Specification

Title of the Invention: Heteroaryl derivative, method for producing the same, and pharmaceutical composition comprising same as effective component

Technical Field

[1] The present invention relates to a heteroaryl derivative. Specifically, the present invention relates to a 6-(isooxazolidine-2-yl)-N-phenylpyrimidine-4-amine derivative. More specifically, the present relates to the compound, stereoisomers thereof, hydrates thereof, or pharmaceutically acceptable salts thereof, a method for preparation of the same, and a pharmaceutical composition for preventing or treating cancer comprising the same as an effective component.

Background Art

[2] The occurrence of cancers is related to a number of environmental factors including chemical substances, radiation, virus, and changes of oncogenes, tumor suppressor genes, genes associated with apoptosis and DNA repair and the like. Recently, the molecular mechanism of cancers is to be understood, and thus, this makes a targeted anticancer therapy, which is a new therapy, become available. Targeted therapeutic agents are generally prepared to show an effect by targeting molecules that cancer cells characteristically have. The molecular targets are genes associated with signal transduction pathway of cancer cells, angiogenesis, cellular matrix, cell cycle regulator, apoptosis and the like. An important targeted therapeutic agent used in the current therapy includes signal transduction pathway inhibitors, including tyrosine kinase inhibitors, and angiogenesis inhibitors and the like. It has been found that a protein tyrosine kinase plays an important role in a number of malignant tumors. In particular, it is known that epidermal growth factor receptor (EGFR), which is a receptor tyrosine kinase of ErbB family, is abnormally activated in a number of epithelial cell tumors including non-small cell lung carcinoma (NSCLC), breast cancer, glioma, squamous cell carcinoma of head and neck, colorectal cancer, rectal adenocarcinoma, head and neck cancer, gastric cancer, and prostate cancer; and the activation of the above EGFR-tyrosine kinase causes a persistent cell proliferation, invasion of the surrounding tissue, remote metastasis, and angiogenesis, and increases a cell survival.

[3] Specifically, the EGFR, which is one of tyrosine kinase receptors of ErbB family,, is a transmembrane tyrosine kinase that has an extracellular ligand-binding domain and an intracellular domain including a tyrosine kinase domain, and may include EGFR (referred to as ErbB1 or HER1), HER2 (referred to as ErbB2 or neu), ErbB3, and ErbB4 (referred to as HER4). If a ligand binds to a receptor forming homodimer or heterodimer, a tyrosine kinase in a cell is activated, and a signal stimulated by EGFR as such activates phosphatidylinositol 3-kinase ((PI3K)/AKT/mTOR, RAS/RAF/MAPK, and JAK/STAT) signal transduction pathway (Non-patent Literature 0001). In particular, EGFR is overexpressed in at least a half of non-small cell lung cancer (NSCLC), and thus, a number of studies have been carried out in which EGFR is a target of a therapy. EGFR TKIs (tyrosine kinase inhibitors), which inhibit an activity of EGFR tyrosine kinase, have been

developed, and representative drugs include Gefitinib (IRESSA™) erlotinib (TARCEVA™), and lapatinib (TYKERB™, TYVERB™).

[4] On the other hand, it was reported that, in 2004, an activating mutation of EGFR is correlated with a response to gefitinib therapy in non-small cell lung cancer (NSCLC) (Non-patent Literature 0002 and 0003). Specifically, it is known that the above EGFR mutation is largely classified into a sensitizing mutation and a resistant mutation, and a deletion of exon 19 and a L858R point mutation of exon 21 are the most important sensitizing mutations and make up about 85 to 90 percent of a sensitizing mutation, and an exon 19 del mutation is more sensitizing to the TKI. On the other hand, it is known that a T790M point mutation of exon 20 is the most important resistant mutation and is found in at least 50 percent of acquired resistant patients (Non-patent Literature 0004).

[5] Somatic mutations identified hitherto include an in-frame deletion in exon 19 or an insertion in exon 20, as well as, a point mutation in which a single nucleic acid residue is modified within an expressed protein (for example, L858R, G719S, G719C, G719A, L861Q) (Non-patent Literature 0005 to 0007).

[6] Despite an early clinical effect of gefitinib/erlotinib in NSCLC patients with an EGFR mutation, a progressive cancer develops in most patients in the end while these patients are receiving a therapy of these drugs. In an early study of recurred samples, a secondary EGFR mutation, T790M, was identified, which made gefitinib and erlotinib to be ineffective inhibitors of EGFR kinase activity (Non-patent Literature 0008 to 0009). It has been proved in the follow-up study that the EGFR T790M mutation was found in approximately 50 percent (24/48) of tumors derived from patients who acquired a resistance against gefitinib or erlotinib (Non-patent Literature 0010 to 0012). The secondary genetic modification is caused in a position similar to a ‘gatekeeper’ residue and a secondary resistance allele associated with the same in patients to be treated with a kinase inhibitor (for example, T3151 within ABL in imatinib resistant CML).

[7] It has been known for a long time that EGFR del19 or EGFR L858R, which is an EGFR mutation, is a major cause of non-small cell lung cancer and head and neck cancer, and IRESSA and TARCEVA, which are therapeutic drugs of the cancers, were developed and are currently used in clinical trials. However, when such drugs were administered for cancer patients, an acquired resistance caused by an EGFR secondary mutation based on the structure of the drug was observed. In addition, it was found that this was actually a major cause of drug resistance. If first generation inhibitors of EGFR have been used for about ten months in average, an acquired resistance, which is a T790M mutation positioned in a gatekeeper of EGFR kinase, occurs to prevent first generation inhibitors of EGFR exerting a medicinal effect. That is, EGFR del19 T790M or EGFR L858R T790M double mutation occurs to prevent conventional therapeutic agents exerting a medicinal effect.

[8] [Prior Art Literature]

[9] [Non-patent Literature]

[10] (Non-patent Literature 0001) Nat Rev Cancer 2007;7:169-81.

[11] (Non-patent Literature 0002) Science 2004;304:1497-500.

[12] (Non-patent Literature 0003) New England Journal of Medicine 2004;350:2129-39.
[13] (Non-patent Literature 0004) Clin Cancer Res 2006;12:6494-6501.
[14] (Non-patent Literature 0005) Fukuoka et al. JCO 2003.
[15] (Non-patent Literature 0006) Kris et al. JAMA 2003.
[16] (Non-patent Literature 0007) Shepherd et al. NEJM 2004.
[17] (Non-patent Literature 0008) Kobayashi et al. NEJM 2005.
[18] (Non-patent Literature 0009) Pao et al. PLOS Medicine 2005.
[19] (Non-patent Literature 0010) Kosaka et al. CCR 2006.
[20] (Non-patent Literature 0011) Balak et al. CCR 2006.
[21] (Non-patent Literature 0012) Engelman et al. Science 2007.

Summary

[21a] In an aspect of the present disclosure, there is provided a compound selected from any one of the compounds 1 through 1059 below, or pharmaceutically acceptable salts of the same:

1) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((S)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

2) N-(4-methoxy-2-morpholino-5-((6-((S)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

3) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((S)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

4) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

5) N-(4-methoxy-2-morpholino-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

6) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

7) N-(2-(4-cyclopropylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

8) N-(2-(2-(dimethylamino)ethoxy)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

9) N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

10) N-(4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

11) N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

12) N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

13) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

14) N-(2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

15) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

16) N-(2-(4-acetylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

17) N-(4-methoxy-2-((2-methoxyethyl)(methyl)amino)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

18) N-(4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

19) N-(4-methoxy-2-(2-methyl-1H-imidazole-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

20) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;

21) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;

22) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;

23) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;

24) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

25) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
26) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
27) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
28) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
29) N-(2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
30) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
31) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
32) N-(4-methoxy-2-(5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
33) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
34) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
35) N-(4-methoxy-2-(3-methyl-3,6-diazabicyclo[3.1.1]heptane-6-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
36) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
37) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
38) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
39) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
40) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
41) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
42) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
43) N-(4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-morpholinophenyl)acrylamide;
44) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
45) N-(4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
46) N-(2-(4-cyclopropylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
47) N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
48) N-(4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
49) N-(2-(4-acetylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
50) N-(2-(4-dimethylaminopiperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

51) N-(2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
52) N-(4-methoxy-2-(4-(5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
53) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
54) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
55) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
56) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
57) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
58) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
59) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
60) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
61) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
62) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
63) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
64) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
65) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
66) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
67) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
68) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
69) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
70) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
71) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
72) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
73) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
74) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
75) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
76) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
77) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-

difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
78) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
79) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
80) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
81) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
82) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
83) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
84) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
85) N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
86) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
87) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
88) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
89) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
90) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
91) N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
92) N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
93) N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
94) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
95) N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
96) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
97) N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
98) N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
99) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
100) N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
101) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
102) N-(4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;

103) N-(2-(4-(2-oxa-6-azaspiro[3.3]heptane-6-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
104) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(5-ethylhexahydropyrrolo[3,4-c]pyrrole-2(1H)-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
105) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aS)-tetrahydro-1H-puro[3,4-c]pyrrole-5(3H)-yl)piperidine-1-yl)phenyl)acrylamide;
106) N-(2-(4-(4-cyclopropyl-3,3-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
107) N-(2-(4-((2R,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
108) N-(2-(4-((2S,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
109) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
110) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
111) N-(2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
112) N-(2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
113) N-(2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
114) N-(2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
115) N-(2-(4-((1R,5S)-8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
116) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-ethoxyphenyl)acrylamide;
117) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)-(E)-4-(dimethylamino)but-2-enamide;
118) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
119) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-(((R)-1,1,1-trifluoropropane-2-yl)oxy)phenyl)acrylamide;
120) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)-2-fluoroacrylamide;
121) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

122) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
123) N-(2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
124) N-(2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
125) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
126) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
127) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
128) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
129) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
130) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
131) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
132) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
133) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
134) N-(2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
135) N-(2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
136) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
137) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
138) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
139) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
140) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
141) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
142) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
143) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
144) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
145) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
146) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
147) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(thiophene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
148) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
149) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
150) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
151) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
152) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
153) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
154) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
155) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
156) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
157) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
158) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
159) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
160) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
161) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
162) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
163) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
164) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
165) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
166) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
167) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
168) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
169) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
170) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
171) N-(2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
172) N-(2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
173) N-(2-(4-((2R,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
174) N-(2-(4-((2S,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
175) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
176) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
177) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
178) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
179) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
180) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
181) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropyl-3,3-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
182) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
183) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

184) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
185) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
186) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
187) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
188) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
189) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
190) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
191) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
192) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
193) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
194) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
195) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
196) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
197) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
198) N-(4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
199) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
200) N-(4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
201) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
202) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
203) N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
204) N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
205) N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
206) N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
207) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
208) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;

209) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
210) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
211) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
212) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
213) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
214) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
215) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
216) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
217) N-(2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
218) N-(4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
219) N-(2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
220) N-(2-(4-isopropylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
221) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
222) N-(2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
223) N-(4-methoxy-2-((2-methoxyethyl)(methyl)amino)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
224) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
225) N-(2-(4-cyclopentylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
226) N-(2-(4-cyclopentylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
227) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
228) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
229) N-(4-methoxy-2-(4-((2-methoxyethyl)(methyl)amino)piperidine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
230) N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
231) N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
232) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
233) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
234) N-(4-methoxy-2-(4-((1R,4R)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-

yl)piperidine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
235) N-(4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-morpholino-[1,4'-bipiperidine]-1'-yl)phenyl)acrylamide;
236) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
237) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
238) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
239) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
240) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
241) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
242) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
243) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
244) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
245) N-(2-(4-(dimethylamino)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
246) N-(2-(4-ethylpiperazine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
247) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
248) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
249) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(3-ethyl-3,6-diazabicyclo[3.1.1]heptane-6-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
250) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
251) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
252) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(6-ethyl-3,6-diazabicyclo[3.1.1]heptane-3-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
253) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-4-(dimethylamino)-1,4'-bipiperidine-1'-yl)-4-methoxyphenyl)acrylamide;
254) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
255) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
256) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;

257) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
258) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
259) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
260) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)phenyl)acrylamide;
261) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-(3-methyl-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
262) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
263) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
264) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
265) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
266) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
267) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
268) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
269) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-methyl-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
270) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-methyl-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
271) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
272) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
273) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
274) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methyl-3-oxopiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
275) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1-isopropylpiperidine-4-yl)amino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
276) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2-(dimethylamino)ethyl)(methyl)amino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
277) N-(2-(4-(cyclopropylmethyl)piperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
278) N-(2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
279) N-(2-(4-cyclopentylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

280) N-(2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
281) N-(2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
282) N-(4-methoxy-2-(4-methyl-1H-imidazole-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
283) N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
284) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
285) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
286) N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
287) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
288) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
289) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
290) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
291) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
292) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
293) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
294) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
295) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
296) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
297) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
298) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
299) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
300) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-propylpiperazine-1-yl)phenyl)acrylamide;
301) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
302) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
303) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
304) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
305) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-(1,4'-bipiperidine)-1'-yl)-4-methoxyphenyl)acrylamide;
306) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-

(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
307) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
308) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
309) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
310) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
311) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
312) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
313) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
314) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
315) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
316) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
317) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
318) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
319) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
320) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
321) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
322) N-(2-(4-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
323) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
324) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
325) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
326) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
327) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
328) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
329) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
330) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(2-methyl-1H-imidazole-1-yl)phenyl)acrylamide;

331) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
332) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
333) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
334) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
335) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
336) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
337) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-2-methylmorpholino)phenyl)acrylamide;
338) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-2-methylmorpholino)phenyl)acrylamide;
339) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
340) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
341) N-(2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
342) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
343) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
344) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
345) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide;
346) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
347) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
348) N-(2-(4-cyclopentylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
349) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
350) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
351) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
352) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
353) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
354) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
355) N-(2-(4-(6-azaspiro[2.5]octan-6-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
356) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
357) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
358) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropyl-1,4-diazepane-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
359) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
360) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
361) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
362) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
363) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
364) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
365) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
366) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
367) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
368) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
369) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
370) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((3S,5R)-4-ethyl-3,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
371) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
372) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
373) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
374) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
375) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
376) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
377) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(5-methyl-1H-imidazole-1-yl)phenyl)acrylamide;
378) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
379) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)phenyl)acrylamide;
380) N-(2-(4-(cyclopropylmethyl)piperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
381) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-

3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
382) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
383) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
384) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
385) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
386) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methyl-1H-imidazole-1-yl)phenyl)acrylamide;
387) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((2-methoxyethyl)(methyl)amino)piperidine-1-yl)phenyl)acrylamide;
388) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-3-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
389) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
390) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-hydroxypiperidine-1-yl)-4-methoxyphenyl)acrylamide;
391) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
392) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
393) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
394) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
395) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
396) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
397) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)-(E)-4-(dimethylamino)but-2-enamide;
398) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
399) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
400) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
401) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
402) N-(1-(2-acrylamido-4-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-5-methoxyphenyl)piperidine-4-yl)-N-(1-isopropylpiperidine-4-yl)acrylamide;
403) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
404) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
405) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

406) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
407) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
408) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
409) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
410) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
411) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
412) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
413) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
414) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
415) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
416) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
417) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
418) N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
419) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
420) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
421) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
422) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2-(dimethylamino)ethyl)(methyl)amino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
423) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
424) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
425) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
426) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholino-[1,4'-bipiperidine]-1'-yl)phenyl)acrylamide;
427) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
428) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
429) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
430) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;

431) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
432) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
433) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
434) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
435) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
436) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
437) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
438) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
439) N-(4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
440) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
441) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
442) N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
443) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
444) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
445) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
446) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
447) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
448) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
449) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
450) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
451) N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
452) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
453) N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
454) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
455) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
456) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
457) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
458) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
459) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
460) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
461) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
462) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
463) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
464) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
465) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
466) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
467) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
468) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
469) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
470) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
471) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
472) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
473) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((1R,4R)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)phenyl)acrylamide;
474) N-(2-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
475) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
476) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
477) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)-[1,4'-bipiperidine]-1'-yl)phenyl)acrylamide;
478) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
479) N-(2-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
480) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-

ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
481) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
482) N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
483) N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
484) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
485) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
486) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
487) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
488) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
489) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
490) N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
491) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
492) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
493) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
494) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
495) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(3-methoxy-3-methylbutoxy)phenyl)acrylamide;
496) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(3-methoxy-3-methylbutoxy)phenyl)-(E)-4-(dimethylamino)but-2-enamide;
497) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
498) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
499) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
500) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
501) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
502) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
503) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;

504) N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
505) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
506) N-(4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
507) N-(4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
508) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
509) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
510) N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
511) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
512) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
513) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
514) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
515) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
516) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
517) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
518) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
519) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
520) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
521) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
522) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
523) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
524) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
525) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
526) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
527) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methyl-1H-imidazole-1-yl)phenyl)acrylamide;
528) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
529) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;

530) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
531) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
532) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
533) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-fluorophenyl)acrylamide;
534) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methylphenyl)acrylamide;
535) N-(4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
536) N-(4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
537) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
538) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
539) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
540) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
541) N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
542) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(3-methyl-3,6-diazabicyclo[3.1.1]heptane-6-yl)phenyl)acrylamide;
543) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
544) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
545) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
546) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
547) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
548) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
549) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
550) N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
551) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
552) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
553) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
554) N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
555) N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
556) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
557) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
558) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
559) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
560) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
561) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)phenyl)acrylamide;
562) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide;
563) N-(2-(4-cyclopentylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
564) N-(2-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
565) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
566) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
567) N-(2-(4-(cyclopropylmethyl)piperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
568) N-(2-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
569) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
570) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
571) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
572) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
573) N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
574) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
575) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
576) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
577) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
578) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-

methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
579) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
580) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
581) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
582) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
583) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
584) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
585) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
586) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
587) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(3-(4-cyclopropylpiperazine-1-yl)azetidine-1-yl)-4-methoxyphenyl)acrylamide;
588) N-(2-(3-(4-cyclopropylpiperazine-1-yl)azetidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
589) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
590) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
591) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-hydroxypiperidine-1-yl)-4-methoxyphenyl)acrylamide;
592) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
593) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
594) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
595) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
596) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
597) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
598) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
599) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
600) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
601) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
602) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
603) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;

604) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
605) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
606) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
607) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
608) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
609) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
610) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
611) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
612) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
613) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2-(dimethylamino)ethyl)(methyl)amino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
614) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholino-[1,4'-bipiperidine]-1'-yl)phenyl)acrylamide;
615) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
616) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
617) N-(5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
618) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
619) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
620) N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
621) N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
622) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
623) N-(4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
624) N-(4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
625) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-((dimethylamino)methyl)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
626) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-((dimethylamino)methyl)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
627) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

628) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
629) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
630) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
631) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
632) N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
633) N-(3-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-5-(4-methylpiperazine-1-yl)phenyl)acrylamide;
634) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
635) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
636) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
637) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
638) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
639) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
640) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
641) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
642) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
643) N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
644) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
645) N-(4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
646) N-(4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
647) N-(2-(4-(dimethylamino)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
648) N-(2-(4-ethylpiperazine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
649) N-(5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
650) N-(5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
651) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(3-

ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
652) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
653) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
654) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
655) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
656) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
657) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-2-methylmorpholino)phenyl)acrylamide;
658) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2S,6S)-2,6-dimethylmorpholino)-4-methoxyphenyl)acrylamide;
659) N-(4-methoxy-2-((S)-2-methylmorpholino)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
660) N-(2-((2S,6S)-2,6-dimethylmorpholino)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
661) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
662) N-(2-((S)-3,4-dimethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
663) N-(4-methoxy-2-((R)-2-methylmorpholino)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
664) N-(2-((2S,6R)-2,6-dimethylmorpholino)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
665) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
666) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-2-methylmorpholino)phenyl)acrylamide;
667) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2S,6R)-2,6-dimethylmorpholino)-4-methoxyphenyl)acrylamide;
668) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
669) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
670) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
671) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
672) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
673) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
674) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((1R,4R)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)phenyl)acrylamide;
675) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
676) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
677) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

678) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
679) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
680) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
681) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
682) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
683) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
684) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)phenyl)acrylamide;
685) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide;
686) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
687) N-(2-(4-(cyclopropylmethyl)piperazine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
688) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
689) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
690) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
691) N-(5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
692) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
693) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
694) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
695) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
696) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
697) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
698) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
699) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
700) N-(2-(4-(6-azaspiro[2.5]octan-6-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
701) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
702) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
703) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
704) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
705) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
706) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
707) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
708) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
709) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
710) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
711) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
712) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
713) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(3-(dimethylamino)azetidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
714) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
715) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
716) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
717) N-(2-(4-(4-cyclopropyl-1,4-diazepane-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
718) N-(2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
719) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
720) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
721) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
722) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methyl-2-oxopiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
723) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
724) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
725) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
726) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
727) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-

(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
728) N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
729) N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
730) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
731) N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
732) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
733) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
734) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
735) N-(2-(4-((2-(dimethylamino)ethyl)(methyl)amino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
736) N-(4-methoxy-2-(4-((2-methoxyethyl)(methyl)amino)piperidine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
737) N-(2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
738) N-(2-(4-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
739) N-(2-(4-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
740) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
741) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
742) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
743) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
744) N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
745) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
746) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
747) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
748) N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-(3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
749) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
750) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
751) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
752) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6S)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
753) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

754) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
755) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
756) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
757) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
758) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
759) N-(2-(4-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
760) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
761) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-2,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
762) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-2,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
763) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
764) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
765) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
766) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
767) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
768) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
769) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
770) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
771) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
772) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
773) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
774) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
775) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
776) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
777) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;

778) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
779) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
780) N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
781) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
782) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
783) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
784) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
785) N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
786) N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
787) N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
788) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
789) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
790) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
791) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
792) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
793) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
794) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
795) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
796) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
797) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
798) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
799) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
800) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
801) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
802) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
803) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;

804) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
805) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
806) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
807) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
808) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
809) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
810) N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
811) N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
812) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
813) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
814) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
815) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
816) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
817) N-(2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
818) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
819) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
820) N-(2-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
821) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
822) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
823) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
824) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
825) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
826) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
827) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((3S,5R)-4-ethyl-3,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
828) N-(2-(4-(6-azaspiro[2.5]octan-6-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-

difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
829) N-(2-(4-(4-cyclopropyl-1,4-diazepane-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
830) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
831) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
832) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
833) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
834) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
835) N-(2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
836) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
837) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)phenyl)acrylamide;
838) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
839) N-(2-((S)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
840) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
841) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((3S,5R)-4-ethyl-3,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
842) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-3-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
843) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-3-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
844) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
845) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
846) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
847) N-(2-(4-ethylpiperazine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
848) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
849) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
850) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
851) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
852) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(hexahydropyrrolo[1,2-a]pyrazine-2(1H)-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
853) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
854) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
855) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
856) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
857) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)phenyl)acrylamide;
858) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
859) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
860) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
861) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(2-methyl-1H-imidazole-1-yl)phenyl)acrylamide;
862) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
863) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
864) N-(2-(4-(dimethylamino)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
865) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
866) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
867) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
868) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
869) N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
870) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
871) N-(2-(4-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
872) N-(2-(4-(6-azaspiro[2.5]octan-6-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
873) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;

874) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
875) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
876) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
877) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)phenyl)acrylamide;
878) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((3S,5R)-4-ethyl-3,5-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
879) N-(2-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
880) N-(2-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
881) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
882) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
883) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
884) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
885) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-2,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
886) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-2,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
887) N-(2-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
888) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-2-methylmorpholino)phenyl)acrylamide;
889) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-2-methylmorpholino)phenyl)acrylamide;
890) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
891) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
892) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
893) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
894) N-(2-(4-(4-(sec-butyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;

895) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
896) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
897) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
898) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
899) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
900) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
901) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
902) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
903) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
904) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
905) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
906) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
907) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
908) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
909) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
910) N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
911) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
912) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
913) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
914) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
915) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
916) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
917) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
918) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-2,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
919) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-2,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
920) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-

methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
921) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
922) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
923) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
924) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
925) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
926) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
927) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
928) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(thiophene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
929) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(thiophene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
930) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(thiophene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
931) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
932) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
933) N-(5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
934) N-(5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
935) N-(5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
936) N-(5-((6-((S)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
937) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
938) N-(5-((6-((R)-3-(3-chloro-2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
939) N-(5-((6-((R)-3-(3-chloro-2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
940) N-(2-(4-cyclopropylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
941) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
942) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
943) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-

5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
944) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
945) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
946) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
947) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
948) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
949) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
950) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
951) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
952) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
953) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
954) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
955) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
956) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
957) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxyphenyl)acrylamide;
958) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
959) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(cyclopropylmethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
960) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(2-methyl-1H-imidazole-1-yl)phenyl)acrylamide;
961) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
962) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxyphenyl)acrylamide;
963) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
964) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
965) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
966) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
967) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(cyclopropylmethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
968) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;

969) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)phenyl)acrylamide;
970) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide;
971) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)phenyl)acrylamide;
972) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopentylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
973) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
974) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide;
975) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)phenyl)acrylamide;
976) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
977) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopentylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
978) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(diethylamino)ethoxy)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
979) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
980) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
981) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
982) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
983) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
984) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
985) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
986) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
987) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
988) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
989) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
990) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
991) N-(5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
992) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;

993) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
994) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
995) N-(2-(4-((1R,5S)-8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
996) N-(5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
997) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
998) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
999) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1000) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1001) N-(5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
1002) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1003) N-(2-(4-ethylpiperazine-1-yl)-5-((6-(S)-(3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1004) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1005) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1006) N-(5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
1007) N-(5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1008) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
1009) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1010) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1011) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
1012) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1013) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
1014) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1015) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1016) N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
1017) N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
1018) N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1019) N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1020) N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1021) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1022) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1023) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1024) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1025) N-(5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1026) N-(5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
1027) N-(5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1028) N-(5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1029) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1030) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1031) N-(5-((6-((S)-3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
1032) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-(S)-(3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1033) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1034) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1035) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1036) N-(5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

1037) N-(5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1038) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1039) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1040) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1041) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1042) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1043) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1044) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1045) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1046) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1047) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1048) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1049) N-(2-(4-cyclopropylpiperazine-1-yl)-4-methoxy-5-((6-((S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1050) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1051) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1052) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1053) N-(5-((6-((S)-3-(3-chloro-2-methoxybenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
1054) N-(5-((6-((S)-3-(3-chloro-2-methoxybenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1055) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-methoxybenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;

1056) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1057) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1058) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(pyridine-2-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1059) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-2-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide.

[21b] In another aspect of the present disclosure, there is provided a compound disclosed herein, or a pharmaceutically acceptable salt thereof, for use in treating cancer.

[21c] In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for the treatment of cancer.

[21d] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound disclosed herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

Disclosure

Technical Problem

[22] The purpose of one aspect of the present invention is to provide a compound which exhibits inhibitory effects against wild type or mutant EGFR and is therefore useful in the treating of cancer, and stereoisomers, hydrates, or pharmaceutically acceptable salts of the compound.

[23] The purpose of another aspect of the present invention is to provide a method for preparation of the compound.

[24] The purpose of yet another aspect of the present invention is to provide a pharmaceutical composition for preventing or treating cancer, the composition comprising the compound or stereoisomers, hydrates or pharmaceutically acceptable salts of the same as an effective component.

[25] The purpose of yet another aspect of the present invention is to provide a pharmaceutical composition which suppresses wild type EGFR (epidermal growth factor receptor) or EGFR mutations to prevent or treat cancer.

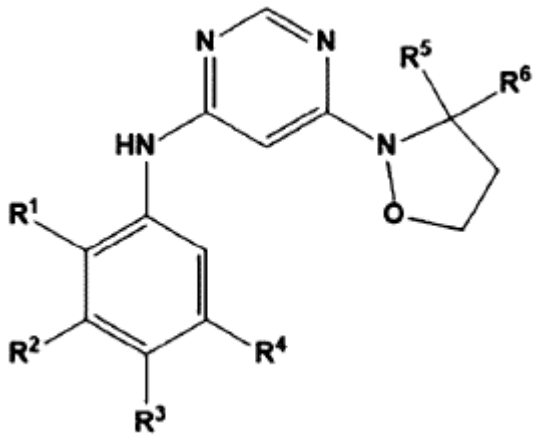
Technical Solution

[26] To achieve the above-stated purposes,

[27] The present invention provides a compound represented by Chemical Formula 1, stereoisomers of the same, hydrates or the same, or pharmaceutically acceptable salts of the same:

[28] [Chemical Formula 1]

[29]



[30] In Chemical Formula 1,

[31] R^1 is hydrogen, halogen, C_{1-8} alkyl, or C_{1-8} alkoxy, where the C_{1-8} alkyl and C_{1-8} alkoxy of R^1 are, respectively and independently, substituted or unsubstituted by at least one halogen,

[32] R^2 is hydrogen or $-NR^7R^8$, where R^7 and R^8 are, respectively and independently, hydrogen or C_{1-8} alkyl, or the R^7 and R^8 are linked together with an N atom to which they are bonded to form a heterocycloalkyl or 3 to 12 atoms, where the C_{1-8} alkyl or heterocycloalkyl of 3 to 12 atoms of R^7 and R^8 are, respectively and independently, substituted or unsubstituted by at least one substituent selected from a group comprised of C_{1-8} alkyl, C_{1-8} alkoxy and C_{1-8} alkylamino,

[33] R^3 is hydrogen, $-NR^9R^{10}$ or $-OR^{11}$, where R^9, R^{10} and R^{11} are, respectively and independently, halogen or C_{1-8} alkyl, or the R^9 and R^{10} are linked together with an N atom to which they are bonded to form a heterocycloalkyl of 3 to 12 atoms or heteroaryl of 3 to 12 atoms, and the C_{1-8} alkyl, heterocycloalkyl of 3 to 12 atoms or heteroaryl of 3 to 12 atoms of R^9, R^{10} and R^{11} are, respectively and independently, substituted or unsubstituted by at least one substituent R selected from among a group comprised of hydroxy, C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkylamino, C_{1-8} alkylcarbonyl, $-NR^{12}R^{13}$, and heterocycloalkyl of 3 to 12 atoms, where the substituents R are, respectively and independently, additionally substituted or unsubstituted by at least one substituent selected from a group comprised of halogen; carbonyl; C_{1-8} alkyl substituted or unsubstituted by hydroxy or C_{1-8} alkylamino; C_{2-8} alkenyl; C_{1-8} alkoxy; C_{1-8} alkylamino; C_{1-8} alkylcarbonyl; and, a heterocycloalkyl of 3 to 12 atoms substituted or unsubstituted by C_{1-8} alkyl, and where the R^{12} and R^{13} are, respectively and independently, hydrogen, C_{1-8} alkyl, C_{2-8} alkenyl, C_{1-8} alkylcarbonyl, C_{2-8} alkenylcarbonyl, or a heterocycloalkyl of 3 to 12 atoms substituted or unsubstituted by C_{1-8} alkyl,

[34] R^4 is $-NH(C=O)R^{14}C=CR^{15}R^{16}$, where the R^{14}, R^{15} and R^{16} are, respectively and independently, hydrogen, halogen, or C_{1-8} alkyl substituted or unsubstituted by C_{1-8} alkylamino,

[35] R^5 is C_{1-8} alkyl, an aryl of 3 to 12 atoms, a heteroaryl of 3 to 12 atoms, or a heterocycloalkyl of 3 to 12 atoms, and the C_{1-8} alkyl, aryl of 3 to 12 atoms, heteroaryl of 3 to 12 atoms, or heterocycloalkyl of 3 to 12 atoms of R^5 are, respectively and independently, substituted or unsubstituted by at least one substituent selected from a group comprised of halogen, cyano, C_{1-8} alkyl substituted or unsubstituted by halogen, C_{2-8} alkenyl, C_{1-8} alkoxy, C_{2-8} alkynyl and C_{1-8} alkylamino,

[36] and R^6 is hydrogen or C_{1-8} alkyl.

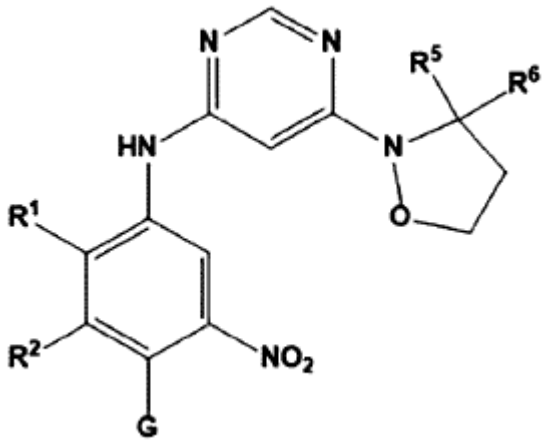
[37] Another aspect of the present invention provides:

[38] a method for preparing the compound of Chemical Formula 5, from the compound of Chemical Formula 4;

[39] a step of preparing the compound of Chemical Formula 6 from the compound of Chemical Formula 5; and,

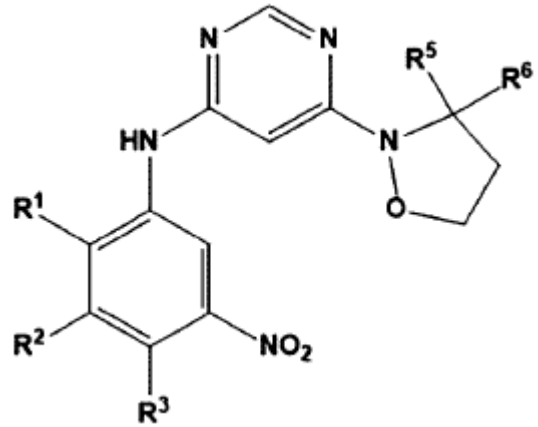
[40] a step of preparing the compound of Chemical Formula 1 from the compound of Chemical Formula 6:

[41] [Chemical Formula 4]



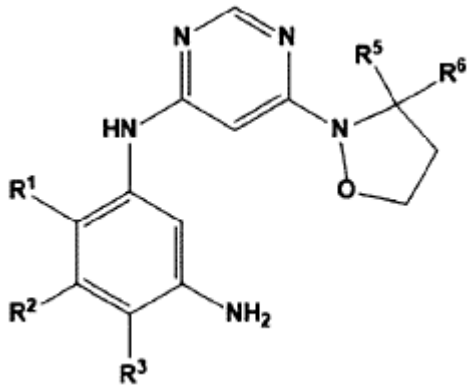
[42]

[43] [Chemical Formula 5]



[44]

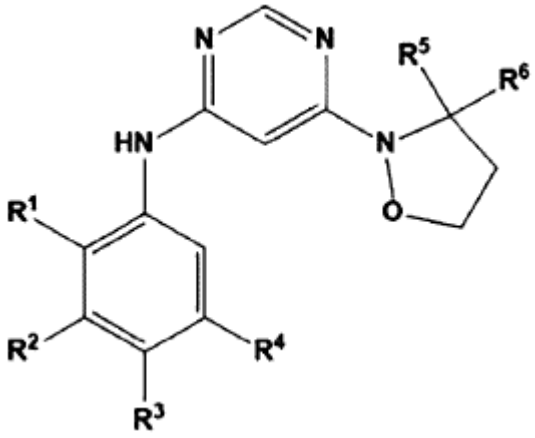
[45] [Chemical Formula 6]



[46]

[47]

[48] [Chemical Formula 1]



[49]

[50] In Chemical Formula 4, G is a leaving group, and R^1 and R^6 are respectively the same as defined in the above.

[51] Yet another aspect of the present invention provides a pharmaceutical composition for preventing or treating cancer, the composition comprising the compound of the present invention, or stereoisomers, hydrates or pharmaceutically acceptable salts of the same as an effective component.

Benefits of the Invention

[52] The compound provided by one aspect of the present invention, and stereoisomers, hydrates or pharmaceutically acceptable salts thereof exhibit high inhibition activity against not only mutants of EGFR (epidermal growth factor receptor) but also wild type or mutants of at least one of ERBB2 and ERBB4, and therefore can be usefully used in the treatment of cancers in which these kinases are expressed.

Brief Description of the Drawings

[53] FIG. 1 show experimental data results in which a PDX (Exon20 ins V769_D770ins ASV) cell line xenograft in vivo was orally administered the Example Compounds for 28 days followed by observation for 21 days without administration to verify whether or not cancer was suppressed.

Best Mode(s) for Carrying Out the Invention

[54] In the following, the present invention will be explained in further detail with reference to embodiments.

[55] Embodiments of the present invention may be modified into various different forms, and the scope of the present invention is not limited to the embodiments explained in the following. The embodiments of the present invention are provided so as to provide persons having ordinary skill in the art to which the present invention belongs with a fuller disclosure of the present invention.

[56] Throughout the specification, to “comprise” a certain component element means, unless specifically stated to the contrary, that other components elements may be further comprised, rather than that other component elements are excluded.

[57] In the structural formulae of the present specification, of the symbols which bonds atoms and/or groups to each other, “-“ may refer to a single bond, and “=” may refer to a double bond. Such symbols may be omitted, and may be indicated in cases necessary for specifying the bonded atoms or the position of a bond.

[58] In the present specification, atoms being “connected” may include not only cases wherein atoms are connected directly but also cases wherein atoms are connected indirectly using other atoms and/or groups as a medium. Here, the other atoms and/or groups may be, but are not limited to, oxygen, sulfur, C_{1-8} alkylamino or C_{1-8} alkylene groups, and these atoms and/or groups may be substituted or unsubstituted.

[59] In the present specification, the expression “substituted or unsubstituted” may refer to , unless otherwise stated, that one or a plurality of hydrogen atoms is substituted or unsubstituted by another atom or substituent. The substituent may be selected from a group comprised of halogen (chloro (Cl), iodo (I), bromo (Br), fluoro(F)), C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, hydroxyl, C_{1-10} alkoxy, amino, nitro, thiol, thioether, imine, cyano, phosphonato, phospine, carboxy, carbamoyl, carbamic acid, acetal, urea, thiocarbonyl, sulfonyl, sulfonamide, ketone, aldehyde,

ester, acetyl, acetoxy, amide, oxygen (=0), haloalkyl (e.g. trifluoromethyl), substituted aminoacyl and aminoalkyl, carbon ring cycloalkyls which are single ring or fused or non-fused multiple ring (e.g. cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl), hetero cycloalkyls which are single ring or fused or non-fused multiple ring (e.g. pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, or thiazinyl, carbon ring or hetero ring, single ring or fused or non-fused multiple ring aryls (e.g. phenyl, naphthalenyl, pyrrolyl, indolyl, furanyl, thienyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, triazolyl, tetrazolyl, pyrazolyl, pyridinyl, quinolinyl, isoquinolinyl, acridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzimidazolyl, benzothienyl, or benzofuranyl), aminos (primary, secondary or tertiary), aryl, aryloxy, and aryl-alkyl, but is not limited hereto. Further, the respective example substituents above may again be substituted or unsubstituted by a substituent selected among these substituents.

[60] In the present specification, “halogen” may be F, Cl, Br or I.

[61] In the present specification, “alkyl” may refer to , unless otherwise stated, a saturated hydrocarbon which is a straight chain or branched chain noncyclic alkyl; a cyclic alkyl; or a combination of the two. Further, “C_{1-8} alkyl” may refer to an alkyl which comprises one to eight carbon atoms. Non-limiting examples of a noncyclic alkyl include methyl, ethyl, N-propyl, N-butyl, N-pentyl, N-hexyl, N-heptyl, N-octyl, isopropyl, secondary (sec)-butyl, tertiary (tert)-butyl, isopentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl and 2,3-dimethylbutyl. Non-examples of a cyclic alkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, or cyclooctyl, etc. Non-limiting examples of an alkyl wherein cyclic and non-cyclic alkyls are combined include methylcyclopropyl, cyclopropylmethyl, ethylcyclopropyl, cyclopropylmethyl, methylcyclobutyl, cyclobutylmethyl, ethylcyclopentyl, and cyclopentylmethyl.

[62] In the present specification, “cycloalkyl” may refer to an alkyl, in particular a cycloalkyl, where an alkyl is as defined in the foregoing.

[63] In the present specification, “alkoxy” is an alkyl ether group which may refer to a -(O-alkyl), where an alkyl is as defined in the foregoing. Further, “C_{1-8} alkoxy” may refer to an alkoxy which comprises a C_{1-8} alkyl, that is, -(O-C_{1-8} alkyl), and examples of a C_{1-8} alkoxy may include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, iso-butoxy, sec-butoxy, tert-butoxy, and n-pentoxy, but is not limited hereto.

[64] In the present specification, “heterocycloalkyl” may refer to a ring comprising one to five heteroatoms selected from among N, O and S are ring-forming atoms, which may be saturated or partially unsaturated. Unless otherwise mentioned, a heterocycloalkyl may be a single ring, or a multiple ring such as a spiro ring, a bridge ring or a fused ring. Further, “heterocycloalkyl of 3 to 12 atoms” may refer to a heterocycloalkyl which comprises 3 to 12 ring-forming atoms. Non-limiting examples of a heterocycloalkyl include pyrrolidine, piperidine, N-methyl piperidine, imidazolidine, pyrazolidine, butylolactam, valerolactam, imidazolinone, hydantoin, dioxolane, phthalimide, piperidine, piperidine-2,4(1H,3H)-dione, 1,4-dioxane, morpholine, thiomorpholine, thiomorpholine-S-oxide, thiomorpholine-S,S-oxide, piperazine, pyran, pyridine, 3-pyrroline, thiopyran, pyrone, tetrahydrofuran, tetrahydrothiophene, quinuclidine, tropane, 2-azaspiro[3.3]heptane, (1R,5S)-3-

azabicyclo[3.2.1]octane, (1s,4s)-2-azabicyclo[2.2.2]octane, or (1R,4R)-2-oxa-5-aza bicyclo[2.2.2]octane.

[65] In the present specification, “alkylamino” may refer to -(NR’R”), where R’ and R” may, respectively and independently, be selected from a group comprised of hydrogen and C_{1-8} alkyls, where the selected R’ and R” may be, respectively and independently, substituted or unsubstituted. Further “C_{1-8} alkylamino” may refer to an amino which comprises a C_{1-8} alkyl, that is, -N-H(C_{1-8} alkyl) or -N-(C_{1-8} alkyl)$_2$, and may include, but is not limited to dimethlyamino, methylethylamino, methylpropylamino, or ethylpropylamino.

[66] In the present specification, “aryl” may refer to an aromatic ring wherein one hydrogen has been removed from an aromatic hydrocarbon ring, and the aryl may be monocyclic or polycyclic. “An aryl of 3 to 12 atoms” may refer to an aryl which includes 3 to 12 ring-forming rings, and non-limiting examples of the same include phenyl, naphthyl, anthracenyl, phenanthryl, biphenyl, and terphenyl.

[67] In the present specification, “heteroaryl” may refer to an aromatic ring which includes at least one heteroatom from among N, O and S as ring-forming atoms, and the heteroaryl may be monocyclic or polycyclic. Further, “heteroaryl of 3 to 12 atoms” may refer to a heteroaryl which includes 3 to 12 ring-forming rings, and non-limiting examples of the same include thienyl, thiophene, furyl, pyrrolyl, pyrazolyl, imidazolyl, thiazolyl, oxazolyl, isothiazolyl, oxadiazolyl, triazolyl, pyridinyl, bipyridyl, pyramidal, triazinyl, triazolyl, acridyl group, pyridazinyl group, pyrazinyl, quinolinyl, quinazoline, quinoxalinyl, phenoxazine, phthalazinyl, pyrimidinyl, pyrido pyrimidinyl, pyrido pyrazinyl, pyrazino pyrazinyl, isoquinoline, indole, carbazole, imidazopyridazinyl, imidazopyridinyl, imidazopyrimidinyl, pyrazolo pyrimidinyl, imidazo pyrazinyl or pyrazolo pyridinyl, N-aryl carbazole, N-heteroaryl carbazole, N-alkyl carbazole group, benzoxazole, benzoimidazole, benzothiazole, benzocarbazole, benzothiophene, dibenzothiophenyl, thienothiophene, benzofuranyl, phenanthroline, isoxazolyl, oxadiazolyl, thiadiazolyl, benzothiazolyl, tetrazolyl, phenothiazolyl, dibenzosilol or dibenzofuranyl, etc.

[68] In the present invention, “hydroxy” may refer to -OH.

[69] In the present specification, “carbonyl” may refer to –(C=(O))-, and may refer to a case wherein a cyclic alkyl, aryl or heterocycloalkyl is substituted by a carbonyl, or a case where a hydrogen atom is substituted by a (=O).

[70] In the present specification, “alkylcarbonyl” may refer to –(C(=O)-alkyl), where the alkyl is as defined in the foregoing. Further, “C_{1-8} alkylcarbonyl” may refer to a carbonyl which includers a C_{1-8} alkyl, that is, -(C(=O)-C_{1-8} alkyl), and non-limiting examples of these include methyl carbonyl (acetyl, -(C=(O)-CH_3)), ethyl carbonyl, n-propyl carbonyl, iso-propyl carbonyl, n-butyl carbonyl, sec-butyl carbonyl, isobutyl carbonyl, tert-butyl carbonyl, n-octyl carbonyl, cyclopropyl carbonyl, cyclobutyl carbonyl, cyclopentyl carbonyl, or cyclohexyl carbonyl.

[71] In the present specification, “alkenyl” may refer to , unless otherwise stated, a noncyclic straight chain or branched chain or cyclic hydrocarbon having at least

one double bond. Further, “C_{2-8} alkenyl” may refer to an alkenyl which comprises two to eight carbon atoms, and may include, but is not limited to, ethenyl, 1-propenyl, prop-2-en-1-yl[-($CH_2CH=CH_2$)](allyl), 2-butenyl, isopropenyl, 3-butenyl, 4-pentenyl, 5-hexenyl, 1-cyclohexenyl, cyclopentadienyl, 1,3-cyclohexadienyl, 1,4-cyclohexadienyl, 1,3-cycloheptadienyl, or 1,3,5-cycloheptatrienyl.

[72] In the present specification, “alkenylcarbonyl” may refer to –(C(=O)-alkenyl), where alkenyl is as defined in the foregoing. Further,k “C_{2-8} alkeylcarbonyl” may refer to a carbonyl which includes a C_{2-8} alkenyl, that is, -(C(=O)-C_{2-8} alkenyl).

[73] In the present specification, “cyano” may refer to –(CN).

[74] In the present specification, “alkynyl” may refer to a straight chain, branched chain noncyclic or cyclic hydrocarbon having at least one triple bond. Further, “C_{2-8} alkynyl” may refer to an alkynyl which comprises 2 to 8 carbon atoms, and non-limiting examples of such include ethinyl, propynyl, hydroxypropynyl, butene-1-yl, butene-2-yl, pentene-1-yl, 3-methylbutene-1-yl, or hexyn-2-yl.

[75] In the present specification, “aralkyl” may refer to –(alkyl-aryl), where alkyl and aryl are as defined in the foregoing. Further, “aralkyl of 3 to 8 atoms” may refer to an aralkyl which comprises 3 to 8 carbon atoms.

[76] In the present specification, “bicycloalkyl” may mean, unless otherwise stated, a fused, spiro or bridged bicyclic hydrocarbon.

[77] In the present specification, “diazabicycloalkyl” may refer to –(diaza-bicycloalkyl), that is, may represent a bicycloalkyl which includes two nitrogen atoms in the cycloalkyl. Non-limiting examples of diazabicycloalkyl include diazabicyclo[3,2,1]heptane, diazabicyclo[3,1,1]heptane, and diazabicyclo[2,2,1]heptane.

[78] In the present specification, “oxazabicycloalkyl” may mean -(oxaza-bicycloalkyl), that is, a bicycloalkyl which comprises one oxygen atom and one nitrogen atom in the cycloalkyl. Non-limiting examples of oxazabicycloalkyl include oxazabicyclo[2,2,1]heptane.

[79] In the present specification, “sulfonic acid ester” may refer to an alkyl sulfonic acid ester or an aryl sulfonic acid ester, where alkyl sulfonic acid ester is represented by –($OS(=O)_2$-alkyl, and aryl sulfonic acid ester is represented by –($(OS)=O_2$-aryl). Here, alkyl and aryl are as defined in the foregoing.

[80] In the present specification, “hydrate” may refer to the compound of the present invention or a salt thereof, comprising a stoichiometric or non-stoichiometric amount of water bonded by a non-covalent intermolecular force. A hydrate of the compound of the present invention represented by Chemical Formula 1 may comprise a stoichiometric or non-stoichiometric amount of water bonded by a non-covalent intermolecular force. The hydrate may comprise at least one equivalents of water, preferably one to five equivalents. Such hydrate may be prepared by crystallizing, from water or solvent comprising water, the compound

of the present invention represented by Chemical Formula 1, isomers of the same, or pharmaceutically acceptable salts thereof.

[81] In the present specification, “solvate” may refer to the compound of the present invention or a salt thereof, comprising a stoichiometric or non-stoichiometric amount of solvent which is bonded by a non-covalent intermolecular force. Preferred solvents include volatile solvents, non-volatile solvents, and/or solvents suitable for administration to humans.

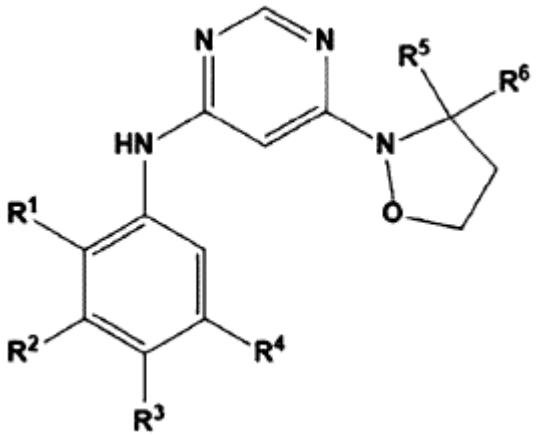
[82] In the present specification, the term “isomer” refers to the compound of the present invention or a salt thereof which has an identical chemical or molecular formula but which is structurally or three-dimensionally different. Included among such isomers are structural isomers such as tautomers, R or S isomers having asymmetric carbon centers, stereoisomers including geometric isomers (trans, cis), and enantiomers. All such isomers and compounds thereof are included in the scope of the present invention.

[83] One aspect of the present invention provides a compound represented by Chemical Formula 1, stereoisomers of the same, hydrates or the same, or pharmaceutically acceptable salts of the same:

[84] In one embodiment:

[85] [Chemical Formula 1]

[86]



[87] In Chemical Formula 1,

[88] R^1 is hydrogen, halogen, C_{1-8} alkyl, or C_{1-8} alkoxy, where the C_{1-8} alkyl and C_{1-8} alkoxy of R^1 are, respectively and independently, substituted or unsubstituted by at least one halogen,

[89] R^2 is hydrogen or $-NR^7R^8$, where R^7 and R^8 are, respectively and independently, hydrogen or C_{1-8} alkyl, or the R^7 and R^8 are linked together with an N atom to which they are bonded to form a heterocycloalkyl of 3 to 12 atoms, where the C_{1-8} alkyl or heterocycloalkyl of 3 to 12 atoms of R^7 and R^8 are, respectively and independently, substituted or unsubstituted by at least one substituent selected from a group comprised of C_{1-8} alkyl, C_{1-8} alkoxy and C_{1-8} alkylamino,

[90] R^3 is hydrogen, $-NR^9R^{10}$ or $-OR^{11}$, where R^9, R^{10} and R^{11} are, respectively and independently, halogen or C_{1-8} alkyl, or the R^9 and R^{10} are linked together with an N atom to which they are bonded to form a heterocycloalkyl of 3 to 12 atoms or heteroaryl of 3 to 12 atoms, and the C_{1-8} alkyl, heterocycloalkyl of 3 to 12 atoms or heteroaryl of 3 to 12 atoms of R^9,

R^{10} and R^{11} are, respectively and independently, substituted or unsubstituted by at least one substituent R selected from among a group comprised of hydroxy, C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkylamino, C_{1-8} alkylcarbonyl, $-NR^{12}R^{13}$, and heterocycloalkyl of 3 to 12 atoms, where the substituents R are, respectively and independently, additionally substituted or unsubstituted by at least one substituent selected from a group comprised of halogen; carbonyl; C_{1-8} alkyl substituted or unsubstituted by hydroxy or C_{1-8} alkylamino; C_{2-8} alkenyl; C_{1-8} alkoxy; C_{1-8} alkylamino; C_{1-8} alkylcarbonyl; and, a heterocycloalkyl of 3 to 12 atoms substituted or unsubstituted by C_{1-8} alkyl, and where the R^{12} and R^{13} are, respectively and independently, hydrogen, C_{1-8} alkyl, C_{2-8} alkenyl, C_{1-8} alkylcarbonyl, C_{2-8} alkenylcarbonyl, or a heterocycloalkyl of 3 to 12 atoms substituted or unsubstituted by C_{1-8} alkyl,

[91] R^4 is $-NH(C=O)R^{14}C=CR^{15}R^{16}$, where the R^{14}, R^{15} and R^{16} are, respectively and independently, hydrogen, halogen, or C_{1-8} alkyl substituted or unsubstituted by C_{1-8} alkylamino,

[92] R^5 is a C_{1-8} alkyl, an aryl of 3 to 12 atoms, a heteroaryl of 3 to 12 atoms, or a heterocycloalkyl of 3 to 12 atoms, and the C_{1-8} alkyl, aryl of 3 to 12 atoms, heteroaryl of 3 to 12 atoms, or heterocycloalkyl of 3 to 12 atoms of R^5 are, respectively and independently, halogen, cyano, a C_{1-8} alkyl substituted or unsubstituted by halogen, an aryl of 3 to 12 atoms, a heteroaryl of 3 to 12 atoms, a heterocycloalkyl of 3 to 12 atoms, C_{2-8} alkenyl, C_{1-8} alkoxy, C_{2-8} alkynyl and C_{1-8} alkylamino, where each of the substituents J are, respectively and independently, halogen, C_{1-8} alkyl substituted or unsubstituted by halogen, C_{1-8} alkoxy, and C_{1-8} alkylamino,

[93] and R^6 may be hydrogen or C_{1-8} alkyl.

[94] In another embodiment, in the compound represented by Chemical Formula 1,

[95] R^1 is hydrogen, halogen, C_{1-8} alkyl, or C_{1-8} alkoxy, where the C_{1-8} alkoxies of R^1 are, respectively and independently, substituted or unsubstituted by at least one halogen,

[96] R^2 is hydrogen or $-NR^7R^8$, where R^7 and R^8 are, respectively and independently, hydrogen or C_{1-8} alkyl, or the R^7 and R^8 are linked together with an N atom to which they are bonded to form a heteroaryl of 3 to 12 atoms, and the C_{1-8} alkyl of R^7 and R^8 are, respectively and independently, substituted or unsubstituted by at least one substituent selected from a group comprised of C_{1-8} alkoxy and C_{1-8} alkylamino, and the heterocycloalkyl of 3 to 12 atoms formed by the bonding of R^7 and R^8 is substituted or unsubstituted by at least one substituent selected from among a group comprised of C_{1-8} alkyl and C_{1-8} alkoxy,

[97] R^3 is hydrogen, $-NR^9R^{10}$ or $-OR^{11}$, where R^9, R^{10} and R^{11} are, respectively and independently, halogen or C_{1-8} alkyl, or the R^9 and R^{10} are linked together with an N atom to which they are bonded to form a heterocycloalkyl of 3 to 12 atoms or a heteroaryl of 3 to 12 atoms, and the C_{1-8} alkyls of R^9, R^{10} and R^{11} are, respectively and independently, substituted or unsubstituted by at least one substituent R selected from among a group comprised of C_{1-8} alkoxy, and C_{1-8} alkylamino, where the heterocycloalkyl of 3 to 12 atoms formed by the bonding of R^9 and R^{10} is substituted or unsubstituted by at least one substituent R^a selected from among a group comprised of hydroxy, C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkylamino, C_{1-8} alkylcarbonyl, $-NR^{12}R^{13}$, and heterocycloalkyl of 3 to 12 atoms, and the C_{1-8} alkyl, C_{1-8} alkylamino,

and C_{1-8} alkylcarbonyl of the substituent R^a are, respectively and independently, additionally substituted or unsubstituted by at least one substituent selected from a group comprised of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkylamino, and heterocycloalkyl of 3 to 12 atoms, the heterocycloalkyl of 3 to 12 atoms of the substituent R^a is additionally substituted or unsubstituted by at least one substituent selected from among a group comprised of halogen; carbonyl; C_{1-8} alkyl substituted or unsubstituted by a hydroxy or a C_{1-8} alkylamino; C_{2-8} alkenyl; C_{1-8} alkoxy; C_{1-8} alkylamino; C_{1-8} alkylcarbonyl; and, a heterocycloalkyl of 3 to 12 atoms substituted or unsubstituted by C_{1-8} alkyl, where the R^{12} and R^{13} are, respectively and independently, hydrogen, C_{1-8} alkylcarbonyl, C_{2-8} alkenylcarbonyl, or a heterocycloalkyl of 3 to 12 atoms substituted or unsubstituted by C_{1-8} alkyl, heterocycloalkyl of 3 to 12 atoms, and the heteroaryl of 3 to 12 atoms formed by the bonding of R^9 and R^{10} is substituted or unsubstituted by C_{1-8} alkyl,

[98] R^4 is $-NH(C=O)R^{14}C=CR^{15}R^{16}$, where the R^{14} is hydrogen or halogen, and the R^{15} and R^{16} are, respectively and independently, hydrogen or C_{1-8} alkyl substituted or unsubstituted by an alkylamino of C_{1-8},

[99] R^5 is a C_{1-8} alkyl substituted by a aryl of 3 to 12 atoms or a heteroaryl of 3 to 12 atoms; an aryl of 3 to 12 atoms; or a heteroaryl of 3 to 12 atoms, where the aryl of 3 to 12 atoms and the heteroaryl of 3 to 12 atoms of R^5 are, respectively and independently, substituted or unsubstituted by at least one substituent selected from a group comprised of halogen, cyano, C_{1-8} substituted or unsubstituted by halogen, C_{1-8} alkoxy, and C_{2-8} alkynyl, and aryl substituted with a aryl of 3 to 12 atoms or heteroaryl of 3 to 12 atoms of R^5 is substituted or unsubstituted by at least one substituent selected from a group comprised of halogen, C_{1-8} alkyl substituted or unsubstituted by halogen, and C_{1-8} alkylamino,

[100] and R^6 may be hydrogen or C_{1-8} alkyl.

[101] In yet another embodiment, in the compound represented by Chemical Formula 1,

[102] R^1 is hydrogen, halogen, C_{1-4} alkyl, or C_{1-4} alkoxy, where the C_{1-4} alkoxies of R^1 are, respectively and independently, substituted or unsubstituted by at least one halogen,

[103] R^2 is hydrogen or $-NR^7R^8$, where R^7 and R^8 are linked, together with the N atoms to which they are bonded, to form a heterocycloalkyl of 3 to 8 atoms, where the heterocycloalkyl of 3 to 8 atoms formed by the bonding of R^7 and R^8 is substituted or unsubstituted by at least one C_{1-4} alkyl,

[104] R^3 is hydrogen, $-NR^9R^{10}$ or $-OR^{11}$, where R^9, R^{10}, and R^{11} are, respectively and independently C_{1-6} alkyl, or R^9 and R^{10} are linked together with the N atoms with which they are bonded to form a heterocycloalkyl of 3 to 10 atoms or heteroaryl of 3 to 8 atoms, the C_{1-6} alkyls of R^9, R^{10}, and R^{11} are, respectively and independently, substituted or unsubstituted by at least one substituent selected from a group comprised of C_{1-4} alkylamino and C_{1-4} alkoxy, and the heterocycloalkyl of 3 to 10 atoms formed by the bonding of R^9 and R^{10} is substituted or unsubstituted by at least one substituent R^b selected from among a group comprised of hydroxy, C_{1-6} alkyl, C_{1-4}, C_{1-4} alkylamino, C_{1-4} alkylcarbonyl, $-NR^{12}R^{13}$ and heterocycloalkyl of 3 to 10 atoms, the C_{1-6} alkyl, C_{1-4} alkoxy, and C_{1-4} alkylamino of the substituent R^b are, respectively and independently, additionally substituted or unsubstituted by at least one

substituent selected from among a group comprised of C_{1-6} alkyl, C_{1-4} alkoxy, and C_{1-4}alkylamino, the heterocycloalkyl of 3 to 10 atoms of substituent R^b is additionally substituted or unsubstituted by at least one substituent selected from among a group comprised of halogen; carbonyl; C_{1-6} alkyl substituted or unsubstituted by C_{1-4} alkylamino; C_{2-4} alkenyl; C_{1-4} alkylamino; C_{1-4} alkylcarbonyl; and, a heterocycloalkyl of 3 to 8 atoms substituted or unsubstituted by C_{1-4} alkyl, R^{12} and R^{13} are, respectively and independently, hydrogen, C_{2-4} alkenyl carbonyl or heterocycloalkyl of 3 to 8 atoms substituted or unsubstituted by C_{1-4} alkyl, the heteroaryl of 3 to 8 atoms formed by the bonding of R^9 and R^{10} is substituted or unsubstituted by C_{1-4} alkyl,

[105] R^4 is $-NH(C=O)R^{14}C=CR^{15}R^{16}$, R^{14} is hydrogen or halogen, and R^{15} and R^{16} are, respectively and independently, hydrogen or C_{1-4} alkyl substituted by an alkylamino of C_{1-4},

[106] R^5 is a C_{1-4} alkyl; an aryl of 3 to 8 atoms; or a heteroaryl of 3 to 8 atoms substituted by an aryl of 3 to 8 atoms or heteroaryl of 3 to 8 atoms; the aryl of 3 to 8 atoms or heteroaryl of 3 to 8 atoms of R^5 are, respectively and independently, substituted or unsubstituted by at least one substituent selected from among a group comprised of halogen, cyano, C_{1-4} alkyl substituted or unsubstituted by halogen, C_{1-4} alkoxy, and C_{2-4} alkynyl, the C_{1-4} alkyl substituted by an aryl of 3 to 8 atoms or heteroaryl of 3 to 8 atoms of R^5 is substituted or unsubstituted by at least one substituent selected from among a group comprised of halogen, C_{1-4} alkyl substituted or unsubstituted by halogen, and C_{1-4} alkylamino,

[107] and R^6 may be hydrogen or C_{1-4} alkyl.

[108] In another embodiment, in a compound represented by Chemical Formula 1,

[109] R^1 is hydrogen, halogen, C_{1-4} alkyl or C_{1-4} alkoxy, where the C_{1-4} alkoxy of R^1 is, respectively and independently, substituted or unsubstituted by at least one halogen,

[110] R^2 is hydrogen or $-NR^7R^8$, where R^7 and R^8 are linked together with an N atom to which they are bonded to form a heterocycloalkyl of 3 to 8 atoms having one or two N atoms, where the heterocycloalkyl of 3 to 8 atoms formed by the bonding of R^7 and R^8 is substituted or unsubstituted by at least one C_{1-4} alkyl,

[111] R^3 is hydrogen, $-NR^9R^{10}$, or $-OR^{11}$, where R^9, R^{10} and R^{11} are, respectively and independently, C_{1-6} alkyl, or R^9 and R^{10} are linked together with an N atom to which they are bonded to form a heterocycloalkyl of 3 to 10 atoms having one or two heteroatoms selected from a group comprised of N and O, or a heteroaryl of 3 to 8 atoms having one or two heteroatoms selected from a group comprised of N and O, the C_{1-6} alkyl of R^9, R^{10} and R^{11} are, respectively and independently, substituted or unsubstituted by at least one substituent selected from among a group comprised of C_{1-4} alkylamino and C_{1-4} alkoxy, the heterocycloalkyl of 3 to 8 atoms formed by the bonding of R^9 and R^{10} is substituted or unsubstituted by at least one substituent R^c selected from among a group comprised of a heterocycloalkyl of 3 to 10 atoms having one or two heteroatoms selected from among a group comprised of hydroxy, C_{1-6} alkyl, C_{1-4} alkoxy, C_{1-4} alkylamino, C_{1-4} carbonyl, $-NR^{12}R^{13}$, and heterocycloalkyl of 3 to 10 atoms having one or two heteroatoms selected from the group consisting of N and O, the C_{1-6} alkyl, C_{1-4} alkoxy and C_{1-4} alkylamino of substituents R^c are, respectively and independently, additionally

substituted or unsubstituted by at least one substituent selected from among C_{1-6} alkyl, C_{1-4} alkoxy and C_{1-4} alkylamino, the heterocycloalkyl of 3 to 10 atoms of substituents R^c is substituted or unsubstituted by halogen; carbonyl; C_{1-6} alkyl substituted or unsubstituted by C_{1-4} alkylamino; C_{2-4} alkenyl; C_{1-4} alkylamino; C_{1-4} alkylcarbonyl; and C_{1-4} alkyl, and additionally substituted or unsubstituted by at least one substituent selected from among a group comprised of heterocycloalkyl of 3 to 8 atoms having one or two heteroatoms selected from a group comprised of N and O, R^{12} and R^{13} are, respectively and independently, substituted or unsubstituted by hydrogen, C_{2-4} alkenylcarbonyl or C_{1-4} alkyl, are heterocycloalkyl of 3 to 8 atoms having one or two N atoms, the heteroaryl of 3 to 8 atoms formed by the bonding of R^9 and R^{10} is substituted or unsubstituted by C_{1-4} alkyl,

[112] R^4 is $-NH(C=O)R^{14}C=CR^{15}R^{16}$, R^{14} is hydrogen or halogen, and R^{15} and R^{16} are, respectively and independently, C_{1-4} alkyl substituted by hydrogen or C_{1-4} alkylamino,

[113] R^5 is a C_{1-4} alkyl substituted by a aryl of 3 to 8 atoms or heteroaryl of 3 to 8 atoms; aryl of 3 to 8 atoms; or heteroaryl of 3 to 8 atoms, the aryl of 3 to 8 atoms or heteroaryl of 3 to 8 atoms of R^5 is, respectively and independently, substituted or unsubstituted by at least one substituent selected from among a group comprised of halogen, cyano, C_{1-4} alkyl substituted or unsubstituted by halogen, C_{1-4} alkoxy, and C_{2-4} alkynyl, the C_{1-4} substituted by a aryl of 3 to 8 atoms or a heteroaryl of 3 to 8 atoms of R^5 is substituted or unsubstituted by at least one substituent selected from among a group comprised of halogen, C_{1-4} alkyl substituted or unsubstituted by halogen, and C_{1-4} alkylamino,

[114] and R^6 may be hydrogen or C_{1-4} alkyl.

[115] In yet another embodiment, in a compound represented by Chemical Formula 1,

[116] R^1 is hydrogen, fluoro, chloro, methyl, ethyl, methoxy, ethoxy or propoxy, where the methoxy, ethoxy, or propoxy of R^1 is, respectively and independently, substituted or unsubstituted by at least one fluoro or chloro,

[117] R^2 is hydrogen or $-NR^7R^8$, where R^7 and R^8 are linked together with an N atom to which they are bonded to form azetidine, pyrrolidine, piperazine, piperidine or diazepane, the azetidine, pyrrolidine, piperazine, piperidine or diazepane formed by the bonding of R^7 and R^8 substituted or unsubstituted by at least one methyl or ethyl,

[118] R^3 is hydrogen, $-NR^9R^{10}$, or $-OR^{11}$, where R^9, R^{10} and R^{11} are, respectively and independently, methyl, ethyl, propyl, butyl or pentyl, or R^9 and R^{10} are linked, together with an N atom to which they are bonded, form an azetidine, pyrrolidine, piperazine, piperidine, diazepane, morpholine, diazabicycloheptane, oxazabicycloheptane, diazabicyclooctane, oxazabicylooctane, imidazole, pyrrole, hexahydropyrrolopyrrole or tetrahydropuropyrrole, the methyl, ethyl, propyl, butyl or pentyl of R^9, R^{10} and R^{11} are, respectively and independently, substituted or unsubstituted by at least one substituent selected from among a group comprised of dimethylamino, diethylamino, methylethylamino, methylpropylamino, ethylpropylamino, methoxy or ethoxy, the azetidine, pyrrolidine, piperazine, piperidine, diazepane, morpholine, diazabicycloheptane, oxazabicycloheptane, diazabicyclooctane, oxazabicylooctane, imidazole, pyrrole,

hexahydropyrrolopyrrole or tetrahydropuropyrrole formed by the bonding of R^9 and R^{10} are, respectively and independently, substituted or unsubstituted by at least one substituent R^d selected from among a group comprised of hydroxy, methyl, ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, methoxy, ethoxy, dimethylamino, diethylamino, methylethylamino, methylpropylamino, ethylpropylamino, acetyl, azetidine, pyrrolidine, piperazine, piperidine, diazepane, morpholine, oxetane, diazabicycloheptane, oxazabicycloheptane, diazabicyclooctane, oxazabicyclooctane , oxazaspiroheptane, azaspirooctane, hexahydropyrrolopirazine, and $-NR^{12}R^{13}$, the methyl, ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, methoxy, ethoxy, dimethylamino, diethylamino, methylethylamino, methylpropylamino or ethylpropylamino of the substituents R^d are, respectively and independently, additionally substituted or unsubstituted by at least one substituent selected from a group comprised of cyclopropyl, cyclobutyl, methoxy, ethoxy, methylamino, diethylamino and methylethylamino, the azetidine, pyrrolidine, piperazine, piperidine, diazepane, morpholine, oxetane, diazabicycloheptane, oxazabicycloheptane, diazabicyclooctane, oxazabicyclooctane , oxazaspiroheptane, azaspirooctane or hexahydropyrrolopirazine of the substituents R^d are, respectively and independently, additionally substituted or unsubstituted by at least one substituent selected from a group comprised of fluoro, chloro, carbonyl, methyl, ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, methyl substituted by dimethylamino, methyl substituted by diethylamino, ethyl substituted by diethylamino, ethenyl, propenyl, butenyl, dimethylamino, diethylamino, methylethylamino, methylpropylamino, ethylpropylamino, acetyl, azetidine substituted or unsubstituted by methyl or ethyl, pyrrolidine substituted or unsubstituted by methyl or ethyl, piperazine substituted or unsubstituted by methyl or ethyl, piperidine substituted or unsubstituted by methyl or ethyl, diazepane substituted or unsubstituted by methyl or ethyl, morpholine substituted or unsubstituted by methyl or ethyl, and oxetane substituted or unsubstituted by methyl or ethyl, R^{12} is, respectively and independently, hydrogen or prop-2-en-1-on, R^{13} is azetidine substituted or unsubstituted by methyl, ethyl or propyl; pyrrolidine substituted or unsubstituted by methyl, ethyl or propyl; or piperidine substituted or unsubstituted by methyl, ethyl or propyl, the imidazole or pyrrole formed by the bonding of R^9 and R^{10} is substituted or unsubstituted by methyl or ethyl,

[119] R^4 is $-NH(C=O)R^{14}C=CR^{15}R^{16}$, R^{14} is hydrogen, fluoro or chloro, R^{15} and R^{16} are, respectively and independently, hydrogen; methyl substituted by dimethylamino or diethylamino; or ethyl substituted by dimethylamino or diethylamino,

[120] R^5 is methyl substituted by phenyl, naphthyl, pyridine or pyrrole; ethyl substituted by phenyl, naphthyl, pyridine or pyrrole; phenyl; naphthyl; pyrrole; pyridine; or thiophene, the phenyl, naphthyl, pyrrole, pyridine or thiophene of R^5 are, respectively and independently, substituted or unsubstituted by at least one substituent selected from among a group comprised of fluoro; chloro; cyano; methyl substituted or unsubstituted by fluoro or chloro; ethyl substituted or unsubstituted by fluoro or chloro; methoxy; ethoxy; and ethinyl, the phenyl, naphthyl, pyridine or pyrrole which is the substituent of the methyl or ethyl of R^5 is,

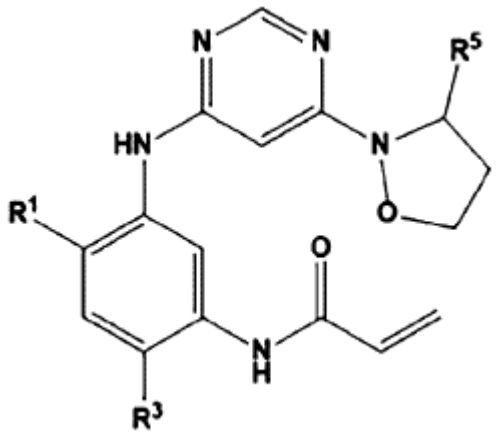
respectively and respectively, substituted or unsubstituted by at least one substituent selected from among a group comprised of fluoro; chloro; methyl substituted or unsubstituted by fluoro or chloro; ethyl substituted or unsubstituted by fluoro or chloro; dimethylamino; and diethylamino,

[121] and R^6 may be hydrogen, methyl or ethyl.

[122] In another embodiment,

[123] A compound represented by Chemical Formula 2, stereoisomers of the same, or pharmaceutically acceptable salts of the same are provided.

[124] [Chemical Formula 2]

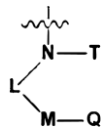


[125]

[126] Where, in Chemical Formula 2,

[127] R^1 is hydrogen or C_{1-4} alkoxy, R^3 is -X-Y-Z, where X and Y are, respectively and independently, single bonds or heterocycloalkyl of 3 to 8 atoms comprising at least one N atom, and Z is $-NR^{17}R^{18}$ or is represented by Chemical Formula 3,

[128] [Chemical Formula 3]



[129]

[130] Where, in a case where Z is $-NR^{17}R^{18}$, at least one of X and Y is the heterocycloalkyl of 3 to 8 atoms comprising at least one N atom, where R^{17} and R^{18} are, respectively and independently, a C_{1-4} alkyl substituted or unsubstituted by hydrogen or C_{1-4} alkylamino, or are linked together with an N atom to which they are bonded to form a heterocycloalkyl of 3 to 12 atoms,

[131] In a case where Z is Chemical Formula 3, L is an alkylene substituted or unsubstituted by C_{1-4} alkyl, M is $-NR^{19}$ or -O-, T and Q are, respectively and independently, C_{1-4} alkyl substituted or unsubstituted by hydrogen or C_{1-4} alkylamino; T and Q are linked to each other to form a heterocycloalkyl of 3 to 12 atoms substituted or unsubstituted by C_{1-4} alkyl; or T and Q are linked to each other, with additional links between at least two different atoms forming a ring, to form a bridged or fused heterocycloalkyl of 3 to 12 atoms substituted or unsubstituted by a C_{1-4} alkyl, R^{19} is hydrogen, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkylcarbonyl, C_{1-4} alkylamino, or a 3 to 8 atom heterocycloalkyl,

[132] R^5 is a aralkyl of 3 to 8 atoms, aryl of 3 to 8 atoms, or heteroaryl of 3 to 8 atoms, where the aralkyl of 3 to 8 atoms, aryl of 3 to 8 atoms, or heteroaryl of 3 to 8 atoms of R^5 may be, respectively and independently, substituted or unsubstituted by at least one

substituent selected from among a group comprised of halogen, cyano, C_{1-4} alkyl, and C_{1-4} alkoxy.

[133] In another embodiment,

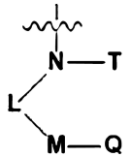
[134] In the compound represented by Chemical Formula 2, R^1 may be hydrogen, methoxy, or ethoxy.

[135] In another embodiment, in the compound represented by Chemical Formula 2,

[136] R^1 and R^5 are as defined in Chemical Formula 2,

[137] R^3 is -X-Y-Z, where X and Y are, respectively and independently, a single bond, azetidine, pyrrolidine, piperidine or piperazine, and Z is represented by -$NR^{17}R^{18}$ or Chemical Formula 3,

[138] [Chemical Formula 3]

[139] 

[140] Where, in a case where Z is -$NR^{17}R^{18}$, at least one of X and Y is azetidine, pyrrolidine, piperidine or piperazine, where R^{17} and R^{18} are, respectively and independently methyl or ethyl, or are linked together with an N atom to which they are bonded to be azaspiroctane,

[141] In a case where Z is Chemical Formula 3, L is methylene, ethylene, propylene or butylene substituted or unsubstituted by methyl or ethyl,

[142] M is -NR^{19} or -O-, and T and Q are, respectively and independently, methyl or ethyl substituted or unsubstituted by dimethyl amino; M is -NR^{19}, and T and Q are linked to each other to form a piperazine substituted or unsubstituted by methyl or ethyl; M is -NR^{19}, and T and Q are linked together, with additional links between at least two different atoms among the atoms forming the ring, forming a 6 to 8 atom diazabicycloalkyl substituted or unsubstituted by methyl or ethyl; M is -O-, and T and Q are linked together, forming a morpholine substituted or unsubstituted by methyl or ethyl; or M is -O-, and T and Q are linked together, with additional links between at least two different atoms among the atoms forming the ring, forming a 6 to 8 atom oxazabicycloalkyl substituted or unsubstituted by methyl or ethyl,

[143] and R^{19} may be methyl, ethyl, propyl, cyclopropyl, cyclopropylmethyl, cyclobutyl, cyclopentyl, prop-2-en-1-yl, acetyl, dimethylamino, or oxetane.

[144] In yet another embodiment,

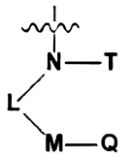
[145] In the compound represented by Chemical Formula 2, R^5 is phenyl, benzyl, pyridine or thiophene, and the phenyl, benzyl, pyridine or thiophene may be, respectively and independently, substituted or unsubstituted by at least one substituent selected from among a group comprised of fluoro, chloro, cyano, methyl substituted or unsubstituted by at least one fluoro, and methoxy.

[146] In another embodiment, in a compound represented by Chemical Formula 2,

[147] R^5 is as defined in Chemical Formula 2,

[148] R^1 is hydrogen or methoxy, R^3 is -X-Y-Z, where X and Y are, respectively and independently, single bonds, pyrrolidine or piperidine, and Z is dimethylamino, azaspirooctane, or represented by Chemical Formula 3,

[149] [Chemical Formula 3]

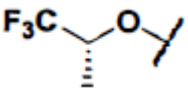
[150] 

[151] Where, in a case where Z is dimethylamino or azaspirooctane, at least one of X and Y is pyrrolidine or piperidine,

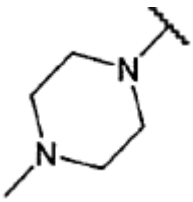
[152] In a case where Z is Chemical Formula 3 and X and Y are single bonds, Chemical Formula 3 is piperazine, morpholine, methylethylamino, hexahydropyrrolopyrrole, or tetrahydropuropyrrole substituted or unsubstituted by at least one substituent selected from among a group comprised of methyl, ethyl, propyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclopropylmethyl, and dimethylamino,

[153] In a case where Z is Chemical Formula 3 and at least one of X and Y is pyrrolidine or piperidine, Chemical Formula 3 may be piperazine, morpholine, diazabicycloheptane, oxazabicycloheptane, hexahydropyrrolopyrrole, or tetrahydropuropyrrole substituted or unsubstituted by at least one substituent selected from among a group comprised of methyl, ethyl, propyl, oxetane, cyclopropyl, cyclobutyl, cyclopentyl, cyclopropylmethyl, acetyl and dimethylamino.

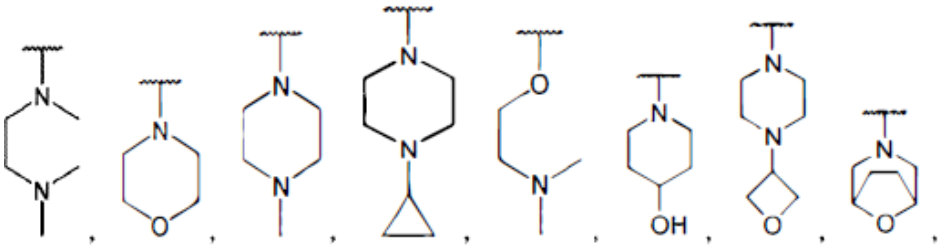
[154] In yet another embodiment, in a compound represented by Chemical Formula 1,

[155] R^1 may be hydrogen, fluoro, chloro, methyl, ethyl, methoxy, ethoxy, propoxy, 

or .

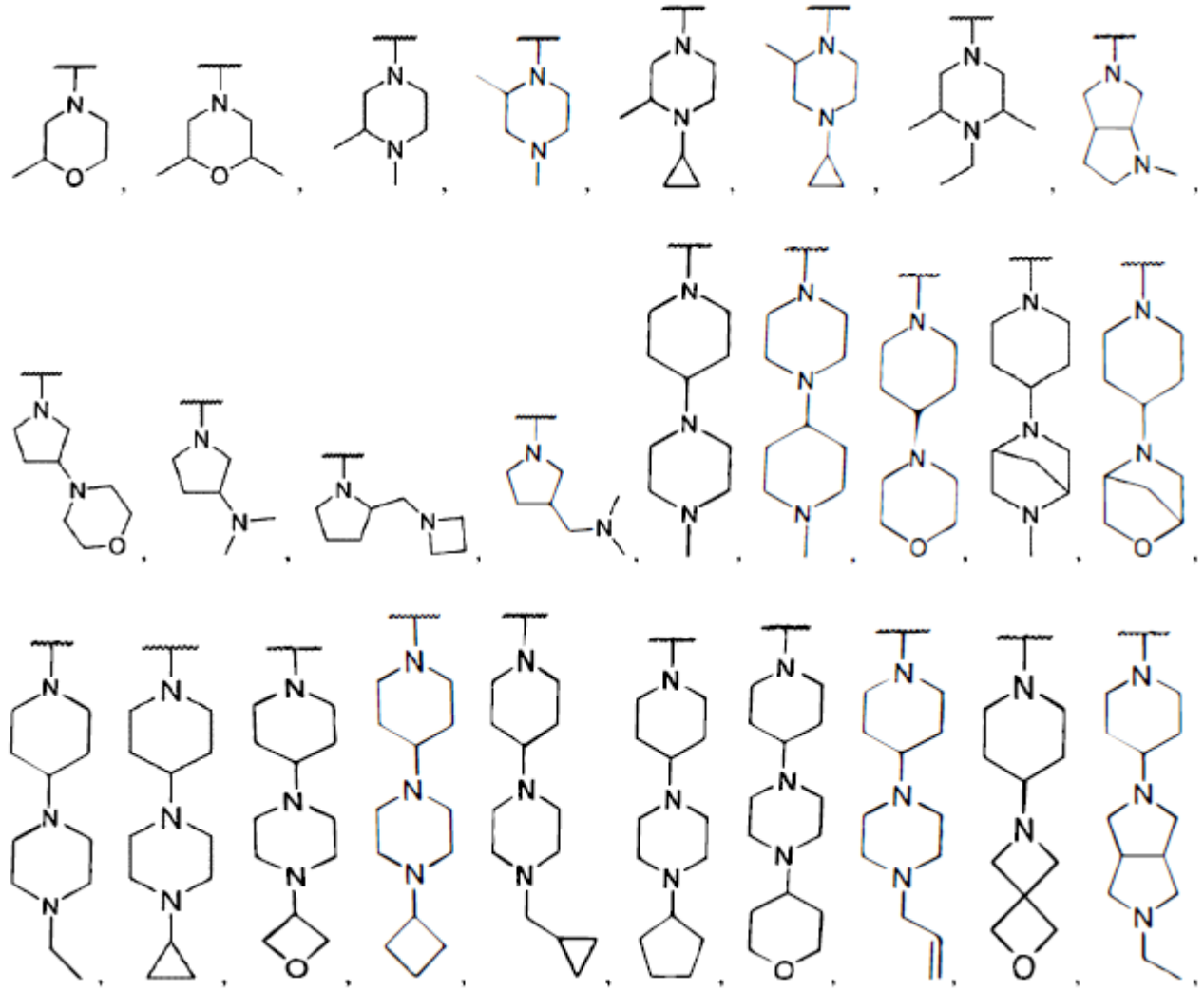
[156] R^2 may be hydrogen or 

.

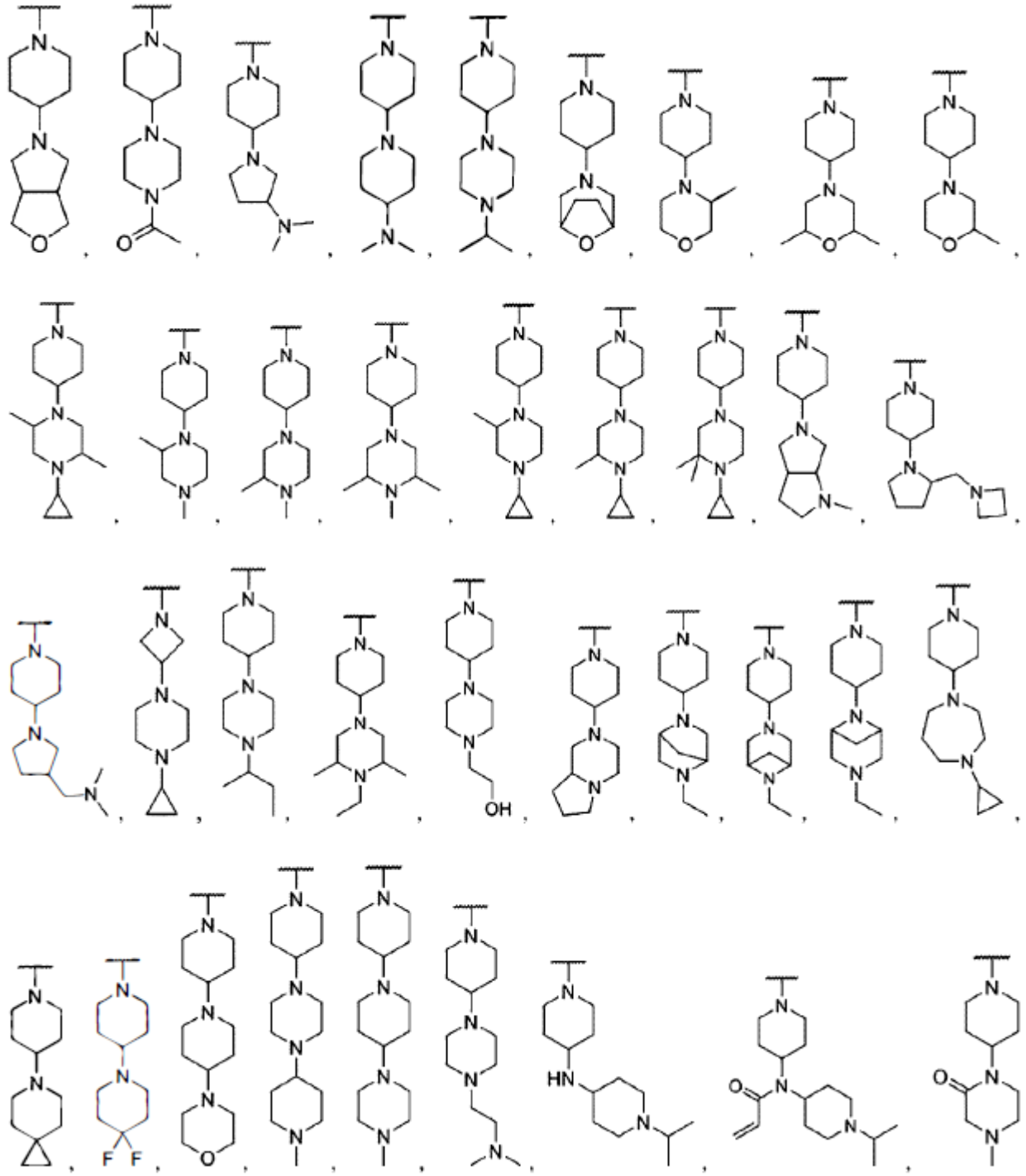
[157] R^3 may be hydrogen, 

.

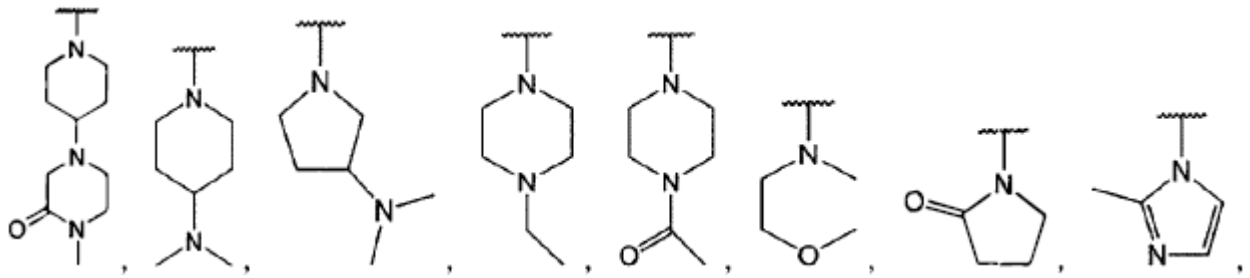
[158]

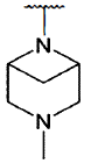


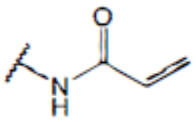
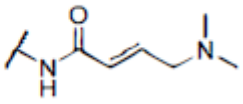
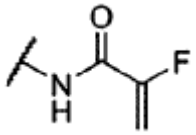
[159]



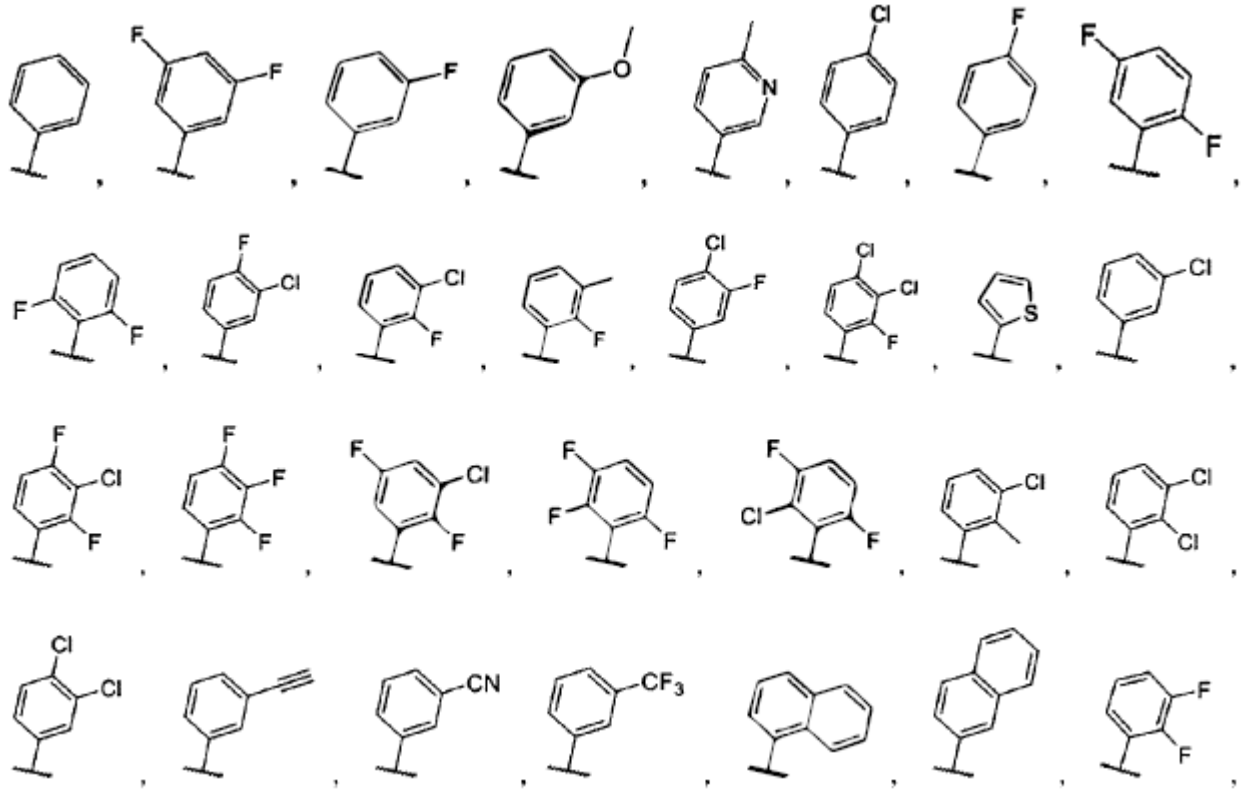
[160]



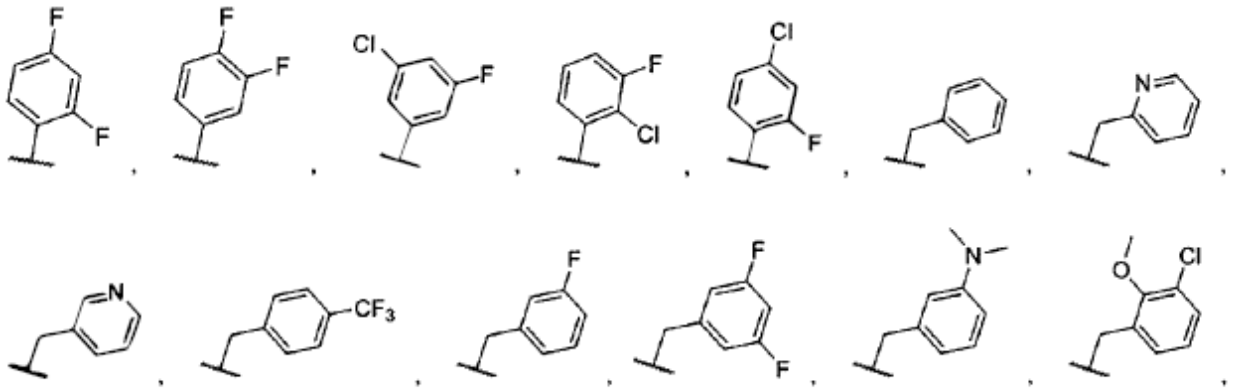
[161] or  .

[162] R^4 may be  ,  , or  . R^5 may be

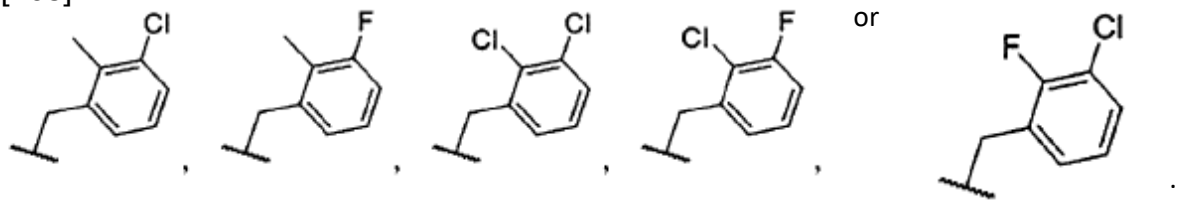
[163]



[164]



[165]



[166] In another embodiment,

[167] The compound represented by Chemical Formula 1 may be any one of Example Compounds 1 through 1059 listed in [Table 1] below.

[168] The compound represented by Chemical Formula 1 of the present invention may be used in the form of pharmaceutically acceptable salts thereof. In particular, the pharmaceutically acceptable salt may be an acid addition salt formed by a free acid. Here, the acid addition salt may be obtained from inorganic acids, such as hydrochloric acid, nitric acid, phosphoric acid, sulfuric acid, hydrobromic acid, hydroiodic acid, nitrous acid, phosphorous acid and the like, nontoxic organic acids, such as aliphatic mono- and dicarboxylate, phenyl-substituted alkanoate, hydroxy alkanoate and alkanthioate, aromatic acids, aliphatic and aromatic sulfonic acids and the like, organic acids, such as acetate, benzoic acid, citric acid, lactic acid, maleic acid, gluconic acid, methanesulfonic acid, 4-toluenesulfonic acid, tartaric acid, fumaric acid and the like. Types of such pharmaceutically acceptable salts include sulfate, pyrosulfate, bisulfate, sulfite, bisulfite, nitrate, phosphate, monohydrogen phosphate, dihydrogen phosphate, metaphosphate, pyrophosphate chloride, bromide, iodide, fluoride, acetate, propionate, decanoate, caprylate, acrylate, formate, isobutyrate, caprate, heptanoate, propiolate, oxalate, malonate, succinate, suberate, sebacate, fumarate, maleate, butyne-1,4-dioate, hexane-1,6-dioate, benzoate, chlorobenzoate, methylbenzoate, dinitrobenzoate, hydroxybenzoate, methoxybenzoate, phthalate, terephthalate, benzene sulfonate, toluene sulfonate, chlorobenzene sulfonate, xylene sulfonate, phenylacetate, phenylpropionate, phenylbutyrate, citrate, lactate, β-hydroxybutyrate, glycolate, malate, tartrate, methane sulfonate, propane sulfonate, naphthalene-1-sulfonate, naphthalene-2-sulfonate, mandelate and the like. The acid addition salt may be prepared using a conventional method, for example, by dissolving the derivative of Formula 1 in an organic solvent, such as methanol, ethanol, acetone, methylene chloride, acetonitrile and the like, adding an organic acid or an inorganic acid,

filtering the resulting precipitate, and drying, or it may be prepared by distilling a solvent and an acid in excess amount under reduced pressure, then drying, and crystallizing under an organic solvent. Further, the pharmaceutically acceptable salt may be a salt or metal salt obtained using a base. As an example of a metal salt, an alkali metal or alkaline earth metal salt may be obtained, for example, by dissolving the compound in surplus alkali metal hydroxide or alkaline earth metal hydroxide solution, filtering the undissolved compound salt, evaporating the filtrate, and drying. Pharmaceutically suitable alkali metal salts may be sodium, potassium or calcium. In addition, the corresponding salt may be obtained by reacting an alkali metal or alkaline earth metal salt with an appropriate silver salt (for example, silver nitrate).

[169] Further, the present invention may be, not only the compound represented by Chemical Formula 1 and pharmaceutically acceptable salts thereof, but also stereoisomers, in particular, enantiomers of the same and hydrates and/or solvates which may be prepared from the same.

[170] Another aspect of the present invention may provide a method for preparing the compound of Chemical Formula 1.

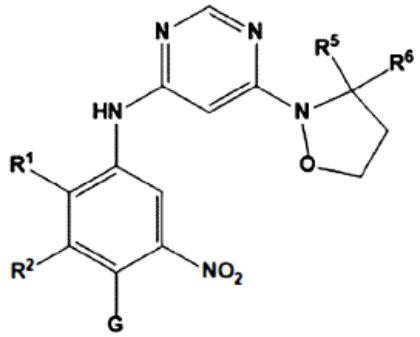
[171] The method for preparing the compound of Chemical Formula 1 may comprise:

[172] A step of preparing a compound of Chemical Formula 5 from a compound of Chemical Formula 4;

[173] A step of preparing a compound of Chemical Formula 6 from the compound of Chemical Formula 5; and,

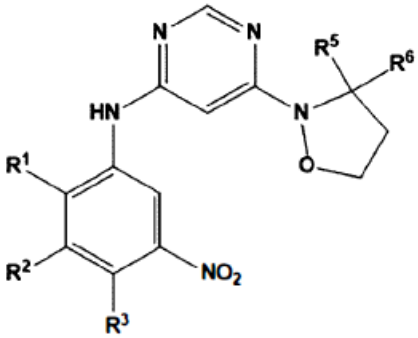
[174] A step of preparing the compound of Chemical Formula 1 from the compound of Chemical Formula 6.

[175] [Chemical Formula 4]



[176]

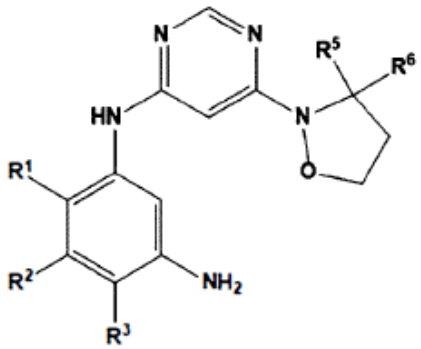
[177] [Chemical Formula 5]



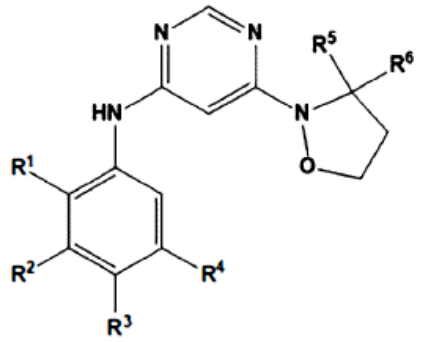
[178]

[179] [Chemical Formula 6]

[180]



[181] [Chemical Formula 1]



[182]

[183] In Chemical Formula 4, G is a leaving group, and R^1 and R^6 are respectively the same as defined in the above. The leaving group may be a functional group such as halogen, sulfonic acid ester or alkoxy, and there is no particular limitation on the functional group so long as it is a functional group where the leaving group can leave from the compound of Chemical Formula 4 to prepare the compound of Chemical Formula 5.

[184] The step of preparing the compound of Chemical Formula 5 from the compound of Chemical Formula 4 may be a step wherein the compound of Chemical Formula 4 reacts with R^3-H. The reaction may be carried out in solvent such as dimethylsulfoxide (DMSO). The reaction temperature may be approximately 40 to 100℃, the reaction time may be 90 to 150 minutes, and conditions may not be limited to the above so long as they allow the reaction to carry on smoothly.

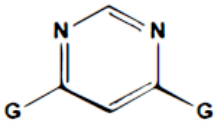
[185] Meanwhile, the step of preparing the compound of Chemical Formula 5 from the compound of Chemical Formula 4 may be a step wherein a step of reacting the compound of Chemical Formula 4 with a heterocycloalkyl such as piperidinone is carried out, and then a step of reacting with R^3-H is carried out.

[186] The step of preparing the compound of Chemical Formula 6 from the compound of Chemical Formula 5 may be a step of reducing nitro groups existing in a para position from R^1, in a meta position from R^2, and in an ortho position from R^3. In particular, the step may be a step wherein only the nitro groups are reduced, without reducing other functional groups or compounds. Any reducing agent may be used without limitation so long as it is a reducing agent which reduces nitro groups, and for example, $SnCl_2$ may be used.

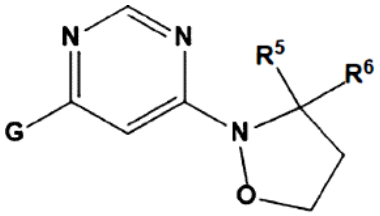
[187] The step of preparing the compound of Chemical Formula 1 from the compound of Chemical Formula 6 may be a step wherein the compound of Chemical Formula 6 reacts with acrylic acid or acryl halide.

[188] Further, the compound of Chemical Formula 4 may be a compound prepared through a step of preparing a compound of Chemical Formula 8 from a compound of Chemical Formula 7; and, a step of preparing the compound of Chemical Formula 4 from the compound of Chemical Formula 8.

[189] [Chemical Formula 7]

[190] 

[191] [Chemical Formula 8]

[192] 

[193] In Chemical Formula 7 or Chemical Formula 8 above, G is, respectively and independently, a leaving group, and R^5 and R^6 may respectively be the same as defined in the present specification. The leaving group may be a functional group such as halogen, sulfonic acid, ester or alkoxy, and there is no particular limitation on the functional group so long as the compound of Chemical Formula 8 can be prepared from the compound of Chemical Formula 7, and the compound of Chemical Formula 4 can be prepared from the compound of Chemical Formula 8.

[194] The step of preparing the compound of Chemical Formula 8 from the compound of Chemical Formula 7 may be performed in a solvent such as dimethylsulfoxide (DMSO). The reaction temperature may be approximately 60 to 120℃, the reaction time may be approximately 30 to 90 minutes, and there is no particular limitation on the above conditions so long as they allow for the reaction(s) to carry out smoothly.

[195] In the case of the step of preparing the compound of Chemical Formula 4 from the compound of Chemical Formula 8, the reaction temperature may be approximately 80 to 120℃, the reaction time may be approximately 45 to 90 minutes, and there is no particular limitation on the above conditions so long as they allow for the reaction(s) to carry out smoothly.

[196] Yet another aspect of the present invention may provide:

[197] A pharmaceutical composition for preventing or treating cancer, the composition comprising the compound of Chemical Formula 1, stereoisomers of the same, hydrates of the same or pharmaceutically acceptable salts of the same as an effective component.

[198] The compound of Chemical Formula 1 may exhibit inhibitory activity against EGFR (epidermal growth factor receptor) mutants and ERBB2 and ERBB4. In other words, the compound of Chemical Formula 1 can inhibit EGFR (epidermal growth factor receptor) mutants, or wild type or mutant kinases of one of ERBB2 and ERBB4.

[199] The EGFR mutant may be at least one selected from among a group comprised of EGFR Del19/T790M, EGFR L858R/T790M, EGFR L858R, EGFR Exon20 ins NPH, EGFR Exon20 ins SVD, EGFR Exon20 ins FQEA,

EGFR Exon20 ins H, and EGFR Exon20 ins ASV.

[200] The ERBB2 mutant may be Her2 Exon20 ins YVMA.

[201] Whereas there is no limitation on the type of cancer, the cancer may be one or more selected from a group comprised of pseudomyxoma, intrahepatic cholangiocarcinoma, hepatoblastoma, liver cancer, thyroid cancer, colon cancer, testis cancer, myelodysplastic syndrome, glioblastoma, oral cancer, lip cancer, mycosis fungoides, acute myeloid leukemia, acute lymphocytic leukemia, basal cell carcinoma, epithelial ovarian cancer, ovarian seminoma, male breast cancer, brain cancer, pituitary adenoma, multiple myeloma, gallbladder cancer, cholangiocarcinoma, colorectal cancer, chronic myeloid leukemia, chronic lymphocytic leukemia, retinoblastoma, choroidal melanoma, ampullar of Vater cancer, bladder cancer, peritoneal cancer, parathyroid cancer, adrenal cancer, nasal and paranasal cavity cancer, non-small cell lung cancer, tongue cancer, astrocytoma, small cell lung cancer, pediatric brain cancer, pediatric lymphoma, pediatric leukemia, small intestine cancer, meningioma, esophageal cancer, glioma, renal pelvis cancer, renal cancer, heart cancer, duodenal cancer, malignant soft tissue cancer, malignant bone cancer, malignant lymphoma, malignant mesothelioma, malignant melanoma, eye cancer, vulvar cancer, ureteral cancer, urethral cancer, cancer of unknown primary site, gastric lymphoma, gastric cancer, gastric carcinoid, gastrointestinal stromal tumor, Wilms' tumor, breast cancer, sarcoma, penile cancer, pharyngeal cancer, gestational choriocarcinoma, cervical cancer, endometrial cancer, uterine sarcoma, prostate cancer, metastatic bone cancer, metastatic brain cancer, mediastinal cancer, rectal cancer, rectal carcinoid, vaginal cancer, spinal cancer, vestibular schwannoma, pancreatic cancer, salivary gland cancer, Kaposi's sarcoma, Paget's disease, tonsillar cancer, squamous cell cancer, adenocarcinoma of lung, lung cancer, squamous cell lung cancer, skin cancer, anal cancer, rhabdomyosarcoma, laryngeal cancer, pleura cancer, hematologic malignancy, and thymic cancer.

[202] The pharmaceutical composition for preventing or treating cancer according to the present invention may be used for clinical administration, and may be prepared for administration as a variety of oral and non-oral dosage forms.

[203] The pharmaceutical composition of the present invention may comprise pharmaceutically acceptable carriers. Examples of such pharmaceutically acceptable carriers include filling agents, bulking agents, binding agents, wetting agents, disintegrating agents, diluents such as surfactants or excipients, and the composition of the present invention may be formulated together with these.

[204] Solid formulations for oral administration may include tablets, pills, powders, granules and capsules, etc., and such solid formulations may be formulated by mixing, with at least one compound, at least one excipient, for example, starch, calcium carbonate, sucrose, lactose or gelatin, etc. Further, in addition to simple excipients, lubricants such as magnesium stearate or talc may be used in formulation.

[205] Liquid formulations for oral administration may include a suspension, a solution, an emulsion and a syrup, etc. In addition to water commonly used as a simple diluent and liquid paraffin, various excipients, for example, wetting agents, sweetening agents, flavors, preservatives, etc. may be included.

[206] Formulations for non-oral administration include sterilized aqueous solutions, non-aqueous solvents, suspending agents, emulsions, freeze-drying agents, suppositories, etc. Propylene glycol, polyethylene glycol, vegetable oils such as olive oil, injectable esters such as ethyl oleate, etc. may be used as non-aqueous solvents and suspending agents.

[207] Further, non-oral administration may be performed using methods such as subcutaneous injection, intravenous injection, intramuscular injection or intrathoracic injection. Here, for formulation into a dosage form for non-oral administration, the pharmaceutical composition may be prepared by mixing the compound represented by Chemical Formula 1 or a pharmaceutically acceptable salt thereof into water together with a stabilizer or buffer to prepare a solution or suspension, which is then prepared into ampoule or vial type unit doses. The composition is/may be sterilized, may contain preservatives, stabilizing agents, wetting agents or emulsifying agents, salts for osmoregulation, and/or adjuvants such as buffer agents, as well as other therapeutically useful substances, and may be formulated using ordinary mixing, granulation or coating methods.

[208]

[209] In the following, the present invention will be explained in detail through embodiments and experimental examples. Provided, that the following embodiments and experimental examples are meant only to exemplify the present invention, and the scope of the present invention is not limited to these.

[210] **<Conditions for Analysis and Purification>**

[211] The compounds synthesized in the embodiments of the present invention were purified or structurally analyzed according to the following HPLC conditions.

[212] **1. Analytical HPLC conditions**

[213] Analytical HPLC conditions (ACQUITY UPLC H-Class Core System)

[214] A UPLC system (ACQUITY UPLC PDA Detector) manufactured by Waters, equipped with a Waters-manufactured mass QDA Detector was used. The column used was the Waters ACQUITY UPLC® BEH C18 (1.7 ㎛, 2.1X50mm), and a column temperature of 30℃ was used.

[215] Water containing 0.1% formic acid was used as mobile phase A, and acetonitrile containing 0.1% formic acid was used as mobile phase B.

[216] Gradient condition (3 minutes with 10-100% B, speed = 0.6ml/min)

[217] Pre-LCMS (Preparative-Liquid chromatography mass spectrometry) for purification

[218] An autopurification HPLC system (2767 sample manager, 2545 binary gradient module, 2998 photodiode array detector) manufactured by Waters equipped with a Waster-manufactured mass QDA detector was used. The column used was the Waters SunFire® Prep C18 OBDTM (5 ㎛, 19X50mm), and the column was carried out at room temperature.

[219] Water containing 0.035% trifluoroacetic acid was used as mobile phase A, and methanol containing 0.035% trifluoroacetic acid was used as mobile phase B.

[220] Gradient condition (10 minutes with 15-100% B, speed = 25ml/min)

[221] Prep-150LC System for purification (Preparative-Liquid chromatography UV spectrometry)

[222] A Prep 150 LC system (2545 quaternary gradient module, 2998 photodiode array detector, Fraction collector^2) manufactured by Waters was used. The column used was the Waters XTERRA® Prep RP18 OBDTM (10 ㎛, 30X300mm), and the column was carried out at room temperature.

[223] Gradient condition (120 minutes with 3-100% B, speed = 40ml/min)

[224] **2. NMR Analysis**

[225] NMR analysis was carried out using the AVANCE III 400 or AVANCE III 400 HD manufactured by Bruker, and data was presented in ppm (parts per million(δ)).

[226] The commercially available reagent used was used without additional purification. In the present invention, room temperature refers to a temperature of about 5℃ to 40℃, 10℃ to 30℃ in one example, and 20℃ to 27℃ in another example, but is not limited to within these ranges. For concentration under pressure and removal of solvent through distillation, a rotary evaporator was used.

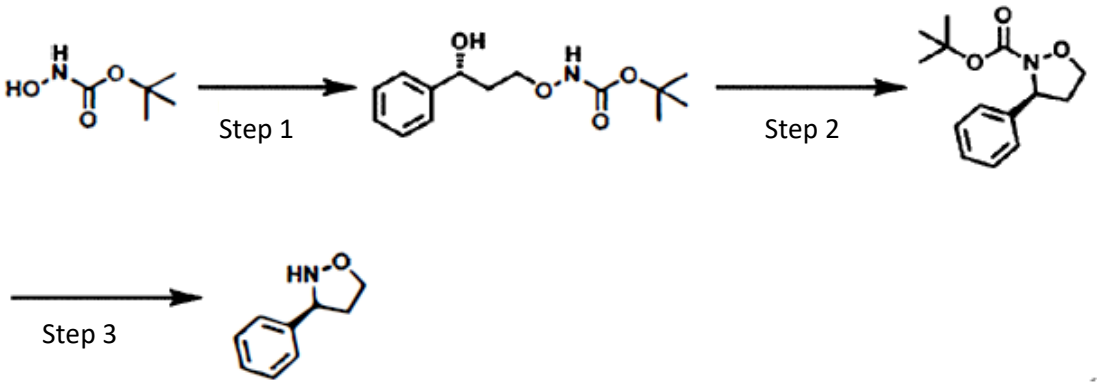
[227]

[228] **<Preparation Examples>**

[229] **1. Preparation of isoxazolidine derivatives**

[230] **<Preparation Example 1> Preparation of (S)-3-phenylisoxazolidine**

[231]



[232] Step 1: Preparation of tert-butyl(R)-(3-hydroxy-3-phenylpropoxy)carbamate

[233] tert-butyl hydroxycarbamate (7.8g, 58.6mmol) was dissolved in dimethylformamide (140ml), then sodium hydride (2.58g, 64.5mmol) was added at 0℃ and reacted for 30 minutes. Then (R)-3-chloro-1-phenylpropane-1-ol (5g, 29.3mmol) dissolved in dimethylformamide (10ml) was slowly added dropwise over 10 minutes at 0℃, and agitated for 72 hours at room temperature. Aqueous solution of ammonium chloride was added to the reaction mixture to end the reaction, then extraction was performed using ethyl acetate and salt water. The organic layers were added. The organic layer was dried using sodium sulfate and concentrated, then purified with medium pressure liquid chromatography (ethyl acetate/n-hexane) to obtain the target compound tert-butyl(R)-(3-hydroxy-3-phenylpropoxy)carbamate (2.8g, 68%).

[234] MS (m/z): 150.17 [M+1]+, UPLC r. t. (min): 1.51

[235] Step 2: Preparation of tert-butyl(S)-3-phenylisoxazolidine-2-carboxylate

[236] The tert-butyl(R)-(3-hydroxy-3-phenylpropoxy)carbamate (2.55g, 94.54mmol) obtained in Step 1 of Preparation Example 1 above and triethylamine (3.13ml, 22.44mmol) were dissolved in dichloromethane (250ml) and chilled to 0℃. Methanesulfonyl chloride (1ml, 13mmol) was added dropwise, then reacted for 2 hours at 0℃. The reaction mixture was extracted with salt water and dichloromethane, and the organic layers were added. The organic layer was dried using sodium sulfate, then vacuum concentrated to obtain the target compound tert-butyl-3-phenylisoxazolidine-2-carboxylate, which was used in the next reaction without purification.

[237] MS (m/z): 194.13 [M+1]+, UPLC r. t. (min): 1.69

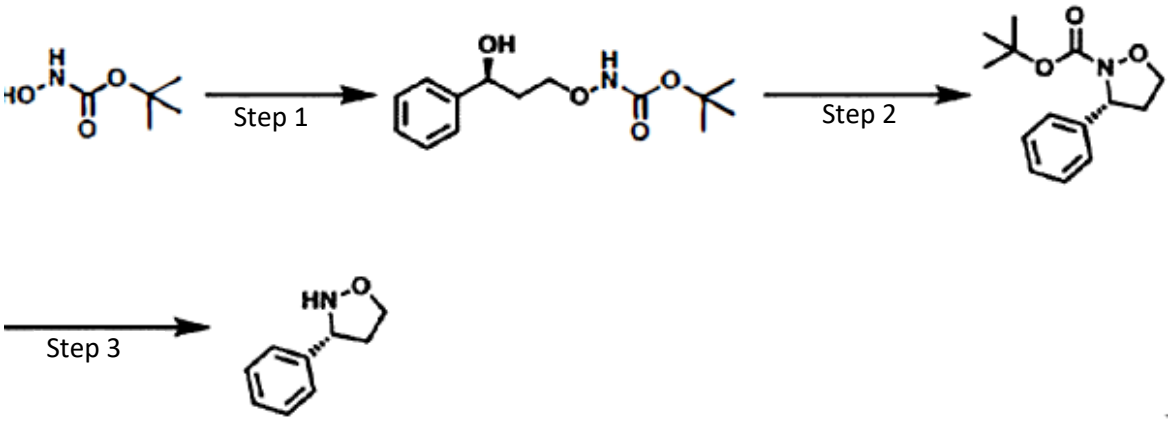
[238] Step 3: Preparation of (S)-3-phenylisoxazolidine

[239] The tert-butyl-3-phenylisoxazolidine-2-carboxylate (2.3g) obtained in Step 2 of Preparation Example 1 above was dissolved in dichloromethane (90ml), then trifluoroacetic acid (14ml) was added and reacted for 1 hour at room temperature. The reaction mixture was neutralized with an aqueous solution of sodium bicarbonate, and the organic layers were added. The organic layer was dried using sodium sulfate and vacuum concentrated and purified using medium pressure liquid chromatography (tetrahydrofuran/n-hexane) to obtain the target compound 3-phenylisoxazolidine (1.3g, 94%).

[240] MS (m/z): 150.08 [M+1]+, UPLC r. t. (min): 0.72

[241] **<Preparation Example 2> Preparation of (R)-3-phenylisoxazolidine**

[242]

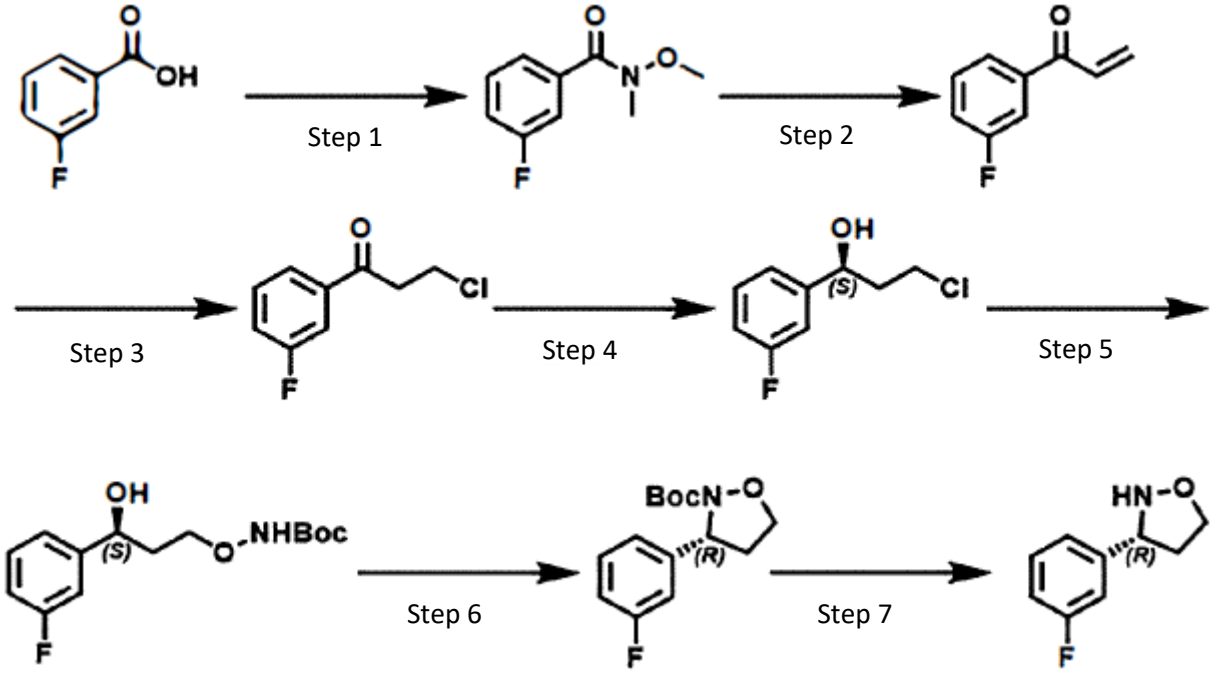


[243] Preparation Example 2 was prepared using method similar to that of Preparation Example 1, and was used in the synthesis of the Example Compounds listed in [Table 1].

[244] MS (m/z): 150.08 [M+1]+, UPLC r. t. (min): 0.72

[245] **<Preparation Example 3> Preparation of (R)-3-(3-fluorophenyl)isoxazolidine**

[246]



[247] Step 1: Preparation of 3-fluoro-N-methoxy-N-methylbenzamide

[248] 3-fluorobenzoic acid (90g, 642.35mmol, 1eq) was dissolved in pyrimidine (150mL, then N-methoxy methanamine (75.19g, 770.81mmol, 1.2eq, HCl) was added. Thereafter, 1-ethyl-3-(-3-dimethylaminopropyl)carbodiimide (EDCI; 147.77g, 770.81mmol. 1.2eq) was added at 15℃. The reaction mixture was agitated for 30 minutes at 50℃. TLC analysis (PE:EA = 3:1) results showed that all of the starting material had disappeared, and new spots with low polarity were detected. Vacuum concentration was performed to remove the pyridine solvent, and dichloromethane (DCM; 500mL), hydrochloric acid (500mL, 2N) and salt water (200mL) were used to extract the organic layer. The organic layer was dried using sodium sulfate and vacuum concentrated to obtain the target compound 3-fluoro-N-methoxy-N-methylbenzamide (110g, 600.50mmol, 93.49% yield) in the form of a yellow oil.

[249] 1H NMR (400 MHz, CHLOROFORM-d) δ ppm 7.47 - 7.40 (m, 1H), 7.39 - 7.38 (m, 2H), 7.14-7.13 (m, 1H), 3.54 (s, 3H), 3.45 (s, 3H)

[250] Step 2: Preparation of 1-(3-fluorophenyl)prop-2-en-1-one

[251] The 3-fluoro-N-methoxy-N-methylbenzamide (110g, 600.50mmol, 1eq) obtained in Step 1 of Preparation Example 3 was dissolved in tetrahydrofuran (THF; 1L), and then at 0℃, bromo(vinyl)magnesium (1M, 630.53mL, 1.05eq) was added dropwise at 78℃. Then, the reaction mixture was agitated for 30 minutes at 0℃. TLC analysis (PE:EA = 4:1) results showed that all of the starting material had disappeared, and new spots having low polarity were detected. Hydrochloric acid (4N, 500mL) was added to end the reaction, and the organic layer was extracted using methyl tert-butyl ether (MTBE; 2000mL) and salt water (500mL). The organic layer was dried using sodium sulfate, then vacuum concentrated. The concentrated compound was purified using chromatography (petroleum ether/ethyl acetate = 30/1) to obtain the target compound 1-3-fluorophenyl)prop-2-en-1-one (80g, 532.80mmol, 88.73% yield) in the form of a yellow oil.

[252] 1H NMR (400 MHz, CHLOROFORM-d) δ ppm 7.65 (m, 1H), 7.58 - 7.52 (m, 1H), 7.39 (m, 1H), 7.24 - 7.17 (m, 1H), 7.04 (dd, J = 17.2, 10.4 Hz, 1H), 6.39 (dd, J = 17.2, 1.6 Hz, 1H), 5.90 (dd, J = 10.4, 1.6 Hz, 1H)

[253] Step 3: Preparation of 3-chloro-1-(3-fluorophenyl)propan-1-one

[254] The 1-3-fluorophenyl)prop-2-en-1-one (71g, 472.86mmol, 1.0eq) obtained in Step 2 of Preparation Example 3 was dissolved in dichloromethane (DCM; 71mL), then HCl/dioxane (4M, 295.54mL, 2.5eq) was added at 0℃. Then, the reaction mixture was agitated for 1.5 hours at 15℃. TLC analysis (PE:EA = 10:1) results showed that all the starting material disappeared, and the target compound was detected. The reaction mixture was concentrated under vacuum, then dichloromethane (DCM; 450mL) and water (200mL * 5) was added to extract the organic layer, which was dried using sodium sulfate and vacuum concentrated to obtain the target compound 3-chloro-1-(3-fluorophenyl)propan-1-one (73g, 391.19mmol. 82.73% yield) in the form of a yellow solid.

[255] 1H NMR (400 MHz, CHLOROFORM-d) δ = 7.78 - 7.72 (m, 1H), 7.69 - 7.60 (m, 1H), 7.53 - 7.44 (m, 1H), 7.37 - 7.24 (m, 1H), 3.93 (t, J =6.8 Hz, 2H), 3.46 (t, J =6.8 Hz, 2H)

[256] Step 4: Preparation of (S)-3-chloro-1-(3-fluorophenyl)propan-1-ol

[257] (3aR)-1-methyl-3,3-diphenyl-3a,4,5,6-tetrahydropyrrolo[1,2-c][1,3,2]oxazaborol (1M, 32.15mL, 0.1eq) was dissolved in tetrahydrofuran (THF; 1.2L), then borane tetrahydrofuran (BH_3THF; 1M, 186.48mL, 0.6eq) was added dropwise at 0℃ in a nitrogen atmosphere. The reaction mixture was agitated for 30 minutes at 0℃. Thereafter, the 3-chloro-1-(3-fluorophenyl)propan-1-one obtained in Step 3 of Preparation Example 3 (60g, 309.02mmol, 1eq) diluted in tetrahydrofuran was added dropwise at 0℃ to the reaction mixture. TLC analysis (PE:EA = 5:1) results showed that all of the starting material had disappeared, with spots of the target compound detected. The reaction was ended by adding methanol (100mL) at 0℃, and the solvent was allowed to volatilize in vacuum. The organic layer was extracted from the concentrated compound using dichloromethane (DCM; 100mL*3) and ammonium chloride (NH_4Cl) solution (300mL). The organic layer was dried using sodium sulfate and vacuum concentrated. The concentrated compound was purified using silica gel chromatography (PE:EA = 50:1 to 5:1) to obtain (3)-3-chloro-1-(3-fluorophenyl)propan-1-ol (140g, 664.2mmol, 71.65% yield, 89.49% purity, 65.5% e.e) as a colorless oil.

[258] 1H NMR (400 MHz, CHLOROFORM-d) δ ppm 7.33 (m, 1H), 7.16 - 7.07 (m, 2H), 7.02 - 6.96 (m, 1H), 4.96 (m, 1H), 3.75 (m, 1H), 3.57 (m, 1H), 2.26 - 2.15(m, 2H)

[259] Step 5: Preparation of tert-butyl(S)-(3-(3-fluorophenyl)-3-hydroxypropoxy)carbamate

[260] Tert-butyl hydroxycarbamate (50.4g, 378.52mmol, 1.05eq) was dissolved in dimethylformamide (DMF; 500mL), and sodium hydride (NaH; 15.86g, 396.55mmol, 60% purity, 1.1eq) was added at 0℃ in a nitrogen atmosphere. The reaction mixture was agitated for 1 hour at 10℃, and the (1R)-3-chloro-1-(3-fluorophenyl)propan-1-ol obtained in Step 4 of Preparation Example 3 diluted in dimethyl formamide (DMF; 180mL) was added dropwise at 0℃, then agitated for 16 hours at 10℃. TLC analysis (PE:EA = 2:1) results showed that all of the starting material had disappeared, and the target compound was detected. An aqueous solution of ammonium chloride (3L) was added to end the reaction, and the organic layer was extracted using ethyl acetate (2000mL) and salt water (2000mL). The organic layer was dried using sodium chlorate, then concentrated under vacuum to obtain tert-butyl(S)-(3-(3-fluorophenyl)-3-hydroxypropoxy)carbamate (176g, 616.87mmol, 85.56% yield) in the form of a bright yellow solid.

[261] 1H NMR (400 MHz, CHLOROFORM-d) δ ppm 7.67 - 7.64 (m, 1H), 7.23- 7. 17 (m, 1H), 7.08 - 7.03 (m, 2H), 6.88 - 6. 81 (m, 1H), 4.99 - 4.84 (m, 1H), 4.02 - 3.97 (m, 1H), 3.96 - 3.89 (m, 1H), 1.95 - 1 .89 (m, 1H), 1 .88 - 1 .78 (m, 1H), 1.42 - 1 .39 (m, 9H)

[262] Step 6: Preparation of tert-butyl(R)-3-(3-fluorophenyl)isoxazolidine-2-carboxylate

[263] The tert-butyl(S)-(3-(3-fluorophenyl)-3-hydroxypropoxy)carbamate obtained in Step 5 of Preparation Example 3 (88g, 308.44mmol, 1eq) and Et_3N (93.63g, 925.31mmol, 128.79mL, 3eq) were dissolved in dichloromethane (DCM; 1L), then anhydrous methanesulfonic acid (80.59g, 462.65mmol, 1.5eq) was slowly added at 0℃. The reaction mixture was agitated for 12 hours at 20℃. TLC analysis (PE:EA

= 3:1) results showed that all of the starting material had disappeared, and new spots were detected. Water (2000mL) was added to end the reaction, and the organic layer was extracted using dichloromethane (DCM; 200mL*3). The organic layer was dried using sodium sulfate, then vacuum concentrated. The concentrated compound was purified using chromatography (PE:EA = 50:1 to 5:1) to extract 88g of the target compound having a 82.5% e.e value. The target compound was purified using SFC (column: DAICEL CHIRALPAK AD (250mm*50mm, 10um); mobile phase: [Neu-MeOH]; B%: 15%-15%, 3.4min; 380min) to obtain the white solid tert-butyl(R)-3-(3-fluorophenyl)isoxazolidine-2-carboxylate (51g, 189.66mmol, 30.74% yield, 99.4% purity).

[264] The enantiomeric purity of the tert-butyl(R)-3-(3-fluorophenyl)isoxazolidine-2-carboxylate obtained in Step 6 was analyzed using the following SFC conditions.

[265] Instrument: CAS-WH-ANA-SFC-C (SHIMADZU LC-30ADsf)

[266] Column: Amycoat 50X4.6mm I.D., 3um

[267] Mobile phase: Phase A for CO2, and Phase B for MeOH (0.05% DEA);

[268] Gradient elution: MeOH (0.05% DEA) in CO_2 from 5% to 40%

[269] Flow rate: 3 mL/min; Detector: PDA;

[270] Column Temp: 35℃, Back Pressure: 100 Bar

[271] In a case where the enantiomeric purity of the tert-butyl(R)-3-(3-fluorophenyl)isoxazolidine-2-carboxylate obtained in Step 6 was low, purification was carried out using the following SFC conditions to obtain the desired enantiomer in the form of a yellow liquid.

[272] (column: DAICEL CHIRALPAK AD-H (250mm * 30mm, 5um) ;

[273] Mobile phase: [0. 1 % NH3H2O MEOH]; B%: 15 % - 15%, 3.8min; 600minmin)

[274] <u>Step 7: Preparation of (R)-3-(3-fluorophenyl)isoxazolidine</u>

[275] Tert-butyl (3R)-3-(3-fluorophenyl)isoxazolidine-2-carboxylate (50g, 185.94mmol, 1eq) was dissolved in ethyl acetate (EA; 200mL), then HCl/EtOAc (4M, 300mL, 6.45eq) was added at 0℃. Then, the reaction mixture was agitated for 1 hour at 10℃. LCMS analysis results showed that all of the starting material had disappeared, and vacuum concentration was performed to obtain a solid. (R)-3-(3-fluorophenyl)isoxazolidine was obtained in the form of a white solid (32g, 150.26mmol, 80.81% yield, 95.62% purity, 100% e.e HCl).

[276] MS: m/z 168.2 [M+H]+

[277] 1H NMR (400 MHz, DMSO-d6) δ ppm 7.53 - 7.43 (m, 2H), 7.39 (d, J = 7.8 Hz, 1H), 7.30 - 7.23 (m, 1H), 5.01 (t, J = 8.0 Hz, 1H), 4.47 (m, 1H), 4.27 (m, 1H), 2.87 (m, 1H), 2.62 - 2.52 (m, 1H)

[278] In Step 7, the following conditions were used for enantiomeric purification or analysis of the compound.

[279] Instrument: CAS-WH-ANA-SFC-C (SHIMADZU LC-30ADsf)

[280] Column: Chiralpak AY-3 50X4.6mm I.D., 3um;

[281] Mobile phase: Phase A for CO_2, and Phase B for IPA (0.05% DEA) ;

[282] Gradient elution: B in A from 5% to 40%;

[283] Flow rate: 3mL/min; Detector: PDA;

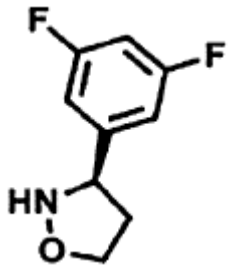
[284] Column Temp: 35℃; Back Pressure: 100 Bar

[285] The compound of Preparation Examples 4 through 52 were prepared using methods similar to those of Preparation Examples 1 through 3 above, and

the Example Compounds of the present invention were prepared using the compounds of Preparation Examples 1 through 52.

[286] **<Preparation Example 4> Preparation of (R)-3-(3,5-difluorophenyl)isoxazolidine**

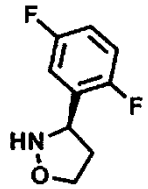
[287]



[288] 1H NMR (400 MHz, DMSO-d6) δ = 7.36 – 7.27 (m, 3H), 5.04 – 4.98 (t, J = 7.6 Hz, 1H), 4.46 – 4.36 (m, 1H), 4.25 – 4.19 (dd, J = 7.6, 15.2 Hz, 1H, 2.90 – 2.78 (m, 1H), 2.56 – 2.51 (m, 1H)

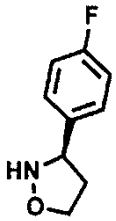
[289] **<Preparation Example 5> Preparation of (R)-3-(2,5-difluorophenyl)isoxazolidine**

[290]



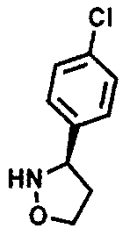
[291] **<Preparation Example 6> Preparation of (R)-3-(4-fluorophenyl)isoxazolidine**

[292]



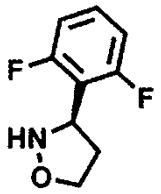
[293] **<Preparation Example 7> Preparation of (R)-3-(4-chlorophenyl)isoxazolidine**

[294]



[295] **<Preparation Example 8> Preparation of (R)-3-(2,6-difluorophenyl)isoxazolidine**

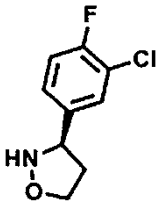
[296]



[297] 1H NMR (400 MHz, METHANOL-d4) δ 7.61 (tt, 1H, J = 6.4, 8.4 Hz), 7.1-7.2 (m, 2H), 5.49 (t, 1H, J = 8.4 Hz), 4.68 (dt, 1H, J = 4.0, 8.0 Hz), 4.4-4.5 (m, 1H), 3.0-3.1 (m, 1H), 2.87 (qd, 1H, J = 8.4, 12.4 Hz)

[298] **<Preparation Example 9> Preparation of (R)-3-(3-chloro-4-fluorophenyl)isoxazolidine**

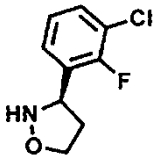
[299]



[300] 1H NMR (400 MHz, DMSO-d6) δ = 7.82-7.89(dd, J =2,7.2, 1H), 7.56-7.51(s, J =15.6, 2H), 5.0-4.96(m, 1H), 4.46-4.4(m, 1H), 4.24-4.20(m, 1H), 2.85-2.82(m, 1H), 2.54-2.52(m, 1H).

[301] **<Preparation Example 10> Preparation of (R)-3-(3-chloro-2-fluorophenyl)isoxazolidine**

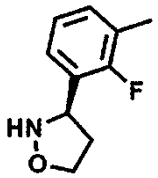
[302]



[303] 1H NMR (400 MHz, DMSO-d6) δ = 7.49 - 7.42 (m, 2H), 7.20 - 7.16 (m, 1H), 6.56 (s, 1H), 4.66 - 4.65 (m, 1H), 3.96 - 3.91 (m, 1H), 3.67 - 3.65 (m, 1H), 2.66 - 2.61 (m, 1H), 2.08 - 2.01 (m, 1H).

[304] **<Preparation Example 11> Preparation of (R)-3-(2-fluoro-3-methylphenyl)isoxazolidine**

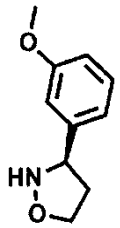
[305]



[306] 1H NMR (400 MHz, CHLOROFORM-d) δ 12.6 (s, 1H), 7.46 (t, 1H, J = 7.2 Hz), 7.3-7.1 (m, 1H), 7.1-7.0 (m, 1H), 5.25 (t, 1H, J = 8.0 Hz), 4.6-4.4 (m, 1H), 4.38 (q, 1H, J = 7.6 Hz), 3.0-2.8 (m, 1H), 2.7-2.5 (m, 1H), 2.26 (s, 3H).

[307] **<Preparation Example 12> Preparation of (R)-3-(3-methoxyphenyl)isoxazolidine**

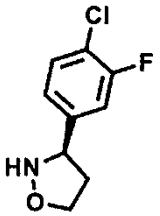
[308]



[309] 1H NMR (400 MHz, $CDCl_3$) δ 7.25 - 7.20 (m, 2 H), 7.11 - 7.09 (m, 1 H), 6.88 - 6.86 (m, 1 H), 4.80 - 4.76 (m, 1 H), 4.46 - 4.44 (m, 1 H), 4.17 - 4.15 (m, 1 H), 3.76 (s, 3 H), 2.69 - 2.66 (m, 2 H)

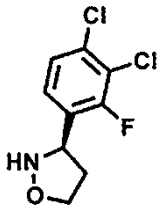
[310] **<Preparation Example 13> Preparation of (R)-3-(4-chloro-3-fluorophenyl)isoxazolidine**

[311]



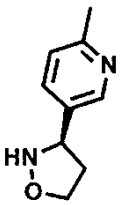
[312] **<Preparation Example 14> Preparation of (R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine**

[313]



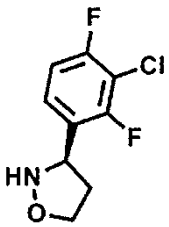
[314] **<Preparation Example 15> Preparation of (R)-3-(6-methylpyridine-3-yl)isoxazolidine**

[315]



[316] **<Preparation Example 16> Preparation of (R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine**

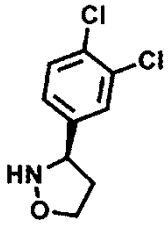
[317]



[318] 1H NMR (DMSO-d6, 400 MHz) δ = 7.51 (dt, J = 6.8, 8.4 Hz, 1H), 7.28 (dt, J = 2.0, 8.8 Hz, 1H), 6.60 (br s, 1H), 4.64 (br s, 1H), 3.94 (dt, J = 5.2, 8.0 Hz, 1H), 3.76 - 3.57 (m, 1H), 2.68 - 2.61 (m, 1H), 2.10 - 2.01 (m, 1H);

[319] **<Preparation Example 17> Preparation of (R)-3-(3,4-dichlorophenyl)isoxazolidine**

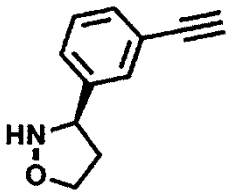
[320]



[321] 1H NMR (400 MHz, DMSO-d6) δ = 7.83 (d, J = 2.0 Hz, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.53 (dd, J = 2.0, 8.4 Hz, 1H), 4.99-4.95 (m, 1H), 4.43-4.38 (m, 1H), 4.21-4.17 (m, 1H), 2.85-2.82 (m, 1H), 2.52-2.48 (m, 1H);

[322] **<Preparation Example 18> Preparation of (R)-3-(3-ethynylphenyl)isoxazolidine**

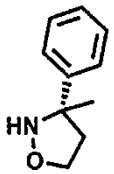
[323]



[324] 1H NMR (400 MHz, DMSO-d6) δ = 7.49 (s, 1H), 7.43 - 7.37 (m, 1H), 7.36 - 7.29 (m, 2H), 6.41 (s, 1H), 4.38 (s, 1H), 4.15 (s, 1H), 3.90 (m, 1H), 3.71 (s, 1H), 2.65 - 2.53 (m, 1H), 2.11 - 2.00 (m, 1H)

[325] **<Preparation Example 19> Preparation of (S)-3-methyl-3-phenylisoxazolidine**

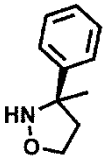
[326]



[327] 1H NMR (400 MHz, DMSO-d6) δ 12.86 (br s, 1H), 7.55-7.45 (m, 2H), 7.44-7.37 (m, 2H), 7.35-7.28 (m, 1H), 3.79-3.63 (m, 1H), 3.44-3.32 (m, 1H), 2.75-2.56 (m, 2H), 1.64 (s, 3H)

[328] **<Preparation Example 20> Preparation of (R)-3-methyl-3-phenylisoxazolidine**

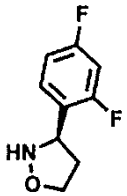
[329]



[330] 1H NMR (400 MHz, DMSO-d6) δ 12.88 (br s, 1H), 7.56-7.46 (m, 2H), 7.44-7.36 (m, 2H), 7.34-7.26 (m, 1H), 3.74-3.62 (m, 1H), 3.46-3.28 (m, 1H), 2.72-2.54 (m, 2H), 1.64 (s, 3H)

[331] **<Preparation Example 21> Preparation of (R)-3-(2,4-difluorophenyl)isoxazolidine**

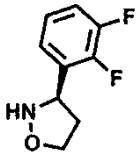
[332]



[333] 1H NMR (400 MHz, CHLOROFORM-d) δ7.52~7.47(m, 1H), 6.87-6.75 (m, 2H), 5.30 (s, 1H), 4.71-4.68 (m, 1H), 4.09-4.04 (m, 1H), 3.91-3.85 (m, 1H), 2.73-2.64 (3, 1H), 2.24-2.20 (m, 1H)

[334] **<Preparation Example 22> Preparation of (R)-3-(2,3-difluorophenyl)isoxazolidine**

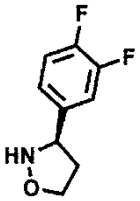
[335]



[336] 1H NMR (CHLOROFORM-d, 400 MHz) δ 7.27-7.29 (m, 1H), 7.02-7.06 (m, 2H), 5.44 (br s, 1H), 4.75 (dd, J1 = 4.4 Hz, J2 = 8.4 Hz, 1H), 4.08 (dt, J1 = 5.2 Hz, J2 = 8.0 Hz, 1H), 3.86 (q, J =8.0 Hz, 1H), 2.66-2.76 (m, 1H), 2.19-2.27 (m, 1H).

[337] **<Preparation Example 23> Preparation of (R)-3-(3,4-difluorophenyl)isoxazolidine**

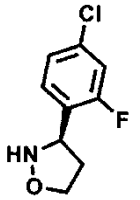
[338]



[339] 1H NMR (400 MHz, CHLOROFORM-d) δ = 7.24-7.19 (m, 1H), 7.12-7.06 (m, 2H), 5.24 (s, 1H), 4.46 (dd, J1 = 8.4 Hz, J2 = 5.6 Hz, 1H), 4.05 (dt, J1 = 8.0 Hz, J2 = 5.2 Hz, 1H), 3.91-3.85 (m, 1H), 2.70-2.61 (m, 1H), 2.25-2.17 (m, 1H).

[340] **<Preparation Example 24> Preparation of (R)-3-(4-chloro-2-fluorophenyl)isoxazolidine**

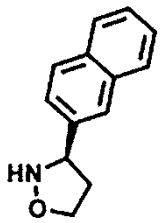
[341]



[342] 1H NMR (400 MHz, DEUTERIUM OXIDE) δ 7.48 - 7.38 (m, 1H), 7.34 - 7.22 (m, 2H), 5.29 - 5.20 (m, 1H), 4.58 - 4.50 (m, 1H), 4.36 - 4.27 (m, 1H), 2.96 - 2.84 (m, 1H), 2.79 - 2.66 (m, 1H).

[343] **<Preparation Example 25> Preparation of (R)-3-(naphthalene-2-yl)isoxazolidine**

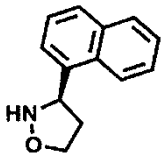
[344]



[345] 1H NMR (400 MHz, CHLOROFORM-d) δ 7.91 - 7.81 (m, 4H), 7.56 - 7.46 (m, 3H), 5.80 - 5.00 (m, 1H), 4.68 (t, J = 7.2 Hz, 1H), 4.19 - 3.99 (m, 2H), 2.8-2.72 (m, 1H), 2.45-2.37 (m, 1H).

[346] **<Preparation Example 26> Preparation of (R)-3-(naphthelene-1-yl)isoxazolidine**

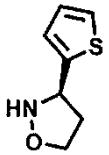
[347]



[348] 1H NMR (400 MHz, CHLOROFORM-d) δ 8.13 (br s, 1H), 7.9-7.9 (m, 1H), 7.7-7.8 (m, 2H), 7.5-7.6 (m, 3H), 5.3-5.9 (m, 1H), 5.22 (br t, 1H, J = 6.4 Hz), 3.9-4.2 (m, 2H), 2.8-2.9 (m, 1H), 2.3-2.5 (m, 1H).

[349] **<Preparation Example 27> Preparation of (R)-3-(thiophene-2-yl)isoxazolidine**

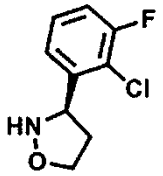
[350]



[351] 1H NMR (400 MHz, CHLOROFORM-d) δ 7.23 (d, J = 5.0 Hz, 1H), 7.04 - 6.99 (m, 1H), 6.99 - 6.94 (m, 1H), 4.97 - 4.58 (m, 2H), 4.11 - 3.96 (m, 2H), 2.75 - 2.58 (m, 1H), 2.44 - 2.33 (m, 1H).

[352] **<Preparation Example 28> Preparation of (R)-3-(2-chloro-3-fluorophenyl)isoxazolidine**

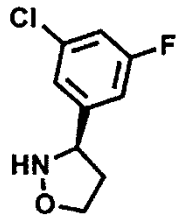
[353]



[354] 1H NMR (400 MHz, CHLOROFORM-d) δ 7.45 (d, J = 7.6 Hz, 1H), 7.22 (m, 1H), 7.02 (m, 1H), 5.44 (m, 1H), 4.87 (dd, J = 4.0, 8.7 Hz, 1H), 4.10 (m, 1H), 3.79 (m, 1H), 2.86 - 2.75 (m, 1H), 2.21 - 2.10 (m, 1H).

[355] **<Preparation Example 29> Preparation of (R)-3-(3-chloro-5-fluorophenyl)isoxazolidine**

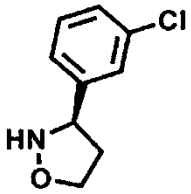
[356]



[357] 1H NMR (400 MHz, CHLOROFORM-d) δ 7.19 (s, 1H), 7.08 - 6.93 (m, 2H), 5.79 - 5.03 (m, 1H), 4.56 - 4.42 (m, 1H), 4.17 - 4.02 (m, 1H), 3.87 (s, 1H), 2.78 - 2.63 (m, 1H), 2.32 - 2.18 (m, 1H).

[358] **<Preparation Example 30> Preparation of (R)-3-(3-chlorophenyl)isoxazolidine**

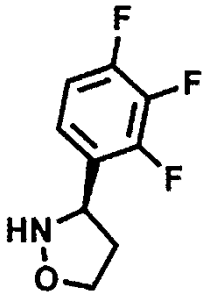
[359]



[360] 1H NMR (400 MHz, DMSO-d6) δ = 7.71 - 7.63 (m, 1H), 7.57 - 7.41 (m, 3H), 5.01 (t, J = 8.0 Hz, 1H), 4.47 (m, 1H), 4.26 (m, 1H), 2.94 - 2.81 (m, 1H), 2.63 - 2.52 (m, 1H)

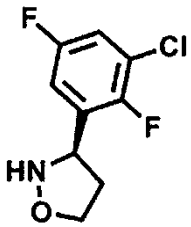
[361] **<Preparation Example 31> Preparation of (R)-3-(2,3,4-trifluorophenyl)isoxazolidine**

[362]



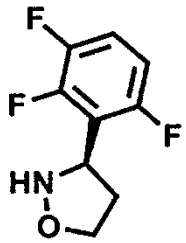
[363] **<Preparation Example 32> Preparation of (R)-3-(3-chloro-2,5-difluorophenyl)isoxazolidine**

[364]



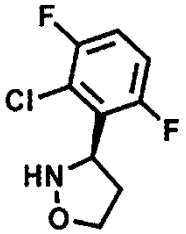
[365] **<Preparation Example 33> Preparation of (R)-3-(2,3,6-trifluorophenyl)isoxazolidine**

[366]



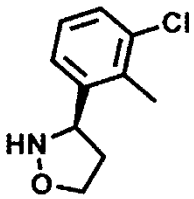
[367] **<Preparation Example 34> Preparation of (R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine**

[368]



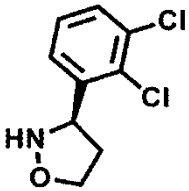
[369] **<Preparation Example 35> Preparation of (R)-3-(3-chloro-2-methylphenyl)isoxazolidine**

[370]



[371] **<Preparation Example 36> Preparation of (R)-3-(2,3-dichlorophenyl)isoxazolidine**

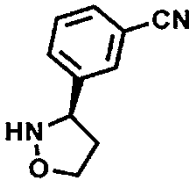
[372]



[373] 1H NMR (DMSO-d6, 400 MHz) HNMR_7, δ = 7.61 - 7.44 (m, 2H), 7.37 - 7.30 (m, 1H), 6.67 (d, J = 6.0 Hz, 1H), 4.79 - 4.63 (m, 1H), 3.94 (td, J = 4.0, 8.0 Hz, 1H), 3.63 (d, J = 8.0 Hz, 1H), 2.78 - 2.74 (m, 1H), 1.99 - 1.91 (m, 1H).

[374] **<Preparation Example 37> Preparation of (R)-3-(isoxazolidine-3-yl)benzonitrile**

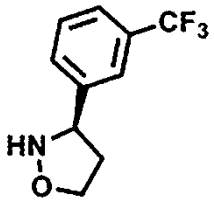
[375]



[376] 1H NMR (400 MHz, DMSO-d6) δ = 8.04 (s, 1H), 7.90-7.87 (m, 2H), 7.69 - 7.62 (m, 1H), 5.05 (t, J = 7.8 Hz, 1H), 4.48-4.43 (m, 1H), 4.27-4.21 (m, 1H), 2.92 - 2.82 (m, 1H), 2.62 - 2.53 (m, 1H).

[377] **<Preparation Example 38> Preparation of (R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine**

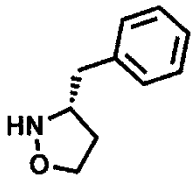
[378]



[379] 1H NMR (400 MHz, Chloroform-d) δ 7.65 (s, 1H), 7.59 (d, J = 7.7 Hz, 1H), 7.53 (d, J = 7.8 Hz, 1H), 7.46 (t, J = 7.7 Hz, 1H), 5.64 - 5.19 (m, 1H), 4.58 (t, J = 7.2 Hz, 1H), 4.11 (td, J = 8.2, 5.2 Hz, 1H), 3.94 (s, 1H), 2.80 - 2.67 (m, 1H), 2.36 - 2.23 (m, 1H).

[380] **<Preparation Example 39> Preparation of (R)-3-benzylisoxazolidine**

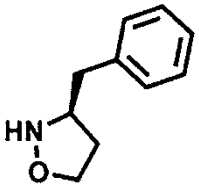
[381]



[382] 1H NMR (400 MHz, CHLOROFORM-d) δ 12.85 - 12.47 (m, 1H), 7.37 - 7.27 (m, 5H), 4.51 - 4.41 (m, 1H), 4.36 - 4.18 (m, 2H), 3.60 (dd, J = 4.8, 13.6 Hz, 1H), 3.12 (dd, J = 10.4, 13.6 Hz, 1H), 2.53 - 2.42 (m, 1H), 2.41 - 2.30 (m, 1H).

[383] **<Preparation Example 40> Preparation of (S)-3-benzylisoxazolidine**

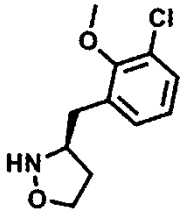
[384]



[385] 1H NMR (400 MHz, CHLOROFORM-d) δ 12.74 - 12.40 (m, 1H), 7.28 - 7.18 (m, 5H), 4.42 - 4.32 (m, 1H), 4.25 - 4.10 (m, 2H), 3.50 (dd, J = 4.8, 13.6 Hz, 1H), 3.03 (dd, J = 10.4, 13.2 Hz, 1H), 2.44 - 2.33 (m, 1H), 2.32 - 2.20 (m, 1H).

[386] **<Preparation Example 41> Preparation of (S)-3-(3-chloro-2-methoxybenzyl)isoxazolidine**

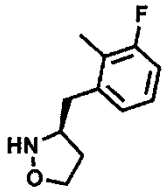
[387]



[388] 1H NMR (400 MHz, CHLOROFORM-d) δ 12.97 - 12.35 (m, 2H), 7.34 (dd, J = 1.6, 8.0 Hz, 1H), 7.24 (dd, J = 1.2, 7.6 Hz, 1H), 7.10 - 7.00 (m, 1H), 4.44 (dt, J = 5.6, 7.6 Hz, 1H), 4.39 - 4.27 (m, 2H), 3.95 (s, 3H), 3.54 (dd, J = 5.2, 13.6 Hz, 1H), 3.22 (dd, J = 10.0, 13.6 Hz, 1H), 2.53 - 2.42 (m, 1H), 2.42 - 2.29 (m, 1H).

[389] **<Preparation Example 42> Preparation of (S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine**

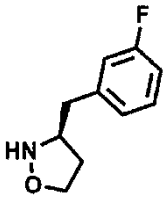
[390]



[391] 1H NMR (400 MHz, CHLOROFORM-d) δ = 7.14 - 7.07 (m, 1H), 6.98 (d, J = 7.6 Hz, 1H), 6.91 (t, J = 8.8 Hz, 1H), 4.08 - 3.98 (m, 1H), 3.82 (q, J = 7.6 Hz, 1H), 3.68 - 3.59 (m, 1H), 2.96 (dd, J = 7.2, 14.0 Hz, 1H), 2.70 (dd, J = 7.2, 14.0 Hz, 1H), 2.25 (d, J = 2.4 Hz, 3H), 1.98 - 1.88 (m, 1H).

[392] **<Preparation Example 43> Preparation of (S)-3-(3-fluorobenzyl)isoxazolidine**

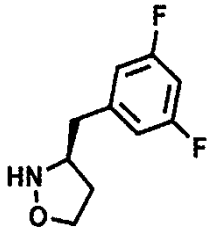
[393]



[394] 1H NMR (400 MHz, CHLOROFORM-d) δ 7.26 (dt, J1 = 6.0 Hz, J2 = 7.6 Hz, 1H), 7.01 (d, J = 7.6 Hz, 1H), 6.96 - 6.89 (m, 2H), 4.87 (s, 1H), 3.99 (dt, J1 = 5.6 Hz, J2 = 8.4 Hz, 1H), 3.80 (q, J = 8.0 Hz, 1H), 3.68 - 3.59 (m, 1H), 2.93 (dd, J1 = 7.2 Hz, J2 = 14.0 Hz, 1H), 2.67 (dd, J1 = 7.2 Hz, J2 = 14.0 Hz, 1H), 2.31 - 2.22 (m, 1H), 1.94 - 1.85 (m, 1H).

[395] **<Preparation Example 44> Preparation of (S)-3-(3,5-difluorobenzyl)isoxazolidine**

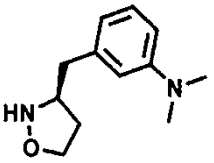
[396]



[397] 1H NMR (400 MHz, CHLOROFORM-d) δ 6.77 (dd,J1 = 2.4 Hz, J2 = 8.4 Hz, 2H), 6.66 (tt, J1 = 2.4 Hz, J2 = 9.2 Hz, 1H), 4.89 (br s, 1H), 4.02 (dt, J1 = 5.2 Hz, J2 = 8.4 Hz, 1H), 3.77 (q, J = 8.0 Hz, 1H), 3.66 - 3.59 (m, 1H), 2.89 (dd, J1 = 7.6 Hz, J2 = 14.0 Hz, 1H), 2.65 (dd, J1 = 6.8 Hz, J2 = 14.0 Hz, 1H), 2.34 - 2.26 (m, 1H), 1.93 - 1.85 (m, 1H).

[398] **<Preparation Example 45> Preparation of (S)-3-(isoxazolidine-3-ylmethyl)-N,N-dimethylaniline**

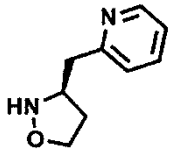
[399]



[400] 1H NMR (400 MHz, CHLOROFORM-d) δ 6.77 (dd,J1 = 2.4 Hz, J2 = 8.4 Hz, 2H), 6.66 (tt, J1 = 2.4 Hz, J2 = 9.2 Hz, 1H), 4.89 (br s, 1H), 4.02 (dt, J1 = 5.2 Hz, J2 = 8.4 Hz, 1H), 3.77 (q, J = 8.0 Hz, 1H), 3.66 - 3.59 (m, 1H), 2.89 (dd, J1 = 7.6 Hz, J2 = 14.0 Hz, 1H), 2.65 (dd, J1 = 6.8 Hz, J2 = 14.0 Hz, 1H), 2.34 - 2.26 (m, 1H), 1.93 - 1.85 (m, 1H).

[401] **<Preparation Example 46> Preparation of (S)-3-(pyridine-2-ylmethyl)isoxazolidine**

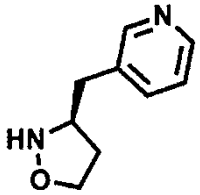
[402]



[403] 1H NMR (DMSO-d6, 400 MHz) δ = 8.54 - 8.41 (m, 1H), 7.70 (dt, J = 2.0, 7.6 Hz, 1H), 7.32 - 7.18 (m, 2H), 5.98 (br s, 1H), 3.86 - 3.54 (m, 3H), 2.91 - 2.70 (m, 2H), 2.18 - 2.10 (m, 1H), 1.85 - 1.74 (m, 1H).

[404] **<Preparation Example 47> Preparation of (S)-3-(pyridine-3-ylmethyl)isoxazolidine**

[405]

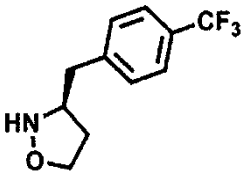


[406]

1H NMR ($CDCl_3$, 400 MHz) δ 8.55 - 8.45 (m, 2H), 7.61 (m, 1H), 7.27 - 7.22 (m, 1H), 4.04 (s, 1H), 3.87 - 3.73 (m, 1H), 3.70 - 3.55 (m, 1H), 2.92 (m, 1H), 2.69 (m, 1H), 2.37 - 2.24 (m, 1H), 1.99 - 1.82 (m, 1H)

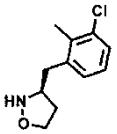
[407] **<Preparation Example 48> Preparation of (S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine**

[408]



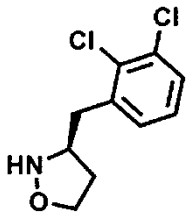
[409] **<Preparation Example 49> Preparation of (S)-3-(3-chloro-2-methylbenzyl)isoxazolidine**

[410]



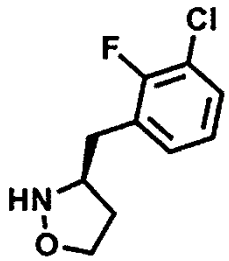
[411] **<Preparation Example 50> Preparation of (S)-3-(2,3-dichlorobenzyl)isoxazolidine**

[412]



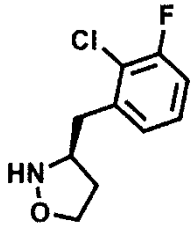
[413] **<Preparation Example 51> Preparation of (S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine**

[414]



[415] **<Preparation Example 52> Preparation of (S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine**

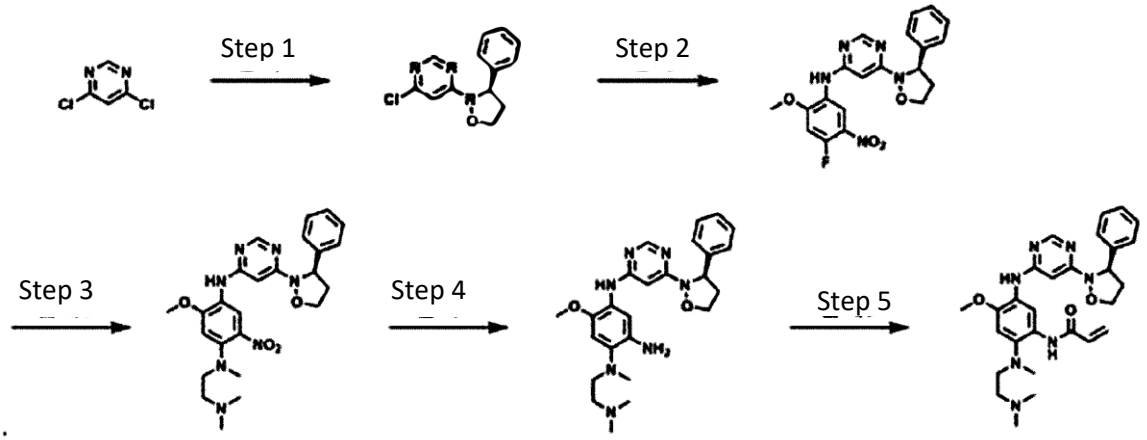
[416]



[417] **2. Preparation of the Example Compounds of the present invention**

[418] **<Preparation Example 1> Preparation of Example Compound 4**

[419]



[420] Step 1: Preparation of (R)-2-(6-chloropyrimidine-4-yl)-3-phenylisoxazolidine

[421] 4,6-dichloropyrimidine (500mg, 3.36mmol) and (R)-3-phenylisoxazolidine (526mg, 3.52mmol) were dissolved in a dimethylsulfoxide (DMSO, 7ml) solvent, and the reaction solution was agitated for 30 minutes at 60℃. After the reaction was completed, extraction was performed using ethylacetate and water. The gathered organic layer was washed with salt water, dried with anhydrous sodium sulfate, then vacuum concentrated, and purified with MPLC (ethylacetate/hexane) to obtain the target compound (R)-2-(6-chloropyrimidine-4-yl)-3-phenylisoxazolidine (800mg, 91%) in the form of a transparent liquid.

[422] MS(m/z): 262.07[M+1], UPLC r. t. (min): 1.58

[423] NMR: 1H NMR (400 MHz, DMSO-d6) δ 8.48 (s, 1H), 7.42 - 7.22 (m, 5H), 7.09 (s, 1H), 5.56 - 5.43 (m, 1H), 4.27 - 4.17 (m, 1H), 4.00 - 3.88 (m, 1H), 2.97 - 2.80 (m, 1H), 2.37 - 2.22 (m, 1H).

[424] Step 2: Preparation of (R)-N-(4-fluoro-2-methoxy-5-nitrophenyl)-6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-amine

[425] The (R)-2-(6-chloropyrimidine-4-yl)-3-phenylisoxazolidine obtained in Step 1 of Preparation Example 1 (800mg, 3.06mmol), 4-fluoro-2-methoxy-5-nitroaniline (626mg, 3.36mmol) and potassium carbonate (1267mg, 9.17mmol) were added to

and dissolved in sec-butanol (12ml), then treated ultrasonically for 5 minutes in a nitrogen atmosphere to remove gases. Tris(dibenzylideneacetone)dipalladium(0) ($Pd_2(dba)_3$; 280mg, 0.306mmol) and Xphos (146mg, 0.306mmol) were added to the reaction mixture, which was then agitated for 1 hour at 100℃. After the reaction was completed, filtration was performed using celite, followed by washing with ethylacetate. The filtrate was concentrated, then purified with MPLC (ethylacetate/hexane) to obtain the target compound (960mg, 76%).

[426] MS(m/z): 412.13[M+1], UPLC r. t. (min): 1.70,

[427] NMR: 1H NMR (400 MHz, DMSO-d6) δ 9.08 (s, 1H), 9.01 (s, 1H), 8.34 (s, 1H), 7.47 - 7.21 (m, 6H), 6.79 (s, 1H), 5.59 - 5.46 (m, 1H), 4.26 - 4.14 (m, 1H), 4.01 (s, 3H), 3.94 - 3.76 (m, 1H), 2.87 - 2.71 (m, 1H), 2.36 - 2.19 (m, 1H).

[428] Step 3: Preparation of (R)-N1-(2-(dimethylamino)ethyl)-5-methoxy-N1-methyl-2-nitro-N4-(6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)benzene-1,4-thiamine

[429] The (R)-N-(4-fluoro-2-methoxy-5-nitrophenyl)-6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-amine obtained in Step 2 of Preparation Example 1 (100mg, 0.243mmol) and potassium carbonate (67.2mg, 0.486mmol) were dissolved in dimethyl sulfoxide (DMSO; 1.5ml). Then N1,N1,N2-trimethylethane-1,2-thiamine (0.035mL, 0.267mmol) was added, and agitated for 2 hours at 70℃. After the reaction ended, extraction was performed using ethylacetate and water. The gathered organic layer was washed with salt water, dried with anhydrous sodium sulfate, and concentrated under vacuum to obtain the target compound (110mg, 92%) which was used in the next reaction without purification.

[430] MS(m/z): 494.24[M+1], UPLC r. t. (min): 1.23

[431] Step 4: Preparation of (R)-N1-(2-(dimethylamino)ethyl)-5-methoxy-N1-methyl-N4-(6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)benzene-1,2,4-triamine

[432] The (R)-N1-(2-(dimethylamino)ethyl)-5-methoxy-N1-methyl-2-nitro-N4-(6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)benzene-1,4-thiamine obtained in Step 3 of Preparation Example 1 (110mg, 0.223mmol) and $SnCl_2 2H_2O$ (251mg, 1.114mmol) were dissolved in ethylacetate (1.5ml), and agitated for 1 hour at 50℃. The temperature of the reaction solution was brought down to room temperature, and aqueous solution of ammonia was added dropwise until pH5 was reached. Anhydrous sodium carbonate was added to the reaction mixture to adjust to pH 7. The reaction mixture was filtered with celite, and washed multiple times with ethylacetate. The filtrate was concentrated under vacuum to obtain the target compound (90mg, 87%), which was used in the next reaction without purification.

[433] MS(m/z): 464.27[M+1], UPLC r. t. (min): 1.03

[434] Step 5:
(R)-N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-(3-phenylisoxazolidin-2-yl)pyrimidin-4-yl)amino)phenyl)acrylamide was prepared.

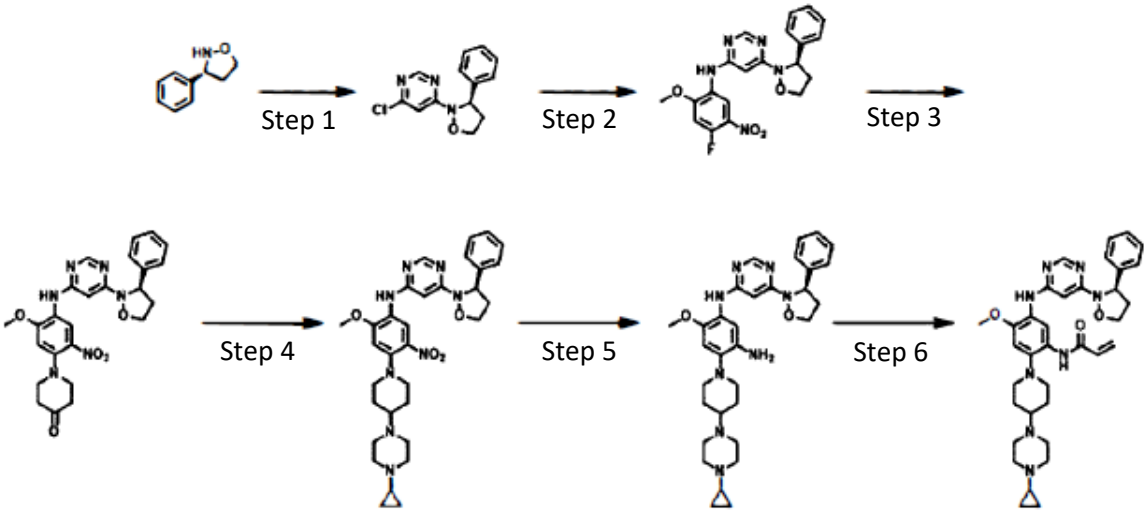
[435] The (R)-N1-(2-(dimethylamino)ethyl)-5-methoxy-N1-methyl-N4-(6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)benzene-1,2,4-triamine obtained in Step 4 of Preparation Example 1 (85mg, 0.183mmol) was dissolved in tetrahydrofuran (THF; 1.5ml), and a saturated sodium bicarbonate ($NaHCO_3$; 1.5ml) aqueous solution was added. While agitating vigorously at 0℃, acryloyl chloride (30μl, 0.367mmol) diluted in tetrahydrofuran (THF; 0.5mL) was added slowly dropwise. After 10 minutes agitation, extraction was performed using ethylacetate and distilled water. The gathered organic layer was dried using anhydrous sodium sulfate. The filtrate was vacuum concentrated, then purified using a Prep-150 LC System to obtain the target compound (58mg, 61%).

[436] MS(m/z): 518.28[M+1], UPLC r. t. (min): 1.11

[437] NMR: 1H NMR (400 MHz, Methanol-d4) δ 8.15 (s, 1H), 7.97 (s, 1H), 7.43 (s, 2H), 7.33 (s, 2H), 7.24 (s, 1H), 6.93 (s, 1H), 6.61 - 6.35 (m, 3H), 5.90 - 5.75 (m, 1H), 5.60 - 5.43 (m, 1H), 4.23 - 4.06 (m, 1H), 4.03 - 3.93 (m, 1H), 3.91 (s, 3H), 3.45 - 3.36 (m, 2H), 3.20 - 3.06 (m, 2H), 2.85 - 2.79 (m, 1H), 2.77 (s, 6H), 2.73 - 2.65 (m, 3H), 2.42 - 2.27 (m, 1H)

[438] **<Preparation Example 2> Preparation of Example Compound 56**

[439]



[440] Step 1: Preparation of (R)-2-(6-chloropyrimidine-4-yl)-3-phenylisoxazolidine

[441] 4,6-dichloropyrimidine (4.23g), the (R)-3-phenylisoxazolidine (6g) obtained in Preparation Example 2 and N,N-diisopropylethylamine (DIPEA; 18.91ml) were placed in dimethylsulfoxide (DMSO; 135ml) solvent and dissolved. The reaction solution was reacted for 30 minutes at 80℃. Ethyl acetate was added to the reaction mixture to dilute, followed by extraction with ethylacetate and salt water. The organic layers were added. The organic layer was dried with sodium sulfate and vacuum concentrated, then purified using medium pressure liquid chromatography (ethylacetate/n-hexane) to obtain the target compound (R)-2-(6-chloropyrimidine-4-yl)-3-phenylisoxazolidine (48.6%).

[442] Step 2: Preparation of (R)-N-(4-fluoro-2-methoxy-5-nitrophenyl)-6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-amine

[443] 4-fluoro-2-methoxy-5-nitroaniline (4.23g) the (R)-2-(6-chloropyridine-4-yl)-3-phenylisoxazolidine obtained in Step 1 of Preparation Example 2 (1.84g) and potassium carbonate (2.56g) were dissolved in a sec-butanol solvent (20.60ml). The temperature of the reaction solution was raised to 60℃, then xphos (0.295g) and tris(dibenzilydeneacetone)dipalladium(0) ($Pd_2(dba)_3$; 0.425g) were placed in the reaction mixture solution. The reaction solution was reacted for 120 minutes at 100℃. After the reaction, the organic layer was vacuum concentrated and purified using medium pressure liquid chromatography (ethylacetate/n-hexane) to obtain the target compound (R)-N-(4-fluoro-2-methoxy-5-nitrophenyl)-6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-amine (58.9% yield).

[444] Step 3: Preparation of (R)-1-(5-methoxy-2-nitro-4((6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)piperidine-4-on

[445] The (R)-N-(4-fluoro-2-methoxy-5-nitrophenyl)-6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-amine obtained in Step 2 of Preparation Example 2 (1.6g) was placed in a dimethylsulfoxide (DMSO; 15ml) solvent and dissolved, and then potassium carbonate (1.98g) and piperidine-4-on hydrochloride (1.45g) were added to the reaction solution. Thereafter, the reaction solution was reacted for 120 minutes at 70℃. After the reaction, water was added to the reaction mixture to dilute the reaction solution. Extraction was performed using ethylacetate and salt

water, followed by vacuum concentration of the organic layer and purification using medium pressure liquid chromatography (dichloromethane/methanol) to obtain the target compound (R)-1-(5-methoxy-2-nitro-4((6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)piperidine-4-on (96% yield).

[446] Step 4: Preparation of (R)-N-(4-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-2-methoxy-5-nitrophenyl)-6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-amine

[447] The (R)-1-(5-methoxy-2-nitro-4((6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)piperidine-4-on obtained in Step 3 of Preparation Example 2 (1.8g) was placed in a dichloromethane (15ml) solvent and dissolved, and 1-cyclopropylpiperazine (0.495mL) and sodium triacetoxy borohydride (1.45g) was added. The reaction solution was reacted for 16 hours at room temperature. The reaction was ended by adding 2 normal sodium hydroxide aqueous solution, and extraction was carried out using dichloromethane solvent and salt water. The organic layer was vacuum concentrated and purified using medium pressure liquid chromatography (dichloromethane/methanol) to obtain the target compound (R)-N-(4-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-2-methoxy-5-nitrophenyl)-6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-amine (73.5% yield).

[448] Step 5: Preparation of (R)-4-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-6-methoxy-N1-(6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)benzene-1,3-thiamine

[449] The (R)-N-(4-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-2-methoxy-5-nitrophenyl)-6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-amine obtained in Step 4 of Preparation Example 2 (1.6g) was placed in an ethylacetate (20ml) and methanol (2ml) solvent and dissolved, then tin(II) chloride dihydrate (2.84g, 12.56mmol) was added. Thereafter, the reaction solution was reacted for 120 minutes at 60℃. The reaction was ended by adding aqueous sodium bicarbonate solution, followed by celite filtration and washing with ethylacetate solvent. The filtrate was extracted using ethylacetate and salt water, and the organic layer was vacuum concentrated and purified using medium pressure liquid chromatography (dichloromethane/methanol) to obtain the target compound (R)-4-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-6-methoxy-N1-(6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)benzene-1,3-thiamine (77% yield).

[450] Step 6: Preparation of (R)-N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide

[451] The (R)-4-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-6-methoxy-N1-(6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)benzene-1,3-thiamine obtained in Step 5 of Preparation Example 2 (1.18g) was dissolved in THF solvent (16mL), then a sodium bicarbonate aqueous solution (16mL) was added. [The mixture was] placed in an ethylacetate (20ml) and methanol (2ml) solvent and dissolved. The temperature of the reaction solution was lowered to 0℃, then THF solution (4ml) in which acryloylchloride (0.315mL) was dissolved was slowly added dropwise. Thereafter, the reaction solution was reacted for 30 minutes at 0℃, and the reaction was ended by adding sodium bicarbonate aqueous solution to end the reaction, followed by extraction using ethylacetate and salt water. The organic layer was vacuum concentrated and purified using medium pressure liquid chromatography (dichloromethane/methanol) to obtain the target compound (R)-N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide (84% yield).

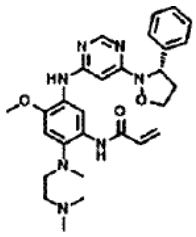
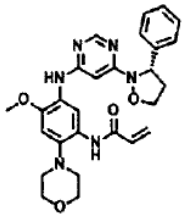
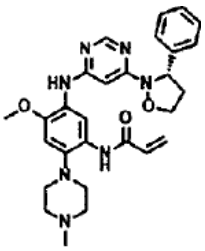
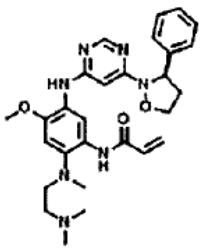
[452] In anot (R)-4-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-6-methoxy-N1-(6-(3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)benzene-1,3-thiamine obtained in Step 5 of Preparation Example 2 for the Example Compounds (128mg) was dissolved in dichloromethane (2ml), followed by addition of ethylene dichloride

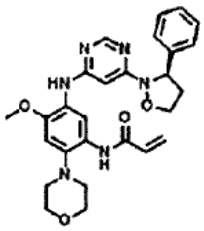
(EDC; 48mg), acrylic acid (0.017mL) and N,N-diisopropylethylamine (DIPEA; 0.108mL). The reaction solution was reacted for 1 hour at room temperature, and the reaction was ended using sodium bicarbonate aqueous solution. The compound was extracted using dichloromethane solvent and salt water. The organic layer was vacuum dried, vacuum concentrated, then purified using medium pressure liquid chromatography (dichloromethane/methanol) to obtain the target compound (86% yield).

[453] All of the example compounds of the present invention (Example Compounds 1 through 1059) were prepared using methods similar to those of Preparation Examples 1 or 2, and the name, chemical structural formula, NMR and UPLC analysis results of the respective Example Compounds are given in Table 1 below.

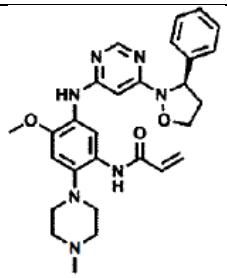
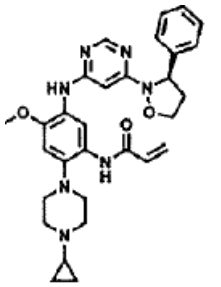
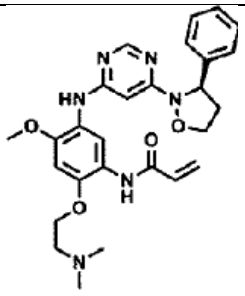
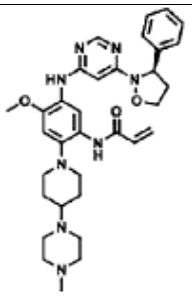
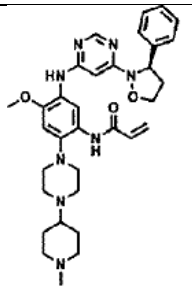
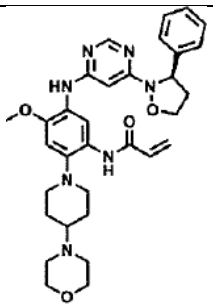
[454] [Table 1]

[455]

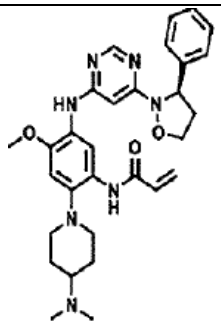
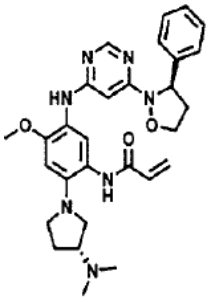
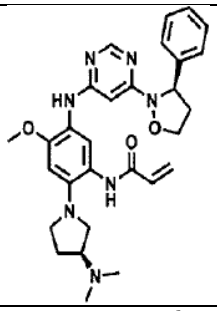
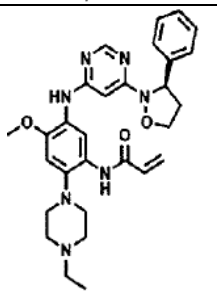
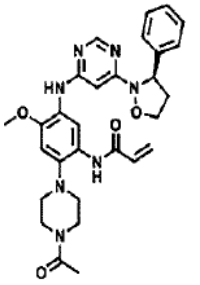
Example Compound	Structure	Name of Compound	^{1}H NMR: MS[M+H]$^+$	UPLC r.t. (min)
1		N-(2((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((S)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d$_4$) δ 8.15 (s, 1H), 7.95 (s, 1H), 7.42 (s, 2H), 7.33 (s, 2H), 7.25 (s, 1H), 6.93 (s, 1H), 6.59 - 6.36 (m, 3H), 5.90 - 5.76 (m, 1H), 5.61 - 5.47 (m, 1H), 4.20 - 4.08 (m, 1H), 4.02 - 3.93 (m, 1H), 3.92 (s, 3H), 3.45 - 3.36 (m, 2H), 3.20 - 3.07 (m, 2H), 2.85 - 2.79 (m, 1H), 2.77 (s, 6H), 2.71 (s, 3H), 2.41 - 2.26 (m, 1H); 518.3[M+H]$^+$	1.12
2		N-(4-methoxy-2-morpholino-5-((6-((S)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d$_4$) δ 8.28 (s, 1H), 8.13 (s, 1H), 7.42 (s, 2H), 7.33 (s, 2H), 7.24 (s, 1H), 6.91 (s, 1H), 6.63 - 6.45 (m, 1H), 6.43 - 6.27 (m, 2H), 5.85 - 5.69 (m, 1H), 5.58 - 5.46 (m, 1H), 4.21 - 4.09 (m, 1H), 4.02 - 3.92 (m, 1H), 3.92 - 3.82 (m, 7H), 2.95 - 2.88 (m, 4H), 2.85 - 2.68 (m, 1H), 2.42 - 2.23 (m, 1H) ; 503.2[M+H]$^+$	1.34
3		N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6((S)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d$_4$) δ 8.31 (s, 1H), 8.14 (s, 1H), 7.42 (s, 2H), 7.33 (s, 2H), 7.24 (s, 1H), 6.92 (s, 1H), 6.62 - 6.47 (m, 1H), 6.45 - 6.39 (m, 1H), 6.39 - 6.30 (m, 1H), 5.86 - 5.71 (m, 1H), 5.60 - 5.47 (m, 1H), 4.20 - 4.07 (m, 1H), 4.01 - 3.89 (m, 1H), 3.89 - 3.82 (m, 4H), 3.09 - 2.95 (m, 7H), 2.87 - 2.72 (m, 1H), 2.65 (s, 3H), 2.41 - 2.24 (m, 1H) ; 516.3[M+H]$^+$	1.04
4		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-(R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-	^{1}H NMR (400 MHz, Methanol-d$_4$) δ 8.15 (s, 1H), 7.97 (s, 1H), 7.43 (s, 2H), 7.33 (s, 2H), 7.24 (s, 1H), 6.93 (s, 1H), 6.61 - 6.35 (m, 3H), 5.90 - 5.75 (m, 1H), 5.60 - 5.43 (m, 1H), 4.23 - 4.06 (m, 1H), 4.03 - 3.93 (m, 1H), 3.91 (s, 3H), 3.45 - 3.36 (m, 2H), 3.20 - 3.06 (m, 2H), 2.85 - 2.79 (m, 1H), 2.77 (s, 6H), 2.73 - 2.65 (m, 3H), 2.42 - 2.27 (m, 1H) ; 518.3[M+H]$^+$	1.11

		yl)amino)phenyl)acrylamide		
5		N-(4-methoxy-2-morpholino-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d$_4$) δ 8.28 (s, 1H), 8.13 (s, 1H), 7.42 (s, 2H), 7.33 (s, 2H), 7.23 (s, 1H), 6.91 (s, 1H), 6.62 - 6.46 (m, 1H), 6.44 - 6.26 (m, 2H), 5.85 - 5.70 (m, 1H), 5.59 - 5.45 (m, 1H), 4.19 - 4.07 (m, 1H), 4.01 - 3.93 (m, 1H), 3.93 - 3.82 (m, 7H), 2.95 - 2.87 (m, 4H), 2.86 - 2.72 (m, 1H), 2.40 - 2.26 (m, 1H) ; 503.2[M+H]$^+$	1.34

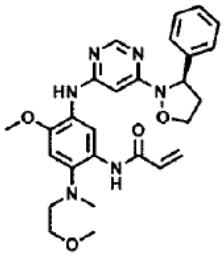
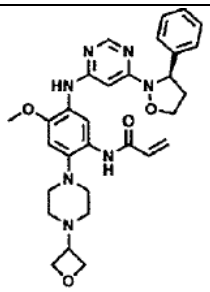
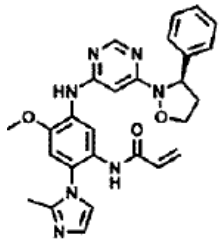
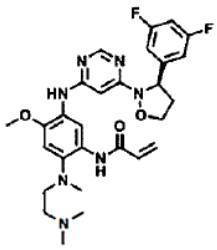
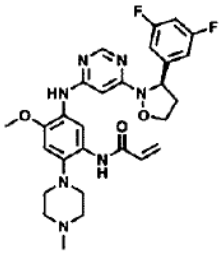
[456]

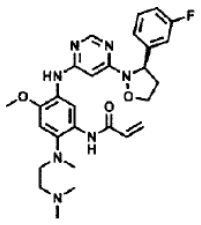
6		N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.31 (s, 1H), 8.14 (s, 1H), 7.42 (s, 2H), 7.33 (s, 2H), 7.24 (s, 1H), 6.92 (s, 1H), 6.61 - 6.49 (m, 1H), 6.43 (s, 1H), 6.40 - 6.29 (m, 1H), 5.87 - 5.73 (m, 1H), 5.59 - 5.45 (m, 1H), 4.20 - 4.02 (m, 1H), 4.02 - 3.91 (m, 1H), 3.91 - 3.81 (m, 4H), 3.12 - 2.92 (m, 7H), 2.85 - 2.70 (m, 1H), 2.63 (s, 3H), 2.40 - 2.26 (m, 1H) ; 516.3[M+H]$^+$	1.04
7		N-(2-(4-cyclopropylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.07 (s, 1H), 8.71 (s, 1H), 8.27 (d, 2H), 7.43 - 6.98 (m, 5H), 6.79 (d, 2H), 6.36 (s, 1H), 5.52 (d, 2H), 3.81 (s, 3H), 3.15 - 3.03 (m, 4H), 2.81 - 2.71 (m, 4H), 2.67 (s, 1H), 2.37 (d, 2H), 2.31 - 2.21 (m, 3H), 1.01 (s, 1H), 1.11 - 1.03 (m, 3H).; 540.3[M+H]$^+$	1.14
8		N-(2-(2-(dimethylamino)ethxy)-4-methoxy-5-((6-(R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl-amino)phenyl)acrylamide	505.3[M+H]$^+$	1.07
9		N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl-pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (d, J = 4.0 Hz, 1H), 8.56 (d, J = 4.2 Hz, 1H), 8.15 (t, J = 3.2 Hz, 1H), 7.43 - 7.23 (m, 5H), 6.82 (d, J = 3.9 Hz, 1H), 6.70 - 6.60 (m, 1H), 6.34 (d, J = 4.3 Hz, 1H), 6.20 (d, J = 16.7 Hz, 1H), 5.72 (d, J = 10.2 Hz, 1H), 5.53 (s, 1H), 4.13 (t, 1H), 3.39 (t, 2H), 3.32 (s, 3H), 3.09 - 2.98 (m, 2H), 2.81 - 2.71 (m, 1H), 2.71 - 2.60 (m, 4H), 2.40 - 2.19 (m, 8H), 2.14 (s, 3H), 1.89 - 1.78 (m, 2H), 1.78 - 1.63 (m, 2H).).; 599.3[M+H]$^+$	1.05
10		N-(4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)-5-((6-(R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.27 (s, 1H), 8.14 (s, 1H), 7.42 (s, 2H), 7.33 (s, 2H), 7.24 (s, 1H), 6.90 (s, 1H), 6.56 - 6.45 (m, 1H), 6.45 - 6.26 (m, 2H), 5.85 - 5.71 (m, 1H), 5.59 - 5.45 (m, 1H), 4.18 - 4.03 (m, 1H), 4.03 - 3.91 (m, 1H), 3.86 (s, 3H), 3.50 - 3.37 (m, 3H), 3.05 - 2.95 (m, 4H), 2.94 - 2.81 (m, 6H), 2.76 (s, 3H), 2.69 - 2.56 (m, 2H), 2.44 - 2.25 (m, 1H), 2.23 - 2.08 (m, 2H) ; 599.3[M+H]$^+$	0.97
11		N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.97 (s, 1H), 9.19 (s, 1H), 8.30 (s, 1H), 7.88 (s, 1H), 7.37 (dd, J = 6.9, 1.3 Hz, 4H), 7.29 (ddd, J = 8.6, 5.4, 2.1 Hz, 1H), 6.90 (s, 1H), 6.67 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 5.79 - 5.73 (m, 1H), 5.52 (d, J = 8.1 Hz, 1H), 4.31 (d, J = 4.5 Hz, 1H), 4.07 (d, J = 7.7 Hz, 1H), 3.98 (d, J = 3.9 Hz, 5H), 3.79 (s, 3H), 3.44 (d, J = 12.0 Hz, 2H), 3.36 - 3.27 (m, 1H), 3.22 (d, J = 11.5 Hz, 2H), 3.14 (d, J = 10.3 Hz, 2H), 2.97 - 2.90 (m, 1H), 2.77 (s, 2H), 2.37 - 2.28 (m, 1H), 2.20 (s, 2H), 2.04 (d, J = 13.4 Hz, 2H); 586.3[M+H]$^+$	1.11

[457]

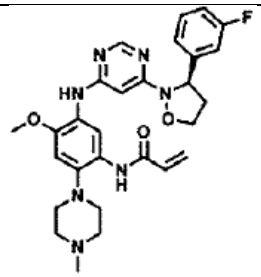
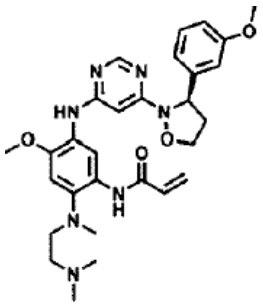
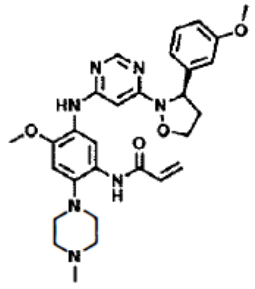
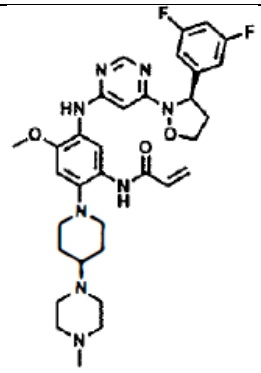
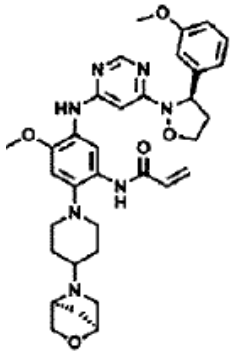
12		N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.28 (s, 1H), 8.14 (s, 1H), 7.42 (s, 2H), 7.33 (s, 2H), 7.24 (s, 1H), 6.89 (s, 1H), 6.65 - 6.48 (m, 1H), 6.47 - 6.28 (m, 2H), 5.86 - 5.73 (m, 1H), 5.58 - 5.43 (m, 1H), 4.20 - 4.08 (m, 1H), 4.02 - 3.90 (m, 1H), 3.86 (s, 3H), 3.64 - 3.55 (m, 4H), 3.26 - 3.13 (m, 4H), 2.93 - 2.71 (m, 7H), 2.41 - 2.28 (m, 1H), 2.21 - 2.09 (m, 1H) ; 544.3[M+H]$^+$	1.09
13		N-2-((R)-3-(dimethylamino)pyrrolidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.10 (s, 1H), 7.69 (s, 1H), 7.42 (s, 2H), 7.32 (s, 2H), 7.24 (s, 1H), 6.69 (s, 1H), 6.56 - 6.43 (m, 1H), 6.40 - 6.23 (m, 2H), 5.87 - 5.72 (m, 1H), 5.57 - 5.44 (m, 1H), 4.17 - 4.04 (m, 1H), 4.00 - 3.89 (m, 1H), 3.86 (s, 3H), 3.49 - 3.34 (m, 5H), 2.86 - 2.72 (m, 1H), 2.63 (s, 6H), 2.41 - 2.24 (m, 2H), 2.11 - 2.01 (m, 1H) ; 530.3[M+H]$^+$	1.05
14		N-(2-((S)-3-(dimethylamino)pyrrolidine-1-yl)-4-methxy-5-((6-(R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.91 (s, 1H), 9.34 (s, 1H), 9.04 (s, 1H), 8.20 (s, 1H), 7.55 (s, 1H), 7.37 (d, J = 1.7 Hz, 2H), 7.36 (s, 1H), 7.27 (s, 1H), 6.64 (s, 1H), 6.51 (dd, J = 17.1, 10.2 Hz, 1H), 6.21 (dd, J = 17.1, 2.1 Hz, 1H), 6.14 (s, 1H), 5.73 (d, J = 10.4 Hz, 1H), 5.52 (dd, J = 8.7, 5.1 Hz, 2H), 4.23 - 4.17 (m, 1H), 3.81 (s, 3H), 3.43 (d, J = 6.7 Hz, 2H), 3.34 (d, J = 3.7 Hz, 2H), 3.25 (t, J = 8.2 Hz, 1H), 2.84 (t, J = 5.8 Hz, 6H), 2.35 - 2.30 (m, 1H), 2.30 - 2.22 (m, 2H), 2.11 (dd, J= 12.6, 6.7 Hz, 1H). ; 530.4[M+H]$^+$	1.07
15		N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.32 (s, 1H), 8.14 (s, 1H), 7.42 (s, 2H), 7.33 (s, 2H), 7.24 (s, 1H), 6.91 (s, 1H), 6.60 - 6.47 (m, 1H), 6.47 - 6.28 (m, 2H), 5.88 - 5.71 (m, 1H), 5.60 - 5.42 (m, 1H), 4.20 - 4.05 (m, 1H), 4.01 - 3.90 (m, 1H), 3.88 (s, 3H), 3.09 (s, 8H), 3.00 - 2.87 (m, 2H), 2.87 - 2.70 (m, 1H), 2.43 - 2.25 (m, 1H), 1.37 - 1.20 (m, 3H) ; 530.3[M+H]$^+$	1.06
16		N-(2-(4-acetylpiperazine-1-yl)-4-methoxy-5-((-6((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.30 (s, 1H), 8.31 (s, 1H), 8.23 (d, J = 4.1 Hz, 1H), 7.45 - 7.19 (m, 5H), 7.00 (s, 1H), 6.42 (dd, J = 13.5 Hz, 1H), 6.23 (d, J = 18.3 Hz, 2H), 5.77 (d, J = 9.8 Hz, 1H), 5.52 (s, 1H), 4.23 (s, 1H), 4.02 - 3.92 (m, 2H), 3.86 - 3.74 (m, 4H), 3.50 (s, 3H), 3.38 - 3.29 (m, 4H), 2.80 (s, 3H), 2.36 - 2.22 (m, 2H). ; 544.3[M+H]$^+$	1.27

[458]

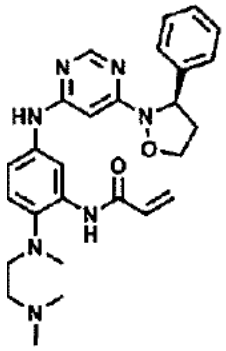
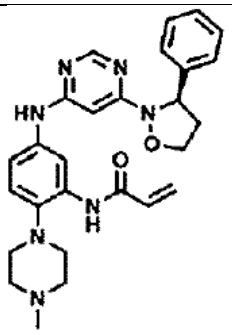
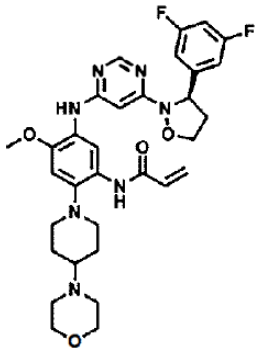
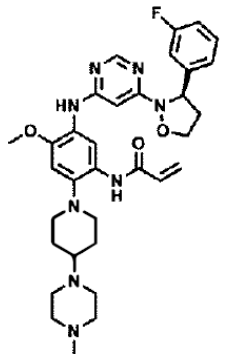
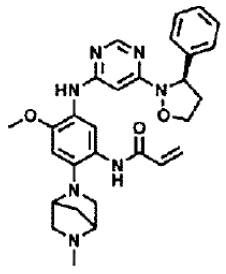
17		N-(4-methoxy-2-((2-methoxyethyl)(methyl)amino-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.45 - 8.34 (m, 1H), 7.12 (d, J = 4.0 Hz, 1H), 7.01 (s, 1H), 6.91 - 6.82 (m, 5H), 6.76 (dd, J = 13.8 Hz, 1H), 6.16 (d, J = 16.4 Hz, 1H), 5.90 (s, 1H), 5.75 - 5.65 (m, 1H), 4.85 - 4.74 (m, 0H), 4.00 (d, J = 4.3 Hz, 2H), 3.31 - 3.17 (m, 6H), 3.05 (s, 1H), 1.93 - 1.76 (m, 2H), : 505.3[M+H]$^+$	1.45
18		N-(4-methoxy-2-(4-oxetane-3-yl)piperazine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.14 (s, 1H), 7.42 (d, J = 7.3 Hz, 2H), 7.32 (dd, J = 6.8, 8.4 Hz, 2H), 7.27 - 7.20 (m, 1H), 6.93 (s, 1H), 6.50 (dd, J = 10.2, 17.0 Hz, 1H), 6.41 (d, J = 1.1 Hz, 1H), 6.33 (dd, J = 1.6, 17.0 Hz, 1H), 5.78 (dd, J = 1.6, 10.2 Hz, 1H), 5.52 (dd, J = 4.7, 8.5 Hz, 1H), 4.73 (t, J = 6.7 Hz, 2H), 4.65 (t, J = 6.2 Hz, 2H), 4.17 - 4.08 (m, 1H), 4.02 - 3.92 (m, 1H), 3.87 (s, 3H), 3.66 - 3.57 (m, 1H), 3.03 - 2.95 (m, 4H), 2.85 - 2.71 (m, 1H), 2.63 - 2.51 (m, 4H), 2.38 - 2.27 (m, 1H) : 558.3[M+H]$^+$	1.07
19		N-(4-methoxy-2-(2-methyl-1H-imidazole-1-yl)-5-((6((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.38 (s, 1H), 8.27 (s, 1H), 7.47 (d, J = 7.6 Hz, 2H), 7.37 (t, J = 7.6 Hz, 2H), 7.27 (t, J = 7.2 Hz, 1H), 7.12 - 7.03 (m, 2H), 7.01 (s, 1H), 6.69 (s, 1H), 6.31 - 6.23 (m, 2H), 5.73 (dd, J = 2.8, 9.1 Hz, 1H), 5.58 (dd, J = 4.8, 8.5 Hz, 1H), 4.24 - 4.16 (m, 2H), 4.08 - 3.98 (m, 2H), 3.96 (s, 3H), 2.30 (s, 3H) : 498.3[M+H]$^+$	1.19
20		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methylamino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (s, 1H), 7.99 (s, 1H), 7.05 (s, 2H), 6.93 (s, 1H), 6.89 - 6.77 (m, 1H), 6.60 - 6.33 (m, 3H), 5.89 - 5.75 (m, 1H), 5.62 - 5.42 (m, 1H), 4.19 - 4.07 (m, 1H), 3.99 - 3.93 (m, 1H), 3.92 (s, 3H), 3.47 - 3.35 (m, 2H), 3.20 - 3.08 (m, 2H), 2.89 - 2.80 (m, 1H), 2.77 (s, 6H), 2.71 (s, 3H), 2.40 - 2.25 (m, 1H) : 554.3[M+H]$^+$	1.23
21		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.33 (s, 1H), 8.17 (s, 1H), 7.05 (s, 2H), 6.93 (s, 1H), 6.88 - 6.74 (m, 1H), 6.59 - 6.42 (m, 2H), 6.40 - 6.28 (m, 1H), 5.85 - 5.72 (m, 1H), 5.61 - 5.41 (m, 1H), 4.21 - 4.05 (m, 1H), 4.01 - 3.91 (m, 1H), 3.88 (s, 3H), 3.10 - 3.01 (m, 4H), 3.01 - 2.91 (m, 4H), 2.89 - 2.74 (m, 1H), 2.62 (s, 3H), 2.40 - 2.22 (m, 1H) : 552.3[M+H]$^+$	1.20

22		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	536.3[M+H]$^+$	1.17

[459]

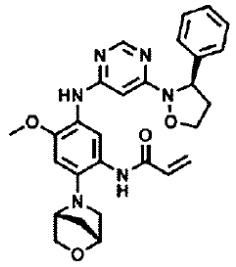
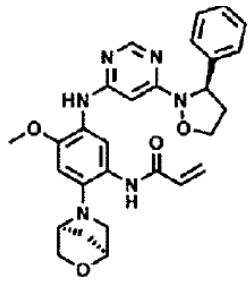
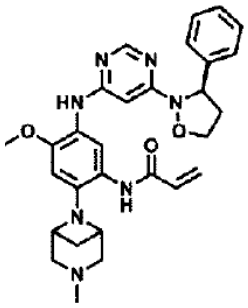
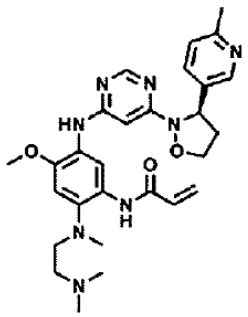
23		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	534.3[M+H]$^+$	1.13
24		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 9.48 (s, 1H), 8.83 (d, J = 2.0 Hz, 1H), 8.29 (d, J = 2.1 Hz, 1H), 7.70 (s, 1H), 7.25 (td, J = 8.3, 2.0 Hz, 1H), 7.02 (dd, J = 4.3, 2.0 Hz, 2H), 6.81 (d, J = 10.2 Hz, 1H), 6.76 (d, J = 9.4 Hz, 1H), 6.74 (s, 1H), 6.67 (d, J = 2.5 Hz, 1H), 6.45 - 6.35 (m, 1H), 5.70 (dd, J = 10.1, 2.1 Hz, 1H), 5.65 (dd, J = 8.6, 4.4 Hz, 1H), 4.16 (td, J = 7.9, 4.4 Hz, 1H), 4.12 - 4.04 (m, 1H), 3.84 (d, J = 2.0 Hz, 3H), 3.80 (d, J = 1.5 Hz, 3H), 3.06 (d, J = 7.1 Hz, 2H), 2.87 (t, J = 5.0 Hz, 2H), 2.76 (tt, J = 8.1, 4.3 Hz, 1H), 2.66 (d, J = 1.0 Hz, 3H), 2.57 (s, 6H), 2.38 (dtd, J = 12.2, 8.0, 4.6 Hz, 1H); 548.3[M+H]$^+$	1.11
25		N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.71 (s, 1H), 8.44 (s, 1H), 8.27 (d, J = 0.9 Hz, 1H), 7.29 (s, 1H), 7.25 (t, J = 8.1 Hz, 1H), 7.03 - 6.99 (m, 2H), 6.83 - 6.76 (m, 2H), 6.57 (s, 1H), 6.41 - 6.27 (m, 2H), 5.76 (dd, J = 8.9, 2.6 Hz, 1H), 5.64 (dd, J = 8.6, 4.5 Hz, 1H), 4.13 (dd, J = 7.9, 4.4 Hz, 1H), 4.03 (q, J = 8.0 Hz, 1H), 3.86 (s, 3H), 3.80 (s, 3H), 3.07 - 3.00 (m, 4H), 2.93 (d, J = 6.2 Hz, 4H), 2.80 - 2.73 (m, 1H), 2.54 (s, 3H), 2.41 - 2.35 (m, 1H); 546.3[M+H]$^+$	1.33
26		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.63 (s, 1H), 8.20 - 8.11 (m, 2H), 7.15 - 7.08 (m, 3H), 6.82 (s, 1H), 6.69 - 6.61 (m, 1H), 6.35 (s, 1H), 6.21 (dd, J = 17.0, 2.0 Hz, 1H), 5.72 (dd, J = 10.1, 2.0 Hz, 1H), 5.56 (dd, J = 8.7, 4.9 Hz, 1H), 4.16 - 4.10 (m, 1H), 3.83 (d, J = 8.0 Hz, 1H), 3.80 (s, 3H), 3.16 - 2.99 (m, 3H), 2.76 (dd, J = 8.1, 4.0 Hz, 1H), 2.68 (d, J = 12.6 Hz, 2H), 2.58 - 2.52 (m, 3H), 2.38 - 2.21 (m, 6H), 2.16 (s, 3H), 1.88 - 1.80 (m, 2H), 1.71 (dd, J = 12.8, 9.2 Hz, 2H); 635.3 [M+H]$^+$	1.16
27		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.05 (d, J = 0.8 Hz, 1H), 7.85 (s, 1H), 7.16 (t, J = 7.9 Hz, 1H), 6.85 - 6.77 (m, 3H), 6.74 (ddd, J = 8.4, 2.6, 1.0 Hz, 1H), 6.42 (dd, J = 17.0, 10.2 Hz, 1H), 6.27 (dd, J = 17.0, 1.6 Hz, 1H), 5.90 (s, 1H), 5.72 (d, J = 10.1 Hz, 1H), 5.33 (s, 1H), 4.66 - 4.56 (m, 2H), 4.24 (dd, J = 7.6, 4.4 Hz, 2H), 4.07 - 3.98 (m, 1H), 3.79 (d, J = 8.8 Hz, 2H), 3.72 (s, 3H), 3.68 (s, 3H), 3.51 (d, J = 13.4 Hz, 2H), 2.90 - 2.68 (m, 4H), 2.32 (dd, J = 12.9, 5.7 Hz, 2H), 2.12 (d, J = 15.6 Hz, 4H), 1.84 (d, J = 3.7 Hz, 2H); 628.3 [M+H]$^+$	1.14

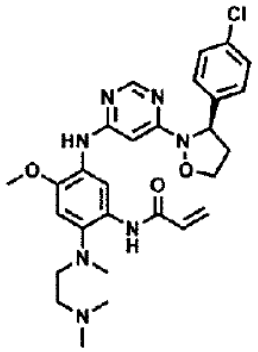
[460]

28		N-(2-((2-(dimethylamino)ethyl)methyl)amino)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.83 (s, 1H), 9.97 (s, 1H), 9.15 (s, 1H), 8.32 (d, J = 4.5 Hz, 1H), 8.25 (s, 1H), 7.44 – 7.14 (m, 5H), 6.78 (dd, J = 16.2, 10.0 Hz, 1H), 6.20 (d, J = 13.6 Hz, 2H), 5.85 – 5.76 (m, 1H), 5.51 (s, 1H), 4.26 (s, 1H), 4.05 – 3.88 (m, 2H), 3.52 – 3.44 (m, 3H), 3.17 (s, 3H), 3.13 – 3.05 (m, 4H), 2.82 (s, 3H), 2.37 – 2.23 (m, 2H). : 488.3[M+H]$^+$	1.11
29		N-(2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.13 (s, 1H), 8.22 (d, J = 4.2 Hz, 1H), 8.11 (s, 1H), 7.38 (d, J = 4.9 Hz, 5H), 7.28 (s, 1H), 6.90 (d, J = 3.9 Hz, 1H), 6.67 (s, 1H), 6.20 (s, 2H), 5.74 (d, J = 10.4 Hz, 1H), 5.51 (d, J = 6.6 Hz, 1H), 4.22 (s, 1H), 4.00 – 3.90 (m, 2H), 3.70 – 3.50 (m, 4H), 2.85 (dd, J = 15.9, 5.7 Hz, 4H), 2.34 – 2.23 (m, 2H), 2.05 (s, 3H). : 486.3[M+H]$^+$	1.08
30		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.73 (s, 1H), 10.22 (s, 1H), 9.26 (s, 1H), 8.34 (s, 1H), 7.88 (s, 1H), 7.17 (tt, J = 9.3, 2.4 Hz, 1H), 7.10 (h, J = 4.5 Hz, 2H), 6.69 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 5.79 - 5.72 (m, 1H), 5.55 (dd, J = 8.6, 5.4 Hz, 1H), 4.05 (d, J = 7.7 Hz, 1H), 4.00 - 3.96 (m, 4H), 3.81 (s, 3H), 3.43 (d, J = 12.0 Hz, 2H), 3.24 (d, J = 11.4 Hz, 2H), 3.15 (d, J = 12.3 Hz, 2H), 2.93 (qd, J = 7.7, 3.4 Hz, 1H), 2.85 - 2.74 (m, 2H), 2.26 - 2.16 (m, 2H), 2.15 - 1.99 (m, 2H), 1.65 - 1.54 (m, 1H), 1.53 - 1.37 (m, 1H), 1.30 - 1.19 (m, 1H), 0.85 (td, J = 8.0, 7.3, 3.1 Hz, 1H).: 622.4 [M+H]$^+$	1.23
31		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.45 (s, 1H), 9.33 (s, 1H), 8.34 (s, 1H), 7.85 (s, 1H), 7.42 (td, J = 8.0, 5.9 Hz, 1H), 7.23 - 7.06 (m, 3H), 6.94 (s, 1H), 6.75 (dd, J = 16.8, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 2.0 Hz, 1H), 6.13 - 6.03 (m, 1H), 5.76 (dd, J = 10.0, 2.0 Hz, 1H), 5.55 (dd, J = 8.4, 5.4 Hz, 2H), 4.08 (q, J = 7.7 Hz, 2H), 3.80 (s, 3H), 3.79 - 3.70 (m, 4H), 3.61 (q, J = 14.1, 11.7 Hz, 5H), 3.48 (d, J = 16.4 Hz, 1H), 3.25 (d, J = 11.3 Hz, 2H), 3.15 (d, J = 7.9 Hz, 1H), 2.96 (qq, J = 7.3, 4.4 Hz, 2H), 2.84 (s, 5H), 2.32 (dtd, J = 12.6, 7.5, 5.2 Hz, 1H), 2.17 (q, J = 12.3 Hz, 4H), 1.67 - 1.49 (m, 4H).: 617.4 [M+H]$^+$	1.09
32		N-(4-methoxy-2-(5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-	528.3[M+H]$^+$	1.08

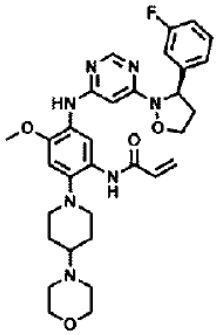
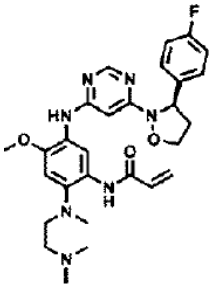
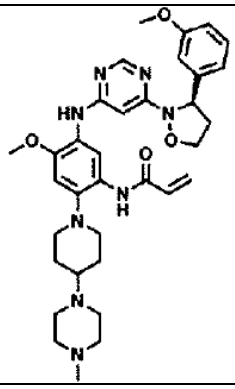
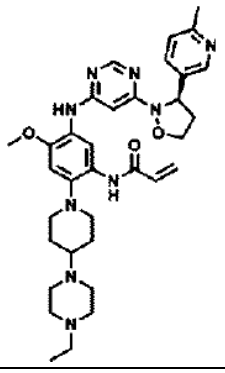
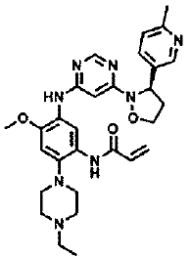
		yl)amino)pheny l)acrylamide		

[461]

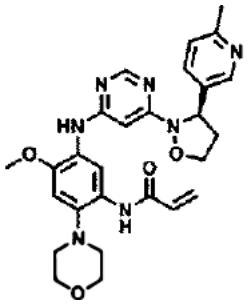
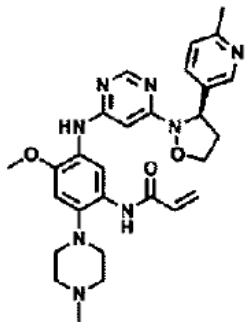
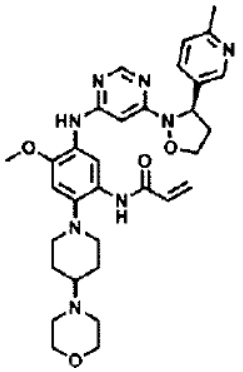
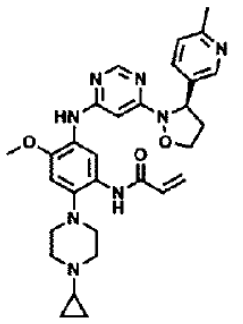
33		N-(2-((1R, 4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxy-5-((6((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.10 (s, 1H), 7.41 - 7.34 (m, 4H), 7.33 - 7.27 (m, 1H), 7.16 (s, 1H), 6.53 - 6.42 (m, 2H), 6.38 (dd, J = 17.0, 2.2 Hz, 1H), 5.95 (s, 1H), 5.82 (dd, J = 9.8, 2.1 Hz, 1H), 5.51 (s, 1H), 4.61 (s, 1H), 4.50 - 4.30 (m, 2H), 4.25 - 4.16 (m, 1H), 4.10 (d, J = 7.6 Hz, 1H), 3.93 - 3.88 (m, 1H), 3.81 (s, 3H), 3.65 (dd, J = 9.6, 1.7 Hz, 1H), 3.35 (d, J = 1.7 Hz, 1H), 3.09 - 2.98 (m, 2H), 2.51 - 2.40 (m, 1H), 2.07 - 2.02 (m, 1H), 1.99 - 1.95 (m, 1H); 515.2[M+H]$^+$	1.15
34		N-(2-((1S, 4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.11 (s, 1H), 7.49 - 7.40 (m, 3H), 7.35 (t, J = 7.6 Hz, 2H), 7.26 (t, J = 7.3 Hz, 1H), 6.56 (s, 1H), 6.49 (dd, J = 10.1, 17.0 Hz, 1H), 6.36 (dd, J = 1.8, 17.1 Hz, 1H), 6.27 (d, J = 3.2 Hz, 1H), 5.79 (dd, J = 1.8, 10.1 Hz, 1H), 5.52 (dd, J = 4.6, 8.5 Hz, 1H), 4.18 - 4.08 (m, 3H), 4.03 - 3.91 (m, 2H), 3.86 (s, 4H), 3.55 - 3.48 (m, 1H), 3.17 - 3.08 (m, 2H), 2.87 - 2.72 (m, 2H), 2.41 - 2.27 (m, 1H) ; 515.2[M+H]$^+$	1.24
35		N-(4-methoxy-2-(3-methyl-3,6-diazabicyclo[3.1.1]heptane-6-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.09 (s, 1H), 7.42 (d, J = 7.3 Hz, 2H), 7.33 (dd, J = 7.7, 15.3 Hz, 3H), 7.28 - 7.17 (m, 1H), 6.46 - 6.32 (m, 2H), 6.29 - 6.25 (m, 2H), 5.76 (dd, J = 2.5, 9.4 Hz, 1H), 5.51 (dd, J = 4.6, 8.7 Hz, 1H), 4.38 - 4.30 (m, 2H), 4.14 - 4.04 (m, 1H), 3.03 (q, J = 7.9 Hz, 1H), 3.83 (s, 3H), 3.19 - 3.11 (m, 2H), 3.06 - 2.96 (m, 2H), 2.82 - 2.71 (m, 1H), 2.65 (q, J = 6.8 Hz, 1H), 2.38 - 2.28 (m, 4H), 2.09 - 2.00 (m, 1H) ; 528.2[M+H]$^+$	1.03
36		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, Chloroform-d) δ 10.11 (s, 1H), 8.95 (s, 1H), 8.57 (d, J = 2.4 Hz, 1H), 8.36 (d, J = 0.9 Hz, 1H), 7.71 (dd, J = 8.1, 2.4 Hz, 1H), 7.12 (d, J = 8.0 Hz, 1H), 7.05 (s, 1H), 6.80 (s, 1H), 6.77 - 6.75 (m, 1H), 6.40 (dd, J = 17.0, 2.1 Hz, 1H), 6.31 (dd, J = 17.0, 9.8 Hz, 1H), 5.70 (ddd, J = 16.4, 9.0, 3.1 Hz, 2H), 4.18 - 4.09 (m, 2H), 3.84 (s, 3H), 2.88 (dt, J = 5.0, 2.4 Hz, 2H), 2.71 (s, 3H), 2.53 (s, 3H), 2.35 - 2.31 (m, 4H), 2.28 (s, 6H); 533.3[M+H]$^+$	1.35

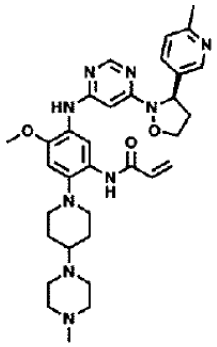
37		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (s, 1H), 8.06 (s, 1H), 7.40 (dd, J = 35.4, 8.1 Hz, 4H), 6.96 (s, 1H), 6.65 - 6.54 (m, 1H), 6.52 - 6.39 (m, 2H), 5.85 (dd, J = 10.2, 1.5 Hz, 1H), 5.57 - 5.50 (m, 1H), 4.16 (td, J = 7.8, 4.6 Hz, 1H), 3.99 (d, J = 7.9 Hz, 1H), 3.93 (s, 3H), 3.42 (t, J = 5.7 Hz, 2H), 3.33 (dt, J = 3.1, 1.6 Hz, 3H), 3.18 (d, J = 13.3 Hz, 2H), 2.80 (d, J = 4.1 Hz, 6H), 2.73 (s, 3H), 2.34 (dt, J = 12.4, 7.5 Hz, 1H) ; 552.5[M+H]$^+$	1.53

[462]

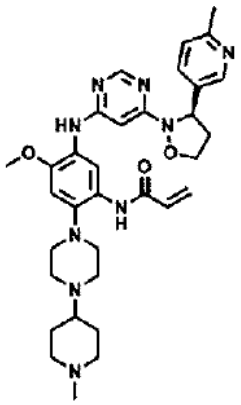
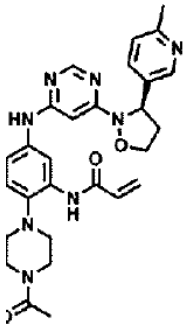
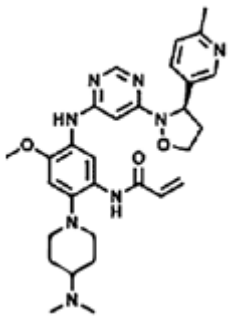
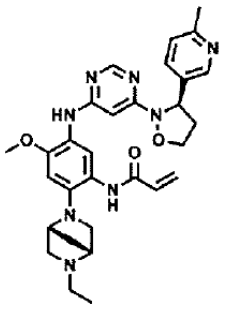
38		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	604.5 $[M+H]^+$	1.17
39		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	536.3$[M+H]^+$ KSS-005-068	
40		N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.17 (s, 1H), 7.93 (s, 1H), 7.28 (t, J = 7.8 Hz, 1H), 6.95 - 6.84 (m, 5H), 6.50 (dd, J = 16.9, 10.2 Hz, 1H), 6.40 (dd, J = 17.0, 1.6 Hz, 1H), 5.84 (dd, J = 10.2, 1.6 Hz, 1H), 5.42 (s, 1H), 4.43 (td, J = 7.5, 4.4 Hz, 1H), 4.19 (td, J = 8.2, 6.6 Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 3.43 (s, 4H), 3.26 (d, J = 12.3 Hz, 5H), 3.02 (dddd, J = 11.1, 8.3, 6.5, 4.3 Hz, 3H), 2.92 (s, 3H), 2.86 (d, J = 11.9 Hz, 2H), 2.50 - 2.41 (m, 1H), 2.20 - 2.11 (m, 2H), 2.02 - 1.80 (m, 3H): 629.3 $[M+H]^+$	1.11
41		N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	628.4 $[M+H]^+$	0.78
42		N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	545.3 $[M+H]^+$	0.74

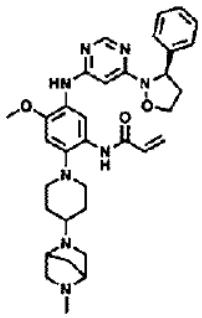
[463]

43		N-(4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino-2-morpholinophenyl)acrylamide	1H NMR (400 MHz, DMSO-$d6$) δ 9.95 (d, J = 23.3 Hz, 1H), 9.47 (s, 1H), 9.24 (s, 1H), 8.76 (d, J = 2.1 Hz, 1H), 8.47 (dd, J = 8.4, 2.2 Hz, 1H), 8.30 (d, J = 3.1 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 6.99 - 6.80 (m, 1H), 6.67 (dd, J = 17.0, 10.2 Hz, 1H), 6.43 - 6.11 (m, 2H), 5.82 - 5.63 (m, 2H), 3.84 - 3.81 (m, 4H), 2.92 (t, J = 4.5 Hz, 3H), 2.76 (s, 3H), 2.50 (q, J = 1.9 Hz, 8H). ; 518.5[M+H]$^+$	1.73
44		N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 11.18 (s, 1H), 9.15 (s, 1H), 8.75 (d, J = 2.1 Hz, 1H), 8.45 (dd, J = 8.5, 2.1 Hz, 1H), 8.27 (s, 1H), 8.15 (s, 1H), 7.01 (d, J = 8.4 Hz, 1H), 6.91 - 6.69 (m, 2H), 6.34 (s, 1H), 6.23 (dd, J = 17.0, 2.0 Hz, 1H), 5.80 - 5.68 (m, 2H), 4.26 (dd, J = 7.8, 4.1 Hz, 2H), 4.01 (q, J = 7.8 Hz, 2H), 3.84 (s, 3H), 3.60 (ddd, J = 9.0, 6.4, 3.1 Hz, 1H), 3.48 (d, J = 11.4 Hz, 2H), 3.17 (d, J = 6.3 Hz, 4H), 2.81 (d, J = 4.6 Hz, 3H), 2.74 (s, 3H), 2.39 (dq, J = 8.7, 4.9, 3.8 Hz, 1H).: 531.5[M+H]$^+$	1.28
45		N-(4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.57 (d, J = 2.3 Hz, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.70 (dd, J = 8.0, 2.4 Hz, 1H), 7.12 (d, J = 8.0 Hz, 1H), 6.95 (s, 1H), 6.73 (d, J = 12.7 Hz, 2H), 6.41 - 6.19 (m, 2H), 5.79 - 5.67 (m, 2H), 4.20 - 4.05 (m, 2H), 3.84 (s, 3H), 3.77 (t, J = 4.6 Hz, 4H), 3.12 - 3.02 (m, 2H), 2.83 - 2.67 (m, 3H), 2.62 (t, J = 4.7 Hz, 4H), 2.54 (s, 3H), 2.34 (m, 2H), 2.08 (d, J = 12.5 Hz, 2H), 1.65 (m, 2H).: 601.7 [M+H]$^+$	1.04
46		N-(2-(4-cyclopropylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.90 (s, 1H), 8.63 - 8.54 (m, 2H), 8.37 (s, 1H), 7.70 (dd, J = 8.1, 2.4 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 6.96 (s, 1H), 6.79 (s, 1H), 6.72 (s, 1H), 6.35 - 6.29 (m, 2H), 5.75 (dd, J = 9.7, 1.8 Hz, 1H), 5.73 - 5.70 (dd, J = 8.5, 4.3 Hz, 1H), 4.16 - 4.09 (m, 2H), 3.81 (s, 3H), 2.91 - 2.73 (m, 9H), 2.54 (s, 3H), 2.41 - 2.32 (m, 1H), 1.73 - 1.72(m, 1H), 0.52 (dd, J = 6.5, 4.4 Hz, 2H), 0.47 - 0.46 (m, 2H). ; 557.6 [M+H]$^+$	1.03

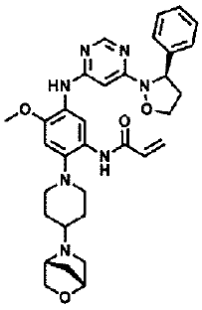
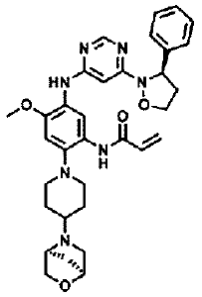
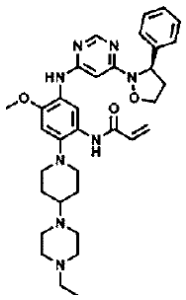
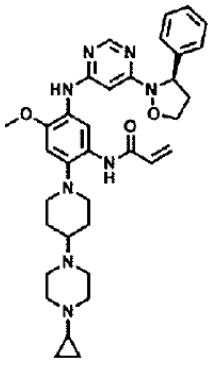
47		N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87(s, 1H), 8.78 (s, 1H), 8.57 (d, *J* = 2.3 Hz, 1H), 8.43 - 8.36 (m, 2H), 7.70 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.93 (s, 1H), 6.74 - 6.71 (m, 2H), 6.38 - 6.21 (m, 1H), 5.74 - 5.68 (m, 2H), 4.15 (td, *J* = 8.1, 4.8 Hz, 1H), 4.11 - 4.03 (m, 1H), 3.91 - 3.86 (m, 1H), 3.84 (s, 3H), 3.06 (d, *J* = 10.9 Hz, 2H), 2.85 - 2.67 (m, 8H), 2.61 (s, 2H), 2.54 (s, 3H), 2.37 (m, 4H), 2.17 (s, 1H), 2.07 (d, *J* = 11.8 Hz, 2H), 1.70 (d, *J* = 12.9 Hz, 2H). : 614.6 $[M+H]^+$	1.00

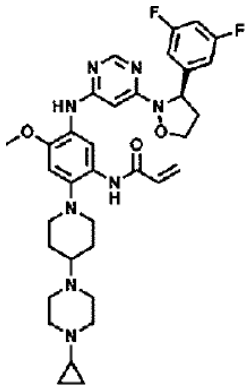
[464]

48		N-(4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl) acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.57 (m, 2H), 8.37 (s, 1H), 7.70 (dd, *J* = 8.0, 2.4 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.94 (s, 1H), 6.81 (s, 1H), 6.72 (s, 1H), 6.36 (dd, *J* = 17.2, 1.6 Hz, 1H), 6.26 (dd, *J* = 17.0, 9.9 Hz, 1H), 5.74 (m, 1H), 5.72 - 5.69 (m, 1H), 4.17 - 4.10 (m, 2H), 3.82 (s, 3H), 2.97 (d, *J* = 11.2 Hz, 2H), 2.91 (m, 4H), 2.82 - 2.71 (m, 4H), 2.54 (s, 3H), 2.29 (m, 3H), 2.17 (s, 3H), 2.01 (t, *J* = 11.7 Hz, 2H), 1.87 (d, *J* = 12.6 Hz, 2H), 1.73 - 1.58 (m, 2H).: 614.5 $[M+H]^+$	0.90
49		N-(2-(4-acetylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl) acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.95 (s, 1H), 8.57 (d, *J* = 2.4 Hz, 1H), δ 8.44 (s, 1H), 8.38 (d, *J* = 1.0 Hz, 1H), 7.70 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.98 (s, 1H), 6.72 (d, *J* = 3.9 Hz, 2H), 6.42 - 6.33 (m, 1H), 6.26 (dd, *J* = 16.9, 10.1 Hz, 1H), 5.76 (dd, *J* = 10.0, 1.5 Hz, 1H), 5.72 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.17 (td, *J* = 8.0, 4.4 Hz, 1H), 4.10 (q, *J* = 8.0 Hz, 1H), 3.85 (s, 3H), 3.67 - 3.64 (m, 2H), 2.81 - 2.74 (m, 2H), 2.88 (m, 4H), 2.81 - 2.74 (m, 1H), 2.54 (s, 3H), 2.37 (dtd, *J* = 12.4, 8.1, 4.5 Hz, 1H), 2.17 (s, 3H).: 550.5 $[M+H]^+$	1.17
50		N-(2-(4-dimethylaminopiperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl) acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.57 (d, *J* = 2.4 Hz, 1H), δ 8.45 (s, 1H), 8.36 (d, *J* = 1.1 Hz, 1H), 7.70 (dd, *J* = 8.0, 2.3 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.94 (s, 1H), 6.74 (d, *J* = 2.6 Hz, 1H), 6.71 (d, *J* = 7.3 Hz, 1H), 6.39 - 6.33 (m, 1H), 6.26 (dd, *J* = 17.0, 9.9 Hz, 1H), 5.77 - 5.72 (m, 1H), 5.73 - 5.68 (m, 1H), 4.16 (m, 1H), 4.09 (m, 1H), 3.84 (s, 3H), 3.08 (d, *J* = 11.3 Hz, 2H), 2.84 (dd, *J* = 12.0, 5.0 Hz, 1H), 2.80 - 2.69 (m, 3H), 2.54 (s, 3H), 2.45 (d, *J* = 4.6 Hz, 6H), 2.30 - 2.32 (m, 1H), 2.10 (d, *J* = 12.5 Hz, 2H), 1.76 (t, *J* = 11.5 Hz, 2H).: 550.5 $[M+H]^+$	1.03
51		N-(2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl) acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.58 - 8.53 (m, 2H), 8.34 (s, 1H), 8.00 (s, 1H), 7.70 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 6.80 (s, 1H), 6.68 (d, *J* = 16.4 Hz, 2H), 6.38 - 6.26 (m, 2H), 5.72 (m, 2H), 4.20 - 4.03 (m, 2H), 3.85 (s, 3H), 3.65- 3.54 (m, 2H), 3.07 (dd, *J* = 9.8, 2.4 Hz, 1H), 2.92 - 2.81 (m, 1H), 2.86 - 2.72 (m, 3H), 2.54 (s, 3H), 2.35 (dtt, *J* = 12.3, 8.6, 4.4 Hz, 1H), 1.33 - 1.30 (m, 2H)1.92 (q, *J* = 9.9 Hz, 2H), 1.15 (t, *J* = 7.2 Hz, 3H).: 557.5 $[M+H]^+$	0.92

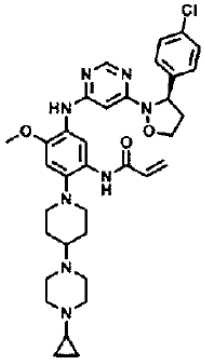
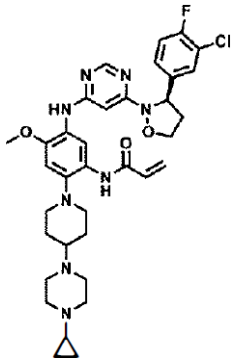
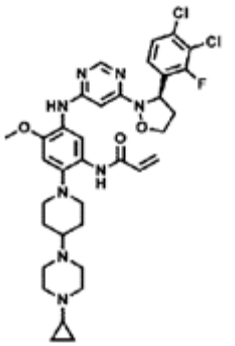
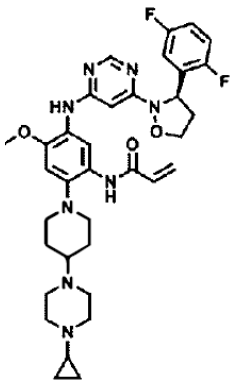
52		N-(4-methoxy-2-(4-(5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-1-yl)amino)phenyl) acrylamide	1H NMR (400 MHz, DMSO-d_6) δ 11.62 (s, 1H), 9.17 (s, 1H), 8.23 (s, 1H), 7.97 (s, 1H), 7.40 - 7.32 (m,4H), 7.30 - 7.24 (m, 1H), 6.87 (d, J = 10.3 Hz, 1H), 6.55 (m, 1H), 6.28 - 6.14 (m, 2H), 5.75 (d, J = 10.3Hz, 1H), 5.52 (d, 1H), 4.74 (s, 1H), 4.48 (d, J = 20.0 Hz, 1H), 4.26 - 4.20 (m, 1H), 3.96 (d, J = 8.9 Hz,2H), 3.81 (s, 3H), 3.21 (m, 4H), 2.92 (m, 5H), 2.67 (m, 4H), 2.36 - 2.25 (m, 2H), 2.07 (d, J = 25.9 Hz,:4H), 611.6[M+H]$^+$	1.35

[465]

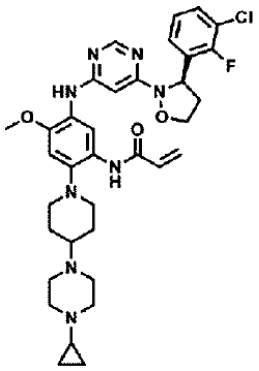
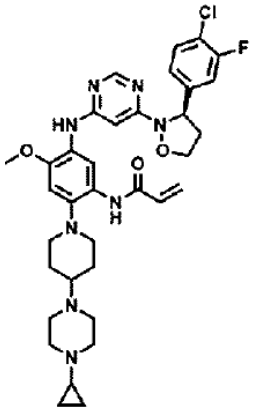
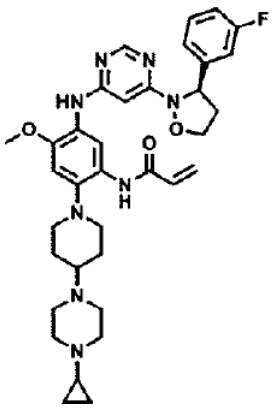
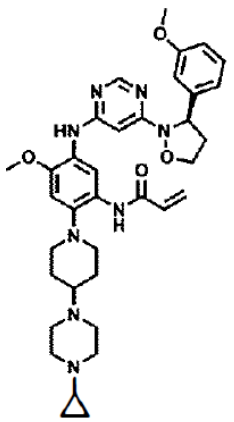
53		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.08 (s, 1H), 7.77 (s, 1H), 7.26 (dd, J = 7.1, 1.4 Hz, 4H), 7.20 (s, 1H), 6.94 (s, 1H), 6.54 (dd, J = 17.0, 10.2 Hz, 1H), 6.33 (dd, J = 16.9, 1.6 Hz, 1H), 5.77 (d, J = 10.2 Hz, 1H), 5.35 (s, 1H), 4.66 (s, 1H), 4.50 (d, J = 12.7 Hz, 1H), 4.33 (t, J = 3.8 Hz, 1H), 4.14 - 4.05 (m, 2H), 3.75 (s, 3H), 3.55 (d, J = 11.5 Hz, 1H), 3.38 (d, J = 1.6 Hz, 1H), 3.20 (s, 2H), 3.04 - 2.88 (m, 3H), 2.37 (ddd, J = 11.8, 8.1, 6.1 Hz, 2H), 2.19 (s, 3H), 2.05 (s, 3H), 1.60 - 1.58 (m, 1H), 1.45 (s, 1H): 598.3 $[M+H]^+$	1.1
54		N-(2-(4-((1S,4S)-2-oxa-5-oxabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.04 (s, 1H), 7.76 (s, 1H), 7.57 (ddd, J = 37.8, 5.8, 3.4 Hz, 1H), 7.28 - 7.23 (m, 3H), 7.23 - 7.16 (m, 2H), 6.83 (s, 1H), 6.53 (d, J = 13.0 Hz, 1H), 6.29 (dd, J = 16.9, 1.6 Hz, 1H), 5.73 (d, J = 10.0 Hz, 1H), 5.30 (s, 1H), 4.68 - 4.54 (m, 2H), 4.33 (d, J = 5.6 Hz, 1H), 4.22 (d, J = 10.7 Hz, 1H), 4.12 - 4.05 (m, 2H), 3.78 (s, 1H), 3.72 (s, 3H), 3.54 (d, J = 11.6 Hz, 1H), 3.38 (d, J = 2.8 Hz, 1H), 2.93 (d, J = 6.8 Hz, 1H), 2.85 - 2.74 (m, 2H), 2.40 - 2.31 (m, 2H), 2.23 - 2.00 (m, 4H), 1.97 (d, J = 12.3 Hz, 3H): 598.3 $[M+H]^+$	1.1
55		N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	613.4$[M+H]^+$	1.07
56		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 7.46 (d, J = 7.4 Hz, 2H), 7.34 (t, J = 7.6 Hz, 2H), 7.23 (d, J = 7.5 Hz, 1H), 6.91 (s, 1H), 6.74 (s, 1H), 6.69 (s, 1H), 6.36 (dd, J = 17.0, 1.6 Hz, 1H), 6.24 (dd, J = 16.9, 10.0 Hz, 1H), 5.76 - 5.71 (m, 1H), 5.71 - 5.67 (m, 1H), 4.15 (td, J = 8.0, 4.5 Hz, 1H), 4.07 (q, J = 8.1 Hz, 1H), 3.83 (s, 3H), 3.05 (d, J = 11.3 Hz, 2H), 2.78 - 2.64 (m, 8H), 2.37 (m, 4H), 2.08 (d, J = 12.4 Hz, 2H), 1.66 (m, 4H), 0.50 - 0.38 (m, 4H) ; 625.50$[M+H]^+$	1.56

57		N-(2-(4-(4-(cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.45 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.04 - 6.98 (m, 2H), 6.97 (s, 1H), 6.77 - 6.64 (m, 3H), 6.42 - 6.23 (m, 2H), 5.74 (dd, *J* = 1.6, 10.0 Hz, 1H), 5.67 (dd, *J* = 4.5, 8.7 Hz, 1H), 4.15 (td, *J* = 4.2, 8.0 Hz, 1H), 4.06 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.11 - 3.01 (m, 2H), 2.82 - 2.61 (m, 10H), 2.43 - 2.28 (m, 2H), 2.12 - 2.04 (m, 2H), 1.74 - 1.61 (m, 3H), 0.51 - 0.40 (m, 4H) ; 661.3[M+H]$^+$	1.23

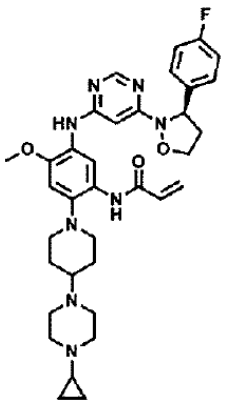
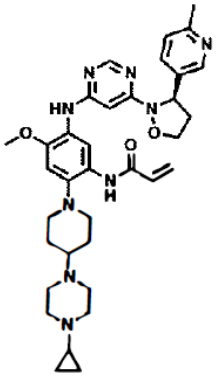
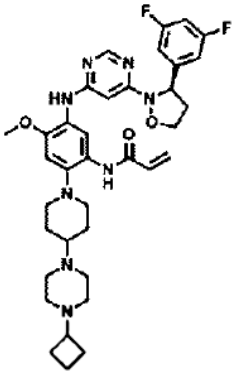
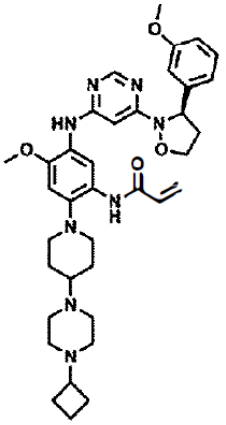
[466]

58		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.74 (s, 1H), 9.16 (s, 1H), 8.27 (s, 2H), 7.95 (s, 1H), 7.44 - 7.33 (m, 7H), 6.88 (s, 2H), 6.68 (dd, J = 17.0, 10.3 Hz, 1H), 6.24 (dd, J = 17.0, 2.0 Hz, 1H), 6.10 (s, 1H), 5.82 - 5.72 (m, 1H), 5.52 (dd, J = 8.4, 5.4 Hz, 2H), 3.88 (q, J = 5.2, 4.0 Hz, 2H), 3.80 (s, 9H), 3.20 (d, J = 11.7 Hz, 5H), 2.96 - 2.84 (m, 3H), 2.78 (t, J = 11.5 Hz, 4H), 2.34 - 2.21 (m, 3H), 2.22 - 1.95 (m, 8H), 1.03 (d, J = 24.0 Hz, 3H), 0.80 - 0.60 (m, 4H); 650.56[M+H]$^+$	1.34
59		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide;	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (d, J = 3.1 Hz, 1H), 8.07 (s, 1H), 7.45 (dd, J = 2.2, 7.1 Hz, 1H), 7.37 - 7.25 (m, 1H), 7.12 (t, J = 8.8 Hz, 1H), 6.81 (s, 1H), 6.45 (dd, J = 10.2, 17.0 Hz, 1H), 6.34 (s, 1H), 6.26 (d, J = 16.8 Hz, 1H), 5.70 (d, J = 10.3 Hz, 1H), 5.47 - 5.37 (m, 1H), 4.05 (td, J = 4.3, 8.0 Hz, 1H), 3.87 (q, J = 8.0 Hz, 1H), 3.77 (s, 3H), 3.13 - 3.05 (m, 2H), 2.97 - 2.88 (m, 3H), 2.83 - 2.66 (m, 8H), 2.23 (dtt, J = 3.5, 8.1, 12.6 Hz, 1H), 2.10 - 1.99 (m, 2H), 1.83 - 1.68 (m, 3H), 0.83 - 0.75 (m, 1H), 0.50- 0.42 (m, 2H), 0.42 - 0.34 (m, 2H) ; 677.3[M+H]$^+$	1.32
60		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl) acrylamide;	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (d, J = 2.9 Hz, 1H), 8.06 (s, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.27 (dd, J = 1.6, 8.6 Hz, 1H), 6.81 (s, 1H), 6.45 (dd, J = 10.2, 16.9 Hz, 1H), 6.37 (s, 1H), 6.26 (d, J = 16.6 Hz, 1H), 5.78 - 5.56 (m, 2H), 4.06 (td, J = 3.9, 7.9 Hz, 1H), 3.88 (q, J = 8.0 Hz, 1H), 3.78 (s, 3H), 3.12 - 3.03 (m, 2H), 2.95 - 2.83 (m, 3H), 2.83 - 2.65 (m, 8H), 2.17 (dtd, J = 4.8, 8.0, 12.8 Hz, 1H), 2.08 - 1.97 (m, 2H), 1.81 - 1.66 (m, 3H), 0.83 - 0.78 (m, 1H), 0.51 - 0.42 (m, 2H), 0.41 - 0.33 (m, 2H) ; 711.3[M+H]$^+$	1.52
61		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl) acrylamide;	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.19 (d, J = 8.8 Hz, 1H), 8.07 (s, 1H), 7.14 (ddt, J = 2.8, 5.9, 8.8 Hz, 1H), 7.04 (td, J = 4.4, 9.3 Hz, 1H), 6.92 (tt, J = 3.6, 8.0 Hz, 1H), 6.81 (s, 1H), 6.53 - 6.34 (m, 2H), 6.26 (d, J = 16.7 Hz, 1H), 5.76 - 5.60 (m, 2H), 4.04 (td, J = 4.2, 8.0 Hz, 1H), 3.88 (q, J = 8.0 Hz, 1H), 3.78 (s, 3H), 3.13 - 3.04 (m, 2H), 2.97 - 2.84 (m, 3H), 2.84 - 2.65 (m, 8H), 2.16 (dtd, J = 4.6, 8.0, 12.5 Hz, 1H), 2.08 - 1.98 (m, 2H), 1.82 - 1.66 (m, 3H), 0.83 - 0.75 (m, 1H), 0.51 - 0.42 (m, 2H), 0.40 - 0.34 (m, 2H) ; 661.3[M+H]$^+$	1.38

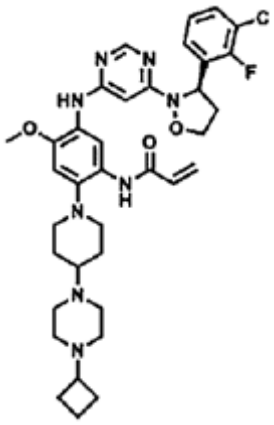
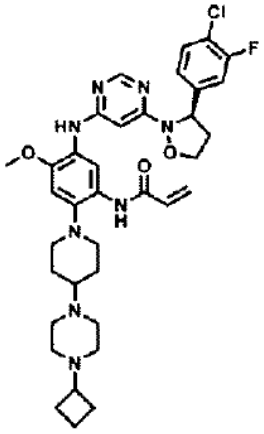
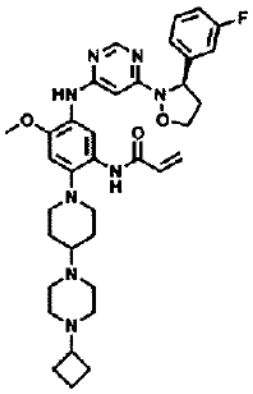
[467]

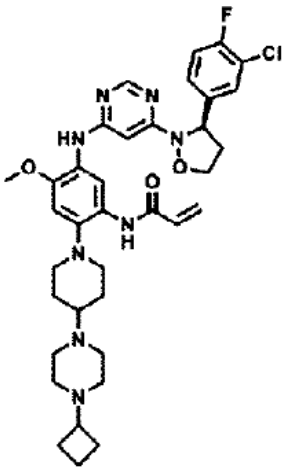
62		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (d, J = 8.5 Hz, 1H), 8.17 (s, 1H), 7.49 (t, J = 7.3 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.16 (t, J = 7.9 Hz, 1H), 6.92 (s, 1H), 6.56 (dd, J = 10.2, 16.9 Hz, 1H), 6.48 (d, J = 6.0 Hz, 1H), 6.37 (d, J = 16.8 Hz, 1H), 5.80 (t, J = 9.9 Hz, 2H), 4.16 (td, J = 4.2, 8.0 Hz, 1H), 3.99 (q, J = 8.0 Hz, 1H), 3.89 (s, 3H), 3.24 - 3.16 (m, 2H), 3.08 - 2.95 (m, 3H), 2.95 - 2.76 (m, 8H), 2.32 - 2.22 (m, 1H), 2.19 - 2.10 (m, 2H), 1.94 - 1.77 (m, 3H), 0.95 - 0.88 (m, 1H), 0.61 - 0.53 (m, 2H), 0.52 - 0.44 (m, 2H) ; 677.3[M+H]$^+$	1.48
63		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.32 (s, 1H), 8.18 (d, J = 0.9 Hz, 1H), 7.45 (t, J = 7.9 Hz, 1H), 7.34 (dd, J = 2.0, 10.5 Hz, 1H), 7.27 (dd, J = 2.0, 8.3 Hz, 1H), 6.92 (s, 1H), 6.57 (dd, J = 10.3, 17.0 Hz, 1H), 6.46 (d, J = 1.0 Hz, 1H), 6.36 (dd, J = 1.5, 17.0 Hz, 1H), 5.81 (dd, J = 1.5, 10.3 Hz, 1H), 5.56 (dd, J = 4.7, 8.6 Hz, 1H), 4.15 (td, J = 4.1, 7.9 Hz, 1H), 3.98 (q, J = 8.0 Hz, 1H), 3.88 (s, 3H), 3.22 - 3.08 (m, 2H), 2.87 - 2.72 (m, 11H), 2.57 - 2.43 (m, 1H), 2.34 (dtd, J = 4.5, 8.0, 12.6 Hz, 1H), 2.17 - 2.03 (m, 2H), 1.86 - 1.66 (m, 3H), 0.61 - 0.48 (m, 2H), 0.48 - 0.38 (m, 2H) ;677.3[M+H]$^+$	1.42
64		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.91 (s, 1H), 9.19 (s, 1H), 8.30 (s, 2H), 7.94 (s, 1H), 7.42 (td, J = 7.9, 6.0 Hz, 2H), 7.24 - 7.16 (m, 3H), 7.12 (td, J = 8.7, 2.7 Hz, 2H), 6.89 (s, 1H), 6.70 (dd, J = 17.0, 10.2 Hz, 2H), 6.25 (dd, J = 17.0, 1.9 Hz, 2H), 6.11 (s, 1H), 5.81 - 5.71 (m, 2H), 5.54 (dd, J = 8.5, 5.4 Hz, 2H), 3.80 (t, J = 6.1 Hz, 3H), 3.80 (s, 11H), 3.22 (d, J = 11.5 Hz, 5H), 2.92 (dtd, J = 12.2, 8.0, 7.5, 4.2 Hz, 3H), 2.79 (t, J = 11.7 Hz, 4H), 2.32 (dtd, J = 12.7, 7.6, 5.2 Hz, 2H), 2.23 - 1.96 (m, 8H), 1.13 (s, 4H), 0.91 - 0.72 (m, 4H) ; 643.59[M+H]$^+$	1.34
65		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.41 (s, 1H), 10.22 (s, 1H), 9.24 (s, 1H), 8.32 (s, 1H), 7.87 (s, 1H), 7.29 (t, J = 7.8 Hz, 1H), 6.89 (dt, J = 14.1, 6.9 Hz, 4H), 6.72 (dd, J = 16.9, 10.3 Hz, 1H), 6.25 (dd, J = 17.0, 1.5 Hz, 1H), 5.76 (d, J = 11.5 Hz, 1H), 5.50 - 5.44 (m, 1H), 4.33 (dd, J = 11.0, 7.4 Hz, 1H), 4.12 - 4.05 (m, 3H), 3.79 (s, 3H), 3.75 (s, 3H), 3.23 (d, J = 10.7 Hz, 2H), 3.00 - 2.87 (m, 2H), 2.81 (t, J = 11.2 Hz, 2H), 2.32 (td, J = 12.7, 7.6 Hz, 1H), 2.22 - 2.06 (m, 4H), 1.61 (dd, J = 8.2, 4.5 Hz, 3H), 1.46 - 1.38 (m, 3H), 1.19 (s, 2H), 0.87 - 0.81 (m, 2H) ; 655.62 [M+H]$^+$.	1.13

[468]

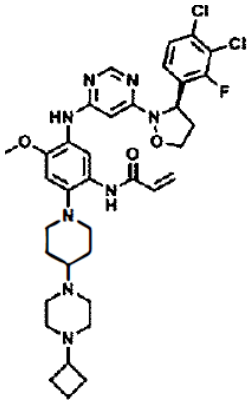
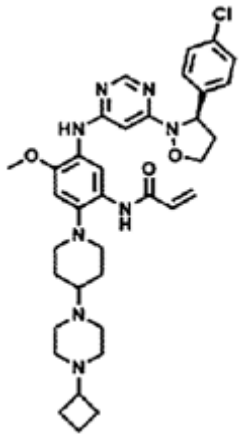
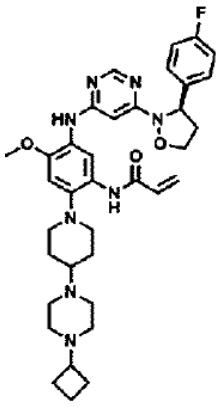
66		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.88 (s, 1H), 9.18 (s, 1H), 8.29 (s, 1H), 7.93 (s, 1H), 7.40 (dd, J = 8.6, 5.6 Hz, 2H), 7.20 (t, J = 8.8 Hz, 2H), 6.80 (s, 1H), 6.60 (dd, J = 17.0, 10.3 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.08 (s, 1H), 5.76 (dd, J = 10.1, 2.0 Hz, 1H), 5.52 (t, J = 7.1 Hz, 1H), 4.32 - 4.26 (m, 1H), 4.04 (d, J = 7.7 Hz, 3H), 3.80 (s, 3H), 3.71 (s, 4H), 3.41 - 3.35 (m, 2H), 3.21 (d, J = 11.5 Hz, 2H), 2.90 (d, J = 9.0 Hz, 1H), 2.80 (d, J = 11.8 Hz, 2H), 2.34 - 2.24 (m, 2H), 2.16 (s, 2H), 2.06 (s, 1H), 1.65 - 1.56 (m, 1H), 1.48 - 1.40 (m, 1H), 1.11 (s, 2H), 0.81 (d, J = 7.0 Hz, 2H) ; 643.34[M+H]$^+$	1.14
67		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.86 (s, 1H), 8.57 (d, J = 2.4 Hz, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.70 (dd, J = 8.0, 2.4 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 6.94 (s, 1H), 6.74 (s, 1H), 6.71 (s, 1H), 6.45 - 6.31 (m, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.74 (dd, J = 9.9, 1.5 Hz, 1H), 5.72 - 5.68 (m, 1H), 4.15 - 4.09 (m, 2H), 3.84 (s, 3H), 3.06 (d, J = 12.6 Hz, 2H), 2.74 (m, 8H), 2.54 (s, 3H), 2.36 (ddt, J = 16.1, 7.9, 4.5 Hz, 4H), 2.08 (d, J = 12.4 Hz, 2H), 1.75 - 1.62 (m, 4H), 0.52 - 0.39 (m, 4H) ; 640.63[M+H]$^+$	0.85
68		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (s, 1H), 8.07 (s, 1H), 7.01 - 6.91 (m, 2H), 6.81 (s, 1H), 6.73 (tt, J = 2.4, 9.1 Hz, 1H), 6.44 (dd, J = 10.2, 17.0 Hz, 1H), 6.35 (s, 1H), 6.25 (dd, J = 1.5, 17.0 Hz, 1H), 5.70 (d, J = 10.3 Hz, 1H), 5.46 (dd, J = 4.8, 8.7 Hz, 1H), 4.04 (td, J = 4.1, 7.9 Hz, 1H), 3.86 (q, J = 8.0 Hz, 1H), 3.77 (s, 3H), 3.14 - 3.03 (m, 3H), 2.88 - 2.66 (m, 11H), 2.55 (tt, J = 3.7, 11.4 Hz, 1H), 2.29 - 2.17 (m, 2H), 2.16 - 2.06 (m, 2H), 2.00 - 1.92 (m, 4H), 1.77 - 1.68 (m, 4H) ;675.4[M+H]$^+$	1.23
69		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.66 (s, 1H), 10.27 (s, 1H), 9.27 (s, 1H), 8.32 (s, 1H), 7.87 (s, 1H), 7.29 (t, J = 7.8 Hz, 1H), 6.88 (dd, J = 12.2, 7.1 Hz, 4H), 6.74 (dd, J = 16.8, 10.2 Hz, 1H), 6.30 - 6.21 (m, 1H), 6.00 (s, 1H), 5.77 (d, J = 11.4 Hz, 1H), 5.52 - 5.42 (m, 1H), 4.33 (dd, J = 11.0, 7.4 Hz, 2H), 4.09 (dd, J = 15.1, 7.6 Hz, 4H), 3.79 (s, 3H), 3.75 (s, 3H), 3.66 (d, J = 12.2 Hz, 4H), 3.46 (d, J = 11.8 Hz, 2H), 3.24 (d, J = 10.6 Hz, 2H), 2.99 - 2.89 (m, 1H), 2.82 (t, J = 11.0 Hz, 2H), 2.45 - 2.28 (m, 3H), 2.19 (d, J = 7.8 Hz, 4H), 1.81 - 1.66 (m, 2H), 1.61 (dd, J = 7.5, 3.8 Hz, 2H), 1.44 (d, J = 2.7 Hz, 2H), 1.24 (s, 1H) ; 669.62[M+H]$^+$.	1.10

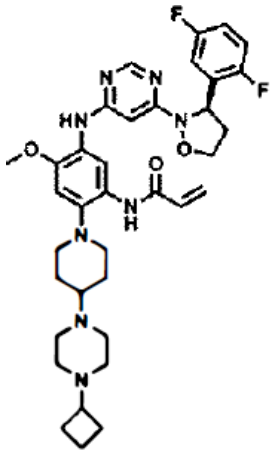
[469]

70		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.99 (s, 1H), 9.16 (s, 1H), 8.67 (t, J = 5.6 Hz, 1H), 8.24 (s, 1H), 8.02 (s, 1H), 7.58 - 7.48 (m, 1H), 7.43 - 7.35 (m, 1H), 7.24 (t, J = 7.9 Hz, 1H), 6.88 (s, 1H), 6.60 (ddd, J = 16.5, 10.4, 5.9 Hz, 2H), 6.25 (ddd, J = 17.1, 5.2, 2.0 Hz, 3H), 5.82 (dd, J = 10.3, 2.0 Hz, 1H), 5.78 - 5.60 (m, 1H), 3.98 (d, J = 7.8 Hz, 1H), 3.81 (s, 3H), 3.60 (q, J = 7.4 Hz, 1H), 3.22 - 3.16 (m, 2H), 3.09 - 3.01 (m, 2H), 2.74 (d, J = 4.9 Hz, 8H), 2.42 - 2.32 (m, 1H), 2.19 (td, J = 14.7, 13.5, 6.9 Hz, 4H), 1.93 - 1.82 (m, 4H), 1.76 (dd, J = 20.2, 10.2 Hz, 2H). ; 691.5[M+H]$^+$	1.26
71		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.19 (s, 1H), 8.29 (d, J = 11.0 Hz, 1H), 8.03 - 7.88 (m, 1H), 7.59 (t, J = 8.1 Hz, 1H), 7.41 (d, J = 10.7 Hz, 1H), 7.25 (d, J = 8.3 Hz, 1H), 6.89 (d, J = 5.7 Hz, 1H), 6.60 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (d, J = 16.9 Hz, 1H), 6.14 (s, 1H), 5.76 (d, J = 10.2 Hz, 1H), 5.54 (dd, J = 8.5, 5.4 Hz, 1H), 4.37 - 4.19 (m, 1H), 3.81 (s, 5H), 3.75 (s, 4H), 3.20 (s, 3H), 2.80 (s, 2H), 2.77 (dd, J = 22.8, 11.2 Hz, 3H), 2.45 - 2.26 (m, 4H), 2.19 (dd, J = 17.1, 9.1 Hz, 5H), 2.05 (d, J = 12.4 Hz, 2H), 1.74 (dt, J = 28.6, 9.7 Hz, 3H) ; 691.5[M+H]$^+$	1.24
72		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.12 (s, 1H), 9.24 (s, 1H), 8.31 (s, 1H), 7.90 (s, 1H), 7.43 (q, J = 7.5 Hz, 1H), 7.16 (dt, J = 24.6, 8.5 Hz, 3H), 6.90 (s, 1H), 6.72 (dd, J = 16.9, 10.2 Hz, 1H), 6.26 (d, J = 17.0 Hz, 1H), 6.07 (s, 1H), 5.77 (d, J = 10.3 Hz, 1H), 5.60 - 5.46 (m, 1H), 4.32 (q, J = 7.0 Hz, 2H), 4.07 (q, J = 7.6 Hz, 2H), 3.80 (s, 3H), 3.23 (d, J = 11.4 Hz, 4H), 2.95 (h, J = 6.8, 6.2 Hz, 2H), 2.80 (t, J = 11.6 Hz, 3H), 2.76 (dd, J = 22.8, 11.2 Hz, 3H), 2.46 - 2.28 (m, 3H), 2.21 (q, J = 10.0, 9.7 Hz, 5H), 2.15 - 2.00 (m, 2H), 1.74 (dt, J = 28.4, 9.0 Hz, 2H) ; 657.57[M+H]$^+$	1.16

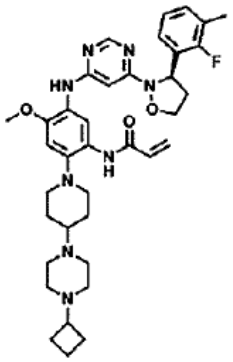
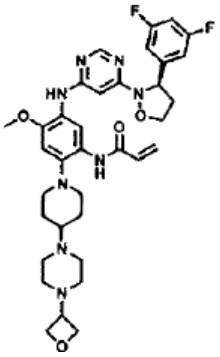
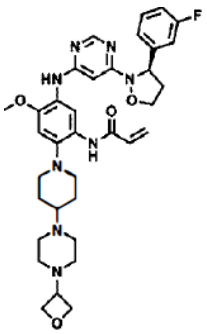
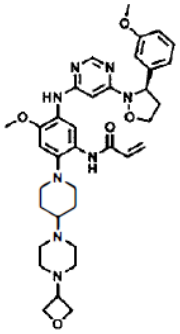
73		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.94 (s, 1H), 9.20 (s, 1H), 8.30 (d, J = 2.2 Hz, 1H), 7.94 (s, 1H), 7.58 (dd, J = 7.1, 2.1 Hz, 1H), 7.43 (s, 1H), 7.41 - 7.35 (m, 2H), 6.90 (s, 1H), 6.70 (dd, J = 16.9, 10.3 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.13 (s, 1H), 5.76 (dd, J = 9.9, 2.0 Hz, 1H), 5.53 (dd, J = 8.5, 5.4 Hz, 1H), 3.89 (t, J = 6.1 Hz, 7H), 3.80 (d, J = 3.2 Hz, 8H), 3.43 (d, J = 12.3 Hz, 6H), 3.22 (d, J = 11.7 Hz, 4H), 3.12 (qd, J = 7.3, 4.2 Hz, 1H), 2.92 (dt, J = 12.3, 5.4 Hz, 2H), 2.40 (t, J = 9.7 Hz, 3H), 2.36 - 2.13 (m, 8H), 1.75 (dq, J = 29.1, 10.0, 9.4 Hz, 3H), 1.28 (dd, J = 12.7, 6.7 Hz, 7H) ; 501.59[M+H]$^+$	1.26

[470]

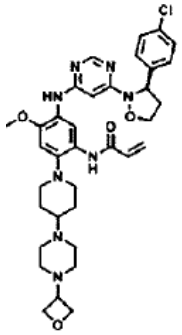
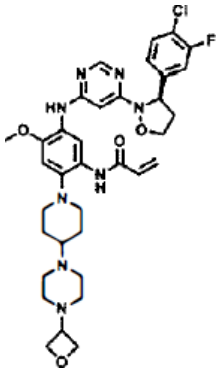
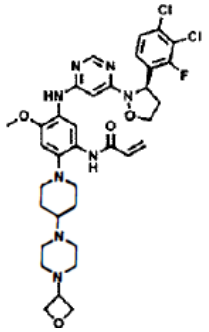
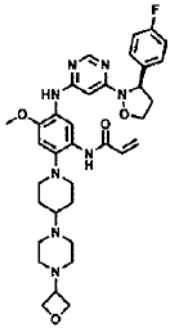
74		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.47 (s, 1H), 9.15 (s, 1H), 8.25 (s, 1H), 8.03 (s, 1H), 7.53 (dd, J = 8.5, 1.5 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 6.88 (s, 1H), 6.67 (dd, J = 16.9, 10.2 Hz, 1H), 6.24 (dd, J = 17.0, 2.0 Hz, 2H), 5.75 (d, J = 11.0 Hz, 1H), 5.70 (dd, J = 8.7, 5.5 Hz, 1H), 4.28 - 4.24 (m, 1H), 3.99 (d, J = 7.6 Hz, 1H), 3.81 (s, 3H), 3.38 (q, J = 7.0 Hz, 5H), 3.21 (d, J = 11.4 Hz, 2H), 2.95 - 2.86 (m, 2H), 2.77 (d, J = 11.7 Hz, 2H), 2.42 - 2.33 (m, 3H), 2.31 - 2.24 (m, 2H), 2.20 (d, J = 10.0 Hz, 5H), 2.04 (d, J = 11.8 Hz, 2H), 1.82 - 1.65 (m, 3H) ; 725.28[M+H]$^+$	1.44
75		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.68 (s, 1H), 10.33 (s, 1H), 9.30 (s, 1H), 8.33 (s, 1H), 7.87 (s, 1H), 7.41 (dd, J = 24.5, 8.5 Hz, 4H), 6.92 (s, 1H), 6.75 (dd, J = 16.6, 10.3 Hz, 1H), 6.26 (dd, J = 17.0, 1.6 Hz, 1H), 6.05 (s, 1H), 5.77 (d, J = 11.7 Hz, 1H), 5.53 (dd, J = 7.8, 5.7 Hz, 1H), 4.36 - 4.29 (m, 3H), 4.12 - 4.05 (m, 4H), 3.81 (s, 3H), 3.66 (d, J = 12.5 Hz, 4H), 3.53 - 3.40 (m, 3H), 3.25 (d, J = 10.4 Hz, 2H), 3.01 - 2.90 (m, 1H), 2.84 (d, J = 10.6 Hz, 2H), 2.40 (dd, J = 19.8, 9.9 Hz, 2H), 2.35 - 2.25 (m, 1H), 2.20 (d, J = 7.7 Hz, 4H), 1.84 - 1.66 (m, 2H), 1.66 - 1.52 (m, 2H), 1.50 - 1.41 (m, 1H), 1.23 (s, 1H) ; 673.60[M+H]$^+$.	1.23
76		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 9.17 (s, 1H), 8.28 (s, 1H), 7.95 (s, 1H), 7.43 - 7.37 (m, 2H), 7.19 (s, 2H), 6.88 (s, 1H), 6.60 (dd, J = 17.0, 10.4 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.09 (s, 1H), 5.76 (d, J = 10.5 Hz, 1H), 5.52 (t, J = 7.1 Hz, 1H), 4.29 (d, J = 4.6 Hz, 1H), 4.03 (d, J = 7.8 Hz, 1H), 3.80 (s, 3H), 3.64 (d, J = 12.5 Hz, 4H), 3.23 (s, 3H), 2.91 (s, 1H), 2.79 (s, 2H), 2.30 (t, J = 9.6 Hz, 2H), 2.34 - 2.27 (m, 2H), 2.19 (t, J = 11.1 Hz, 5H), 1.83 - 1.67 (m, 3H), 1.62 (d, J = 5.0 Hz, 2H), 1.43 (d, J = 5.1 Hz, 2H) ; 657.36[M+H]$^+$	1.12

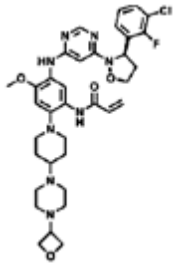
77		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.95 (s, 1H), 9.21 (s, 1H), 8.30 (s, 1H), 7.95 (s, 1H), 7.32 (td, J = 9.3, 4.5 Hz, 1H), 7.25 - 7.12 (m, 3H), 6.90 (s, 1H), 6.71 (dd, J = 16.9, 10.3 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.19 (s, 1H), 5.81 - 5.72 (m, 2H), 5.66 (dd, J = 8.7, 5.6 Hz, 1H), 3.80 (t, J = 6.2 Hz, 1H), 3.81 (s, 4H), 3.53 - 3.33 (m, 4H), 3.27 - 3.18 (m, 2H), 3.11 (tt, J = 7.4, 3.7 Hz, 1H), 2.92 (ddd, J = 13.1, 8.7, 5.2 Hz, 2H), 2.40 (t, J = 9.9 Hz, 2H), 2.34 - 2.00 (m, 9H), 1.73 (dt, J = 29.2, 9.9 Hz, 3H), 1.34 - 1.21 (m, 8H) ; 675.67[M+H]$^+$	1.20

[471]

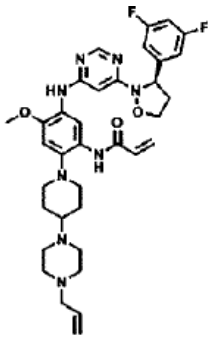
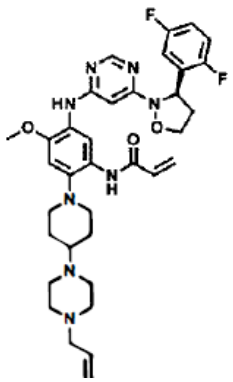
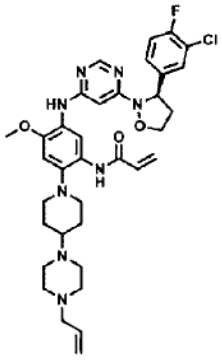
78		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.99 (s, 1H), 8.61 (s, 1H), 8.14 (s, 2H), 7.28 (t, J = 7.4 Hz, 1H), 7.19 (t, J = 7.4 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.83 (s, 1H), 6.64 (dd, J = 17.0, 10.2 Hz, 1H), 6.36 (s, 1H), 6.23 (ddd, J = 16.7, 14.9, 1.9 Hz, 2H), 6.08 (dd, J = 17.3, 10.3 Hz, 1H), 5.88 (dd, J = 10.3, 1.9 Hz, 1H), 5.73 (dq, J = 8.6, 4.6 Hz, 2H), 4.14 (td, J = 7.9, 3.8 Hz, 1H), 3.80 (s, 3H), 3.50 (h, J = 6.6 Hz, 4H), 3.15 - 3.05 (m, 8H), 2.78 (dtd, J = 11.8, 7.9, 3.9 Hz, 2H), 2.26 (d, J = 1.9 Hz, 3H), 2.19 - 2.09 (m, 2H), 2.04 (s, 4H), 1.77 (s, 2H), 1.68 (q, J = 9.5 Hz, 2H). ; 671.6[M+H]$^+$	1.22
79		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (s, 1H), 8.07 (s, 1H), 7.04 - 6.91 (m, 2H), 6.81 (s, 1H), 6.77 - 6.68 (m, 1H), 6.45 (dd, J = 10.3, 16.9 Hz, 1H), 6.35 (d, J = 3.8 Hz, 1H), 6.25 (dd, J = 1.6, 17.0 Hz, 1H), 5.70 (dd, J = 1.6, 10.2 Hz, 1H), 5.46 (dd, J = 4.8, 8.7 Hz, 1H), 4.04 (td, J = 4.0, 7.8 Hz, 1H), 3.86 (q, J = 8.0 Hz, 1H), 3.77 (s, 3H), 3.51 - 3.44 (m, 1H), 3.11 - 3.01 (m, 3H), 2.89 - 2.62 (m, 8H), 2.60 - 2.50 (m, 1H), 2.43 (s, 3H), 2.20 - 2.16 (m, 2H), 2.06 - 1.96 (m, 2H), 1.77 - 1.64 (m, 2H), 0.83 - 0.75 (m, 2H) ; 677.3[M+H]$^+$	1.26
80		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.28 (s, 1H), 9.08 (s, 1H), 8.24 (s, 1H), 8.04 (s, 1H), 7.41 (q, J = 7.5 Hz, 1H), 7.21 (dd, J = 17.1, 9.1 Hz, 2H), 7.11 (td, J = 8.6, 2.7 Hz, 1H), 6.86 (s, 1H), 6.62 (dd, J = 16.9, 10.3 Hz, 1H), 6.33 - 6.15 (m, 2H), 5.75 (d, J = 10.3 Hz, 1H), 5.54 (dd, J = 8.6, 5.3 Hz, 1H), 4.61 (t, J = 6.7 Hz, 2H), 4.47 (t, J = 6.1 Hz, 2H), 4.22 (td, J = 7.7, 4.0 Hz, 2H), 3.94 (q, J = 7.8 Hz, 3H), 3.81 (s, 3H), 3.38 - 3.30 (m, 4H), 3.21 - 3.13 (m, 2H), 2.85 (dtd, J = 12.0, 7.8, 4.1 Hz, 2H), 2.76 (t, J = 11.7 Hz, 3H), 2.28 (ddd, J = 12.8, 10.5, 6.6 Hz, 2H), 2.13 (d, J = 11.9 Hz, 2H), 1.94 (tt, J = 14.2, 7.0 Hz, 2H) ; 650.56[M+H]$^+$	1.16
81		N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.12 (s, 1H), 9.16 (d, J = 5.5 Hz, 1H), 8.33 (s, 1H), 7.85 (s, 1H), 7.33 - 7.25 (m, 1H), 6.91 - 6.86 (m, 4H), 6.76 - 6.67 (m, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 2H), 5.49 - 5.42 (m, 2H), 4.77 (d, J = 6.4 Hz, 2H), 4.62 (t, J = 3.8 Hz, 1H), 4.34 (td, J = 7.5, 4.4 Hz, 1H), 4.10 (q, J = 7.7 Hz, 1H), 3.79 (s, 3H), 3.75 (s, 3H), 3.34 (s, 2H), 3.24 (d, J = 11.3 Hz, 2H), 2.95 (dp, J = 12.3, 4.6, 3.6 Hz, 1H), 2.84 (t, J = 11.6 Hz, 2H), 2.39 - 2.25 (m, 2H), 2.16 (d, J = 12.3 Hz, 2H), 2.08 (s, 8H), 1.29 - 1.22 (m, 2H); 671.65 [M+H]$^+$	1.11

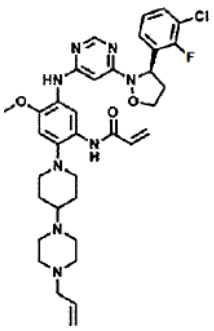
[472]

82		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	676.23 $[M+H]^+$	1.21
83		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.10 (s, 1H), 9.15 (d, J = 4.7 Hz, 1H), 8.33 (s, 1H), 7.87 (s, 1H), 7.60 (t, J = 8.1 Hz, 1H), 7.41 (dd, J = 10.3, 2.0 Hz, 1H), 7.24 (dd, J = 8.4, 1.9 Hz, 1H), 6.91 (s, 1H), 6.70 (ddd, J = 15.7, 10.4, 4.2 Hz, 1H), 6.31 - 6.17 (m, 1H), 6.05 (d, J = 31.5 Hz, 1H), 5.77 (d, J = 10.4 Hz, 1H), 5.53 (dd, J = 8.5, 5.5 Hz, 1H), 4.74 (t, J = 6.0 Hz, 2H), 4.32 (dd, J = 7.6, 4.4 Hz, 2H), 3.80 (s, 3H), 3.32 (d, J = 3.2 Hz, 2H), 3.23 (d, J = 11.4 Hz, 4H), 3.05 - 2.80 (m, 2H), 2.80 - 2.63 (m, 2H), 2.44 (s, 8H), 2.40 - 2.23 (m, 2H), 2.22 - 1.94 (m, 2H) : 603.5$[M+H]^+$	1.25
84		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.95 (s, 1H), 9.12 (d, J = 4.7 Hz, 1H), 8.32 (s, 1H), 7.91 (s, 1H), 7.54 (dd, J = 8.6, 1.6 Hz, 1H), 7.38 (t, J = 8.1 Hz, 1H), 6.90 (s, 1H), 6.66 (d, J = 13.4 Hz, 1H), 6.25 (d, J = 16.5 Hz, 1H), 6.11 (s, 1H), 5.77 (s, 1H), 5.68 (t, J = 7.2 Hz, 1H), 4.67 (d, J = 27.0 Hz, 5H), 4.34 (d, J = 4.2 Hz, 1H), 4.07 (d, J = 7.8 Hz, 2H), 3.81 (s, 3H), 3.71 (d, J = 16.1 Hz, 3H), 3.41 (dd, J = 22.8, 7.0 Hz, 5H), 3.01 - 2.95 (m, 1H), 2.79 (d, J = 8.6 Hz, 3H), 2.14 (s, 2H) :727.26$[M+H]^+$	1.42
85		N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 9.10 (s, 1H), 8.30 (s, 1H), 7.92 (s, 1H), 7.44 - 7.36 (m, 2H), 7.20 (t, J = 8.8 Hz, 2H), 6.88 (s, 1H), 6.67 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.03 (s, 1H), 5.80 - 5.73 (m, 1H), 5.51 (s, 1H), 4.64 (d, J = 6.8 Hz, 2H), 4.55 (s, 2H), 4.30 (s, 1H), 4.05 (d, J = 7.7 Hz, 1H), 3.80 (s, 3H), 3.63 (s, 2H), 3.38 (d, J = 6.9 Hz, 3H), 3.20 (d, J = 11.6 Hz, 6H), 2.91 (dd, J = 8.5, 4.6 Hz, 1H), 2.77 (d, J = 11.9 Hz, 2H), 2.33 - 2.27 (m, 1H), 2.14 (d, J = 11.2 Hz, 2H), 2.01 (s, 2H), 1.10 (d, J = 7.0 Hz, 1H) : 659.34$[M+H]^+$	1.15

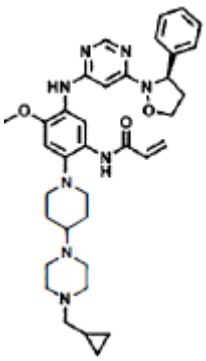
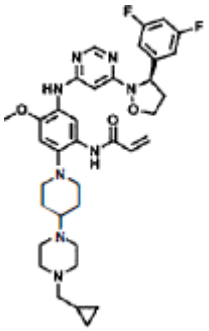
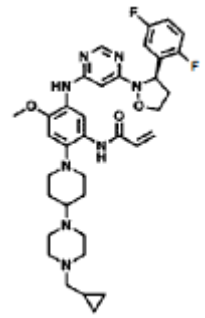
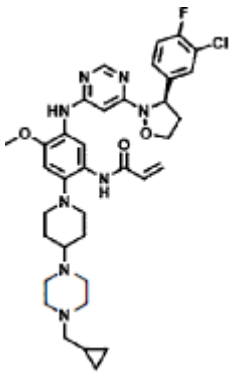
86		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.05 (s, 1H), 8.89 (s, 1H), 8.19 (s, 1H), 8.11 (s, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.23 (t, J = 7.9 Hz, 1H), 6.85 (s, 1H), 6.60 (dd, J = 17.0, 10.1 Hz, 1H), 6.34 (s, 1H), 6.29 - 6.18 (m, 1H), 5.73 (td, J = 9.2, 8.4, 3.8 Hz, 2H), 4.60 (t, J = 6.6 Hz, 2H), 4.46 (t, J = 6.1 Hz, 2H), 4.20 (dd, J = 8.0, 3.7 Hz, 1H), 3.89 (t, J = 8.0 Hz, 1H), 3.81 (s, 3H), 3.16 (d, J = 12.0 Hz, 8H), 2.97 (s, 2H), 2.85 (dtd, J = 11.8, 7.7, 3.5 Hz, 2H), 2.75 (t, J = 11.8 Hz, 2H), 2.31 - 2.16 (m, 2H), 2.12 (d, J = 11.5 Hz, 2H), 1.98 - 1.81 (m, 2H) ; 603.5[M+H]$^+$	1.30

[473]

87		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.74 (s, 1H), 9.17 (s, 1H), 8.29 (s, 1H), 7.97 (s, 1H), 7.21 - 7.05 (m, 4H), 6.89 (s, 1H), 6.68 (dd, J = 17.0, 10.2 Hz, 1H), 6.31 - 6.12 (m, 3H), 6.07 - 5.91 (m, 2H), 5.76 (dd, J = 10.1, 2.0 Hz, 1H), 5.63 (d, J = 17.0 Hz, 2H), 3.81 (s, 13H), 3.57 (s, 8H), 3.21 (d, J = 11.6 Hz, 3H), 2.96 - 2.86 (m, 2H), 2.81 (q, J = 14.1, 11.5 Hz, 3H), 2.32 (dq, J = 12.8, 7.6 Hz, 2H), 2.23 - 1.96 (m, 6H) ; 661.59[M+H]$^+$	1.61
88		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.90 (s, 1H), 9.19 (s, 1H), 8.30 (s, 1H), 7.95 (s, 1H), 7.32 (td, J = 9.3, 4.4 Hz, 1H), 7.26 - 7.11 (m, 2H), 6.90 (s, 1H), 6.69 (dd, J = 16.9, 10.2 Hz, 1H), 6.31 - 6.10 (m, 2H), 5.99 (ddt, J = 17.1, 10.2, 7.0 Hz, 1H), 5.80 - 5.71 (m, 2H), 5.70 - 5.52 (m, 3H), 3.81 (s, 4H), 3.74 - 3.49 (m, 8H), 3.22 (d, J = 11.4 Hz, 2H), 2.92 (ddd, J = 11.9, 7.7, 4.4 Hz, 1H), 2.80 (t, J = 11.7 Hz, 2H), 2.36 - 2.22 (m, 1H), 2.22 - 2.00 (m, 4H) ; 661.54[M+H]$^+$	1.16
89		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.53 (s, 1H), 10.39 (s, 1H), 9.31 (s, 1H), 8.35 (s, 1H), 7.88 (s, 1H), 7.58 (dd, J = 7.1, 2.0 Hz, 1H), 7.40 (ddd, J = 11.7, 8.6, 6.2 Hz, 2H), 6.93 (s, 1H), 6.73 (td, J = 16.1, 10.3 Hz, 1H), 6.31 - 6.18 (m, 1H), 6.10 (dd, J = 17.1, 10.2 Hz, 1H), 6.06 - 5.95 (m, 1H), 5.76 (dd, J = 7.1, 4.5 Hz, 1H), 5.64 (d, J = 16.8 Hz, 1H), 5.50 - 5.48 (m, 2H), 4.36 - 4.30 (m, 3H), 3.82 (s, 3H), 3.73 - 3.69 (m, 3H), 3.29 - 3.16 (m, 3H), 2.84 (s, 2H), 2.71 (d, J = 4.9 Hz, 3H), 2.33 (dd, J = 12.9, 5.1 Hz, 1H), 2.13 (dd, J = 23.6, 14.7 Hz, 3H) ; 677.56[M+H]$^+$.	1.27

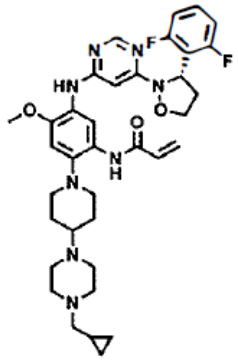
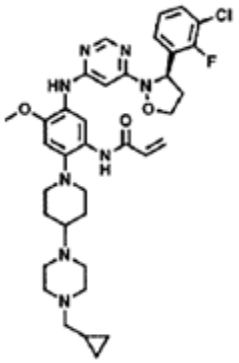
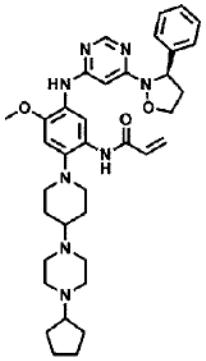
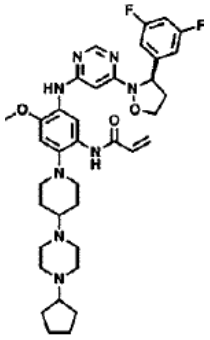
90		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-(R-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.04 (s, 1H), 8.88 (s, 1H), 8.19 (s, 1H), 8.11 (s, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.23 (t, J = 7.9 Hz, 1H), 6.84 (s, 1H), 6.61 (dd, J = 17.0, 10.2 Hz, 1H), 6.34 (s, 1H), 6.23 (d, J = 16.9 Hz, 1H), 5.86 (dt, J = 16.6, 8.0 Hz, 1H), 5.78 - 5.67 (m, 2H), 5.46 (s, 1H), 5.41 (d, J = 8.5 Hz, 1H), 4.20 (td, J = 8.0, 3.5 Hz, 2H), 3.89 (q, J = 6.9, 5.5 Hz, 2H), 3.81 (s, 3H), 3.17 (s, 4H), 3.13 (s, 2H), 2.90 - 2.79 (m, 2H), 2.73 (t, J = 11.7 Hz, 2H), 2.27 - 2.14 (m, 1H), 2.08 - 1.99 (m, 2H), 1.91 (s, 4H), 1.85 (s, 2H) :677.51[M+H]$^+$	1.25

[474]

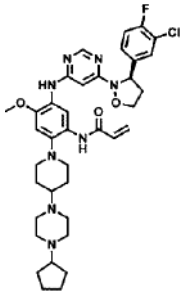
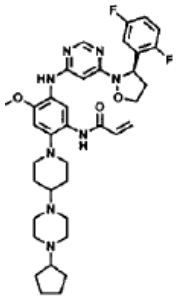
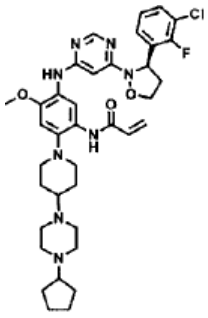
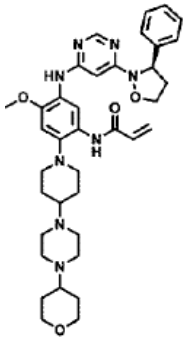
91		N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.46 (s, 1H), 8.37 (s, 1H), 7.46 (d, J = 7.2 Hz, 2H), 7.34 (t, J = 7.6 Hz, 2H), 7.24 (dd, J = 8.4, 6.5 Hz, 1H), 6.91 (s, 1H), 6.75 (s, 1H), 6.69 (s, 1H), 6.36 (dd, J = 16.9, 1.5 Hz, 1H), 6.24 (dd, J = 16.9, 10.0 Hz, 1H), 5.72 (ddd, J = 14.4, 9.3, 3.0 Hz, 2H), 4.15 (td, J = 8.0, 4.5 Hz, 1H), 4.07 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.06 (d, J = 11.2 Hz, 2H), 2.79 - 2.68 (m, 6H), 2.38 (dtt, J = 16.3, 8.2, 4.2 Hz, 2H), 2.20 (d, J = 6.6 Hz, 2H), 2.09 (d, J = 12.5 Hz, 2H), 1.80 - 1.75 (m, 3H), 1.68 (td, J = 12.0, 3.7 Hz, 3H), 0.93 - 0.83 (m, 2H), 0.57 - 0.49 (m, 2H), 0.12 (dt, J = 5.9, 4.5 Hz, 2H) ; 630.67[M+H]$^+$	1.33 min
92		N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.32 (s, 1H), 8.19 (s, 1H), 7.11 - 7.00 (m, 2H), 6.92 (s, 1H), 6.84 (tt, J = 2.4, 9.0 Hz, 1H), 6.56 (dd, J = 10.3, 17.0 Hz, 1H), 6.48 (s, 1H), 6.36 (dd, J = 1.6, 17.0 Hz, 1H), 5.81 (dd, J = 1.6, 10.2 Hz, 1H), 5.58 (dd, J = 4.7, 8.7 Hz, 1H), 4.20 - 4.11 (m, 1H), 3.98 (q, J = 8.0 Hz, 1H), 3.88 (s, 3H), 3.20 - 3.11 (m, 2H), 3.03 - 2.69 (m, 11H), 2.61 - 2.56 (m, 2H), 2.56 - 2.47 (m, 1H), 2.41 - 2.26 (m, 1H), 2.10 - 2.02 (m, 2H), 1.87 - 1.71 (m, 2H), 1.06 - 0.94 (m, 1H), 0.69 - 0.61 (m, 2H), 0.28 (dt, J = 4.6, 6.1 Hz, 2H) ; 675.3[M+H]$^+$	1.23
93		N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.32 (s, 1H), 8.18 (d, J = 1.0 Hz, 1H), 7.26 (ddd, J = 3.3, 5.8, 9.1 Hz, 1H), 7.15 (td, J = 4.4, 9.3 Hz, 1H), 7.08 - 6.99 (m, 1H), 6.93 (s, 1H), 6.62 - 6.46 (m, 2H), 6.36 (dd, J = 1.6, 17.0 Hz, 1H), 5.79 (td, J = 3.1, 9.3, 9.8 Hz, 2H), 4.19 - 4.10 (m, 1H), 4.00 (q, J = 8.0 Hz, 1H), 3.20 - 3.13 (m, 2H), 3.02 - 2.74 (m, 11H), 2.61 - 2.55 (m, 2H), 2.55 - 2.48 (m, 1H), 2.32 - 2.23 (m, 1H), 2.11 - 2.03 (m, 2H), 1.86 - 1.72 (m, 2H), 1.04 - 0.95 (m, 1H), 0.69 - 0.61 (m, 2H), 0.31 - 0.23 (m, 2H) ; 675.4[M+H]$^+$	1.17
94		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.20 (s, 1H), 10.35 (s, 1H), 9.30 (s, 1H), 8.35 (s, 1H), 7.88 (s, 1H), 7.58 (dd, J = 7.0, 2.0 Hz, 1H), 7.46 - 7.35 (m, 3H), 6.93 (s, 1H), 6.74 (dt, J = 16.7, 8.4 Hz, 1H), 6.26 (dd, J = 17.0, 1.6 Hz, 1H), 6.12 (s, 1H), 5.77 (d, J = 11.7 Hz, 1H), 5.55 (dd, J = 8.0, 5.5 Hz, 1H), 4.32 (dd, J = 7.2, 4.4 Hz, 2H), 4.07 (dd, J = 15.4, 7.8 Hz, 3H), 3.82 (s, 3H), 3.50 (d, J = 11.3 Hz, 4H), 3.25 (d, J = 10.2 Hz, 4H), 3.11 (d, J = 7.5 Hz, 3H), 2.90 - 2.82 (m, 6H), 2.71 (d, J = 4.9 Hz, 1H), 2.32 (dt, J = 12.7, 6.4 Hz, 1H), 2.17 (d, J = 19.0 Hz, 4H), 2.09 (s, 1H), 2.05 (s, 1H), 1.28 (ddd, J = 16.7, 13.1, 8.3 Hz, 3H), 1.12 (ddd, J = 21.3, 10.8, 5.9 Hz, 3H), 0.69 - 0.50 (m, 4H), 0.46 (q, J = 4.8 Hz, 3H), 0.43 - 0.37 (m, 1H) ; 601.59[M+H]$^+$.	1.26

		yl)-4-methoxyphenyl)acrylamide		

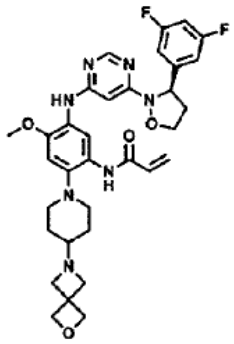
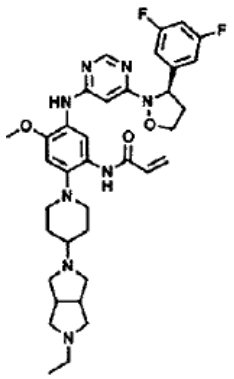
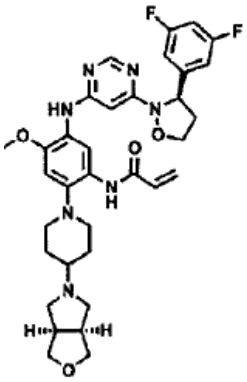
[475]

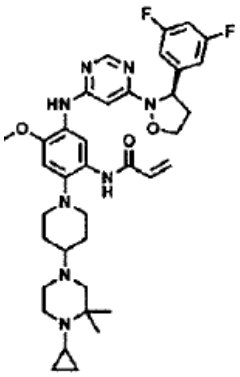
95		N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.34 (s, 1H), 9.28 (s, 1H), 8.30 (s, 1H), 7.84 (s, 1H), 7.48 - 7.39 (m, 1H), 7.13 (t, J = 8.5 Hz, 2H), 6.93 (s, 1H), 6.80 - 6.71 (m, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 5.95 (s, 1H), 5.76 (dd, J = 10.1, 1.9 Hz, 1H), 5.70 (s, 1H), 4.53 - 4.48 (m, 1H), 4.10 - 4.03 (m, 1H), 3.79 (s, 3H), 3.66 (s, 2H), 3.43 (t, J = 5.4 Hz, 7H), 3.14 - 3.07 (m, 2H), 2.94 (dd, J = 6.0, 3.0 Hz, 1H), 2.85 (t, J = 11.6 Hz, 2H), 2.46 (d, J = 4.2 Hz, 1H), 2.17 (d, J = 19.8 Hz, 4H), 1.00 (t, J = 7.0 Hz, 3H), 0.68 - 0.60 (m, 2H), 0.50 - 0.41 (m, 2H) ; 643.34[M+H]$^+$	1.18
96		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.96 (s, 1H), 8.63 (s, 1H), 8.14 (d, J = 8.3 Hz, 2H), 7.55 - 7.47 (m, 1H), 7.47 - 7.41 (m, 1H), 7.23 (t, J = 7.9 Hz, 1H), 6.83 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.21 (dd, J = 16.9, 2.0 Hz, 1H), 5.77 - 5.67 (m, 2H), 4.07 (s, 4H), 3.90 - 3.81 (m, 2H), 3.80 (s, 3H), 3.05 (d, J = 11.1 Hz, 2H), 2.81 (dd, J = 8.4, 4.0 Hz, 2H), 2.71 - 2.62 (m, 2H), 2.15 (d, J = 6.5 Hz, 2H), 1.91 (s, 4H), 1.85 (d, J = 12.0 Hz, 2H), 1.60 (d, J = 11.5 Hz, 2H), 1.18 (t, J = 7.1 Hz, 1H), 0.82 (dd, J = 12.6, 5.5 Hz, 1H), 0.45 (dt, J = 8.5, 2.9 Hz, 2H), 0.06 (q, J = 4.8 Hz, 2H) ; 691.50[M+H]$^+$	1.28
97		N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.47 (s, 1H), 8.35 (s, 1H), 7.46 (d, J = 7.2 Hz, 2H), 7.35 (d, J = 3.5 Hz, 2H), 7.25 (q, J = 6.9 Hz, 1H), 6.96 (s, 1H), 6.76 (s, 1H), 6.67 (s, 1H), 6.40 - 6.32 (m, 1H), 6.25 (dd, J = 16.9, 9.9 Hz, 1H), 5.70 - 5.64 (m, 2H), 4.15 (td, J = 7.7, 4.3 Hz, 1H), 4.06 (q, J = 7.6 Hz, 1H), 3.84 (s, 3H), 3.06 (d, J = 11.0 Hz, 2H), 2.80 - 2.70 (m, 4H), 2.59 (dq, J = 3.9, 2.5, 1.9 Hz, 2H), 2.50 (s, 2H), 2.33 (s, 6H), 2.00 (d, J = 12.2 Hz, 2H), 1.89 (s, 2H), 1.76 - 1.64 (m, 4H), 1.57 (t, J = 6.2 Hz, 2H), 1.42 (d, J = 9.7 Hz, 2H) ;653.61 [M+H]$^+$	1.29 min
98		N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.20 (s, 1H), 8.06 (s, 1H), 7.00 - 6.89 (m, 2H), 6.80 (s, 1H), 6.72 (tt, J = 2.4, 9.1 Hz, 1H), 6.44 (dd, J = 10.3, 17.0 Hz, 1H), 6.35 (s, 1H), 6.24 (dd, J = 1.5, 16.9 Hz, 1H), 5.68 (dd, J = 1.6, 10.3 Hz, 1H), 5.46 (dd, J = 4.7, 8.7 Hz, 1H), 4.08 - 3.97 (m, 1H), 3.85 (q, J = 7.9 Hz, 1H), 3.76 (s, 3H), 3.09 - 2.98 (m, 3H), 2.86 - 2.58 (m, 12H), 2.44 - 2.32 (m, 1H), 2.22 (dtd, J = 4.6, 8.1, 12.6 Hz, 1H), 1.98 - 1.86 (m, 5H), 1.73 - 1.60 (m, 5H), 1.58 - 1.48 (m, 2H), 1.45 - 1.36 (m, 2H) ; 680.3[M+H]$^+$	1.23

[476]

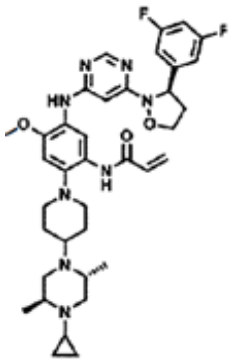
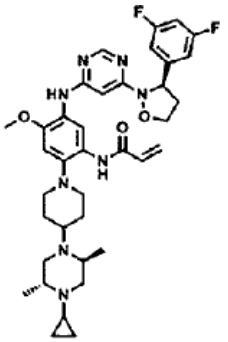
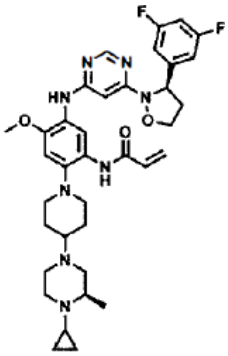
99		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.42 (s, 1H), 10.33 (s, 1H), 9.30 (s, 1H), 8.34 (s, 1H), 7.89 (s, 1H), 7.58 (dd, J = 7.0, 2.0 Hz,13H), 7.47 - 7.35 (m, 2H), 6.93 (s, 1H), 6.74 (dt, J = 16.7, 8.3 Hz, 1H), 6.26 (dd, J = 17.0, 1.6 Hz, 1H), 6.11 (s, 1H), 5.77 (d, J = 11.6 Hz, 1H), 5.58 - 5.51 (m, 1H), 4.37 - 4.28 (m, 2H), 4.07 (dd, J = 15.5, 7.8 Hz, 4H), 3.81 (s, 3H), 3.44 (d, J = 7.6 Hz, 2H), 3.25 (d, J = 10.6 Hz, 2H), 3.00 - 2.88 (m, 2H), 2.83 (t, J = 10.6 Hz, 3H), 2.72 (d, J = 4.9 Hz, 1H), 2.33 (td, J = 12.7, 7.6 Hz, 2H), 2.16 (d, J = 15.4 Hz, 3H), 2.05 (s, 4H), 1.88 - 1.67 (m, 6H), 1.63 - 1.48 (m, 5H), 1.28 (ddd, J = 16.5, 13.1, 8.4 Hz, 2H) ; 705.58[M+H]$^+$.	1.28
100		N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.33 (s, 1H), 8.18 (d, J = 0.9 Hz, 1H), 7.26 (ddd, J = 3.2, 5.8, 9.1 Hz, 1H), 7.15 (td, J = 4.3, 9.3 Hz, 1H), 7.08 - 6.98 (m, 1H), 6.92 (s, 1H), 6.61 - 6.49 (m, 2H), 6.36 (dd, J = 1.6, 17.0 Hz, 1H), 5.79 (td, J = 3.1, 9.2, 9.7 Hz, 2H), 4.19 - 4.10 (m, 1H), 3.99 (q, J = 8.0 Hz, 1H), 3.89 (s, 3H), 3.20 - 3.12 (m, 2H), 3.06 - 2.76 (m, 12H), 2.59 - 2.50 (m, 1H), 2.27 (dtd, J = 4.6, 8.1, 12.7 Hz, 1H), 2.11 - 2.00 (m, 5H), 1.87 - 1.73 (m, 5H), 1.72 - 1.63 (m, 2H), 1.62 - 1.51 (m, 2H) ;680.4[M+H]$^+$	1.22
101		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.96 (s, 1H), 8.63 (s, 1H), 8.14 (d, J = 7.9 Hz, 2H), 7.51 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 7.1 Hz, 1H), 7.23 (t, J = 7.9 Hz, 1H), 6.83 (s, 1H), 6.64 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.21 (d, J = 17.9 Hz, 1H), 5.73 (dd, J = 9.1, 5.0 Hz, 2H), 4.17 (td, J = 7.9, 3.6 Hz, 2H), 3.85 (q, J = 8.0 Hz, 2H), 3.79 (s, 3H), 3.17 (s, 2H), 3.04 (d, J = 11.0 Hz, 2H), 2.81 (dtd, J = 12.1, 8.1, 3.6 Hz, 2H), 2.72 - 2.61 (m, 2H), 2.41 (q, J = 8.1 Hz, 2H), 2.21 (tdd, J = 12.7, 9.5, 5.8 Hz, 2H), 1.88 (s, 4H), 1.76 (td, J = 11.0, 5.9 Hz, 2H), 1.68 (d, J = 11.1 Hz, 2H), 1.66 - 1.54 (m, 2H), 1.50 (ddt, J = 12.4, 9.3, 3.7 Hz, 2H), 1.37 - 1.20 (m, 2H) ; 705.62[M+H]$^+$	1.28
102		N-(4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.36 (s, 1H), 7.46 (d, J = 7.3 Hz, 2H), 7.34 (t, J = 7.6 Hz, 2H), 7.24 (t, J = 7.3 Hz, 1H), 6.91 (s, 1H), 6.74 (s, 1H), 6.60 (s, 1H), 6.36 (d, J = 16.2 Hz, 1H), 6.24 (dd, J = 16.9, 10.0 Hz, 1H), 5.76 - 5.71 (m, 1H), 5.71 - 5.66 (m, 1H), 4.15 (td, J = 7.9, 4.4 Hz, 1H), 4.10 - 4.05 (m, 1H), 4.05 - 3.99 (m, 2H), 3.84 (s, 3H), 3.39 (td, J = 11.9, 1.9 Hz, 2H), 3.06 (d, J = 11.2 Hz, 2H), 2.73 (dt, J = 22.3, 7.0 Hz, 11H), 2.49 - 2.32 (m, 4H), 2.09 (d, J = 12.3 Hz, 2H), 1.85 - 1.77 (m, 2H), 1.74 - 1.54 (m, 4H) ; 669.75[M+H]$^+$	1.87

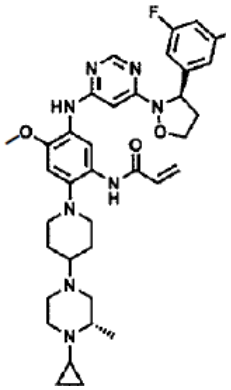
[477]

103		N-(2-(4-(2-oxa-6-azaspiro[3.3]heptane-6-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO) δ 9.00 (s, 1H), 8.64 (s, 1H), 8.17 (s, 1H), 8.12 (s, 1H), 7.17 - 7.06 (m, 3H), 6.84 (s, 1H), 6.63 - 6.52 (m, 1H), 6.36 (s, 1H), 6.20 (d, *J* = 17.4 Hz, 1H), 5.72 (d, *J* = 10.5 Hz, 1H), 5.56 (dd, *J* = 8.6, 5.0 Hz, 1H), 4.83 - 4.68 (m, 1H), 4.62 (s, 3H), 4.43 - 4.20 (m, 2H), 4.13 (td, *J* = 7.8, 4.0 Hz, 1H), 3.88 - 3.75 (m, 4H), 3.67 - 3.54 (m, 1H), 3.22 - 2.92 (m, 5H), 2.80 - 2.58 (m, 4H), 2.30 - 2.19 (m, 1H), 2.09 - 1.85 (m, 2H); 634.54 [M+H]$^+$.	1.39
104		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(5-ethylhexahydropyrrolo[3,4-c]pyrrole-2(1H)-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO) δ 8.98 (s, 1H), 8.64 (s, 1H), 8.16 (s, 1H), 8.11 (s, 1H), 7.16 - 7.08 (m, 3H), 6.82 (s, 1H), 6.62 (dd, *J* = 16.9, 10.3 Hz, 1H), 6.35 (s, 1H), 6.24 - 6.17 (m, 1H), 5.87 (dd, *J* = 10.3, 1.8 Hz, 1H), 5.72 (d, *J* = 11.0 Hz, 1H), 5.56 (dd, *J* = 8.6, 5.0 Hz, 1H), 4.13 (td, *J* = 7.8, 3.9 Hz, 1H), 3.97 - 3.76 (m, 5H), 3.62 - 3.47 (m, 2H), 3.12 - 2.98 (m, 5H), 2.90 - 2.62 (m, 9H), 2.29 - 2.16 (m, 2H), 1.98 - 1.88 (m, 2H), 1.78 - 1.66 (m, 2H), 1.14 (t, *J* = 10.7 Hz, 3H) ; 675.62 [M+H]$^+$	1.28
105		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aS)-tetrahydro-1H-puro[3,4-c]pyrrole-5(3H)-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO) δ 9.12 - 8.91 (m, 1H), 8.65 (s, 1H), 8.17 (s, 1H), 8.12 (s, 1H), 7.17 - 7.07 (m, 3H), 6.84 (s, 1H), 6.56 (s, 1H), 6.38 (s, 1H), 6.22 (d, *J* = 17.0 Hz, 1H), 5.77 - 5.67 (m, 1H), 5.56 (dd, *J* = 8.6, 5.0 Hz, 1H), 4.13 (td, *J* = 7.8, 3.9 Hz, 1H), 3.94 - 3.69 (m, 7H), 3.66 - 3.44 (m, 3H), 3.19 - 2.97 (m, 5H), 2.81 - 2.64 (m, 4H), 2.29 - 2.18 (m, 1H), 2.14 - 1.82 (m, 4H) ; 648.57 [M+H]$^+$	1.42

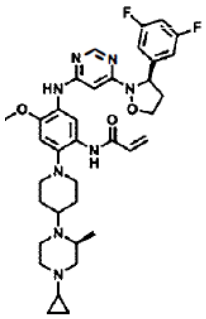
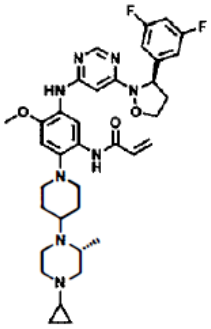
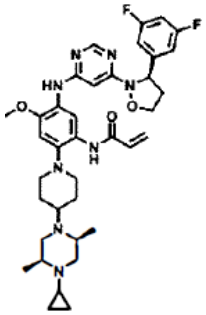
106		N-(2-(4-(4-cyclopropyl-3,3-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	689.7 $[M+H]^+$	1.33

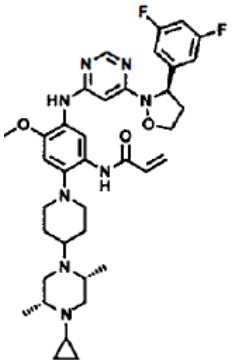
[478]

107		N-(2-(4-((2R,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.62 (s, 1H), 8.16 (s, 1H), 7.12 (ddd, J = 8.2, 6.2, 3.2 Hz, 3H), 6.84 (s, 1H), 6.68 (dd, J = 16.9, 10.1 Hz, 1H), 6.34 (s, 1H), 6.21 (dd, J = 16.9, 2.1 Hz, 1H), 5.72 (d, J = 10.9 Hz, 1H), 5.55 (dt, J = 10.5, 5.1 Hz, 1H), 3.85 (dd, J = 15.5, 7.4 Hz, 2H), 3.79 (s, 3H), 3.17 (s, 2H), 3.05 (q, J = 14.6, 13.2 Hz, 4H), 2.88 (d, J = 11.5 Hz, 2H), 2.80 (d, J = 2.4 Hz, 1H), 2.75 (dt, J = 12.6, 3.8 Hz, 3H), 2.67 (q, J = 1.8 Hz, 1H), 2.55 (d, J = 6.1 Hz, 1H), 2.39 - 2.32 (m, 2H), 2.30 - 2.19 (m, 2H), 2.00 (td, J = 10.6, 5.5 Hz, 4H), 1.71 (s, 3H), 1.23 (s, 3H), 1.11 (d, J = 6.2 Hz, 3H), 0.99 (d, J = 6.1 Hz, 2H).; 680.6 $[M+H]^+$	1.32
108		N-(2-(4-((2S,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	680.6 $[M+H]^+$	1.29
109		N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.23 (s, 1H), 8.11 (s, 1H), 7.00 (d, J = 4.3 Hz, 2H), 6.85 (s, 1H), 6.77 (tt, J = 2.5, 9.1 Hz, 1H), 6.50 (dd, J = 10.2, 17.0 Hz, 1H), 6.39 (s, 1H), 6.30 (d, J = 16.4 Hz, 1H), 5.75 (d, J = 10.6 Hz, 1H), 5.50 (dd, J = 4.8, 8.6 Hz, 1H), 4.12 - 4.05 (m, 1H), 3.91 (q, J = 8.0 Hz, 1H), 3.82 (s, 3H), 3.14 - 3.05 (m, 4H), 2.80 - 2.70 (m, 3H), 2.68 - 2.58 (m, 2H), 2.58 - 2.50 (m, 2H), 2.33 - 2.19 (m, 2H), 2.11 - 2.00 (m, 2H), 1.83 - 1.71 (m, 2H), 1.71 - 1.59 (m, 1H), 1.22 (d, 3H), 0.67 (dt, J = 5.8, 11.5 Hz, 1H), 0.58 (dt, J = 4.8, 10.2 Hz, 1H), 0.49 (q, J = 7.5, 9.1 Hz, 1H), 0.32 (dt, J = 5.4, 10.8 Hz, 1H) ; 675.4$[M+H]^+$	1.41

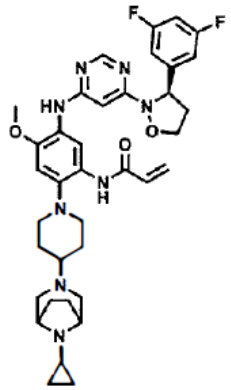
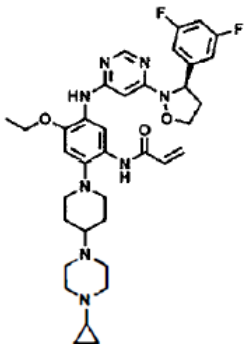
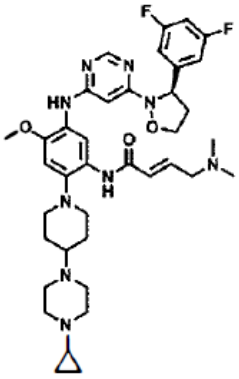
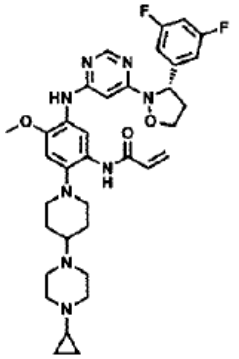
110		N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.18 (s, 1H), 7.07 (d, J = 4.5 Hz, 2H), 6.92 (s, 1H), 6.84 (tt, J = 2.5, 9.1 Hz, 1H), 6.57 (dd, J = 10.3, 17.0 Hz, 1H), 6.46 (s, 1H), 6.37 (d, J = 16.8 Hz, 1H), 5.82 (d, J = 10.4 Hz, 1H), 5.57 (dd, J = 4.7, 8.7 Hz, 1H), 4.15 (dd, J = 4.2, 7.9 Hz, 1H), 3.97 (q, J = 8.0 Hz, 1H), 3.89 (s, 3H), 3.22 - 3.15 (m, 4H), 2.86 - 2.70 (m, 5H), 2.68 - 2.58 (m, 2H), 2.42 - 2.28 (m, 2H), 2.17 - 2.08 (m, 2H), 1.89 - 1.79 (m, 2H), 1.78 - 1.68 (m, 1H), 1.30 (d, J = 6.5 Hz, 3H), 0.75 (dt, J = 5.8, 11.6 Hz, 1H), 0.65 (dt, J = 4.8, 10.2 Hz, 1H), 0.61 - 0.51 (m, 1H), 0.39 (dt, J = 5.2, 10.5 Hz, 1H) ; 675.4[M+H]$^+$	1.41

[479]

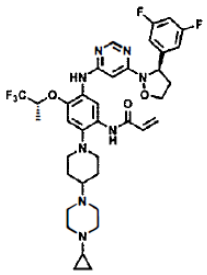
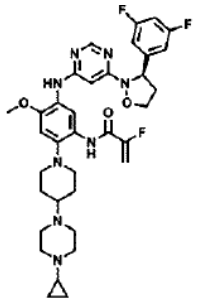
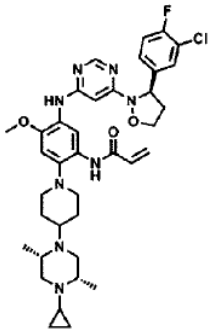
111		N-(2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.14 - 7.02 (m, 2H), 6.94 (s, 1H), 6.87 - 6.78 (m, 1H), 6.57 (dd, J = 10.3, 17.0 Hz, 1H), 6.47 (s, 1H), 6.37 (dd, J = 1.5, 17.0 Hz, 1H), 5.82 (d, J = 9.8 Hz, 1H), 5.57 (dd, J = 4.8, 8.7 Hz, 1H), 4.19 - 4.12 (m, 2H), 3.98 (q, J = 7.9 Hz, 2H), 3.89 (s, 3H), 3.21 (d, J = 11.5 Hz, 4H), 3.14 (d, J = 8.0 Hz, 1H), 3.08 - 3.02 (m, 2H), 2.96 - 2.81 (m, 5H), 2.76 - 2.57 (m, 2H), 2.53 - 2.44 (m, 1H), 2.30 - 2.31 (m, 1H), 1.30 (d, J = 6.4 Hz, 3H), 0.56 (d, J = 6.3 Hz, 2H), 0.47 (s, 2H) ; 675.4[M+H]$^+$	1.3
112		N-(2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.11 - 7.02 (m, 2H), 6.94 (s, 1H), 6.91 - 6.78 (m, 1H), 6.57 (dd, J = 10.2, 16.9 Hz, 1H), 6.47 (s, 1H), 6.37 (dd, J = 1.5, 16.8 Hz, 1H), 5.82 (d, J = 10.3 Hz, 1H), 5.57 (dd, J = 4.8, 8.6 Hz, 1H), 4.19 - 4.12 (m, 2H), 3.98 (q, J = 7.9 Hz, 2H), 3.89 (s, 3H), 3.21 (d, J = 12.7 Hz, 4H), 3.10 - 3.01 (m, 3H), 2.99 - 2.79 (m, 5H), 2.65 (d, J = 18.7 Hz, 2H), 2.54 - 2.42 (m, 1H), 2.36 - 2.29 (m, 1H), 1.32 - 1.30 (m, 3H), 0.56 (d, J = 6.4 Hz, 2H), 0.47 (s, 2H) ; 675.4[M+H]$^+$	1.31
113		N-(2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.01 (s, 1H), 9.29 (s, 1H), 8.32 (s, 1H), 7.22 - 7.06 (m, 4H), 6.94 (d, J = 18.2 Hz, 1H), 6.65 (ddd, J = 52.1, 16.8, 10.2 Hz, 1H), 6.25 (d, J = 17.0 Hz, 1H), 6.15 (s, 1H), 5.81 - 5.71 (m, 2H), 5.55 (dd, J = 8.6, 5.4 Hz, 2H), 4.04 (q, J = 7.7 Hz, 4H), 3.81 (d, J = 4.2 Hz, 6H), 3.57 (s, 6H), 3.21 (d, J = 33.4 Hz, 5H), 3.03 - 2.87 (m, 4H), 2.88 - 2.63 (m, 2H), 2.39 - 2.23 (m, 3H), 2.11 (d, J = 20.3 Hz, 3H), 1.74 (s, 2H), 1.57 (s, 6H).: 680.6 [M+H]$^+$	1.40

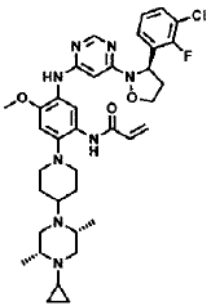
114		N-(2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.62 (s, 1H), 8.16 (d, J = 1.0 Hz, 1H), 7.12 (dq, J = 7.7, 3.0, 1.7 Hz, 4H), 6.83 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.34 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.75 - 5.67 (m, 1H), 5.56 (dd, J = 8.7, 5.0 Hz, 1H), 4.13 (d, J = 3.9 Hz, 1H), 3.79 (s, 4H), 3.32 (s, 3H), 3.11 - 2.93 (m, 4H), 2.77 (ddd, J = 12.1, 8.3, 3.9 Hz, 1H), 2.73 - 2.64 (m, 3H), 2.60 (dd, J = 10.9, 4.9 Hz, 3H), 2.44 (dd, J = 11.0, 3.2 Hz, 2H), 2.31 - 2.18 (m, 3H), 1.88 - 1.77 (m, 3H), 1.77 - 1.65 (m, 2H), 1.55 (d, J = 10.4 Hz, 2H), 1.00 (d, J = 6.2 Hz, 4H), 0.95 (d, J = 6.3 Hz, 4H), 0.58 - 0.49 (m, 1H), 0.42 - 0.31 (m, 3H), 0.13 (d, J = 9.6 Hz, 1H).: 689.6 $[M+H]^+$	1.41

[480]

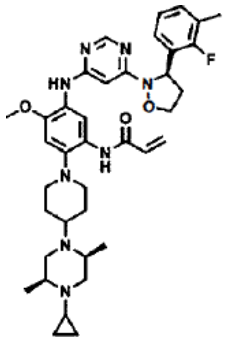
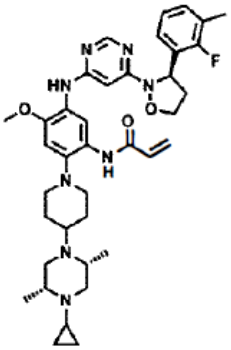
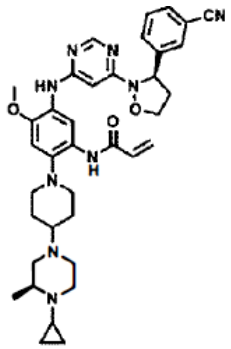
115		N-(2-(4-((1R,5S)-8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.44 (s, 1H), 8.34 (s, 1H), 7.16 (s, 1H), 7.01 (s, 1H), 6.99 (s, 1H), 6.75 (s, 1H), 6.71 - 6.65 (m, 2H), 6.40 - 6.23 (m, 2H), 5.77 - 5.72 (m, 1H), 5.66 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.18 - 4.11 (m, 1H), 4.05 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.37 (s, 2H), 3.06 - 2.99 (m, 2H), 2.82 - 2.63 (m, 5H), 2.55 - 2.40 (m, 2H), 2.38 - 2.28 (m, 2H), 2.01 - 1.85 (m, 7H), 1.60 - 1.57 (m, 2H), 0.63 - 0.56 (m, 2H), 0.50 - 0.43 (m, 2H); 687.53 $[M+H]^+$	1.21
116		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-ethoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.17 (s, 2H), 7.11 - 7.02 (m, 2H), 6.91 - 6.77 (m, 2H), 6.58 (dd, *J* = 10.3, 16.9 Hz, 1H), 6.36 (d, *J* = 18.5 Hz, 2H), 5.79 (dd, *J* = 1.6, 10.2 Hz, 1H), 5.56 (dd, *J* = 4.9, 8.6 Hz, 1H), 4.23 - 4.11 (m, 4H), 3.96 (t, *J* = 8.0 Hz, 1H), 3.02 - 2.89 (m, 4H), 2.91 - 2.76 (m, 7H), 2.76 - 2.68 (m, 2H), 2.41 - 2.28 (m, 2H), 2.10 - 2.03 (m, 2H), 1.82 - 1.70 (m, 2H), 1.59 (td, *J* = 4.1, 12.0 Hz, 1H), 1.48 (t, *J* = 7.0 Hz, 3H), 0.54 (dd, *J* = 4.5, 6.7 Hz, 2H), 0.49 - 0.40 (m, 2H) ; 675.4$[M+H]^+$	1.33
117		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)-(E)-4-(dimethylamino)but-2-enamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.32 (s, 1H), 8.18 (s, 1H), 7.11 - 7.02 (m, 2H), 6.95 - 6.80 (m, 4H), 6.76 - 6.72 (m, 2H), 6.56 - 6.44 (m, 2H), 5.57 (dd, *J* = 4.8, 8.7 Hz, 1H), 4.16 (td, *J* = 3.9, 7.7 Hz, 2H), 3.97 (d, *J* = 8.0 Hz, 1H), 3.89 (s, 4H), 3.16 (s, 3H), 3.03 (s, 3H), 2.89 - 2.78 (m, 10H), 2.41 - 2.28 (m, 2H), 2.14 - 2.09 (m, 2H), 1.87 - 1.76 (m, 4H), 0.59 - 0.53 (m, 2H), 0.50 - 0.44 (m, 2H) ; 718.4$[M+H]^+$	1.1
118		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.04 - 6.97 (m, 2H), 6.94 (s, 1H), 6.75 (s, 1H), 6.73 - 6.64 (m, 2H), 6.39 - 6.19 (m, 2H), 5.74 (d, *J* = 11.1 Hz, 1H), 5.67 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.19 - 4.11 (m, 1H), 4.06 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.12 - 3.00 (m, 2H), 2.81 - 2.59 (m, 10H), 2.40 - 2.29 (m, 2H), 2.14 - 2.03 (m, 2H), 1.76 - 1.60 (m, 4H), 0.51 - 0.38 (m, 4H); 661.54 $[M+H]^+$	1.19

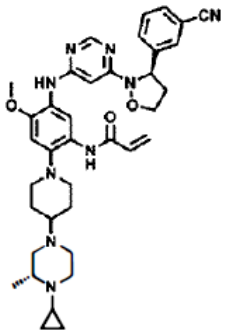
[481]

119		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-(((R)-1,1,1-trifluoropropane-2-yl)oxy)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.25 (s, 1H), 8.17 (s, 1H), 7.11 - 6.98 (m, 3H), 6.90 - 6.77 (m, 1H), 6.63 - 6.49 (m, 1H), 6.41 (d, J = 6.0 Hz, 2H), 5.83 (d, J = 10.3 Hz, 1H), 5.57 (dd, J = 4.8, 8.7 Hz, 1H), 4.19 - 4.13 (m, 1H), 3.97 (q, J = 8.0 Hz, 1H), 3.23 - 3.14 (m, 3H), 3.06 - 2.91 (m, 4H), 2.91 - 2.76 (m, 8H), 2.40 - 2.29 (m, 1H), 2.17 - 2.11 (m, 2H), 1.93 - 1.75 (m, 4H), 1.44 (d, J = 6.5 Hz, 3H), 0.60 - 0.52 (m, 2H), 0.52 - 0.45 (m, 2H) ; 743.3[M+H]$^+$	1.42
120		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)-2-fluoroacrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.30 (d, J = 3.6 Hz, 1H), 8.70 (s, 1H), 8.42 (d, J = 1.2 Hz, 1H), 8.19 (s, 1H), 7.13 (ddd, J = 7.9, 5.4, 2.9 Hz, 3H), 6.95 (s, 1H), 6.44 (s, 1H), 5.79 - 5.61 (m, 1H), 5.29 (dd, J = 13.9, 3.9 Hz, 1H), 4.14 (td, J = 7.9, 3.9 Hz, 1H), 3.82 (s, 4H), 3.06 (d, J = 11.4 Hz, 2H), 2.88 (d, J = 30.1 Hz, 5H), 2.77 (ddt, J = 15.4, 7.4, 4.0 Hz, 8H), 2.32 - 2.18 (m, 1H), 2.11 - 2.03 (m, 2H), 1.65 (td, J = 11.9, 3.6 Hz, 2H), 1.24 (dd, J = 4.6, 2.5 Hz, 2H), 0.45 (dt, J = 6.2, 2.9 Hz, 2H), 0.36 (q, J = 3.4, 2.9 Hz, 2H).; 679.5 [M+H]$^+$	1.35
121		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.31 (s, 1H), 9.38 (s, 1H), 8.35 (s, 1H), 7.88 (d, J = 73.3 Hz, 1H), 7.50 (dd, J = 7.1, 2.2 Hz, 1H), 7.46 - 7.34 (m, 2H), 6.96 (d, J = 22.5 Hz, 1H), 6.68 (ddd, J = 55.9, 17.0, 10.2 Hz, 1H), 6.25 (d, J = 17.0 Hz, 1H), 6.13 (s, 1H), 5.77 (dd, J = 10.1, 1.9 Hz, 1H), 5.54 (t, J = 7.0 Hz, 1H), 4.32 (d, J = 4.6 Hz, 1H), 4.19 - 4.00 (m, 3H), 3.97 (s, 1H), 3.82 (d, J = 4.1 Hz, 3H), 3.71 (s, 1H), 3.57 (d, J = 2.2 Hz, 2H), 3.44 - 3.35 (m, 1H), 3.24 (d, J = 30.2 Hz, 3H), 2.96 (ddd, J = 17.0, 8.7, 4.8 Hz, 3H), 2.83 - 2.67 (m, 1H), 2.33 (dt, J = 9.5, 5.2 Hz, 2H), 2.15 (s, 2H), 1.77 (s, 2H), 1.61 (d, J = 13.5 Hz, 4H), 1.46 - 1.34 (m, 1H), 0.84 (d, J = 6.8 Hz, 3H). 705.3[M+H]$^+$	1.45

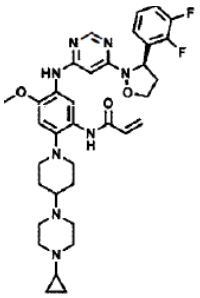
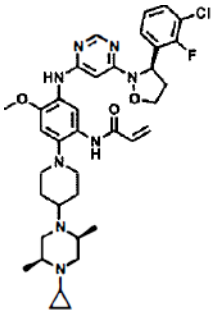
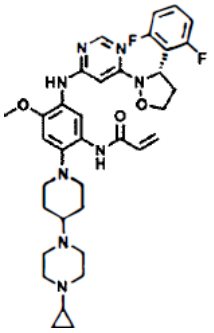
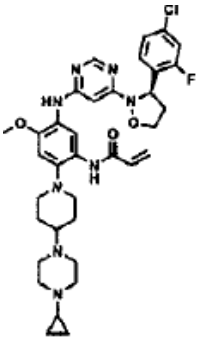
122		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.04 (d, J = 35.7 Hz, 3H), 8.21 (s, 1H), 7.56 - 7.49 (m, 1H), 7.46 - 7.39 (m, 2H), 7.23 (t, J = 7.9 Hz, 2H), 6.85 (s, 1H), 6.51 (t, J = 13.9 Hz, 1H), 6.32 (s, 2H), 6.28 - 6.17 (m, 2H), 5.80 - 5.67 (m, 4H), 4.21 (dt, J = 7.9, 4.1 Hz, 2H), 3.91 (q, J = 7.9 Hz, 2H), 3.81 (s, 6H), 3.45 (d, J = 9.5 Hz, 1H), 3.16 (d, J = 9.3 Hz, 3H), 2.94 (d, J = 12.1 Hz, 2H), 2.89 - 2.77 (m, 4H), 2.68 (d, J = 11.1 Hz, 4H), 2.22 (dq, J = 13.1, 7.8, 6.6 Hz, 3H), 2.14 (s, 2H), 1.79 (s, 2H), 1.60 (s, 1H), 1.32 - 1.14 (m, 10H), 0.67 (s, 2H), 0.48 (d, J = 35.5 Hz, 3H). ; 705.6[M+H]+	1.42

[482]

123		N-(2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 8.94 (s, 1H), 8.59 (s, 1H), 8.14 (s, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.19 (t, J = 7.3 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.83 (s, 1H), 6.66 (dd, J = 16.9, 10.2 Hz, 1H), 6.34 (s, 1H), 6.20 (dd, J = 16.9, 2.0 Hz, 1H), 5.72 (dd, J = 9.3, 4.4 Hz, 2H), 4.14 (td, J = 7.8, 3.8 Hz, 1H), 3.84 (q, J = 8.0 Hz, 1H), 3.79 (s, 3H), 3.02 (d, J = 11.0 Hz, 2H), 2.95 (s, 1H), 2.77 (dt, J = 8.1, 4.2 Hz, 1H), 2.67 (q, J = 9.5, 8.4 Hz, 2H), 2.64 - 2.54 (m, 3H), 2.43 (dd, J = 11.0, 3.2 Hz, 2H), 2.26 (d, J = 2.0 Hz, 3H), 2.22 - 2.09 (m, 2H), 1.82 (t, J = 12.9 Hz, 2H), 1.55 (d, J = 11.1 Hz, 2H), 1.24 (s, 3H), 1.09 (d, J = 6.2 Hz, 3H), 0.94 (d, J = 6.3 Hz, 3H), 0.53 (q, J = 6.0 Hz, 1H), 0.42 - 0.31 (m, 2H).; 685.6[M+H]+	1.40
124		N-(2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 9.09 (s, 1H), 8.21 (s, 1H), 8.03 (s, 1H), 7.22 (dt, J = 13.8, 7.4 Hz, 2H), 7.07 (t, J = 7.6 Hz, 1H), 6.86 (s, 1H), 6.51 (t, J = 13.9 Hz, 1H), 6.32 - 6.17 (m, 2H), 5.74 (d, J = 10.4 Hz, 1H), 5.70 (dd, J = 8.7, 5.2 Hz, 1H), 4.21 (q, J = 6.0, 4.7 Hz, 1H), 3.92 (q, J = 7.9 Hz, 1H), 3.81 (s, 3H), 3.45 (s, 1H), 3.15 (s, 3H), 3.02 - 2.88 (m, 1H), 2.84 (d, J = 8.3 Hz, 2H), 2.69 (d, J = 13.1 Hz, 3H), 2.54 (s, 1H), 2.26 (d, J = 2.0 Hz, 3H), 2.24 - 2.08 (m, 3H), 1.80 (s, 2H), 1.57 (d, J = 10.0 Hz, 1H), 1.38 - 1.12 (m, 8H), 0.67 (s, 1H), 0.49 (d, J = 35.7 Hz, 2H), 0.21 (s, 1H). ; 685.7[M+H]+	1.41
125		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.44 (s, 1H), 8.33 (s, 1H), 7.78 (s, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.54 (d, J = 7.7 Hz, 1H), 7.45 (t, J = 7.8 Hz, 1H), 6.75 (s, 1H), 6.70 (s, 1H), 6.40 - 6.23 (m, J = 17.0, 12.9 Hz, 2H), 5.77 - 5.68 (m, 2H), 4.19 - 4.13 (m, 1H), 4.08 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.11 - 3.02 (m, 4H), 2.99 - 2.92 (m, 1H), 2.85 - 2.68 (m, 3H), 2.65 - 2.51 (m, 2H), 2.49 - 2.29 (m, 3H), 2.14 - 2.08 (m, 3H), 1.79 - 1.67 (m, 2H), 1.61 - 1.53 (m, 1H), 1.23 (d, J = 6.3 Hz, 3H), 0.70 - 0.58 (m, 2H), 0.50 - 0.30 (m, 2H); 664.54 [M+H]+	1.10

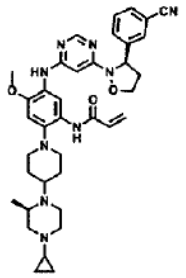
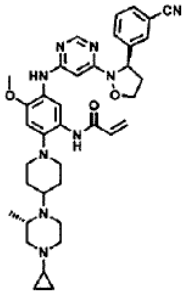
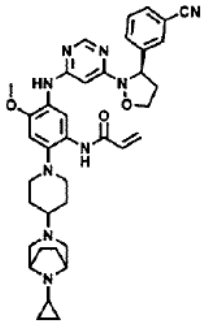
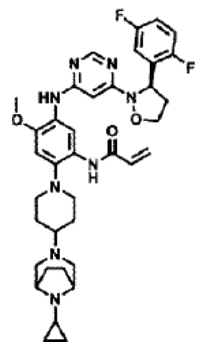
126		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.43 (s, 1H), 8.31 (s, 1H), 7.78 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.48 - 7.41 (m, 2H), 6.73 (d, *J* = 13.3 Hz, 1H), 6.68 (s, 1H), 6.40 - 6.24 (m, 2H), 5.78 - 5.67 (m, 2H), 4.20 - 4.12 (m, 1H), 4.07 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.15 - 3.00 (m, 5H), 2.84 - 2.46 (m, 7H), 2.38 - 2.28 (m, 1H), 2.22 - 2.08 (m, 3H), 1.83 - 1.72 (m, 2H), 1.66 - 1.56 (m, 1H), 1.24 (d, *J* = 6.3 Hz, 3H), 0.72 - 0.61 (m, 2H), 0.51 - 0.33 (m, 2H); 664.59 $[M+H]^+$	1.10

[483]

127		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.62 (s, 1H), 8.16 (s, 1H), 7.40 - 7.25 (m, 2H), 7.24 - 7.15 (m, 1H), 6.82 (s, 1H), 6.65 (dd, *J* = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.20 (dd, *J* = 16.9, 2.0 Hz, 1H), 5.75 (d, *J* = 3.9 Hz, 2H), 5.74 - 5.69 (m, 1H), 3.85 (q, *J* = 7.0 Hz, 1H), 3.79 (s, 3H), 3.04 (d, *J* = 11.1 Hz, 3H), 2.81 (dtd, *J* = 12.0, 8.0, 3.7 Hz, 1H), 2.70 - 2.60 (m, 3H), 2.34 - 2.15 (m, 3H), 1.91 (s, 7H), 1.82 (t, *J* = 7.2 Hz, 2H), 1.70 (tt, *J* = 12.8, 6.6 Hz, 3H), 1.57 (dq, *J* = 6.7, 3.4 Hz, 1H), 1.23 (s, 1H), 0.39 (dt, *J* = 6.2, 3.0 Hz, 2H), 0.27 (p, *J* = 3.9 Hz, 2H).; 661.5 [M+H]$^+$	1.23
128		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 8.94 (s, 1H), 8.63 (s, 1H), 8.15 (s, 1H), 7.55 - 7.48 (m, 1H), 7.45 (t, *J* = 7.1 Hz, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 6.83 (s, 1H), 6.66 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.35 (s, 1H), 6.20 (dd, *J* = 17.0, 2.0 Hz, 1H), 5.72 (dt, *J* = 9.5, 4.2 Hz, 2H), 4.17 (td, *J* = 7.0, 3.7 Hz, 1H), 3.90 - 3.82 (m, 1H), 3.79 (s, 3H), 3.02 (d, *J* = 11.0 Hz, 2H), 2.86 - 2.75 (m, 1H), 2.69 (d, *J* = 12.4 Hz, 2H), 2.64 - 2.53 (m, 2H), 2.26 (t, *J* = 10.0 Hz, 1H), 2.22 - 2.15 (m, 1H), 1.87 (s, 6H), 1.80 (d, *J* = 13.5 Hz, 2H), 1.61 - 1.50 (m, 2H), 1.00 (d, *J* = 6.2 Hz, 3H), 0.94 (d, *J* = 6.3 Hz, 3H), 0.57 - 0.49 (m, 1H), 0.37 (d, *J* = 7.0 Hz, 2H), 0.13 (d, *J* = 9.8 Hz, 1H).; 705.5[M+H]$^+$	1.43
129		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.87 (s, 1H), 9.17 (s, 1H), 8.26 (s, 1H), 7.90 (s, 1H), 7.42 (ddd, *J* = 8.5, 6.5, 2.0 Hz, 1H), 7.12 (t, *J* = 8.5 Hz, 2H), 6.89 (s, 1H), 6.69 (dd, *J* = 17.0, 10.3 Hz, 1H), 6.24 (dd, *J* = 17.0, 2.0 Hz, 1H), 5.99 (s, 1H), 5.76 (dd, *J* = 10.2, 1.9 Hz, 1H), 5.69 (s, 1H), 4.48 - 4.41 (m, 1H), 4.01 (d, *J* = 11.2 Hz, 2H), 3.79 (s, 3H), 3.70 (s, 4H), 3.57 (s, 2H), 3.21 (d, *J* = 11.4 Hz, 2H), 2.91 (s, 1H), 2.79 (t, *J* = 11.8 Hz, 2H), 2.46 (s, 1H), 2.16 (s, 2H), 2.09 (s, 3H), 1.24 (s, 2H), 1.10 (s, 2H), 0.80 (d, *J* = 6.4 Hz, 2H).; 661.3[M+H]$^+$	1.14
130		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-	676.3[M+H]$^+$	1.34

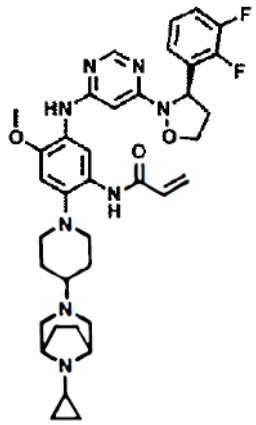
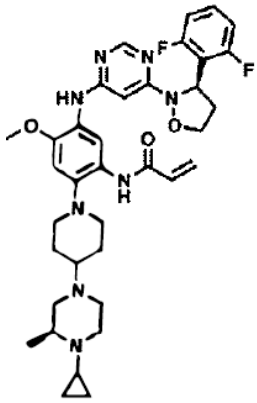
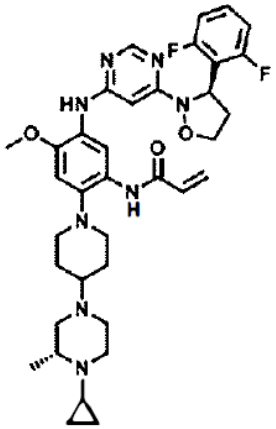
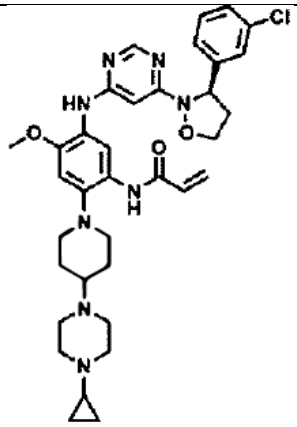
		yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide		

[484]

131		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.42 (s, 1H), 8.31 (s, 1H), 7.78 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.50 - 7.42 (m, 2H), 6.76 (s, 1H), 6.68 (s, 1H), 6.40 - 6.24 (m, 2H), 5.76 (dd, *J* = 9.7, 1.6 Hz, 1H), 5.71 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.19 - 4.11 (m, 1H), 4.07 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.17 - 3.04 (m, 3H), 3.02 - 2.91 (m, 4H), 2.87 - 2.77 (m, 2H), 2.76 - 2.58 (m, 3H), 2.45 - 2.28 (m, 2H), 2.00 - 1.87 (m, 3H), 1.76 - 1.65 (m, 2H), 1.18 (d, *J* = 6.3 Hz, 3H), 0.53 - 0.42 (m, *J* = 5.7 Hz, 4H); 664.54 $[M+H]^+$	1.12
132		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.42 (s, 1H), 8.32 (s, 1H), 7.78 (s, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.38 (s, 1H), 6.76 (s, 1H), 6.69 (s, 1H), 6.39 - 6.23 (m, 2H), 5.76 (dd, *J* = 9.8, 1.6 Hz, 1H), 5.71 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.19 - 4.13 (m, 1H), 4.08 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.12 - 3.04 (m, 3H), 3.00 - 2.89 (m, 4H), 2.86 - 2.78 (m, 2H), 2.72 - 2.55 (m, 3H), 2.41 - 2.29 (m, 2H), 1.98 - 1.86 (m, 3H), 1.74 - 1.63 (m, 2H), 1.16 (d, *J* = 6.2 Hz, 3H), 0.52 - 0.43 (m, 4H); 664.59 $[M+H]^+$	1.12
133		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.44 (s, 1H), 8.31 (s, 1H), 7.78 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.47 - 7.38 (m, 2H), 6.75 (s, 1H), 6.68 (s, 1H), 6.40 - 6.24 (m, 2H), 5.75 (dd, *J* = 9.7, 1.6 Hz, 1H), 5.71 (dd, *J* = 8.6, 4.6 Hz, 1H), 4.19 - 4.11 (m, 1H), 4.07 (q, *J* = 8.1 Hz, 1H), 3.84 (s, 3H), 3.49 (s, 2H), 3.08 - 2.98 (m, 2H), 2.85 - 2.65 (m, 7H), 2.44 - 2.29 (m, 2H), 2.04 - 1.91 (m, 7H), 1.73 - 1.60 (m, 2H), 0.81 - 0.73 (m, 2H), 0.56 - 0.48 (m, 2H); 676.59 $[M+H]^+$	1.13
134		N-(2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.44 (s, 1H), 8.34 (s, 1H), 7.35 - 7.28 (m, 1H), 7.12 (s, 1H), 7.03 - 6.95 (m, 1H), 6.93 - 6.85 (m, 1H), 6.75 (s, 1H), 6.74 (s, 1H), 6.40 - 6.23 (m, 2H), 5.89 (dd, *J* = 8.7, 4.4 Hz, 1H), 5.75 (dd, *J* = 9.8, 1.6 Hz, 1H), 4.14 - 4.03 (m, 2H), 3.84 (s, 3H), 3.35 (s, 2H), 3.06 - 2.99 (m, 2H), 2.87 - 2.78 (m, 1H), 2.74 - 2.63 (m, 4H), 2.53 - 2.46 (m, 2H), 2.36 - 2.25 (m, 2H), 1.99 - 1.83 (m, 7H), 1.68 - 1.57 (m, 2H), 0.59 - 0.52 (m, 2H), 0.49 - 0.41 (m, 2H); 687.53 $[M+H]^+$	1.22

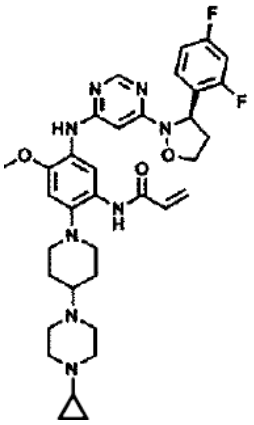
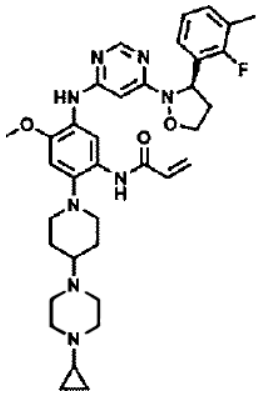
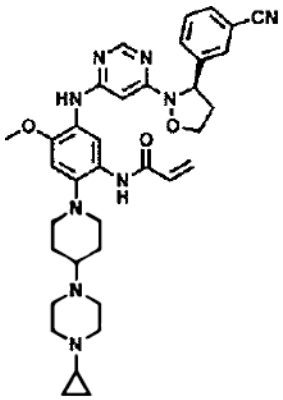
		yl)amino)-4-methoxyphenyl) acrylamide		

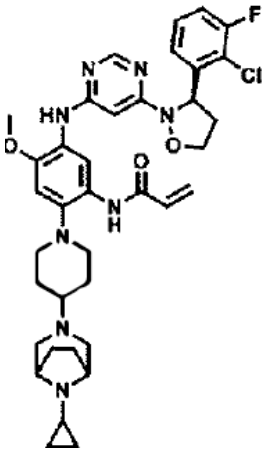
[485]

135		N-(2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.43 (s, 1H), 8.32 (s, 1H), 7.37 - 7.28 (m, 2H), 7.10 - 7.00 (m, 2H), 6.75 (s, 1H), 6.71 (s, 1H), 6.40 - 6.23 (m, 2H), 5.92 (dd, *J* = 8.5, 4.5 Hz, 1H), 5.75 (dd, *J* = 9.8, 1.6 Hz, 1H), 4.16 - 4.02 (m, 2H), 3.84 (s, 3H), 3.42 (s, 2H), 3.08 - 2.98 (m, 2H), 2.92 - 2.53 (m, 7H), 2.40 - 2.26 (m, 2H), 2.03 - 1.87 (m, 7H), 1.71 - 1.58 (m, 2H), 0.71 - 0.62 (m, 2H), 0.53 - 0.44 (m, 2H); 687.53 $[M+H]^+$	1.22
136		N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.82 (s, 1H), 8.42 (s, 1H), 8.35 (s, 1H), 7.82 (s, 1H), 7.24 - 7.20 (m, 1H), 6.91 - 6.87 (m, 2H), 6.73 (s, 1H), 6.40 - 6.31 (m, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.94 - 5.88 (m, 1H), 5.78 - 5.64 (m, 2H), 4.45 - 4.30 (m, 2H), 3.97 (p, *J* = 7.5 Hz, 2H), 3.00 (d, *J* = 26.2 Hz, 4H), 2.90 (d, *J* = 10.8 Hz, 1H), 2.82 - 2.67 (m, 4H), 2.61 - 2.53 (m, 2H), 2.48 (d, *J* = 11.2 Hz, 1H), 2.33 (t, *J* = 10.8 Hz, 2H), 1.69 - 1.64 (m, 2H), 1.56 - 1.53 (m, 1H), 1.21 (d, *J* = 6.3 Hz, 3H), 0.67 - 0.57 (m, 2H), 0.48 - 0.41 (m, 1H), 0.36 - 0.29 (m, 1H); 675.6$[M+H]^+$	1.11
137		N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.80 (s, 1H), 8.41 (s, 1H), 8.34 (d, *J* = 1.0 Hz, 1H), 7.83 (s, 1H), 7.24 - 7.20 (m, 1H), 6.90 - 6.88 (m, 2H), 6.72 (s, 1H), 6.39 - 6.32 (m, 1H), 6.25 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.91 (dd, *J* = 9.0, 6.5 Hz, 1H), 5.76 - 5.68 (m, 2H), 4.44 - 4.33 (m, 2H), 3.97 (p, *J* = 7.2 Hz, 2H), 3.81 (s, 3H), 3.08 - 2.98 (m, 4H), 2.92 (d, *J* = 11.1 Hz, 1H), 2.78 - 2.67 (m, 4H), 2.61 - 2.56 (m, 2H), 2.54 - 2.48 (m, 1H), 2.40 - 2.33 (m, 2H), 1.73 - 1.65 (m, 2H), 1.55 (dt, *J* = 6.7, 3.2 Hz, 1H), 1.22 (d, *J* = 6.3 Hz, 3H), 0.67 - 0.59 (m, 2H), 0.48 - 0.40 (m, 1H), 0.37 - 0.30 (m, 1H); 675.6$[M+H]^+$	1.10
138		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-	1H NMR (400 MHz,DMSO-d6) δ 9.20 (s, 1H), 9.06 (s, 1H), 8.23 (d, *J* = 2.1 Hz, 1H), 8.05 (s, 1H), 7.43 (d, *J* = 3.6 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.37 - 7.33 (m, 2H), 6.85 (s, 1H), 6.61 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.28 - 6.19 (m, 2H), 5.74 (d, *J* = 10.3 Hz, 1H), 5.53 (dd, *J* = 8.6, 5.3 Hz, 1H), 4.26 - 4.18 (m, 2H), 3.91 (t, *J* = 7.9 Hz, 3H), 3.80 (s, 3H), 3.29 (d, *J* = 11.6 Hz, 2H), 3.22 - 3.09 (m, 4H), 2.85 (d, *J* = 9.0 Hz, 2H), 2.74 (t, *J* = 11.7 Hz, 3H), 2.28 (dtd, *J* = 17.0, 9.1, 7.9, 4.8 Hz, 1H), 2.09 (d, *J* = 11.9 Hz, 3H), 1.98 - 1.84 (m, 2H), 0.63 - 0.44 (m, 4H).; 650.5$[M+H]^+$	1.19

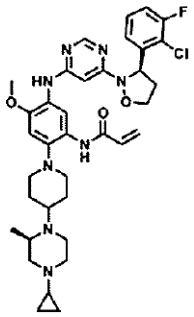
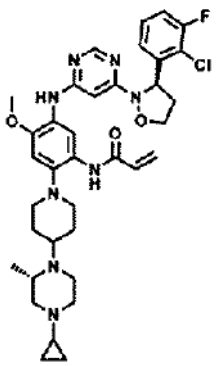
		methoxyphenyl)acrylamide		

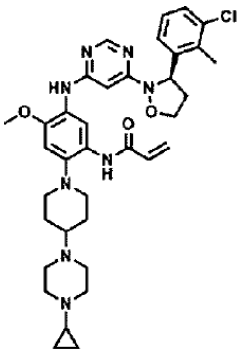
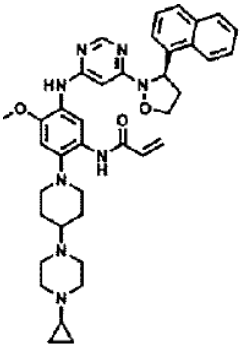
[486]

139		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.67 (s, 1H), 9.15 (s, 1H), 8.27 (s, 1H), 7.98 (s, 1H), 7.40 - 7.38 (m, 1H), 7.35 - 7.25 (m, 1H), 7.09 (td, J = 8.4, 2.6 Hz, 1H), 6.80 (s, 1H), 6.67 (dd, J = 16.9, 10.2 Hz, 1H), 6.29 - 6.12 (m, 2H), 5.76 (d, J = 10.3 Hz, 1H), 5.66 (t, J = 7.3 Hz, 1H), 4.29 (q, J = 7.7, 6.4 Hz, 2H), 4.05 - 3.98 (m, 4H), 3.81 (s, 3H), 3.76 - 3.58 (m, 5H), 3.21 (d, J = 11.5 Hz, 2H), 2.94 - 2.85 (m, 1H), 2.78 (t, J = 11.6 Hz, 2H), 2.30 - 2.22 (m, 1H), 2.20 - 2.11 (m, 2H), 2.09 - 1.93 (m, 2H), 1.26 - 1.22 (m, 1H), 0.89 - 0.67 (m, 4H) ;661.5[M+H]$^+$	1.19
140		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.59 (s, 1H), 8.14 (d, J = 1.0 Hz, 2H), 7.28 (t, J = 7.4 Hz, 1H), 7.18 (t, J = 6.0 Hz, 2H), 7.06 (t, J = 7.6 Hz, 1H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.70 (s, 1H), 4.14 (td, J = 8.0, 3.0 Hz, 1H), 3.70 (s, 3H), 3.17 (s, 2H), 3.03 (dd, J = 12.0, 6.7 Hz, 3H), 2.95 - 2.85 (m, 1H), 2.82 - 2.71 (m, 2H), 2.66 (t, J = 11.6 Hz, 3H), 2.21 - 2.06 (m, 2H), 1.88 (s, 8H), 1.83 (d, J = 12.3 Hz, 3H), 1.70 (d, J = 12.1 Hz, 3H), 1.58 (tt, J = 6.6, 3.7 Hz, 1H), 0.30 (dt, J = 6.2, 3.0 Hz, 3H), 0.30 - 0.26 (m, 2H).; 657.5 [M+H]$^+$	1.26
141		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.03 (s, 1H), 9.19 (s, 1H), 8.30 (s, 1H), 7.94 (s, 1H), 7.83 (d, J = 1.8 Hz, 1H), 7.78 (d, J = 7.5 Hz, 2H), 7.72 (d, J = 7.9 Hz, 1H), 7.60 (t, J = 7.8 Hz, 1H), 6.90 (s, 1H), 6.69 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.14 (s, 1H), 5.80 - 5.72 (m, 1H), 5.58 (dd, J = 8.5, 5.5 Hz, 1H), 3.89 (t, J = 6.1 Hz, 1H), 3.81 (s, 3H), 3.57 (s, 2H), 3.43 (d, J = 16.8 Hz, 2H), 3.37 (t, J = 7.0 Hz, 1H), 3.22 (d, J = 11.6 Hz, 2H), 3.07 - 2.58 (m, 7H), 2.40 - 2.28 (m, 2H), 2.16 (s, 3H), 2.13 - 2.00 (m, 3H), 1.15 (d, J = 7.0 Hz, 2H), 0.82 (d, J = 7.0 Hz, 3H).; 650.5 [M+H]$^+$	1.15

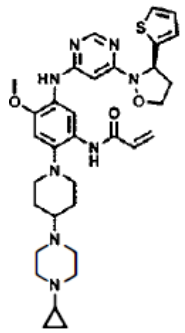
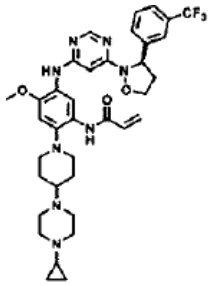
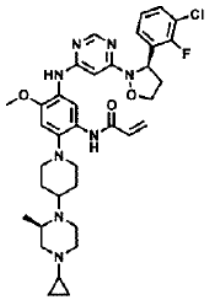
142		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.44 (s, 1H), 8.32 (d, J = 0.6 Hz, 1H), 7.46 (d, J = 7.9 Hz, 1H), 7.24 - 7.18 (m, 1H), 7.07 - 7.02 (m, 1H), 6.75 (s, 1H), 6.72 (s, 1H), 6.40 - 6.24 (m, 2H), 5.95 (dd, J = 8.7, 4.4 Hz, 1H), 5.75 (dd, J = 9.8, 1.7 Hz, 1H), 4.14 - 4.04 (m, 2H), 3.84 (s, 3H), 3.41 (s, 2H), 3.08 - 2.99 (m, 2H), 2.99 - 2.88 (m, 1H), 2.76 - 2.63 (m, 4H), 2.62 - 2.53 (m, 2H), 2.40 - 2.32 (m, 1H), 2.28 - 2.19 (m, 1H), 2.03 - 1.86 (m, 7H), 1.70 - 1.57 (m, 2H), 0.69 - 0.61 (m, 2H), 0.52 - 0.45 (m, 2H); 703.50 $[M+H]^+$	1.37

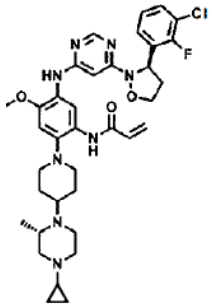
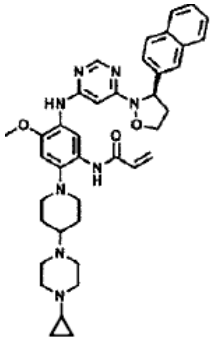
[487]

143		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.43 (s, 1H), 8.32 (s, 1H), 7.46 (d, J = 7.9 Hz, 1H), 7.32 (s, 1H), 7.24 - 7.18 (m, 1H), 7.05 (dd, J = 12.3, 4.7 Hz, 1H), 6.74 (d, J = 7.1 Hz, 1H), 6.71 (s, 1H), 6.39 - 6.23 (m, 2H), 5.94 (dd, J = 8.7, 4.4 Hz, 1H), 5.74 (dd, J = 9.8, 1.6 Hz, 1H), 4.13 - 4.03 (m, 2H), 3.84 (s, 3H), 3.10 - 3.01 (m, 4H), 2.99 - 2.89 (m, 2H), 2.79 - 2.67 (m, 2H), 2.67 - 2.51 (m, 2H), 2.50 - 2.37 (m, 2H), 2.29 - 2.19 (m, 1H), 2.14 - 2.07 (m, 3H), 1.80 - 1.67 (m, 2H), 1.61 - 1.54 (m, 1H), 1.23 (d, J = 6.3 Hz, 3H), 0.69 - 0.59 (m, 2H), 0.50 - 0.31 (m, 2H); 691.45 $[M+H]^+$	1.34
144		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.42 (s, 1H), 8.31 (s, 1H), 7.48 - 7.40 (m, 2H), 7.08 - 7.01 (m, 1H), 6.74 (s, 1H), 6.71 (s, 1H), 6.40 - 6.24 (m, 2H), 5.94 (dd, J = 8.7, 4.4 Hz, 1H), 5.74 (dd, J = 9.7, 1.7 Hz, 1H), 4.15 - 4.02 (m, 2H), 3.84 (s, 3H), 3.14 - 2.89 (m, 6H), 2.79 - 2.43 (m, 6H), 2.27 - 2.20 (m, 1H), 2.15 - 2.07 (m, 3H), 1.82 - 1.70 (m, 2H), 1.64 - 1.55 (m, 1H), 1.24 (d, J = 6.3 Hz, 3H), 0.71 - 0.60 (m, 2H), 0.51 - 0.32 (m, 2H); 691.50 $[M+H]^+$	1.32

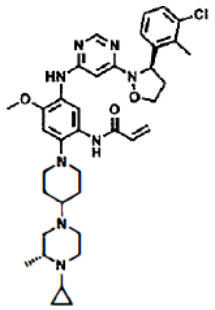
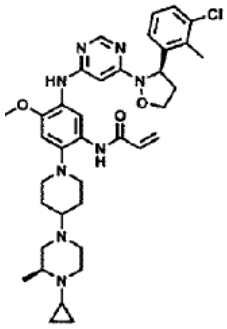
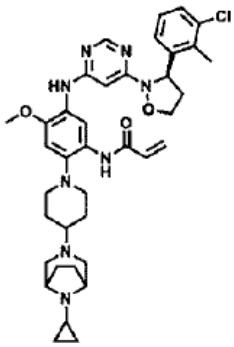
145		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.58 (s, 1H), 8.14 (d, J = 1.0 Hz, 1H), 7.40 (d, J = 7.8 Hz, 2H), 7.34 (dd, J = 8.0, 1.3 Hz, 2H), 7.20 (t, J = 7.9 Hz, 2H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.34 (s, 1H), 6.20 (dd, J = 17.1, 2.0 Hz, 1H), 5.69 (dd, J = 8.9, 4.6 Hz, 2H), 4.16 - 4.13 (m, 1H), 3.79 (s, 3H), 2.89 (t, J = 6.2 Hz, 1H), 2.86 - 2.78 (m, 2H), 2.65 (d, J = 11.4 Hz, 4H), 2.27 (s, 2H), 2.11 - 2.07 (m, 1H), 1.89 (s, 8H), 1.83 (d, J = 12.4 Hz, 3H), 1.71 (s, 2H), 1.58 (dt, J = 6.5, 3.1 Hz, 2H), 0.39 (dd, J = 6.4, 2.2 Hz, 2H), 0.28 - 0.26 (m, 2H).; 673.5 $[M+H]^+$	1.31
146		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.90 (s, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 8.15 (d, J = 8.3 Hz, 1H), 7.88 (dd, J = 8.0, 1.5 Hz, 1H), 7.79 - 7.75 (m, 2H), 7.55 - 7.45 (m, 3H), 6.91 (s, 1H), 6.78 - 6.75 (m, 2H), 6.42 - 6.21 (m, 4H), 5.74 (dd, J = 9.9, 1.6 Hz, 1H), 4.20 - 4.15 (m, 2H), 3.84 (s, 3H), 3.09 - 3.03 (m, 2H), 2.99 - 2.94 (m, 1H), 2.75 - 2.60 (m, 10H), 2.42 - 2.32 (m, 2H), 2.10 - 2.05 (m, 2H), 1.72 - 1.66 (m, 2H), 0.49 - 0.42 (m, 4H) ; 675.5[M+H]$^+$	1.24

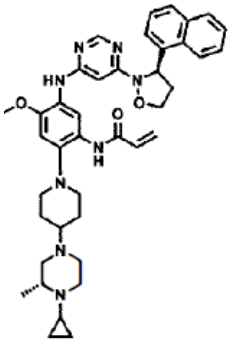
[488]

147		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(thiophene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.41 (s, 1H), 8.36 (s, 1H), 7.43 (s, 1H), 7.19 (d, *J* = 5.1 Hz, 1H), 7.06 (d, *J* = 3.4 Hz, 1H), 6.95 (dd, *J* = 4.9, 3.6 Hz, 1H), 6.72 (s, 1H), 6.62 (s, 1H), 6.30 - 6.11 (m, 2H), 5.99 (dd, *J* = 8.2, 3.2 Hz, 1H), 5.80 (d, *J* = 10.4 Hz, 1H), 5.73 (dd, *J* = 9.8, 1.5 Hz, 1H), 4.23 - 4.16 (m, 1H), 4.12 (q, *J* = 7.0 Hz, 1H), 3.82 (s, 3H), 3.12 - 3.01 (m, 2H), 2.98 - 2.61 (m, 12H), 2.55 - 2.46 (m, 1H), 2.16 - 2.08 (m, 2H), 1.87 - 1.70 (m, 3H), 0.55 - 0.46 (m, 4H); 631.50 $[M+H]^+$	1.17
148		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.45 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.73 (s, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.50 - 7.44 (m, 2H), 6.95 (s, 1H), 6.74 (d, *J* = 6.5 Hz, 2H), 6.38 - 6.20 (m, 3H), 5.77 - 5.73 (m, 2H), 4.17 - 4.07 (m, 2H), 3.84 (s, 3H), 3.07 - 3.03 (m, 2H), 2.78 - 2.61 (m, 12H), 2.36 - 2.33 (m, 1H), 2.10 - 2.05 (m, 2H), 1.72 - 1.65 (m, 2H), 0.47 - 0.42 (m, 4H) ; 603.5$[M+H]^+$	1.42
149		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d_6) δ 9.06 (d, *J* = 26.6 Hz, 2H), 8.21 (d, *J* = 3.5 Hz, 1H), 7.53 (td, *J* = 7.6, 1.7 Hz, 1H), 7.42 (t, *J* = 6.9 Hz, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 6.85 (s, 1H), 6.65 (d, *J* = 11.5 Hz, 1H), 6.33 - 6.17 (m, 2H), 5.79 - 5.65 (m, 2H), 4.22 (dt, *J* = 7.9, 4.3 Hz, 2H), 3.03 (d, *J* = 8.0 Hz, 4H), 3.80 (s, 3H), 3.47 (d, *J* = 31.1 Hz, 4H), 3.22 (s, 2H), 3.15 (d, *J* = 13.8 Hz, 3H), 2.88 (d, *J* = 13.8 Hz, 3H), 2.23 (h, *J* = 7.6 Hz, 1H), 2.14 (s, 1H), 2.00 - 1.83 (m, 2H), 1.31 (d, *J* = 6.2 Hz, 3H), 0.61 - 0.30 (m, 4H).; 601.5$[M+H]^+$	1.41

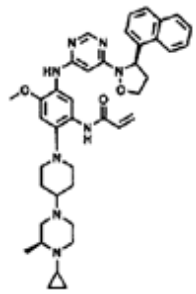
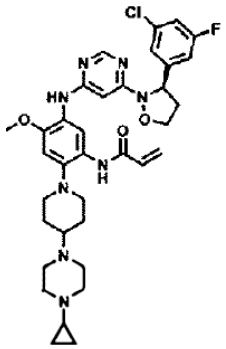
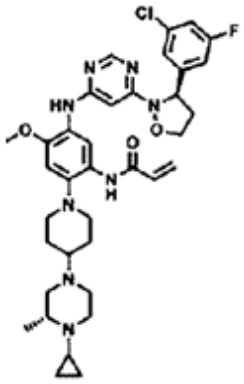
150		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d_6) δ 9.22 (d, J = 24.5 Hz, 1H), 9.05 (s, 1H), 8.23 (d, J = 2.5 Hz, 1H), 7.53 (td, J = 7.6, 1.7 Hz, 1H), 7.45 - 7.37 (m, 1H), 7.23 (t, J = 7.9 Hz, 1H), 6.86 (s, 1H), 6.66 (s, 1H), 6.31 - 6.20 (m, 2H), 5.73 (td, J = 9.7, 8.8, 3.6 Hz, 2H), 4.30 - 4.17 (m, 4H), 3.95 (td, J = 9.9, 8.7, 5.9 Hz, 3H), 3.80 (s, 3H), 3.63 (s, 1H), 3.50 (d, J = 24.8 Hz, 2H), 3.27 (s, 2H), 3.14 (t, J = 10.9 Hz, 2H), 2.95 - 2.72 (m, 4H), 2.33 - 2.21 (m, 1H), 2.15 (s, 1H), 2.02 - 1.84 (m, 2H), 1.32 (d, J = 6.2 Hz, 3H), 0.53 (d, J = 25.6 Hz, 4H) ; 691.5[M+H]$^+$	1.41
151		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 2H), 9.85 (s, 1H), 9.16 (s, 1H), 8.28 (s, 1H), 8.00 - 7.83 (m, 5H), 7.61 - 7.44 (m, 3H), 6.86 (s, 1H), 6.68 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.10 (s, 1H), 5.84 - 5.71 (m, 1H), 5.67 (s, 1H), 4.37 (d, J = 4.7 Hz, 1H), 4.10 (q, J = 7.7 Hz, 3H), 3.77 (s, 3H), 3.70 (s, 4H), 3.20 (d, J = 11.3 Hz, 2H), 3.00 (d, J = 6.4 Hz, 1H), 2.77 (t, J = 11.9 Hz, 2H), 2.41 (dq, J = 12.9, 7.3 Hz, 2H), 2.17 (d, J = 11.0 Hz, 2H), 2.07 (d, J = 16.1 Hz, 2H), 1.32 - 1.20 (m, 1H), 1.09 (t, J = 7.0 Hz, 2H), 0.80 (s, 2H); 675.53 [M+H]+	1.26

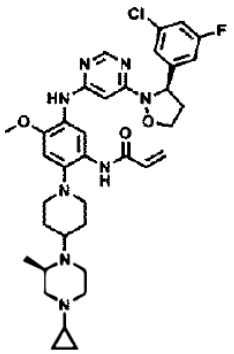
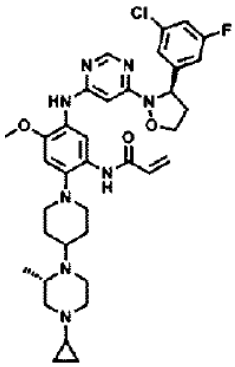
[489]

152		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.00 (s, 1H), 8.63 (s, 1H), 8.20 - 8.10 (m, 2H), 7.39 (dd, J = 7.8, 1.3 Hz, 1H), 7.34 (dd, J = 8.1, 1.4 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.83 (s, 1H), 6.61 (dd, J = 16.9, 10.2 Hz, 1H), 6.38 (s, 1H), 6.22 (dd, J = 16.9, 1.9 Hz, 1H), 5.71 (ddd, J = 14.0, 9.4, 3.5 Hz, 2H), 4.15 (td, J = 7.9, 3.8 Hz, 1H), 3.81 (s, 3H), 3.44 - 3.27 (m, 8H), 3.12 (t, J = 10.9 Hz, 4H), 2.84 (tq, J = 8.0, 3.9 Hz, 2H), 2.72 (s, 4H), 2.42 (s, 4H), 2.08 (ddq, J = 12.8, 8.1, 5.2 Hz, 3H), 1.91 (s, 2H), 1.23 (d, J = 14.1 Hz, 4H).; 687.5 $[M+H]^+$	1.32
153		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.58 (s, 1H), 8.14 (t, J = 1.6 Hz, 2H), 7.40 (dd, J = 7.8, 1.3 Hz, 1H), 7.34 (dd, J = 7.9, 1.3 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.81 (s, 1H), 6.66 (dd, J = 17.0, 10.2 Hz, 1H), 6.34 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.71 (td, J = 9.0, 8.3, 3.5 Hz, 2H), 4.14 (td, J = 7.9, 3.8 Hz, 1H), 3.79 (s, 3H), 3.32 (s, 6H), 3.04 (d, J = 11.0 Hz, 2H), 2.80 - 2.60 (m, 7H), 2.42 (s, 3H), 2.36 - 2.15 (m, 4H), 1.92 (t, J = 9.7 Hz, 1H), 1.83 (d, J = 11.8 Hz, 2H), 1.76 - 1.63 (m, 3H), 1.10 (d, J = 6.3 Hz, 3H).; 687.5 $[M+H]^+$	1.31
154		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.58 (s, 1H), 8.14 (d, J = 1.0 Hz, 1H), 7.40 (dd, J = 7.7, 1.3 Hz, 1H), 7.34 (dd, J = 8.0, 1.3 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.80 (s, 1H), 6.66 (dd, J = 17.0, 10.2 Hz, 1H), 6.34 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.70 (ddd, J = 8.6, 5.6, 3.4 Hz, 2H), 4.14 (td, J = 7.9, 3.8 Hz, 1H), 3.79 (s, 3H), 3.32 (s, 2H), 3.19 (s, 2H), 3.03 (d, J = 11.1 Hz, 2H), 2.82 (dtd, J = 11.9, 7.9, 3.8 Hz, 1H), 2.63 (ddd, J = 14.5, 10.1, 2.8 Hz, 4H), 2.42 (s, 3H), 2.28 (d, J = 9.6 Hz, 2H), 2.18 (dq, J = 10.4, 5.6, 3.4 Hz, 1H), 2.14 - 2.02 (m, 1H), 1.92 - 1.75 (m, 5H), 1.66 (dq, J = 20.8, 8.9, 6.4 Hz, 4H), 0.36 (dd, J = 6.4, 4.1 Hz, 2H), 0.30 (d, J = 3.5 Hz, 2H).; 600.5 $[M+H]^+$	1.35

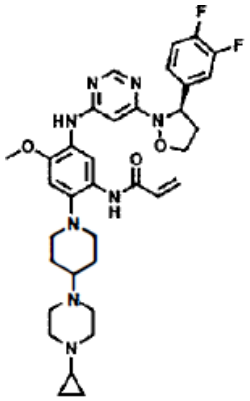
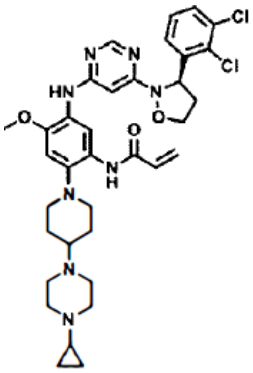
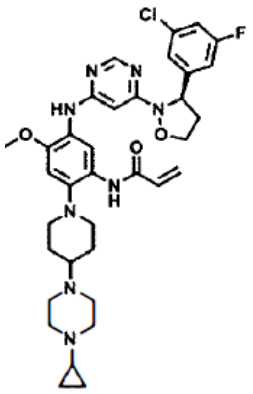
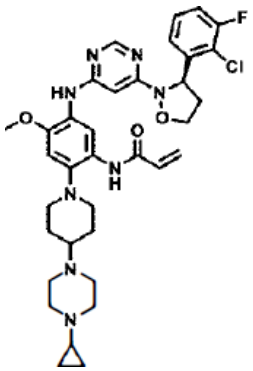
155		N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.90 (s, 1H), 8.45 (s, 1H), 8.37 (s, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.88 (dd, J = 8.1, 1.5 Hz, 1H), 7.70 - 7.75 (m, 2H), 7.55 - 7.45 (m, 3H), 6.92 (s, 1H), 6.78 - 6.75 (m, 2H), 6.43 - 6.21 (m, 4H), 5.75 - 5.72 (m, 1H), 4.20 - 4.15 (m, 2H), 3.84 (s, 3H), 3.05 - 2.85 (m, 7H), 2.75 - 2.67 (m, 2H), 2.50 - 2.41 (m, 2H), 2.31 - 2.28 (m, 1H), 2.08 - 1.97 (m, 3H), 1.68 - 1.64 (m, 2H), 1.56 - 1.51 (m, 1H), 1.21 (d, J = 6.3 Hz, 3H), 0.66 - 0.50 (m, 2H), 0.46 - 0.41 (m, 1H), 0.35 - 0.20 (m, 1H) ; 680.5[M+H]$^+$	1.26

[490]

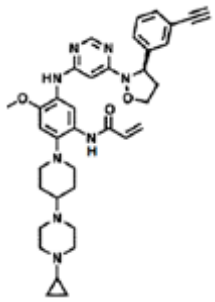
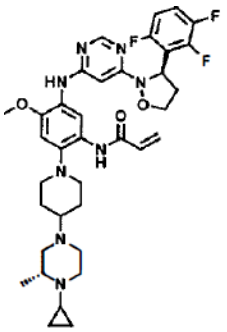
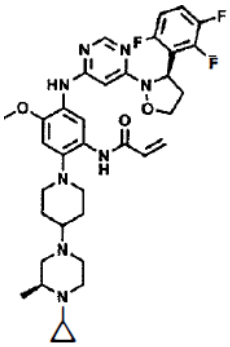
156		N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.45 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 8.16 - 8.13 (m, 1H), 7.90 - 7.86 (m, 1H), 7.77 (dd, *J* = 7.8, 6.4 Hz, 2H), 7.56 - 7.44 (m, 3H), 6.92 (s, 1H), 6.76 (d, *J* = 11.9 Hz, 2H), 6.43 - 6.20 (m, 4H), 5.74 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.20 - 4.15 (m, 2H), 3.84 (s, 3H), 3.08 - 2.86 (m, 7H), 2.76 - 2.68 (m, 2H), 2.52 - 2.42 (m, 2H), 2.32 - 2.28 (m, 1H), 2.02 (dd, *J* = 22.0, 11.6 Hz, 3H), 1.60 - 1.64 (m, 2H), 1.56 - 1.51 (m, 1H), 1.21 (d, *J* = 6.4 Hz, 3H), 0.66 - 0.58 (m, 2H), 0.47 - 0.41 (m, 1H), 0.34 - 0.28 (m, 1H) ; 689.5[M+H]$^+$	1.27
157		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 7.10 (d, *J* = 9.4 Hz, 1H), 6.99 - 6.94 (m, 1H), 6.92 (s, 1H), 6.75 (s, 1H), 6.71 (s, 1H), 6.39 - 6.11 (m, 2H), 5.77 - 5.70 (m, 2H), 5.66 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.19 - 4.12 (m, 1H), 4.06 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.10 - 2.85 (m, 5H), 2.81 - 2.67 (m, 3H), 2.57 - 2.44 (m, 2H), 2.38 - 2.25 (m, 3H), 2.11 - 1.96 (m, 3H), 1.72 - 1.65 (m, 2H), 1.57 - 1.50 (m, 1H), 1.21 (d, *J* = 6.3 Hz, 3H), 0.69 - 0.55 (m, 2H), 0.48 - 0.28 (m, 2H); 691.45 [M+H]$^+$	1.34
158		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.10 (d, *J* = 9.4 Hz, 1H), 6.97 (dt, *J* = 8.4, 2.0 Hz, 1H), 6.93 (s, 1H), 6.75 (s, 1H), 6.71 (s, 1H), 6.40 - 6.19 (m, 2H), 5.74 (dd, *J* = 10.0, 1.3 Hz, 1H), 5.66 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.15 (dt, *J* = 8.0, 4.1 Hz, 1H), 4.06 (q, *J* = 8.1 Hz, 1H), 3.84 (s, 3H), 3.09 - 2.86 (m, 5H), 2.81 - 2.67 (m, 3H), 2.57 - 2.43 (m, 2H), 2.38 - 2.26 (m, 3H), 2.11 - 1.97 (m, 3H), 1.69 - 1.60 (m, 2H), 1.57 - 1.49 (m, 1H), 1.21 (d, *J* = 6.3 Hz, 3H), 0.68 - 0.56 (m, 2H), 0.47 - 0.27 (m, 2H); 691.50 [M+H]$^+$	1.32

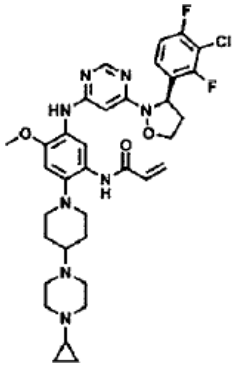
159		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.10 (d, *J* = 9.4 Hz, 1H), 6.97 (dt, *J* = 8.5, 2.0 Hz, 1H), 6.94 (s, 1H), 6.76 (s, 1H), 6.71 (s, 1H), 6.40 - 6.22 (m, 2H), 5.75 (dd, *J* = 10.0, 1.4 Hz, 1H), 5.66 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.15 (td, *J* = 8.0, 4.2 Hz, 1H), 4.06 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.12 - 3.01 (m, 2H), 2.99 - 2.66 (m, 8H), 2.57 - 2.41 (m, 2H), 2.38 - 2.28 (m, 1H), 2.26 - 2.19 (m, 1H), 1.93 - 1.81 (m, 3H), 1.64 - 1.55 (m, 2H), 1.00 (d, *J* = 6.1 Hz, 3H), 0.50 - 0.37 (m, 4H); 691.45 $[M+H]^+$	1.35
160		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.10 (d, *J* = 9.4 Hz, 1H), 6.99 - 6.95 (m, 1H), 6.93 (s, 1H), 6.76 (s, 1H), 6.71 (s, 1H), 6.29 (dt, *J* = 16.9, 13.3 Hz, 2H), 5.77 - 5.73 (m, 1H), 5.66 (dd, *J* = 8.6, 4.6 Hz, 1H), 4.16 (td, *J* = 8.1, 4.3 Hz, 1H), 4.06 (q, *J* = 8.1 Hz, 1H), 3.84 (s, 3H), 3.11 - 3.02 (m, 2H), 2.99 - 2.63 (m, 8H), 2.57 - 2.41 (m, 2H), 2.38 - 2.28 (m, 1H), 2.27 - 2.19 (m, 1H), 1.94 - 1.81 (m, 3H), 1.60 - 1.53 (m, 2H), 1.00 (d, *J* = 6.2 Hz, 3H), 0.49 - 0.37 (m, 4H); 691.45 $[M+H]^+$	1.36

[491]

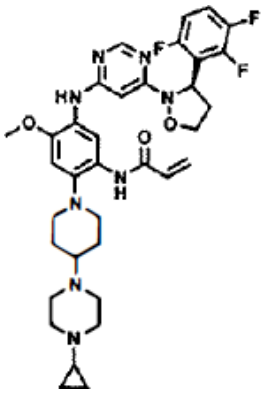
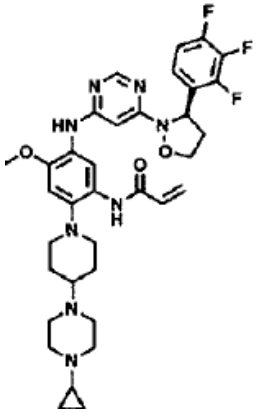
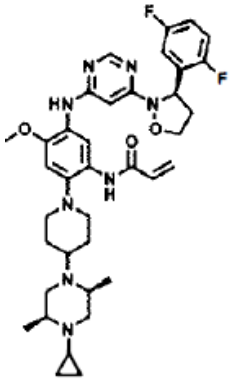
161		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.31 (s, 1H), 8.17 (s, 1H), 7.40 - 7.32 (m, 1H), 7.28 - 7.21 (m, 2H), 6.91 (s, 1H), 6.57 (dd, *J* = 17.0, 10.3 Hz, 1H), 6.45 (s, 1H), 6.36 (dd, *J* = 17.0, 1.3 Hz, 1H), 5.81 (d, *J* = 10.4 Hz, 1H), 5.54 (dd, *J* = 8.5, 4.6 Hz, 1H), 4.15 (td, *J* = 7.9, 4.3 Hz, 1H), 3.98 (q, *J* = 7.9 Hz, 1H), 3.88 (s, 3H), 3.17 (d, *J* = 11.0 Hz, 2H), 2.67 (t, *J* = 11.5 Hz, 1H), 2.40 - 2.27 (m, 1H), 2.16 - 2.06 (m, 2H), 1.89 - 1.74 (m, 3H), 1.30 (s, 1H), 0.59 - 0.51 (m, 2H), 0.51 - 0.43 (m, 2H) ; 661.5[M+H]$^+$	1.25
162		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.84 (s, 1H), 8.44 (s, 1H), 8.35 (d, *J* = 1.0 Hz, 1H), 7.50 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.37 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.96 (s, 1H), 6.75 (s, 2H), 6.36 (dd, *J* = 17.0, 1.6 Hz, 1H), 6.26 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.96 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.7 Hz, 1H), 4.15 - 4.02 (m, 2H), 3.85 (s, 3H), 3.65 (p, *J* = 6.7 Hz, 1H), 3.08 (d, *J* = 7.4 Hz, 2H), 2.95 (dtd, *J* = 12.3, 8.0, 4.3 Hz, 1H), 2.81 - 2.66 (m, 8H), 2.11 (d, *J* = 12.3 Hz, 2H), 1.83 (s, 6H), 1.55 (t, *J* = 7.4 Hz, 2H), 0.50 - 0.40 (m, 4H).: 603.5[M+H]$^+$	1.35
163		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	677.5[M+H]$^+$	1.33
164		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.81 (s, 1H), 8.43 (s, 1H), 8.35 (s, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.20 (dt, *J* = 8.1, 4.1 Hz, 1H), 6.74 (d, *J* = 8.6 Hz, 2H), 6.42 - 6.16 (m, 2H), 5.95 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.7 Hz, 1H), 4.17 - 3.98 (m, 2H), 3.84 (s, 3H), 3.81 - 3.74 (m, 2H), 3.06 (dd, *J* = 9.4, 5.2 Hz, 2H), 2.81 - 2.67 (m, 7H), 2.06 (s, 3H), 1.43 (s, 5H), 1.39 (d, *J* = 6.7 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 4H). ; 677.5 [M+H]$^+$	1.30

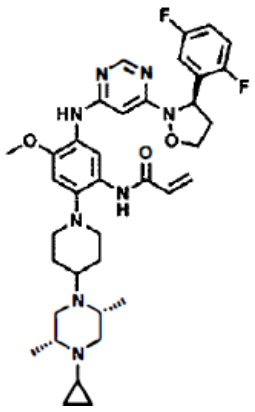
[492]

165		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.08 (s, 1H), 9.21 (s, 1H), 8.31 (s, 1H), 7.91 (s, 1H), 7.43 (d, J = 21.5 Hz, 4H), 6.90 (s, 1H), 6.70 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.07 (s, 1H), 5.79 - 5.74 (m, 1H), 5.56 - 5.47 (m, 1H), 4.32 (d, J = 4.4 Hz, 1H), 4.24 (s, 1H), 4.10 - 4.01 (m, 2H), 3.80 (s, 3H), 3.77 - 3.71 (m, 4H), 3.22 (d, J = 11.3 Hz, 2H), 2.93 (ddt, J = 11.9, 8.6, 4.8 Hz, 2H), 2.80 (t, J = 11.6 Hz, 2H), 2.35 - 2.26 (m, 1H), 2.17 (s, 2H), 2.00 (s, 2H), 1.67 - 1.54 (m, 2H), 1.49 - 1.36 (m, 2H), 1.16 (t, J = 3.6 Hz, 2H), 0.83 (d, J = 7.1 Hz, 2H). : 649.3[M+H]$^+$	1.13
166		N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.84 (s, 1H), 8.43 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.10 - 7.02 (m, 1H), 6.87 - 6.80 (m, 2H), 6.73 (s, 1H), 6.65 - 6.61 (m, 1H), 6.43 - 6.17 (m, 3H), 5.90 (dd, J = 9.1, 6.6 Hz, 1H), 5.74 (dd, J = 10.0, 1.5 Hz, 1H), 4.40 - 4.34 (m, 1H), 4.03 - 3.94 (m, 1H), 3.82 (s, 3H), 3.07 - 2.86 (m, 6H), 2.77 - 2.68 (m, 3H), 2.56 - 2.48 (m, 2H), 2.31 - 2.27 (m, 1H), 2.00 - 1.97 (m, 3H), 1.70 - 1.62 (m, 2H), 1.56 - 1.50 (m, 1H), 1.21 (d, J = 2.7 Hz, 3H), 0.67 - 0.57 (m, 2H), 0.46 - 0.31 (m, 2H) : 603.5[M+H]$^+$	1.20
167		N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.84 (s, 1H), 8.43 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.10 - 7.01 (m, 1H), 6.87 - 6.81 (m, 2H), 6.73 (s, 1H), 6.64 - 6.61 (m, 1H), 6.42 - 6.18 (m, 3H), 5.90 (dd, J = 9.0, 6.6 Hz, 1H), 5.74 (dd, J = 10.0, 1.5 Hz, 1H), 4.39 - 4.33 (m, 1H), 4.02 - 3.95 (m, 1H), 3.82 (s, 3H), 3.07 - 2.86 (m, 6H), 2.76 - 2.68 (m, 3H), 2.57 - 2.49 (m, 2H), 2.32 - 2.28 (m, 1H), 2.00 - 1.98 (m, 3H), 1.69 - 1.59 (m, 2H), 1.56 - 1.50 (m, 1H), 1.21 (d, 3H), 0.66 - 0.58 (m, 2H), 0.48 - 0.40 (m, 1H), 0.35 - 0.28 (m, 1H) : 603.5[M+H]$^+$	1.20

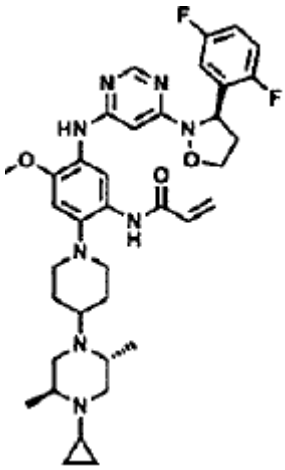
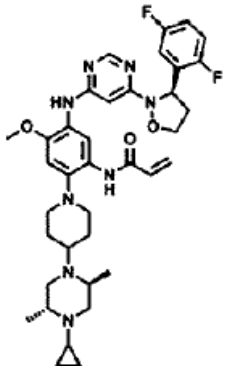
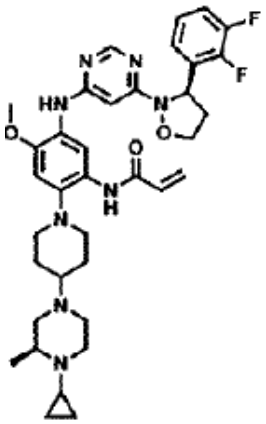
168		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.84 (s, 1H), 8.40 (s, 1H), 8.34 (d, *J* = 1.0 Hz, 1H), 7.40 (td, *J* = 8.4, 6.0 Hz, 1H), 7.00 (s, 1H), 6.95 (td, *J* = 8.5, 1.8 Hz, 1H), 6.74 (d, *J* = 1.8 Hz, 2H), 6.41 - 6.21 (m, 2H), 5.86 (dd, *J* = 8.8, 4.6 Hz, 1H), 5.74 (dd, *J* = 9.7, 1.8 Hz, 1H), 4.10 - 3.99 (m, 2H), 3.84 (s, 3H), 3.08 (d, *J* = 11.6 Hz, 2H), 2.80 (dp, *J* = 24.7, 12.3, 8.2 Hz, 10H), 2.12 (d, *J* = 12.1 Hz, 2H), 2.07 (s, 1H), 1.91 - 1.68 (m, 3H), 1.26 (d, *J* = 4.6 Hz, 1H), 0.92 - 0.81 (m, 1H), 0.55 - 0.39 (m, 4H).; 695.5[M+H]$^+$	1.35

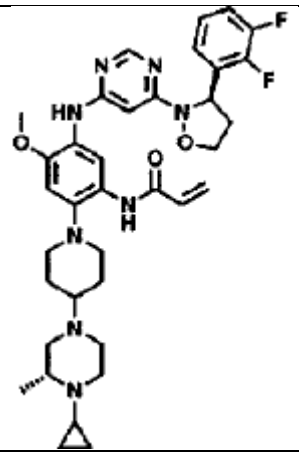
[493]

169		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.83 (s, 1H), 8.43 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.08 - 7.03 (m, 1H), 6.86 - 6.82 (m, 2H), 6.73 (s, 1H), 6.63 (s, 1H), 6.42 - 6.17 (m, 3H), 5.91 - 5.87 (m, 1H), 5.73 (dd, J = 10.0, 1.5 Hz, 1H), 4.38 - 4.34 (m, 1H), 4.01 - 3.96 (m, 1H), 3.82 (s, 3H), 3.07 - 3.03 (m, 2H), 2.75 - 2.59 (m, 12H), 2.36 - 2.30 (m, 1H), 2.09 - 2.05 (m, 2H), 1.72 - 1.66 (m, 2H), 0.47 - 0.42 (m, 4H) ; 679.5[M+H]$^+$	1.23
170		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.17 (s, 1H), 9.25 (s, 1H), 8.33 (s, 1H), 7.91 (s, 1H), 7.33 (dt, J = 9.8, 2.3 Hz, 1H), 7.24 (dd, J = 8.3, 5.3 Hz, 1H), 6.92 (s, 1H), 6.71 (dd, J = 17.0, 10.2 Hz, 1H), 6.29 - 6.12 (m, 2H), 5.73 (ddd, J = 28.1, 9.3, 3.7 Hz, 2H), 4.37 - 4.31 (m, 3H), 4.07 (t, J = 7.9 Hz, 2H), 3.77 (s, 4H), 3.67 (s, 2H), 3.50 (d, J = 16.0 Hz, 1H), 3.23 (d, J = 11.5 Hz, 2H), 2.94 (t, J = 6.3 Hz, 2H), 2.82 (s, 2H), 2.37 - 2.29 (m, 1H), 2.17 (s, 2H), 2.10 (d, J = 7.0 Hz, 2H), 1.61 (d, J = 12.5 Hz, 1H), 1.48 - 1.38 (m, 1H), 1.23 - 1.15 (m, 2H), 0.84 (d, J = 7.0 Hz, 2H). ; 679.3[M+H]$^+$	1.28
171		N-(2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.95 (s, 1H), 9.27 (s, 1H), 8.31 (s, 1H), 7.32 (td, J = 9.3, 4.4 Hz, 1H), 7.26 - 7.12 (m, 3H), 6.94 (d, J = 17.4 Hz, 1H), 6.80 - 6.51 (m, 1H), 6.28 - 6.11 (m, 2H), 5.76 (t, J = 5.3 Hz, 2H), 5.66 (dd, J = 8.6, 5.5 Hz, 2H), 4.03 (d, J = 8.2 Hz, 10H), 3.81 (d, J = 3.8 Hz, 6H), 3.56 (s, 3H), 3.35 - 3.10 (m, 5H), 3.02 - 2.87 (m, 4H), 2.86 - 2.67 (m, 2H), 2.20 (dt, J = 13.1, 6.5 Hz, 3H), 2.13 (s, 3H), 1.73 (s, 2H), 1.56 (s, 6H).; 689.6 [M+H]$^+$	1.41

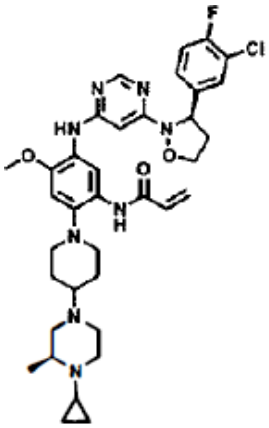
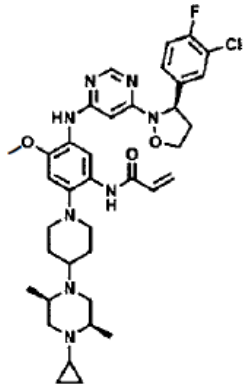
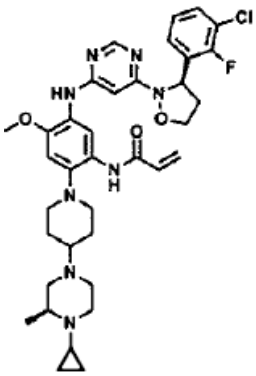
172		N-(2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.00 (s, 1H), 9.25 (d, J = 28.6 Hz, 1H), 8.31 (s, 1H), 7.32 (td, J = 9.3, 4.5 Hz, 2H), 7.26 - 7.10 (m, 3H), 6.94 (d, J = 18.3 Hz, 1H), 6.79 - 6.49 (m, 1H), 6.31 - 6.12 (m, 3H), 5.75 (d, J = 3.5 Hz, 1H), 5.66 (dd, J = 8.6, 5.6 Hz, 2H), 4.05 (t, J = 7.9 Hz, 4H), 3.81 (d, J = 4.1 Hz, 6H), 3.56 (s, 12H), 3.21 (d, J = 33.4 Hz, 5H), 3.03 - 2.87 (m, 4H), 2.88 - 2.64 (m, 3H), 2.36 - 2.22 (m, 3H), 2.14 (s, 3H), 1.74 (s, 3H), 1.57 (s, 6H).; 689.6 $[M+H]^+$	1.38

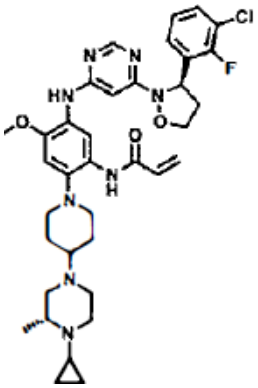
[494]

173		N-(2-(4-((2R,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	680.6 $[M+H]^+$	1.37
174		N-(2-(4-((2S,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	680.6 $[M+H]^+$	1.36
175		N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.42 (s, 1H), 8.32 (s, 1H), 7.41 - 7.31 (m, 2H), 7.09 - 7.00 (m, 2H), 6.74 (s, 1H), 6.70 (s, 1H), 6.39 - 6.23 (m, 2H), 5.92 (dd, *J* = 8.6, 4.5 Hz, 1H), 5.74 (dd, *J* = 9.8, 1.6 Hz, 1H), 4.16 - 4.10 (m, 1H), 4.05 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.12 - 2.97 (m, 5H), 2.90 - 2.81 (m, 1H), 2.78 - 2.42 (m, 6H), 2.34 - 2.25 (m, 1H), 2.18 - 2.08 (m, 3H), 1.82 - 1.69 (m, 2H), 1.65 - 1.55 (m, 1H), 1.24 (d, *J* = 6.3 Hz, 3H), 0.72 - 0.59 (m, 2H), 0.51 - 0.32 (m, 2H); 675.62 $[M+H]^+$	1.27

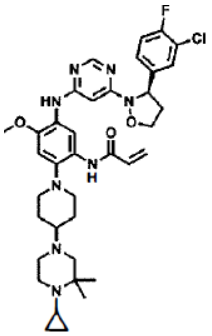
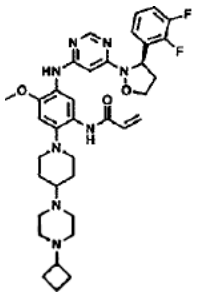
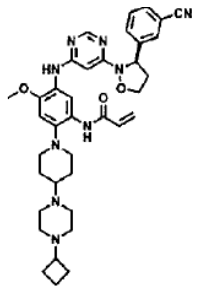
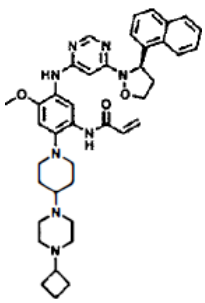
176		N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.42 (s, 1H), 8.32 (s, 1H), 7.41 - 7.30 (m, 2H), 7.11 - 6.99 (m, 2H), 6.74 (s, 1H), 6.70 (s, 1H), 6.39 - 6.23 (m, 2H), 5.92 (dd, *J* = 8.6, 4.5 Hz, 1H), 5.74 (dd, *J* = 9.8, 1.6 Hz, 1H), 4.17 - 4.10 (m, 1H), 4.06 (q, *J* = 8.1 Hz, 1H), 3.84 (s, 3H), 3.12 - 3.02 (m, 4H), 3.02 - 2.96 (m, 1H), 2.90 - 2.81 (m, 1H), 2.78 - 2.41 (m, 6H), 2.35 - 2.26 (m, 1H), 2.17 - 2.07 (m, 3H), 1.80 - 1.68 (m, 2H), 1.63 - 1.55 (m, 1H), 1.23 (d, *J* = 6.3 Hz, 3H), 0.70 - 0.58 (m, 2H), 0.50 - 0.32 (m, 2H); 675.58 $[M+H]^+$	1.25

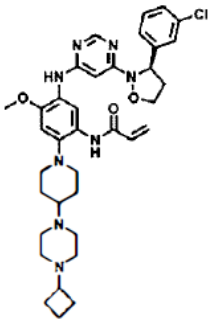
[495]

177		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H), 9.25 (s, 1H), 8.34 (s, 1H), 7.90 (s, 1H), 7.58 (dd, J = 7.1, 2.1 Hz, 1H), 7.46 - 7.35 (m, 2H), 6.92 (s, 1H), 6.78 - 6.68 (m, 1H), 6.26 (dd, J = 16.9, 2.0 Hz, 1H), 6.12 (s, 1H), 5.81 - 5.74 (m, 1H), 5.54 (dd, J = 8.5, 5.4 Hz, 1H), 4.35 - 4.27 (m, 1H), 4.15 - 4.05 (m, 2H), 3.81 (s, 3H), 3.74 - 3.66 (m, 2H), 3.54 - 3.37 (m, 3H), 3.23 (s, 2H), 3.00 - 2.75 (m, 5H), 2.33 (dt, J = 7.8, 5.2 Hz, 1H), 2.25 - 2.09 (m, 4H), 1.58 - 1.40 (m, 3H), 1.43 (s, 1H), 0.91 (d, J = 52.0 Hz, 4H).; 691.3[M+H]$^+$	1.32
178		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.35 (s, 1H), 9.40 (s, 1H), 8.35 (s, 1H), 7.88 (d, J = 60.9 Hz, 1H), 7.50 (dd, J = 7.1, 2.2 Hz, 1H), 7.46 - 7.35 (m, 2H), 6.97 (d, J = 21.7 Hz, 1H), 6.80 - 6.55 (m, 1H), 6.26 (dd, J = 16.9, 1.9 Hz, 1H), 6.13 (s, 1H), 5.77 (dd, J = 10.2, 1.9 Hz, 1H), 5.54 (dd, J = 8.4, 5.5 Hz, 1H), 4.37 - 4.20 (m, 2H), 4.14 - 4.01 (m, 3H), 3.82 (d, J = 3.5 Hz, 3H), 3.72 (s, 1H), 3.67 - 3.53 (m, 2H), 3.38 (d, J = 6.7 Hz, 1H), 3.22 (dd, J = 29.9, 15.5 Hz, 3H), 3.08 - 2.88 (m, 3H), 2.81 (d, J = 29.2 Hz, 1H), 2.32 (dd, J = 7.9, 5.0 Hz, 2H), 2.17 (d, J = 14.7 Hz, 2H), 1.77 (d, J = 7.0 Hz, 2H), 1.65 - 1.57 (m, 4H), 1.46 - 1.33 (m, 1H), 0.94 - 0.74 (m, 3H).; 705.3[M+H]$^+$	1.39
179		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.08 (s, 1H), 8.22 (s, 1H), 8.07 (s, 1H), 7.56 - 7.50 (m, 1H), 7.41 (t, J = 7.3 Hz, 1H), 7.23 (t, J = 7.9 Hz, 1H), 6.86 (s, 1H), 6.65 (dd, J = 16.8, 10.0 Hz, 1H), 6.33 - 6.19 (m, 2H), 5.79 - 5.68 (m, 2H), 4.29 - 4.19 (m, 1H), 3.94 (q, J = 8.1 Hz, 2H), 3.81 (s, 3H), 3.18 (d, J = 11.1 Hz, 4H), 2.87 (d, J = 9.3 Hz, 2H), 2.75 (t, J = 11.5 Hz, 3H), 2.29 - 2.20 (m, 2H), 2.16 (s, 3H), 1.99 (s, 3H), 1.91 (s, 3H), 1.38 (d, J = 16.4 Hz, 3H), 1.24 (s, 3H).; 691.5[M+H]$^+$	1.38

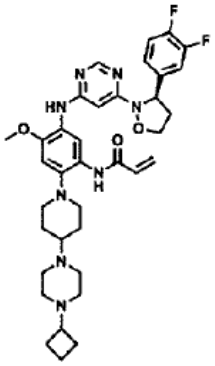
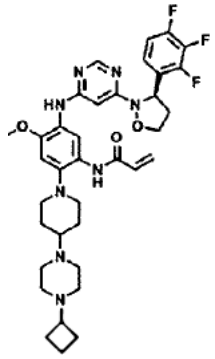
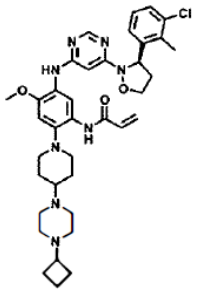
180		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 9.03 (s, 1H), 8.76 (s, 1H), 8.18 (s, 1H), 7.52 (t, J = 7.4 Hz, 1H), 7.48 - 7.38 (m, 1H), 7.23 (t, J = 7.9 Hz, 1H), 6.84 (s, 1H), 6.60 (d, J = 12.0 Hz, 1H), 6.37 (s, 1H), 6.29 - 6.17 (m, 1H), 5.73 (t, J = 7.5 Hz, 2H), 4.19 (d, J = 3.8 Hz, 1H), 3.88 (q, J = 7.9 Hz, 1H), 3.81 (s, 3H), 3.15 (d, J = 11.1 Hz, 4H), 2.83 (d, J = 8.7 Hz, 2H), 2.72 (s, 3H), 2.25 - 2.05 (m, 5H), 1.91 (s, 5H), 1.28 - 1.21 (m, 4H), 1.17 (s, 4H). : 601.5[M+H]+	1.38

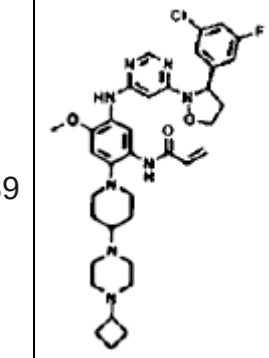
[496]

181		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropyl-3,3-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, Methanol-d_4) δ 8.28 (s, 1H), 8.16 (s, 1H), 7.54 (dd, J = 7.1, 2.3 Hz, 1H), 7.39 (ddd, J = 8.6, 4.6, 2.3 Hz, 1H), 7.21 (t, J = 8.9 Hz, 1H), 6.89 (s, 1H), 6.53 (dd, J = 17.0, 10.2 Hz, 1H), 6.43 (s, 1H), 6.35 (dd, J = 17.0, 1.6 Hz, 1H), 5.84 - 5.76 (m, 1H), 5.52 (dd, J = 8.6, 4.7 Hz, 1H), 4.14 (td, J = 7.9, 4.2 Hz, 1H), 3.96 (q, J = 8.0 Hz, 1H), 3.86 (s, 3H), 3.15 (d, J = 11.6 Hz, 2H), 3.09 (t, J = 5.2 Hz, 2H), 2.82 - 2.76 (m, 2H), 2.72 - 2.64 (m, 2H), 2.35 - 2.28 (m, 1H), 2.20 (tt, J = 7.1, 3.9 Hz, 1H), 2.03 (d, J = 12.1 Hz, 2H), 1.87 - 1.77 (m, 2H), 1.37 (s, 6H), 1.28 (s, 4H), 0.74 (d, J = 6.9 Hz, 2H), 0.69 - 0.59 (m, 2H); 705.5[M+H]$^+$	1.33
182		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.63 (s, 1H), 8.16 (s, 1H), 7.41 - 7.13 (m, 4H), 6.82 (s, 1H), 6.65 (dd, J = 17.0, 10.2 Hz, 1H), 6.35 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.75 (d, J = 4.6 Hz, 2H), 5.74 - 5.69 (m, 1H), 3.85 (q, J = 8.1 Hz, 2H), 3.79 (s, 4H), 3.04 (d, J = 11.1 Hz, 3H), 2.88 - 2.74 (m, 2H), 2.71 - 2.59 (m, 4H), 2.38 - 2.14 (m, 6H), 1.94 (dq, J = 9.6, 5.8, 5.2 Hz, 3H), 1.82 (s, 8H), 1.80 - 1.66 (m, 5H), 1.66 - 1.56 (m, 3H), 1.23 (s, 1H).; 675.6 [M+H]$^+$	1.21
183		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.62 (s, 1H), 8.16 (s, 1H), 7.83 (d, J = 1.8 Hz, 1H), 7.79 - 7.72 (m, 2H), 7.58 (t, J = 7.8 Hz, 1H), 6.82 (s, 1H), 6.65 (dd, J = 17.0, 10.2 Hz, 1H), 6.36 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.71 (dd, J = 10.1, 2.0 Hz, 1H), 5.59 (dd, J = 8.7, 5.0 Hz, 1H), 4.14 (td, J = 7.9, 3.9 Hz, 1H), 3.79 (s, 3H), 3.33 (s, 8H), 3.04 (d, J = 11.1 Hz, 2H), 2.78 (dtd, J = 12.0, 7.8, 3.9 Hz, 2H), 2.71 - 2.60 (m, 4H), 2.25 (tq, J = 8.2, 5.1 Hz, 6H), 2.08 (s, 3H), 2.01 - 1.90 (m, 3H), 1.66 - 1.56 (m, 3H).; 664.5 [M+H]$^+$	1.09
184		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-	^{1}H NMR (400 MHz, chloroform-d) δ 8.90 (s, 1H), 8.46 (s, 1H), 8.37 (s, 1H), 8.15 (d, J = 8.3 Hz, 1H), 7.89 - 7.87 (m, 1H), 7.79 - 7.75 (m, 2H), 7.55 - 7.45 (m, 3H), 6.93 (s, 1H), 6.78 - 6.75 (m, 2H), 6.41 - 6.21 (m, 4H), 5.73 (dd, J = 10.0, 1.6 Hz, 1H), 4.20 - 4.15 (m, 2H), 3.85 (s, 3H), 3.08 - 3.04 (m, 2H), 2.99 - 2.94 (m, 1H), 2.78 - 2.64 (m, 8H), 2.41 - 2.31 (m, 4H), 2.10 - 2.07 (m, 2H), 1.95 - 1.83 (m, 4H), 1.75 - 1.69 (m, 4H) ; 680.6[M+H]$^+$	1.24

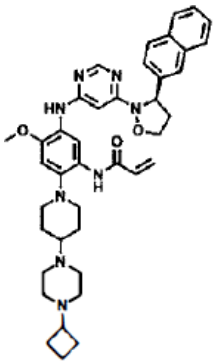
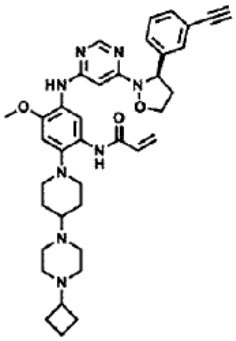
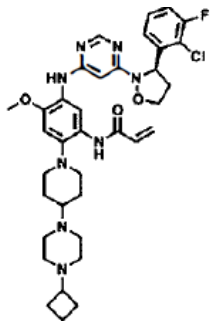
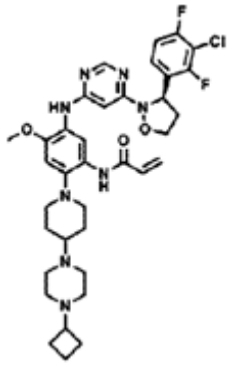
		4-yl)amino)phenyl)acrylamide		
185		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.07 (s, 1H), 8.23 (d, *J* = 3.1 Hz, 1H), 8.06 (s, 1H), 7.43 (q, *J* = 2.9, 2.4 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.35 (ddd, *J* = 7.4, 5.0, 1.8 Hz, 2H), 6.85 (s, 1H), 6.63 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.28 - 6.19 (m, 2H), 5.77 - 5.70 (m, 1H), 5.53 (dd, *J* = 8.6, 5.3 Hz, 1H), 4.21 (dq, *J* = 7.4, 3.7, 2.8 Hz, 4H), 3.91 (ddd, *J* = 13.2, 8.5, 4.8 Hz, 4H), 3.81 (s, 5H), 3.17 (d, *J* = 11.5 Hz, 4H), 2.89 - 2.81 (m, 1H), 2.76 (t, *J* = 11.7 Hz, 3H), 2.28 (dq, *J* = 8.9, 5.1, 3.8 Hz, 1H), 2.18 (d, *J* = 8.9 Hz, 4H), 2.04 (s, 2H), 1.94 - 1.83 (m, 2H), 1.75 (dt, *J* = 18.8, 10.1 Hz, 2H).; 673.5[M+H]+	1.22

[497]

186		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.11 (s, 1H), 9.23 (s, 1H), 8.32 (s, 1H), 7.92 (s, 1H), 7.49 - 7.38 (m, 2H), 7.22 (dq, J = 7.9, 2.7 Hz, 1H), 6.91 (s, 1H), 6.72 (dd, J = 16.9, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.12 (s, 1H), 5.75 (d, J = 5.4 Hz, 1H), 5.53 (dd, J = 8.5, 5.4 Hz, 1H), 4.29 (dd, J = 7.6, 4.5 Hz, 1H), 4.10 - 4.00 (m, 1H), 3.81 (s, 3H), 3.63 (s, 6H), 3.46 (d, J = 13.8 Hz, 3H), 3.23 (d, J = 11.5 Hz, 2H), 2.97 - 2.87 (m, 1H), 2.81 (t, J = 11.8 Hz, 2H), 2.44 - 2.20 (m, 3H), 2.24 - 2.14 (m, 4H), 2.00 (s, 1H), 1.84 - 1.69 (m, 2H), 1.63 - 1.55 (m, 1H), 1.48 - 1.40 (m, 1H).; 675.3[M+H]$^+$	1.21
187		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.70 (s, 1H), 9.17 (s, 1H), 8.28 (s, 1H), 7.99 (s, 1H), 7.40 - 7.24 (m, 2H), 6.89 (s, 1H), 6.60 (dd, J = 16.9, 10.2 Hz, 1H), 6.24 (dd, J = 17.1, 2.0 Hz, 2H), 5.78 - 5.74 (m, 1H), 5.70 (dd, J = 8.6, 5.5 Hz, 1H), 4.30 (d, J = 4.2 Hz, 1H), 4.09 (d, J = 5.2 Hz, 1H), 4.01 (d, J = 7.9 Hz, 1H), 3.81 (s, 3H), 3.74 (s, 1H), 3.65 (d, J = 12.7 Hz, 3H), 3.47 - 3.35 (m, 3H), 3.22 (d, J = 11.3 Hz, 2H), 2.96 - 2.88 (m, 1H), 2.79 (t, J = 11.8 Hz, 2H), 2.30 (s, 1H), 2.34 - 2.28 (m, 1H), 2.19 (t, J = 11.3 Hz, 4H), 2.07 (d, J = 16.0 Hz, 3H), 1.74 (dd, J = 20.6, 10.5 Hz, 2H), 1.63 - 1.54 (m, 1H), 1.46 - 1.39 (m, 1H).; 603.3[M+H]$^+$	1/28
188		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.59 (s, 1H), 8.14 (t, J = 1.4 Hz, 2H), 7.40 (dd, J = 7.8, 1.3 Hz, 1H), 7.34 (dd, J = 8.0, 1.3 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.70 (td, J = 9.2, 8.5, 3.5 Hz, 2H), 4.15 (td, J = 7.9, 3.8 Hz, 1H), 3.79 (s, 3H), 3.05 (d, J = 11.1 Hz, 2H), 2.83 (dtd, J = 12.0, 7.9, 3.7 Hz, 2H), 2.71 - 2.62 (m, 3H), 2.54 (s, 1H), 2.42 (s, 4H), 2.37 - 2.16 (m, 5H), 2.13 - 2.04 (m, 2H), 1.96 (s, 3H), 1.83 (s, 3H), 1.64 (d, J = 6.4 Hz, 2H), 1.24 (d, J = 6.0 Hz, 5H).; 687.5 [M+H]$^+$	1.25

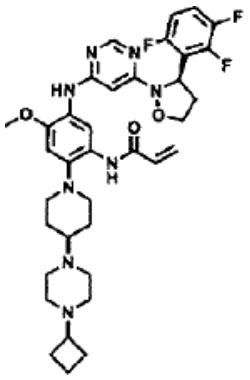
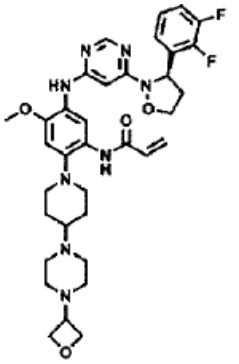
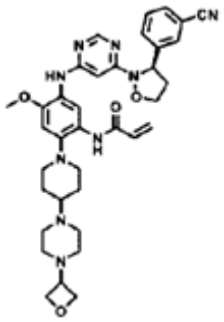
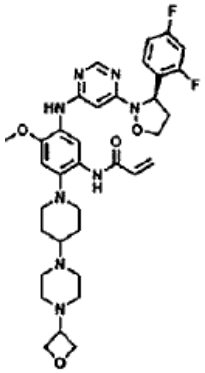
189		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	691.45 $[M+H]^+$	1.28

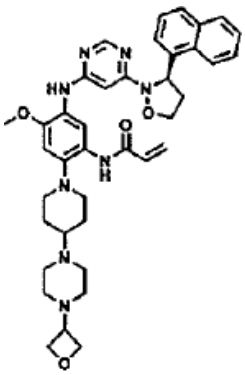
[498]

190		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.06 (s, 1H), 8.22 (d, J = 3.7 Hz, 1H), 8.07 (s, 1H), 7.96 - 7.85 (m, 4H), 7.52 (dtd, J = 14.9, 8.1, 7.4, 3.5 Hz, 3H), 6.84 (s, 1H), 6.63 (dd, J = 16.9, 10.2 Hz, 1H), 6.24 (dd, J = 17.0, 1.9 Hz, 2H), 5.78 - 5.62 (m, 2H), 4.26 (dd, J = 8.4, 4.5 Hz, 2H), 4.01 - 3.93 (m, 2H), 3.79 (s, 3H), 3.67 - 3.59 (m, 6H), 3.16 (d, J = 11.4 Hz, 4H), 2.96 - 2.85 (m, 2H), 2.73 (q, J = 14.7, 13.3 Hz, 2H), 2.37 (tdd, J = 11.2, 5.9, 3.9 Hz, 1H), 2.16 (d, J = 9.6 Hz, 4H), 2.02 (s, 2H), 1.89 (d, J = 15.9 Hz, 2H), 1.73 (dd, J = 18.6, 9.5 Hz, 2H).; 680.6[M+H]+	1.23
191		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.13 (s, 1H), 9.22 (s, 1H), 8.32 (s, 1H), 7.91 (s, 1H), 7.46 (s, 1H), 7.40 (s, 3H), 6.90 (s, 1H), 6.72 (dd, J = 17.0, 10.3 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 5.79 - 5.74 (m, 2H), 5.52 (dd, J = 8.4, 5.6 Hz, 1H), 4.32 (d, J = 4.4 Hz, 1H), 4.24 (s, 1H), 4.06 (d, J = 7.8 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 1H), 3.65 (d, J = 12.4 Hz, 4H), 3.45 (d, J = 13.8 Hz, 3H), 3.23 (d, J = 11.3 Hz, 2H), 2.94 (dd, J = 8.2, 4.4 Hz, 1H), 2.80 (t, J = 11.5 Hz, 2H), 2.41 (t, J = 10.2 Hz, 2H), 2.35 - 2.20 (m, 1H), 2.25 - 2.16 (m, 4H), 2.00 (d, J = 6.6 Hz, 2H), 1.73 (dd, J = 20.1, 10.2 Hz, 2H), 1.64 - 1.58 (m, 1H), 1.47 - 1.30 (m, 1H), 663.4[M+H]+	1.09
192		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.09 (d, J = 13.7 Hz, 1H), 8.22 (s, 1H), 8.08 (s, 1H), 7.44 - 7.31 (m, 3H), 6.85 (s, 1H), 6.62 (dd, J = 17.0, 10.2 Hz, 1H), 6.33 - 6.18 (m, 2H), 5.82 - 5.70 (m, 2H), 4.20 (td, J = 7.9, 4.0 Hz, 3H), 3.95 (d, J = 8.0 Hz, 4H), 3.81 (s, 3H), 3.71 (s, 3H), 3.17 (d, J = 11.6 Hz, 4H), 2.94 (dtd, J = 12.1, 7.9, 4.0 Hz, 2H), 2.76 (t, J = 11.7 Hz, 2H), 2.23 - 2.08 (m, 5H), 2.04 (d, J = 11.6 Hz, 2H), 1.90 (d, J = 10.4 Hz, 2H), 1.75 (dt, J = 18.8, 8.6 Hz, 2H).; 691.5[M+H]+	1.21
193		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpipe	1H NMR (400 MHz, DMSO-d6) δ 9.04 (d, J = 15.4 Hz, 1H), 8.21 (d, J = 2.2 Hz, 1H), 8.10 (s, 1H), 7.47 (td, J = 8.5, 6.1 Hz, 1H), 7.32 (td, J = 8.8, 1.7 Hz, 1H), 6.84 (s, 1H), 6.62 (dd, J = 17.0, 10.2 Hz, 1H), 6.32 (s, 1H), 6.23 (dd, J = 16.9, 1.9 Hz, 1H), 5.78 - 5.66 (m, 2H), 4.22 (td, J = 7.9, 3.6 Hz, 2H), 3.91 (s, 4H), 3.81 (s, 3H), 3.43 (t, J = 7.0 Hz, 4H), 3.20 - 3.11 (m, 4H), 2.85 (dq, J = 8.5, 5.6, 4.3 Hz, 2H), 2.80 - 2.71 (m, 2H), 2.28 - 2.21 (m, 1H), 2.16 (q, J = 10.9, 10.3 Hz, 4H), 2.03 (d, J = 11.2 Hz, 2H), 1.89 (d, J = 16.1 Hz, 2H), 1.74 (dt, J = 18.6, 9.6 Hz, 2H). ; 709.5[M+H]+	1.33

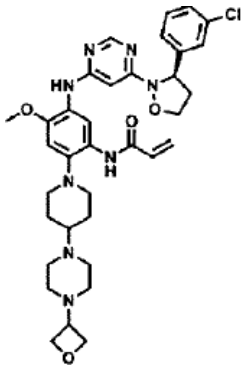
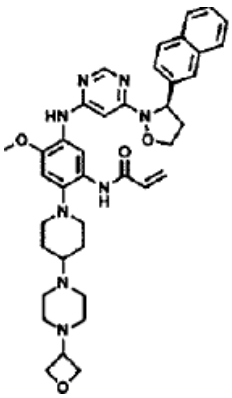
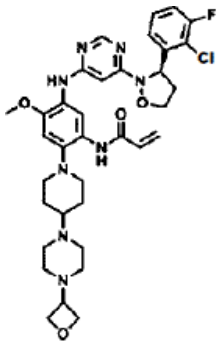
		razine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide		

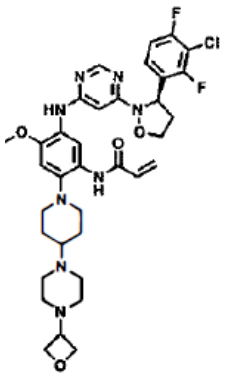
[499]

194		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.84 (s, 1H), 8.43 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.08 - 7.03 (m, 1H), 6.86 - 6.82 (m, 2H), 6.74 (s, 1H), 6.63 (s, 1H), 6.45 - 6.14 (m, 3H), 5.91 - 5.87 (m, 1H), 5.73 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.38 - 4.32 (m, 1H), 4.01 - 3.95 (m, 1H), 3.82 (s, 3H), 3.07 - 3.02 (m, 2H), 2.77 - 2.54 (m, 12H), 2.34 - 2.30 (m, 1H), 2.10 - 2.07 (m, 2H), 1.94 - 1.83 (m, 4H), 1.72 - 1.64 (m, 4H) ; 603.5[M+H]$^+$	1.19
195		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.43 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.37 - 7.33 (m, 1H), 7.07 - 7.02 (m, 2H), 6.94 (s, 1H), 6.76 - 6.74 (m, 2H), 6.39 - 6.20 (m, 3H), 5.94 - 5.91 (m, 1H), 5.75 - 5.72 (m, 1H), 4.70 - 4.63 (m, 4H), 4.17 - 4.04 (m, 3H), 3.85 (s, 3H), 3.55 - 3.51 (m, 1H), 3.09 - 3.04 (m, 2H), 2.90 - 2.70 (m, 7H), 2.42 - 2.29 (m, 4H), 2.11 - 2.06 (m, 2H), 1.70 - 1.67 (m, 2H) ; 677.5[M+H]$^+$	1.24
196		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.45 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.79 (d, *J* = 1.9 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.56 - 7.52 (m, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 6.94 (s, 1H), 6.76 - 6.71 (m, 2H), 6.45 - 6.14 (m, 3H), 5.76 - 5.70 (m, 2H), 4.70 - 4.62 (m, 4H), 4.18 - 4.07 (m, 2H), 3.85 (s, 3H), 3.55 - 3.46 (m, 2H), 3.09 - 3.03 (m, 2H), 2.86 - 2.67 (m, 7H), 2.43 - 2.31 (m, 4H), 2.10 - 2.04 (m, 2H), 1.71 - 1.66 (m, 2H) ; 666.5[M+H]$^+$	1.10
197		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-	1H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.43 (s, 1H), 8.37 (s, 1H), 7.56 (m, 1H), 6.92 (s, 1H), 6.79 (m, 4H), 6.36 (d, *J* = 16.8 Hz, 1H), 6.26 m, 1H), 5.87 (m, 1H), 5.74 (d, *J* = 10.3 Hz, 1H), 4.10 (m, 2H), 3.85 (s, 3H), 3.51 (m, 2H), 3.07 (d, *J* = 11.7 Hz, 2H), 2.87 - 2.63 (m, 8H), 2.36 (d, *J* = 67.9 Hz, 6H), 2.11 - 2.04 (m, 2H), 1.68 (m, 4H):677.5[M+H]$^+$	1.21

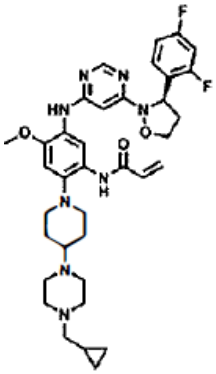
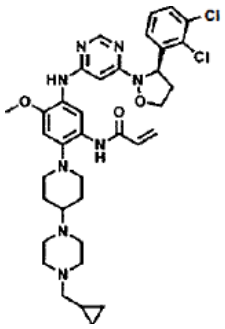
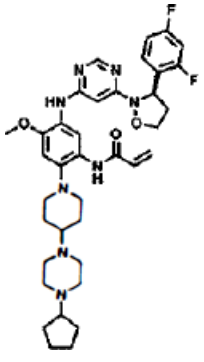
		yl)phenyl)acrylamide		
198		N-(4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.91 (s, 1H), 8.44 (s, 1H), 8.37 (s, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.77 (dd, *J* = 7.8, 4.7 Hz, 2H), 7.55 - 7.44 (m, 3H), 6.94 (s, 1H), 6.77 (d, *J* = 10.4 Hz, 2H), 6.43 - 6.22 (m, 4H), 5.74 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.60 - 4.63 (m, 4H), 4.20 - 4.14 (m, 2H), 3.85 (s, 3H), 3.55 - 3.47 (m, 2H), 3.10 - 3.05 (m, 2H), 2.98 - 2.94 (m, 1H), 2.78 - 2.68 (m, 6H), 2.45 - 2.38 (m, 4H), 2.10 - 2.05 (m, 2H), 1.70 - 1.67 (m, 2H) ; 691.5[M+H]$^+$	1.22

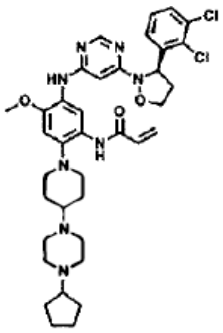
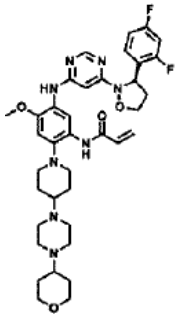
[500]

199		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.21 (s, 1H), 9.07 (s, 1H), 8.24 (s, 1H), 8.05 (s, 1H), 7.43 (d, *J* = 1.9 Hz, 1H), 7.42 - 7.39 (m, 1H), 7.36 (dd, *J* = 4.7, 2.5 Hz, 2H), 6.86 (s, 1H), 6.62 (dd, *J* = 16.9, 10.2 Hz, 1H), 6.28 - 6.20 (m, 2H), 5.75 (d, *J* = 10.3 Hz, 1H), 5.53 (dd, *J* = 8.6, 5.3 Hz, 1H), 4.60 (t, *J* = 6.6 Hz, 2H), 4.47 (t, *J* = 6.1 Hz, 2H), 4.22 (td, *J* = 7.8, 3.9 Hz, 3H), 3.81 (s, 3H), 3.63 (q, *J* = 6.2 Hz, 2H), 3.32 (s, 2H), 3.17 (t, *J* = 6.1 Hz, 4H), 3.06 - 2.93 (m, 2H), 2.85 (dtd, *J* = 12.0, 7.6, 3.9 Hz, 1H), 2.75 (t, *J* = 11.7 Hz, 2H), 2.28 (tdd, *J* = 12.8, 9.7, 5.7 Hz, 2H), 2.10 (d, *J* = 10.1 Hz, 2H), 1.92 (d, *J* = 10.1 Hz, 2H). : 675.5[M+H]+	1.24
200		N-(4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.07 (d, *J* = 3.3 Hz, 1H), 8.24 (d, *J* = 6.6 Hz, 1H), 8.04 (d, *J* = 8.3 Hz, 1H), 7.97 - 7.88 (m, 4H), 7.52 (qt, *J* = 7.5, 3.4 Hz, 3H), 6.85 (s, 1H), 6.68 - 6.58 (m, 1H), 6.28 - 6.18 (m, 2H), 5.79 - 5.63 (m, 2H), 4.60 (t, *J* = 6.6 Hz, 2H), 4.47 (dt, *J* = 9.5, 4.7 Hz, 2H), 4.33 - 4.24 (m, 2H), 3.99 (dd, *J* = 16.2, 7.9 Hz, 4H), 3.79 (s, 3H), 3.65 - 3.58 (m, 2H), 3.32 (s, 2H), 3.16 (d, *J* = 4.6 Hz, 4H), 3.00 - 2.91 (m, 1H), 2.75 (t, *J* = 11.8 Hz, 2H), 2.43 - 2.30 (m, 2H), 2.12 (dd, *J* = 17.1, 7.3 Hz, 2H), 1.92 (d, *J* = 10.5 Hz, 2H). : 691.5[M+H]+	1.23
201		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 9.06 (s, 1H), 8.22 (s, 1H), 8.07 (s, 1H), 7.45 - 7.31 (m, 3H), 6.86 (s, 1H), 6.62 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.34 - 6.17 (m, 2H), 5.83 - 5.71 (m, 2H), 4.60 (t, *J* = 6.6 Hz, 2H), 4.47 (t, *J* = 6.1 Hz, 2H), 4.21 (td, *J* = 7.8, 3.9 Hz, 2H), 3.97 - 3.95 (m, 4H), 3.81 (s, 3H), 3.62 (p, *J* = 6.4 Hz, 2H), 3.44 (q, *J* = 7.0 Hz, 1H), 3.32 (t, *J* = 12.1 Hz, 1H), 3.21 - 3.11 (m, 3H), 2.96 (tq, *J* = 8.1, 3.9 Hz, 2H), 2.75 (t, *J* = 11.9 Hz, 2H), 2.32 (s, 1H), 2.14 (ddd, *J* = 12.3, 8.1, 4.5 Hz, 3H), 1.98 - 1.86 (m, 2H).: 693.5[M+H]+	1.25

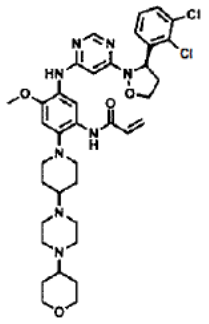
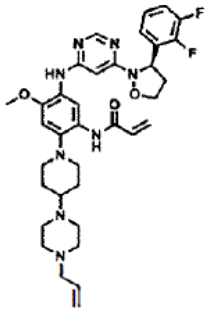
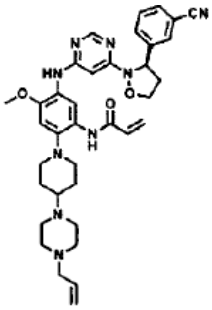
202		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.05 (s, 1H), 8.21 (s, 1H), 8.10 (s, 1H), 7.47 (td, *J* = 8.6, 6.2 Hz, 1H), 7.32 (td, *J* = 8.8, 1.7 Hz, 1H), 6.85 (s, 1H), 6.61 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.33 (s, 1H), 6.23 (dd, *J* = 17.0, 1.9 Hz, 1H), 5.77 - 5.66 (m, 2H), 4.60 (t, *J* = 6.6 Hz, 2H), 4.46 (t, *J* = 6.1 Hz, 2H), 4.22 (td, *J* = 7.8, 3.7 Hz, 1H), 3.91 (q, *J* = 8.2 Hz, 3H), 3.81 (s, 3H), 3.44 (d, *J* = 7.0 Hz, 1H), 3.31 (s, 2H), 3.17 (d, *J* = 11.7 Hz, 4H), 2.99 (s, 2H), 2.84 (qd, *J* = 8.2, 3.9 Hz, 1H), 2.73 (q, *J* = 18.0, 15.1 Hz, 2H), 2.34 - 2.19 (m, 3H), 2.11 (t, *J* = 10.0 Hz, 2H), 1.90 (dd, *J* = 15.0, 9.0 Hz, 2H).; 711.4[M+H]+	1.33

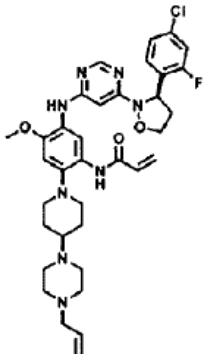
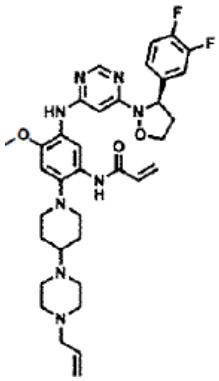
[501]

203		N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 7.56 (q, *J* = 8.2 Hz, 1H), 6.93 (s, 1H), 6.82 (td, *J* = 12.6, 11.4, 7.9 Hz, 2H), 6.75 (d, *J* = 3.0 Hz, 2H), 6.30 - 6.32 (m, 1H), 6.24 (dd, *J* = 17.0, 10.0 Hz, 1H), 5.87 (dd, *J* = 8.6, 4.3 Hz, 1H), 5.73 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.14 - 4.06 (m, 2H), 3.85 (s, 3H), 3.06 (d, *J* = 11.3 Hz, 2H), 2.83 - 2.65 (m, 8H), 2.35 - 2.26 (m, 4H), 2.00 (d, *J* = 12.8 Hz, 2H), 0.90 - 0.82 (m, 6H), 0.53 (d, *J* = 7.7 Hz, 2H), 0.13 (d, *J* = 5.0 Hz, 2H).; 675.5[M+H]$^+$	1.18
204		N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.42 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.60 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.37 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.93 (s, 1H), 6.75 (s, 2H), 6.40 - 6.32 (m, 1H), 6.30 - 6.21 (m, 1H), 5.96 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.74 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.15 - 4.04 (m, 2H), 3.85 (s, 3H), 3.64 (s, 2H), 3.07 (d, *J* = 10.7 Hz, 4H), 3.00 - 2.90 (m, 2H), 2.88 - 2.68 (m, 7H), 2.45 - 2.30 (m, 3H), 2.27 - 2.19 (m, 1H), 2.14 - 2.04 (m, 2H), 0.91 - 0.80 (m, 1H), 0.60 (s, 2H), 0.20 (s, 2H); 707.4[M+H]$^+$	1.31
205		N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.56 (q, *J* = 8.3 Hz, 1H), 6.93 (s, 1H), 6.87 - 6.74 (m, 4H), 6.35 (d, *J* = 17.3 Hz, 1H), 6.24 (dd, *J* = 17.0, 10.1 Hz, 1H), 5.87 (dd, *J* = 8.7, 4.3 Hz, 1H), 5.74 (dd, *J* = 10.2, 1.5 Hz, 1H), 4.14 - 4.05 (m, 2H), 3.85 (s, 3H), 3.06 (d, *J* = 11.8 Hz, 4H), 2.87 - 2.66 (m, 8H), 2.32 - 2.21 (m, 2H), 2.09 (d, *J* = 12.4 Hz, 2H), 1.91 (s, 2H), 1.70 (s, 4H), 1.45 (s, 6H).; 680.5[M+H]$^+$	1.22

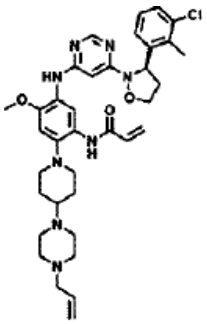
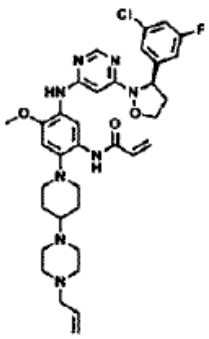
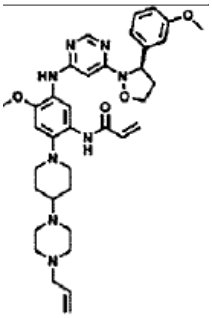
206		N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.85 (s, 1H), 8.39 - 8.34 (m, 2H), 7.50 (d, J = 7.2 Hz, 1H), 7.37 (d, J = 7.9 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 7.06 (s, 1H), 6.74 (s, 2H), 6.30 - 6.33 (m, 1H), 6.31 - 6.21 (m, 1H), 5.96 (dd, J = 8.8, 4.4 Hz, 1H), 5.75 (d, J = 10.1 Hz, 1H), 4.15 - 4.03 (m, 2H), 3.85 (s, 3H), 3.66 (hept, J = 6.6 Hz, 6H), 3.12 - 3.05 (m, 10H), 2.79 - 2.69 (m, 3H), 2.11 - 1.99 (m, 6H), 1.93 - 1.81 (m, 3H); 721.5[M+H]$^+$	1.35
207		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, chloroform-d) δ 8.88 (s, 1H), 8.37 (s, 2H), 7.56 (m, 1H), 6.95 (s, 1H), 6.82 (m, 2H), 6.75 (m, 2H), 6.35 (m, 2H), 5.89 (m, 1H), 5.75 (d, J = 11.2 Hz, 1H), 4.08 (s, 4H), 3.85 (s, 3H), 3.40 (m, 5H), 3.31 (s, 2H), 3.08 (m, 4H), 2.79 (m, 7H), 2.30 (s, 4H), 1.44 (d, J = 6.5 Hz, 1H), 1.23 - 1.13 (m, 3H) ; 705.5[M+H]$^+$	1.21

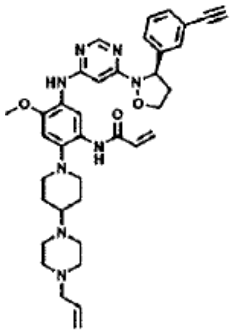
[502]

208		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.36 (s, 1H), 7.50 (d, J = 7.9 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 7.9 Hz, 2H), 6.98 (s, 1H), 6.74 (d, J = 8.9 Hz, 2H), 6.49 - 6.21 (m, 2H), 5.96 (dd, J = 8.7, 4.4 Hz, 1H), 5.74 (d, J = 10.1 Hz, 1H), 4.12 - 4.03 (m, 3H), 3.85 (s, 3H), 3.40 (t, J = 11.9 Hz, 2H), 3.35 - 3.27 (m, 2H), 3.15 - 3.04 (m, 3H), 3.01 - 2.86 (m, 3H), 2.86 - 2.67 (m, 6H), 2.27 - 2.18 (m, 2H), 2.10 - 2.02 (m, 2H), 1.48 - 1.42 (m, 4H), 1.39 (d, J = 6.7 Hz, 3H); 737.5[M+H]$^+$	1.30
209		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.63 (s, 1H), 8.16 (s, 1H), 7.40 - 7.26 (m, 2H), 7.25 - 7.15 (m, 1H), 6.82 (s, 1H), 6.65 (dd, J = 17.0, 10.2 Hz, 1H), 6.35 (s, 1H), 6.20 (dd, J = 16.9, 2.0 Hz, 1H), 5.74 (d, J = 10.1 Hz, 4H), 5.22 - 5.06 (m, 2H), 3.85 (q, J = 8.0 Hz, 2H), 3.79 (s, 4H), 3.04 (d, J = 11.0 Hz, 3H), 2.92 (d, J = 6.4 Hz, 2H), 2.81 (dtd, J = 12.0, 7.9, 3.7 Hz, 2H), 2.71 - 2.61 (m, 3H), 2.46 - 2.29 (m, 4H), 2.22 (dddd, J = 20.8, 12.9, 7.8, 4.3 Hz, 2H), 1.85 (s, 8H), 1.78 - 1.63 (m, 2H).: 661.5 [M+H]$^+$	1.20
210		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	650.5 [M+H]$^+$	1.11

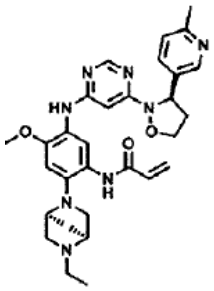
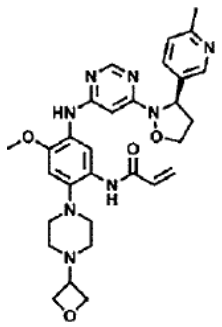
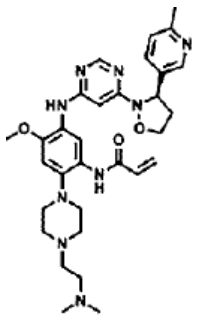
211		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.35 (s, 1H), 8.17 (d, *J* = 0.7 Hz, 1H), 7.54 (t, *J* = 8.2 Hz, 1H), 7.26 - 7.16 (m, 2H), 6.91 (s, 1H), 6.57 (dd, *J* = 17.0, 10.3 Hz, 1H), 6.50 (s, 1H), 6.36 (dd, *J* = 17.0, 1.4 Hz, 1H), 5.97 - 5.83 (m, 2H), 5.82 - 5.72 (m, 2H), 5.25 (d, *J* = 11.0 Hz, 3H), 4.14 (td, *J* = 7.9, 4.3 Hz, 1H), 4.00 (t, *J* = 8.0 Hz, 1H), 3.88 (s, 6H), 3.64 - 3.54 (m, 1H), 3.10 (d, *J* = 6.9 Hz, 3H), 2.81 - 2.73 (m, 4H), 2.52 (dd, *J* = 10.9, 5.7 Hz, 1H), 2.49 - 2.41 (m, 2H), 2.26 (ddd, *J* = 20.5, 10.3, 6.5 Hz, 1H), 2.06 (d, *J* = 11.4 Hz, 2H), 1.77 (tt, *J* = 11.7, 6.0 Hz, 2H) ; 677.5[M+H]$^+$	1.29
212		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.34 (s, 1H), 8.18 (s, 1H), 7.40 - 7.32 (m, 1H), 7.27 - 7.23 (m, 2H), 6.92 (s, 1H), 6.60 (dd, *J* = 16.9, 10.3 Hz, 1H), 6.47 (s, 1H), 6.39 (s, 1H), 6.34 (d, *J* = 1.8 Hz, 1H), 6.29 (d, *J* = 1.8 Hz, 1H), 6.14 (dd, *J* = 17.3, 10.3 Hz, 2H), 5.99 - 5.87 (m, 2H), 5.82 (dt, *J* = 7.6, 2.3 Hz, 2H), 5.55 (dd, *J* = 8.5, 4.6 Hz, 1H), 5.39 (s, 1H), 4.15 (td, *J* = 7.9, 4.3 Hz, 1H), 3.98 (q, *J* = 7.9 Hz, 1H), 3.88 (s, 3H), 3.38 - 3.34 (m, 2H), 3.18 (s, 4H), 2.98 (d, *J* = 3.4 Hz, 4H), 2.81 (dt, *J* = 7.8, 6.2 Hz, 3H), 2.39 - 2.28 (m, 1H), 2.15 (d, *J* = 10.9 Hz, 2H), 1.95 (dt, *J* = 23.4, 11.8 Hz, 3H) ; 661.5[M+H]$^+$	1.18

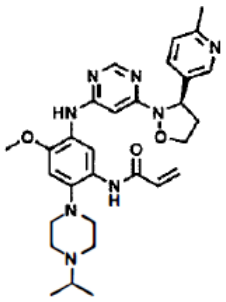
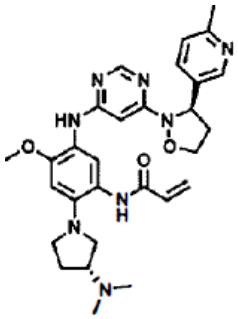
[503]

213		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.59 (s, 1H), 8.15 - 8.14 (m, 2H), 7.40 (dd, J = 7.8, 1.3 Hz, 1H), 7.34 (dd, J = 8.0, 1.3 Hz, 1H), 7.21 (d, J = 7.9 Hz, 1H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.87 - 5.74 (m, 1H), 5.70 (td, J = 8.9, 8.2, 3.4 Hz, 2H), 5.23 - 5.10 (m, 2H), 4.14 (td, J = 7.9, 3.9 Hz, 1H), 3.79 (s, 3H), 3.09 - 3.01 (m, 3H), 2.95 (d, J = 6.4 Hz, 3H), 2.83 (dtd, J = 12.1, 8.0, 3.8 Hz, 2H), 2.66 (t, J = 11.6 Hz, 3H), 2.58 (s, 3H), 2.54 (s, 2H), 2.42 (s, 4H), 2.08 (dtd, J = 12.6, 8.1, 5.0 Hz, 2H), 1.91 (s, 4H), 1.85 (d, J = 12.0 Hz, 3H), 1.78 - 1.65 (m, 3H).; 673.5 $[M+H]^+$	1.28
214		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	677.4 $[M+H]^+$	1.29
215		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.17 (s, 1H), 7.26 (t, J = 8.2 Hz, 1H), 7.00 (d, J = 6.8 Hz, 2H), 6.91 (s, 1H), 6.83 (dd, J = 8.2, 1.7 Hz, 1H), 6.63 (dd, J = 16.9, 10.3 Hz, 1H), 6.41 - 6.32 (m, 2H), 5.98 - 5.88 (m, 1H), 5.81 (d, J = 11.3 Hz, 1H), 5.50 (dd, J = 8.4, 4.8 Hz, 1H), 5.41 (t, J = 14.1 Hz, 2H), 4.19 (td, J = 7.8, 4.5 Hz, 1H), 4.01 (q, J = 7.9 Hz, 1H), 3.86 (s, 3H), 3.80 (s, 3H), 3.18 (s, 2H), 2.87 - 2.78 (m, 3H), 2.41 - 2.30 (m, 1H), 2.18 (s, 2H), 1.99 (d, J = 9.8 Hz, 2H) ; 655.5$[M+H]^+$	1.08

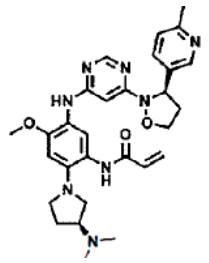
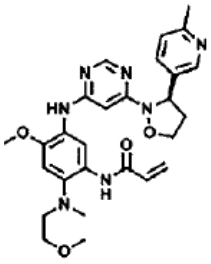
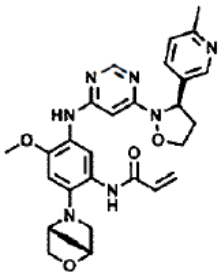
216		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.17 (s, 1H), 8.03 (s, 1H), 7.48 (s, 1H), 7.30 (s, 1H), 6.93 (s, 1H), 6.58 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.39 (dd, *J* = 17.0, 1.3 Hz, 1H), 6.00 (s, 1H), 5.94 (dd, *J* = 17.1, 10.2 Hz, 1H), 5.83 (d, *J* = 11.3 Hz, 1H), 5.53 - 5.42 (m, 3H), 4.36 (td, *J* = 7.6, 4.3 Hz, 1H), 4.13 (dd, *J* = 15.3, 8.0 Hz, 1H), 3.85 (s, 3H), 3.55 (s, 1H), 3.49 (d, *J* = 6.5 Hz, 2H), 3.25 (d, *J* = 11.2 Hz, 4H), 2.90 - 2.80 (m, 2H), 2.47 - 2.36 (m, 1H), 2.20 - 2.11 (m, 2H), 2.01 (s, 2H), 1.95 (d, *J* = 8.7 Hz, 1H), 1.31 (s, 1H) ; 649.5[M+H]$^+$	1.17

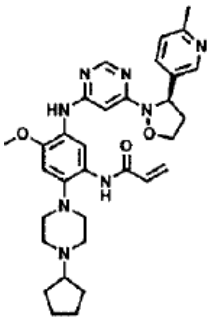
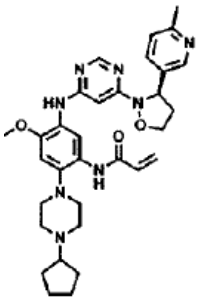
[504]

217		N-(2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.58 - 8.51 (m, 2H), 8.35 (s, 1H), 8.03 (s, 1H), 7.70 (dd, J = 8.1, 2.4 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 6.88 (s, 1H), 6.77 (s, 1H), 6.62 (s, 1H), 6.38 (s, 2H), 5.79 - 5.61 (m, 2H), 4.22 - 4.13 (m, 1H), 4.03 (q, J = 7.9 Hz, 1H), 3.91 (t, J = 6.3 Hz, 2H), 3.87 (s, 3H), 3.18 - 3.11 (m, 1H), 2.92 - 2.88 (m, 1H), 2.70 - 2.70 (m, 2H), 2.54 (s, 3H), 2.43 - 2.24 (m, 2H), 2.01 (s, 2H), 1.47 - 1.30 (m, 2H), 1.22 - 1.02 (m, 3H).; 557.5 $[M+H]^+$	0.93
218		N-(4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.91 (s, 1H), 8.57 (d, J = 2.4 Hz, 1H), 8.49 (s, 1H), 8.37 (s, 1H), 7.70 (dd, J = 8.1, 2.4 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 7.00 (s, 1H), 6.81 (s, 1H), 6.72 (s, 1H), 6.36 (dd, J = 16.9, 1.6 Hz, 1H), 6.25 (dd, J = 17.0, 10.0 Hz, 1H), 5.74 (dd, J = 10.0, 1.5 Hz, 1H), 5.72 - 5.69 (m, 1H), 4.60 (dt, J = 21.2, 6.3 Hz, 4H), 4.20 - 4.06 (m, 2H), 3.84 (s, 3H), 3.61 (p, J = 6.4 Hz, 1H), 2.95 (dt, J = 4.6, 2.7 Hz, 4H), 2.84 - 2.73 (m, 2H), 2.54 (s, 6H), 2.37 (dp, J = 11.8, 3.9, 3.5 Hz, 1H).; 573.4 $[M+H]^+$	0.99
219		N-(2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.89 (s, 1H), 8.57 (d, J = 2.3 Hz, 1H), 8.52 (s, 1H), 8.36 (s, 1H), 7.70 (dd, J = 8.0, 2.4 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 6.99 (s, 1H), 6.80 (s, 1H), 6.71 (s, 1H), 6.36 (dd, J = 16.9, 1.7 Hz, 1H), 6.26 - 6.23 (m, 1H), 5.75 (dd, J = 9.8, 1.7 Hz, 1H), 5.71 - 5.69(m, 1H), 4.20 - 4.04 (m, 2H), 3.84 (s, 3H), 3.67 - 3.63 (m, 1H), 2.96 - 2.91 (m, 4H), 2.80 - 2.70 (m, 8H), 2.53 - 2.52 (m, 8H), 2.36 (dq, J = 11.8, 3.6 Hz, 2H).; 588.5 $[M+H]^+$	0.96

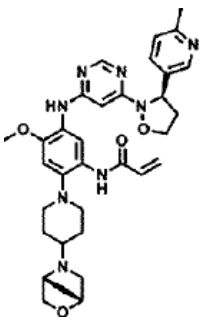
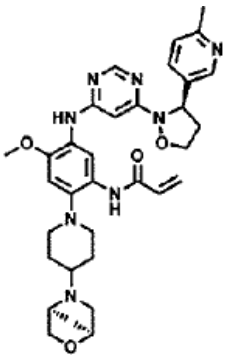
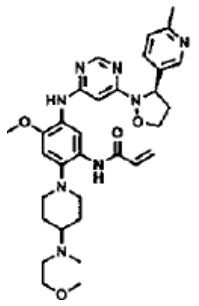
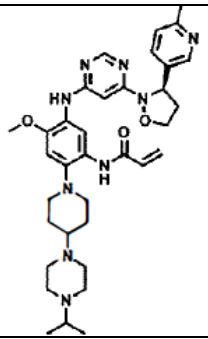
220		N-(2-(4-isopropylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-$d6$) δ 11.09 (s, 1H), 9.36 (s, 1H), 9.27 (s, 1H), 8.75 (d, J = 2.1 Hz, 1H), 8.46 (dd, J = 8.3, 2.1 Hz, 1H), 8.28 (s, 1H), 8.11 (s, 1H), 7.92 (d, J = 8.4 Hz, 1H), 6.82 (s, 1H), 6.40 - 6.14 (m, 2H), 5.78 - 5.68 (m, 2H), 4.29 (q, J = 7.0, 6.4 Hz, 2H), 4.03 (q, J = 7.8 Hz, 2H), 3.84 (s, 3H), 3.60 (dd, J = 6.6, 2.7 Hz, 1H), 3.57 (s, 3H), 3.41 (s, 3H), 3.34 (d, J = 11.7 Hz, 2H), 3.25 - 3.16 (m, 2H), 3.11 (tt, J = 7.3, 3.7 Hz, 2H), 2.92 (dq, J = 11.9, 7.5, 6.0 Hz, 1H), 2.75 (s, 3H), 2.40 (td, J = 13.0, 7.8 Hz, 1H).; 589.5[M+H]$^+$	1.03
221		N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-$d6$) δ 11.27 (s, 1H), 9.98 (s, 1H), 9.66 (s, 1H), 8.76 (d, J = 2.1 Hz, 1H), 8.46 (d, J = 8.4 Hz, 1H), 8.30 (s, 1H), 7.93 (d, J = 8.3 Hz, 1H), 7.50 (s, 1H), 6.88 (dd, J = 17.2, 10.1 Hz, 1H), 6.60 (s, 1H), 6.21 (dd, J = 17.1, 2.1 Hz, 1H), 5.72 (td, J = 11.9, 10.1, 4.7 Hz, 2H), 4.31 (s, 1H), 4.07 - 4.02 (m, 3H), 3.88 (t, J = 6.1 Hz, 3H), 3.82 (s, 3H), 3.63 (d, J = 10.4 Hz, 1H), 3.57 (s, 2H), 3.51 (s, 1H), 3.43 - 3.36 (m, 1H), 3.17 (s, 1H), 3.06 (q, J = 8.2 Hz, 1H), 2.96 (d, J = 6.4 Hz, 1H), 2.80 (d, J = 2.8 Hz, 3H), 2.76 (s, 1H), 2.30 (s, 1H).; 545.5[M+H]$^+$	0.92

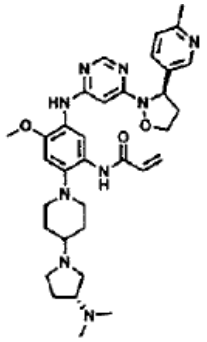
[505]

222		N-(2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d_6) δ 11.18 (s, 1H), 9.61 (s, 1H), 8.75 (d, J = 2.1 Hz, 1H), 8.44 (d, J = 8.5 Hz, 1H), 8.27 (s, 1H), 7.91 (d, J = 8.4 Hz, 1H), 7.65 (s, 1H), 6.94 - 6.81 (m, 1H), 6.69 (s, 1H), 6.21 (dd, J = 17.1, 2.1 Hz, 2H), 5.77 - 5.68 (m, 2H), 4.28 (d, J = 6.2 Hz, 1H), 4.06 - 4.00 (m, 1H), 3.88 (d, J = 5.8 Hz, 1H), 3.82 (d, J = 3.2 Hz, 3H), 3.57 (s, 3H), 3.09 (s, 1H), 3.05 - 2.98 (m, 3H), 2.80 (dd, J = 8.0, 4.7 Hz, 5H), 2.74 (s, 3H), 2.30 (dq, J = 13.1, 6.3, 5.3 Hz, 2H).; 545.5[M+H]$^+$	0.93
223		N-(4-methoxy-2-((2-methoxyethyl)(methyl)amino)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d_6) δ 9.67 (s, 2H), 8.76 (d, J = 2.1 Hz, 1H), 8.48 (d, J = 8.7 Hz, 1H), 8.32 (d, J = 7.4 Hz, 2H), 7.93 (d, J = 8.7 Hz, 1H), 7.17 (s, 1H), 6.48 (s, 2H), 6.25 (d, J = 16.8 Hz, 1H), 5.82 - 5.71 (m, 2H), 4.32 - 4.24 (m, 2H), 4.04 (d, J = 8.7 Hz, 2H), 3.86 (s, 3H), 3.57 (s, 1H), 3.47 (s, 2H), 3.28 (s, 3H), 2.93 (s, 3H), 2.76 (s, 3H), 2.44 - 2.37 (m, 1H).; 520.5[M+H]$^+$	1.23
224		N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d_6) δ 9.64 (s, 1H), 9.36 (d, J = 24.6 Hz, 1H), 8.75 (d, J = 2.2 Hz, 1H), 8.43 (d, J = 8.4 Hz, 1H), 8.26 (d, J = 2.4 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.16 (d, J = 47.7 Hz, 1H), 6.47 (d, J = 11.2 Hz, 1H), 6.19 (dd, J = 17.1, 2.1 Hz, 1H), 5.78 - 5.66 (m, 2H), 4.60 - 4.45 (m, 2H), 4.29 (td, J = 7.6, 4.0 Hz, 1H), 4.04 (t, J = 7.8 Hz, 1H), 3.95 (dd, J = 7.8, 2.6 Hz, 1H), 3.86 (t, J = 6.3 Hz, 2H), 3.80 (d, J = 4.2 Hz, 3H), 3.57 (s, 2H), 2.96 - 2.92 (m, 1H), 2.79 (t, J = 6.1 Hz, 1H), 2.73 (s, 3H), 2.44 - 2.37 (m, 1H), 1.85 (q, J = 9.8 Hz, 2H).; 530.4[M+H]$^+$	1.08

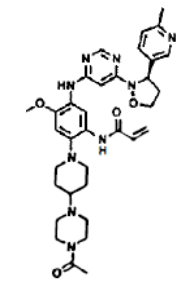
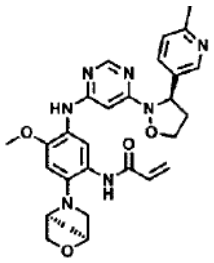
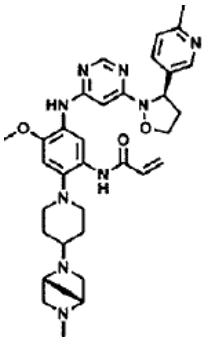
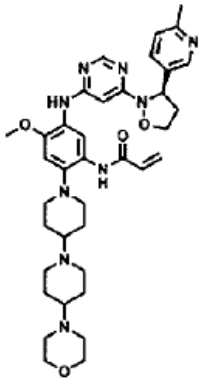
225		N-(2-(4-cyclopentylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.91 (s, 1H), 8.59 - 8.57 (s, 2H), 8.37 (s, 1H), 7.70 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.95 (s, 1H), 6.83 (s, 1H), 6.72 (s, 1H), 6.36 (dd, *J* = 16.9, 1.6 Hz, 1H), 6.30 - 6.23 (m, 1H), 5.77 - 5.73 (m, 1H), 5.73 - 5.60 (m, 1H), 4.20 - 4.05 (m, 2H), 3.82 (s, 3H), 2.94 (t, *J* = 5.0 Hz, 4H), 2.80 - 2.72 (m, 3H), 2.63 - 2.60 (m, 2H), 2.54 (s, 3H), 2.40 - 2.32 (m, 1H), 2.18 (d, *J* = 7.7 Hz, 1H), 1.97 - 1.80 (m, 2H), 1.78 - 1.71 (m, 2H), 1.65 - 1.58 (m, 2H), 1.50 - 1.42 (m, 2H).; 585.6 [M+H]$^+$	0.89
226		N-(2-(4-cyclopentylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.57 (d, *J* = 2.3 Hz, 1H), 8.47 (s, 1H), 8.36 (s, 1H), 7.70 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.92 (s, 1H), 6.75 (s, 1H), 6.72 (s, 1H), 6.40 - 6.31 (m, 1H), 6.26 (dd, *J* = 16.9, 0.9 Hz, 1H), 5.77 - 5.73 (m, 1H), 5.73 - 5.69 (m, 1H), 4.21 - 4.06 (m, 2H), 3.84 (s, 3H), 3.27 - 3.15 (m, 4H), 3.05 (d, *J* = 11.5 Hz, 2H), 2.82 - 2.62 (m, 6H), 2.48 - 2.42 (m, 3H), 2.37 (s, 3H), 2.29 (s, 3H), 2.27 (s, 6H).; 616.6 [M+H]$^+$	0.46

[506]

227		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.57 (d, *J* = 2.4 Hz, 1H), 8.48 (s, 1H), 8.36 (s, 1H), 7.70 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.94 (s, 1H), 6.76 (s, 1H), 6.72 (s, 1H), 6.35 (dd, *J* = 17.0, 1.5 Hz, 1H), 6.24 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.72 (m, 2H), 4.21 - 4.04 (m, 3H), 3.85 (s, 3H), 3.78 (s, 1H), 3.67 (dd, *J* = 8.0, 1.6 Hz, 1H), 3.20 - 3.13 (m, 1H), 3.03 (d, *J* = 11.7 Hz, 2H), 2.83 - 2.71 (m, 3H), 2.54 (m, 5H), 2.36 (m, 1H), 2.10 - 1.91 (m, 4H), 1.83 (d, *J* = 9.8 Hz, 1H), 1.68 (m, 2H).; 613.6 [M+H]$^+$	0.75
228		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.57 (d, *J* = 2.3 Hz, 1H), 8.48 (s, 1H), 8.36 (s, 1H), 7.70 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.96 (s, 1H), 6.76 (s, 1H), 6.72 (s, 1H), 6.44 - 6.32 (m, 1H), 6.24 (dd, *J* = 17.0, 10.0 Hz, 1H), 5.81 - 5.68 (m, 2H), 4.20 - 4.07 (m, 3H), 3.85 (s, 3H), 3.78 (m, 1H), 3.67 (dd, *J* = 7.9, 1.7 Hz, 1H), 3.15 (d, *J* = 9.8 Hz, 1H), 3.03 (m, 2H), 2.76 (m, 3H), 2.63 - 2.48 (m, 5H), 2.35 (m, 1H), 2.08 - 1.90 (m, 4H), 1.83 (d, *J* = 9.5 Hz, 1H), 1.68 (t, *J* = 11.1 Hz, 2H).; 613.6 [M+H]$^+$	0.81
229		N-(4-methoxy-2-(4-((2-methoxyethyl)(methyl)amino)piperidine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.57 (d, *J* = 2.2 Hz, 1H), 8.46 (s, 1H), 8.36 (s, 1H), 7.70 (dd, *J* = 8.0, 2.3 Hz, 1H), 7.13 (d, *J* = 8.1 Hz, 1H), 6.93 (s, 1H), 6.73 (d, *J* = 13.1 Hz, 2H), 6.43 - 6.19 (m, 2H), 5.79 - 5.66 (m, 2H), 4.22 - 4.05 (m, 2H), 3.84 (s, 3H), 3.53 (t, *J* = 5.7 Hz, 2H), 3.39 (s, 3H), 3.06 (d, *J* = 11.0 Hz, 2H), 2.83 - 2.66 (m, 5H), 2.54 (s, 3H), 2.41 (s, 3H), 2.00 (m, 2H), 1.92 - 1.79 (m, 2H), 1.70 (m, 2H).; 603.5 [M+H]$^+$	0.83
230		N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.57 (d, *J* = 2.3 Hz, 1H), 8.41 (s, 1H), 8.36 (s, 1H), 7.71 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.13 (d, *J* = 8.1 Hz, 1H), 6.97 (s, 1H), 6.73 (d, *J* = 10.5 Hz, 2H), 6.36 (dd, *J* = 16.9, 1.6 Hz, 1H), 6.28 - 6.16 (m, 1H), 5.76 - 5.73 (m, 1H), 5.71 (m 1H), 4.16 (tt, *J* = 8.7, 4.3 Hz, 1H), 4.12 - 4.06 (m, 1H), 3.84 (s, 3H), 3.06 (dd, *J* = 9.6, 4.8 Hz, 4H), 2.94 (s, 8H), 2.82 - 2.68 (m, 4H), 2.46 (d, *J* = 4.5 Hz, 1H), 2.36 (dtd, *J* = 12.3, 8.0, 4.4 Hz, 2H), 2.12 - 2.05 (m, 2H), 1.69 (d, *J* = 11.9 Hz, 2H), 1.26 (d, *J* = 6.2 Hz, 6H).; 642.6 [M+H]$^+$	0.80

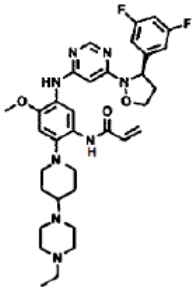
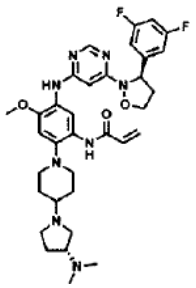
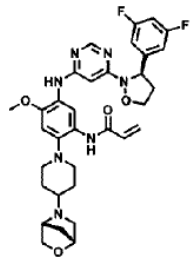
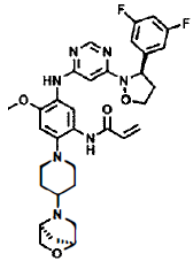
		-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide		
231		N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.57 (d, *J* = 2.3 Hz, 1H), 8.40 (s, 1H), 8.36 (s, 1H), 7.73 - 7.69 (m, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.92 (s, 1H), 6.75 (s, 1H), 6.72 (s, 1H), 6.34 (dd, *J* = 16.7, 1.4 Hz, 1H), 6.23 (dd, *J* = 16.9, 10.1 Hz, 1H), 5.72 (m, 2H), 4.19 - 4.07 (m, 2H), 3.84 (s, 3H), 3.29 - 3.14 (m, 5H), 3.12 - 2.99 (m, 3H), 2.94 (m, 1H), 2.83 - 2.68 (m, 5H), 2.54 (s, 3H), 2.47 (t, *J* = 6.3 Hz, 2H), 2.35 (m, 2H), 2.30 (s, 6H).; 628.6 $[M+H]^+$	0.36

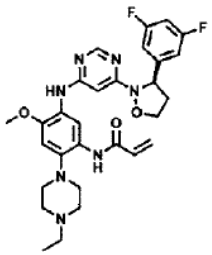
[507]

232		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.86 (s, 1H), 8.57 (d, J = 2.4 Hz, 1H), 8.41 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.73 - 7.68 (m, 1H), 7.13 (d, J = 8.0 Hz, 1H), 7.01 (s, 1H), 6.73 (d, J = 13.9 Hz, 2H), 6.43 - 6.34 (m, 1H), 6.28 - 6.11 (m, 1H), 5.77 - 5.73 (m, 1H), 5.73 - 5.60 (m, 1H), 4.15 (dd, J = 8.0, 4.5 Hz, 1H), 4.10 (d, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.67 (m, 2H), 3.52 (t, J = 5.0 Hz, 2H), 3.07 (m, 2H), 2.81 - 2.69 (m, 4H), 2.62 (dt, J = 14.2, 5.1 Hz, 4H), 2.44 - 2.32 (m, 4H), 2.11 (s, 3H), 2.04 (m, 2H), 1.68 (m, 2H).; 642.6 $[M+H]^+$	0.76
233		N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, chloroform-d) δ 8.67 (s, 1H), 8.57 (d, J = 2.3 Hz, 1H), 8.36 (s, 1H), 7.97 (s, 1H), 7.70 (dd, J = 8.1, 2.4 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 6.88 (s, 1H), 6.67 (d, J = 26.7 Hz, 2H), 6.39 (d, J = 17.2 Hz, 1H), 6.28 (dd, J = 16.9, 10.0 Hz, 1H), 5.75 (d, J = 10.0 Hz, 1H), 5.70 (dd, J = 8.7, 4.4 Hz, 1H), 4.65 (s, 1H), 4.15 (td, J = 8.0, 4.5 Hz, 1H), 4.05 (d, J = 7.7 Hz, 2H), 3.86 (s, 4H), 3.75 (d, J = 7.8 Hz, 1H), 3.42 (d, J = 10.2 Hz, 1H), 3.24 (d, J = 10.1 Hz, 1H), 2.76 (dtd, J = 12.5, 8.2, 4.5 Hz, 1H), 2.54 (s, 3H), 2.36 (dtd, J = 12.3, 7.9, 4.4 Hz, 1H), 2.08 (d, J = 9.9 Hz, 1H), 1.99 (d, J = 9.8 Hz, 1H).; 530.5$[M+H]^+$	0.87
234		N-(4-methoxy-2-(4-((1R,4R)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.57 (d, J = 2.4 Hz, 1H), 8.35 (s, 1H), 7.72 (dd, J = 8.1, 2.4 Hz, 1H), 7.15 (d, J = 8.1 Hz, 1H), 7.04 (s, 1H), 6.76 (s, 1H), 6.69 (s, 1H), 6.54 (s, 2H), 6.34 (s, 1H), 5.77 - 5.68 (m, 2H), 5.61 (s, 2H), 4.17 (td, J = 8.0, 4.3 Hz, 1H), 4.09 (q, J = 8.0 Hz, 1H), 3.86 (s, 3H), 3.35 (q, J = 6.0 Hz, 5H), 3.19 (dd, J = 7.2, 5.6 Hz, 4H), 3.13 (t, J = 6.9 Hz, 5H), 2.55 (s, 3H), 2.01 (p, J = 6.6 Hz, 6H).; 626.6$[M+H]^+$	0.74
235		N-(4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-morpholino-[1,4'-bipiperidine]-1'-	1H NMR (400 MHz, DMSO-$d6$) δ 8.94 (s, 1H), 8.59 (s, 1H), 8.47 (d, J = 2.3 Hz, 1H), 8.15 (d, J = 8.6 Hz, 2H), 7.67 (dd, J = 8.1, 2.4 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 6.81 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.33 (s, 1H), 6.20 (dd, J = 16.9, 2.0 Hz, 1H), 5.72 (d, J = 10.3 Hz, 1H), 5.54 (dd, J = 8.6, 4.9 Hz, 1H), 4.15 (td, J = 7.9, 4.1 Hz, 1H), 3.86 (q, J = 7.9 Hz, 1H), 3.79 (s, 2H), 3.56 (t, J = 4.6 Hz, 3H), 3.33 (s, 10H), 3.05 (d, J = 10.4 Hz, 2H), 3.00 - 2.91 (m, 2H), 2.74 (dt, J = 8.3, 4.2 Hz, 1H), 2.70 - 2.61 (m, 2H), 2.45 (s, 3H), 1.86 - 1.64 (m, 6H), 1.36 (d, J = 12.2 Hz, 2H), 1.24 (s, 1H).; 684.6$[M+H]^+$	0.45

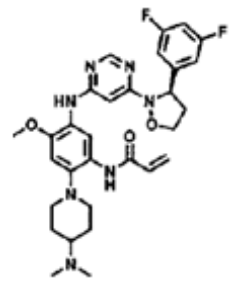
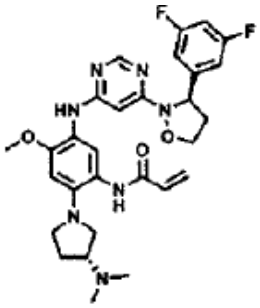
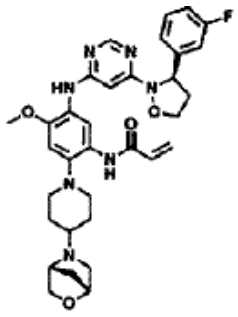
		yl)phenyl)acrylamide		

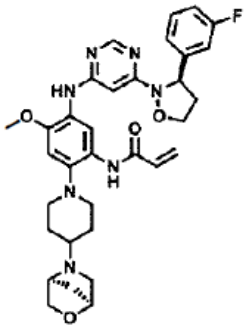
[508]

236		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.12 - 7.01 (m, 2H), 6.92 (s, 1H), 6.84 (tt, J = 2.5, 9.1 Hz, 1H), 6.55 (dd, J = 10.2, 17.0 Hz, 1H), 6.46 (s, 1H), 6.36 (dd, J = 1.5, 17.0 Hz, 1H), 5.81 (d, J = 10.3 Hz, 1H), 5.57 (dd, J = 4.7, 8.7 Hz, 1H), 4.19 - 4.11 (m, 1H), 3.97 (q, J = 8.0 Hz, 1H), 3.88 (s, 3H), 3.22 - 3.12 (m, 2H), 3.08 - 2.87 (m, 9H), 2.87 - 2.74 (m, 4H), 2.66 - 2.58 (m, 1H), 2.38 - 2.29 (m, 1H), 2.10 - 2.02 (m, 2H), 1.88 - 1.75 (m, 2H), 1.27 (t, J = 7.3 Hz, 3H) ; 649.3[M+H]$^+$	1.15
237		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.18 (s, 1H), 7.10 - 7.02 (m, 2H), 6.92 (s, 1H), 6.90 - 6.80 (m, 1H), 6.61 - 6.51 (m, 1H), 6.47 (s, 1H), 6.42 - 6.31 (m, 1H), 5.81 (d, J = 10.5 Hz, 1H), 5.57 (dd, J = 4.8, 8.7 Hz, 1H), 4.20 - 4.12 (m, 1H), 3.98 (q, J = 8.0 Hz, 1H), 3.89 (s, 3H), 3.26 - 3.19 (m, 1H), 3.19 - 3.10 (m, 3H), 3.06 - 2.97 (m, 2H), 2.92 - 2.75 (m, 4H), 2.63 - 2.53 (m, 7H), 2.38 - 2.20 (m, 2H), 2.17 - 2.09 (m, 2H), 1.87 - 1.75 (m, 2H) ; 649.3[M+H]$^+$	1.09
238		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.33 (s, 1H), 8.18 (d, J = 1.0 Hz, 1H), 7.10 - 7.03 (m, 2H), 6.93 (s, 1H), 6.87 - 6.81 (m, 1H), 6.58 (dd, J = 17.0, 10.3 Hz, 1H), 6.47 (d, J = 1.0 Hz, 1H), 6.36 (dd, J = 17.0, 1.6 Hz, 1H), 5.80 (dd, J = 10.3, 1.6 Hz, 1H), 5.57 (dd, J = 8.6, 4.8 Hz, 1H), 4.47 (t, J = 2.0 Hz, 1H), 4.19 - 4.10 (m, 2H), 3.98 (d, J = 8.0 Hz, 1H), 3.88 (s, 4H), 3.67 (dd, J = 8.3, 1.7 Hz, 1H), 3.15 - 3.08 (m, 3H), 2.88 - 2.78 (m, 3H), 2.70 - 2.50 (m, 2H), 2.36 - 2.30 (m, 1H), 2.11 - 1.03 (m, 3H), 1.89 - 1.84 (m, 1H), 1.73 (d, J = 12.0 Hz, 2H); 634.3 [M+H]$^+$	1.2
239		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.33 (s, 1H), 8.18 (d, J = 1.0 Hz, 1H), 7.09 - 7.03 (m, 2H), 6.92 (s, 1H), 6.87 - 6.81 (m, 1H), 6.58 (dd, J = 17.0, 10.3 Hz, 1H), 6.47 (d, J = 1.0 Hz, 1H), 6.36 (dd, J = 17.0, 1.5 Hz, 1H), 5.80 (dd, J = 10.3, 1.6 Hz, 1H), 5.57 (dd, J = 8.7, 4.7 Hz, 1H), 4.47 (t, J = 2.0 Hz, 1H), 4.17 - 4.10 (m, 2H), 3.97 (q, J = 8.0 Hz, 1H), 3.90 (s, 1H), 3.88 (s, 3H), 3.67 (dd, J = 8.3, 1.7 Hz, 1H), 3.13 - 3.07 (m, 3H), 2.85 - 2.76 (m, 3H), 2.70 - 2.58 (m, 2H), 2.37 - 2.31 (m, 1H), 2.06 (d, J = 13.6 Hz, 1H), 2.02 (d, J = 3.4 Hz, 1H), 1.94 (dd, J = 10.2, 2.1 Hz, 1H), 1.86 (d, J = 10.1 Hz, 1H), 1.77 - 1.67 (m, 2H); 634.3 [M+H]$^+$	1.21

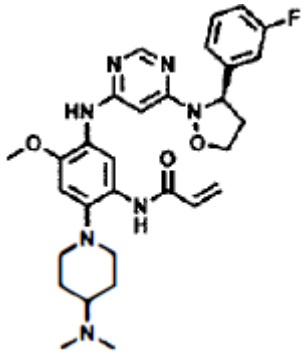
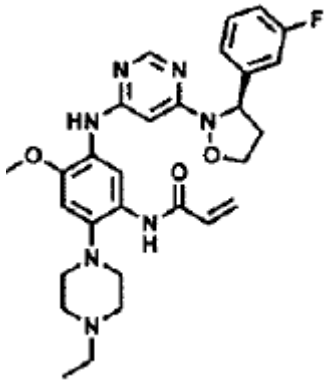
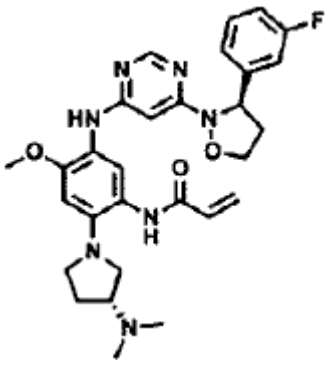
		methoxyphenyl)acrylamide		
240		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.34 (s, 1H), 10.19 (s, 1H), 9.31 (s, 1H), 8.32 (s, 1H), 7.16 (tt, J = 9.4, 2.5 Hz, 1H), 7.10 (h, J = 4.4 Hz, 2H), 6.88 (q, J = 9.6, 9.0 Hz, 2H), 6.24 (dd, J = 17.0, 2.0 Hz, 1H), 5.74 (dd, J = 10.1, 2.0 Hz, 1H), 5.56 (dd, J = 8.6, 5.4 Hz, 1H), 4.04 (q, J = 7.8 Hz, 3H), 3.82 (s, 3H), 3.50 (d, J = 11.2 Hz, 2H), 3.41 (d, J = 10.2 Hz, 2H), 3.31 - 3.19 (m, 4H), 3.20 - 3.10 (m, 3H), 2.92 (qd, J = 7.8, 3.5 Hz, 1H), 2.32 (dtd, J = 12.8, 7.7, 5.2 Hz, 1H), 1.32 (t, J = 7.2 Hz, 3H), 1.23 (d, J = 3.4 Hz, 1H), 0.88 - 0.78 (m, 1H).; 566.3 $[M+H]^+$	1.16

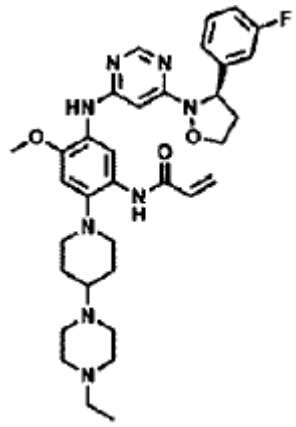
[509]

241		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.48 (s, 1H), 9.49 - 9.24 (m, 1H), 8.36 (s, 1H), 7.87 (s, 1H), 7.17 (tt, J = 9.3, 2.4 Hz, 1H), 7.10 (h, J = 4.5 Hz, 3H), 6.96 (s, 1H), 6.78 (dd, J = 16.9, 10.2 Hz, 1H), 6.25 (dd, J = 16.9, 1.9 Hz, 2H), 6.14 (s, 1H), 5.79 - 5.71 (m, 1H), 5.56 (dd, J = 8.6, 5.4 Hz, 1H), 4.06 (q, J = 7.7 Hz, 1H), 3.81 (s, 4H), 3.25 (d, J = 12.2 Hz, 2H), 3.00 - 2.80 (m, 4H), 2.73 (d, J = 4.9 Hz, 7H), 2.33 (dtd, J = 12.7, 7.6, 5.3 Hz, 1H), 2.20 - 2.00 (m, 5H), 1.23 (d, J = 3.4 Hz, 2H), 0.84 (td, J = 7.6, 7.1, 3.1 Hz, 1H).; 580.4 $[M+H]^+$	1.13
242		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.63 (s, 1H), 8.34 (s, 1H), 8.20 (s, 1H), 6.93 (s, 1H), 6.73 (s, 1H), 6.71 - 6.63 (m, 2H), 6.41 - 6.25 (m, 2H), 5.72 (dd, J = 9.5, 2.2 Hz, 1H), 5.66 (dd, J = 8.8, 4.6 Hz, 1H), 4.04 (q, J = 8.2 Hz, 1H), 3.83 (s, 3H), 3.22 - 3.04 (m, 4H), 2.93 - 2.68 (m, 2H), 2.29 (s, 8H), 2.16 (ddd, J = 16.5, 9.4, 3.3 Hz, 3H).; 566.3 $[M+H]^+$	1.11
243		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.60 (s, 1H), 8.17 (d, J = 4.7 Hz, 2H), 7.40 (td, J = 8.0, 6.1 Hz, 1H), 7.26 (d, J = 7.7 Hz, 1H), 7.20 (dt, J = 10.3, 2.2 Hz, 1H), 7.08 (td, J = 8.6, 2.7 Hz, 1H), 6.84 (s, 1H), 6.68 - 6.61 (m, 1H), 6.35 (s, 1H), 6.21 (dd, J = 17.0, 1.9 Hz, 1H), 5.72 (dd, J = 10.0, 2.0 Hz, 1H), 5.56 (dd, J = 8.7, 5.0 Hz, 1H), 4.34 (d, J = 2.6 Hz, 1H), 4.12 (dd, J = 7.9, 3.9 Hz, 1H), 3.90 - 3.83 (m, 2H), 3.80 (s, 3H), 3.70 (s, 1H), 3.54 - 3.50 (m, 1H), 3.05 - 2.94 (m, 3H), 2.78 - 2.67 (m, 3H), 2.47 (d, J = 4.6 Hz, 1H), 2.35 (d, J = 9.7 Hz, 1H), 2.20 - 2.19 (m, 1H), 1.83 (s, 2H), 1.60 - 1.57 (m, 4H); 616.3 $[M+H]^+$	1.13

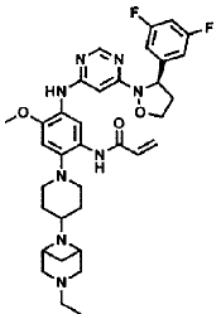
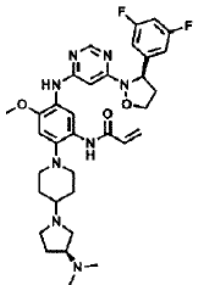
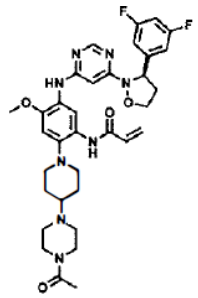
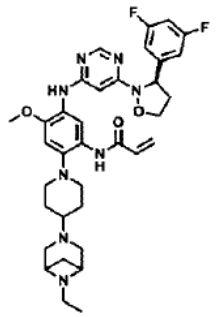
244		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (s, 1H), 7.89 (s, 1H), 7.39 (dd, J = 8.0, 5.8 Hz, 1H), 7.22 - 7.17 (m, 1H), 7.12 (dd, J = 9.8, 2.0 Hz, 1H), 7.05 (d, J = 2.6 Hz, 1H), 6.97 (d, J = 3.6 Hz, 1H), 6.64 (ddd, J = 17.0, 10.3, 2.1 Hz, 1H), 6.44 - 6.37 (m, 1H), 6.01 (s, 1H), 5.85 (dd, J = 10.3, 1.6 Hz, 1H), 5.52 (d, J = 6.6 Hz, 1H), 4.82 - 4.67 (m, 3H), 4.44 (td, J = 7.6, 4.3 Hz, 1H), 4.34 (d, J = 10.7 Hz, 1H), 4.20 (td, J = 8.4, 6.7 Hz, 2H), 3.92 - 3.89 (m, 1H), 3.87 (s, 3H), 3.66 (d, J = 15.6 Hz, 2H), 3.10 - 3.00 (m, 1H), 2.91 (dd, J = 23.0, 11.8 Hz, 2H), 2.53 - 2.43 (m, 2H), 2.31 - 2.05 (m, 6H); 616.3 $[M+H]^+$	1.13

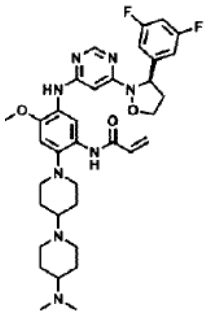
[510]

245		N-(2-(4-(dimethylamino)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.04 (s, 1H), 8.63 (s, 1H), 8.18 (d, J = 4.9 Hz, 2H), 7.40 (td, J = 7.9, 6.1 Hz, 1H), 7.26 (d, J = 7.7 Hz, 1H), 7.20 (dd, J = 10.4, 2.0 Hz, 1H), 7.09 (td, J = 8.6, 2.6 Hz, 1H), 6.84 (s, 1H), 6.69 (dd, J = 16.9, 10.2 Hz, 1H), 6.37 (s, 1H), 6.23 (dd, J = 17.1, 2.0 Hz, 1H), 5.76 - 5.68 (m, 1H), 5.56 (dd, J = 8.7, 5.0 Hz, 1H), 4.14 (td, J = 7.8, 3.8 Hz, 1H), 3.87 - 3.83 (m, 1H), 3.81 (s, 3H), 3.17 (s, 3H), 3.12 (d, J = 11.7 Hz, 2H), 3.01 - 2.90 (m, 1H), 2.78 - 2.71 (m, 2H), 2.60 (s, 6H), 2.25 (ddt, J = 11.8, 7.8, 4.0 Hz, 1H), 2.03 (d, J = 11.7 Hz, 2H); 562.3 $[M+H]^+$	1.14
246		N-(2-(4-ethylpiperazine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.19 (d, J = 2.8 Hz, 1H), 8.00 (s, 1H), 7.44 - 7.39 (m, 1H), 7.22 - 7.19 (m, 1H), 7.14 - 6.97 (m, 3H), 6.72 - 6.66 (m, 1H), 6.42 (dd, J = 16.9, 1.6 Hz, 1H), 6.00 (s, 1H), 5.85 (dd, J = 10.3, 1.6 Hz, 1H), 5.53 (s, 1H), 4.43 (dt, J = 7.5, 3.9 Hz, 1H), 4.23 - 4.17 (m, 1H), 3.96 (t, J = 5.7 Hz, 1H), 3.88 (d, J = 3.2 Hz, 3H), 3.70 (d, J = 11.8 Hz, 2H), 3.47 - 3.35 (m, 4H), 3.29 - 3.22 (m, 2H), 3.10 - 3.00 (m, 2H), 2.48 (dddd, J = 12.6, 8.4, 7.1, 5.8 Hz, 1H), 1.46 (t, J = 7.3 Hz, 3H); 548.3 $[M+H]^+$	1.14
247		N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.40 (s, 1H), 8.50 (s, 1H), 8.14 (d, J = 1.0 Hz, 1H), 7.46 (s, 1H), 7.38 (dd, J = 8.0, 6.1 Hz, 1H), 7.26 (d, J = 7.8 Hz, 1H), 7.20 (dt, J = 10.3, 2.1 Hz, 1H), 7.09 (dd, J = 8.4, 2.4 Hz, 1H), 6.58 - 6.50 (m, 2H), 6.26 - 6.16 (m, 2H), 5.69 (dd, J = 10.1, 2.1 Hz, 1H), 5.57 - 5.50 (m, 1H), 4.12 (q, J = 4.0 Hz, 1H), 3.82 (s, 1H), 3.80 (s, 3H), 3.27 (dd, J = 11.8, 5.7 Hz, 4H), 2.92 (d, J = 7.5 Hz, 1H), 2.79 - 2.71 (m, 1H), 2.29 (s, 6H), 2.26 - 2.21 (m, 1H), 2.16 - 2.06 (m, 1H), 1.87 - 1.76 (m, 1H); 548.3 $[M+H]^+$	1.09

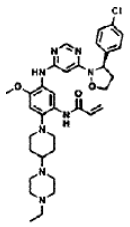
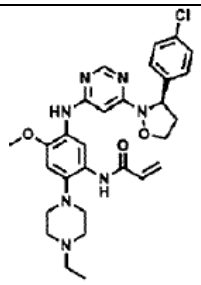
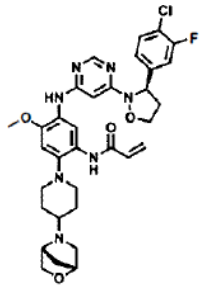
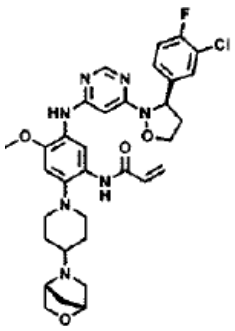
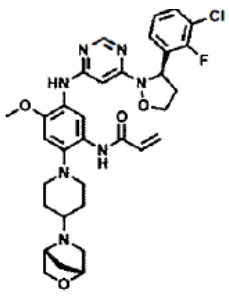
248		N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.60 (s, 1H), 8.15 (d, J = 3.4 Hz, 2H), 7.40 (td, J = 7.9, 6.1 Hz, 1H), 7.20 - 7.18 (m, 2H), 7.08 (td, J = 8.6, 2.7 Hz, 1H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.3 Hz, 1H), 6.34 (s, 1H), 6.23 - 6.15 (m, 1H), 5.77 - 5.69 (m, 1H), 5.55 (dd, J = 8.7, 5.0 Hz, 1H), 4.13 (d, J = 4.0 Hz, 1H), 3.83 (d, J = 8.1 Hz, 1H), 3.80 (s, 3H), 3.05 (d, J = 11.1 Hz, 2H), 2.80 - 2.72 (m, 1H), 2.66 (ddd, J = 12.2, 9.4, 3.6 Hz, 2H), 2.54 (s, 3H), 2.37 (s, 2H), 2.34 - 2.10 (m, 6H), 1.83 (s, 3H), 1.70 (dd, J = 11.7, 3.7 Hz, 2H), 0.99 (t, J = 7.2 Hz, 3H): 631.3 $[M+H]^+$	1.08

[511]

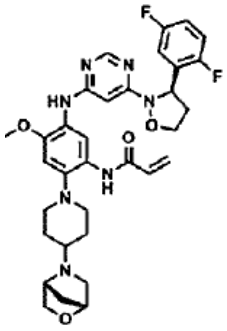
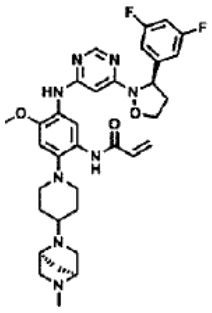
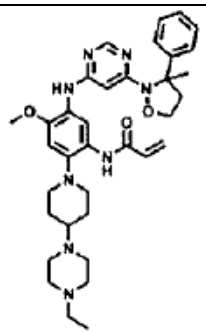
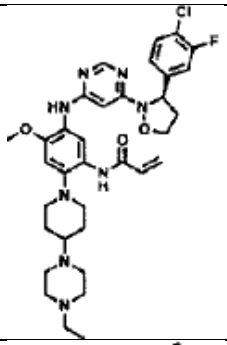
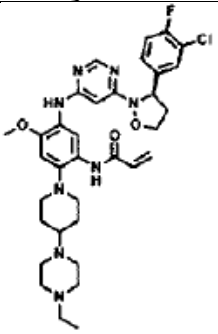
249		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(3-ethyl-3,6-diazabicyclo[3.1.1]heptane-6-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.19 (s, 1H), 7.10 - 7.04 (m, 2H), 6.94 (s, 1H), 6.84 (tt, J = 2.4, 9.1 Hz, 1H), 6.60 - 6.43 (m, 2H), 6.42 - 6.29 (m, 1H), 5.82 (d, J = 10.2 Hz, 1H), 5.57 (dd, J = 4.8, 8.7 Hz, 1H), 4.36 - 4.28 (m, 2H), 4.18 - 4.12 (m, 1H), 3.97 (q, J = 8.0 Hz, 1H), 3.89 (s, 3H), 3.42 - 3.34 (m, 2H), 3.22 - 3.13 (m, 4H), 2.98 - 2.79 (m, 7H), 2.40 - 2.26 (m, 2H), 2.23 - 2.02 (m, 3H), 1.71 (td, J = 3.7, 11.7 Hz, 1H), 1.23 (t, J = 7.2 Hz, 3H) ; 661.3[M+H]$^+$	1.13
250		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino) pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.18 (s, 1H), 7.10 - 7.02 (m, 2H), 6.92 (s, 1H), 6.90 - 6.80 (m, 1H), 6.61 - 6.51 (m, 1H), 6.47 (s, 1H), 6.42 - 6.31 (m, 1H), 5.81 (d, J = 10.5 Hz, 1H), 5.57 (dd, J = 4.8, 8.7 Hz, 1H), 4.20 - 4.12 (m, 1H), 3.98 (q, J = 8.0 Hz, 1H), 3.89 (s, 3H), 3.26 - 3.19 (m, 1H), 3.19 - 3.10 (m, 3H), 3.06 - 2.97 (m, 2H), 2.92 - 2.75 (m, 4H), 2.63 - 2.53 (m, 7H), 2.38 - 2.20 (m, 2H), 2.17 - 2.09 (m, 2H), 1.87 - 1.75 (m, 2H) ; 649.3[M+H]$^+$	1.10
251		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.11 - 7.00 (m, 2H), 6.92 (s, 1H), 6.89 - 6.77 (m, 1H), 6.56 (dd, J = 10.2, 17.0 Hz, 1H), 6.46 (s, 1H), 6.36 (d, J = 16.9 Hz, 1H), 5.81 (d, J = 10.3 Hz, 1H), 5.56 (dd, J = 4.8, 8.7 Hz, 1H), 4.18 - 4.12 (m, 1H), 3.97 (q, J = 8.0 Hz, 1H), 3.88 (s, 3H), 3.71 - 3.57 (m, 4H), 3.20 - 3.11 (m, 2H), 2.88 - 2.73 (m, 5H), 2.73 - 2.65 (m, 2H), 2.59 - 2.47 (m, 1H), 2.39 - 2.28 (m, 1H), 2.13 (s, 3H), 2.05 (d, J = 12.2 Hz, 2H), 1.86 - 1.72 (m, 2H) ; 663.3[M+H]$^+$	1.18
252		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(6-ethyl-3,6-diazabicyclo[3.1.1]heptane-3-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.18 (s, 1H), 7.13 - 7.00 (m, 2H), 6.94 (s, 1H), 6.91 - 6.78 (m, 1H), 6.54 (dd, J = 10.2, 17.0 Hz, 1H), 6.46 (s, 1H), 6.37 (d, J = 16.9 Hz, 1H), 5.81 (d, J = 10.2 Hz, 1H), 5.57 (dd, J = 4.8, 8.7 Hz, 1H), 4.16 (td, J = 4.1, 7.9 Hz, 1H), 3.98 (q, J = 8.0 Hz, 1H), 3.89 (s, 3H), 3.53 - 3.30 (m, 3H), 3.30 - 3.23 (m, 3H), 3.21 - 3.12 (m, 3H), 2.91 - 2.70 (m, 5H), 2.41 - 2.31 (m, 2H), 2.15 - 2.03 (m, 2H), 1.93 - 1.77 (m, 3H), 1.35 - 1.26 (m, 3H); 661.3[M+H]$^+$	1.20

253		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-4-(dimethylamino)-1,4'-bipiperidine-1'-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.18 (s, 1H), 7.12 - 7.01 (m, 2H), 6.92 (s, 1H), 6.88 - 6.79 (m, 1H), 6.56 (dd, J = 10.2, 17.0 Hz, 1H), 6.46 (s, 1H), 6.37 (d, J = 16.9 Hz, 1H), 5.81 (d, J = 10.3 Hz, 1H), 5.57 (dd, J = 4.8, 8.7 Hz, 1H), 4.16 (td, J = 4.1, 7.9 Hz, 1H), 3.97 (q, J = 7.9 Hz, 1H), 3.88 (s, 3H), 3.23 - 3.13 (m, 2H), 3.05 - 2.94 (m, 1H), 2.91 - 2.75 (m, 4H), 2.73 (s, 7H), 2.61 - 2.50 (m, 2H), 2.40 - 2.29 (m, 1H), 2.15 (dd, J = 6.3, 9.4 Hz, 2H), 2.07 (d, J = 11.9 Hz, 2H), 1.92 - 1.70 (m, 5H) ; 663.4[M+H]$^+$	1.08

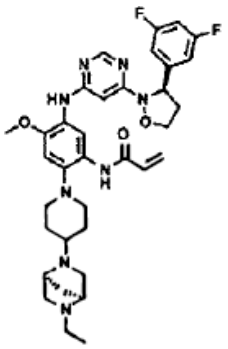
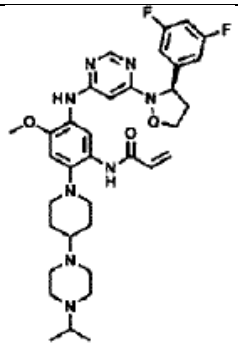
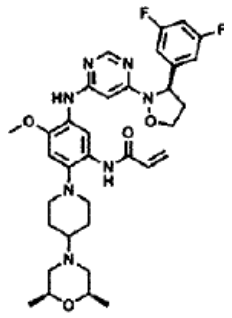
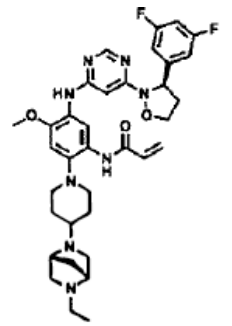
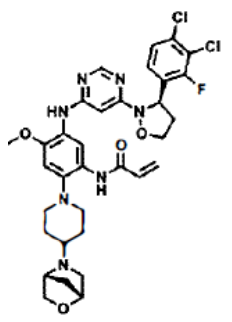
[512]

254		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	647.3 $[M+H]^+$	1.18
255		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	564.2 $[M+H]^+$	1.23
256		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.85 (s, 1H), 9.24 (d, J = 32.0 Hz, 1H), 8.30 (d, J = 6.7 Hz, 1H), 7.88 (s, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.42 (dd, J = 10.4, 2.0 Hz, 1H), 7.25 (d, J = 8.4 Hz, 1H), 6.90 (s, 1H), 6.50 (s, 1H), 6.28 - 6.20 (m, 1H), 6.13 (s, 1H), 5.76 (d, J = 10.4 Hz, 1H), 5.54 (dd, J = 8.6, 5.4 Hz, 1H), 4.72 - 4.55 (m, 3H), 4.28 (s, 1H), 4.20 (d, J = 10.2 Hz, 1H), 3.82 (d, J = 2.0 Hz, 3H), 3.71 (d, J = 9.7 Hz, 1H), 3.47 (t, J = 9.4 Hz, 2H), 3.19 (d, J = 20.5 Hz, 3H), 2.87 (d, J = 35.1 Hz, 3H), 2.31 (d, J = 13.0 Hz, 2H), 2.12 (d, J = 38.0 Hz, 5H); 650.3 $[M+H]^+$	1.27
257		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.10 (s, 1H), 9.29 (d, J = 33.0 Hz, 1H), 8.33 (s, 1H), 7.86 (d, J = 12.2 Hz, 1H), 7.58 (dd, J = 7.1, 2.1 Hz, 1H), 7.45 - 7.36 (m, 2H), 6.92 (d, J = 9.0 Hz, 1H), 6.71 - 6.53 (m, 1H), 6.29 - 6.23 (m, 1H), 6.12 (s, 1H), 5.76 (d, J = 10.4 Hz, 1H), 5.54 (dd, J = 8.5, 5.4 Hz, 1H), 4.73 - 4.56 (m, 3H), 4.46 (d, J = 9.2 Hz, 1H), 4.31 (d, J = 4.3 Hz, 1H), 4.22 (s, 1H), 4.06 (s, 2H), 3.82 (d, J = 2.3 Hz, 3H), 3.72 - 3.68 (m, 1H), 3.50 - 3.41 (m, 2H), 3.24 (d, J = 11.4 Hz, 2H), 2.97 - 2.78 (m, 3H), 2.33 (t, J = 6.6 Hz, 2H), 2.11 - 2.03 (m, 3H); 650.3 $[M+H]^+$	1.27
258		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.01 (s, 1H), 9.27 (d, J = 33.1 Hz, 1H), 8.31 (s, 1H), 7.88 (d, J = 12.1 Hz, 1H), 7.57 - 7.52 (m, 1H), 7.36 (t, J = 7.1 Hz, 1H), 7.24 (t, J = 7.9 Hz, 1H), 6.92 (d, J = 8.2 Hz, 1H), 6.63 (dt, J = 17.7, 8.8 Hz, 1H), 6.27 - 6.14 (m, 2H), 5.77 - 5.68 (m, 2H), 4.72 - 4.64 (m, 2H), 4.57 (s, 1H), 4.44 (d, J = 9.2 Hz, 1H), 4.32 (d, J = 4.1 Hz, 1H), 4.10 (s, 1H), 3.82 (d, J = 2.1 Hz, 3H), 3.71 (d, J = 3.2 Hz, 1H), 3.46 (t, J = 9.6 Hz, 3H), 3.23 (d, J = 11.2 Hz, 2H), 3.00 - 2.94 (m, 1H), 2.84 (t, J = 11.2 Hz, 2H), 2.31 (d, J = 10.6 Hz, 3H), 2.12 - 2.05 (m, 3H); 650.3 $[M+H]^+$	1.29

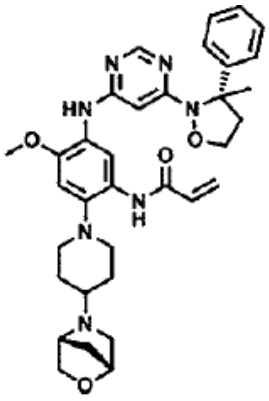
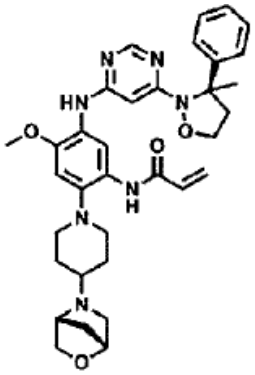
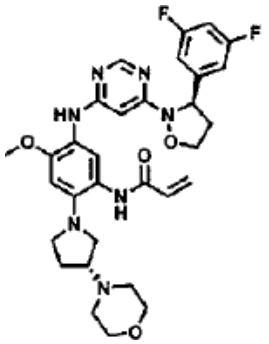
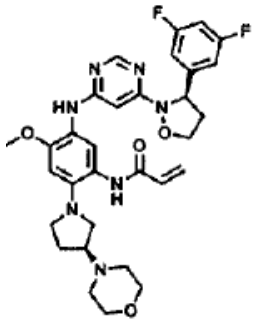
[513]

259		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.23 (s, 1H), 9.33 (d, J = 35.9 Hz, 1H), 8.34 (s, 1H), 7.85 (d, J = 11.6 Hz, 1H), 7.33 (td, J = 9.3, 4.4 Hz, 1H), 7.19 (dtd, J = 18.1, 9.1, 8.7, 3.7 Hz, 2H), 6.95 (d, J = 10.9 Hz, 1H), 6.64 (ddd, J = 21.2, 16.9, 10.2 Hz, 1H), 6.29 - 6.15 (m, 2H), 5.77 (dd, J = 10.0, 1.9 Hz, 1H), 5.66 (dd, J = 8.6, 5.6 Hz, 1H), 4.73 - 4.64 (m, 2H), 4.57 (s, 1H), 4.40 (s, 1H), 4.33 (d, J = 3.7 Hz, 1H), 3.83 (d, J = 2.2 Hz, 3H), 3.70 (td, J = 5.7, 3.0 Hz, 1H), 3.51 - 3.42 (m, 2H), 3.25 (d, J = 11.7 Hz, 2H), 3.15 (dd, J = 11.4, 3.6 Hz, 1H), 2.99 - 2.80 (m, 3H), 2.37 - 2.27 (m, 2H), 2.08 (d, J = 10.8 Hz, 3H); 634.3 [M+H]$^+$	1.23
260		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.06 (s, 1H), 9.29 (s, 1H), 8.33 (s, 1H), 7.85 (s, 1H), 7.10 - 7.14 (m, 1H), 7.12 - 7.08 (m, 2H), 6.93 (d, J = 23.4 Hz, 1H), 6.58 (d, J = 21.7 Hz, 1H), 6.25 (dd, J = 17.0, 1.8 Hz, 1H), 6.14 (s, 1H), 5.80 - 5.70 (m, 1H), 5.55 (dd, J = 8.6, 5.4 Hz, 1H), 4.70 (s, 2H), 4.48 (s, 1H), 4.20 (dd, J = 7.6, 4.3 Hz, 2H), 4.05 (s, 2H), 3.82 (s, 3H), 3.69 (s, 2H), 3.25 (s, 3H), 2.98 - 2.92 (m, 2H), 2.88 (d, J = 4.1 Hz, 3H), 2.75 (d, J = 9.3 Hz, 2H), 2.33 (dq, J = 10.4, 3.9, 2.5 Hz, 2H), 2.08 (d, J = 35.2 Hz, 3H); 647.3 [M+H]$^+$	1.13
261		N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-(3-methyl-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	627.6 [M+H]$^+$	1.06
262		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	665.5 [M+H]$^+$	1.27
263		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	665.5 [M+H]$^+$	1.26

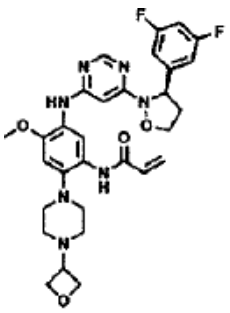
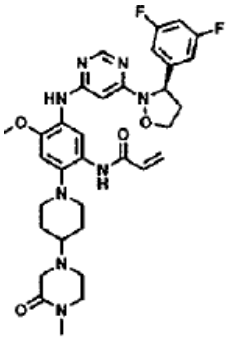
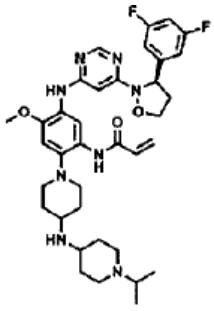
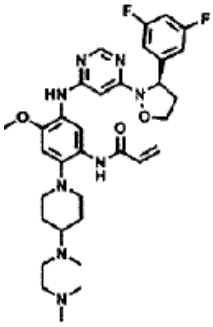
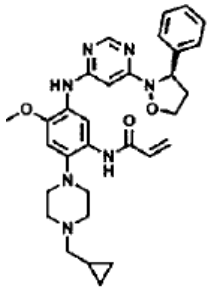
[514]

264		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	661.3 $[M+H]^+$	1.17
265		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.12 - 7.02 (m, 2H), 6.92 (s, 1H), 6.90 - 6.79 (m, 1H), 6.55 (dd, J = 10.2, 17.0 Hz, 1H), 6.46 (s, 1H), 6.37 (dd, J = 1.5, 17.0 Hz, 1H), 5.81 (d, J = 10.3 Hz, 1H), 5.57 (dd, J = 4.7, 8.7 Hz, 1H), 4.16 (td, J = 4.1, 7.9 Hz, 1H), 3.97 (q, J = 8.0 Hz, 1H), 3.88 (s, 3H), 3.30 - 3.23 (m, 2H), 3.19 - 3.10 (m, 5H), 2.97 (s, 4H), 2.88 - 2.75 (m, 3H), 2.68 - 2.56 (m, 1H), 2.40 - 2.28 (m, 1H), 2.10 - 2.01 (m, 2H), 1.80 - 1.74 (m, 2H), 1.33 - 1.20 (m, 6H) ; 663.4[M+H]$^+$	1.18
266		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.11 - 7.01 (m, 2H), 6.92 (s, 1H), 6.84 (tt, J = 2.5, 9.1 Hz, 1H), 6.57 (dd, J = 10.3, 17.0 Hz, 1H), 6.46 (s, 1H), 6.37 (d, J = 16.9 Hz, 1H), 5.81 (d, J = 10.3 Hz, 1H), 5.56 (dd, J = 4.8, 8.7 Hz, 1H), 4.16 (td, J = 4.1, 7.9 Hz, 1H), 3.97 (q, J = 7.9 Hz, 1H), 3.88 (s, 3H), 3.77 (dt, J = 6.5, 12.4 Hz, 2H), 3.22 - 3.14 (m, 2H), 3.14 - 3.07 (m, 2H), 2.87 - 2.75 (m, 3H), 2.66 - 2.56 (m, 1H), 2.38 - 2.28 (m, 1H), 2.14 - 2.09 (m, 2H), 1.87 - 1.75 (m, 2H), 1.25 - 1.18 (m, 6H) ; 650.3[M+H]$^+$	1.31
267		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.48 (s, 1H), 8.35 (s, 1H), 7.06 (s, 1H), 7.03 - 6.98 (m, 2H), 6.75 (s, 1H), 6.72 - 6.65 (m, 2H), 6.38 - 6.22 (m, 2H), 5.73 (dd, J = 9.8, 1.5 Hz, 1H), 5.66 (dd, J = 8.7, 4.5 Hz, 1H), 4.15 (td, J = 8.0, 4.2 Hz, 1H), 4.06 (q, J = 8.0 Hz, 1H), 3.85 (s, 3H), 3.74 (d, J = 18.2 Hz, 2H), 3.26 - 3.20 (m, 1H), 3.10 - 3.06 (m, 1H), 3.04 - 2.99 (m, 2H), 2.96 - 2.87 (m, 4H), 2.83 - 2.73 (m, 7H), 2.67 - 2.62 (m, 1H), 2.38 - 2.29 (m, 1H), 1.78 - 1.66 (m, 2H), 1.21 (t, J = 7.2 Hz, 3H); 661.6[M+H]$^+$	1.2
268		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.18 (s, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.38 (d, J = 8.6 Hz, 1H), 6.93 (s, 1H), 6.56 (dd, J = 10.2, 17.0 Hz, 1H), 6.49 (s, 1H), 6.37 (d, J = 16.9 Hz, 1H), 5.87 - 5.70 (m, 2H), 4.23 - 4.14 (m, 3H), 3.99 (q, J = 8.0 Hz, 1H), 3.80 (s, 3H), 3.77 (d, J = 9.0 Hz, 1H), 3.31 - 3.25 (m, 2H), 3.20 - 3.12 (m, 2H), 3.01 - 2.79 (m, 5H), 2.34 - 2.22 (m, 1H), 2.22 - 2.13 (m, 1H), 2.13 - 2.02 (m, 3H), 1.87 - 1.73 (m, 2H) ; 684.2[M+H]$^+$	1.51

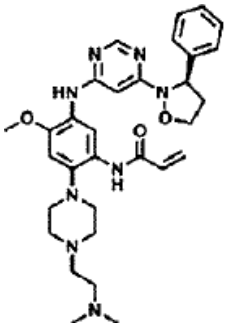
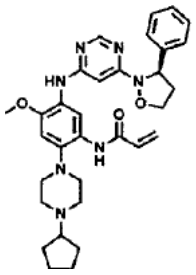
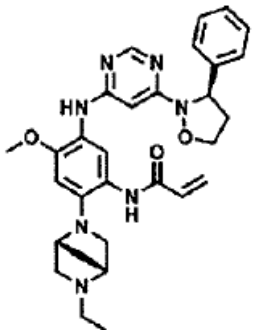
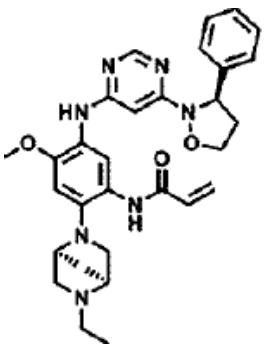
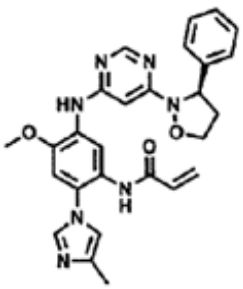
[515]

269		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-methyl-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.26 (s, 1H), 8.12 (s, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.33 (t, J = 7.6 Hz, 2H), 7.25 (t, J = 7.3 Hz, 1H), 6.03 (s, 1H), 6.55 (dd, J = 10.3, 17.0 Hz, 1H), 6.39 - 6.30 (m, 2H), 5.80 (d, J = 10.3 Hz, 1H), 4.23 - 4.19 (m, 1H), 4.19 - 4.14 (m, 1H), 3.98 (td, J = 5.0, 9.0 Hz, 1H), 3.89 (s, 3H), 3.79 - 3.73 (m, 1H), 3.73 - 3.63 (m, 1H), 3.31 - 3.25 (m, 2H), 3.19 - 3.13 (m, 2H), 3.02 - 2.90 (m, 2H), 2.90 - 2.77 (m, 2H), 2.73 - 2.64 (m, 1H), 2.56 - 2.46 (m, 1H), 2.21 - 2.10 (m, 1H), 2.12 - 2.01 (m, 3H), 1.85 - 1.75 (m, 2H), 1.62 (s, 3H) ; 612.3[M+H]$^+$	1.27
270		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-methyl-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.27 (s, 1H), 8.12 (s, 1H), 7.48 (d, J = 7.6 Hz, 2H), 7.33 (t, J = 7.6 Hz, 2H), 7.25 (t, J = 7.3 Hz, 1H), 6.03 (s, 1H), 6.55 (dd, J = 10.2, 17.0 Hz, 1H), 6.40 - 6.28 (m, 2H), 5.79 (d, J = 10.3 Hz, 1H), 4.20 - 4.22 (m, 1H), 4.21 - 4.12 (m, 1H), 4.03 - 3.92 (m, 1H), 3.89 (s, 3H), 3.81 - 3.74 (m, 1H), 3.74 - 3.62 (m, 1H), 3.32 - 3.27 (m, 2H), 3.22 - 3.11 (m, 2H), 3.06 - 2.94 (m, 2H), 2.91 - 2.78 (m, 2H), 2.73 - 2.63 (m, 1H), 2.58 - 2.46 (m, 1H), 2.24 - 2.13 (m, 1H), 2.13 - 2.02 (m, 3H), 1.88 - 1.75 (m, 2H), 1.62 (s, 3H)) ; 612.3[M+H]$^+$	1.26
271		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.01 (d, J = 9.5 Hz, 1H), 10.22 (s, 1H), 9.70 (s, 1H), 7.56 (s, 1H), 7.18 (tt, J = 9.3, 2.4 Hz, 1H), 7.12 - 7.06 (m, 2H), 6.89 (dd, J = 17.0, 10.2 Hz, 1H), 6.71 (s, 1H), 6.22 (dd, J = 17.0, 2.1 Hz, 1H), 6.05 (s, 1H), 5.71 (dd, J = 10.1, 2.1 Hz, 1H), 5.56 (dd, J = 8.6, 5.4 Hz, 1H), 4.11 - 4.03 (m, 1H), 3.96 (tp, J = 18.1, 5.8, 5.1 Hz, 6H), 3.82 (s, 3H), 3.73 (dd, J = 11.0, 4.5 Hz, 1H), 3.61 - 3.45 (m, 4H), 3.41 (dd, J = 10.9, 6.3 Hz, 1H), 3.13 (dt, J = 24.6, 7.8 Hz, 4H), 3.00 - 2.88 (m, 1H), 2.47 - 2.26 (m, 4H).; 608.5 [M+H]$^+$	1.34
272		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.03 (d, J = 9.4 Hz, 1H), 10.28 (s, 1H), 9.72 (s, 1H), 7.55 (s, 1H), 7.18 (tt, J = 9.3, 2.4 Hz, 1H), 7.10 (h, J = 4.5 Hz, 2H), 6.90 (dd, J = 17.0, 10.2 Hz, 1H), 6.71 (s, 1H), 6.22 (dd, J = 16.9, 2.1 Hz, 1H), 6.06 (s, 1H), 5.71 (dd, J = 10.1, 2.1 Hz, 1H), 5.56 (dd, J = 8.6, 5.4 Hz, 1H), 4.11 - 4.04 (m, 1H), 3.97 (q, J = 12.6, 9.9 Hz, 5H), 3.82 (s, 3H), 3.73 (dd, J = 11.0, 4.5 Hz, 1H), 3.54 (dtd, J = 17.8, 12.9, 11.4, 7.3 Hz, 3H), 3.42 (dd, J = 11.0, 6.3 Hz, 1H), 3.14 (dt, J = 28.6, 9.4 Hz, 4H), 3.00 - 2.80 (m, 1H), 2.36 (dddd, J = 26.2, 13.2, 10.7, 6.7 Hz, 3H).; 608.5 [M+H]$^+$	1.32

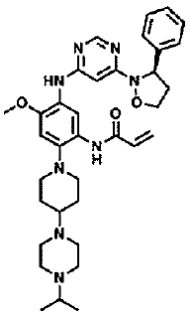
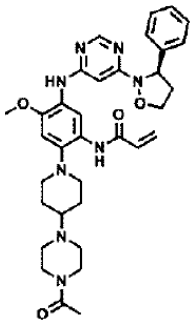
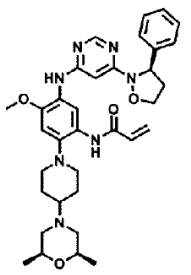
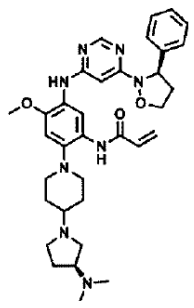
[516]

273		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	594.5 $[M+H]^+$	1.37
274		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methyl-3-oxopiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.71 (s, 1H), 8.41 (s, 1H), 8.27 (d, *J* = 0.9 Hz, 1H), 6.97 (h, *J* = 4.5 Hz, 3H), 6.74 (s, 1H), 6.66 (tt, *J* = 8.9, 2.4 Hz, 1H), 6.62 (s, 1H), 6.40 - 6.20 (m, 2H), 5.74 (dd, *J* = 9.8, 1.7 Hz, 1H), 5.62 (dd, *J* = 8.8, 4.6 Hz, 1H), 4.02 (q, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.46 (s, 2H), 3.35 (d, *J* = 8.1 Hz, 4H), 3.11 - 3.02 (m, 2H), 2.97 (s, 3H), 2.84 (dd, *J* = 6.3, 4.6 Hz, 2H), 2.82 - 2.67 (m, 4H), 2.44 (tt, *J* = 11.0, 3.8 Hz, 1H), 2.31 (dtd, *J* = 12.6, 8.1, 4.7 Hz, 1H), 2.04 - 1.97 (m, 2H), 1.74 - 1.62 (m, 2H).; 649.5 $[M+H]^+$	1.38
275		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1-isopropylpiperidine-4-yl)amino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	677.5 $[M+H]^+$	1.31
276		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2-(dimethylamino)ethyl)(methyl)amino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.45 (s, 1H), 8.37 (s, 1H), 7.03 - 6.99 (m, 2H), 6.93 (s, 1H), 6.75 (s, 1H), 6.72 - 6.65 (m, 2H), 6.40 - 6.25 (m, 2H), 5.75 (dd, *J* = 9.7, 1.8 Hz, 1H), 5.67 (dd, *J* = 8.8, 4.5 Hz, 1H), 4.15 (td, *J* = 8.1, 4.3 Hz, 1H), 4.11 - 3.84 (m, 4H), 3.85 (s, 2H), 3.11 - 3.02 (m, 2H), 2.80 - 2.50 (m, 8H), 2.49 - 2.29 (m, 10H), 2.02 - 1.96 (m, 2H), 1.78 - 1.67 (m, 2H): 637.6$[M+H]^+$	1.25
277		N-(2-(4-(cyclopropylmethyl)piperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, CDCl3) δ 8.92 (s, 1H), 8.57 (s, 1H), 8.37 (s, 1H), 7.47 (d, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.24 (s, 1H), 6.92 (s, 1H), 6.83 (s, 1H), 6.70 (s, 1H), 6.37 (d, *J* = 16.8 Hz, 1H), 6.26 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.77 - 5.73 (m, 1H), 5.73 - 5.68 (m, 1H), 4.16 (td, *J* = 7.9, 4.6 Hz, 1H), 4.07 (q, *J* = 7.9 Hz, 1H), 3.83 (s, 3H), 2.95 (s, 4H), 2.81 - 2.72 (m, 3H), 2.44 - 2.38 (m, 1H), 2.36 (d, *J* = 6.8 Hz, 2H), 0.87 (m, 3H), 0.63 - 0.52 (m, 2H), 0.17 (m, 2H).; 556.5 $[M+H]^+$	1.38

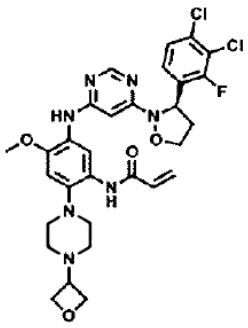
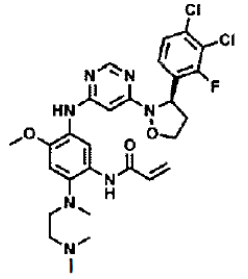
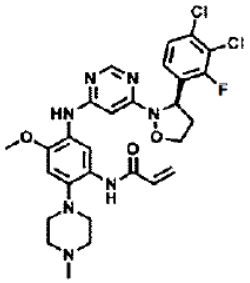
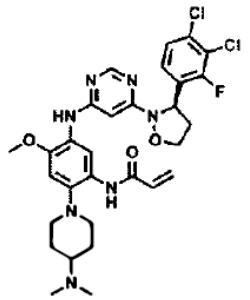
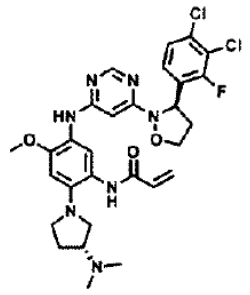
[517]

278		N-(2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, CDCl3) δ 8.90 (s, 1H), 8.55 (s, 1H), 8.37 (s, 1H), 7.46 (d, J = 7.6 Hz, 2H), 7.34 (t, J = 7.6 Hz, 2H), 7.23 (t, J = 7.3 Hz, 1H), 6.94 (s, 1H), 6.80 (s, 1H), 6.60 (s, 1H), 6.36 (d, J = 16.0 Hz, 1H), 6.27 (dd, J = 16.9, 9.9 Hz, 1H), 5.78 - 5.73 (m, 1H), 5.71 - 5.65 (m, 1H), 4.16 (td, J = 7.9, 4.6 Hz, 1H), 4.06 (dt, J = 8.0, 5.8 Hz, 1H), 3.82 (s, 3H), 2.98 - 2.88 (m, 4H), 2.80 - 2.64 (m, 4H), 2.62 - 2.57 (m, 2H), 2.54 - 2.48 (m, 2H), 2.44 -2.34 (m, 2H), 2.31 (s, 6H).; 573.5 [M+H]$^+$	1.28
279		N-(2-(4-cyclopentylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, CDCl$_3$) δ 8.91 (s, 1H), 8.59 (s, 1H), 8.37 (s, 1H), 7.46 (d, J = 7.5 Hz, 2H), 7.34 (t, J = 7.6 Hz, 2H), 7.23 (d, J = 7.3 Hz, 1H), 6.95 (s, 1H), 6.82 (s, 1H), 6.70 (s, 1H), 6.36 (d, J = 16.9 Hz, 1H), 6.27 (dd, J = 16.9, 9.9 Hz, 1H), 5.74 (dd, J = 10.0, 1.4 Hz, 1H), 5.72 - 5.67 (m, 1H), 4.16 (td, J = 7.9, 4.6 Hz, 1H), 4.07 (q, J = 7.9 Hz, 1H), 3.82 (s, 3H), 2.94 (s, 4H), 2.80 - 2.66 (m, 3H), 2.64 - 2.54 (m, 2H), 2.44 - 2.30 (m, 2H), 1.92 (m, 2H), 1.73 (m, 2H), 1.61 (m, 2H), 1.52 - 1.39 (m, 2H).; 570.5 [M+H]$^+$	1.41
280		N-(2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, CDCl3) δ 8.56 (s, 1H), 8.35 (s, 1H), 7.95 (s, 1H), 7.48 (d, J = 7.6 Hz, 2H),7.34 (t, J = 7.6 Hz, 2H), 7.23 (d, J = 7.3 Hz, 1H), 6.80 (s, 1H), 6.68 (s, 1H), 6.64 (s, 1H), 6.38(d, J = 16.7 Hz, 1H), 6.28 (dd, J = 16.8, 10.0 Hz, 1H), 5.74 (d, J = 10.6 Hz, 1H), 5.70 (dd, J =8.6, 4.5 Hz, 1H), 4.21 - 4.12 (m, 1H), 4.05 (dd, J = 15.9, 8.1 Hz, 1H), 3.84 (s, 3H), 3.73 (s, 1H),3.57 (s, 1H), 3.48 (d, J = 9.2 Hz, 1H), 3.07 (d, J = 8.1 Hz, 1H), 2.81 (s, 2H), 2.78 - 2.70 (m,2H), 2.58 (m, 1H), 2.44 - 2.33 (m, 1H), 1.90 (dd, J = 21.0, 9.5 Hz, 2H), 1.13 (t, J = 7.0 Hz, 3H).; 542.5 [M+H]$^+$	1.34
281		N-(2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, CDCl3) δ 8.55 (s, 1H), 8.34 (s, 1H), 7.95 (s, 1H), 7.46 (d, J = 7.6 Hz, 2H), 7.33 (t, J= 7.6 Hz, 2H), 7.24 (m, 1H), 6.86 (s, 1H), 6.65 (s, 1H), 6.60 (s, 1H), 6.38 (d, J = 16.5 Hz, 1H), 6.20 (dd, J= 16.9, 9.9 Hz, 1H), 5.73 (d, J = 10.5 Hz, 1H), 5.60 (dd, J = 8.6, 4.4 Hz, 1H), 4.14 (td, J = 7.8, 4.6 Hz,1H), 4.02 (q, J = 7.8 Hz, 1H), 3.83 (s, 3H), 3.72 (s, 1H), 3.58 (s, 1H), 3.46 (d, J = 9.6 Hz, 1H), 3.11 (d, J = 8.2 Hz, 1H), 2.82 (s, 2H), 2.79 - 2.66 (m, 2H), 2.58 (m, 1H), 2.43 - 2.33 (m, 1H), 1.90 (dd, J = 21.0, 9.6Hz, 2H), 1.12 (t, J = 7.1 Hz, 3H).; 542.4 [M+H]$^+$	1.35
282		N-(4-methoxy-2-(4-methyl-1H-imidazole-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, CDCl3) δ 9.40 (s, 1H), 8.92 (s, 1H), 8.42 (s, 1H), 7.50 - 7.43 (m, 3H), 7.36 (t, J =7.6 Hz, 2H), 7.28 - 7.25 (m, 1H), 7.15 (s, 1H), 6.79 (s, 1H), 6.75 (s, 1H), 6.72 (s, 1H), 6.44 - 6.31 (m,1H), 6.27 - 6.15 (m, 1H), 5.80 - 5.73 (m, 1H), 5.73 - 5.66 (m, 1H), 4.20 (m, 1H), 4.11 - 3.99 (m, 1H),3.88 (s, 3H), 2.77 (m, 1H), 2.49 - 2.37 (m, 1H) 2.23 (s, 3H).; 408.4 [M+H]$^+$	1.49

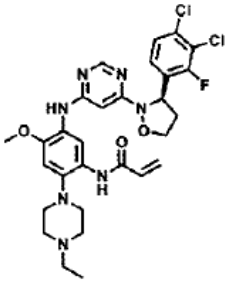
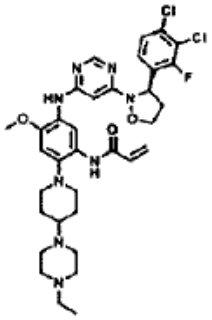
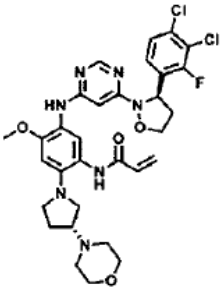
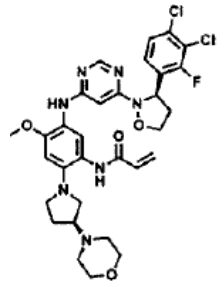
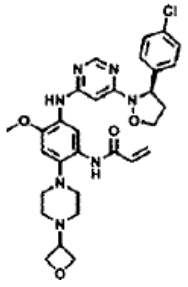
[518]

283		N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl) acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.88 (s, 1H), 8.45 (s, 1H), 8.37 (s, 1H), 7.46 (d, *J* = 7.3 Hz, 2H), 7.34 (dd, *J* = 8.3, 6.8 Hz, 2H), 7.24 (s, 1H), 6.89 (s, 1H), 6.74 (s, 1H), 6.69 (s, 1H), 6.35 (dd, *J* = 16.9, 1.5 Hz, 1H), 6.24 (dd, *J* = 16.9, 10.1 Hz, 1H), 5.72 (ddd, *J* = 13.2, 9.3, 3.0 Hz, 2H), 4.15 (td, *J* = 7.9, 4.4 Hz, 1H), 4.07 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.06 (d, *J* = 11.4 Hz, 2H), 2.76 - 2.70 (m, 4H), 2.44 - 2.25 (m, 3H), 2.09 (d, *J* = 12.0 Hz, 2H), 1.69 - 1.64 (m, 3H), 1.09 (d, *J* = 6.5 Hz, 8H).: 627.6[M+H]$^+$	1.10
284		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl) acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.42 (s, 1H), 8.38 - 8.34 (m, 1H), 7.46 (d, *J* = 7.3 Hz, 2H), 7.33 (dd, *J* = 8.4, 6.8 Hz, 2H), 7.26 - 7.21 (m, 1H), 6.97 (s, 1H), 6.74 (s, 1H), 6.69 (s, 1H), 6.37 (dd, *J* = 17.0, 1.6 Hz, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.72 (ddd, *J* = 18.4, 9.3, 3.0 Hz, 2H), 4.15 (td, *J* = 8.0, 4.4 Hz, 1H), 4.06 (q, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.66 (t, *J* = 5.1 Hz, 2H), 3.51 (t, *J* = 5.0 Hz, 2H), 3.06 (d, *J* = 11.0 Hz, 2H), 2.77 - 2.69 (m, 3H), 2.62 - 2.58 (m, 3H), 2.40 (ddd, *J* = 10.5, 8.2, 4.3 Hz, 2H), 2.10 (s, 3H), 2.03 (d, *J* = 13.6 Hz, 2H), 1.71 - 1.61 (m, 2H), 1.26 (s, 1H).: 627.6[M+H]$^+$	1.35
285		N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl) acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.43 (s, 1H), 8.37 (s, 1H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 7.3 Hz, 1H), 6.96 (s, 1H), 6.74 (s, 1H), 6.69 (s, 1H), 6.41 - 6.33 (m, 1H), 6.26 (dd, *J* = 16.9, 9.8 Hz, 1H), 5.72 (ddd, *J* = 16.7, 9.3, 3.0 Hz, 2H), 4.16 (td, *J* = 7.9, 4.5 Hz, 1H), 4.07 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.72 (s, 2H), 3.07 (d, *J* = 11.2 Hz, 2H), 2.89 (d, *J* = 10.7 Hz, 2H), 2.77 - 2.67 (m, 3H), 2.42 - 2.35 (m, 1H), 2.30 (dd, *J* = 13.2, 7.6 Hz, 2H), 2.07 (d, *J* = 13.3 Hz, 3H), 1.91 (t, *J* = 10.1 Hz, 3H), 1.73 - 1.63 (m, 5H).: 614.6[M+H]$^+$	1.33
286		N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl) acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.49 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.48 - 7.44 (m, 2H), 7.33 (dd, *J* = 8.5, 6.8 Hz, 2H), 7.26 - 7.20 (m, 1H), 6.94 (s, 1H), 6.75 (s, 1H), 6.69 (s, 1H), 6.34 (dd, *J* = 16.9, 1.5 Hz, 1H), 6.23 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.71 (ddd, *J* = 12.4, 9.3, 3.0 Hz, 2H), 4.15 (td, *J* = 8.0, 4.5 Hz, 1H), 4.07 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.05 (ddd, *J* = 21.8, 9.9, 5.4 Hz, 3H), 2.93 (td, *J* = 8.4, 5.1 Hz, 1H), 2.75 (tdd, *J* = 11.7, 5.7, 2.4 Hz, 4H), 2.56 (td, *J* = 9.0, 6.5 Hz, 1H), 2.42 - 2.34 (m, 2H), 2.26 (s, 6H), 2.22 - 2.16 (m, 1H), 2.10 - 2.01 (m, 3H), 1.81 - 1.67 (m, 3H).: 613.6[M+H]$^+$	1.27

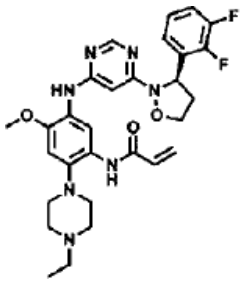
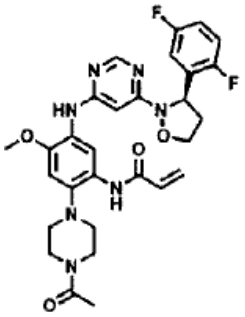
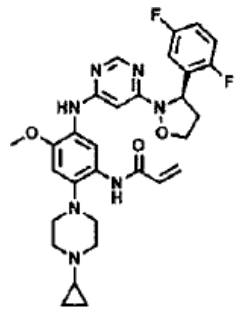
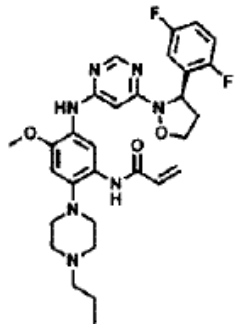
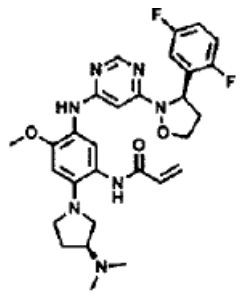
[519]

287		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.95 (s, 1H), 9.18 (s, 1H), 8.32 (s, 1H), 8.04 - 7.99 (m, 1H), 7.54 (dd, J = 8.5, 1.5 Hz, 1H), 7.38 (t, J = 8.1 Hz, 1H), 6.92 (s, 1H), 6.70 (dd, J = 17.0, 10.2 Hz, 1H), 6.24 (dd, J = 17.0, 2.0 Hz, 1H), 6.13 (s, 1H), 5.76 (dd, J = 9.7, 2.3 Hz, 1H), 5.68 (dd, J = 8.7, 5.7 Hz, 1H), 4.85 - 4.77 (m, 4H), 4.54 (s, 1H), 4.07 (d, J = 7.8 Hz, 2H), 3.83 (s, 3H), 3.52 (s, 2H), 3.30 - 3.34 (m, 1H), 3.26 (s, 4H), 3.16 (d, J = 12.1 Hz, 2H), 2.97 (d, J = 8.0 Hz, 1H); 644.2 $[M+H]^+$	1.65
288		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.88 (s, 1H), 9.73 (s, 1H), 8.28 (s, 1H), 8.09 (s, 1H), 7.53 (dd, J = 8.6, 1.5 Hz, 1H), 7.41 (t, J = 8.1 Hz, 1H), 7.20 (dd, J = 17.0, 10.2 Hz, 1H), 6.96 (s, 1H), 6.30 - 6.19 (m, 2H), 5.73 - 5.66 (m, 2H), 4.33 - 4.27 (m, 1H), 4.03 (d, J = 7.9 Hz, 1H), 3.83 (s, 3H), 3.32 (s, 4H), 2.93 (d, J = 8.3 Hz, 1H), 2.73 (d, J = 4.8 Hz, 6H), 2.61 (s, 3H), 2.30 (dd, J = 13.2, 6.1 Hz, 1H); 604.2 $[M+H]^+$	1.76
289		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.77 (s, 1H), 9.17 (s, 1H), 8.28 (s, 1H), 8.07 (s, 1H), 7.53 (dd, J = 8.6, 1.5 Hz, 1H), 7.40 (t, J = 8.1 Hz, 1H), 6.88 (s, 1H), 6.81 - 6.72 (m, 1H), 6.28 - 6.18 (m, 2H), 5.78 - 5.65 (m, 2H), 4.28 (dd, J = 7.8, 4.0 Hz, 1H), 4.03 (s, 1H), 3.83 (s, 3H), 3.48 (d, J = 11.5 Hz, 2H), 3.42 - 3.36 (m, 2H), 3.20 (s, 4H), 2.97 - 2.87 (m, 1H), 2.82 (d, J = 4.6 Hz, 3H), 2.36 - 2.24 (m, 1H); 602.2 $[M+H]^+$	1.64
290		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.25 (s, 1H), 8.75 (s, 1H), 8.32 (s, 1H), 7.93 (s, 1H), 7.53 (dd, J = 8.5, 1.5 Hz, 1H), 7.30 (t, J = 8.1 Hz, 1H), 6.92 (s, 1H), 6.75 (dd, J = 16.9, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 2H), 5.79 - 5.74 (m, 1H), 5.71 - 5.66 (m, 1H), 4.33 - 4.30 (m, 1H), 4.06 (d, J = 7.8 Hz, 1H), 3.82 (s, 3H), 3.68 (d, J = 7.3 Hz, 1H), 3.38 (d, J = 6.9 Hz, 1H), 3.08 (s, 1H), 2.95 (d, J = 4.9 Hz, 1H), 2.81 (s, 1H), 2.73 (d, J = 5.5 Hz, 6H), 2.36 - 2.28 (m, 1H), 2.13 (d, J = 9.5 Hz, 2H), 2.03 (d, J = 11.0 Hz, 2H), 1.90 (d, J = 7.1 Hz, 1H); 630.2 $[M+H]^+$	1.72
291		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.54 (d, J = 30.1 Hz, 1H), 8.25 (d, J = 2.9 Hz, 1H), 7.64 (s, 1H), 7.53 (dd, J = 8.5, 1.5 Hz, 1H), 7.40 (t, J = 8.1 Hz, 2H), 6.85 (dd, J = 17.0, 10.2 Hz, 1H), 6.66 (d, J = 21.0 Hz, 1H), 6.25 - 6.08 (m, 2H), 5.74 - 5.65 (m, 2H), 4.27 (q, J = 6.7, 5.3 Hz, 1H), 3.90 (d, J = 7.8 Hz, 1H), 3.88 (s, 1H), 3.81 (d, J = 3.1 Hz, 3H), 3.50 (s, 1H), 3.48 (s, 1H), 3.41 - 3.36 (m, 1H), 3.05 (d, J = 8.4 Hz, 1H), 2.80 (dd, J = 8.3, 4.6 Hz, 6H), 2.36 - 2.21 (m, 4H); 616.2 $[M+H]^+$	1.64

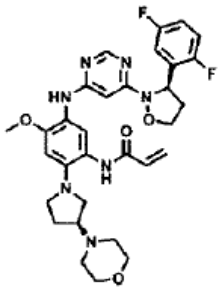
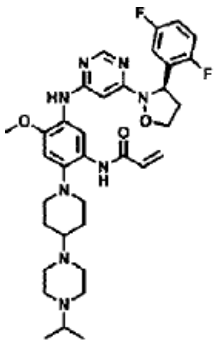
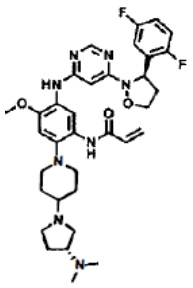
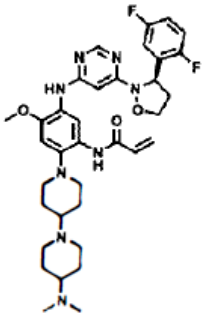
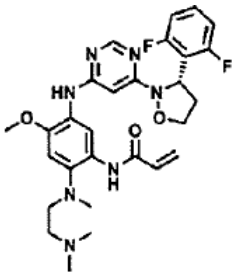
[520]

292		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.81 (s, 1H), 9.21 (s, 1H), 8.29 (s, 1H), 8.07 (s, 1H), 7.53 (dd, J = 8.5, 1.5 Hz, 1H), 7.40 (t, J = 8.1 Hz, 1H), 6.90 - 6.72 (m, 2H), 6.31 - 6.17 (m, 2H), 5.73 (ddd, J = 23.7, 9.4, 3.8 Hz, 2H), 4.31 - 4.27 (m, 1H), 4.02 (d, J = 8.0 Hz, 2H), 3.83 (s, 3H), 3.52 (d, J = 11.3 Hz, 2H), 3.40 - 3.29 (m, 3H), 3.22 - 3.14 (m, 4H), 2.93 (dd, J = 8.1, 4.3 Hz, 1H), 2.34 - 2.24 (m, 1H), 1.32 (t, J = 7.2 Hz, 3H); 616.2 $[M+H]^+$	1.68
293		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	608.3 $[M+H]^+$	1.63
294		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.67 (s, 1H), 9.60 (s, 1H), 8.26 (s, 1H), 7.64 (s, 1H), 7.53 (dd, J = 8.6, 1.5 Hz, 1H), 7.39 (t, J = 8.1 Hz, 1H), 6.86 (dd, J = 17.0, 10.2 Hz, 1H), 6.70 (s, 1H), 6.21 (dd, J = 17.0, 2.1 Hz, 1H), 6.13 (s, 1H), 5.70 (dd, J = 9.9, 2.4 Hz, 2H), 4.31 - 4.27 (m, 1H), 3.97 (s, 2H), 3.82 (s, 3H), 3.56 (d, J = 12.1 Hz, 2H), 3.50 - 3.47 (m, 1H), 3.38 (d, J = 7.0 Hz, 3H), 3.11 (dd, J = 15.7, 7.3 Hz, 4H), 2.98 - 2.87 (m, 1H), 2.32 (dd, J = 14.0, 6.7 Hz, 3H), 1.09 (t, J = 7.0 Hz, 2H).; 658.4 $[M+H]^+$	1.37
295		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 9.59 (d, J = 33.2 Hz, 1H), 8.27 (d, J = 2.6 Hz, 1H), 7.62 (s, 1H), 7.53 (dd, J = 8.6, 1.5 Hz, 1H), 7.40 (dd, J = 8.1, 2.3 Hz, 1H), 6.87 (dd, J = 17.0, 10.2 Hz, 1H), 6.68 (d, J = 22.7 Hz, 1H), 6.21 (dd, J = 17.0, 2.1 Hz, 1H), 6.12 (s, 1H), 5.73 - 5.66 (m, 2H), 4.31 - 4.26 (m, 1H), 4.05 (s, 1H), 3.81 (d, J = 3.2 Hz, 3H), 3.53 (d, J = 20.3 Hz, 4H), 3.43 - 3.38 (m, 1H), 3.16 (d, J = 7.6 Hz, 4H), 2.96 (d, J = 6.3 Hz, 2H), 2.44 - 2.27 (m, 4H), 1.65 - 1.55 (m, 1H), 1.50 - 1.40 (m, 1H).; 658.4 $[M+H]^+$	1.38
296		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	592.5 $[M+H]^+$	1.48

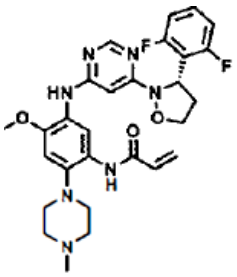
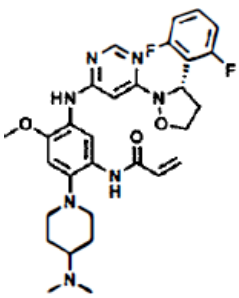
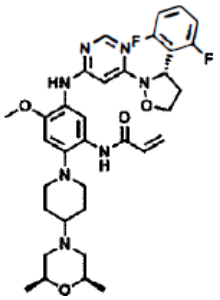
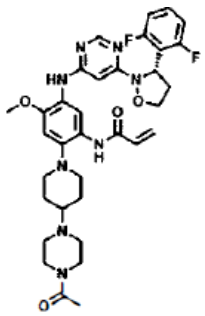
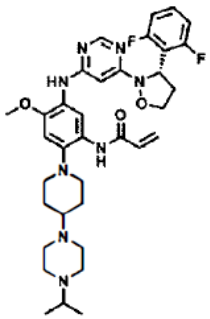
[521]

297		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.56 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 7.40 - 7.31 (m, 1H), 7.08 - 7.01 (m, 2H), 6.08 (s, 1H), 6.82 (s, 1H), 6.75 (s, 1H), 6.37 (dd, *J* = 17.0, 1.6 Hz, 1H), 6.26 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.93 (dd, *J* = 8.8, 4.5 Hz, 1H), 5.75 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.19 - 4.11 (m, 1H), 4.11 - 4.01 (m, 1H), 3.83 (s, 3H), 2.96 - 2.91 (m, 4H), 2.88 - 2.81 (m, 1H), 2.75 - 2.55 (m, 4H), 2.52 (q, *J* = 7.2 Hz, 2H), 2.36 - 2.27 (m, 1H), 1.16 (t, *J* = 7.2 Hz, 3H) ; 566.4[M+H]$^+$	1.21
298		N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.43 (s, 1H), 8.36 (s, 1H), 7.35 - 7.28 (m, 1H), 7.21 (s, 1H), 7.04 - 6.94 (m, 1H), 6.94 - 6.86 (m, 1H), 6.75 (s, 1H), 6.73 (s, 1H), 6.30 (dt, *J* = 16.9, 13.2 Hz, 2H), 5.90 (dd, *J* = 8.7, 4.3 Hz, 1H), 5.77 (dd, *J* = 10.0, 1.2 Hz, 1H), 4.16 - 4.03 (m, 2H), 3.86 (s, 3H), 3.84 - 3.75 (m, 2H), 3.68 - 3.63 (m, 2H), 2.93 - 2.80 (m, 5H), 2.34 - 2.26 (m, 1H), 2.17 (s, 3H); 580.4[M+H]$^+$	1.41
299		N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.60 (s, 1H), 8.37 (s, 1H), 7.36 - 7.28 (m, *J* = 9.0, 5.8, 3.2 Hz, 1H), 7.00 (td, *J* = 9.2, 4.4 Hz, 1H), 6.95 (s, 1H), 6.93 - 6.86 (m, 1H), 6.80 (s, 1H), 6.77 (s, 1H), 6.40 - 6.25 (m, 2H), 5.90 (dd, *J* = 8.7, 4.3 Hz, 1H), 5.75 (dd, *J* = 9.8, 1.6 Hz, 1H), 4.16 - 4.04 (m, 2H), 3.82 (s, 3H), 2.92 - 2.77 (m, 9H), 2.34 - 2.24 (m, 1H), 1.76 - 1.70 (m, 1H), 0.55 - 0.50 (m, 2H), 0.49 - 0.43 (m, 2H); 578.5[M+H]$^+$	1.23
300		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-propylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.57 (s, 1H), 8.37 (s, 1H), 7.36 - 7.28 (m, 1H), 7.04 - 6.94 (m, 2H), 6.93 - 6.87 (m, 1H), 6.82 (s, 1H), 6.77 (s, 1H), 6.30 (dt, *J* = 17.0, 13.1 Hz, 2H), 5.90 (dd, *J* = 8.6, 4.2 Hz, 1H), 5.74 (dd, *J* = 10.0, 1.1 Hz, 1H), 4.16 - 4.03 (m, 2H), 3.84 (s, 3H), 2.96 - 2.88 (m, 4H), 2.87 - 2.70 (m, 1H), 2.70 - 2.63 (m, 2H), 2.43 - 2.38 (m, 2H), 2.34 - 2.24 (m, 1H), 1.64 - 1.53 (m, 4H), 0.95 (t, *J* = 7.4 Hz, 3H); 580.5[M+H]$^+$	1.24
301		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.36 (s, 1H), 8.17 (s, 1H), 7.35 - 7.29 (m, 1H), 7.00 (td, *J* = 9.2, 4.4 Hz, 1H), 6.92 - 6.85 (m, *J* = 10.9, 5.4 Hz, 2H), 6.77 (s, 1H), 6.72 (s, 1H), 6.42 - 6.23 (m, 2H), 5.90 (dd, *J* = 8.6, 4.1 Hz, 1H), 5.73 (dd, *J* = 10.0, 1.3 Hz, 1H), 4.15 - 4.01 (m, 2H), 3.85 (s, 3H), 3.22 - 3.03 (m, 3H), 2.93 - 2.76 (m, 2H), 2.35 - 2.12 (m, 9H), 1.99 - 1.80 (m, 1H); 566.5[M+H]$^+$	1.17

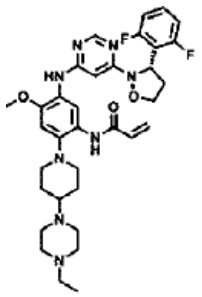
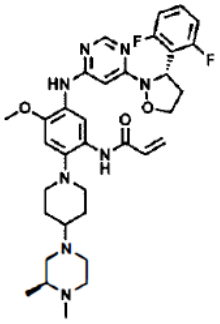
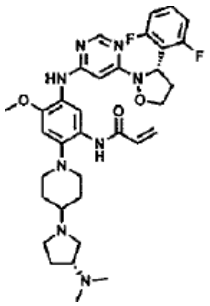
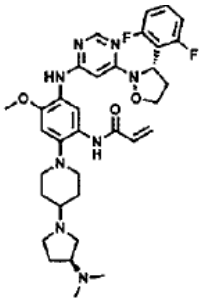
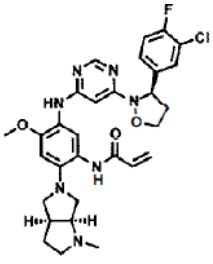
[522]

302		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, CDCl3) δ 8.73 (s, 1H), 8.36 (s, 1H), 8.14 (s, 1H), 7.35 - 7.29 (m, 1H), 7.02 - 6.87 (m, 3H), 6.77 (s, 1H), 6.72 (s, 1H), 6.41 - 6.22 (m, 2H), 5.90 (dd, J = 8.6, 4.2 Hz, 1H), 5.76 - 5.71 (m, 1H), 4.15 - 4.01 (m, 2H), 3.85 (s, 1H), 3.78 - 3.74 (m, 4H), 3.21 - 3.08 (m, 3H), 3.02 - 2.96 (m, 1H), 2.85 - 2.77 (m, 1H), 2.60 - 2.55 (m, 2H), 2.52 - 2.44 (m, 2H), 2.33 - 2.14 (m, 3H), 2.00 - 1.90 (m, 1H); 608.46[M+H]+	1.18
303		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, Methanol-d4) δ 8.29 (s, 1H), 8.18 (s, 1H), 7.29 - 7.20 (m, 1H), 7.15 (td, J = 4.3, 9.3 Hz, 1H), 7.04 (tt, J = 3.6, 8.2 Hz, 1H), 6.93 (s, 1H), 6.63 - 6.45 (m, 2H), 6.45 - 6.27 (m, 1H), 5.88 - 5.68 (m, 2H), 4.16 (dt, J = 4.0, 8.1 Hz, 1H), 3.99 (q, J = 8.0 Hz, 1H), 3.89 (s, 3H), 3.29 - 3.21 (m, 1H), 3.20 - 3.09 (m, 6H), 3.05 - 2.92 (m, 3H), 2.92 - 2.74 (m, 4H), 2.67 - 2.57 (m, 1H), 2.33 - 2.21 (m, 1H), 2.11 - 2.02 (m, 2H), 1.89 - 1.73 (m, 2H), 1.32 (s, 3H), 1.30 (s, 3H) : 663.4[M+H]+	1.19
304		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, Methanol-d4) δ 8.17 (s, 1H), 8.06 (s, 1H), 7.17 - 7.08 (m, 1H), 7.08 - 6.98 (m, 1H), 6.98 - 6.87 (m, 1H), 6.81 (s, 1H), 6.49 - 6.34 (m, 2H), 6.31 - 6.20 (m, 1H), 5.73 - 5.60 (m, 2H), 4.04 (td, J = 4.2, 7.9 Hz, 1H), 3.88 (q, J = 8.0 Hz, 1H), 3.78 (s, 3H), 3.29 - 3.22 (m, 2H), 3.15 - 3.08 (m, 1H), 3.08 - 2.99 (m, 3H), 2.97 - 2.84 (m, 2H), 2.83 - 2.65 (m, 4H), 2.47 (s, 6H), 2.22 - 2.10 (m, 2H), 2.07 - 1.98 (m, 2H), 1.76 - 1.63 (m, 2H) : 649.3[M+H]+	1.11
305		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-(1,4'-bipiperidine)-1'-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, Methanol-d4) δ 8.18 (s, 1H), 8.06 (s, 1H), 7.18 - 7.08 (m, 1H), 7.08 - 6.98 (m, 1H), 6.98 - 6.87 (m, 1H), 6.80 (s, 1H), 6.52 - 6.35 (m, 2H), 6.28 - 6.20 (m, 1H), 5.75 - 5.59 (m, 2H), 4.08 - 3.98 (m, 1H), 3.87 (q, J = 8.0 Hz, 1H), 3.77 (s, 3H), 3.12 - 3.01 (m, 5H), 2.98 - 2.92 (m, 1H), 2.91 - 2.80 (m, 1H), 2.80 - 2.63 (m, 7H), 2.48 - 2.37 (m, 2H), 2.21 - 2.10 (m, 1H), 2.07 - 1.99 (m, 2H), 1.99 - 1.90 (m, 2H), 1.80 - 1.59 (m, 5H) ; 649.3[M+H]+	1.11
306		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.85 (s, 1H), 8.25 (s, 1H), 8.02 (s, 1H), 7.46 - 7.37 (m, 1H), 7.20 - 7.09 (m, 3H), 6.96 (s, 1H), 6.23 (dd, J = 17.0, 2.2 Hz, 1H), 6.05 (s, 1H), 5.71 (dd, J = 10.1, 2.2 Hz, 1H), 4.46 (t, J = 8.0 Hz, 1H), 3.80 (s, 3H), 3.32 (s, 4H), 2.94 - 2.86 (m, 1H), 2.73 (d, J = 4.8 Hz, 6H), 2.61 (s, 3H), 2.44 (s, 1H), 1.53 (d, J = 72.7 Hz, 2H) : 554.5[M+H]+	1.16

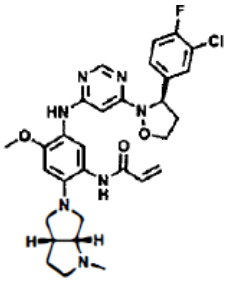
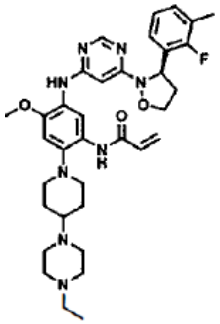
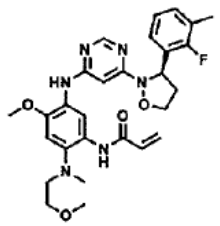
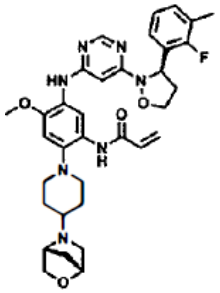
[523]

307		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.73 (s, 1H), 9.14 (s, 1H), 8.25 (s, 1H), 8.02 (s, 1H), 7.42 (ddd, J = 14.7, 8.4, 6.4 Hz, 1H), 7.12 (t, J = 8.4 Hz, 2H), 6.88 (s, 1H), 6.76 (dd, J = 17.0, 10.3 Hz, 1H), 6.24 (dd, J = 17.0, 2.0 Hz, 1H), 6.02 (s, 1H), 5.76 (dd, J = 10.1, 2.0 Hz, 1H), 5.68 (t, J = 7.7 Hz, 1H), 4.44 (t, J = 7.5 Hz, 1H), 3.80 (s, 3H), 3.50 (d, J = 11.6 Hz, 2H), 3.35 (d, J = 10.8 Hz, 2H), 3.21 - 3.14 (m, 4H), 2.93 - 2.86 (m, 1H), 2.83 (d, J = 4.5 Hz, 3H), 2.47 - 2.42 (m, 1H), 1.64 - 1.40 (m, 2H) ; 552.5[M+H]$^+$	1.11
308		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.03 (s, 1H), 9.17 (s, 1H), 8.27 (s, 1H), 7.88 (s, 1H), 7.46 - 7.37 (m, 1H), 7.12 (t, J = 8.5 Hz, 2H), 6.90 (s, 1H), 6.72 (dd, J = 16.9, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 5.96 (s, 1H), 5.76 (dd, J = 10.1, 2.0 Hz, 1H), 5.68 (t, 2H), 4.49 - 4.45 (m, 1H), 4.05 - 4.02 (m, 1H), 3.79 (s, 3H), 3.30 (d, J = 14.0 Hz, 1H), 3.21 (d, J = 11.5 Hz, 2H), 2.96 - 2.88 (m, 1H), 2.80 (d, J = 11.6 Hz, 2H), 2.75 (d, J = 4.9 Hz, 6H), 2.12 (d, J = 11.8 Hz, 2H), 2.05 - 1.95 (m, 2H) ; 580.5[M+H]$^+$	1.14
309		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.41 (s, 1H), 9.29 (s, 1H), 8.31 (s, 1H), 7.80 (s, 1H), 7.43 (ddd, J = 8.5, 6.4, 2.0 Hz, 1H), 7.14 (d, J = 8.5 Hz, 2H), 6.95 (s, 1H), 6.73 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 5.96 (s, 1H), 5.77 (dd, J = 10.2, 1.9 Hz, 1H), 5.72 - 5.67 (m, 1H), 4.52 - 4.45 (m, 1H), 4.23 - 4.12 (m, 2H), 4.11 - 4.02 (m, 1H), 3.80 (s, 3H), 3.49 - 3.43 (m, 2H), 3.38 (q, J = 7.0 Hz, 2H), 3.26 (d, J = 11.4 Hz, 2H), 2.98 - 2.90 (m, 1H), 2.83 (d, J = 11.6 Hz, 2H), 2.75 - 2.64 (m, 2H), 2.26 (d, J = 11.3 Hz, 2H), 2.20 - 2.09 (m, 2H), 1.17 (d, J = 6.3 Hz, 6H).; 650.3 [M+H]$^+$	1.23
310		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.37 (s, 1H), 9.31 (s, 1H), 8.31 (s, 1H), 7.80 (s, 1H), 7.46 - 7.41 (m, 1H), 7.13 (t, J = 8.5 Hz, 2H), 6.93 (s, 1H), 6.74 (dd, J = 17.0, 10.2 Hz, 1H), 6.27 - 6.23 (m, 1H), 5.96 (s, 1H), 5.78 - 5.67 (m, 2H), 4.53 - 4.46 (m, 2H), 4.09 - 4.00 (m, 2H), 3.79 (s, 3H), 3.73 (d, J = 12.9 Hz, 1H), 3.48 (d, J = 8.8 Hz, 2H), 3.39 - 3.36 (m, 3H), 3.05 - 2.93 (m, 2H), 2.83 (s, 2H), 2.51 (q, J = 1.9 Hz, 3H), 2.48 - 2.43 (m, 1H), 2.20 (s, 2H), 2.12 (s, 1H), 2.07 (s, 3H).; 663.6 [M+H]$^+$	1.17
311		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.29 (s, 1H), 9.26 (s, 1H), 8.29 (s, 1H), 7.86 (s, 1H), 7.43 (ddd, J = 8.4, 6.4, 2.0 Hz, 1H), 7.13 (t, J = 8.5 Hz, 2H), 6.91 (s, 1H), 6.76 (dd, J = 16.9, 10.3 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 5.97 (s, 1H), 5.80 - 5.74 (m, 1H), 5.69 (s, 1H), 4.52 - 4.48 (m, 1H), 4.08 - 4.01 (m, 1H), 3.79 (s, 7H), 3.69 (s, 4H), 3.60 (t, J = 6.7 Hz, 1H), 3.53 - 3.45 (m, 1H), 3.41 - 3.35 (m, 1H), 3.24 (d, J = 11.1 Hz, 2H), 2.97 - 2.90 (m, 1H), 2.82 (t, J = 11.4 Hz, 2H), 2.46 (d, J = 8.8 Hz, 1H), 2.15 (d, J = 15.1 Hz, 4H), 1.32 (d, J = 6.6 Hz, 6H).; 663.3 [M+H]$^+$	1.14

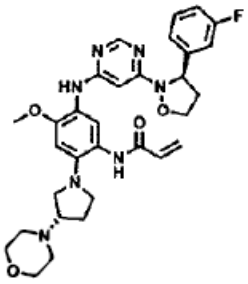
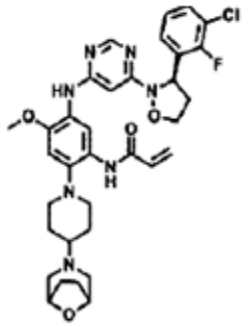
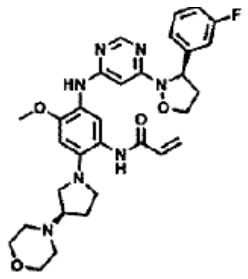
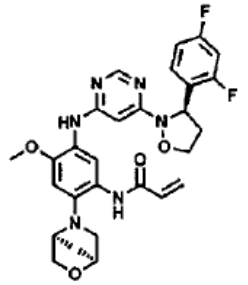
[524]

312		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	649.6 $[M+H]^+$	1.10
313		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.31 (s, 1H), 9.25 (s, 1H), 8.30 (s, 1H), 7.84 (s, 1H), 7.43 (ddd, J = 8.4, 6.4, 2.0 Hz, 1H), 7.13 (t, J = 8.5 Hz, 2H), 6.92 (s, 1H), 6.77 - 6.69 (m, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 5.98 (d, J = 20.2 Hz, 1H), 5.77 (dd, J = 10.1, 1.9 Hz, 1H), 5.70 (s, 1H), 4.51 - 4.46 (m, 1H), 4.10 - 4.02 (m, 1H), 3.84 (d, J = 12.7 Hz, 2H), 3.79 (s, 3H), 3.76 (s, 1H), 3.66 (d, J = 8.0 Hz, 2H), 3.50 - 3.36 (m, 3H), 3.29 - 3.22 (m, 2H), 2.93 (d, J = 3.2 Hz, 1H), 2.84 (s, 3H), 2.80 (d, J = 12.4 Hz, 1H), 2.45 (d, J = 3.7 Hz, 1H), 2.26 - 2.06 (m, 4H), 1.62 (dd, J = 5.1, 2.7 Hz, 1H), 1.42 (d, J = 6.1 Hz, 3H).: 649.3 $[M+H]^+$	1.13
314		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	649.5 $[M+H]^+$	1.10
315		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	649.5 $[M+H]^+$	1.04
316		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.05 (d, J = 1.2 Hz, 1H), 7.44 (dd, J = 7.1, 2.0 Hz, 1H), 7.31 - 7.25 (m, 1H), 7.10 (t, J = 8.9 Hz, 1H), 6.74 (s, 1H), 6.49 (dd, J = 17.0, 10.2 Hz, 1H), 6.28 (dd, J = 17.8, 2.4 Hz, 1H), 5.68 (dd, J = 10.3, 1.5 Hz, 1H), 5.41 (dd, J = 8.5, 4.7 Hz, 1H), 4.03 (td, J = 7.8, 4.2 Hz, 1H), 3.84 (dd, J = 15.9, 7.9 Hz, 1H), 3.75 (s, 3H), 3.21 (dt, J = 3.2, 1.6 Hz, 4H), 3.01 (dt, J = 11.6, 5.9 Hz, 1H), 2.92 (t, J = 8.0 Hz, 12H), 2.84 - 2.63 (m, 4H), 2.39 (s, 2H), 2.31 - 2.05 (m, 3H) ; 594.1 $[M+H]^+$	1.30

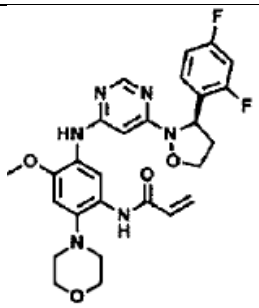
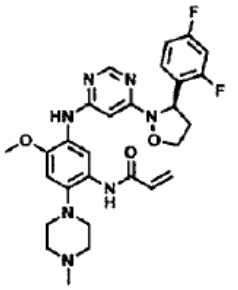
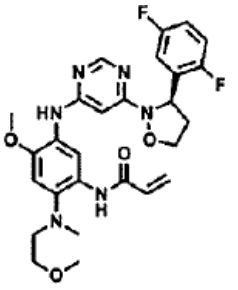
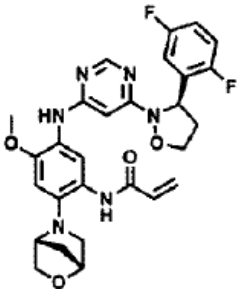
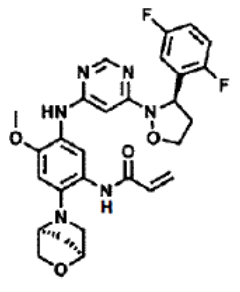
[525]

317		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.15 (d, J = 3.7 Hz, 1H), 7.56 - 7.47 (m, 1H), 7.41 - 7.32 (m, 1H), 7.20 (td, J = 8.9, 2.3 Hz, 1H), 6.84 (s, 1H), 6.59 (dd, J = 17.0, 10.2 Hz, 1H), 6.42 - 6.38 (m, 1H), 5.77 (dd, J = 10.3, 1.4 Hz, 1H), 5.51 (dd, J = 8.4, 4.8 Hz, 1H), 4.12 (td, J = 7.9, 4.2 Hz, 1H), 3.99 - 3.91 (m, 1H), 3.84 (s, 3H), 3.33 - 3.27 (m, 3H), 3.14 - 3.06 (m, 1H), 3.01 (dd, J = 11.4, 7.1 Hz, 2H), 2.93 - 2.72 (m, 4H), 2.48 (s, 3H), 2.40 - 2.14 (m, 3H), 1.68 (ddd, J = 10.5, 12.2, 7.3 Hz, 1H) ; 504.4 [M+H]$^+$	1.30
318		N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.28 (s, 1H), 8.33 (s, 1H), 7.89 (s, 1H), 7.23 (td, J = 7.5, 1.9 Hz, 1H), 7.15 (t, J = 7.4 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 6.93 (s, 1H), 6.74 (dtd, J = 21.5, 10.7, 4.0 Hz, 1H), 6.26 (dd, J = 17.0, 2.0 Hz, 1H), 6.12 (s, 1H), 5.81 - 5.73 (m, 1H), 5.69 (dd, J = 8.6, 5.5 Hz, 1H), 4.32 (td, J = 7.6, 4.3 Hz, 2H), 4.09 (q, J = 7.7 Hz, 2H), 3.82 (s, 4H), 3.70 (q, J = 12.8, 10.0 Hz, 3H), 3.64 - 3.56 (m, 2H), 3.30 - 3.14 (m, 5H), 2.83 (t, J = 11.2 Hz, 2H), 2.71 (d, J = 4.8 Hz, 1H), 2.29 - 2.05 (m, 8H), 1.36 - 1.24 (m, 4H).; 645.5 [M+H]$^+$	1.16
319		N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 9.12 (s, 1H), 8.89 (s, 1H), 8.28 (s, 1H), 7.32 (s, 1H), 7.08 (t, J = 7.3 Hz, 1H), 6.99 (t, J = 7.6 Hz, 1H), 6.78 (s, 1H), 6.60 (s, 1H), 6.40 (dd, J = 17.0, 1.9 Hz, 1H), 6.30 (dd, J = 16.9, 9.9 Hz, 1H), 5.89 (dd, J = 8.8, 4.5 Hz, 1H), 5.69 (dd, J = 9.9, 1.9 Hz, 1H), 4.18 - 4.04 (m, 2H), 3.84 (s, 3H), 3.47 (t, J = 4.9 Hz, 2H), 3.43 (s, 3H), 2.98 (h, J = 4.1 Hz, 2H), 2.85 (dtd, J = 12.7, 8.0, 4.7 Hz, 1H), 2.76 (s, 3H), 2.38 - 2.23 (m, 5H).; 537.3 [M+H]$^+$	1.58
320		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.32 (s, 1H), 8.33 (s, 1H), 7.83 (d, J = 13.0 Hz, 1H), 7.23 (td, J = 7.5, 1.9 Hz, 1H), 7.15 (t, J = 7.3 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 6.95 (d, J = 11.7 Hz, 1H), 6.65 (ddd, J = 25.1, 17.0, 10.2 Hz, 1H), 6.25 (dt, J = 17.1, 2.1 Hz, 1H), 6.12 (s, 1H), 5.77 (dd, J = 10.0, 1.9 Hz, 1H), 5.68 (dd, J = 8.6, 5.5 Hz, 1H), 4.74 - 4.68 (m, 1H), 4.65 (d, J = 2.5 Hz, 1H), 4.57 (s, 1H), 4.51 (d, J = 9.1 Hz, 1H), 4.32 (td, J = 7.6, 4.3 Hz, 1H), 4.21 (d, J = 10.2 Hz, 1H), 4.09 (q, J = 7.7 Hz, 1H), 3.83 (d, J = 2.6 Hz, 3H), 3.69 (td, J = 7.2, 6.7, 3.7 Hz, 1H), 3.60 (pt, J = 6.6, 3.5 Hz, 1H), 3.49 - 3.42 (m, 1H), 3.29 (dd, J = 30.1, 12.5 Hz, 2H), 3.11 (tt, J = 7.3, 3.6 Hz, 1H), 2.97 (ddd, J = 12.4, 7.7, 4.4 Hz, 1H), 2.87 (p, J = 11.5, 9.2 Hz, 1H), 2.35 (d, J = 10.8 Hz, 1H), 2.26 (d, J = 2.0 Hz, 4H), 2.08 (t, J = 8.8 Hz, 3H), 1.33 (s, 2H).; 630.4 [M+H]$^+$	1.21

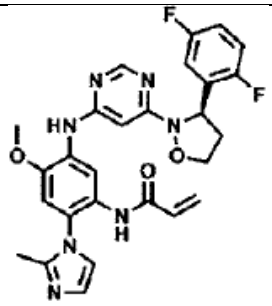
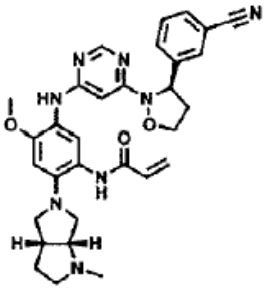
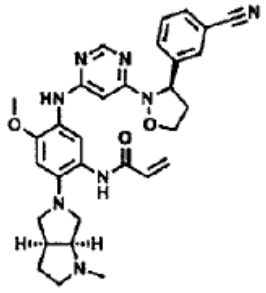
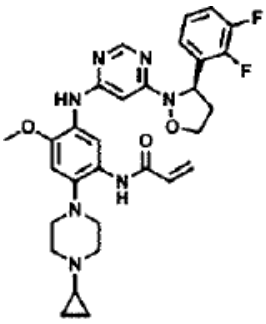
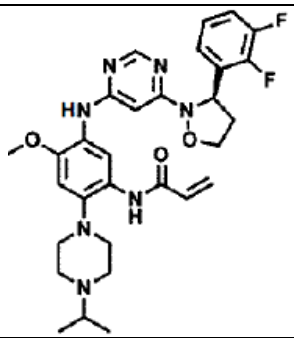
[526]

321		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-$d6$) δ 9.43 - 9.25 (m, 1H), 8.49 (s, 1H), 8.13 (s, 1H), 7.39 (td, J = 8.0, 6.1 Hz, 2H), 7.28 - 7.14 (m, 2H), 7.08 (td, J = 8.6, 2.7 Hz, 1H), 6.49 (s, 1H), 6.26 - 6.14 (m, 2H), 5.68 (dd, J = 10.1, 2.1 Hz, 1H), 5.54 (dd, J = 8.7, 5.0 Hz, 1H), 4.12 (td, J = 7.9, 3.8 Hz, 1H), 3.80 (s, 5H), 3.59 (s, 3H), 3.17 (d, J = 36.8 Hz, 3H), 2.75 (dtd, J = 12.0, 8.0, 3.8 Hz, 3H), 2.38 (s, 2H), 2.29 - 2.15 (m, 2H), 2.10 (s, 1H), 1.72 (s, 1H), 1.26 (td, J = 7.2, 4.8 Hz, 2H) ; 590.4 $[M+H]^+$	1.11
322		N-(2-(4-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-$d6$) δ 10.00 (s, 1H), 9.02 (s, 1H), 8.23 (s, 1H), 8.05 (s, 1H), 7.53 (t, J = 7.4 Hz, 1H), 7.40 (t, J = 7.3 Hz, 1H), 7.23 (t, J = 7.9 Hz, 1H), 6.88 (s, 1H), 6.59 (dd, J = 17.1, 10.2 Hz, 1H), 6.24 (d, J = 17.4 Hz, 2H), 5.81 - 5.65 (m, 2H), 4.51 (s, 2H), 4.29 - 4.20 (m, 2H), 3.81 (s, 3H), 3.40 - 3.33 (m, 3H), 3.28 (dd, J = 10.8, 5.7 Hz, 2H), 3.20 - 3.12 (m, 3H), 2.88 (s, 1H), 2.73 (t, J = 11.8 Hz, 2H), 2.21 (d, J = 7.9 Hz, 3H), 2.12 (s, 2H), 2.06 (d, J = 11.6 Hz, 1H), 1.95 (s, 2H) ; 664.5 $[M+H]^+$	1.24
323		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-$d6$) δ 9.34 (s, 1H), 8.48 (s, 1H), 8.12 (s, 1H), 7.45 - 7.33 (m, 2H), 7.25 (d, J = 7.8 Hz, 1H), 7.22 - 7.16 (m, 1H), 7.08 (td, J = 8.6, 2.6 Hz, 1H), 6.50 (d, J = 3.0 Hz, 1H), 6.48 - 6.42 (m, 1H), 6.20 (d, J = 2.2 Hz, 2H), 5.68 (dd, J = 10.2, 2.1 Hz, 1H), 5.54 (dd, J = 8.7, 4.9 Hz, 1H), 4.12 (td, J = 7.9, 3.9 Hz, 1H), 3.80 (s, 4H), 3.59 (t, J = 4.7 Hz, 4H), 3.38 (dt, J = 9.5, 4.8 Hz, 1H), 3.28 (t, J = 8.1 Hz, 1H), 3.24 - 3.15 (m, 2H), 2.84 - 2.69 (m, 2H), 2.47 - 2.42 (m, 2H), 2.38 (q, J = 5.7, 5.1 Hz, 2H), 2.23 (dtd, J = 12.7, 8.0, 4.9 Hz, 1H), 2.09 (d, J = 7.4 Hz, 1H), 1.77 - 1.66 (m, 1H) ; 590.5 $[M+H]^+$	1.10
324		N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-d) δ 8.68 (s, 1H), 8.36 (s, 1H), 7.95 (s, 1H), 7.56 (d, J = 7.0 Hz, 1H), 6.90 (s, 1H), 6.82 (m, 3H), 6.69 (d, J = 15.8 Hz, 1H), 6.39 (d, J = 16.7 Hz, 1H), 6.32 - 6.23 (m, 1H), 5.85 (s, 1H), 5.75 (d, J = 10.0 Hz, 1H), 4.65 (s, 1H), 4.11 (d, J = 4.5 Hz, 1H), 4.06 (d, J = 7.8 Hz, 1H), 3.86 (s, 3H), 3.75 (d, J = 7.5 Hz, 1H), 3.43 (d, J = 10.2 Hz, 1H), 3.24 (d, J = 10.1 Hz, 1H), 2.79 (d, J = 12.3 Hz, 1H), 2.35 - 2.22 (m, 1H), 2.17 (s, 2H), 2.08 (d, J = 10.1 Hz, 1H), 1.99 (d, J = 9.6 Hz, 1H).; 551.4 $[M+H]^+$	1.36

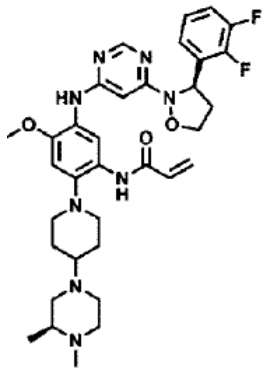
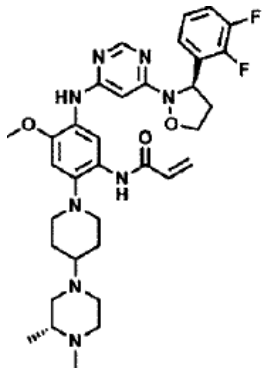
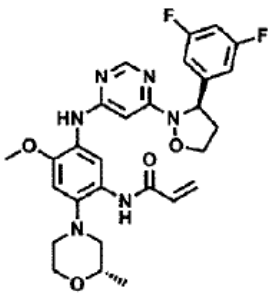
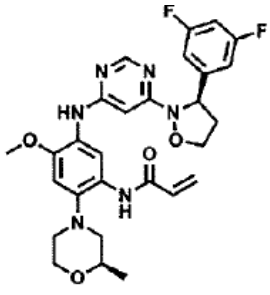
[527]

325		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.03 (s, 1H), 8.51 (s, 1H), 8.38 (d, *J* = 1.0 Hz, 1H), 7.56 (dt, *J* = 14.6, 7.1 Hz, 1H), 6.96 (s, 1H), 6.88 - 6.80 (m, 2H), 6.77 (d, *J* = 7.7 Hz, 2H), 6.42 - 6.34 (m, 1H), 6.27 (dd, *J* = 17.0, 10.0 Hz, 1H), 5.88 (dd, *J* = 8.7, 4.4 Hz, 1H), 5.76 (dd, *J* = 9.9, 1.5 Hz, 1H), 4.16 - 4.04 (m, 2H), 3.91 - 3.87 (m, 6H), 2.80 (q, *J* = 3.8 Hz, 4H), 2.81 (ddt, *J* = 12.7, 8.2, 4.2 Hz, 1H), 2.33 - 2.23 (m, 1H), 2.17 (s, 1H).: 530.4[M+H]	1.50
326		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.01 (s, 1H), 8.53 (s, 1H), 8.37 (s, 1H), 7.56 (dt, *J* = 15.2, 7.4 Hz, 1H), 6.94 (s, 1H), 6.87 - 6.78 (m, 3H), 6.75 (s, 1H), 6.43 - 6.34 (m, 1H), 6.27 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.88 (dd, *J* = 8.6, 4.4 Hz, 1H), 5.75 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.14 - 4.06 (m, 2H), 3.84 (s, 3H), 2.92 (s, 3H), 2.84 - 2.76 (m, 1H), 2.40 (s, 3H), 2.31 - 2.25 (m, 1H), 2.23 (s, 1H), 2.17 (s, 1H), 2.02 (s, 1H), 1.26 (s, 1H), 1.19 (t, *J* = 7.3 Hz, 1H).: 552.4[M+H]	1.21
327		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.99 (s, 1H), 8.37 (s, 1H), 7.36 - 7.28 (m, 1H), 7.04 - 6.96 (m, 2H), 6.92 - 6.85 (m, 1H), 6.79 (s, 1H), 6.78 (s, 1H), 6.35 (qd, *J* = 16.9, 5.8 Hz, 2H), 5.90 (dd, *J* = 8.7, 4.3 Hz, 1H), 5.60 (dd, *J* = 9.8, 1.9 Hz, 1H), 4.15 - 4.06 (m, 2H), 3.85 (s, 3H), 3.47 (t, *J* = 4.9 Hz, 2H), 3.43 (s, 3H), 3.02 - 2.93 (m, 2H), 2.88 - 2.78 (m, 1H), 2.76 (s, 3H), 2.35 - 2.24 (m, 1H): 541.5[M+H]$^+$	1.63
328		N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.33 (s, 1H), 7.94 (s, 1H), 7.35 - 7.28 (m, 1H), 7.14 (s, 1H), 7.00 (td, *J* = 9.2, 4.3 Hz, 1H), 6.93 - 6.87 (m, 1H), 6.73 (s, 1H), 6.71 (s, 1H), 6.41 - 6.24 (m, 2H), 5.80 (dd, *J* = 8.3, 4.0 Hz, 1H), 5.78 - 5.73 (m, 1H), 4.65 (s, 1H), 4.19 - 4.03 (m, 4H), 3.91 - 3.88 (m, 1H), 3.86 (s, 3H), 3.80 - 3.74 (m, 2H), 3.48 - 3.43 (m, 1H), 3.23 - 3.18 (m, 1H), 2.87 - 2.78 (m, 1H), 2.34 - 2.24 (m, 1H): 551.4[M+H]$^+$	1.28
329		N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.35 (s, 1H), 7.95 (s, 1H), 7.35 - 7.28 (m, 1H), 7.07 - 6.96 (m, 2H), 6.93 - 6.86 (m, 1H), 6.71 (s, 1H), 6.67 (s, 1H), 6.42 - 6.23 (m, 2H), 5.80 (dd, *J* = 8.6, 4.3 Hz, 1H), 5.79 - 5.72 (m, 1H), 4.26 - 3.97 (m, 4H), 3.91 - 3.83 (m, 4H), 3.83 - 3.72 (m, 2H), 3.46 - 3.38 (m, 1H), 3.28 - 3.20 (m, 1H), 2.86 - 2.76 (m, 1H), 2.34 - 2.22 (m, 2H): 551.4[M+H]$^+$	1.28

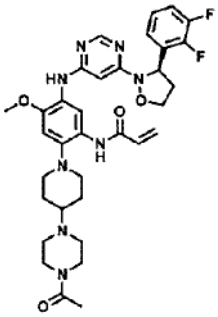
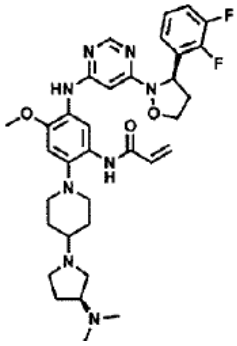
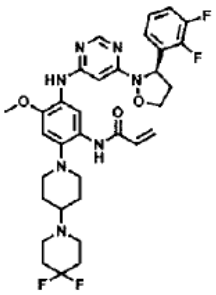
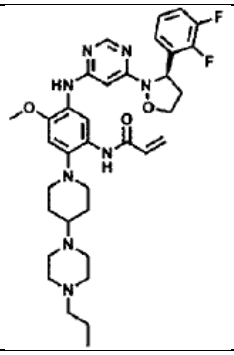
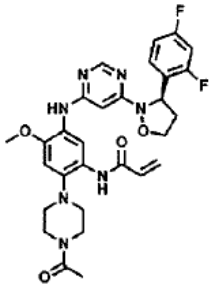
[528]

330		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(2-methyl-1H-imidazole-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.43 (s, 1H), 7.40 (s, 1H), 7.35 - 7.28 (m, 1H), 7.15 (s, 1H), 7.02 (td, *J* = 9.1, 4.3 Hz, 1H), 6.96 - 6.88 (m, 2H), 6.82 (s, 1H), 6.79 - 6.72 (m, 2H), 6.29 (d, *J* = 16.9 Hz, 1H), 6.06 (dd, *J* = 16.8, 10.3 Hz, 1H), 5.91 (dd, *J* = 8.5, 4.5 Hz, 1H), 5.74 - 5.68 (m, 1H), 4.18 (td, *J* = 7.9, 4.3 Hz, 1H), 4.06 (q, *J* = 8.0 Hz, 1H), 3.90 (s, 3H), 2.90 - 2.79 (m, 1H), 2.37 - 2.30 (m, 1H), 2.26 (s, 3H): 534.4[M+H]$^+$	1.26
331		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (s, 1H), 8.45 (s, 1H), 8.30 (s, 1H), 7.78 (s, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 6.68 - 6.50 (m, 2H), 6.56 - 6.42 (m, 2H), 5.77 - 5.64 (m, 2H), 4.16 (td, *J* = 8.0, 4.1 Hz, 1H), 4.04 (q, *J* = 8.1 Hz, 1H), 3.83 (s, 3H), 3.65 - 3.54 (m, 2H), 3.31 - 3.23 (m, 1H), 3.00 - 3.02 (m, 1H), 3.00 - 2.87 (m, 2H), 2.85 - 2.70 (m, 2H), 2.63 (s, 3H), 2.51 - 2.40 (m, 1H), 2.38 - 2.23 (m, 2H), 1.80 - 1.77 (m, 1H): 567.5[M+H]$^+$	1.03
332		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (s, 1H), 8.52 (s, 1H), 8.31 (s, 1H), 7.79 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.21 (s, 1H), 6.71 - 6.62 (m, 2H), 6.52 - 6.41 (m, 2H), 5.72 (dd, *J* = 7.8, 4.2 Hz, 2H), 4.16 (td, *J* = 8.0, 4.1 Hz, 1H), 4.07 (q, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.51 - 3.41 (m, 2H), 3.23 - 3.17 (m, 1H), 3.08 - 3.01 (m, 1H), 2.99 - 2.88 (m, 1H), 2.88 - 2.75 (m, 3H), 2.64 - 2.54 (m, 3H), 2.47 - 2.38 (m, 1H), 2.38 - 2.22 (m, 2H), 1.88 - 1.75 (m, 1H): 567.5[M+H]$^+$	1.04
333		N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.59 (s, 1H), 8.37 (s, 1H), 7.40 - 7.30 (m, 1H), 7.12 - 7.00 (m, 2H), 6.96 (s, 1H), 6.82 - 6.73 (m, 2H), 6.42 - 6.33 (m, 1H), 6.33 - 6.23 (m, 1H), 5.93 (dd, *J* = 8.9, 4.6 Hz, 1H), 5.75 (dd, *J* = 9.0, 1.7 Hz, 1H), 4.19 - 4.10 (m, 1H), 4.10 - 4.01 (m, 1H), 3.82 (s, 3H), 2.93 - 2.66 (m, 9H), 2.38 - 2.25 (m, 1H), 1.76 - 1.70 (m, 1H), 0.57 - 0.42 (m, 4H) : 578.4[M+H]$^+$	1.17
334		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.89 (s, 1H), 8.56 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.40 - 7.31 (m, 1H), 7.12 - 7.01 (m, 2H), 7.00 (s, 1H), 6.83 (s, 1H), 6.75 (s, 1H), 6.37 (dd, *J* = 16.8, 1.7 Hz, 1H), 6.27 (dd, *J* = 17.0, 9.9 Hz, 1H), 5.93 (dd, *J* = 8.8, 4.6 Hz, 1H), 5.75 (dd, *J* = 9.9, 1.7 Hz, 1H), 4.19 - 4.12 (m, 1H), 4.12 - 4.01 (m, 1H), 3.83 (s, 3H), 2.99 - 2.91 (m, 4H), 2.90 - 2.84 (m, 1H), 2.83 - 2.78 (m, 1H), 2.77 - 2.68 (m, 4H), 2.35 - 2.26 (m, 1H), 1.13 (d, *J* = 6.5 Hz, 6H) : 580.5[M+H]$^+$	1.21

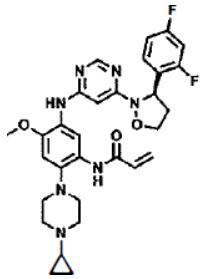
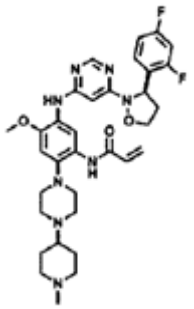
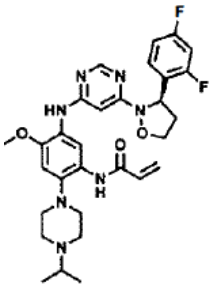
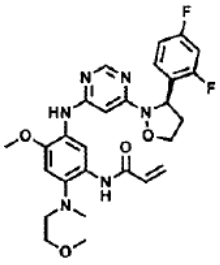
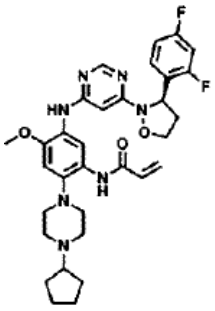
[529]

335		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.44 (s, 1H), 8.36 (d, J = 0.9 Hz, 1H), 7.40 - 7.31 (m, 1H), 7.12 - 6.98 (m, 2H), 6.93 (s, 1H), 6.75 (d, J = 2.4 Hz, 2H), 6.36 (dd, J = 17.0, 1.6 Hz, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.93 (dd, J = 8.8, 4.6 Hz, 1H), 5.74 (dd, J = 9.9, 1.6 Hz, 1H), 4.19 - 4.11 (m, 1H), 4.10 - 4.03 (m, 1H), 3.85 (s, 3H), 3.10 - 3.02 (m, 2H), 3.02 - 2.95 (m, 1H), 2.94 - 2.79 (m, 3H), 2.78 - 2.66 (m, 2H), 2.43 - 2.34 (m, 2H), 2.32 (s, 3H), 2.32 - 2.27 (m, 2H), 2.21 - 2.14 (m, 1H), 2.11 - 2.05 (m, 2H), 2.05 - 1.98 (m, 1H), 1.70 - 1.60 (m, 2H), 1.10 (d, J = 6.1 Hz, 3H) ; 649.5[M+H]$^+$	1.10
336		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.44 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.39 - 7.31 (m, 1H), 7.12 - 6.98 (m, 2H), 6.94 (s, 1H), 6.75 (d, J = 1.9 Hz, 2H), 6.36 (dd, J = 17.0, 1.6 Hz, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.93 (dd, J = 8.8, 4.5 Hz, 1H), 5.74 (dd, J = 9.9, 1.6 Hz, 1H), 4.19 - 4.10 (m, 1H), 4.10 - 4.01 (m, 1H), 3.85 (s, 3H), 3.10 - 3.02 (m, 2H), 3.02 - 2.95 (m, 1H), 2.95 - 2.81 (m, 3H), 2.78 - 2.65 (m, 2H), 2.45 - 2.35 (m, 2H), 2.33 (s, 3H), 2.32 - 2.27 (m, 2H), 2.24 - 2.13 (m, 1H), 2.12 - 1.99 (m, 3H), 1.72 - 1.61 (m, 2H), 1.11 (d, J = 6.2 Hz, 3H) ; 649.5[M+H]$^+$	1.09
337		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-2-methylmorpholino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.06 (s, 1H), 8.65 (s, 1H), 8.18 (d, J = 2.6 Hz, 2H), 7.13 (ddd, J = 8.2, 5.8, 3.2 Hz, 4H), 6.86 (s, 1H), 6.62 (dd, J = 17.0, 10.2 Hz, 1H), 6.37 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.72 (dd, J = 10.1, 2.0 Hz, 1H), 5.56 (dd, J = 8.7, 5.0 Hz, 1H), 4.13 (td, J = 7.9, 3.9 Hz, 1H), 3.87 - 3.74 (m, 9H), 2.87 - 2.70 (m, 4H), 1.78 (s, 2H), 1.11 (d, J = 6.2 Hz, 4H),: 553.3[M+H]$^+$	1.51
338		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-2-methylmorpholino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.07 (s, 1H), 8.71 (s, 1H), 8.18 (s, 1H), 7.13 (td, J = 7.7, 7.1, 3.1 Hz, 3H), 6.86 (s, 1H), 6.62 (dd, J = 17.0, 10.2 Hz, 1H), 6.36 (s, 1H), 6.21 (dd, J = 17.0, 2.0 Hz, 1H), 5.72 (dd, J = 10.2, 1.9 Hz, 1H), 5.56 (dd, J = 8.8, 5.0 Hz, 1H), 4.14 (td, J = 7.9, 3.9 Hz, 1H), 3.82 (d, J = 7.8 Hz, 8H), 2.93 - 2.71 (m, 4H), 2.30 - 2.19 (m, 1H), 1.91 (s, 1H), 1.10 (d, J = 6.2 Hz, 3H), : 553.4[M+H]$^+$	1.52

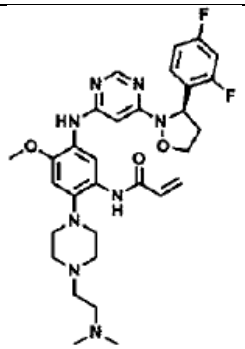
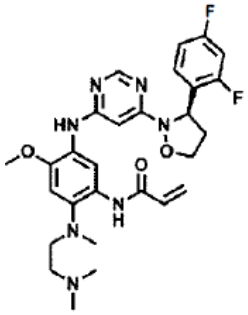
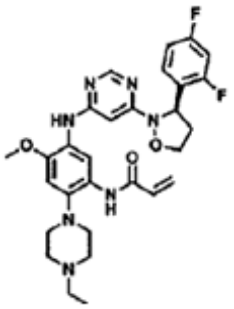
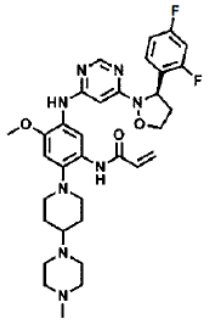
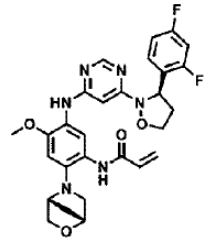
[530]

339		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.96 (s, 1H), 8.63 (s, 1H), 8.16 (s, 1H), 7.40 - 7.24 (m, 2H), 7.20 (td, J = 8.1, 4.6 Hz, 1H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.21 (dd, J = 17.0, 2.0 Hz, 1H), 5.80 - 5.68 (m, 2H), 3.85 (q, J = 8.0 Hz, 1H), 3.79 (s, 3H), 3.06 (d, J = 11.3 Hz, 3H), 2.88 - 2.75 (m, 1H), 2.72 - 2.61 (m, 2H), 2.41 - 2.29 (m, 2H), 2.27 - 2.12 (m, 2H), 1.99 (s, 4H), 1.88 - 1.69 (m, 5H), 1.67 (s, 4H), 1.24 (s, 5H), 0.89 - 0.79 (m, 1H).; 663.5[M+H]$^+$	1.21
340		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.63 (s, 1H), 8.16 (s, 1H), 7.30 - 7.24 (m, 3H), 7.20 (td, J = 8.0, 4.7 Hz, 2H), 6.82 (s, 1H), 6.64 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.73 (s, 1H), 3.84 (dd, J = 9.0, 7.2 Hz, 3H), 3.80 (s, 5H), 3.10 (d, J = 11.9 Hz, 2H), 3.01 (d, J = 11.4 Hz, 5H), 2.86 - 2.75 (m, 4H), 2.73 - 2.58 (m, 6H), 2.35 - 2.26 (m, 2H), 2.25 - 2.15 (m, 2H), 1.96 - 1.80 (m, 5H), 1.72 - 1.52 (m, 5H), 1.24 (s, 2H).; 649.5[M+H]$^+$	1.10
341		N-(2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.00 (s, 1H), 8.67 (s, 1H), 8.25 - 8.09 (m, 2H), 7.42 - 7.26 (m, 2H), 7.26 - 7.11 (m, 1H), 6.83 (s, 1H), 6.62 (dd, J = 17.0, 10.2 Hz, 1H), 6.39 (s, 1H), 6.23 (dd, J = 16.9, 1.9 Hz, 1H), 5.75 (s, 1H), 3.87 (t, J = 8.1 Hz, 1H), 3.81 (s, 3H), 3.37 (s, 8H), 3.14 (d, J = 10.2 Hz, 3H), 2.88 - 2.65 (m, 4H), 2.27 - 2.16 (m, 2H), 2.08 (d, J = 7.8 Hz, 2H), 1.91 (s, 7H).; 656.5[M+H]$^+$	1.29
342		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.63 (s, 1H), 8.16 (s, 1H), 7.30 - 7.25 (m, 3H), 7.20 (qd, J = 7.7, 6.7, 3.0 Hz, 2H), 6.82 (s, 1H), 6.65 (dd, J = 16.6, 10.1 Hz, 1H), 6.35 (s, 1H), 6.20 (dd, J = 16.9, 2.0 Hz, 1H), 5.77 - 5.71 (m, 2H), 4.16 (dt, J = 7.9, 4.0 Hz, 1H), 3.79 (s, 3H), 3.05 (d, J = 10.8 Hz, 4H), 2.97 (td, J = 7.1, 5.7 Hz, 2H), 2.88 - 2.75 (m, 3H), 2.71 - 2.61 (m, 3H), 2.18 (dt, J = 14.4, 7.3 Hz, 8H), 2.09 (s, 2H), 1.84 (d, J = 12.0 Hz, 3H), 1.69 (d, J = 11.4 Hz, 2H), 1.23 (s, 3H).; 663.6[M+H]$^+$	1.19
343		N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.95 (s, 1H), 8.44 (s, 1H), 8.38 (s, 1H), 7.56 (d, J = 6.7 Hz, 1H), 6.98 (s, 1H), 6.82 (s, 2H), 6.74 (d, J = 14.8 Hz, 2H), 6.38 (d, J = 16.6 Hz, 1H), 6.31 - 6.22 (m, 1H), 5.87 (s, 1H), 5.76 (d, J = 11.1 Hz, 1H), 4.16 - 4.03 (m, 2H), 3.85 (s, 3H), 3.80 (s, 2H), 3.65 (s, 2H), 2.89 (s, 4H), 2.80 (d, J = 4.4 Hz, 1H), 2.28 (d, J = 16.7 Hz, 1H), 2.17 (s, 3H).; 580.5 [M+H]$^+$	1.40

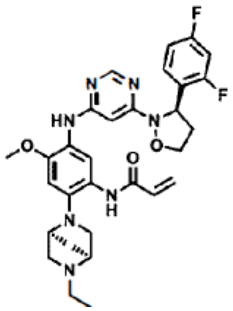
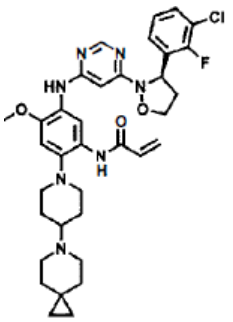
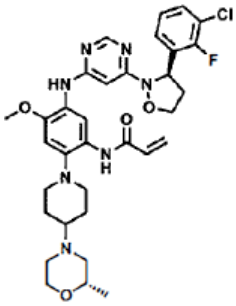
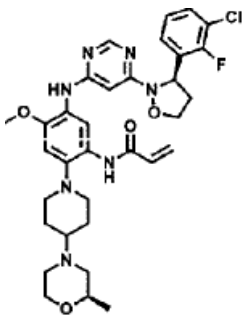
[531]

344		N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.91 (s, 1H), 8.59 (s, 1H), 8.37 (s, 1H), 7.57 (d, *J* = 6.7 Hz, 1H), 6.94 (s, 1H), 6.82 (d, *J* = 17.0 Hz, 3H), 6.75 (s, 1H), 6.37 (d, *J* = 16.9 Hz, 1H), 6.28 (dd, *J* = 17.0, 9.8 Hz, 1H), 5.88 (s, 1H), 5.75 (d, *J* = 9.8 Hz, 1H), 4.11 (d, *J* = 16.8 Hz, 2H), 3.82 (s, 3H), 2.88 (s, 4H), 2.82 (s, 2H), 2.29 (m, 2H), 1.74 (m, 2H), 0.96 (dd, 1H), 0.52 (d, *J* = 6.5 Hz, 2H), 0.47 (d, *J* = 3.4 Hz, 2H).; 578.4 $[M+H]^+$	1.21
345		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.89 (s, 1H), 8.55 (s, 1H), 8.36 (s, 1H), 7.56 (d, *J* = 6.9 Hz, 1H), 7.02 (s, 1H), 6.78 (d, *J* = 20.1 Hz, 4H), 6.39 - 6.22 (m, 2H), 5.88 (m, 1H), 5.74 (d, *J* = 10.6 Hz, 1H), 4.12 (s, 2H), 3.83 (s, 3H), 2.92 (s, 6H), 2.75 (s, 5H), 2.29 (s, 5H), 1.99 (t, 2H), 1.88 (d, 2H), 1.65 (m, 2H).; 635.5 $[M+H]^+$	1.06
346		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.91 (s, 1H), 8.58 (s, 1H), 8.37 (s, 1H), 7.57 (d, *J* = 6.6 Hz, 1H), 6.94 (s, 1H), 6.88 - 6.74 (m, 4H), 6.37 (d, *J* = 16.5 Hz, 1H), 6.27 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.88 (m, 1H), 5.75 (d, *J* = 9.9 Hz, 1H), 4.11 (d, *J* = 16.8 Hz, 2H), 3.83 (s, 3H), 2.93 (s, 4H), 2.72 (s, 6H), 2.25 (s, 1H), 1.59 (s, 6H).; 580.5 $[M+H]^+$	1.24
347		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 9.13 (s, 1H), 8.99 (s, 1H), 8.37 (s, 1H), 7.57 (d, *J* = 6.7 Hz, 1H), 6.94 (s, 1H), 6.81 (m, *J* = 25.7 Hz, 4H), 6.40 (d, *J* = 18.7 Hz, 1H), 6.32 (d, *J* = 9.8 Hz, 1H), 5.86 (m, 1H), 5.69 (d, *J* = 11.7 Hz, 1H), 4.11 (t, *J* = 7.8 Hz, 2H), 3.85 (s, 3H), 3.47 (d, *J* = 4.9 Hz, 2H), 3.43 (s, 3H), 2.97 (m, 2H), 2.79 (s, 1H), 2.76 (s, 3H), 2.28 (s, 1H).; 541.4 $[M+H]^+$	1.55
348		N-(2-(4-cyclopentylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.91 (s, 1H), 8.59 (s, 1H), 8.37 (s, 1H), 7.57 (d, *J* = 6.7 Hz, 1H), 6.94 (s, 1H), 6.83 (m, 3H), 6.75 (s, 1H), 6.36 (d, *J* = 16.1 Hz, 1H), 6.20 (m, 1H), 5.86 (m, 1H), 5.75 (d, *J* = 10.0 Hz, 1H), 4.16 - 4.04 (m, 2H), 3.82 (s, 3H), 2.94 (s, 4H), 2.81 (d, *J* = 8.0 Hz, 2H), 2.71 (s, 2H), 2.62 - 2.58 (m, 4H), 2.27 (m, 1H), 1.92 (m, 2H), 1.74 (m, 2H), 1.52 - 1.40 (m, 2H).; 606.5 $[M+H]^+$	1.25

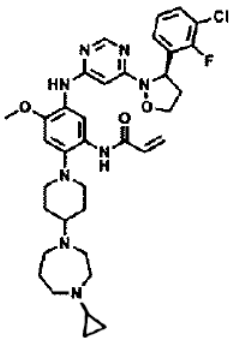
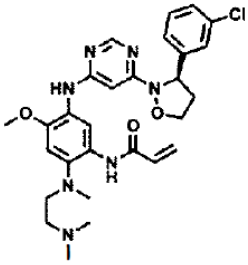
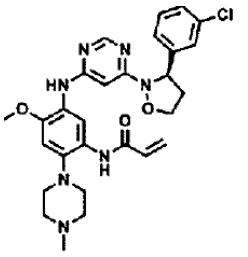
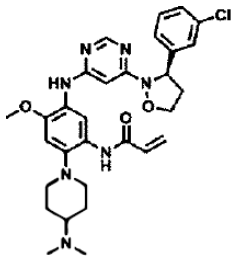
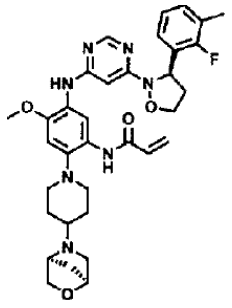
[532]

349		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.90 (s, 1H), 8.54 (s, 1H), 8.37 (s, 1H), 7.57 (m, 1H), 6.94 (s, 1H), 6.82 (m, 3H), 6.75 (s, 1H), 6.36 (d, J = 18.1 Hz, 1H), 6.30 - 6.21 (m, 1H), 5.89 (m, 1H), 5.75 (d, J = 11.3 Hz, 1H), 4.10 (d, J = 13.1 Hz, 2H), 3.84 (s, 3H), 2.94 (s, 4H), 2.82 (m, 3H), 2.66 (s, 6H), 2.37 (s, 5H), 2.27 (dt, J = 8.3, 4.4 Hz, 2H).; 609.5 [M+H]$^+$	1.14
350		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 10.11 (s, 1H), 8.96 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.57 (td, J = 8.6, 6.5 Hz, 1H), 6.96 (s, 1H), 6.87 - 6.82 (m, 1H), 6.80 (d, J = 1.3 Hz, 3H), 6.40 (dd, J = 17.0, 1.9 Hz, 1H), 6.28 (dd, J = 17.0, 10.0 Hz, 1H), 5.88 (dd, J = 8.7, 4.3 Hz, 1H), 5.68 (dd, J = 9.9, 1.9 Hz, 1H), 4.15 - 4.09 (m, 2H), 3.85 (s, 3H), 2.87 (q, J = 2.6 Hz, 2H), 2.72 (s, 3H), 2.32 (t, J = 5.5 Hz, 2H), 2.27 (s, 6H), 1.26 (s, 2H).; 554.5[M+H]	1.24
351		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.91 (s, 1H), 8.56 (s, 1H), 8.37 (s, 1H), 7.61 - 7.53 (m, 1H), 6.95 (s, 1H), 6.87 - 6.78 (m, 3H), 6.75 (s, 1H), 6.40 - 6.33 (m, 1H), 6.26 (dd, J = 16.9, 9.9 Hz, 1H), 5.88 (dd, J = 8.6, 4.3 Hz, 1H), 5.75 (dd, J = 9.9, 1.6 Hz, 1H), 4.15 - 4.04 (m, 2H), 3.83 (s, 3H), 2.93 (d, J = 5.0 Hz, 4H), 2.52 (q, J = 7.2 Hz, 2H), 1.61 (s, 4H), 1.25 (s, 2H), 1.15 (t, J = 7.2 Hz, 3H).; 566.4[M+H]	1.21
352		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.45 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.56 (td, J = 8.6, 6.5 Hz, 1H), 6.92 (s, 1H), 6.87 - 6.77 (m, 2H), 6.75 (d, J = 2.1 Hz, 2H), 6.36 (dd, J = 17.0, 1.6 Hz, 1H), 6.24 (dd, J = 16.9, 10.0 Hz, 1H), 5.87 (dd, J = 8.6, 4.3 Hz, 1H), 5.74 (dd, J = 10.0, 1.6 Hz, 1H), 4.14 - 4.05 (m, 2H), 3.85 (s, 3H), 3.06 (d, J = 11.6 Hz, 2H), 2.80 (dt, J = 11.6, 3.6 Hz, 1H), 2.76 - 2.71 (m, 2H), 2.52 (s, 2H), 2.32 (s, 3H), 2.17 (s, 1H), 2.08 (d, J = 12.5 Hz, 2H), 1.66 (d, J = 10.2 Hz, 8H), 1.26 (d, J = 2.2 Hz, 1H).; 635.5[M+H]	1.14
353		N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.64 (s, 1H), 8.36 (s, 1H), 7.95 (s, 1H), 7.56 (q, J = 7.9 Hz, 1H), 6.90 - 6.77 (m, 3H), 6.73 (s, 2H), 6.39 (d, J = 16.9 Hz, 1H), 6.28 (dd, J = 16.9, 10.0 Hz, 1H), 5.88 (dd, J = 8.7, 4.5 Hz, 1H), 5.76 (d, J = 10.0 Hz, 1H), 4.65 (s, 1H), 4.16 - 4.03 (m, 3H), 3.86 (s, 3H), 3.75 (d, J = 7.9 Hz, 1H), 3.46 (d, J = 10.1 Hz, 1H), 3.20 (d, J = 10.1 Hz, 1H), 2.85 - 2.75 (m, 1H), 2.33 - 2.23 (m, 1H), 2.17 (s, 1H), 2.09 (d, J = 10.0 Hz, 1H), 2.00 (d, J = 9.7 Hz, 1H).; 551.4[M+H]	1.32

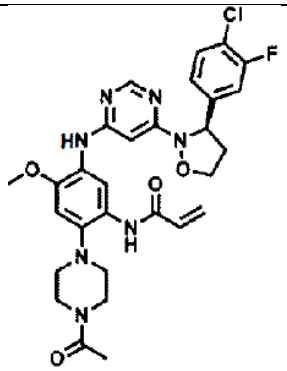
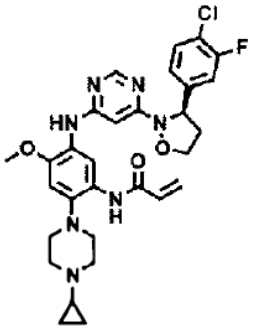
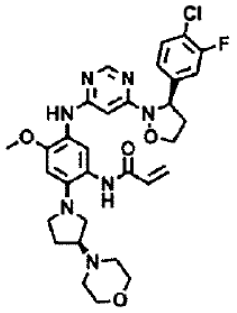
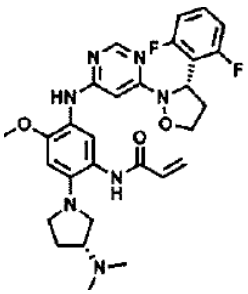
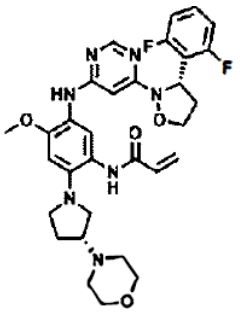
[533]

354		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.58 (s, 1H), 8.34 (s, 1H), 7.93 (s, 1H), 7.55 (dt, *J* = 13.5, 6.9 Hz, 1H), 6.87 - 6.77 (m, 3H), 6.67 (s, 2H), 6.38 (d, *J* = 16.8 Hz, 1H), 6.28 (dd, *J* = 17.0, 10.0 Hz, 1H), 5.87 (dd, *J* = 8.7, 4.3 Hz, 1H), 5.74 (d, *J* = 9.9 Hz, 1H), 4.10 (dd, *J* = 8.1, 4.6 Hz, 1H), 4.03 (q, *J* = 7.9 Hz, 1H), 3.85 (s, 3H), 3.72 (s, 1H), 3.58 (s, 1H), 3.45 (d, *J* = 9.6 Hz, 1H), 3.11 (d, *J* = 9.7 Hz, 1H), 2.82 (s, 2H), 2.31 - 2.22 (m, 1H), 2.17 (s, 1H), 1.92 (t, *J* = 11.4 Hz, 2H), 1.26 (s, 2H), 1.12 (t, *J* = 7.1 Hz, 3H).; 578.5[M+H]	1.16
355		N-(2-(4-(6-azaspiro[2.5]octan-6-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.01 (s, 1H), 8.17 (d, *J* = 12.9 Hz, 2H), 7.56 - 7.48 (m, 1H), 7.44 (t, *J* = 7.1 Hz, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 6.84 (s, 1H), 6.63 (dd, *J* = 16.9, 10.1 Hz, 1H), 6.36 (s, 1H), 6.24 (dd, *J* = 17.0, 1.9 Hz, 1H), 5.77 - 5.70 (m, 2H), 4.24 - 4.14 (m, 1H), 3.88 (q, *J* = 7.9 Hz, 1H), 3.82 (s, 3H), 3.51 (d, *J* = 11.5 Hz, 2H), 3.17 (d, *J* = 11.3 Hz, 2H), 3.08 (q, *J* = 11.4 Hz, 2H), 2.88 - 2.81 (m, 1H), 2.76 (t, *J* = 12.0 Hz, 2H), 2.26 - 2.16 (m, 2H), 2.13 (d, *J* = 14.6 Hz, 4H), 1.98 (d, *J* = 12.0 Hz, 2H), 1.23 (s, 1H), 1.17 (d, *J* = 13.8 Hz, 2H), 0.51 - 0.36 (m, 4H).; 662.5[M+H]+	1.40
356		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.03 (s, 1H), 8.68 (s, 1H), 8.17 (s, 1H), 7.56 - 7.47 (m, 1H), 7.47 - 7.39 (m, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 6.84 (s, 1H), 6.59 (s, 1H), 6.39 (s, 1H), 6.23 (dd, *J* = 17.1, 1.9 Hz, 1H), 5.73 (dd, *J* = 8.9, 4.9 Hz, 2H), 4.18 (td, *J* = 8.0, 3.7 Hz, 1H), 4.05 (d, *J* = 12.7 Hz, 1H), 3.87 (t, *J* = 8.1 Hz, 1H), 3.82 (s, 3H), 3.62 (td, *J* = 6.7, 4.0 Hz, 1H), 3.14 (qd, *J* = 7.4, 4.1 Hz, 4H), 2.81 (dd, *J* = 8.1, 4.1 Hz, 2H), 2.78 - 2.68 (m, 2H), 2.25 - 2.17 (m, 1H), 2.15 (d, *J* = 9.8 Hz, 2H), 1.91 (s, 3H), 1.25 (q, *J* = 7.2, 6.7 Hz, 4H), 1.18 (d, *J* = 6.2 Hz, 2H). ; 652.4[M+H]+	1.32
357		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.64 (s, 1H), 8.15 (s, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.1 Hz, 1H), 7.22 (t, *J* = 7.9 Hz, 1H), 6.83 (s, 1H), 6.64 (s, 1H), 6.36 (s, 1H), 6.21 (d, *J* = 17.0 Hz, 1H), 5.77 - 5.71 (m, 2H), 4.17 (dt, *J* = 9.1, 4.5 Hz, 1H), 3.86 (q, *J* = 8.0 Hz, 1H), 3.80 (s, 3H), 3.06 (s, 3H), 2.89 - 2.75 (m, 3H), 2.18 (dt, *J* = 12.8, 6.9 Hz, 4H), 1.91 (s, 3H), 1.87 (s, 3H), 1.73 (d, *J* = 14.7 Hz, 2H), 1.07 (d, *J* = 6.5 Hz, 4H). ; 652.4[M+H]+	1.32

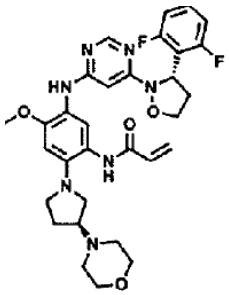
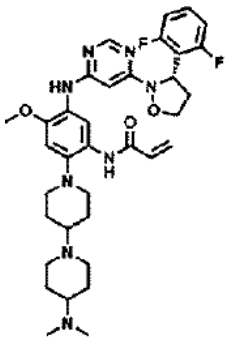
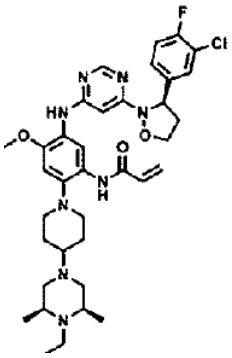
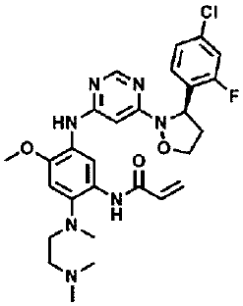
[534]

358		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropyl-1,4-diazepane-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.96 (s, 1H), 8.67 (s, 1H), 8.16 (s, 1H), 7.57 - 7.47 (m, 1H), 7.47 - 7.40 (m, 1H), 7.23 (t, J = 7.9 Hz, 1H), 6.82 (s, 1H), 6.66 (dd, J = 16.8, 10.1 Hz, 1H), 6.39 (s, 1H), 6.24 (dd, J = 17.0, 2.0 Hz, 1H), 5.74 (dt, J = 8.7, 4.8 Hz, 2H), 4.18 (td, J = 8.0, 3.7 Hz, 1H), 3.87 (t, J = 8.1 Hz, 1H), 3.81 (s, 4H), 3.13 (d, J = 11.5 Hz, 3H), 3.05 (s, 2H), 2.88 (s, 2H), 2.86 - 2.78 (m, 2H), 2.74 (t, J = 11.6 Hz, 2H), 2.26 - 2.14 (m, 2H), 2.05 (d, J = 14.8 Hz, 3H), 1.95 (s, 2H), 1.91 (s, 5H), 0.48 (d, J = 30.7 Hz, 3H). : 601.5[M+H]+	1.20
359		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-$d6$) δ 10.05 (s, 1H), 8.62 (s, 1H), 8.47 (s, 1H), 8.17 (s, 1H), 7.48 - 7.27 (m, 4H), 6.99 (s, 1H), 6.46 - 6.31 (m, 2H), 6.22 (dd, J = 16.9, 2.2 Hz, 1H), 5.81 - 5.65 (m, 1H), 5.54 (dd, J = 8.7, 5.1 Hz, 1H), 4.14 (td, J = 7.9, 3.8 Hz, 1H), 3.80 (s, 3H), 2.87 (t, J = 5.8 Hz, 2H), 2.78 (dtd, J = 12.0, 7.8, 3.7 Hz, 1H), 2.71 (s, 3H), 2.33 (s, 2H), 2.21 (s, 8H) ; 552.4 [M+H]$^+$	1.21
360		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-$d6$) δ 8.97 (s, 1H), 8.62 (s, 1H), 8.14 (d, J = 13.7 Hz, 2H), 7.48 - 7.30 (m, 4H), 6.84 (s, 1H), 6.50 (dd, J = 17.0, 10.2 Hz, 1H), 6.36 (s, 1H), 6.21 (dt, J = 17.0, 3.9 Hz, 1H), 5.72 (d, J = 10.6 Hz, 1H), 5.54 (dd, J = 8.6, 5.1 Hz, 1H), 4.14 (td, J = 7.9, 3.7 Hz, 1H), 3.88 - 3.76 (m, 4H), 2.88 (t, J = 4.8 Hz, 4H), 2.77 (qq, J = 7.7, 3.7 Hz, 1H), 2.55 (d, J = 10.5 Hz, 3H), 2.36 - 2.16 (m, 5H) ; 550.4 [M+H]$^+$	1.16
361		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-$d6$) δ 8.98 (s, 1H), 8.61 (s, 1H), 8.15 (d, J = 6.5 Hz, 2H), 7.47 - 7.30 (m, 4H), 6.83 (s, 1H), 6.65 (dd, J = 17.0, 10.1 Hz, 1H), 6.35 (s, 1H), 6.23 (ddd, J = 17.0, 12.9, 2.0 Hz, 1H), 5.77 - 5.68 (m, 1H), 5.54 (dd, J = 8.7, 5.1 Hz, 1H), 4.14 (td, J = 7.9, 3.8 Hz, 1H), 3.80 (s, 4H), 3.09 - 3.03 (m, 2H), 2.77 (dtd, J = 12.0, 7.9, 3.7 Hz, 1H), 2.71 - 2.63 (m, 2H), 2.30 (s, 6H), 1.86 (d, J = 11.5 Hz, 2H), 1.78 - 1.64 (m, 2H), 1.13 - 1.02 (m, 2H) ; 578.4 [M+H]$^+$	1.18
362		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.88 (s, 1H), 8.46 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.44 - 7.33 (m, 1H), 7.11 - 7.03 (m, 1H), 6.99 (t, J = 7.6 Hz, 1H), 6.92 (s, 1H), 6.74 (d, J = 8.9 Hz, 2H), 6.41 - 6.16 (m, 2H), 5.91 (dd, J = 8.8, 4.4 Hz, 1H), 5.73 (dd, J = 9.8, 1.6 Hz, 1H), 4.47 (s, 1H), 4.16 - 4.01 (m, 3H), 3.85 (s, 3H), 3.66 (dq, J = 13.3, 7.3, 6.6 Hz, 2H), 3.08 (dd, J = 15.6, 8.1 Hz, 3H), 2.79 (dtdd, J = 20.3, 11.7, 8.3, 3.4 Hz, 4H), 2.36 - 2.22 (m, 4H), 1.97 (d, J = 12.6 Hz, 2H), 1.55 - 1.41 (m, 5H). : 630.5 [M+H]$^+$	1.15

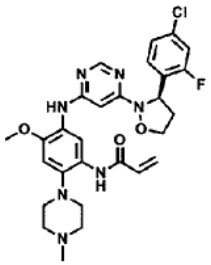
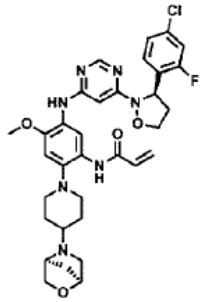
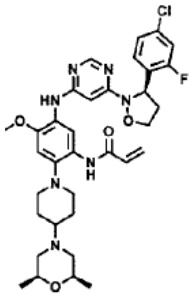
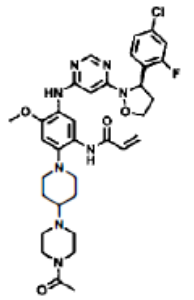
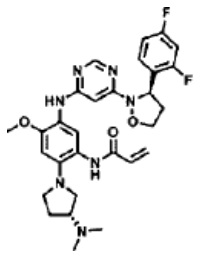
[535]

363		N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.95 (s, 1H), 8.44 (s, 1H), 8.38 (d, *J* = 1.0 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.29 (dd, *J* = 10.1, 2.0 Hz, 1H), 7.19 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.98 (s, 1H), 6.72 (s, 2H), 6.38 (dd, *J* = 16.9, 1.5 Hz, 1H), 6.26 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.77 (dd, *J* = 10.0, 1.5 Hz, 1H), 5.66 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.16 (td, *J* = 8.0, 4.2 Hz, 1H), 4.06 (q, *J* = 8.1 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 1H), 3.65 (t, *J* = 5.0 Hz, 2H), 2.88 (td, *J* = 6.3, 3.2 Hz, 4H), 2.77 (dtd, *J* = 12.2, 8.0, 4.2 Hz, 1H), 2.34 (dtd, *J* = 12.5, 8.1, 4.6 Hz, 1H), 2.17 (s, 3H), 1.66 - 1.50 (m, 1H).; 506.3 [M+H]$^+$	1.44
364		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.60 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 7.29 (dd, *J* = 10.2, 2.1 Hz, 1H), 7.19 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.94 (s, 1H), 6.79 (s, 1H), 6.71 (s, 1H), 6.37 (dd, *J* = 16.9, 1.7 Hz, 1H), 6.28 (dd, *J* = 16.9, 9.8 Hz, 1H), 5.76 (dd, *J* = 9.8, 1.7 Hz, 1H), 5.66 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.15 (td, *J* = 8.0, 4.2 Hz, 1H), 4.07 (q, *J* = 8.0 Hz, 1H), 3.81 (s, 3H), 2.92 - 2.71 (m, 9H), 2.33 (dtd, *J* = 12.5, 8.1, 4.6 Hz, 1H), 1.72 (tt, *J* = 6.6, 3.7 Hz, 1H), 0.57 - 0.38 (m, 4H).; 504.4 [M+H]$^+$	1.28
365		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.71 (s, 1H), 8.35 (s, 1H), 8.16 (s, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 7.29 (dd, *J* = 10.2, 2.0 Hz, 1H), 7.19 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.91 (s, 1H), 6.77 (s, 1H), 6.67 (s, 1H), 6.45 - 6.20 (m, 2H), 5.74 (dd, *J* = 10.0, 1.6 Hz, 1H), 5.65 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.14 (td, *J* = 7.9, 4.2 Hz, 1H), 4.04 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.76 (t, *J* = 4.7 Hz, 3H), 3.24 - 2.94 (m, 4H), 2.76 (dtd, *J* = 12.3, 8.0, 4.2 Hz, 1H), 2.64 - 2.42 (m, 4H), 2.33 (dtd, *J* = 12.3, 8.0, 4.5 Hz, 1H), 2.26 - 2.13 (m, 1H), 2.02 (s, 3H).; 624.4 [M+H]$^+$	1.23
366		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	566.5 [M+H]$^+$	1.06
367		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d$_4$) δ 7.99 (s, 1H), 7.55 (s, 1H), 7.25 - 7.14 (m, 1H), 6.83 (t, *J* = 8.4 Hz, 2H), 6.52 (s, 1H), 6.41 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.23 (d, *J* = 16.3 Hz, 1H), 6.11 (s, 1H), 5.63 (dd, *J* = 10.9, 9.7 Hz, 2H), 4.19 (dd, *J* = 7.7, 6.1 Hz, 1H), 3.80 - 3.74 (m, 1H), 3.71 (s, 3H), 3.64 (t, *J* = 4.0 Hz, 4H), 3.45 (ddd, *J* = 17.1, 11.1, 5.4 Hz, 2H), 3.21 (dt, *J* = 3.2, 1.6 Hz, 3H), 3.17 (d, *J* = 7.1 Hz, 2H), 2.99 - 2.92 (m, 1H), 2.70 - 2.46 (m, 5H), 2.39 (dt, *J* = 11.7, 7.7 Hz, 2H), 2.12 (d, *J* = 4.8 Hz, 1H), 1.88 (s, 5H) ; 608.5 [M+H]$^+$	1.05

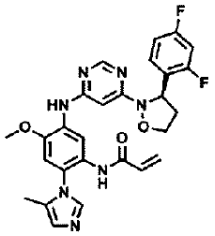
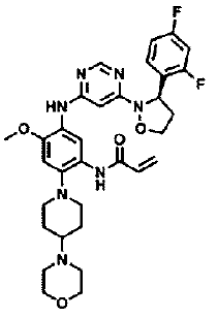
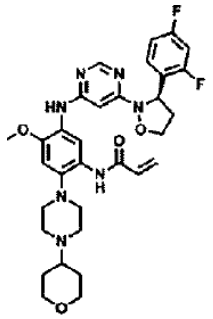
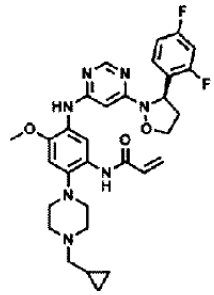
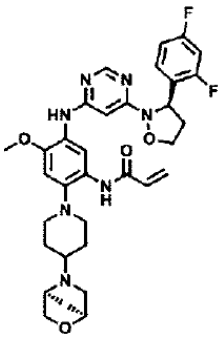
[536]

368		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.09 (s, 1H), 7.64 (s, 1H), 7.34 - 7.25 (m, 1H), 6.93 (t, J = 8.4 Hz, 2H), 6.62 (s, 1H), 6.51 (dd, J = 17.0, 10.2 Hz, 1H), 6.37 - 6.29 (m, 1H), 6.22 (s, 1H), 5.73 (dd, J = 17.8, 9.8 Hz, 2H), 4.29 (dd, J = 7.9, 5.9 Hz, 1H), 3.87 (dd, J = 11.6, 6.3 Hz, 2H), 3.82 (s, 3H), 3.72 (t, J = 4.5 Hz, 4H), 3.55 (ddd, J = 17.1, 11.1, 5.4 Hz, 1H), 3.32 - 3.29 (m, 2H), 3.24 (dd, J = 14.3, 7.3 Hz, 2H), 3.02 - 2.90 (m, 1H), 2.75 (dt, J = 9.0, 8.2 Hz, 1H), 2.67 - 2.45 (m, 4H), 2.25 - 2.14 (m, 1H), 1.97 (s, 4H) ; 608.5 [M+H]$^+$	1.07
369		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide	663.6 [M+H]$^+$	0.99
370		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((3S,5R)-4-ethyl-3,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.42 (s, 1H), 8.32 (s, 1H), 7.52 (dd, J = 7.0, 1.8 Hz, 1H), 7.37 (s, 1H), 7.34 - 7.29 (m, 1H), 7.10 (t, J = 8.7 Hz, 1H), 6.74 (s, 1H), 6.67 (s, 1H), 6.31 (dt, J = 16.9, 13.1 Hz, 2H), 5.75 (d, J = 10.8 Hz, 1H), 5.63 (dd, J = 8.5, 4.6 Hz, 1H), 4.15 (td, J = 7.9, 4.2 Hz, 1H), 4.05 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.15 - 2.92 (m, 8H), 2.81 - 2.65 (m, 3H), 2.54 - 2.38 (m, 3H), 2.38 - 2.26 (m, 1H), 2.08 (d, J = 12.1 Hz, 2H), 2.04 (s, 4H), 1.72 (dd, J = 21.0, 11.5 Hz, 2H), 1.22 (d, J = 6.1 Hz, 6H), 1.02 (t, J = 7.1 Hz, 3H) ; 603.6 [M+H]$^+$	1.22
371		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 9.87 (s, 1H), 8.93 (s, 1H), 8.34 (s, 1H), 7.54 (t, J = 8.3 Hz, 1H), 7.18 (s, 1H), 7.13 - 7.06 (m, 2H), 6.78 (d, J = 2.2 Hz, 2H), 6.40 (s, 1H), 6.30 (s, 1H), 5.87 (dd, J = 8.8, 4.4 Hz, 1H), 5.68 (t, J = 5.9 Hz, 1H), 4.11 (td, J = 8.0, 6.5, 3.1 Hz, 2H), 3.85 (s, 3H), 2.93 (dt, J = 5.6, 2.9 Hz, 2H), 2.86 - 2.79 (m, 1H), 2.70 (s, 3H), 2.44 (t, J = 5.7 Hz, 2H), 2.33 (s, 6H), 2.29 - 2.24 (m, 1H); 570.4[M+H]$^+$	1.33

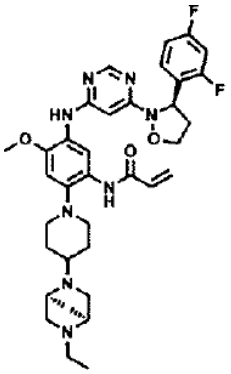
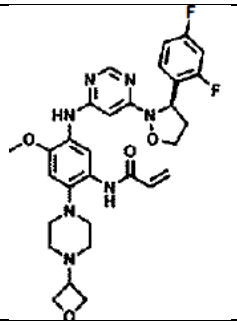
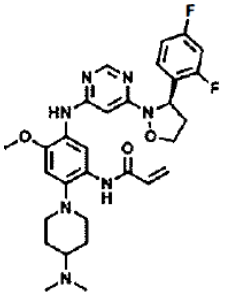
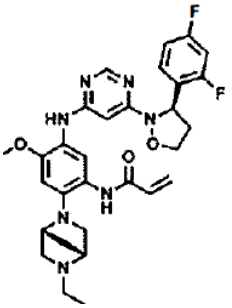
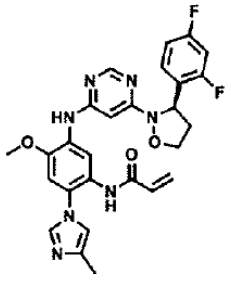
[537]

372		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.32 (s, 1H), 8.15 (d, J = 5.0 Hz, 1H), 7.52 (t, J = 8.2 Hz, 1H), 7.24 - 7.16 (m, 2H), 6.92 (d, J = 13.1 Hz, 1H), 6.53 (dd, J = 16.9, 10.2 Hz, 1H), 6.48 (d, J = 3.7 Hz, 1H), 6.35 (d, J = 16.8 Hz, 1H), 5.80 (d, J = 10.2 Hz, 1H), 5.73 (dd, J = 8.7, 4.7 Hz, 1H), 4.13 (td, J = 8.0, 4.2 Hz, 1H), 3.99 (d, J = 7.8 Hz, 1H), 3.88 (d, J = 2.3 Hz, 3H), 3.04 (t, J = 4.9 Hz, 4H), 2.99 - 2.88 (m, 4H), 2.82 (ddd, J = 12.5, 8.2, 4.4 Hz, 1H), 2.57 (d, J = 7.6 Hz, 3H), 2.28 - 2.21 (m, 1H); 568.4[M+H]$^+$	1.29
373		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.89 (s, 1H), 9.23 (d, J = 30.9 Hz, 1H), 8.26 (s, 1H), 7.95 (d, J = 12.8 Hz, 1H), 7.51 - 7.40 (m, 2H), 7.30 (dd, J = 8.4, 2.1 Hz, 1H), 6.88 (d, J = 5.6 Hz, 1H), 6.59 (td, J = 15.9, 10.2 Hz, 1H), 6.24 (dt, J = 17.0, 2.4 Hz, 2H), 5.78 - 5.62 (m, 2H), 4.72 - 4.54 (m, 3H), 3.82 (d, J = 1.3 Hz, 3H), 3.70 (d, J = 9.7 Hz, 1H), 3.37 (d, J = 4.8 Hz, 4H), 2.95 - 2.66 (m, 4H), 2.34 - 2.17 (m, 3H), 2.08 (d, J = 11.5 Hz, 3H).: 650.3 [M+H]$^+$	1.38
374		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.36 (s, 1H), 9.28 (s, 1H), 8.34 (s, 1H), 7.86 (s, 1H), 7.50 (dd, J = 10.3, 2.1 Hz, 1H), 7.38 (t, J = 8.3 Hz, 1H), 7.31 (dd, J = 8.4, 2.1 Hz, 1H), 6.94 (s, 1H), 6.72 (dd, J = 17.0, 10.2 Hz, 1H), 6.26 (dd, J = 17.0, 1.9 Hz, 1H), 6.15 (s, 1H), 5.77 (dd, J = 10.1, 1.9 Hz, 1H), 5.67 (dd, J = 8.6, 5.6 Hz, 1H), 4.36 - 4.31 (m, 1H), 4.17 (ddd, J = 9.8, 6.8, 3.4 Hz, 2H), 4.08 (d, J = 7.7 Hz, 1H), 3.82 (s, 3H), 3.36 (dd, J = 10.9, 5.1 Hz, 5H), 2.95 (dd, J = 7.9, 4.1 Hz, 1H), 2.81 (s, 2H), 2.70 (d, J = 10.6 Hz, 2H), 2.31 - 2.22 (m, 3H), 2.16 - 2.05 (m, 2H), 1.17 (d, J = 6.3 Hz, 6H).: 666.3 [M+H]$^+$	1.32
375		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.67 (s, 1H), 9.15 (s, 1H), 8.27 (s, 1H), 7.96 (s, 1H), 7.52 - 7.37 (m, 2H), 7.30 (dd, J = 8.3, 2.1 Hz, 1H), 6.89 (s, 1H), 6.67 (dd, J = 17.0, 10.2 Hz, 1H), 6.28 - 6.15 (m, 2H), 5.80 - 5.63 (m, 2H), 4.50 (d, J = 14.0 Hz, 1H), 4.28 (s, 1H), 4.01 (s, 2H), 3.81 (s, 3H), 3.49 (s, 3H), 3.34 (s, 2H), 3.18 (d, J = 10.4 Hz, 4H), 3.05 - 2.88 (m, 3H), 2.77 (s, 2H), 2.17 (s, 3H), 2.06 (s, 3H).: 679.3 [M+H]$^+$	1.28
376		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.67 (s, 1H), 8.35 (s, 1H), 8.14 (s, 1H), 7.56 (q, J = 8.1 Hz, 1H), 6.88 - 6.77 (m, 3H), 6.74 (d, J = 11.0 Hz, 2H), 6.41 - 6.35 (m, 1H), 6.28 (dd, J = 16.9, 9.8 Hz, 1H), 5.88 (dd, J = 8.7, 4.3 Hz, 1H), 5.73 (dd, J = 9.9, 1.8 Hz, 1H), 4.15 - 4.04 (m, 2H), 3.84 (s, 3H), 3.19 (q, J = 7.9 Hz, 1H), 3.11 (d, J = 7.0 Hz, 2H), 2.90 - 2.75 (m, 2H), 2.30 (s, 6H), 1.62 (s, 4H).: 586.4[M+H]	1.15

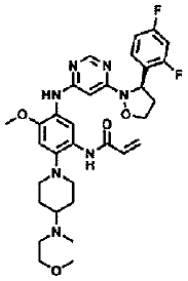
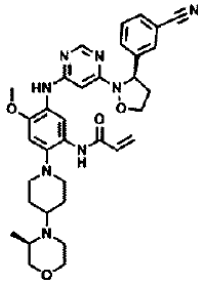
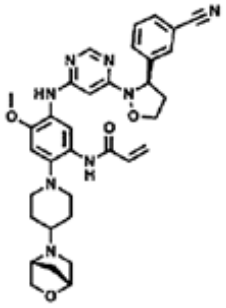
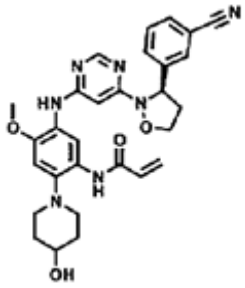
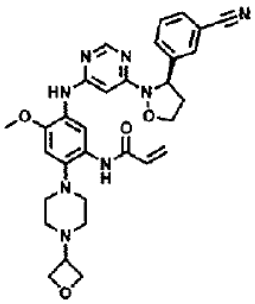
[538]

377		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(5-methyl-1H-imidazole-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 9.11 (s, 1H), 8.45 (s, 1H), 7.56 (q, J = 8.0 Hz, 1H), 7.21 (s, 1H), 7.14 (d, J = 1.4 Hz, 1H), 6.95 (d, J = 1.4 Hz, 1H), 6.84 (dd, J = 10.1, 9.0 Hz, 3H), 6.75 (s, 1H), 6.68 (s, 1H), 6.27 (d, J = 16.9 Hz, 1H), 6.03 (dd, J = 16.8, 10.3 Hz, 1H), 5.89 (dd, J = 8.7, 4.7 Hz, 1H), 5.71 (d, J = 10.3 Hz, 1H), 4.17 (dt, J = 7.9, 3.9 Hz, 1H), 4.06 (q, J = 7.9 Hz, 1H), 3.90 (s, 3H), 2.25 (s, 2H), 2.17 (s, 3H).: 534.4[M+H]	1.26
378		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.88 (s, 1H), 8.44 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.56 (td, J = 8.6, 6.5 Hz, 1H), 6.93 (s, 1H), 6.87 - 6.78 (m, 2H), 6.75 (d, J = 1.8 Hz, 2H), 6.36 (dd, J = 17.0, 1.5 Hz, 1H), 6.24 (dd, J = 16.9, 10.0 Hz, 1H), 5.88 (dd, J = 8.7, 4.3 Hz, 1H), 5.74 (dd, J = 10.0, 1.6 Hz, 1H), 4.16 - 4.04 (m, 2H), 3.85 (s, 3H), 3.78 (t, J = 4.7 Hz, 4H), 3.07 (d, J = 11.6 Hz, 2H), 2.80 (dt, J = 11.7, 3.7 Hz, 1H), 2.77 - 2.67 (m, 2H), 2.62 (t, J = 4.7 Hz, 4H), 2.29 (ddd, J = 12.5, 9.8, 5.8 Hz, 2H), 2.08 (d, J = 12.5 Hz, 2H), 1.70 - 1.61 (m, 2H).: 622.5[M+H]	1.14
379		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.91 (s, 1H), 8.54 (s, 1H), 8.37 (s, 1H), 7.61 - 7.53 (m, 1H), 6.96 (s, 1H), 6.87 - 6.78 (m, 3H), 6.75 (s, 1H), 6.40 - 6.34 (m, 1H), 6.26 (dd, J = 17.0, 9.9 Hz, 1H), 5.88 (dd, J = 8.6, 4.3 Hz, 1H), 5.75 (dd, J = 9.9, 1.6 Hz, 1H), 4.14 - 4.04 (m, 4H), 3.83 (s, 3H), 3.42 (dd, J = 12.7, 10.7 Hz, 2H), 2.93 (q, J = 3.9 Hz, 4H), 2.83 - 2.74 (m, 4H), 2.52 (ddd, J = 11.3, 7.5, 3.8 Hz, 1H), 1.84 (d, J = 12.6 Hz, 2H), 1.66 (dd, J = 12.1, 4.4 Hz, 4H).: 635.6[M+H]	1.20
380		N-(2-(4-(cyclopropylmethyl)piperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.92 (s, 1H), 8.57 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.60 - 7.53 (m, 1H), 6.94 (s, 1H), 6.87 - 6.75 (m, 4H), 6.40 - 6.33 (m, 1H), 6.26 (dd, J = 16.9, 9.9 Hz, 1H), 5.88 (dd, J = 8.7, 4.3 Hz, 1H), 5.74 (dd, J = 9.9, 1.6 Hz, 1H), 4.14 - 4.05 (m, 2H), 3.84 (s, 3H), 2.94 (d, J = 5.1 Hz, 4H), 2.80 (ddd, J = 12.8, 8.4, 4.7 Hz, 2H), 2.36 (d, J = 6.6 Hz, 2H), 2.28 (dq, J = 12.0, 3.7 Hz, 1H), 2.17 (s, 4H), 0.60 - 0.54 (m, 2H), 0.16 (q, J = 5.0 Hz, 2H).: 592.5[M+H]	1.20
381		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.88 (s, 1H), 8.48 (s, 1H), 8.37 (d, J = 0.9 Hz, 1H), 7.61 - 7.53 (m, 1H), 6.93 (s, 1H), 6.82 (dddd, J = 12.0, 11.2, 8.6, 2.6 Hz, 2H), 6.76 (d, J = 5.3 Hz, 2H), 6.35 (dd, J = 17.0, 1.5 Hz, 1H), 6.23 (dd, J = 16.9, 10.1 Hz, 1H), 5.88 (dd, J = 8.7, 4.3 Hz, 1H), 5.73 (dd, J = 10.1, 1.5 Hz, 1H), 4.44 (s, 1H), 4.09 (q, J = 7.0, 7.3 Hz, 3H), 3.86 (s, 3H), 3.77 (d, J = 2.2 Hz, 1H), 3.66 (dd, J = 8.1, 1.6 Hz, 1H), 3.14 (dd, J = 9.9, 1.8 Hz, 1H), 3.03 (dd, J = 12.0, 3.7 Hz, 2H), 2.78 (ddd, J = 12.0, 8.4, 3.3 Hz, 2H), 2.62 - 2.55 (m, 1H), 2.50 (d, J = 9.9 Hz, 1H), 2.27 (dtd, J = 12.3, 8.0, 4.2 Hz, 1H), 2.04 (d, J = 13.1 Hz, 1H), 2.00 - 1.89 (m, 2H), 1.83 (d, J = 9.8 Hz, 1H), 1.65 (dd, J = 22.6, 11.4 Hz, 3H).: 634.5[M+H]	1.15

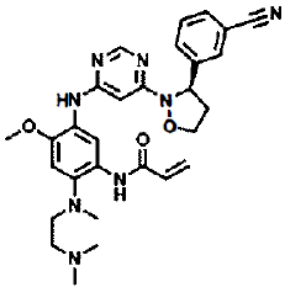
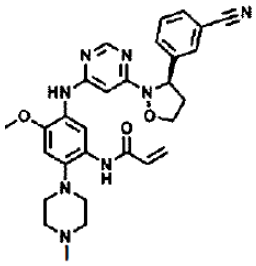
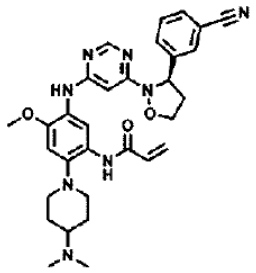
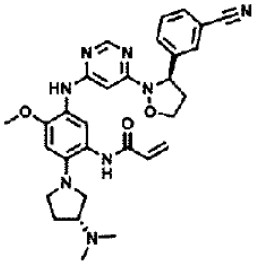
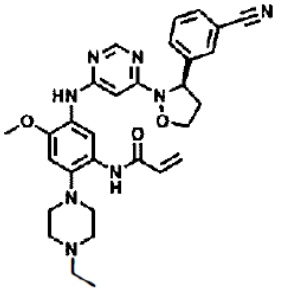
[539]

382		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.88 (s, 1H), 8.47 (s, 1H), 8.37 (s, 1H), 7.56 (q, J = 8.2 Hz, 1H), 6.92 (s, 1H), 6.87 - 6.77 (m, 2H), 6.75 (d, J = 3.4 Hz, 2H), 6.39 - 6.31 (m, 1H), 6.29 - 6.19 (m, 1H), 5.87 (dd, J = 8.6, 4.3 Hz, 1H), 5.73 (d, J = 10.1 Hz, 1H), 4.15 - 4.05 (m, 2H), 3.85 (s, 3H), 3.66 (s, 1H), 3.02 (s, 3H), 2.85 - 2.73 (m, 4H), 2.30 - 2.23 (m, 1H), 2.17 (s, 3H), 2.06 (d, J = 12.8 Hz, 1H), 1.90 (s, 2H), 1.69 (d, J = 31.5 Hz, 4H), 1.28 (d, J = 18.2 Hz, 3H), 1.17 (s, 2H).; 661.5[M+H]	1.07
383		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.92 (s, 1H), 8.49 (s, 1H), 8.38 (s, 1H), 7.56 (d, J = 6.7 Hz, 1H), 6.97 (s, 1H), 6.79 (m, 4H), 6.36 (d, J = 16.2 Hz, 1H), 6.27 (m, 1H), 5.88 (m, 1H) 5.74 (d, J = 11.3 Hz, 1H), 4.69 (td, J = 21.8 Hz, 4H), 4.08 (m, 2H), 3.85 (s, 3H), 3.61 (m, 1H), 2.96 (s, 4H), 2.81 (m, 1H) 2.54 (s, 4H), 2.28 (s, 1H).; 594.4 [M+H]$^+$	1.16
384		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.49 (s, 1H), 8.37 (s, 1H), 7.57 (m, 1H), 6.92 (s, 1H), 6.79 (m, 4H), 6.35 (d, J = 15.9 Hz, 1H), 6.27 (m, 1H), 5.87 (m, 1H), 5.74 (d, J = 11.3 Hz, 1H), 4.08 (m, 2H), 3.85 (s, 3H), 3.06 (d, J = 11.6 Hz, 2H), 2.80 (m, 1H), 2.73 (m, 2H), 2.36 (s, 6H), 2.27 (m, 2H), 2.06 (d, J = 13.0 Hz, 2H), 1.66 (d, J = 9.9 Hz, 2H).; 580.5 [M+H]$^+$	1.19
385		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.56 (s, 1H), 8.34 (s, 1H), 7.96 (s, 1H), 7.56 (m, 1H), 6.85 (m, 3H), 6.69 (s, 2H), 6.38 (m, 1H), 6.31 (m, 1H), 5.89 (m, 1H), 5.74 (d, J = 10.2 Hz, 1H), 4.15 - 4.02 (m, 2H), 3.85 (s, 3H), 3.73 (s, 1H), 3.57 (s, 1H), 3.49 (d, 1H), 3.06 (d, J = 9.4 Hz, 1H), 2.75 (m, 4H), 2.60 (m, 1H), 2.27 (m, 1H), 1.91 (q, J = 10.6, 10.0 Hz, 2H), 1.13 (t, J = 7.1 Hz, 3H).; 578.4 [M+H]$^+$	1.14
386		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methyl-1H-imidazole-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.96 (s, 1H), 8.47 - 8.38 (m, 1H), 7.61 - 7.52 (m, 1H), 7.51 - 7.45 (m, 1H), 7.15 (d, J = 8.0 Hz, 1H), 6.90 - 6.72 (m, 6H), 6.44 - 6.25 (m, 1H), 6.13 (dd, J = 16.8, 10.3 Hz, 1H), 5.88 (dd, J = 8.6, 4.5 Hz, 1H), 5.80 - 5.67 (m, 1H), 4.17 (td, J = 8.0, 4.3 Hz, 1H), 4.09 - 4.03 (m, 1H), 3.90 (s, 3H), 2.90 - 2.77 (m, 1H), 2.30 (s, 3H), 1.82 (p, J = 7.0 Hz, 1H).; 534.3 [M+H]$^+$	1.29

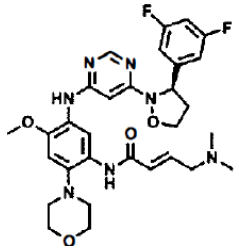
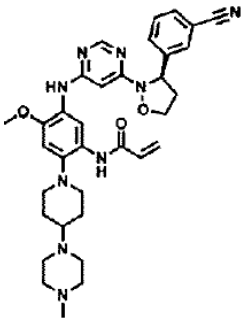
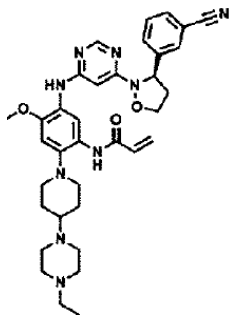
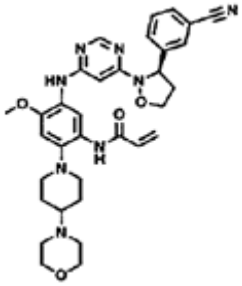
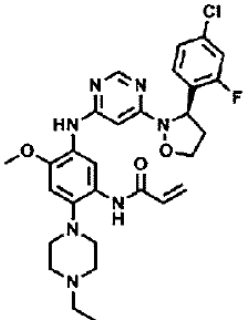
[540]

387		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((2-methoxyethyl)(methyl)amino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 7.62 - 7.51 (m, 1H), 6.94 (s, 1H), 6.80 - 6.71 (m, 4H), 6.40 - 6.33 (m, 1H), 6.31 - 6.22 (m, 1H), 5.90 - 5.85 (m, 1H), 5.75 (d, *J* = 10.1 Hz, 1H), 4.16 - 4.03 (m, 2H), 3.85 (s, 3H), 3.50 - 3.51 (m, 2H), 3.39 (s, 3H), 3.35 - 3.26 (m, 1H), 3.07 (d, *J* = 11.1 Hz, 2H), 2.87 - 2.67 (m, 7H), 2.61 (s, 2H), 2.44 (s, 4H).; 624.5 [M+H]$^+$	1.19
388		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-3-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.44 (s, 1H), 8.31 (s, 1H), 7.78 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.58 - 7.50 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 1H), 6.77 (s, 1H), 6.68 (s, 1H), 6.40 - 6.23 (m, 2H), 5.76 (dd, *J* = 9.0, 1.5 Hz, 1H), 5.71 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.16 (td, *J* = 8.0, 4.1 Hz, 1H), 4.07 (q, *J* = 8.1 Hz, 1H), 3.80 - 3.81 (m, 4H), 3.78 - 3.70 (m, 2H), 3.47 - 3.38 (m, 1H), 3.13 - 3.03 (m, 2H), 2.98 - 2.89 (m, 2H), 2.86 - 2.64 (m, 5H), 2.30 - 2.29 (m, 1H), 1.98 - 1.79 (m, 3H), 1.74 - 1.61 (m, 1H), 1.08 (d, *J* = 6.4 Hz, 3H); 625.5[M+H]$^+$	1.08
389		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.49 (s, 1H), 8.36 (s, 1H), 7.79 (s, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 6.96 (s, 1H), 6.77 (s, 1H), 6.74 (s, 1H), 6.39 - 6.20 (m, 2H), 5.77 - 5.69 (m, 2H), 4.44 (s, 1H), 4.17 (td, *J* = 8.1, 4.2 Hz, 1H), 4.12 - 4.05 (m, 2H), 3.86 (s, 3H), 3.81 - 3.74 (m, 1H), 3.69 - 3.64 (m, 1H), 3.17 - 3.11 (m, 1H), 3.07 - 2.99 (m, 2H), 2.86 - 2.71 (m, 3H), 2.63 - 2.54 (m, 1H), 2.53 - 2.47 (m, 1H), 2.30 - 2.29 (m, 1H), 2.09 - 2.00 (m, 1H), 1.99 - 1.90 (m, 2H), 1.86 - 1.80 (m, 1H), 1.74 - 1.62 (m, 2H); 623.5[M+H]$^+$	1.05
390		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-hydroxypiperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.35 (s, 1H), 7.79 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.04 (s, 1H), 6.78 (s, 1H), 6.73 (s, 1H), 6.30 (dt, *J* = 16.9, 13.4 Hz, 2H), 5.78 - 5.70 (m, 2H), 4.17 (td, *J* = 7.9, 4.1 Hz, 1H), 4.08 (q, *J* = 8.0 Hz, 1H), 3.98 - 3.91 (m, 1H), 3.85 (s, 3H), 3.10 - 3.01 (m, 2H), 2.86 - 2.72 (m, 3H), 2.40 - 2.29 (m, 1H), 2.11 - 2.03 (m, 2H), 1.81 - 1.73 (m, 2H); 542.4[M+H]$^+$	1.21
391		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.92 (s, 1H), 8.50 (s, 1H), 8.37 (d, *J* = 0.9 Hz, 1H), 7.79 (d, *J* = 1.8 Hz, 1H), 7.75 - 7.67 (m, 1H), 7.58 - 7.51 (m, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 6.98 (s, 1H), 6.82 (s, 1H), 6.74 (s, 1H), 6.36 (dd, *J* = 17.0, 1.5 Hz, 1H), 6.26 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.79 - 5.69 (m, 2H), 4.69 (dt, *J* = 21.4, 6.3 Hz, 4H), 4.22 - 4.14 (m, 1H), 4.14 - 4.03 (m, 1H), 3.85 (s, 3H), 3.66 - 3.55 (m, 1H), 3.02 - 2.91 (m, 4H), 2.88 - 2.75 (m, 1H), 2.63 - 2.43 (m, 4H), 2.41 - 2.28 (m, 1H) ; 583.4[M+H]$^+$	1.09

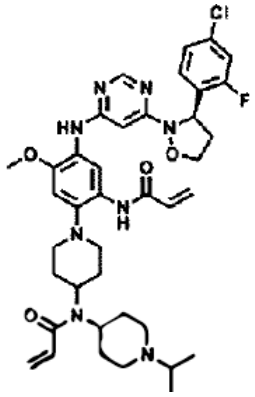
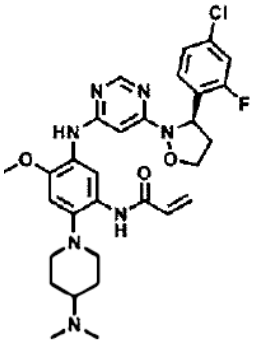
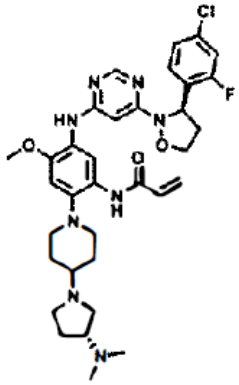
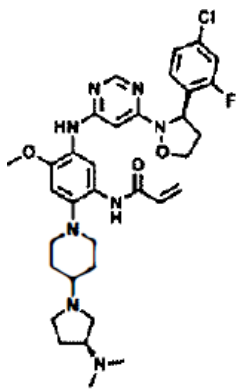
[541]

392		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 10.12 (s, 1H), 8.96 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 7.79 (d, *J* = 1.8 Hz, 1H), 7.72 (dt, *J* = 8.0, 1.7 Hz, 1H), 7.54 (dt, *J* = 7.6, 1.5 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 6.98 (s, 1H), 6.81 - 6.78 (m, 2H), 6.40 (dd, *J* = 17.0, 2.0 Hz, 1H), 6.34 - 6.22 (m, 1H), 5.74 (dd, *J* = 8.8, 4.5 Hz, 1H), 5.72 - 5.65 (m, 1H), 4.19 - 4.10 (m, 2H), 3.85 (s, 3H), 2.91 - 2.86 (m, 2H), 2.84 - 2.78 (m, 1H), 2.72 (s, 3H), 2.37 - 2.31 (m, 3H), 2.20 (s, 6H) ; 543.5[M+H]$^+$	1.08
393		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.54 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.79 (d, *J* = 1.8 Hz, 1H), 7.71 (dt, *J* = 7.8, 1.7 Hz, 1H), 7.55 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 6.99 (s, 1H), 6.80 (s, 1H), 6.73 (s, 1H), 6.37 (dd, *J* = 17.1, 1.6 Hz, 1H), 6.27 (dd, *J* = 17.0, 9.9 Hz, 1H), 5.79 - 5.68 (m, 2H), 4.22 - 4.13 (m, 1H), 4.13 - 4.03 (m, 1H), 3.84 (s, 3H), 2.96 - 2.89 (m, 4H), 2.86 - 2.77 (m, 1H), 2.73 - 2.53 (m, 4H), 2.40 (s, 3H), 2.37 - 2.28 (m, 1H) ; 541.5[M+H]$^+$	1.02
394		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.46 (s, 1H), 8.36 (d, *J* = 0.9 Hz, 1H), 7.79 (d, *J* = 1.9 Hz, 1H), 7.74 - 7.67 (m, 1H), 7.55 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 6.95 (s, 1H), 6.75 (d, *J* = 8.4 Hz, 2H), 6.36 (dd, *J* = 17.0, 1.7 Hz, 1H), 6.27 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.79 - 5.68 (m, 2H), 4.22 - 4.14 (m, 1H), 4.14 - 4.03 (m, 1H), 3.85 (s, 3H), 3.12 - 3.05 (m, 2H), 2.86 - 2.77 (m, 1H), 2.79 - 2.70 (m, 2H), 2.45 (s, 6H), 2.37 (dd, *J* = 8.1, 4.5 Hz, 1H), 2.34 - 2.20 (m, 1H), 2.15 - 2.07 (m, 2H), 1.80 - 1.68 (m, 2H) ; 569.5[M+H]$^+$	1.05
395		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.67 (s, 1H), 8.35 (s, 1H), 8.17 (s, 1H), 7.79 (d, *J* = 1.7 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.55 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 6.90 (s, 1H), 6.76 (s, 1H), 6.71 (s, 1H), 6.43 - 6.35 (m, 1H), 6.30 (dd, *J* = 16.9, 9.8 Hz, 1H), 5.77 - 5.69 (m, 2H), 4.22 - 4.13 (m, 1H), 4.13 - 4.03 (m, 1H), 3.84 (s, 3H), 3.24 - 3.15 (m, 1H), 3.13 - 3.00 (m, 2H), 2.96 - 2.74 (m, 2H), 2.40 - 2.31 (m, 1H), 2.31 (s, 6H), 2.20 - 2.16 (m, 1H), 2.01 - 1.88 (m, 1H), 1.72 - 1.60 (m, 1H) ; 555.5[M+H]$^+$	1.00
396		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.91 (s, 1H), 8.57 (s, 1H), 8.37 (d, *J* = 0.9 Hz, 1H), 7.79 (d, *J* = 1.8 Hz, 1H), 7.71 (dt, *J* = 7.9, 1.6 Hz, 1H), 7.55 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 6.96 (s, 1H), 6.83 (s, 1H), 6.74 (s, 1H), 6.37 (dd, *J* = 16.9, 1.6 Hz, 1H), 6.27 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.77 - 5.71 (m, 2H), 4.22 - 4.14 (m, 1H), 4.14 - 4.03 (m, 1H), 3.83 (s, 3H), 2.96 - 2.92 (m, 4H), 2.86 - 2.77 (m, 1H), 2.74 - 2.56 (m, 4H), 2.52 (q, *J* = 7.2 Hz, 2H), 2.30 - 2.30 (m, 1H), 1.16 (t, *J* = 7.2 Hz, 3H) ; 555.5[M+H]$^+$	1.05

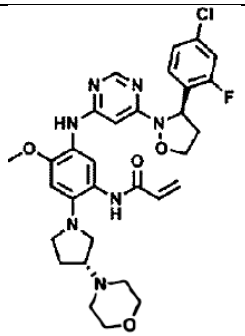
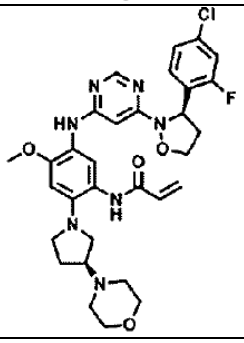
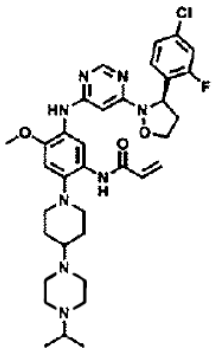
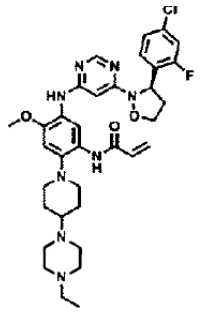
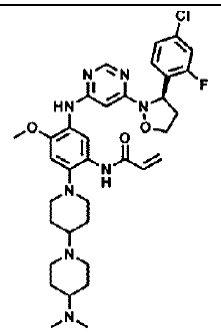
[542]

397		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)-(E)-4-(dimethylamino)but-2-enamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.97 (s, 1H), 8.64 (s, 1H), 8.17 (s, 2H), 7.12 (dq, J = 9.0, 3.0 Hz, 4H), 6.86 (s, 1H), 6.74 - 6.61 (m, 2H), 5.56 (dd, J = 8.7, 5.0 Hz, 2H), 4.13 (td, J = 8.0, 3.9 Hz, 2H), 3.88 - 3.75 (m, 9H), 2.85 (t, J = 4.6 Hz, 4H), 2.76 (dtd, J = 12.2, 7.8, 3.8 Hz, 3H), 2.25 (ddt, J = 12.1, 7.9, 3.7 Hz, 2H), 1.77 (s, 3H), 1.23 (s, 4H).: 596.4[M+H]$^+$	1.15
398		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.97 (s, 1H), 8.63 (s, 1H), 8.16 (s, 1H), 8.14 (s, 1H), 7.79 - 7.72 (m, 2H), 7.58 (t, J = 7.8 Hz, 1H), 6.82 (s, 1H), 6.70 - 6.50 (m, 1H), 6.36 (s, 1H), 6.25 - 6.17 (m, 1H), 5.72 (dd, J = 10.1, 2.0 Hz, 1H), 5.50 (dd, J = 8.7, 5.1 Hz, 1H), 4.15 (td, J = 7.9, 3.9 Hz, 1H), 3.80 (s, 3H), 3.07 (d, J = 11.4 Hz, 3H), 2.98 - 2.50 (m, 11H), 2.56 (s, 1H), 2.30 - 2.21 (m, 1H), 1.94 - 1.65 (m, 5H), 1.25 (dd, J = 11.4, 4.7 Hz, 4H).: 624.4[M+H]$^+$	1.21
399		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (s, 1H), 8.63 (s, 1H), 8.16 (s, 1H), 7.83 (d, J = 1.9 Hz, 1H), 7.75 (dd, J = 8.8, 6.9 Hz, 2H), 7.58 (t, J = 7.8 Hz, 1H), 6.82 (s, 1H), 6.67 (ddd, J = 19.8, 16.8, 10.3 Hz, 2H), 6.36 (s, 1H), 6.23 (q, J = 2.3 Hz, 1H), 5.75 - 5.70 (m, 1H), 5.50 (dd, J = 8.6, 5.1 Hz, 1H), 4.15 (td, J = 7.9, 3.9 Hz, 1H), 3.80 (s, 3H), 3.58 (q, J = 5.1, 3.4 Hz, 2H), 2.78 (dq, J = 8.2, 4.2 Hz, 3H), 2.60 (s, 3H), 2.31 - 2.21 (m, 2H), 1.78 - 1.64 (m, 3H), 1.26 (t, J = 7.1 Hz, 15H), 1.16 (s, 3H).: 638.5[M+H]$^+$	1.21
400		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.62 (s, 1H), 8.16 (d, J = 2.9 Hz, 2H), 7.83 (d, J = 1.8 Hz, 1H), 7.79 - 7.72 (m, 2H), 7.58 (t, J = 7.8 Hz, 1H), 6.83 (s, 1H), 6.65 (dd, J = 17.0, 10.2 Hz, 1H), 6.36 (s, 1H), 6.21 (dd, J = 17.0, 2.0 Hz, 1H), 5.72 (dd, J = 10.1, 2.0 Hz, 1H), 5.50 (dd, J = 8.7, 5.0 Hz, 1H), 4.15 (td, J = 7.9, 3.9 Hz, 1H), 3.80 (s, 3H), 3.50 (t, J = 4.5 Hz, 4H), 3.33 (s, 6H), 3.05 (d, J = 11.0 Hz, 2H), 2.78 (dtd, J = 12.1, 7.9, 3.8 Hz, 1H), 2.66 (ddd, J = 12.4, 9.5, 3.9 Hz, 2H), 2.26 (dtd, J = 12.6, 8.2, 4.9 Hz, 2H), 1.91 - 1.80 (m, 2H), 1.75 - 1.62 (m, 2H), 1.24 (d, J = 3.4 Hz, 2H), 0.85 (td, J = 8.1, 7.4, 3.1 Hz, 1H).: 611.4[M+H]$^+$	1.22
401		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.53 (s, 1H), 8.34 (d, J = 1.0 Hz, 1H), 7.53 (t, J = 8.2 Hz, 1H), 7.18 (s, 1H), 7.13 - 7.06 (m, 2H), 6.82 (s, 1H), 6.73 (s, 1H), 6.36 (dd, J = 17.0, 1.5 Hz, 1H), 6.26 (dd, J = 17.0, 10.0 Hz, 1H), 5.87 (dd, J = 8.8, 4.4 Hz, 1H), 5.75 (dd, J = 9.0, 1.6 Hz, 1H), 4.11 (td, J = 7.2, 6.2, 3.5 Hz, 1H), 4.06 (q, J = 8.0, 7.0 Hz, 1H), 3.84 (s, 3H), 3.02 - 2.90 (m, 4H), 2.84 - 2.78 (m, 1H), 2.76 - 2.58 (m, 4H), 2.56 (q, J = 7.2 Hz, 2H), 2.30 - 2.23 (m, 1H), 1.16 (t, J = 7.2 Hz, 3H): 582.4[M+H]$^+$	1.25

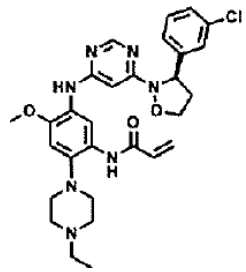
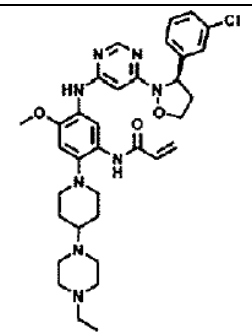
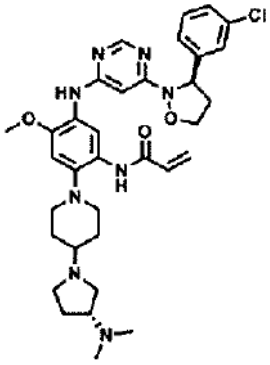
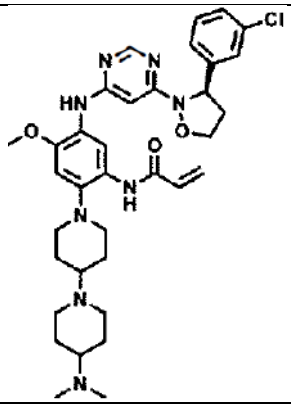
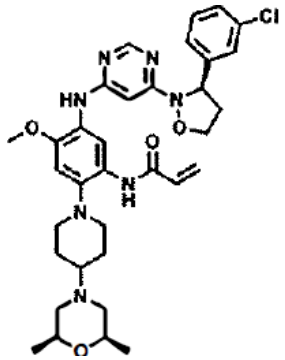
[543]

402		N-(1-(2-acrylamido-4-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-5-methoxyphenyl)piperidine-4-yl)-N-(1-isopropylpiperidine-4-yl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.10 (s, 1H), 9.48 (s, 1H), 8.31 (s, 1H), 7.95 (s, 1H), 7.51 - 7.47 (m, 1H), 7.40 (t, J = 8.3 Hz, 1H), 7.30 (dd, J = 8.4, 2.0 Hz, 1H), 6.90 (d, J = 38.7 Hz, 2H), 6.25 (dd, J = 17.0, 2.0 Hz, 2H), 6.08 (d, J = 16.5 Hz, 1H), 5.82 - 5.50 (m, 4H), 4.30 (dd, J = 7.7, 4.1 Hz, 2H), 4.06 (d, J = 7.8 Hz, 1H), 3.83 (s, 3H), 3.43 (s, 2H), 3.39 - 3.24 (m, 6H), 3.10 (d, J = 16.3 Hz, 2H), 3.04 - 2.87 (m, 4H), 2.30 - 2.21 (m, 1H), 1.69 (s, 5H), 1.29 (d, J = 6.6 Hz, 6H).; 747.3 [M+H]$^+$	1.5
403		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.79 (s, 1H), 8.44 (s, 1H), 8.32 (d, J = 1.0 Hz, 1H), 7.52 (t, J = 8.3 Hz, 1H), 7.33 (s, 1H), 7.13 - 7.06 (m, 2H), 6.74 (s, 1H), 6.71 (s, 1H), 6.42 - 6.27 (m, 2H), 5.86 (dd, J = 8.7, 4.4 Hz, 1H), 5.75 (dd, J = 9.0, 2.5 Hz, 1H), 4.12 (dt, J = 8.0, 4.0 Hz, 1H), 4.09 - 4.01 (m, 1H), 3.85 (s, 3H), 3.11 (d, J = 11.9 Hz, 2H), 2.73 (d, J = 12.3 Hz, 4H), 2.54 (s, 6H), 2.30 - 2.24 (m, 1H), 2.12 (d, J = 12.8 Hz, 2H), 1.88 - 1.79 (m, 2H); 506.4[M+H]$^+$	1.24
404		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.05 (s, 1H), 7.91 (s, 1H), 7.28 (t, J = 8.2 Hz, 1H), 7.15 - 7.07 (m, 2H), 6.83 (s, 1H), 6.49 (dd, J = 16.9, 10.2 Hz, 1H), 6.30 - 6.23 (m, 1H), 6.08 (s, 1H), 5.69 (d, J = 10.8 Hz, 1H), 5.62 (dd, J = 8.4, 5.6 Hz, 1H), 4.23 (td, J = 7.6, 4.3 Hz, 1H), 4.14 - 4.07 (m, 1H), 4.02 (dd, J = 15.4, 8.0 Hz, 1H), 3.85 (s, 2H), 3.76 (s, 3H), 3.60 (s, 1H), 3.43 (d, J = 5.8 Hz, 1H), 3.20 (s, 1H), 3.25 - 3.18 (m, 3H), 3.13 (d, J = 11.3 Hz, 2H), 2.80 (s, 7H), 2.76 (t, J = 12.4 Hz, 2H), 2.62 - 2.50 (m, 1H), 2.28 (td, J = 12.6, 5.2 Hz, 2H), 2.18 (d, J = 9.5 Hz, 2H), 1.98 (d, J = 11.4 Hz, 2H), 1.89 (s, 2H) ; 665.5 [M+H]$^+$	1.18
405		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 11.08 (s, 1H), 8.36 (d, J = 9.3 Hz, 2H), 8.08 (s, 1H), 7.23 (t, J = 8.3 Hz, 1H), 7.15 - 7.08 (m, 2H), 6.74 (s, 1H), 6.35 (d, J = 4.3 Hz, 2H), 6.09 (s, 1H), 5.75 (dd, J = 8.5, 4.9 Hz, 2H), 4.22 (dd, J = 12.7, 7.4 Hz, 1H), 4.08 (dd, J = 15.3, 7.6 Hz, 1H), 3.82 (s, 3H), 3.12 (s, 2H), 2.93 (s, 6H), 2.81 (d, J = 10.1 Hz, 2H), 2.35 (dt, J = 12.5, 7.2 Hz, 1H), 2.20 (s, 3H), 2.06 (s, 2H) ; 665.5 [M+H]$^+$	1.20

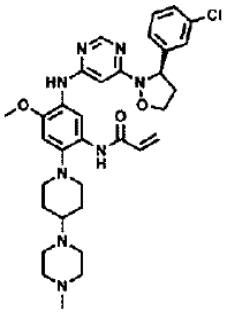
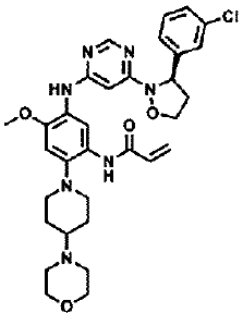
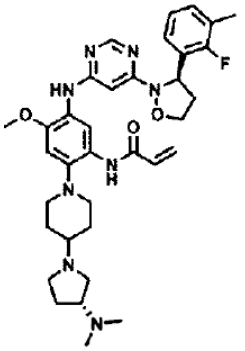
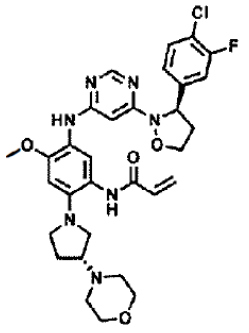
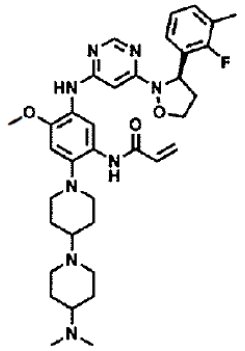
[544]

406		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 8.70 (s, 1H), 8.17 (s, 2H), 7.37 (t, *J* = 8.1 Hz, 1H), 7.11 (d, *J* = 9.1 Hz, 2H), 6.69 - 6.58 (m, 2H), 6.42 - 6.30 (m, 2H), 5.79 (dd, *J* = 8.4, 4.6 Hz, 1H), 5.71 (d, *J* = 10.3 Hz, 1H), 4.18 (dd, *J* = 12.5, 7.7 Hz, 1H), 4.06 (dd, *J* = 15.8, 7.9 Hz, 1H), 3.97 (d, *J* = 3.1 Hz, 4H), 3.81 (s, 3H), 3.74 (d, *J* = 11.0 Hz, 1H), 3.51 (s, 1H), 3.23 (d, *J* = 7.0 Hz, 2H), 3.11 - 3.02 (m, 2H), 2.83 (ddd, *J* = 24.6, 12.9, 7.1 Hz, 2H), 2.41 (d, *J* = 6.5 Hz, 1H), 2.38 - 2.24 (m, 2H), 2.06 (s, 2H) : 624.4 [M+H]$^+$	1.29
407		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 10.96 (s, 1H), 8.86 (s, 1H), 8.06 (s, 1H), 7.94 (s, 1H), 7.23 (t, *J* = 8.3 Hz, 1H), 7.15 - 7.08 (m, 2H), 6.60 (dd, *J* = 16.8, 10.2 Hz, 1H), 6.57 (s, 1H), 6.32 (d, *J* = 16.8 Hz, 1H), 5.84 (s, 1H), 5.76 - 5.65 (m, 2H), 4.20 (dd, *J* = 12.8, 7.5 Hz, 1H), 4.03 (dd, *J* = 15.0, 7.2 Hz, 5H), 3.81 (s, 1H), 3.79 (s, 3H), 3.65 (d, *J* = 4.6 Hz, 1H), 3.25 (s, 1H), 2.98 (dd, *J* = 16.5, 8.2 Hz, 1H), 2.93 - 2.84 (m, 1H), 2.58 (dd, *J* = 10.8, 7.8 Hz, 1H), 2.45 - 2.28 (m, 3H), 2.06 (s, 2H) : 624.5 [M+H]$^+$	1.29
408		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.70 (s, 1H), 9.17 (s, 1H), 8.27 (s, 1H), 8.00 (s, 1H), 7.52 - 7.35 (m, 2H), 7.30 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.90 (s, 1H), 6.70 (dd, *J* = 16.9, 10.2 Hz, 1H), 6.25 (dd, *J* = 17.1, 2.0 Hz, 2H), 5.71 (ddd, *J* = 35.7, 8.4, 4.3 Hz, 2H), 4.29 - 4.25 (m, 1H), 4.01 (d, *J* = 7.0 Hz, 1H), 3.81 (s, 3H), 3.76 (s, 6H), 3.42 (d, *J* = 5.4 Hz, 1H), 3.38 - 3.33 (m, 1H), 3.30 - 3.25 (m, 1H), 3.21 (d, *J* = 10.8 Hz, 2H), 2.93 - 2.87 (m, 1H), 2.79 (t, *J* = 11.8 Hz, 2H), 2.20 - 2.02 (m, 6H), 1.32 (d, *J* = 6.5 Hz, 6H).: 679.3 [M+H]$^+$	1.41
409		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.05 (s, 1H), 9.22 (s, 1H), 8.30 (s, 1H), 7.93 (s, 1H), 7.40 (dd, *J* = 10.3, 2.0 Hz, 1H), 7.40 (t, *J* = 8.3 Hz, 1H), 7.30 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.91 (s, 1H), 6.77 - 6.64 (m, 1H), 6.25 (dd, *J* = 17.0, 1.9 Hz, 2H), 5.83 - 5.62 (m, 2H), 4.36 - 4.30 (m, 4H), 4.06 (d, *J* = 7.8 Hz, 1H), 3.81 (s, 3H), 3.67 (s, 2H), 3.57 (d, *J* = 11.1 Hz, 2H), 3.45 (s, 1H), 3.22 (s, 4H), 2.93 (d, *J* = 8.9 Hz, 1H), 2.81 (s, 2H), 2.30 - 2.01 (m, 6H), 1.29 (t, *J* = 7.2 Hz, 3H).: 665.3 [M+H]$^+$	1.4
410		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.07 (s, 1H), 9.24 (s, 1H), 8.31 (s, 1H), 7.92 (s, 1H), 7.40 (dd, *J* = 10.3, 2.1 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 7.30 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.90 (s, 1H), 6.75 (dd, *J* = 17.0, 10.3 Hz, 1H), 6.28 - 6.14 (m, 2H), 5.71 (dd, *J* = 24.0, 3.0 Hz, 2H), 4.31 (td, *J* = 7.5, 4.1 Hz, 1H), 4.05 (q, *J* = 7.8 Hz, 1H), 3.82 (d, *J* = 2.6 Hz, 3H), 3.63 (s, 1H), 3.50 (d, *J* = 8.0 Hz, 1H), 3.40 - 3.33 (m, 1H), 3.23 (d, *J* = 11.1 Hz, 2H), 3.14 (s, 2H), 2.97 - 2.88 (m, 1H), 2.79 (s, 2H), 2.71 (d, *J* = 4.6 Hz, 6H), 2.54 (s, 1H), 2.30 (d, *J* = 8.8 Hz, 5H), 2.18 (d, *J* = 10.3 Hz, 2H), 2.08 (d, *J* = 11.9 Hz, 2H).:679.3 [M+H]$^+$	1.33

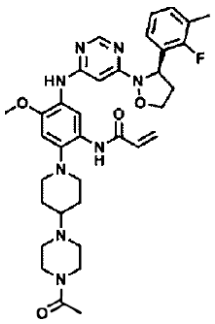
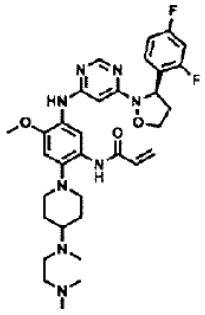
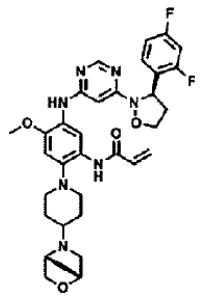
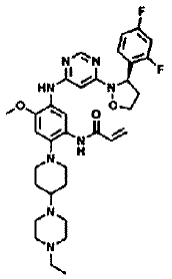
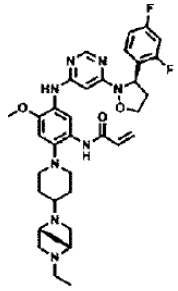
[545]

411		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (s, 1H), 8.62 (s, 1H), 8.18 - 8.11 (m, 2H), 7.47 - 7.29 (m, 4H), 6.86 (s, 1H), 6.59 (dd, J = 17.0, 10.2 Hz, 1H), 6.36 (s, 1H), 6.20 (dd, J = 16.9, 2.0 Hz, 1H), 5.72 (dd, J = 9.9, 2.0 Hz, 1H), 5.54 (dd, J = 8.7, 5.0 Hz, 1H), 4.14 (td, J = 7.9, 3.8 Hz, 1H), 3.89 - 3.75 (m, 4H), 2.87 (t, J = 4.8 Hz, 4H), 2.77 (dtd, J = 12.0, 7.8, 3.8 Hz, 2H), 2.57 (s, 3H), 2.40 (q, J = 7.1 Hz, 2H), 2.30 - 2.17 (m, 1H), 1.04 (t, J = 7.1 Hz, 3H) : 564.5 [M+H]$^+$	1.15
412		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.60 (s, 1H), 8.15 (d, J = 4.8 Hz, 2H), 7.47 - 7.28 (m, 4H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.34 (s, 1H), 6.21 (dd, J = 17.0, 2.0 Hz, 1H), 5.77 - 5.66 (m, 1H), 5.54 (dd, J = 8.7, 5.1 Hz, 1H), 4.14 (td, J = 7.9, 3.8 Hz, 1H), 3.87 - 3.75 (m, 4H), 3.05 (d, J = 11.1 Hz, 2H), 2.77 (dtd, J = 11.6, 7.8, 3.5 Hz, 1H), 2.72 - 2.61 (m, 3H), 2.53 (s, 3H), 2.44 - 2.17 (m, 8H), 1.85 (d, J = 12.0 Hz, 2H), 1.76 - 1.61 (m, 2H), 0.99 (t, J = 7.1 Hz, 3H) : 647.5 [M+H]$^+$	1.14
413		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.60 (s, 1H), 8.15 (d, J = 5.2 Hz, 2H), 7.48 - 7.29 (m, 4H), 6.82 (s, 1H), 6.64 (dd, J = 17.0, 10.2 Hz, 1H), 6.34 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.71 (d, J = 10.3 Hz, 1H), 5.54 (dd, J = 8.7, 5.1 Hz, 1H), 4.14 (td, J = 7.9, 3.8 Hz, 1H), 3.89 - 3.74 (m, 4H), 3.01 (d, J = 11.3 Hz, 2H), 2.86 - 2.72 (m, 2H), 2.67 (t, J = 10.6 Hz, 4H), 2.34 (d, J = 8.5 Hz, 1H), 2.29 - 2.18 (m, 1H), 2.12 (s, 6H), 1.97 - 1.77 (m, 4H), 1.76 - 1.52 (m, 4H) : 647.5 [M+H]$^+$	1.06
414		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.60 (s, 1H), 8.15 (d, J = 6.3 Hz, 2H), 7.46 - 7.29 (m, 4H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.34 (s, 1H), 6.21 (dd, J = 17.0, 2.0 Hz, 1H), 5.72 (d, J = 10.3 Hz, 1H), 5.54 (dd, J = 8.7, 5.1 Hz, 1H), 4.14 (td, J = 7.8, 3.7 Hz, 1H), 3.89 - 3.75 (m, 4H), 3.01 (dd, J = 31.8, 11.2 Hz, 4H), 2.77 (dtd, J = 11.9, 7.8, 3.6 Hz, 1H), 2.72 - 2.60 (m, 2H), 2.35 (d, J = 13.0 Hz, 1H), 2.24 (s, 6H), 2.17 (q, J = 11.9, 9.8 Hz, 4H), 1.85 - 1.65 (m, 6H), 1.37 (d, J = 11.9 Hz, 2H)) : 661.5 [M+H]$^+$	1.04
415		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.05 (s, 1H), 8.20 (d, J = 16.0 Hz, 1H), 8.06 (s, 1H), 7.44 (s, 1H), 7.41 - 7.29 (m, 3H), 6.86 (s, 1H), 6.62 (t, J = 13.9 Hz, 1H), 6.30 - 6.21 (m, 2H), 5.75 (d, J = 10.4 Hz, 1H), 5.53 (t, J = 6.9 Hz, 1H), 4.20 (s, 1H), 3.89 (d, J = 22.7 Hz, 4H), 3.81 (s, 3H), 3.51 (d, J = 11.0 Hz, 4H), 3.29 (s, 1H), 3.18 (d, J = 11.4 Hz, 2H), 2.74 (t, J = 11.3 Hz, 4H), 2.27 (s, 1H), 2.15 (d, J = 11.7 Hz, 2H), 1.99 - 1.77 (m, 2H), 1.18 (d, J = 6.2 Hz, 5H). : 648.5[M+H]+	1.25

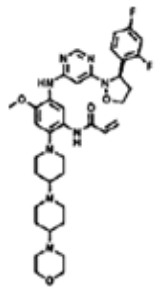
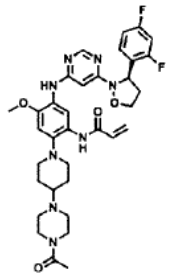
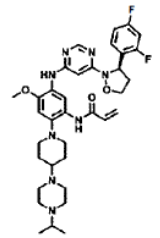
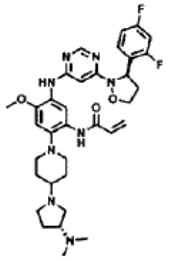
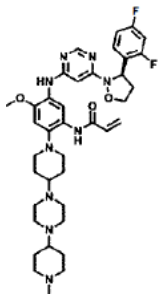
[546]

416		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.06 (s, 1H), 8.24 (s, 1H), 8.06 (s, 1H), 7.43 (q, J = 2.3 Hz, 1H), 7.42 - 7.32 (m, 3H), 6.86 (s, 1H), 6.63 (dd, J = 17.0, 10.2 Hz, 1H), 6.24 (d, J = 16.6 Hz, 2H), 5.74 (d, J = 10.4 Hz, 1H), 5.53 (dd, J = 8.5, 5.2 Hz, 1H), 4.21 (s, 1H), 3.93 (d, J = 8.5 Hz, 1H), 3.81 (s, 3H), 3.63 (s, 2H), 3.17 (d, J = 11.7 Hz, 8H), 2.93 - 2.82 (m, 4H), 2.76 (t, J = 10.9 Hz, 3H), 2.30 (dd, J = 15.8, 10.4 Hz, 2H), 2.05 (s, 2H), 1.89 (d, J = 13.3 Hz, 2H). : 633.5[M+H]+	1.13
417		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.08 (d, J = 10.5 Hz, 1H), 8.22 (d, J = 11.7 Hz, 1H), 8.06 (s, 1H), 7.43 (d, J = 6.2 Hz, 1H), 7.42 - 7.28 (m, 3H), 6.86 (s, 1H), 6.59 (d, J = 11.0 Hz, 1H), 6.32 - 6.16 (m, 2H), 5.74 (d, J = 10.4 Hz, 1H), 5.53 (dd, J = 8.6, 5.2 Hz, 1H), 4.20 (s, 1H), 4.05 (d, J = 12.6 Hz, 3H), 3.97 - 3.85 (m, 2H), 3.81 (s, 3H), 3.71 (s, 3H), 3.49 (d, J = 12.2 Hz, 2H), 3.32 (s, 1H), 3.18 (d, J = 9.5 Hz, 4H), 2.90 - 2.67 (m, 2H), 2.35 - 2.20 (m, 1H), 2.14 (d, J = 11.4 Hz, 2H), 1.91 (s, 1H).: 620.5[M+H]+	1.16
418		N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.85 (s, 1H), 8.48 (s, 1H), 8.35 (s, 1H), 7.39 (td, J = 7.5, 1.9 Hz, 1H), 7.12 - 7.04 (m, 1H), 7.02 - 6.94 (m, 2H), 6.73 (d, J = 11.0 Hz, 2H), 6.39 - 6.27 (m, 1H), 6.27 - 6.20 (m, 1H), 5.90 (dd, J = 8.8, 4.4 Hz, 1H), 5.73 (dd, J = 9.8, 1.7 Hz, 1H), 4.17 - 4.01 (m, 2H), 3.84 (s, 3H), 3.55 (h, J = 6.7 Hz, 1H), 3.09 - 2.88 (m, 7H), 2.83 - 2.62 (m, 4H), 2.51 (dd, J = 9.1, 7.2 Hz, 1H), 2.33 (s, 6H), 2.14 - 2.00 (m, 3H), 1.93 - 1.66 (m, 3H), 1.36 (d, J = 6.6 Hz, 3H).: 645.6[M+H]$^+$	1.05
419		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.65 (s, 1H), 8.34 (s, 1H), 8.16 (s, 1H), 7.35 (t, J = 7.9 Hz, 1H), 7.31 - 7.28 (m, 1H), 7.18 (dd, J = 8.4, 2.0 Hz, 1H), 6.95 (s, 1H), 6.75 (s, 1H), 6.67 (s, 1H), 6.43 - 6.23 (m, 2H), 5.74 (dd, J = 9.7, 1.8 Hz, 1H), 5.65 (dd, J = 8.7, 4.5 Hz, 1H), 4.15 (td, J = 8.0, 4.2 Hz, 1H), 4.05 (q, J = 8.0 Hz, 1H), 3.83 (s, 3H), 3.76 (t, J = 4.7 Hz, 4H), 3.25 - 3.05 (m, 4H), 2.98 (p, J = 7.4 Hz, 1H), 2.76 (dtd, J = 12.3, 8.1, 4.2 Hz, 1H), 2.53 (ddt, J = 39.6, 11.1, 4.6 Hz, 4H), 2.33 (ddt, J = 11.9, 7.9, 4.0 Hz, 1H), 2.19 (ddt, J = 12.1, 7.6, 4.3 Hz, 1H), 1.99 - 1.91 (m, 1H).: 624.4[M+H]$^+$	1.15
420		N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.23 (s, 1H), 7.93 (s, 1H), 7.10 (dt, J = 24.4, 7.6 Hz, 3H), 7.08 (t, J = 7.6 Hz, 1H), 6.72 (dd, J = 16.9, 10.2 Hz, 1H), 6.48 (d, J = 16.9 Hz, 1H), 6.10 (s, 1H), 5.90 (d, J = 10.4 Hz, 1H), 5.73 (t, J = 7.0 Hz, 1H), 4.44 (td, J = 7.5, 4.4 Hz, 1H), 4.23 (q, J = 7.7 Hz, 1H), 3.93 (d, J = 8.2 Hz, 5H), 3.79 - 3.64 (m, 2H), 3.53 (ddq, J = 12.7, 8.5, 4.1 Hz, 2H), 3.37 (d, J = 12.1 Hz, 2H), 3.30 - 3.22 (m, 1H), 3.07 (ddd, J = 13.4, 8.5, 5.5 Hz, 1H), 2.97 (s, 6H), 2.91 (d, J = 3.6 Hz, 2H), 2.48 (dd, J = 10.1, 12.2 Hz, 5H), 2.39 - 2.24 (m, 7H).: 659.6[M+H]$^+$	1.06

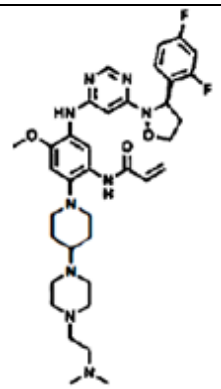
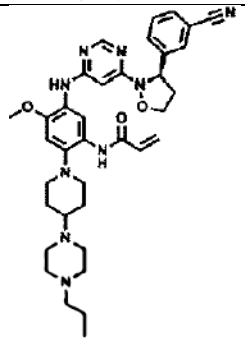
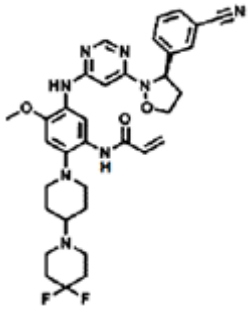
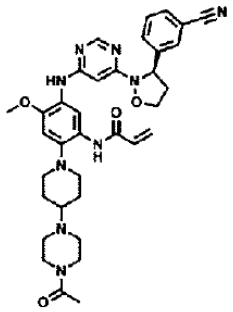
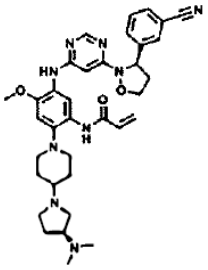
[547]

421		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.42 (s, 1H), 8.36 (d, *J* = 0.9 Hz, 1H), 7.39 (td, *J* = 7.4, 1.9 Hz, 1H), 7.07 (dt, *J* = 7.4, 3.8 Hz, 1H), 7.02 - 6.91 (m, 2H), 6.73 (d, *J* = 8.9 Hz, 2H), 6.45 - 6.20 (m, 2H), 5.90 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.78 - 5.71 (m, 1H), 4.17 - 4.03 (m, 2H), 3.84 (s, 3H), 3.66 (t, *J* = 5.0 Hz, 2H), 3.51 (t, *J* = 5.0 Hz, 2H), 3.12 - 3.03 (m, 2H), 2.84 (td, *J* = 8.1, 4.3 Hz, 1H), 2.73 (qd, *J* = 11.9, 2.2 Hz, 2H), 2.61 (dt, *J* = 13.8, 5.0 Hz, 4H), 2.28 (d, *J* = 2.0 Hz, 3H), 2.11 (s, 3H), 2.06 - 2.00 (m, 2H), 1.67 (qd, *J* = 12.0, 3.9 Hz, 2H), 1.43 (d, *J* = 6.6 Hz, 2H).; 650.5[M+H]$^+$	1.15
422		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2-(dimethylamino)ethyl)(methyl)amino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.88 (s, 1H), 8.46 (s, 1H), 8.37 (s, 1H), 7.56 (dt, *J* = 14.8, 7.4 Hz, 1H), 6.92 (s, 1H), 6.87 - 6.70 (m, 4H), 6.40 - 6.22 (m, 2H), 5.88 (dd, *J* = 8.9, 4.3 Hz, 1H), 5.80 - 5.71 (m, 1H), 4.16 - 4.03 (m, 2H), 3.85 (s, 3H), 3.06 (d, *J* = 11.6 Hz, 2H), 2.86 - 2.62 (m, 5H), 2.37 (s, 3H), 2.30 (s, 6H), 1.99 (d, *J* = 12.5 Hz, 2H), 1.80 - 1.68 (m, 6H).; 637.6 [M+H]$^+$	1.06
423		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 - 8.85 (s, 1H), 8.48 (s, 1H), 8.37 (s, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 6.93 (s, 1H), 6.80 (m, 4H), 6.35 (d, *J* = 16.6 Hz, 1H), 6.26 (m, 1H), 5.88 (m, 1H), 5.73 (d, *J* = 11.0 Hz, 1H), 4.44 (s, 1H), 4.00 (m, 4H), 3.86 (s, 3H), 3.77 (s, 1H), 3.67 (d, *J* = 7.7 Hz, 1H), 3.14 (d, *J* = 9.6 Hz, 1H), 3.03 (d, *J* = 11.8 Hz, 2H), 2.78 (m, 4H), 2.58 (m, 1H), 2.50 (d, *J* = 9.8 Hz, 1H), 2.27 (m, 1H), 2.06 (m 1H), 1.92 (d, *J* = 11.3 Hz, 2H), 1.84 (s, 1H).; 634.5 [M+H]$^+$	1.16
424		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 7.56 (m, 1H), 6.92 (s, 1H), 6.83 (q, 2H), 6.75 (s, 2H), 6.35 (d, *J* = 16.8 Hz, 1H), 6.26 (m, 1H), 5.87 (m, 1H), 5.73 (d, *J* = 10.3 Hz, 1H), 4.10 (s, 2H), 3.85 (s, 3H), 3.06 (d, *J* = 11.5 Hz, 2H), 2.86 - 2.63 (m, 8H), 2.54 (s, 3H), 2.44 (m, 3H), 2.30 (m, 3H), 2.09 (d, *J* = 5.0 Hz, 2H), 1.11 (s, 3H).; 649.5 [M+H]$^+$	1.10
425		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.47 (s, 1H), 8.36 (s, 1H), 7.56 m, 1H), 6.91 (s, 1H), 6.80 m, 4H), 6.34 (d, *J* = 16.9 Hz, 1H), 6.25 (m, 1H), 5.86 (m, 1H), 5.72 (d, *J* = 11.0 Hz, 1H), 4.00 (m, 2H), 3.85 (s, 3H), 3.61 (s, 1H), 3.36 (s, 1H), 3.00 (m, 3H), 2.88 (d, *J* = 9.9 Hz, 2H), 2.76 (d, *J* = 23.4 Hz, 3H), 2.58 (m, 6H), 2.27 (m, 1H), 2.02 (m, 1H), 1.91 (m, 1H), 1.80 (m, 2H), 1.10 (t, 3H).; 661.5 [M+H]$^+$	1.07

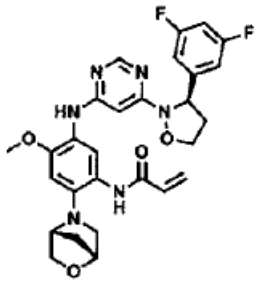
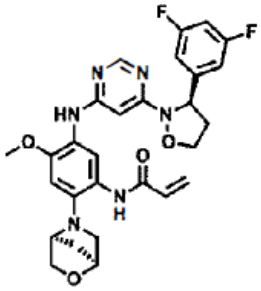
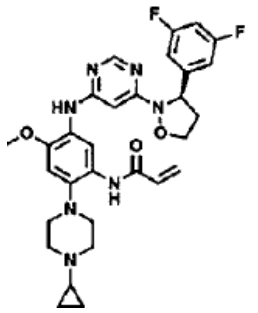
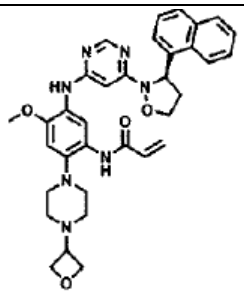
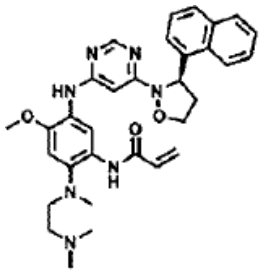
[548]

426		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholino-[1,4'-bipiperidine]-1'-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.56 (m, 1H), 6.92 (s, 1H), 6.82 (m, 2H), 6.75 (m, 2H), 6.36 (d, *J* = 17.0 Hz, 1H), 6.27 (m, 1H), 5.87 (m, 1H), 5.74 (d, *J* = 10.9 Hz, 1H), 4.10 (d, *J* = 11.3 Hz, 3H), 3.85 (s, 3H), 3.73 (m, 4H), 3.15 - 3.02 (m, 4H), 2.79 (m, 2H), 2.72 (m, 2H), 2.57 (m, 4H), 2.38 (m, 2H), 2.22 (m, 5H), 2.03 (d, *J* = 14.6 Hz, 2H), 1.87 (d, *J* = 13.5 Hz, 2H).; 705.6 [M+H]$^+$	1.12
427		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.88 (s, 1H), 8.41 (s, 1H), 8.37 (d, *J* = 0.9 Hz, 1H), 7.56 (q, *J* = 8.4 Hz, 1H), 6.93 (s, 1H), 6.87 - 6.78 (m, 2H), 6.75 (s, 2H), 6.40 - 6.33 (m, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.88 (dd, *J* = 8.7, 4.3 Hz, 1H), 5.74 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.14 - 4.05 (m, 2H), 3.85 (s, 3H), 3.67 (t, *J* = 5.1 Hz, 2H), 3.52 (t, *J* = 5.1 Hz, 2H), 3.07 (d, *J* = 11.5 Hz, 2H), 2.81 (dd, *J* = 8.2, 4.2 Hz, 1H), 2.77 - 2.68 (m, 2H), 2.61 (dt, *J* = 13.9, 5.0 Hz, 4H), 2.44 - 2.36 (m, 1H), 2.32 - 2.23 (m, 1H), 2.11 (s, 3H), 2.04 (d, *J* = 12.4 Hz, 2H), 1.60 (t, *J* = 11.8 Hz, 2H).; 663.5[M+H]	1.33
428		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 7.56 (td, *J* = 8.6, 6.5 Hz, 1H), 6.92 (s, 1H), 6.87 - 6.77 (m, 2H), 6.75 (d, *J* = 2.4 Hz, 2H), 6.39 - 6.32 (m, 1H), 6.24 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.87 (dd, *J* = 8.8, 4.3 Hz, 1H), 5.73 (dd, *J* = 9.9, 1.5 Hz, 1H), 4.15 - 4.05 (m, 2H), 3.84 (s, 3H), 3.06 (d, *J* = 11.5 Hz, 2H), 2.82 - 2.61 (m, 10H), 2.35 - 2.22 (m, 2H), 2.10 (d, *J* = 12.4 Hz, 2H), 1.72 - 1.60 (m, 4H), 1.08 (d, *J* = 6.5 Hz, 6H).; 663.6[M+H]	1.09
429		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.48 (s, 1H), 8.36 (s, 1H), 7.56 (q, *J* = 8.3 Hz, 1H), 6.99 (s, 1H), 6.88 - 6.77 (m, 2H), 6.75 (s, 1H), 6.38 - 6.31 (m, 1H), 6.30 - 6.12 (m, 2H), 5.87 (dd, *J* = 8.8, 4.3 Hz, 1H), 5.75 - 5.70 (m, 1H), 4.14 - 4.04 (m, 2H), 3.85 (s, 3H), 3.01 (t, *J* = 16.2 Hz, 5H), 2.87 - 2.60 (m, 5H), 2.53 (d, *J* = 8.7 Hz, 1H), 2.34 (s, 6H), 2.07 (d, *J* = 10.6 Hz, 2H), 1.88 (t, *J* = 10.2 Hz, 1H), 1.75 (t, *J* = 11.2 Hz, 2H), 1.38 (s, 2H).; 640.5[M+H]	1.04
430		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.56 (q, *J* = 8.0 Hz, 1H), 6.92 (s, 1H), 6.87 - 6.77 (m, 2H), 6.75 (s, 2H), 6.35 (d, *J* = 16.9 Hz, 1H), 6.23 (dd, *J* = 16.8, 10.0 Hz, 1H), 5.87 (dd, *J* = 8.8, 4.3 Hz, 1H), 5.73 (d, *J* = 10.4 Hz, 1H), 4.14 - 4.04 (m, 2H), 3.84 (s, 3H), 3.24 (t, *J* = 6.1 Hz, 2H), 3.19 - 3.16 (m, 2H), 3.06 (d, *J* = 11.7 Hz, 2H), 2.92 (d, *J* = 11.2 Hz, 2H), 2.66 (s, 4H), 2.30 (t, *J* = 6.2 Hz, 2H), 2.27 (s, 3H), 2.09 (d, *J* = 12.5 Hz, 2H), 1.95 (t, *J* = 11.6 Hz, 2H), 1.83 (d, *J* = 12.3 Hz, 2H), 1.65 (t, *J* = 6.2 Hz, 4H), 1.14 (t, *J* = 7.2 Hz, 4H).; 718.6[M+H]	1.13

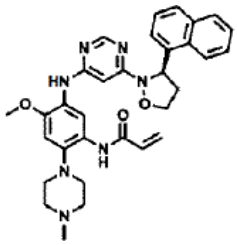
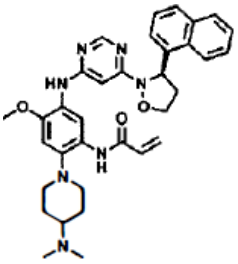
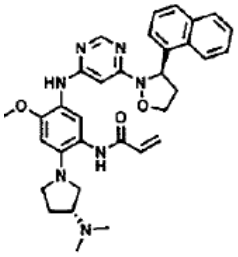
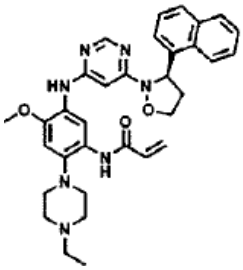
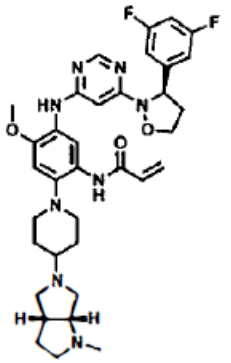
[549]

431		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.46 (d, J = 10.8 Hz, 1H), 8.35 (d, J = 8.7 Hz, 1H), 7.58 - 7.52 (m, 1H), 6.93 (d, J = 4.0 Hz, 1H), 6.88 - 6.78 (m, 3H), 6.75 (s, 1H), 6.35 (d, J = 17.1 Hz, 1H), 6.24 (dd, J = 16.8, 10.1 Hz, 1H), 5.85 (s, 1H), 5.74 (d, J = 10.0 Hz, 1H), 4.14 - 4.07 (m, 2H), 3.94 (d, J = 7.7 Hz, 1H), 3.85 (s, 3H), 3.27 (dd, J = 7.7, 4.5 Hz, 4H), 3.22 (d, J = 4.5 Hz, 2H), 3.18 (dd, J = 7.3, 5.5 Hz, 4H), 2.60 - 2.55 (m, 8H), 2.30 (s, 6H), 1.77 - 1.72 (m, 4H).: 692.6[M+H]	1.12
432		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.05 (s, 1H), 8.69 (s, 1H), 8.17 (d, J = 1.0 Hz, 1H), 7.83 (d, J = 1.8 Hz, 1H), 7.80 - 7.72 (m, 2H), 7.58 (t, J = 7.8 Hz, 1H), 6.84 (s, 1H), 6.66 (dd, J = 16.9, 10.2 Hz, 1H), 6.37 (s, 1H), 6.22 (dd, J = 17.0, 2.0 Hz, 1H), 5.73 (d, J = 10.4 Hz, 1H), 5.50 (dd, J = 8.7, 5.1 Hz, 1H), 4.15 (td, J = 7.9, 3.8 Hz, 1H), 3.81 (s, 3H), 3.59 (pd, J = 6.6, 3.9 Hz, 7H), 3.34 (s, 14H), 3.11 (dt, J = 7.4, 3.7 Hz, 6H), 2.08 (s, 3H).: 652.5[M+H]$^+$	1.10
433		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.62 (s, 1H), 8.16 (s, 1H), 7.83 (d, J = 1.9 Hz, 1H), 7.81 - 7.70 (m, 2H), 7.58 (t, J = 7.8 Hz, 1H), 6.82 (s, 1H), 6.66 (dd, J = 16.9, 10.2 Hz, 1H), 6.36 (s, 1H), 6.21 (dd, J = 17.0, 2.0 Hz, 1H), 5.72 (dd, J = 10.3, 2.0 Hz, 1H), 5.50 (dd, J = 8.7, 5.0 Hz, 1H), 4.15 (td, J = 7.9, 3.9 Hz, 1H), 3.80 (s, 3H), 3.33 (s, 5H), 3.06 (d, J = 11.1 Hz, 2H), 2.78 (dtd, J = 12.0, 7.9, 3.8 Hz, 1H), 2.72 - 2.55 (m, 6H), 2.31 - 2.20 (m, 1H), 1.95 (tt, J = 13.8, 5.4 Hz, 4H), 1.84 - 1.70 (m, 4H).: 645.4 [M+H]$^+$	1.18
434		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.96 (s, 1H), 8.62 (s, 1H), 8.16 (s, 1H), 7.83 (d, J = 1.8 Hz, 1H), 7.80 - 7.72 (m, 2H), 7.58 (t, J = 7.8 Hz, 1H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.36 (s, 1H), 6.23 (dd, J = 33.1, 2.0 Hz, 2H), 5.72 (dd, J = 10.2, 2.0 Hz, 1H), 5.50 (dd, J = 8.6, 5.0 Hz, 1H), 4.15 (td, J = 7.8, 3.8 Hz, 1H), 3.80 (s, 3H), 3.46 - 3.21 (m, 8H), 3.06 (d, J = 11.1 Hz, 2H), 2.78 (dtd, J = 12.0, 7.9, 3.8 Hz, 1H), 2.66 (td, J = 10.4, 9.6, 6.0 Hz, 2H), 2.53 (t, J = 4.9 Hz, 2H), 2.47 (d, J = 4.4 Hz, 2H), 1.99 (s, 3H), 1.87 - 1.79 (m, 2H), 1.79 - 1.66 (m, 2H).: 652.5[M+H]$^+$	1.10
435		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	638.6[M+H]$^+$	1.01

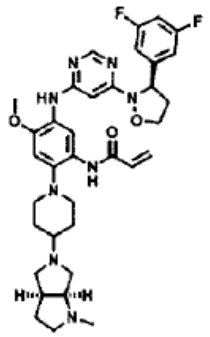
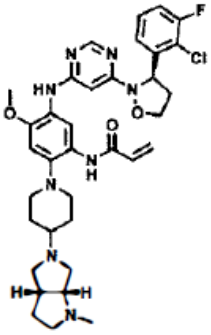
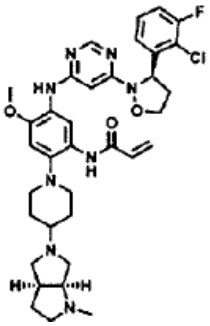
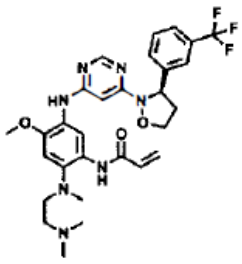
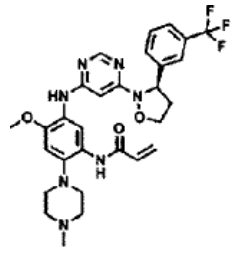
[550]

436		N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.13 (s, 1H), 7.52 (s, 1H), 7.07 (d, J = 6.6 Hz, 2H), 6.84 (dd, J = 10.1, 8.0 Hz, 1H), 6.57 (s, 1H), 6.48 (dd, J = 17.0, 10.1 Hz, 1H), 6.41 - 6.26 (m, 2H), 5.79 (dd, J = 10.1, 1.7 Hz, 1H), 5.56 (dd, J = 8.5, 4.8 Hz, 1H), 4.60 (s, 1H), 4.38 (s, 1H), 4.17 - 4.10 (m, 2H), 3.98 - 3.84 (m, 5H), 3.51 (d, J = 8.3 Hz, 1H), 3.14 (d, J = 9.2 Hz, 1H), 2.88 - 2.75 (m, 1H), 2.33 (dt, J = 8.7, 6.4 Hz, 1H), 2.06 (d, J = 8.3 Hz, 1H), 1.98 - 1.89 (m, 1H). : 551.4[M+H]$^+$	1.38
437		N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.14 (s, 1H), 7.52 (s, 1H), 7.08 (t, J = 6.4 Hz, 2H), 6.84 (ddd, J = 9.1, 5.7, 2.2 Hz, 1H), 6.57 (s, 1H), 6.49 (dd, J = 17.0, 10.1 Hz, 1H), 6.41 - 6.33 (m, 2H), 5.79 (dd, J = 10.1, 1.7 Hz, 1H), 5.56 (dd, J = 8.6, 4.6 Hz, 1H), 4.60 (s, 1H), 4.38 (s, 1H), 4.20 - 4.00 (m, 2H), 3.98 - 3.86 (m, 5H), 3.53 (d, J = 9.5 Hz, 1H), 3.13 (d, J = 9.6 Hz, 1H), 2.87 - 2.73 (m, 1H), 2.38 - 2.26 (m, 1H), 2.06 (d, J = 8.2 Hz, 1H), 1.98 - 1.90 (m, 1H). : 551.4[M+H]$^+$	1.37
438		N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.35 (s, 1H), 8.20 (d, J = 7.2 Hz, 1H), 7.07 (d, J = 6.7 Hz, 2H), 6.92 (s, 1H), 6.84 (ddd, J = 9.1, 5.6, 2.2 Hz, 1H), 6.58 - 6.46 (m, 2H), 6.37 (dd, J = 17.0, 1.3 Hz, 1H), 5.82 (d, J = 10.5 Hz, 1H), 5.57 (dd, J = 8.6, 4.8 Hz, 1H), 4.15 (td, J = 7.8, 4.2 Hz, 1H), 3.97 (q, J = 8.0 Hz, 1H), 3.80 (d, J = 7.7 Hz, 3H), 2.97 - 2.78 (m, 9H), 2.38 - 2.28 (m, 1H), 1.86 - 1.77 (m, 1H), 0.52 (ddd, J = 14.7, 10.7, 6.9 Hz, 4H). : 578.4 [M+H]$^+$	1.26
439		N-(4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.96 (s, 1H), 8.50 (s, 1H), 8.38 (d, J = 0.9 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.92 - 7.85 (m, 1H), 7.77 (dd, J = 7.7, 4.6 Hz, 2H), 7.60 - 7.41 (m, 3H), 6.95 (s, 1H), 6.81 (d, J = 11.5 Hz, 2H), 6.45 - 6.32 (m, 2H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.74 (dd, J = 10.0, 1.5 Hz, 1H), 4.60 (dt, J = 20.7, 6.3 Hz, 4H), 4.22 - 4.12 (m, 2H), 3.85 (s, 3H), 3.61 (p, J = 6.4 Hz, 1H), 3.03 - 2.90 (m, 5H), 2.63 - 2.43 (m, 4H), 2.46 - 2.37 (m, 1H). : 608.5 [M+H]$^+$	1.25
440		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 10.10 (s, 1H), 9.00 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.88 (dd, J = 8.0, 1.5 Hz, 1H), 7.78 (dd, J = 10.6, 7.7 Hz, 2H), 7.60 - 7.41 (m, 3H), 6.96 (s, 1H), 6.86 - 6.77 (m, 2H), 6.45 - 6.36 (m, 2H), 6.20 (dd, J = 17.0, 10.0 Hz, 1H), 5.68 (dd, J = 9.9, 2.0 Hz, 1H), 4.27 - 4.11 (m, 2H), 3.85 (s, 3H), 3.04 - 2.92 (m, 1H), 2.92 - 2.84 (m, 2H), 2.72 (s, 3H), 2.45 - 2.37 (m, 1H), 2.36 - 2.30 (m, 2H), 2.28 (s, 6H). : 568.4 [M+H]$^+$	1.29

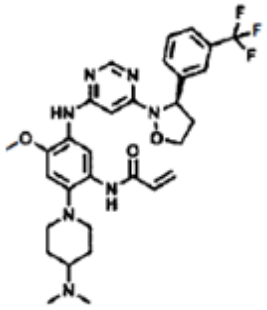
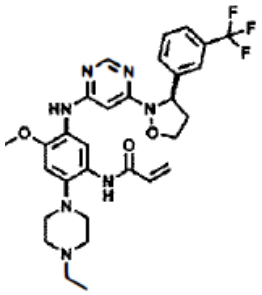
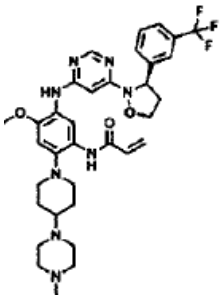
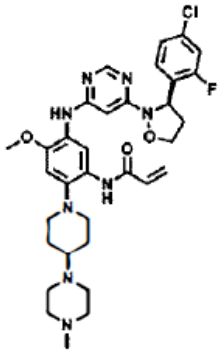
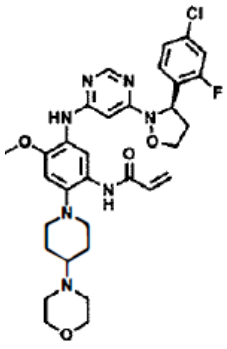
[551]

441		N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.95 (s, 1H), 8.53 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 7.92 - 7.85 (m, 1H), 7.77 (t, *J* = 6.9 Hz, 2H), 7.60 - 7.41 (m, 3H), 6.95 (s, 1H), 6.79 (d, *J* = 6.6 Hz, 2H), 6.45 - 6.33 (m, 2H), 6.27 (dd, *J* = 17.0, 10.0 Hz, 1H), 5.75 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.24 - 4.11 (m, 2H), 3.85 (s, 3H), 3.03 - 2.90 (m, 5H), 2.74 - 2.50 (m, 4H), 2.47 - 2.35 (m, 4H). : 566.4 [M+H]$^+$	1.23
442		N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.91 (s, 1H), 8.48 (s, 1H), 8.37 (d, *J* = 0.9 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.88 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.77 (t, *J* = 6.8 Hz, 2H), 7.60 - 7.41 (m, 3H), 6.93 (s, 1H), 6.77 (d, *J* = 11.0 Hz, 2H), 6.45 - 6.40 (m, 1H), 6.40 - 6.31 (m, 1H), 6.26 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.74 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.25 - 4.11 (m, 2H), 3.85 (s, 3H), 3.11 - 3.02 (m, 2H), 3.01 - 2.92 (m, 1H), 2.80 - 2.67 (m, 2H), 2.45 - 2.40 (m, 1H), 2.30 (s, 6H), 2.35 - 2.24 (m, 1H), 2.11 - 2.03 (m, 2H), 1.72 - 1.62 (m, 2H). : 594.5 [M+H]$^+$	1.24
443		N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.71 (s, 1H), 8.35 (s, 1H), 8.18 - 8.12 (m, 2H), 7.88 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.81 - 7.73 (m, 2H), 7.60 - 7.41 (m, 3H), 6.88 (s, 1H), 6.76 (d, *J* = 2.1 Hz, 2H), 6.45 - 6.34 (m, 2H), 6.29 (dd, *J* = 16.9, 9.8 Hz, 1H), 5.73 (dd, *J* = 9.9, 1.8 Hz, 1H), 4.24 - 4.13 (m, 2H), 3.84 (s, 3H), 3.24 - 3.15 (m, 1H), 3.13 - 3.10 (m, 2H), 3.00 - 2.93 (m, 1H), 2.93 - 2.86 (m, 1H), 2.47 - 2.35 (m, 1H), 2.30 (s, 6H), 2.19 (d, *J* = 7.5 Hz, 1H), 2.01 - 1.87 (m, 2H). : 580.5 [M+H]$^+$	1.21
444		N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.95 (s, 1H), 8.57 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 7.88 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.81 - 7.73 (m, 2H), 7.60 - 7.41 (m, 3H), 6.95 (s, 1H), 6.81 (d, *J* = 13.3 Hz, 2H), 6.45 - 6.32 (m, 2H), 6.27 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.24 - 4.11 (m, 2H), 3.84 (s, 3H), 3.03 - 2.88 (m, 5H), 2.76 - 2.53 (m, 4H), 2.51 (t, *J* = 7.2 Hz, 2H), 2.47 - 2.35 (m, 1H), 1.16 (t, *J* = 7.2 Hz, 3H). : 580.4 [M+H]$^+$	1.25
445		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.47 (s, 1H), 8.33 (s, 1H), 7.23 (s, 1H), 7.04 - 6.96 (m, 2H), 6.74 (s, 1H), 6.72 - 6.64 (m, 2H), 6.30 - 6.23 (m, 2H), 5.75 (dd, *J* = 9.7, 1.7 Hz, 1H), 5.66 (dd, *J* = 8.6, 4.5 Hz, 1H), 4.14 (td, *J* = 7.9, 4.2 Hz, 1H), 4.06 (q, *J* = 16.0, 8.0 Hz, 1H), 3.84 (s, 3H), 3.18 - 3.10 (m, 2H), 3.07 - 2.97 (m, 3H), 2.85 - 2.67 (m, 5H), 2.63 - 2.56 (m, 1H), 2.55 - 2.48 (m, 2H), 2.46 (s, 3H), 2.37 - 2.28 (m, 1H), 2.26 - 2.18 (m, 1H), 2.13 - 1.95 (m, 3H), 1.87 - 1.65 (m, 3H): 661.50[M+H]$^+$	1.14

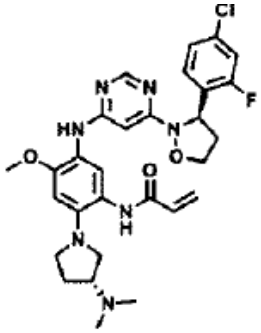
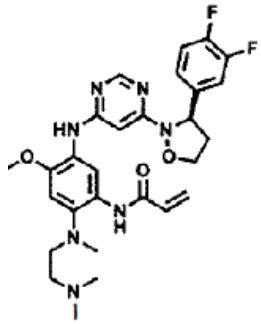
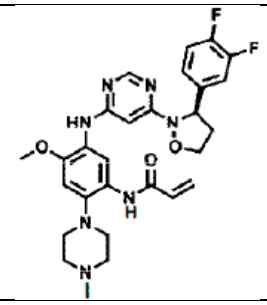
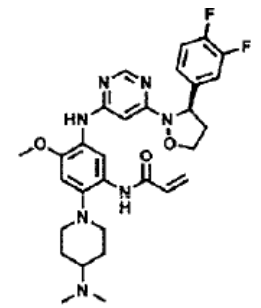
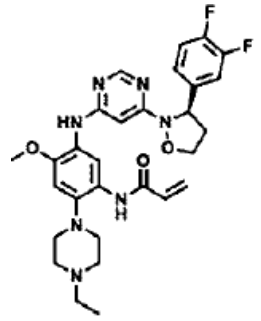
[552]

446		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.48 (s, 1H), 8.33 (s, 1H), 7.20 (s, 1H), 7.03 - 6.97 (m, 2H), 6.74 (s, 1H), 6.71 - 6.65 (m, 2H), 6.38 - 6.23 (m, 2H), 5.75 (dd, *J* = 9.7, 1.6 Hz, 1H), 5.66 (dd, *J* = 8.6, 4.5 Hz, 1H), 4.14 (td, *J* = 8.1, 4.3 Hz, 1H), 4.06 (q, *J* = 8.1 Hz, 1H), 3.84 (s, 3H), 3.16 - 3.07 (m, 2H), 3.05 - 2.99 (m, 3H), 2.83 - 2.67 (m, 5H), 2.60 - 2.53 (m, 1H), 2.51 - 2.40 (m, 5H), 2.38 - 2.29 (m, 1H), 2.25 - 2.16 (m, 1H), 2.11 - 2.00 (m, 3H), 1.86 - 1.64 (m, 3H): 661.50[M+H]$^+$	1.14
447		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.47 (s, 1H), 8.32 (s, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.24 - 7.18 (m, 2H), 7.05 (t, *J* = 8.0 Hz, 1H), 6.75 (s, 1H), 6.73 (s, 1H), 6.38 - 6.23 (m, 2H), 5.95 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.74 (dd, *J* = 9.7, 1.6 Hz, 1H), 4.14 - 4.03 (m, 2H), 3.85 (s, 3H), 3.15 - 3.07 (m, 2H), 3.05 - 2.98 (m, 3H), 2.97 - 2.89 (m, 1H), 2.85 - 2.64 (m, 5H), 2.60 - 2.53 (m, 1H), 2.51 - 2.45 (m, 2H), 2.44 (s, 3H), 2.27 - 2.18 (m, 2H), 2.11 - 2.00 (m, 2H), 1.86 - 1.66 (m, 3H): 677.56[M+H]$^+$	1.19
448		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.48 (s, 1H), 8.33 (s, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.24 - 7.17 (m, 2H), 7.12 (s, 1H), 7.05 (t, *J* = 7.9 Hz, 1H), 6.76 - 6.71 (m, 2H), 6.38 - 6.22 (m, 2H), 5.95 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.77 - 5.71 (m, 1H), 4.14 - 4.03 (m, 2H), 3.85 (s, 3H), 3.13 - 3.05 (m, 1H), 3.05 - 2.90 (m, 5H), 2.81 - 2.64 (m, 5H), 2.52 - 2.40 (m, 5H), 2.28 - 2.12 (m, 2H), 2.04 - 1.99 (m, 2H), 1.84 - 1.72 (m, 2H), 1.69 - 1.62 (m, 1H): 677.47[M+H]$^+$	1.18
449		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 8.77 (s, 1H), 8.33 (s, 1H), 7.73 (s, 1H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.48 (dt, *J* = 15.3, 7.7 Hz, 2H), 6.72 (d, *J* = 25.1 Hz, 2H), 6.40 (dd, *J* = 16.8, 1.8 Hz, 1H), 5.76 (dd, *J* = 8.6, 4.5 Hz, 1H), 5.70 (dd, *J* = 10.2, 1.7 Hz, 1H), 4.20 (td, *J* = 8.0, 4.3 Hz, 1H), 4.11 (q, *J* = 8.0 Hz, 1H), 3.85 (s, 3H), 3.32 - 3.14 (m, 4H), 3.09 (q, *J* = 7.4 Hz, 2H), 2.81 (s, 6H), 2.72 (s, 3H), 2.41 - 2.33 (m, 1H), 1.54 (t, *J* = 7.4 Hz, 4H) : 586.4[M+H]$^+$	1.31
450		N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.52 (s, 1H), 8.34 (s, 1H), 7.71 (s, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.48 (dt, *J* = 15.5, 7.8 Hz, 2H), 7.31 (s, 1H), 6.78 (s, 1H), 6.67 (s, 1H), 6.45 - 6.32 (m, 2H), 5.73 (dd, *J* = 8.9, 2.5 Hz, 1H), 4.16 (td, *J* = 7.9, 4.2 Hz, 1H), 4.05 (dd, *J* = 16.1, 8.0 Hz, 1H), 3.84 (s, 3H), 3.10 (d, *J* = 5.9 Hz, 4H), 3.09 - 3.02 (m, 4H), 2.86 - 2.73 (m, 1H), 2.64 (s, 3H), 2.41 - 2.30 (m, 1H), 1.51 (t, *J* = 7.4 Hz, 1H): 584.4[M+H]$^+$	1.31

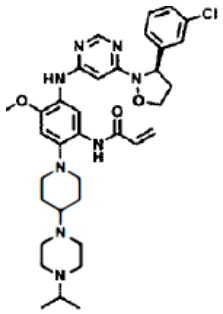
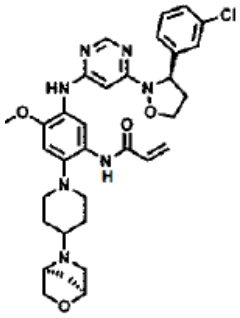
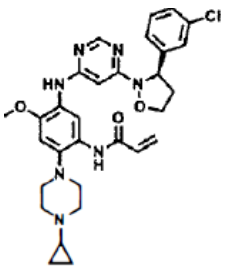
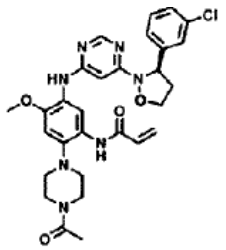
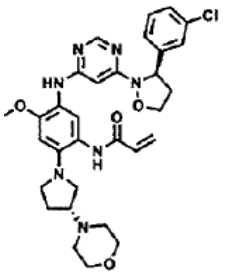
[553]

451		N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.85 (s, 1H), 8.46 (s, 1H), 8.35 (d, J = 1.0 Hz, 1H), 7.73 (s, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.48 (dt, J = 15.3, 7.7 Hz, 2H), 6.75 (d, J = 1.1 Hz, 1H), 6.72 (d, J = 1.9 Hz, 1H), 6.35 (d, J = 1.8 Hz, 1H), 6.29 (dd, J = 17.0, 9.6 Hz, 1H), 5.75 (ddd, J = 9.7, 6.6, 3.3 Hz, 2H), 4.17 (td, J = 8.1, 4.3 Hz, 1H), 4.08 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.10 - 3.05 (m, 2H), 2.83 - 2.68 (m, 4H), 2.44 (d, J = 1.3 Hz, 6H), 2.38 (q, J = 3.8 Hz, 1H), 2.08 (d, J = 12.7 Hz, 2H), 1.74 (dt, J = 12.5, 6.2 Hz, 2H): 612.5[M+H]$^+$	1.29
452		N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.50 (s, 1H), 8.37 (s, 1H), 7.73 (s, 1H), 7.66 (d, J = 7.5 Hz, 1H), 7.48 (dt, J = 15.3, 7.7 Hz, 2H), 7.09 (s, 1H), 6.82 (s, 1H), 6.72 (s, 1H), 6.40 - 6.26 (m, 2H), 5.78 - 5.72 (m, 2H), 4.17 (td, J = 8.0, 4.2 Hz, 1H), 4.07 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.04 (d, J = 13.0 Hz, 4H), 2.81 (dtd, J = 12.1, 8.1, 4.3 Hz, 4H), 2.66 (dd, J = 13.0, 6.8 Hz, 2H), 2.41 - 2.32 (m, 1H), 1.23 (t, J = 7.2 Hz, 3H): 508.4[M+H]$^+$	1.30
453		N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	667.5[M+H]$^+$	1.21
454		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.84 (s, 1H), 8.43 (s, 1H), 8.34 (d, J = 1.0 Hz, 1H), 7.53 (t, J = 8.2 Hz, 1H), 7.00 (td, J = 7.1, 6.6, 4.0 Hz, 3H), 6.75 (s, 1H), 6.73 (s, 1H), 6.40 - 6.31 (m, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.86 (dd, J = 8.7, 4.4 Hz, 1H), 5.74 (dd, J = 9.9, 1.6 Hz, 1H), 4.13 - 4.04 (m, 2H), 3.85 (s, 3H), 3.06 (d, J = 11.5 Hz, 2H), 2.82 (dd, J = 8.1, 4.4 Hz, 1H), 2.80 - 2.53 (m, 10H), 2.40 (d, J = 11.1 Hz, 1H), 2.35 (s, 3H), 2.30 - 2.25 (m, 1H), 2.12 - 2.06 (m, 2H), 1.68 (d, J = 11.5 Hz, 2H): 651.5[M+H]$^+$	1.18
455		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.81 (s, 1H), 8.43 (s, 1H), 8.32 (d, J = 1.0 Hz, 1H), 7.52 (t, J = 8.5 Hz, 1H), 7.33 (s, 1H), 7.14 - 7.05 (m, 2H), 6.75 (s, 1H), 6.71 (s, 1H), 6.36 (dd, J = 17.0, 1.6 Hz, 1H), 6.26 (dd, J = 16.9, 9.9 Hz, 1H), 5.86 (dd, J = 8.8, 4.4 Hz, 1H), 5.74 (dd, J = 9.9, 1.6 Hz, 1H), 4.16 - 4.07 (m, 1H), 4.00 - 4.03 (m, 1H), 3.85 (s, 3H), 3.79 (t, J = 4.7 Hz, 4H), 3.08 (d, J = 11.4 Hz, 2H), 2.88 - 2.77 (m, 1H), 2.74 (q, J = 12.3 Hz, 2H), 2.65 (t, J = 4.7 Hz, 4H), 2.41 - 2.31 (m, 1H), 2.32 - 2.20 (m, 1H), 2.13 - 2.08 (m, 2H), 1.69 (qd, J = 13.7, 13.0, 3.6 Hz, 2H): 638.4[M+H]$^+$	1.27

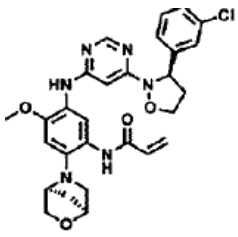
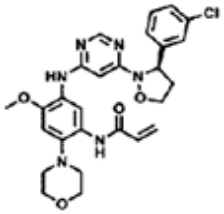
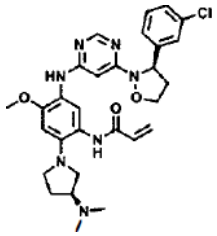
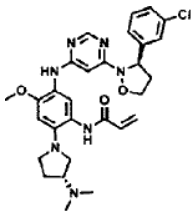
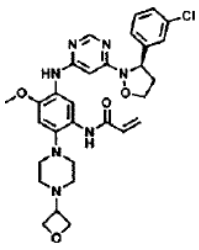
[554]

456		N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.24 (d, J = 16.6 Hz, 2H), 7.44 (t, J = 8.3 Hz, 1H), 7.14 - 7.04 (m, 2H), 6.60 (s, 1H), 6.50 (s, 1H), 6.40 (d, J = 16.8 Hz, 1H), 5.81 (dd, J = 8.4, 4.5 Hz, 1H), 5.71 (d, J = 10.8 Hz, 1H), 4.15 (dd, J = 12.3, 7.8 Hz, 1H), 4.04 (q, J = 7.8 Hz, 1H), 3.82 (s, 3H), 3.74 (d, J = 11.0 Hz, 1H), 3.60 (s, 1H), 3.37 (s, 1H), 3.05 - 2.92 (m, 2H), 2.85 (s, 6H), 2.37 (d, J = 4.4 Hz, 2H), 2.32 - 2.23 (m, 1H) ; 582.4[M+H]$^+$	1.26
457		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.19 (s, 1H), 9.95 (s, 1H), 8.33 (s, 1H), 8.02 (s, 1H), 7.45 (tdd, J = 10.4, 7.3, 4.1 Hz, 2H), 7.33 - 7.20 (m, 2H), 6.97 (s, 1H), 6.26 - 6.11 (m, 2H), 5.70 (dd, J = 10.1, 2.2 Hz, 1H), 5.54 (dd, J = 8.4, 5.3 Hz, 1H), 4.32 (dt, J = 7.6, 3.7 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 3.82 (s, 3H), 3.32 (s, 4H), 2.97 - 2.88 (m, 1H), 2.72 (d, J = 4.8 Hz, 6H), 2.62 (s, 3H), 2.34 (ddd, J = 9.9, 7.7, 5.2 Hz, 1H).; 554.3 [M+H]$^+$	1.26
458		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.75 (s, 1H), 9.17 (s, 1H), 8.29 (s, 1H), 8.07 (s, 1H), 7.48 - 7.30 (m, 2H), 7.27 - 7.20 (m, 1H), 6.88 (s, 1H), 6.82 - 6.74 (m, 1H), 6.28 - 6.12 (m, 2H), 5.76 (dd, J = 10.2, 2.0 Hz, 1H), 5.53 (dd, J = 8.5, 5.2 Hz, 1H), 4.26 (q, J = 4.5, 4.0 Hz, 1H), 4.01 (t, J = 7.8 Hz, 1H), 3.83 (s, 3H), 3.48 (d, J = 11.6 Hz, 2H), 3.37 (d, J = 10.6 Hz, 2H), 3.18 (d, J = 8.8 Hz, 4H), 2.93 - 2.87 (m, 1H), 2.82 (d, J = 4.5 Hz, 3H), 2.31 (dt, J = 12.8, 3.8 Hz, 1H).; 552.3 [M+H]$^+$	1.20
459		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.03 (s, 1H), 9.20 (s, 1H), 8.32 (s, 1H), 7.93 (s, 1H), 7.47 - 7.39 (m, 2H), 7.22 (d, J = 8.4 Hz, 1H), 6.90 (s, 1H), 6.73 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 2.0 Hz, 1H), 6.12 (s, 1H), 5.79 - 5.72 (m, 1H), 5.53 (dd, J = 8.4, 5.2 Hz, 1H), 4.29 (td, J = 7.5, 4.3 Hz, 1H), 4.04 (q, J = 7.7 Hz, 1H), 3.81 (s, 3H), 3.33 - 3.16 (m, 3H), 2.97 - 2.88 (m, 1H), 2.80 (d, J = 11.8 Hz, 2H), 2.75 (d, J = 5.0 Hz, 6H), 2.33 (ddd, J = 13.0, 8.5, 5.4 Hz, 1H), 2.12 (d, J = 11.5 Hz, 2H), 2.01 (d, J = 12.1 Hz, 2H).; 580.3 [M+H]$^+$	1.22
460		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.80 (s, 1H), 9.22 (s, 1H), 8.29 (s, 1H), 8.06 (s, 1H), 7.44 (tdd, J = 10.8, 6.8, 4.0 Hz, 2H), 7.23 (dq, J = 7.7, 2.6 Hz, 1H), 6.83 (d, J = 27.4 Hz, 2H), 6.27 - 6.14 (m, 2H), 5.78 - 5.70 (m, 1H), 5.53 (dd, J = 8.5, 5.3 Hz, 1H), 4.27 (d, J = 4.4 Hz, 1H), 4.02 (t, J = 7.8 Hz, 1H), 3.83 (s, 3H), 3.52 (d, J = 11.3 Hz, 2H), 3.33 (s, 2H), 3.19 (ddd, J = 19.8, 7.7, 4.1 Hz, 6H), 2.94 - 2.82 (m, 1H), 2.31 (dd, J = 12.8, 5.1 Hz, 1H), 1.32 (t, J = 7.2 Hz, 3H).; 566.3 [M+H]$^+$	1.21

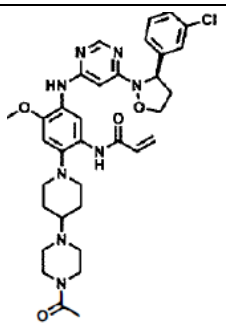
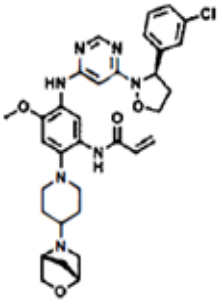
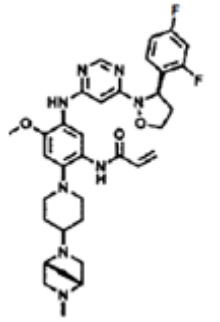
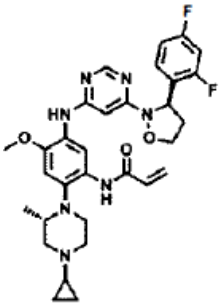
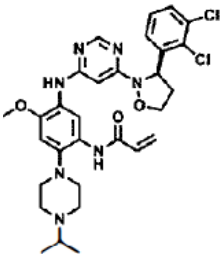
[555]

461		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.05 (s, 1H), 8.21 (s, 1H), 8.09 (s, 1H), 7.43 (d, J = 5.9 Hz, 1H), 7.41 - 7.32 (m, 3H), 6.84 (s, 1H), 6.62 (dd, J = 17.1, 10.3 Hz, 1H), 6.31 - 6.25 (m, 1H), 6.21 (d, J = 2.0 Hz, 1H), 5.74 (d, J = 10.4 Hz, 1H), 5.53 (dd, J = 8.6, 5.2 Hz, 1H), 4.20 (td, J = 7.8, 3.8 Hz, 2H), 3.95 - 3.86 (m, 2H), 3.81 (s, 3H), 3.16 (d, J = 11.2 Hz, 6H), 2.89 - 2.64 (m, 5H), 2.39 - 2.16 (m, 2H), 2.10 - 1.96 (m, 2H), 1.87 (t, J = 15.5 Hz, 3H), 1.26 (d, J = 6.5 Hz, 7H), ; 661.5[M+H]+	1.10
462		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.10 (d, J = 17.9 Hz, 1H), 8.24 (d, J = 6.0 Hz, 1H), 8.02 (s, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.41 - 7.31 (m, 3H), 6.85 (s, 1H), 6.62 - 6.50 (m, 1H), 6.23 (dd, J = 16.3, 3.1 Hz, 2H), 5.79 - 5.60 (m, 1H), 5.53 (dd, J = 8.6, 5.3 Hz, 1H), 4.72 (s, 1H), 4.66 (d, J = 7.7 Hz, 2H), 4.22 (dd, J = 9.0, 5.0 Hz, 2H), 3.96 (dt, J = 23.7, 8.8 Hz, 2H), 3.81 (s, 3H), 3.75 (t, J = 9.8 Hz, 1H), 3.55 - 3.36 (m, 2H), 3.28 - 3.10 (m, 3H), 2.93 - 2.65 (m, 3H), 2.38 - 2.21 (m, 1H), 2.21 - 1.99 (m, 3H), 1.88 (d, J = 21.4 Hz, 2H), ; 632.5[M+H]+	1.14
463		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.13 (s, 2H), 8.22 (s, 1H), 8.13 (s, 1H), 7.43 (q, J = 3.9, 3.0 Hz, 1H), 7.37 (dt, J = 12.7, 7.3 Hz, 3H), 6.90 (s, 1H), 6.67 (dd, J = 16.9, 10.2 Hz, 1H), 6.25 (d, J = 1.9 Hz, 1H), 5.74 (dd, J = 10.0, 2.0 Hz, 1H), 5.53 (dd, J = 8.6, 5.3 Hz, 1H), 4.21 (td, J = 7.7, 3.9 Hz, 4H), 3.92 (q, J = 7.0 Hz, 3H), 3.80 (s, 3H), 3.65 (q, J = 5.9, 5.3 Hz, 4H), 2.84 (dt, J = 16.2, 5.0 Hz, 4H), 2.34 - 2.20 (m, 1H), 2.05 (s, 3H).; 576.4[M+H]+	1.25
464		N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 26.2 Hz, 2H), 8.26 - 8.15 (m, 1H), 7.43 (d, J = 8.1 Hz, 1H), 7.35 (dt, J = 19.1, 6.1 Hz, 4H), 6.96 - 6.74 (m, 1H), 6.39 (d, J = 33.6 Hz, 1H), 5.54 (dd, J = 8.9, 5.4 Hz, 1H), 4.17 (s, 1H), 3.83 (qd, J = 11.6, 11.0, 6.0 Hz, 5H), 3.30 (s, 3H), 3.17 (s, 2H), 3.13 - 3.00 (m, 3H), 2.88 - 2.74 (m, 2H), 2.33 - 2.19 (m, 2H), 1.91 (s, 3H), ; 578.4[M+H]+	1.41
465		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.67 (s, 1H), 8.35 (s, 1H), 8.14 (s, 1H), 7.47 (t, J = 1.9 Hz, 1H), 7.34 (dt, J = 7.5, 1.6 Hz, 1H), 7.29 - 7.18 (m, 2H), 6.93 (s, 1H), 6.75 (s, 1H), 6.67 (s, 1H), 6.42 - 6.23 (m, 2H), 5.73 (dd, J = 9.0, 1.8 Hz, 1H), 5.67 (dd, J = 8.7, 4.5 Hz, 1H), 4.21 - 3.99 (m, 2H), 3.83 (s, 3H), 3.76 (t, J = 4.7 Hz, 4H), 3.26 - 3.05 (m, 4H), 2.98 (p, J = 7.4 Hz, 1H), 2.76 (dtd, J = 12.3, 8.0, 4.2 Hz, 1H), 2.53 (ddt, J = 30.6, 10.6, 4.6 Hz, 4H), 2.35 (dtd, J = 12.4, 8.1, 4.5 Hz, 1H), 2.19 (dtd, J = 12.1, 7.5, 4.5 Hz, 1H), 2.02 - 1.88 (m, 1H).; 606.3[M+H]$^+$	1.18

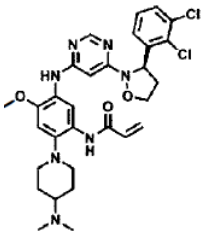
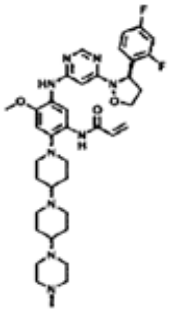
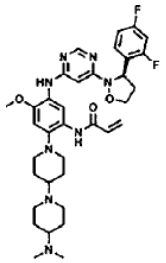
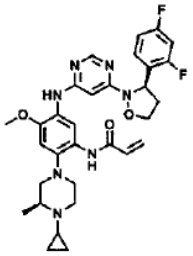
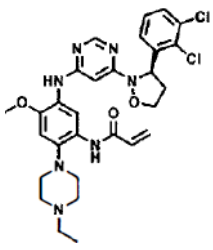
[556]

466		N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.67 (s, 1H), 8.36 (s, 1H), 7.97 (s, 1H), 7.47 (d, J = 2.0 Hz, 1H), 7.34 (dt, J = 7.6, 1.7 Hz, 1H), 7.20 - 7.19 (m, 2H), 6.90 (s, 1H), 6.66 (d, J = 29.6 Hz, 2H), 6.32 (tq, J = 26.5, 16.6, 15.3 Hz, 2H), 5.75 (dd, J = 10.0, 1.5 Hz, 1H), 5.67 (dd, J = 8.7, 4.5 Hz, 1H), 4.65 (s, 1H), 4.13 (qd, J = 9.0, 8.5, 5.7 Hz, 1H), 4.03 (dd, J = 15.5, 7.9 Hz, 2H), 3.86 (s, 3H), 3.42 (d, J = 10.1 Hz, 1H), 3.24 (d, J = 10.1 Hz, 1H), 2.76 (dtd, J = 12.3, 8.0, 4.2 Hz, 1H), 2.61 (s, 2H), 2.35 (dtd, J = 12.5, 8.1, 4.6 Hz, 1H), 2.08 (d, J = 9.9 Hz, 1H), 1.99 (d, J = 10.3 Hz, 1H).; 549.3[M+H]$^+$	1.37
467		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.93 (s, 1H), 8.51 (s, 1H), 8.38 (d, J = 0.9 Hz, 1H), 7.47 (d, J = 1.9 Hz, 1H), 7.34 (dt, J = 7.7, 1.6 Hz, 1H), 7.28 - 7.19 (m, 2H), 7.00 (s, 1H), 6.77 (s, 1H), 6.71 (s, 1H), 6.43 - 6.20 (m, 2H), 5.76 (dd, J = 9.0, 1.6 Hz, 1H), 5.68 (dd, J = 8.7, 4.5 Hz, 1H), 4.21 - 4.01 (m, 2H), 3.88 (t, J = 4.5 Hz, 4H), 3.86 (s, 3H), 2.80 (td, J = 4.1, 1.7 Hz, 4H), 2.77 (dtd, J = 12.3, 8.0, 4.2 Hz, 1H), 2.36 (dtd, J = 12.5, 8.1, 4.6 Hz, 1H).; 537.2[M+H]$^+$	1.51
468		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.62 (s, 1H), 8.44 (s, 1H), 8.33 (s, 1H), 7.47 (t, J = 1.9 Hz, 1H), 7.37 - 7.28 (m, 1H), 7.27 - 7.15 (m, 2H), 7.01 (s, 1H), 6.68 (d, J = 29.5 Hz, 1H), 6.47 - 6.38 (m, 1H), 6.24 - 6.08 (m, 1H), 5.82 - 5.55 (m, 2H), 4.14 (tt, J = 7.2, 3.7 Hz, 1H), 4.02 (q, J = 8.0 Hz, 1H), 3.83 (s, 3H), 3.60 (p, J = 6.7 Hz, 1H), 3.24 (ddt, J = 21.5, 8.6, 4.7 Hz, 2H), 3.14 - 3.06 (m, 2H), 3.03 (q, J = 7.4 Hz, 2H), 2.76 (dtd, J = 12.3, 8.0, 4.2 Hz, 1H), 2.63 (dd, J = 25.4, 15.0 Hz, 1H), 2.41 (s, 4H), 2.21 (td, J = 12.3, 6.6 Hz, 1H), 1.43 (d, J = 15.6 Hz, 3H).; 564.4[M+H]$^+$	1.17
469		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.91 (s, 1H), 9.33 (s, 1H), 8.87 (s, 1H), 8.19 (s, 1H), 7.60 (s, 1H), 7.49 - 7.31 (m, 4H), 6.64 (s, 1H), 6.51 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 - 6.20 (m, 1H), 5.80 - 5.69 (m, 1H), 5.53 (dd, J = 8.7, 5.2 Hz, 1H), 4.17 (td, J = 7.7, 3.8 Hz, 1H), 3.93 (q, J = 7.1, 6.5 Hz, 1H), 3.90 - 3.77 (m, 4H), 3.47 - 3.40 (m, 2H), 3.32 (t, J = 4.6 Hz, 1H), 3.22 (q, J = 8.2 Hz, 1H), 2.84 (t, J = 5.7 Hz, 7H), 2.39 - 2.20 (m, 2H), 2.12 (dt, J = 13.4, 7.3 Hz, 1H). ; 564.4[M+H]$^+$	1.19
470		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.05 (s, 1H), 8.75 (s, 1H), 8.25 (s, 1H), 8.18 (s, 1H), 7.46 - 7.30 (m, 4H), 6.84 (s, 1H), 6.63 (dd, J = 17.1, 10.2 Hz, 1H), 6.39 (s, 1H), 6.23 (dd, J = 17.1, 2.0 Hz, 1H), 5.74 (d, J = 9.7 Hz, 1H), 5.54 (dd, J = 8.7, 5.1 Hz, 1H), 4.76 (s, 4H), 4.20 - 4.10 (m, 1H), 3.84 (s, 4H), 3.63 (s, 4H), 3.42 - 3.35 (m, 1H), 3.17 (s, 4H), 2.83 - 2.73 (m, 1H), 2.30 - 2.18 (m, 1H) ; 592.4[M+H]$^+$	1.22

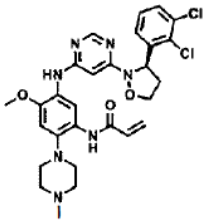
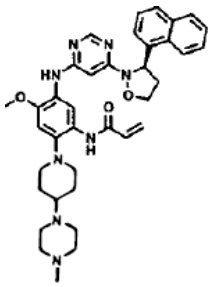
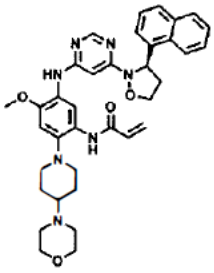
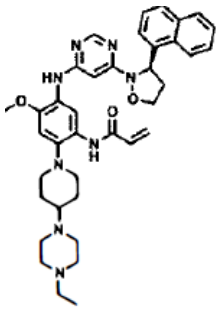
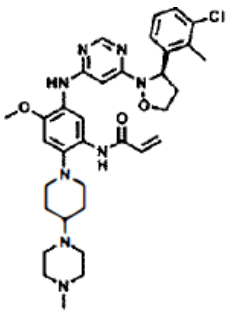
[557]

471		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.53 (s, 1H), 9.20 (s, 1H), 9.08 (s, 1H), 8.25 (s, 1H), 8.10 (s, 1H), 7.48 - 7.30 (m, 4H), 6.87 (s, 1H), 6.66 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.30 - 6.23 (m, 1H), 5.82 - 5.66 (m, 1H), 5.54 (dd, *J* = 8.6, 5.3 Hz, 1H), 4.21 (td, *J* = 7.8, 3.9 Hz, 1H), 4.06 (s, 1H), 3.93 (t, *J* = 7.9 Hz, 1H), 3.82 (s, 3H), 3.52 (s, 3H), 3.39 (dq, *J* = 11.7, 7.6, 6.2 Hz, 2H), 3.18 (d, *J* = 11.5 Hz, 3H), 3.10 - 2.91 (m, 2H), 2.85 (tt, *J* = 8.1, 4.0 Hz, 1H), 2.77 (t, *J* = 12.8 Hz, 2H), 2.32 - 2.20 (m, 1H), 2.12 (d, *J* = 11.4 Hz, 2H), 2.08 (s, 3H), 2.00 (dt, *J* = 12.1, 6.4 Hz, 2H). : 661.4[M+H]$^+$	1.22
472		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.08 (d, *J* = 16.7 Hz, 1H), 8.71 (s, 1H), 8.18 (s, 1H), 8.11 (s, 1H), 7.47 - 7.29 (m, 4H), 6.82 (s, 1H), 6.52 (dt, *J* = 19.2, 10.2 Hz, 1H), 6.37 (s, 1H), 6.22 (d, *J* = 16.9 Hz, 1H), 5.74 (d, *J* = 10.1 Hz, 1H), 5.54 (dd, *J* = 8.6, 5.2 Hz, 1H), 4.76 - 4.61 (m, 2H), 4.15 (dd, *J* = 7.9, 3.9 Hz, 1H), 3.90 - 3.79 (m, 4H), 3.75 (t, *J* = 10.5 Hz, 2H), 3.44 - 3.36 (m, 3H), 3.23 (d, *J* = 11.8 Hz, 1H), 3.18 - 3.07 (m, 2H), 2.81 - 2.73 (m, 2H), 2.65 (d, *J* = 12.3 Hz, 1H), 2.33 (s, 1H), 2.29 - 2.20 (m, 1H), 2.16 (d, *J* = 14.6 Hz, 1H), 2.01 (d, *J* = 11.4 Hz, 1H), 1.87 - 1.73 (m, 2H). : 632.5[M+H]$^+$	1.24
473		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((1R,4R)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.88 (s, 1H), 8.47 (s, 1H), 8.37 (s, 1H), 7.56 (q, *J* = 8.3 Hz, 1H), 6.93 (s, 1H), 6.87 - 6.73 (m, 4H), 6.38 - 6.31 (m, 1H), 6.24 (dd, *J* = 17.0, 10.0 Hz, 1H), 5.87 (dd, *J* = 8.7, 4.3 Hz, 1H), 5.73 (d, *J* = 10.1 Hz, 1H), 4.14 - 4.05 (m, 2H), 3.86 (s, 3H), 3.02 (s, 2H), 2.78 (q, *J* = 11.7, 9.9 Hz, 4H), 2.50 (d, *J* = 9.6 Hz, 2H), 2.32 - 2.24 (m, 1H), 2.06 (d, *J* = 10.5 Hz, 2H), 1.90 (s, 2H), 1.25 (s, 3H).: 647.5[M+H]	1.13
474		N-(2-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 9.02 (s, 1H), 8.96 (s, 1H), 8.38 (s, 1H), 7.57 (q, *J* = 8.3 Hz, 1H), 7.07 (s, 1H), 6.81 (dd, *J* = 12.2, 8.4 Hz, 4H), 6.35 - 6.23 (m, 2H), 5.88 (dd, *J* = 8.7, 4.1 Hz, 1H), 5.74 (dd, *J* = 9.6, 1.9 Hz, 1H), 4.15 - 4.08 (m, 2H), 3.80 (s, 3H), 3.16 - 2.97 (m, 4H), 2.85 - 2.79 (m, 2H), 2.53 - 2.45 (m, 1H), 2.31 - 2.24 (m, 1H), 2.20 (t, *J* = 10.4 Hz, 1H), 1.70 (d, *J* = 4.1 Hz, 1H), 0.82 (d, *J* = 6.1 Hz, 3H), 0.50 (dd, *J* = 17.3, 5.1 Hz, 4H).: 502.4[M+H]	1.31
475		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.57 (s, 1H), 8.36 (s, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.30 - 7.34 (m, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.95 (s, 1H), 6.84 (s, 1H), 6.76 (s, 1H), 6.37 (d, *J* = 16.7 Hz, 1H), 6.27 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.97 (dd, *J* = 8.9, 4.4 Hz, 1H), 5.77 - 5.72 (m, 1H), 4.10 (dt, *J* = 10.3, 6.3 Hz, 2H), 3.83 (s, 3H), 2.94 (dt, *J* = 8.1, 4.1 Hz, 4H), 2.78 - 2.67 (m, 4H), 2.23 (dtd, *J* = 12.6, 8.2, 4.4 Hz, 1H), 1.64 (s, 2H), 1.13 (d, *J* = 6.4 Hz, 6H).: 612.3[M+H]	1.37

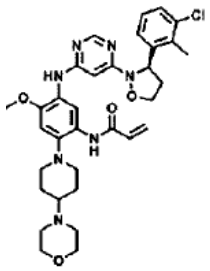
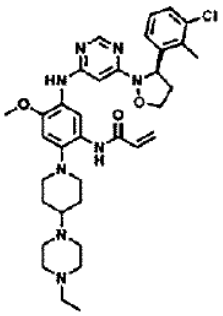
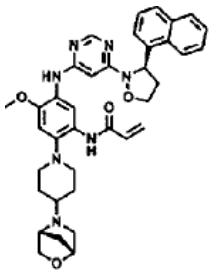
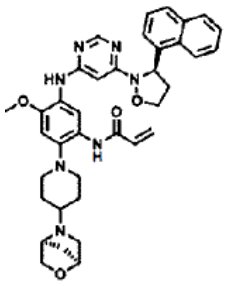
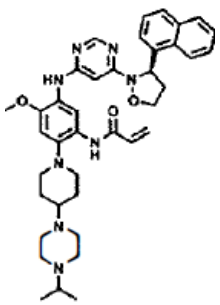
[558]

476		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.43 (s, 1H), 8.35 (s, 1H), 7.50 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.37 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 7.05 (s, 1H), 6.75 (s, 1H), 6.36 - 6.26 (m, 2H), 6.16 (dd, *J* = 17.3, 10.1 Hz, 1H), 5.96 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.73 (ddd, *J* = 16.3, 9.8, 2.0 Hz, 1H), 4.16 - 4.05 (m, 2H), 3.85 (s, 3H), 2.96 (ddt, *J* = 12.2, 8.1, 4.0 Hz, 2H), 2.81 - 2.71 (m, 2H), 2.53 (s, 6H), 2.23 (dq, *J* = 12.2, 3.8 Hz, 1H), 1.88 - 1.76 (m, 2H), 1.33 - 1.22 (m, 4H).: 612.4[M+H]	1.34
477		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)-[1,4'-bipiperidine]-1'-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.56 (m, 1H), 6.92 (s, 1H), 6.84 (m, 2H), 6.75 (m, 2H), 6.34 (m, 1H), 6.27 (d, *J* = 10.1 Hz, 1H), 5.89 (m, 1H), 5.74 (d, *J* = 11.1 Hz, 1H), 4.08 (d, *J* = 16.0 Hz, 2H), 3.85 (s, 3H), 3.12 (m, 5H), 2.79 (m, 2H), 2.72 m, 2H), 2.63 (m, 5H), 2.50 (m, 3H), 2.30 (m, 5H), 2.02(m, 3H), 1.86 (m, 3H), 1.71 (m, 3H).: 718.6 [M+H]$^+$	1.11
478		N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 9.25 (s, 1H), 8.86 (s, 1H), 8.43 (s, 2H), 8.36 (s, 1H), 8.31 (s, 1H), 7.54 (m, 2H), 6.94 (s, 1H), 6.36 (d, *J* = 17.4 Hz, 1H), 6.26 (dd, *J* = 16.7, 10.4 Hz, 1H), 5.83 (m, 1H), 5.75 (d, *J* = 10.4 Hz, 1H), 4.14 - 4.04 (m, 2H), 3.85 (s, 3H), 3.78 - 3.69 (m, 4H), 3.44 - 3.36 (m, 3H), 3.31 - 3.26 (m, 5H), 2.40 (s, 6H), 1.81 - 1.73 (m, 4H), 1.71 - 1.56 (m, 4H).: 663.5 [M+H]$^+$	1.11
479		N-(2-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.60 (s, 1H), 8.37 (s, 1H), 7.56 (m, 1H), 6.93 (s, 1H), 6.80 (m, 4H), 6.35 (m, 1H), 6.28 (m, 1H), 5.80 (m, 1H), 5.75 (d, *J* = 11.0 Hz, 1H), 4.11 (m,2H), 3.82 (s, 3H), 3.12 (d, *J* = 11.7 Hz, 1H), 2.89 (m, 2H), 2.82 (m, 2H), 2.69 (m, 1H), 2.64 - 2.55 (m, 1H), 2.27 (m, 1H), 1.66 (s, 1H), 1.57 (s, 1H), 1.26 (d, *J* = 6.2 Hz, 3H), 0.65 (d, *J* = 32.1 Hz, 2H), 0.50 (m, 1H), 0.36 (m, 1H).: 592.4 [M+H]$^+$	1.24
480		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.56 (s, 1H), 8.36 (s, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 9.0 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.95 (s, 1H), 6.82 (s, 1H), 6.76 (s, 1H), 6.36 (d, *J* = 16.2Hz, 1H), 6.29 (d, *J* = 10.0 Hz, 1H), 5.98 (m, 1H), 5.75 (d, *J* = 11.1 Hz, 1H), 4.09 (m, 2H), 3.84 (s, 3H),3.07 (m, 1H), 2.94 (m, 5H), 2.66 (s, 3H), 2.53 (m, 2H), 2.24 (m, 1H), 1.16 (t, *J* = 7.2 Hz, 3H).: 598.3 [M+H]$^+$	1.35

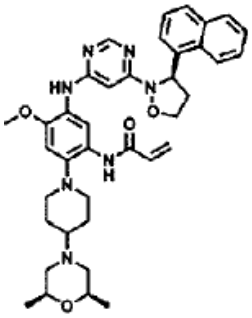
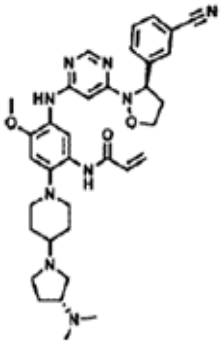
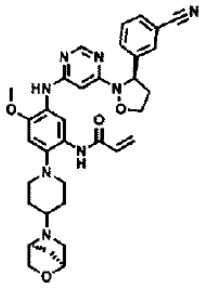
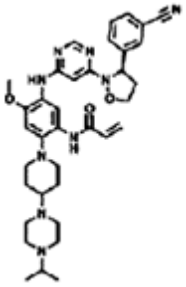
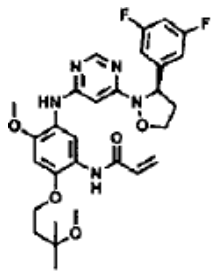
[559]

481		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 11.33 (s, 1H), 8.92 (s, 1H), 8.37 (s, 1H), 7.58 (s, 1H), 7.38 (s,1H), 7.19 (s, 1H), 6.98 (s, 1H), 6.81 (s, 1H), 6.75 (s, 1H), 6.36 (s, 1H), 6.30 (d, *J* = 10.4 Hz, 1H), 5.98 (m,1H), 5.75 (d, *J* = 11.1 Hz, 1H), 4.08 (m, 2H), 3.84 (s, 3H), 3.65 (m, 2H), 3.08 (m, 2H), 2.91 (m, 2H), 2.49(m, 2H), 2.22 (m, 2H), 1.45 (d, *J* = 6.6 Hz, 3H).; 584.3 $[M+H]^+$	1.33
482		N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.89 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 8.14 (d, *J* = 8.3 Hz, 1H), 7.88 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.57 - 7.42 (m, 4H), 6.98 (s, 1H), 6.77 (s, 1H), 6.74 (s, 1H), 6.43 - 6.37 (m, 2H), 6.34 (d, *J* = 1.6 Hz, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.74 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.16 (d, *J* = 6.5 Hz, 2H), 3.84 (s, 4H), 3.35 - 3.17 (m, 2H), 3.16 - 3.00 (m, 4H), 2.84 (s, 1H), 2.72 (tdd, *J* = 11.6, 9.3, 8.8, 4.5 Hz, 8H), 2.67 - 2.50 (m, 5H), 2.07 (d, *J* = 12.9 Hz, 2H), 1.71 - 1.65 (m, 2H).; 640.5$[M+H]^+$	1.20
483		N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.89 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 8.14 (d, *J* = 8.3 Hz, 1H), 7.87 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.63 - 7.36 (m, 4H), 7.00 (s, 1H), 6.76 (d, *J* = 10.8 Hz, 2H), 6.43 - 6.18 (m, 4H), 5.74 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.16 (d, *J* = 7.0 Hz, 1H), 3.84 (s, 3H), 3.77 (t, *J* = 4.6 Hz, 4H), 3.06 (dq, *J* = 9.4, 3.3 Hz, 2H), 3.01 - 2.89 (m, 1H), 2.79 - 2.66 (m, 2H), 2.61 (dd, *J* = 7.6, 3.3 Hz, 5H), 2.40 (dtd, *J* = 11.8, 7.8, 3.9 Hz, 1H), 2.30 (tt, *J* = 11.1, 3.8 Hz, 1H), 2.07 (d, *J* = 12.7 Hz, 3H), 1.65 (qd, *J* = 12.1, 3.9 Hz, 3H), 1.33 - 1.22 (m, 2H).; 363.5$[M+H]^+$	1.23
484		N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.02 (s, 1H), 8.63 (s, 1H), 8.27 (d, *J* = 8.2 Hz, 1H), 8.16 (d, *J* = 9.4 Hz, 2H), 7.99 - 7.94 (m, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.63 - 7.52 (m, 2H), 7.48 (t, *J* = 7.7 Hz, 1H), 6.83 (s, 1H), 6.73 - 6.66 (m, 1H), 6.26 - 6.20 (m, 2H), 5.76 (s, 2H), 3.95 (q, *J* = 8.0 Hz, 1H), 3.81 (s, 3H), 3.57 (p, *J* = 6.6 Hz, 3H), 3.05 - 2.96 (m, 4H), 2.22 (ddt, *J* = 12.1, 8.0, 4.2 Hz, 1H), 1.32 - 1.25 (m, 12H), 1.21 (d, *J* = 6.8 Hz, 4H), 1.08 (td, *J* = 7.4, 5.2 Hz, 3H).; 663.5$[M+H]^+$	1.14
485		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.82 (s, 1H), 8.43 (s, 1H), 8.32 (s, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.16 - 7.07 (m, 2H), 6.74 (s, 1H), 6.60 (s, 1H), 6.39 - 6.31 (m, 1H), 6.25 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.83 (dd, *J* = 8.8, 4.5 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.13 (dd, *J* = 8.0, 4.2 Hz, 2H), 3.84 (s, 4H), 3.06 (d, *J* = 11.6 Hz, 3H), 2.90 - 2.52 (m, 13H), 2.47 (s, 4H), 2.37 (s, 4H), 2.17 (dtd, *J* = 12.5, 8.1, 4.5 Hz, 2H), 2.06 (d, *J* = 12.0 Hz, 3H), 1.68 (qd, *J* = 12.1, 3.9 Hz, 3H).; 647.5$[M+H]^+$	1.24

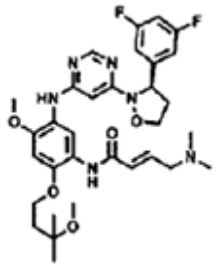
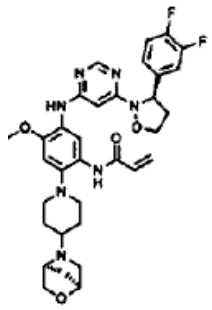
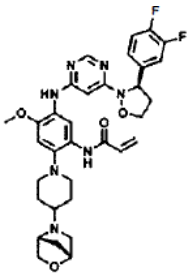
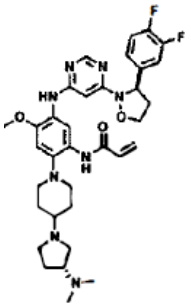
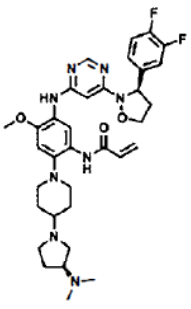
[560]

486		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.84 (s, 1H), 8.44 (s, 1H), 8.33 (d, *J* = 1.0 Hz, 1H), 7.49 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.15 - 7.05 (m, 2H), 6.75 (s, 1H), 6.70 (d, *J* = 1.1 Hz, 1H), 6.36 (dd, *J* = 16.9, 1.5 Hz, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.84 (dd, *J* = 8.8, 4.5 Hz, 1H), 5.74 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.14 (td, *J* = 8.1, 4.2 Hz, 1H), 3.84 (s, 3H), 3.78 (t, *J* = 4.7 Hz, 4H), 3.07 (d, *J* = 11.4 Hz, 2H), 2.87 - 2.66 (m, 4H), 2.63 (t, *J* = 4.6 Hz, 4H), 2.47 (s, 4H), 2.31 (dtd, *J* = 12.9, 9.2, 8.3, 4.6 Hz, 3H), 2.18 (dtd, *J* = 12.5, 8.1, 4.5 Hz, 3H), 1.72 - 1.60 (m, 3H).: 634.4[M+H]$^+$	1.27
487		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	661.5[M+H]$^+$	1.25
488		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.91 (s, 1H), 8.49 (s, 1H), 8.37 (d, *J* = 0.9 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.81 – 7.73 (m, 2H), 7.60 – 7.41 (m, 3H), 6.92 (s, 1H), 6.78 (d, *J* = 8.9 Hz, 2H), 6.45 – 6.40 (m, 1H), 6.40 – 6.31 (m, 1H), 6.24 (dd, *J* = 17.0, 10.0 Hz, 1H), 5.73 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.44 (s, 1H), 4.25 – 4.12 (m, 2H), 4.09 (d, *J* = 7.9 Hz, 1H), 3.86 (s, 3H), 3.77 (s, 1H), 3.67 (dd, *J* = 7.9, 1.6 Hz, 1H), 3.14 (dd, *J* = 9.8, 1.7 Hz, 1H), 3.07 – 3.00 (m, 2H), 2.99 – 2.92 (m, 1H), 2.83 – 2.70 (m, 2H), 2.61 – 2.56 (m, 1H), 2.51 (d, *J* = 9.9 Hz, 1H), 2.47 – 2.35 (m, 1H), 2.04 (d, 1H), 2.00 – 1.88 (m, 2H), 1.83 (d, *J* = 9.8 Hz, 1H), 1.72 – 1.62 (m, 2H). ; 648.5 [M+H]$^+$	1.25
489		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.91 (s, 1H), 8.49 (s, 1H), 8.37 (s, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.77 (dd, *J* = 7.6, 5.7 Hz, 2H), 7.60 – 7.41 (m, 3H), 6.92 (s, 1H), 6.78 (d, *J* = 7.5 Hz, 2H), 6.45 – 6.31 (m, 2H), 6.24 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.73 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.44 (s, 1H), 4.24 – 4.12 (m, 2H), 4.09 (d, *J* = 7.9 Hz, 1H), 3.86 (s, 3H), 3.77 (s, 1H), 3.67 (dd, *J* = 7.9, 1.6 Hz, 1H), 3.14 (dd, *J* = 10.0, 1.8 Hz, 1H), 3.07 – 2.99 (m, 2H), 2.99 – 2.92 (m, 1H), 2.82 – 2.71 (m, 2H), 2.61 – 2.56 (m, 1H), 2.51 (d, *J* = 9.9 Hz, 1H), 2.47 – 2.35 (m, 1H), 2.04 (d, *J* = 13.7 Hz, 1H), 1.99 – 1.88 (m, 2H), 1.83 (d, *J* = 9.8 Hz, 1H), 1.73 – 1.64 (m, 2H). ; 648.5 [M+H]$^+$	1.25
490		N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (s, 1H), 8.46 (s, 1H), 8.37 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.91 – 7.85 (m, 1H), 7.81 – 7.73 (m, 2H), 7.60 – 7.41 (m, 3H), 6.91 (s, 1H), 6.77 (d, *J* = 10.2 Hz, 2H), 6.43 – 6.31 (m, 2H), 6.24 (dd, *J* = 17.0, 10.0 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.24 – 4.11 (m, 2H), 3.85 (s, 3H), 3.06 (d, *J* = 9.6 Hz, 2H), 3.01 – 2.92 (m, 1H), 2.82 – 2.53 (m, 11H), 2.45 – 2.36 (m, 1H), 2.30 (d, *J* = 10.9 Hz, 1H), 2.10 (d, *J* = 12.5 Hz, 2H), 1.73 – 1.64 (m, 2H), 1.08 (d, *J* = 6.5 Hz, 6H). ; 677.5 [M+H]$^+$	1.22

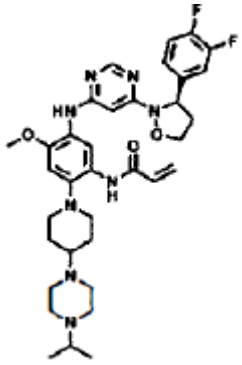
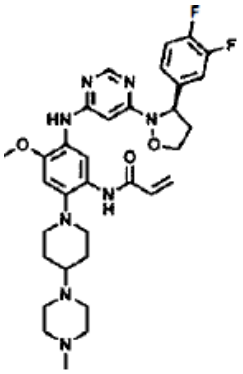
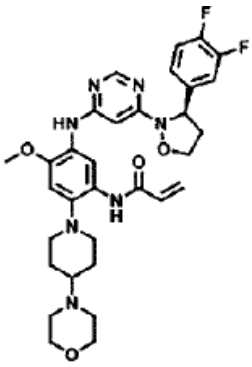
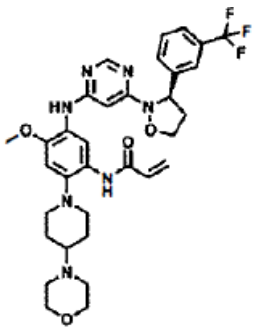
[561]

491		N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (s, 1H), 8.44 (s, 1H), 8.37 (s, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 7.88 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.77 (dd, *J* = 7.7, 5.2 Hz, 2H), 7.60 – 7.41 (m, 3H), 6.92 (s, 1H), 6.77 (d, *J* = 12.4 Hz, 2H), 6.45 – 6.33 (m, 2H), 6.26 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.24 – 4.11 (m, 2H), 3.85 (s, 3H), 3.78 – 3.65 (m, 2H), 3.06 (s, 2H), 3.03 – 2.91 (m, 1H), 2.88 (d, *J* = 10.8 Hz, 2H), 2.72 (dt, *J* = 12.7, 10.3 Hz, 2H), 2.41 (dtd, *J* = 11.9, 7.9, 3.9 Hz, 1H), 2.29 (d, *J* = 4.0 Hz, 1H), 2.07 (d, *J* = 12.4 Hz, 2H), 1.90 (t, *J* = 10.6 Hz, 2H), 1.67 (dt, *J* = 12.2, 6.0 Hz, 2H), 1.21 (d, *J* = 6.2 Hz, 6H). ; 664.5 [M+H]$^+$	1.30
492		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, CDCl$_3$) δ 8.85 (s, 1H), 8.49 (s, 1H), 8.35 (s, 1H), 7.79 (s, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.01 (s, 1H), 6.75 (s, 1H), 6.73 (s, 1H), 6.38 - 6.12 (m, 2H), 5.75 - 5.65 (m, 2H), 4.16 (td, *J* = 8.0, 4.1 Hz, 1H), 4.08 (q, *J* = 8.0 Hz, 1H), 3.85 (s, 3H), 3.13 - 3.06 (m, 1H), 3.06 - 2.98 (m, 2H), 2.98 - 2.90 (m, 2H), 2.85 - 2.69 (m, 3H), 2.68 - 2.62 (m, 1H), 2.54 - 2.47 (m, 1H), 2.38 - 2.23 (m, 8H), 2.13 - 2.02 (m, 3H), 1.90 - 1.68 (m, 3H); 638.56[M+H]$^+$	0.99
493		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	; 623.60[M+H]$^+$	1.11
494		N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, CDCl$_3$) δ 8.86 (s, 1H), 8.46 (s, 1H), 8.36 (s, 1H), 7.79 (s, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 6.93 (s, 1H), 6.76 (s, 1H), 6.73 (s, 1H), 6.38 - 6.20 (m, 2H), 5.76 - 5.60 (m, 2H), 4.16 (td, *J* = 8.0, 4.1 Hz, 1H), 4.08 (q, *J* = 8.0 Hz, 1H), 3.85 (s, 3H), 3.10 - 3.02 (m, 2H), 2.86 - 2.68 (m, 7H), 2.38 - 2.29 (m, 2H), 2.14 - 2.06 (m, 2H), 1.73 - 1.60 (m, 7H), 1.10 (s, 3H), 1.08 (s, 3H); 652.68[M+H]$^+$	1.07
495		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(3-methoxy-3-methylbutoxy)phenyl)acrylamide	^{1}H NMR (400 MHz, CDCl$_3$) δ 8.79 (s, 1H), 8.33 (s, 1H), 8.15 (s, 1H), 7.03 - 6.97 (m, 2H), 6.75 (s, 1H), 6.71 - 6.64 (m, 1H), 6.61 (s, 1H), 6.58 (s, 1H), 6.42 - 6.26 (m, 2H), 5.72 (dd, *J* = 9.7, 1.9 Hz, 1H), 5.66 (dd, *J* = 8.6, 4.5 Hz, 1H), 4.18 - 4.09 (m, 3H), 4.06 - 3.99 (m, 1H), 3.84 (s, 3H), 3.27 (s, 3H), 2.80 - 2.72 (m, 1H), 2.37 - 2.28 (m, 1H), 2.04 (t, *J* = 6.5 Hz, 2H), 1.29 (s, 6H); 570.38[M+H]$^+$	1.60

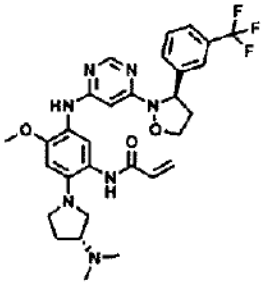
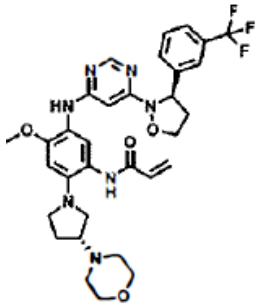
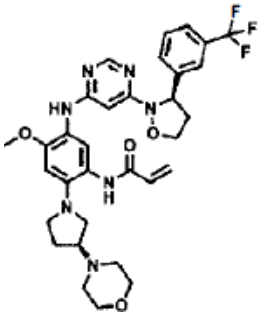
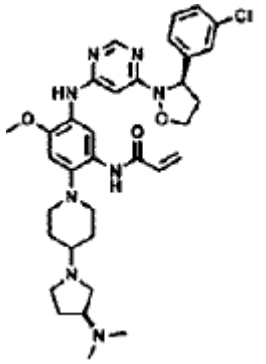
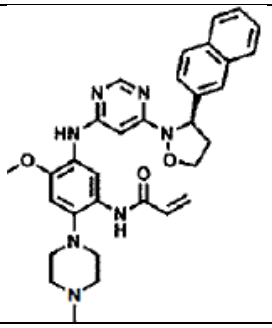
[562]

496		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(3-methoxy-3-methylbutoxy)phenyl)-(E)-4-(dimethylamino)but-2-enamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.31 (s, 1H), 7.99 (s, 1H), 7.04 - 6.85 (m, 4H), 6.70 - 6.64 (m, 1H), 6.60 (s, 1H), 6.57 (s, 1H), 6.15 (d, J = 15.3 Hz, 1H), 5.66 (dd, J = 8.6, 4.6 Hz, 1H), 4.18 - 4.09 (m, 3H), 4.03 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.27 (s, 3H), 3.15 (d, J = 6.1 Hz, 2H), 2.80 - 2.71 (m, 1H), 2.35 - 2.28 (m, 7H), 2.07 - 2.02 (m, 2H), 1.29 (s, 6H); 627.53[M+H]$^+$	1.29
497		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	634.4[M+H]$^+$	1.21
498		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	634.5[M+H]$^+$	1.22
499		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.50 (s, 1H), 9.47 (s, 1H), 8.37 (s, 1H), 7.83 (s, 1H), 7.48 - 7.39 (m, 2H), 7.26 - 7.20 (m, 1H), 7.02 (s, 1H), 6.70 - 6.68 (m, 1H), 6.27 (dd, J = 17.0, 1.9 Hz, 1H), 6.17 - 6.08 (m, 1H), 5.80 - 5.76 (m, 1H), 5.58 - 5.54 (m, 2H), 4.32 (dd, J = 7.6, 4.5 Hz, 1H), 4.12 - 3.95 (m, 3H), 3.84 (s, 3H), 3.65 (d, J = 9.5 Hz, 2H), 3.46 (s, 1H), 3.34 - 3.27 (m, 2H), 2.95 (dd, J = 8.1, 4.4 Hz, 1H), 2.85 (s, 3H), 2.46 (d, J = 8.9 Hz, 2H), 2.38 - 2.31 (m, 1H), 2.21 (d, J = 25.6 Hz, 4H).: 631.3 [M+H]$^+$	1.17
500		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H), 9.34 (s, 1H), 8.34 (s, 1H), 7.85 (s, 1H), 7.44 (dtd, J = 10.5, 8.5, 7.2, 3.0 Hz, 2H), 7.26 - 7.16 (m, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.76 - 6.66 (m, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.11 (s, 1H), 5.76 (dd, J = 10.1, 1.9 Hz, 1H), 5.54 (dd, J = 8.5, 5.3 Hz, 1H), 4.31 (q, J = 3.2 Hz, 2H), 4.04 (dd, J = 18.6, 11.1 Hz, 3H), 3.82 (s, 3H), 3.75 (s, 1H), 3.66 - 3.50 (m, 2H), 3.39 (d, J = 11.8 Hz, 1H), 3.26 (d, J = 11.4 Hz, 2H), 2.93 (ddd, J = 18.3, 9.0, 5.0 Hz, 1H), 2.87 - 2.77 (m, 8H), 2.47 - 2.39 (m, 1H), 2.36 - 2.28 (m, 1H), 2.24 - 2.05 (m, 4H).: 631.3 [M+H]$^+$	1.1

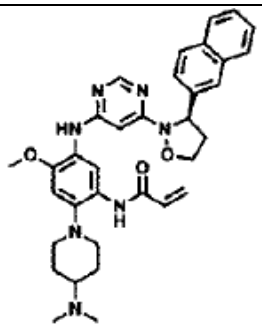
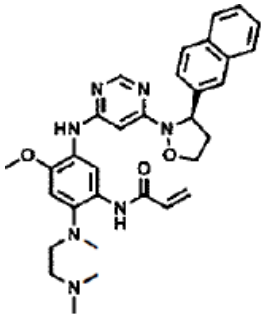
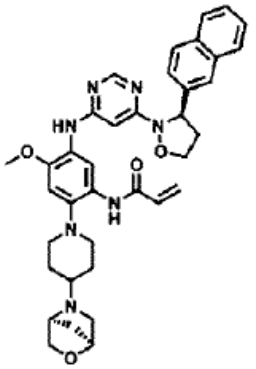
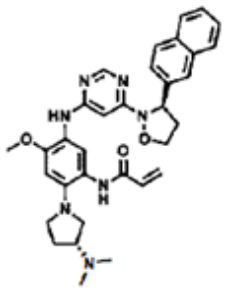
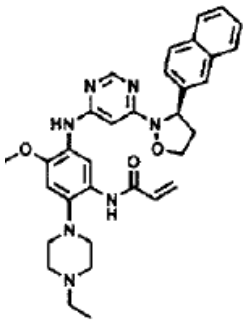
[563]

501		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	663.5[M+H]$^+$	1.16
502		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.19 (s, 1H), 9.24 (s, 1H), 8.33 (s, 1H), 7.90 (s, 1H), 7.48 - 7.41 (m, 2H), 7.25 - 7.19 (m, 1H), 6.92 (s, 1H), 6.75 - 6.67 (m, 1H), 6.25 (dd, *J* = 17.0, 1.9 Hz, 1H), 6.11 (s, 1H), 5.76 (dd, *J* = 10.0, 2.0 Hz, 1H), 5.53 (dd, *J* = 8.5, 5.4 Hz, 1H), 4.31 (d, *J* = 4.5 Hz, 1H), 4.06 (d, *J* = 7.8 Hz, 1H), 3.81 (s, 3H), 3.76 (d, *J* = 18.4 Hz, 3H), 3.62 (d, *J* = 8.9 Hz, 5H), 3.44 (s, 1H), 3.24 (d, *J* = 11.3 Hz, 2H), 2.92 (dd, *J* = 8.2, 4.4 Hz, 1H), 2.83 (d, *J* = 14.2 Hz, 5H), 2.37 - 2.28 (m, 1H), 2.23 - 2.06 (m, 4H).; 635.3 [M+H]$^+$	1.13
503		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.11 (s, 1H), 9.23 (s, 1H), 8.33 (s, 1H), 7.89 (s, 1H), 7.44 (ddq, *J* = 11.4, 6.3, 3.0, 2.3 Hz, 2H), 7.26 - 7.20 (m, 1H), 6.92 (s, 1H), 6.69 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.25 (dd, *J* = 17.0, 1.9 Hz, 1H), 6.11 (s, 1H), 5.76 (dd, *J* = 10.1, 1.9 Hz, 1H), 5.56 - 5.52 (m, 1H), 4.29 (dd, *J* = 7.6, 4.4 Hz, 1H), 4.08 - 4.03 (m, 1H), 3.99 (d, *J* = 7.5 Hz, 4H), 3.44 (d, *J* = 12.0 Hz, 2H), 3.24 (d, *J* = 11.3 Hz, 3H), 3.17 - 3.08 (m, 2H), 2.97 - 2.87 (m, 1H), 2.79 (t, *J* = 11.8 Hz, 2H), 2.33 (ddd, *J* = 10.0, 7.8, 5.2 Hz, 1H), 2.22 (d, *J* = 10.3 Hz, 2H), 2.13 - 2.01 (m, 2H).; 622.3 [M+H]$^+$	1.17
504		N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.74 (s, 1H), 8.44 (s, 1H), 8.29 (s, 1H), 7.75 (s, 1H), 7.71 (s, 1H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.48 (dt, *J* = 15.3, 7.7 Hz, 2H), 6.75 (s, 1H), 6.66 (s, 1H), 6.40 - 6.33 (m, 1H), 6.28 (dd, *J* = 16.9, 9.7 Hz, 1H), 5.74 (dt, *J* = 9.0, 2.4 Hz, 2H), 4.15 (td, *J* = 8.0, 4.2 Hz, 1H), 4.07 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.81 (t, *J* = 4.7 Hz, 4H), 3.08 (t, *J* = 8.8 Hz, 2H), 2.83 (tt, *J* = 8.1, 4.0 Hz, 1H), 2.77 (d, *J* = 11.7 Hz, 2H), 2.73 (d, *J* = 3.8 Hz, 4H), 2.45 (tt, *J* = 11.2, 3.8 Hz, 1H), 2.36 (dq, *J* = 11.0, 3.5 Hz, 1H), 2.12 - 2.07 (m, 2H), 1.74 (qd, *J* = 12.1, 4.0 Hz, 2H): 654.5[M+H]$^+$	1.29

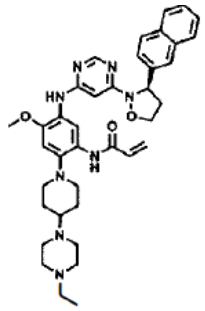
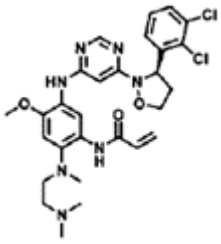
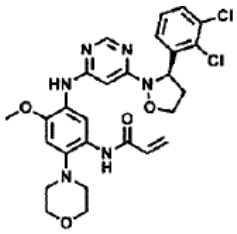
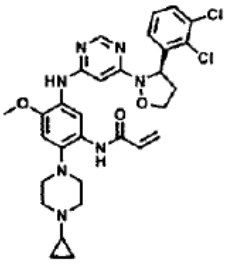
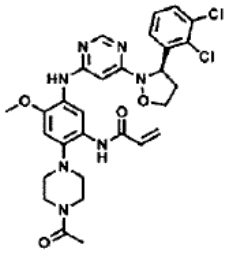
[564]

505		N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	508.4[M+H]+	1.24
506		N-(4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.15 (d, J = 0.5 Hz, 1H), 7.78 - 7.60 (m, 3H), 7.60 - 7.53 (m, 2H), 6.71 (s, 1H), 6.58 (dd, J = 17.0, 10.3 Hz, 1H), 6.41 - 6.32 (m, 2H), 5.80 (dd, J = 10.3, 1.4 Hz, 1H), 5.65 (dd, J = 8.5, 4.8 Hz, 1H), 4.17 (td, J = 7.9, 4.2 Hz, 1H), 4.01 - 3.94 (m, 1H), 3.88 (s, 3H), 3.84 (t, J = 4.4 Hz, 4H), 3.30 - 3.20 (m, 8H), 2.95 - 2.83 (m, 4H), 2.40 - 2.28 (m, 2H), 2.05 (t, J = 15.6 Hz, 1H) : 640.4 [M+H]$^+$	1.25
507		N-(4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.14 (s, 1H), 7.73 (t, J = 11.3 Hz, 3H), 7.60 - 7.51 (m, 2H), 6.67 (s, 1H), 6.54 (dd, J = 17.0, 10.2 Hz, 1H), 6.40 - 6.31 (m, 2H), 5.79 (dd, J = 10.3, 1.5 Hz, 1H), 5.64 (dd, J = 8.5, 4.8 Hz, 1H), 4.15 (td, J = 7.9, 4.2 Hz, 1H), 3.97 (d, J = 7.9 Hz, 1H), 3.87 (s, 3H), 3.77 (t, J = 4.6 Hz, 4H), 3.39 - 3.25 (m, 7H), 3.11 - 3.01 (m, 1H), 2.91 - 2.78 (m, 1H), 2.76 - 2.56 (m, 4H), 2.40 - 2.30 (m, 1H), 2.25 (dtd, J = 12.9, 6.5, 3.3 Hz, 1H), 2.01 - 1.86 (m, 1H) : 640.4 [M+H]$^+$	1.22
508		N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	: 647.5[M+H]+	1.14
509		N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.92 (s, 1H), 8.54 (s, 1H), 8.38 (d, J = 0.9 Hz, 1H), 7.94 (d, J = 1.7 Hz, 1H), 7.85 - 7.79 (m, 3H), 7.44 (td, J = 7.4, 6.7, 3.8 Hz, 2H), 6.97 (s, 1H), 6.77 (d, J = 24.0 Hz, 2H), 6.44 - 6.22 (m, 2H), 5.85 (dd, J = 8.7, 4.5 Hz, 1H), 5.76 (dd, J = 9.0, 1.6 Hz, 1H), 4.20 (td, J = 7.9, 4.4 Hz, 1H), 4.11 (q, J = 7.9 Hz, 1H), 3.84 (s, 3H), 3.64 - 3.57 (m, 2H), 3.03 (d, J = 7.4 Hz, 2H), 2.94 - 2.90 (m, 3H), 2.40 (s, 3H), 1.51 (t, J = 7.4 Hz, 4H).: 566.4[M+H]$^+$	1.21

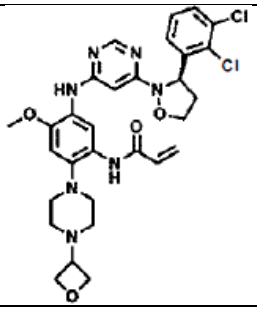
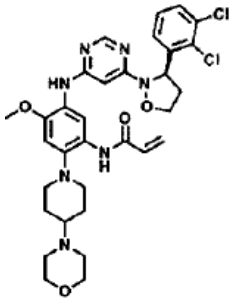
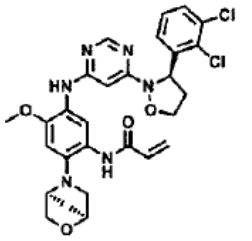
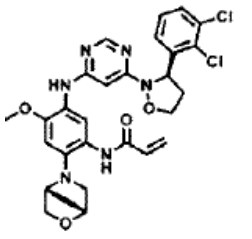
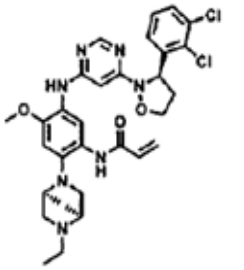
[565]

510		N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.94 (s, 1H), 7.81 (dt, J = 9.3, 3.7 Hz, 2H), 7.44 (ddt, J = 9.1, 6.8, 3.3 Hz, 2H), 7.02 (s, 1H), 6.73 (d, J = 5.2 Hz, 2H), 6.41 - 6.27 (m, 2H), 6.22 - 6.17 (m, 1H), 5.85 (dd, J = 8.6, 4.5 Hz, 1H), 5.75 (dd, J = 9.7, 1.8 Hz, 1H), 5.62 (dd, J = 9.1, 3.1 Hz, 1H), 4.20 (td, J = 8.0, 4.5 Hz, 1H), 4.11 (q, J = 7.0 Hz, 1H), 3.84 (s, 3H), 3.72 (dd, J = 14.8, 5.8 Hz, 2H), 3.55 (h, J = 6.7 Hz, 2H), 2.99 (t, J = 7.4 Hz, 1H), 2.77 - 2.71 (m, 2H), 2.46 (s, 6H), 2.09 (d, J = 12.4 Hz, 2H), 1.76 (qd, J = 12.1, 3.9 Hz, 2H), 1.41 (d, J = 7.4 Hz, 1H).; 504.4[M+H]$^+$	1.21
511		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 9.57 (s, 1H), 8.87 (s, 1H), 8.36 (s, 1H), 7.94 (s, 1H), 7.81 (dd, J = 8.2, 3.8 Hz, 3H), 7.57 (dd, J = 8.5, 1.8 Hz, 1H), 7.44 (dq, J = 7.6, 5.3, 3.9 Hz, 2H), 7.10 (s, 1H), 6.73 (d, J = 28.7 Hz, 2H), 6.42 (dd, J = 16.8, 2.1 Hz, 1H), 5.85 (dd, J = 8.7, 4.6 Hz, 1H), 5.71 (dd, J = 10.1, 2.0 Hz, 1H), 4.23 (td, J = 7.9, 4.3 Hz, 1H), 4.15 (t, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.69 - 3.62 (m, 2H), 3.23 - 3.19 (m, 2H), 3.12 - 3.07 (m, 2H), 2.99 (s, 1H), 2.72 (s, 3H), 2.70 (s, 6H).; 568.4[M+H]$^+$	1.28
512		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.80 (s, 1H), 8.52 (s, 1H), 8.35 (s, 1H), 7.93 (d, J = 1.7 Hz, 1H), 7.86 - 7.79 (m, 3H), 7.56 (dd, J = 8.5, 1.8 Hz, 1H), 7.45 (qd, J = 7.4, 3.6 Hz, 2H), 6.70 (d, J = 3.7 Hz, 2H), 6.54 - 6.34 (m, 2H), 5.83 (dd, J = 8.7, 4.7 Hz, 1H), 5.77 (dd, J = 9.6, 2.0 Hz, 1H), 4.61 (s, 1H), 4.30 (s, 1H), 4.22 (tt, J = 7.9, 4.6 Hz, 2H), 4.11 (q, J = 7.9 Hz, 1H), 3.83 (d, J = 4.7 Hz, 3H), 3.69 - 3.62 (m, 3H), 3.12 (d, J = 8.5 Hz, 3H), 2.89 - 2.68 (m, 4H), 2.60 - 2.38 (m, 4H), 2.07 (dt, J = 33.4, 13.3 Hz, 3H).; 648.6[M+H]$^+$	1.24
513		N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.33 (s, 1H), 8.53 (s, 1H), 8.14 (s, 1H), 7.90 (td, J = 7.5, 6.8, 3.3 Hz, 4H), 7.61 - 7.44 (m, 4H), 6.59 (s, 1H), 6.49 (dd, J = 17.1, 10.2 Hz, 1H), 6.30 (s, 1H), 6.20 (dd, J = 17.1, 2.1 Hz, 1H), 5.70 (dq, J = 11.1, 5.1, 3.6 Hz, 2H), 4.18 (td, J = 7.8, 3.7 Hz, 1H), 3.90 - 3.79 (m, 4H), 3.32 (s, 6H), 2.83 (dtd, J = 12.1, 8.1, 3.8 Hz, 2H), 2.65 (d, J = 19.7 Hz, 3H), 2.30 - 2.31 (m, 2H), 2.25 (s, 1H), 1.97 (s, 1H), .; 580.4[M+H]$^+$	1.19
514		N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.54 (s, 1H), 9.06 (s, 1H), 8.86 (s, 1H), 8.26 (s, 1H), 8.20 (s, 1H), 7.94 - 7.88 (m, 3H), 7.56 (dd, J = 8.5, 1.7 Hz, 1H), 7.50 (tt, J = 8.1, 3.7 Hz, 2H), 6.84 (s, 1H), 6.66 (dd, J = 17.1, 10.2 Hz, 1H), 6.38 (s, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 5.79 - 5.74 (m, 1H), 5.70 (dd, J = 8.6, 5.3 Hz, 1H), 4.23 (d, J = 3.9 Hz, 1H), 3.92 (t, J = 7.9 Hz, 1H), 3.83 (s, 3H), 3.58 (d, J = 11.6 Hz, 2H), 3.22 (d, J = 11.8 Hz, 6H), 3.04 (t, J = 12.5 Hz, 2H), 2.91 - 2.82 (m, 1H), 2.36 (dt, J = 8.8, 5.1 Hz, 1H), 1.28 (t, J = 7.2 Hz, 3H), .; 580.4[M+H]$^+$	1.25

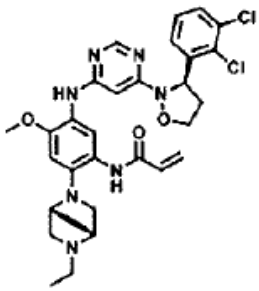
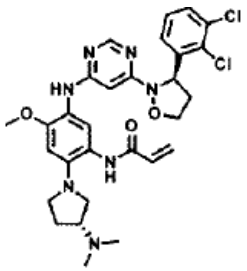
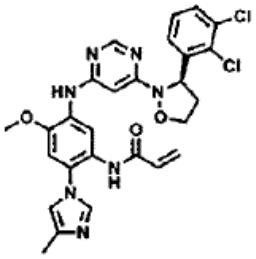
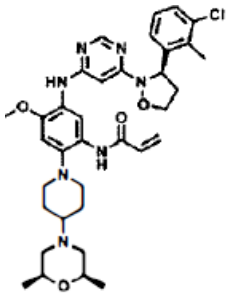
[566]

515		N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.01 (s, 1H), 8.76 (s, 1H), 8.16 (d, J = 16.7 Hz, 2H), 7.95 - 7.86 (m, 4H), 7.56 (dd, J = 8.4, 1.8 Hz, 1H), 7.50 (qd, J = 7.6, 6.9, 3.7 Hz, 2H), 6.83 (s, 1H), 6.63 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.23 (dd, J = 17.0, 1.9 Hz, 1H), 5.77 - 5.62 (m, 2H), 4.21 (dd, J = 7.7, 3.9 Hz, 1H), 3.91 (q, J = 8.1 Hz, 1H), 3.81 (s, 3H), 3.51 (s, 3H), 3.31 (s, 2H), 3.11 (d, J = 11.6 Hz, 4H), 2.94 (s, 1H), 2.91 - 2.81 (m, 2H), 2.72 (t, J = 11.8 Hz, 3H), 2.41 - 2.32 (m, 2H), 1.94 (s, 2H), 1.79 (s, 2H), 1.20 (t, J = 7.2 Hz, 3H). : 663.5[M+H]$^+$	1.2
516		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-d) δ 11.32 (s, 1H), 9.96 (s, 1H), 8.92 (s, 1H), 8.36 (s, 1H), 7.60 (d, J =8.9 Hz, 1H), 7.37 (d, J = 9.4 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.96 (s, 1H), 6.82 (s, 1H), 6.77 (s, 1H),6.40 (d, J = 16.5 Hz, 1H), 5.99 (s, 1H), 5.60 (d, J = 11.9 Hz, 1H), 4.12 (m, 2H), 3.85 (s, 3H), 3.60 - 3.61(m, 1H), 3.08 (d, J = 7.4 Hz, 1H), 2.95 (d, J = 3.3 Hz, 2H), 2.73 (s, 3H), 2.43 (s, 6H), 2.24 (d, J = 12.4Hz, 2H).: 586.3 [M+H]$^+$	1.37
517		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide	1H NMR (400 MHz, chloroform-d) δ 8.93 (s, 1H), 8.51 (s, 1H), 8.37 (s, 1H), 7.60 (d, J = 8.8 Hz, 1H),7.37 (d, J = 9.2 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.96 (s, 1H), 6.78 (d, J = 4.6 Hz, 2H), 6.37 (d, J = 17.0Hz, 1H), 6.28 (m, 1H), 5.96 (m, 1H), 5.76 (d, J = 11.3 Hz, 1H), 4.11 (m, 2H), 3.87 (m, 7H), 2.96 (m, 1H),2.80 (m, 4H), 2.24 (m, 1H).: 571.3 [M+H]$^+$	1.64
518		N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-d) δ 8.90 (s, 1H), 8.60 (s, 1H), 8.36 (s, 1H), 7.60 (d, J = 7.7 Hz, 1H),7.37 (d, J = 9.3 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.94 (s, 1H), 6.78 (d, J = 13.6 Hz, 2H), 6.37 (d, J = 18.3Hz, 1H), 6.30 (m, 1H), 5.96 (m, 1H), 5.75 (d, J = 9.8 Hz, 1H), 4.11 (m, 2H), 3.82 (s, 3H), 2.90 m, 8H),2.23 (m, 2H), 1.73 (m, 1H), 0.52 (d, J = 6.4 Hz, 2H), 0.47 (t, J = 3.8 Hz, 2H).: 610.3 [M+H]$^+$	1.36
519		N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-d) δ 8.94 (s, 1H), 8.44 (s, 1H), 8.37 (s, 1H), 7.60 (d, J = 8.9 Hz, 1H),7.36 (d, J = 9.3 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.98 (s, 1H), 6.75 (d, J = 17.0 Hz, 2H), 6.38 (d, J = 16.0Hz, 1H), 6.28 (m, 1H), 5.96 (m, 1H), 5.76 (d, J = 10.0 Hz, 1H), 4.09 (m, 2H), 3.86 (s, 3H), 3.80 (s, 2H),3.64 (m, 2H), 2.96 (m, 1H), 2.87 (m, 3H), 2.61 (s, 3H), 2.21 (m, 1H), 2.02 (s, 1H).: 612.3 [M+H]$^+$	1.54

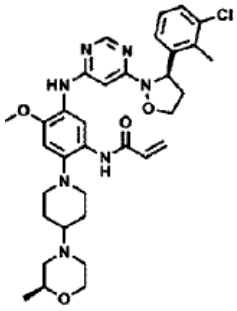
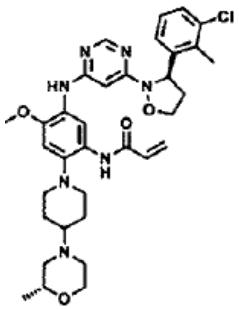
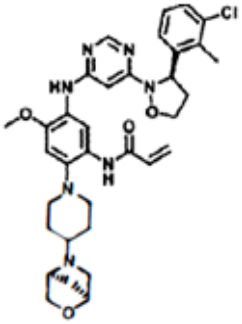
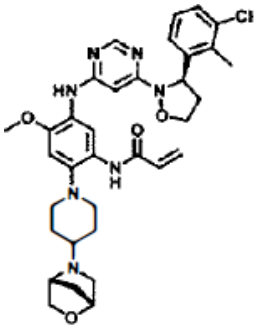
[567]

520		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.92 (s, 1H), 8.49 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 7.63 - 7.56 (m,1H), 7.37 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.96 (s, 1H), 6.82 (s, 1H), 6.76 (s, 1H), 6.36(dd, *J* = 17.0, 1.5 Hz, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.97 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.74 (dd, *J* =10.0, 1.5 Hz, 1H), 4.72 (t, *J* = 6.6 Hz, 2H), 4.67 (t, *J* = 6.2 Hz, 2H), 4.16 - 4.03 (m, 2H), 3.86 (s, 3H), 3.61(p, *J* = 6.5 Hz, 1H), 3.01 - 2.89 (m, 5H), 2.64 - 2.45 (m, 4H), 2.24 (dp, *J*= 12.1, 4.1 Hz, 1H).: 626.33 $[M+H]^+$	1.34
521		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.60 (d, *J* = 7.8 Hz, 1H),7.37 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.93 (s, 1H), 6.76 (s, 2H), 6.36 (d, *J* = 16.8 Hz,1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.96 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.81 - 5.70 (m, 1H), 4.16 - 4.04 (m,2H), 3.85 (s, 3H), 3.78 (t, *J* = 4.7 Hz, 4H), 3.07 (d, *J* = 11.4 Hz, 2H), 3.00 - 2.90 (m, 1H), 2.73 (q, *J* =12.3 Hz, 3H), 2.65 - 2.56 (m, 4H), 2.37 - 2.17 (m, 3H), 2.08 (d, *J* = 12.5 Hz, 2H).: 654.4 $[M+H]^+$	1.34
522		N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.68 (s, 1H), 8.35 (s, 1H), 7.95 (s, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.37 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.90 (s, 1H), 6.69 (d, *J* = 13.7 Hz, 2H), 6.39 (d, *J* = 16.8 Hz, 1H), 6.28 (dd, *J* = 16.8, 10.0 Hz, 1H), 5.96 (dd, *J* = 8.8, 4.5 Hz, 1H), 5.75 (d, *J* = 10.2 Hz, 1H), 4.65 (s, 1H), 4.14 - 3.99 (m, 3H), 3.86 (s, 3H), 3.76 (d, *J* = 7.8 Hz, 1H), 3.43 (d, *J* = 10.1 Hz, 1H), 3.24 (d, *J* = 10.1 Hz, 1H), 2.94 (dtd, *J* = 12.4, 8.1, 4.2 Hz, 1H), 2.61 (s, 1H), 2.22 (tdd, *J* = 12.9, 8.7, 4.6 Hz, 1H), 2.09 (d, *J* = 9.8 Hz, 1H), 1.99 (d, *J* = 10.6 Hz, 1H).: 583.3[M+H]	1.48
523		N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.64 (s, 1H), 8.35 (s, 1H), 7.95 (s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.37 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.88 (s, 1H), 6.73 (s, 2H), 6.39 (d, *J* = 16.8 Hz, 1H), 6.28 (dd, *J* = 17.0, 10.0 Hz, 1H), 5.97 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.76 (d, *J* = 9.9 Hz, 1H), 4.65 (s, 1H), 4.16 - 4.01 (m, 3H), 3.86 (s, 3H), 3.75 (d, *J* = 7.8 Hz, 1H), 3.46 (d, *J* = 10.1 Hz, 1H), 3.20 (d, *J* = 10.1 Hz, 1H), 3.00 - 2.89 (m, 1H), 2.62 (s, 1H), 2.23 (dtd, *J* = 12.6, 8.2, 4.6 Hz, 1H), 2.09 (d, *J* = 10.0 Hz, 1H), 2.00 (d, *J* = 9.9 Hz, 1H).: 583.3[M+H]	1.48
524		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.65 (s, 1H), 8.34 (s, 1H), 8.15 (s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.37 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.95 (s, 1H), 6.81 (s, 1H), 6.66 (s, 1H), 6.39 (d, *J* = 16.5 Hz, 1H), 6.26 - 6.13 (m, 1H), 5.95 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.75 - 5.66 (m, 1H), 4.09 (dd, *J* = 7.9, 4.2 Hz, 1H), 4.03 (q, *J* = 8.1 Hz, 1H), 3.88 (s, 3H), 3.13 (d, *J* = 9.6 Hz, 1H), 2.98 - 2.90 (m, 1H), 2.83 (d, *J* = 10.8 Hz, 1H), 2.35 (d, *J* = 25.1 Hz, 1H), 2.22 (dtd, *J* = 12.6, 8.2, 4.5 Hz, 1H), 1.51 (t, *J* = 7.6 Hz, 1H), 1.45 (d, *J* = 6.7 Hz, 2H), 1.37 - 1.21 (m, 7H).: 610.3[M+H]	1.29

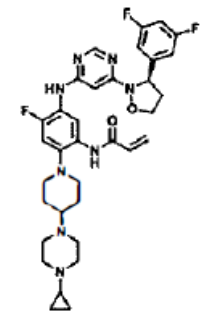
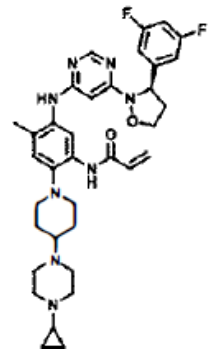
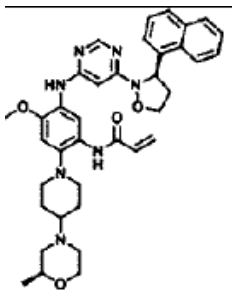
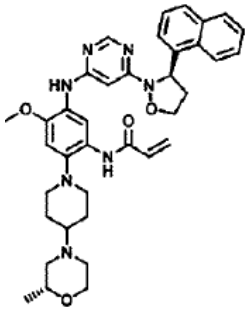
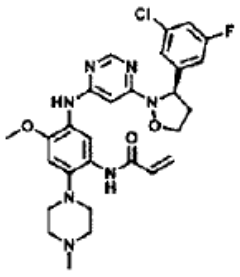
[568]

525		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.62 (s, 1H), 8.34 (s, 1H), 8.09 (s, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.37 (dd, J = 8.0, 1.6 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.92 (s, 1H), 6.73 (s, 1H), 6.38 (d, J = 15.9 Hz, 1H), 6.32 - 6.14 (m, 1H), 5.96 (dd, J = 8.7, 4.4 Hz, 1H), 5.78 - 5.66 (m, 2H), 4.14 - 4.04 (m, 2H), 3.88 (s, 3H), 3.09 (d, J = 10.5 Hz, 1H), 2.95 (ddt, J = 12.2, 8.0, 4.0 Hz, 2H), 2.80 (s, 2H), 2.32 (d, J = 21.0 Hz, 1H), 2.25 - 2.20 (m, 1H), 2.07 (s, 2H), 1.39 - 1.17 (m, 6H).; 610.3[M+H]	1.29
526		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 11.35 (s, 1H), 8.58 (s, 1H), 8.33 (d, J = 1.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.36 (dd, J = 8.0, 1.6 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.86 (s, 1H), 6.74 (s, 1H), 6.68 (s, 1H), 6.41 (d, J = 16.3 Hz, 1H), 5.96 (dd, J = 8.8, 4.4 Hz, 1H), 5.72 (d, J = 11.7 Hz, 1H), 4.14 - 4.02 (m, 2H), 3.84 (s, 3H), 3.69 - 3.61 (m, 1H), 3.32 (dd, J = 7.3, 5.3 Hz, 1H), 3.12 - 3.05 (m, 2H), 2.95 (dq, J = 8.4, 4.0 Hz, 1H), 2.32 (d, J = 18.1 Hz, 1H), 2.23 (ddd, J = 12.4, 8.3, 4.4 Hz, 1H), 1.58 - 1.52 (m, 3H), 1.45 (d, J = 6.6 Hz, 2H), 1.26 (d, J = 4.8 Hz, 3H), 1.19 (t, J = 7.3 Hz, 1H).; 508.4[M+H]	1.29
527		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methyl-1H-imidazole-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.96 (s, 1H), 8.43 (dd, J = 7.8, 1.0 Hz, 1H), 7.59 (dd, J = 7.9, 1.6 Hz, 1H), 7.53 - 7.47 (m, 1H), 7.39 (dd, J = 8.0, 1.6 Hz, 1H), 7.24 - 7.14 (m, 2H), 6.99 (d, J = 9.0 Hz, 1H), 6.82 - 6.76 (m, 2H), 6.33 (d, J = 17.0 Hz, 1H), 6.11 (dd, J = 17.0, 10.2 Hz, 1H), 5.98 (dd, J = 8.7, 4.5 Hz, 1H), 5.73 (dd, J = 10.3, 1.2 Hz, 1H), 4.16 (td, J = 8.0, 4.1 Hz, 1H), 4.06 (q, J = 8.1 Hz, 1H), 3.90 (d, J = 2.4 Hz, 3H), 2.97 (dtd, J = 12.4, 7.9, 4.1 Hz, 1H), 2.31 (d, J = 1.0 Hz, 3H), 2.29 - 2.24 (m, 1H), 2.07 - 2.01 (m, 1H).; 566.3[M+H]	1.46
528		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.59 (s, 1H), 8.14 (d, J = 1.0 Hz, 2H), 7.40 (dd, J = 7.8, 1.3 Hz, 1H), 7.34 (dd, J = 8.0, 1.3 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.82 (s, 1H), 6.66 (dd, J = 16.9, 10.2 Hz, 1H), 6.34 (s, 1H), 6.21 (dd, J = 16.9, 2.0 Hz, 1H), 5.74 - 5.66 (m, 2H), 4.14 (td, J = 7.9, 3.8 Hz, 1H), 3.79 (s, 3H), 3.54 (dqd, J = 12.5, 6.1, 3.1 Hz, 2H), 3.05 (d, J = 11.1 Hz, 2H), 2.88 - 2.77 (m, 3H), 2.65 (td, J = 10.9, 9.6, 6.1 Hz, 2H), 2.42 (s, 3H), 2.25 (dq, J = 11.0, 5.6, 3.7 Hz, 1H), 2.12 - 2.02 (m, 1H), 1.91 - 1.77 (m, 6H), 1.70 (qd, J = 11.3, 10.5, 3.2 Hz, 2H), 1.06 (d, J = 6.3 Hz, 6H).; 662.5[M+H]$^+$	1.33

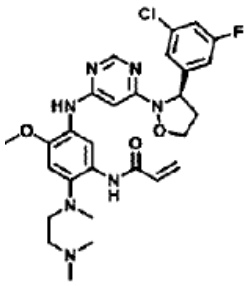
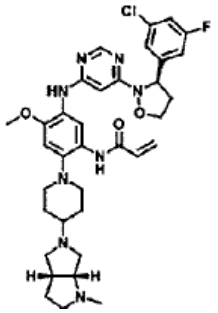
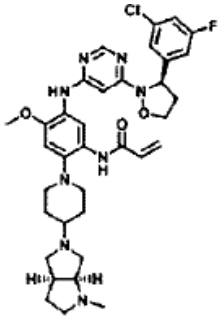
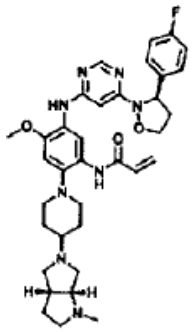
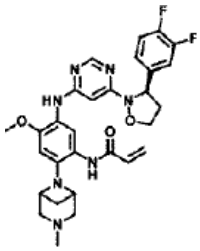
[569]

529		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.59 (s, 1H), 8.17 - 8.12 (m, 2H), 7.40 (dd, J = 7.9, 1.3 Hz, 1H), 7.34 (dd, J = 8.0, 1.3 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.21 (dd, J = 17.0, 2.0 Hz, 1H), 5.71 (td, J = 9.4, 3.4 Hz, 2H), 4.15 (td, J = 7.8, 3.7 Hz, 1H), 3.80 (s, 3H), 3.50 (t, J = 10.6 Hz, 2H), 3.42 - 3.22 (m, 4H), 3.11 - 3.00 (m, 3H), 2.83 (dtd, J = 11.0, 7.9, 3.7 Hz, 4H), 2.67 (t, J = 11.4 Hz, 2H), 2.36 - 2.18 (m, 2H), 2.08 (dtd, J = 12.6, 8.1, 5.0 Hz, 2H), 1.91 (s, 3H), 1.87 (s, 2H), 1.71 (d, J = 12.4 Hz, 3H), 1.07 (d, J = 6.2 Hz, 3H).; 648.5[M+H]$^+$	1.30
530		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.59 (s, 1H), 8.14 (d, J = 1.0 Hz, 2H), 7.40 (dd, J = 7.8, 1.3 Hz, 1H), 7.34 (dd, J = 8.0, 1.3 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.21 (dd, J = 17.0, 2.0 Hz, 1H), 5.71 (td, J = 9.0, 3.4 Hz, 2H), 4.14 (td, J = 7.8, 3.8 Hz, 1H), 3.80 (s, 3H), 3.53 - 3.45 (m, 2H), 3.33 (s, 4H), 3.12 - 3.00 (m, 3H), 2.87 - 2.71 (m, 4H), 2.66 (td, J = 10.5, 9.4, 6.1 Hz, 2H), 2.42 (s, 3H), 2.34 - 2.16 (m, 2H), 2.14 - 2.02 (m, 1H), 1.91 (s, 2H), 1.86 (d, J = 12.6 Hz, 3H), 1.70 - 1.63 (m, 3H), 1.07 (d, J = 6.3 Hz, 4H).; 648.5[M+H]$^+$	1.29
531		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.59 (s, 1H), 8.14 (d, J = 1.0 Hz, 1H), 7.40 (dd, J = 7.8, 1.3 Hz, 1H), 7.34 (dd, J = 8.0, 1.3 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.83 (s, 1H), 6.64 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.70 (td, J = 8.8, 7.7, 3.4 Hz, 2H), 4.15 (td, J = 7.9, 3.8 Hz, 1H), 3.87 (dd, J = 12.8, 7.8 Hz, 2H), 3.80 (s, 3H), 3.04 - 2.90 (m, 4H), 2.83 (dtd, J = 11.9, 8.0, 3.8 Hz, 2H), 2.70 (tdd, J = 10.0, 7.8, 2.3 Hz, 2H), 2.42 (s, 3H), 2.34 (d, J = 9.7 Hz, 1H), 2.14 - 2.01 (m, 2H), 1.90 (s, 5H), 1.76 - 1.52 (m, 5H).; 646.5[M+H]$^+$	1.27
532		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.59 (s, 1H), 8.14 (d, J = 1.0 Hz, 1H), 7.40 (dd, J = 7.9, 1.4 Hz, 1H), 7.34 (dd, J = 8.0, 1.3 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.83 (s, 1H), 6.64 (dd, J = 17.0, 10.2 Hz, 1H), 6.34 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.70 (td, J = 8.9, 7.8, 3.4 Hz, 2H), 4.15 (td, J = 7.9, 3.8 Hz, 1H), 3.87 (dd, J = 12.9, 7.8 Hz, 3H), 3.80 (s, 3H), 3.04 - 2.93 (m, 4H), 2.82 (dq, J = 8.0, 4.1 Hz, 1H), 2.71 (dt, J = 11.4, 9.1 Hz, 3H), 2.42 (s, 4H), 2.34 (d, J = 9.7 Hz, 1H), 2.10 - 2.05 (m, 1H), 1.90 (s, 6H), 1.73 - 1.55 (m, 5H).; 646.5[M+H]$^+$	1.26

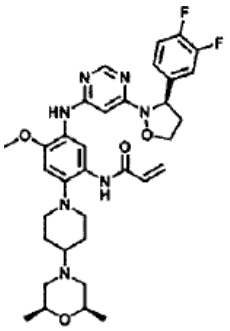
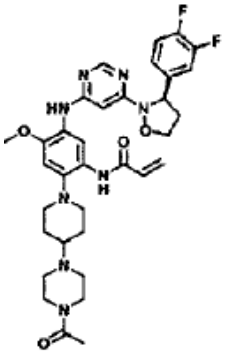
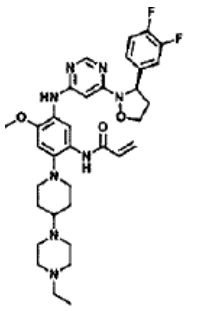
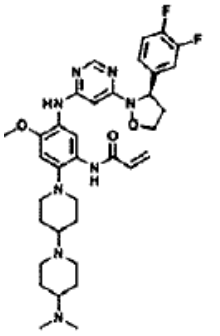
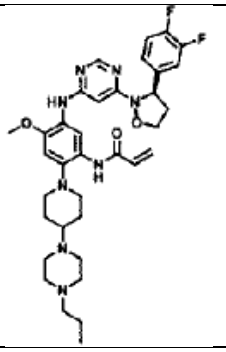
[570]

533		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-fluorophenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.32 (d, J = 8.4 Hz, 1H), 8.19 (s, 1H), 7.14 - 7.01 (m, 3H), 6.88 - 6.80 (m, 1H), 6.57 (dd, J = 10.1, 17.0 Hz, 1H), 6.46 - 6.33 (m, 2H), 5.84 (d, J = 10.3 Hz, 1H), 5.61 - 5.52 (m, 1H), 4.20 - 4.14 (m, 1H), 4.00 - 3.94 (m, 1H), 3.23 - 3.16 (m, 2H), 3.08 - 2.94 (m, 4H), 2.91 - 2.73 (m, 8H), 2.38 - 2.31 (m, 1H), 2.18 - 2.00 (m, 2H), 1.92 - 1.78 (m, 3H), 0.50 - 0.53 (m, 2H), 0.53 - 0.44 (m, 2H) : 640.3[M+H]$^+$	1.34
534		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methylphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.13 (s, 1H), 8.06 (s, 1H), 7.17 (s, 1H), 7.00 - 7.00 (m, 2H), 6.84 (tt, J = 2.5, 9.1 Hz, 1H), 6.56 (dd, J = 10.3, 17.0 Hz, 1H), 6.43 - 6.32 (m, 1H), 6.21 (s, 1H), 5.82 (d, J = 10.3 Hz, 1H), 5.55 (dd, J = 4.8, 8.7 Hz, 1H), 4.16 - 4.09 (m, 1H), 3.94 (q, J = 7.9 Hz, 1H), 3.21 - 3.14 (m, 2H), 3.10 - 2.95 (m, 4H), 2.93 - 2.76 (m, 8H), 2.37 - 2.28 (m, 1H), 2.23 (s, 3H), 2.20 - 2.11 (m, 2H), 1.93 - 1.79 (m, 3H), 0.60 - 0.53 (m, 2H), 0.52 - 0.45 (m, 2H) : 645.3[M+H]$^+$	1.24
535		N-(4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	650.5[M+H]$^+$	1.28
536		N-(4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.91 (s, 1H), 8.44 (s, 1H), 8.37 (s, 1H), 8.15 (d, J = 8.3 Hz, 1H), 7.88 (dd, J = 8.0, 1.5 Hz, 1H), 7.77 (dd, J = 7.7, 5.2 Hz, 2H), 7.60 - 7.41 (m, 3H), 6.93 (s, 1H), 6.77 (d, J = 12.2 Hz, 2H), 6.45 - 6.32 (m, 2H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.74 (dd, J = 10.0, 1.6 Hz, 1H), 4.24 - 4.09 (m, 2H), 3.96 - 3.90 (m, 1H), 3.85 (s, 3H), 3.76 - 3.60 (m, 2H), 3.12 - 3.02 (m, 2H), 3.01 - 2.93 (m, 1H), 2.93 - 2.82 (m, 2H), 2.80 - 2.66 (m, 2H), 2.45 - 2.37 (m, 1H), 2.34 - 2.26 (m, 2H), 2.11 - 2.04 (m, 2H), 1.69 - 1.63 (m, 3H), 1.26 (s, 3H). : 650.5 [M+H]$^+$	1.27
537		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	: 568.35[M+H]$^+$	1.29

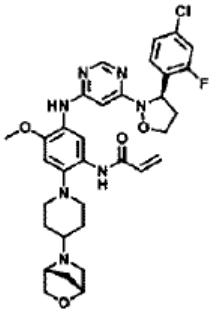
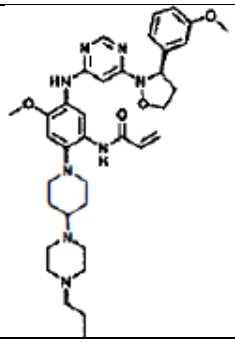
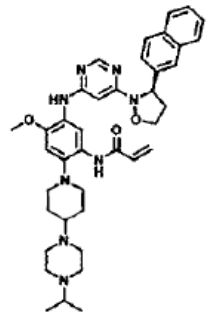
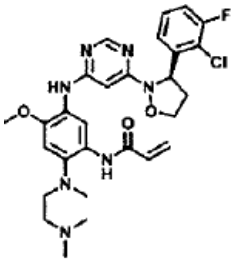
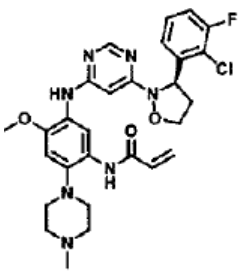
[571]

538		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	: 570.38[M+H]$^+$	1.31
539		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide	: 677.47[M+H]$^+$	1.21
540		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide	: 677.47[M+H]$^+$	1.21
541		N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide	643.3[M+H]$^+$	1.18
542		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(3-methyl-3,6-diazabicyclo[3.1.1]heptane-6-yl)phenyl)acrylamide	564.4[M+H]$^+$	1.16

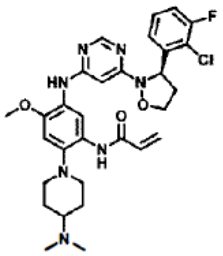
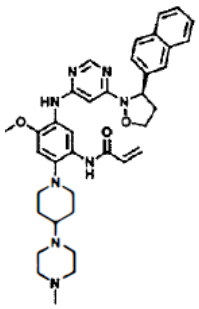
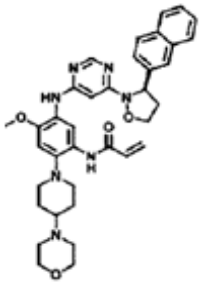
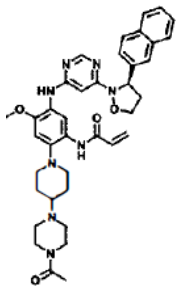
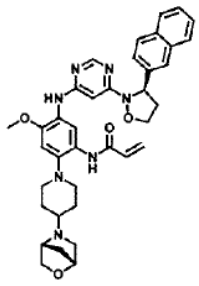
[572]

543		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.08 (s, 1H), 9.20 (s, 1H), 8.32 (s, 1H), 7.89 (s, 1H), 7.43 (ddt, *J* = 10.5, 4.7, 2.7 Hz, 2H), 7.26 - 7.21 (m, 1H), 6.92 (s, 1H), 6.60 (dd, *J* = 16.9, 10.2 Hz, 1H), 6.25 (dd, *J* = 17.0, 1.9 Hz, 1H), 6.11 (s, 1H), 5.78 (d, *J* = 1.9 Hz, 1H), 5.53 (dd, *J* = 8.4, 5.3 Hz, 1H), 4.30 (d, *J* = 4.5 Hz, 1H), 4.15 (dt, *J* = 7.7, 4.0 Hz, 2H), 4.05 (d, *J* = 7.7 Hz, 1H), 3.81 (s, 3H), 3.46 (d, *J* = 11.7 Hz, 2H), 3.23 (d, *J* = 11.8 Hz, 3H), 2.93 - 2.87 (m, 1H), 2.78 (s, 2H), 2.60 (d, *J* = 10.7 Hz, 2H), 2.32 (d, *J* = 7.7 Hz, 1H), 2.24 (d, *J* = 11.4 Hz, 2H), 2.13 - 2.03 (m, 2H), 1.17 (d, *J* = 6.2 Hz, 6H).; 650.3[M+H]$^+$	1.28
544		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	663.5[M+H]+	1.20
545		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	649.5[M+H]+	1.18
546		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide	663.5[M+H]+	1.09
547		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.08 (s, 1H), 7.24 (dd, *J* = 11.8, 7.7 Hz, 1H), 7.13 (dd, *J* = 9.2, 4.5 Hz, 2H), 6.78 (s, 1H), 6.53 (dd, *J* = 16.9, 10.3 Hz, 1H), 6.36 (s, 1H), 6.26 - 6.20 (m, 1H), 5.78 - 5.65 (m, 1H), 5.41 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.05 (td, *J* = 7.8, 4.3 Hz, 1H), 3.87 (d, *J* = 7.9 Hz, 1H), 3.75 (s, 3H), 3.22 - 3.19 (m, 1H), 3.00 (dd, *J* = 7.1, 4.0 Hz, 5H), 2.81 - 2.74 (m, 2H), 2.73 - 2.62 (m, 4H), 2.26 - 2.16 (m, 1H), 2.05 (s, 1H), 1.95 (d, *J* = 10.7 Hz, 2H), 1.79 (dd, *J* = 16.3, 7.3 Hz, 2H), 1.66 - 1.58 (m, 2H), 0.88 (t, *J* = 7.4 Hz, 3H) ; 663.5 [M+H]$^+$	1.08

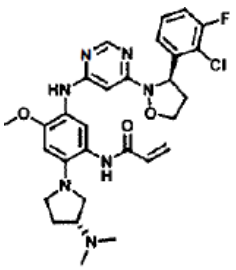
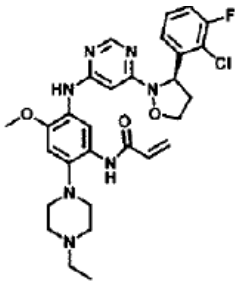
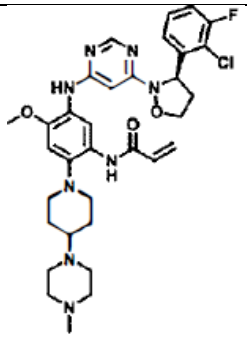
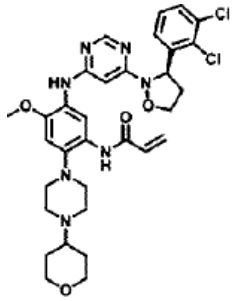
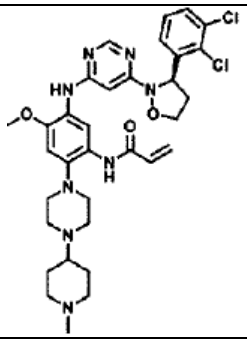
[573]

548		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.92 (s, 1H), 9.26 (d, J = 33.7 Hz, 1H), 8.30 (s, 1H), 7.80 (d, J = 12.7 Hz, 1H), 7.49 (dd, J = 10.3, 2.1 Hz, 1H), 7.40 (t, J = 8.3 Hz, 1H), 7.30 (dd, J = 8.4, 2.1 Hz, 1H), 6.92 (d, J = 7.7 Hz, 1H), 6.59 (dd, J = 17.3, 10.3 Hz, 1H), 6.20 - 6.13 (m, 2H), 5.75 (d, J = 4.5 Hz, 1H), 5.66 (dd, J = 8.6, 5.5 Hz, 1H), 4.71 - 4.55 (m, 2H), 4.33 - 4.25 (m, 1H), 4.20 (d, J = 10.3 Hz, 1H), 4.04 (d, J = 7.8 Hz, 1H), 3.82 (d, J = 1.8 Hz, 3H), 3.70 (d, J = 9.9 Hz, 1H), 3.52 - 3.40 (m, 2H), 3.30 - 3.13 (m, 3H), 2.95 - 2.67 (m, 4H), 2.20 (dd, J = 18.8, 10.0 Hz, 2H), 2.18 - 2.02 (m, 4H).: 650.3[M+H]$^+$	1.3
549		N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.10 (s, 1H), 8.07 (s, 1H), 7.15 (t, J = 8.2 Hz, 1H), 6.85 (s, 1H), 6.80 (s, 1H), 6.75 - 6.60 (m, 1H), 6.54 (dd, J = 16.9, 10.3 Hz, 1H), 6.30 - 6.21 (m, 1H), 6.14 (s, 1H), 5.70 (d, J = 10.5 Hz, 1H), 5.36 (dd, J = 8.3, 5.2 Hz, 1H), 4.14 (td, J = 7.6, 4.4 Hz, 1H), 3.93 (dd, J = 15.7, 7.8 Hz, 1H), 3.73 (s, 3H), 3.23 - 3.19 (m, 3H), 3.05 - 3.00 (m, 3H), 2.78 (ddd, J = 23.2, 18.3, 11.7 Hz, 7H), 2.31 - 2.19 (m, 1H), 2.06 (s, 3H), 2.01 (d, J = 10.6 Hz, 1H), 1.85 (d, J = 10.1 Hz, 1H), 1.77 - 1.60 (m, 2H), 1.65 (dd, J = 15.7, 7.8 Hz, 2H), 0.92 (t, J = 7.3 Hz, 3H) : 657.5 [M+H]$^+$	1.10
550		N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.97 (s, 1H), 8.59 (s, 1H), 8.16 (s, 1H), 7.95 - 7.86 (m, 4H), 7.49 (qd, J = 7.4, 7.0, 3.4 Hz, 2H), 6.83 (s, 1H), 6.66 (dd, J = 16.9, 10.2 Hz, 1H), 6.38 (s, 1H), 6.25 - 6.02 (m, 2H), 5.76 - 5.65 (m, 2H), 4.19 (td, J = 7.9, 3.8 Hz, 1H), 3.88 (q, J = 7.9 Hz, 1H), 3.80 (s, 3H), 3.11 - 3.02 (m, 2H), 2.94 - 2.79 (m, 2H), 2.68 (q, J = 11.7, 9.6 Hz, 5H), 2.34 (dtd, J = 13.7, 9.3, 8.7, 5.8 Hz, 2H), 1.86 (d, J = 12.1 Hz, 2H), 1.78 - 1.63 (m, 2H), 1.17 (d, J = 6.6 Hz, 6H), 1.02 (d, J = 6.5 Hz, 6H).: 677.5[M+H]$^+$	1.18
551		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.84 (s, 1H), 8.36 - 8.30 (m, 1H), 7.49 - 7.43 (m, 1H), 7.24 - 7.17 (m, 1H), 7.05 (td, J = 8.5, 1.6 Hz, 1H), 6.76 (d, J = 13.8 Hz, 2H), 6.45 - 6.24 (m, 2H), 6.21 - 6.00 (m, 1H), 5.95 (dd, J = 8.7, 4.4 Hz, 1H), 5.70 (dt, J = 8.3, 3.1 Hz, 1H), 4.16 - 4.07 (m, 2H), 3.85 (s, 3H), 3.70 (d, J = 7.5 Hz, 1H), 3.16 (d, J = 5.3 Hz, 2H), 2.92 - 2.88 (m, 2H), 2.70 (s, 3H), 2.63 (s, 6H), 2.24 (dtd, J = 12.4, 8.1, 5.0 Hz, 2H).: 570.3[M+H]$^+$	1.26
552		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.53 (s, 1H), 8.23 (d, J = 9.4 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 7.6 Hz, 1H), 7.21 (td, J = 8.0, 5.3 Hz, 1H), 7.09 - 6.93 (m, 2H), 6.73 (s, 1H), 6.42 - 6.24 (m, 2H), 5.95 (dd, J = 8.7, 4.5 Hz, 1H), 5.78 - 5.70 (m, 1H), 4.17 - 3.98 (m, 3H), 3.85 (s, 3H), 3.74 (s, 3H), 3.15 (s, 3H), 2.96 (dt, J = 20.7, 3.7 Hz, 3H), 2.78 (s, 4H).: 568.3[M+H]$^+$	1.24

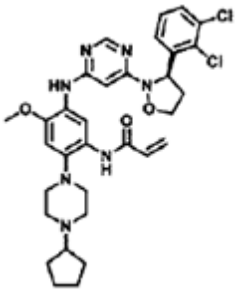
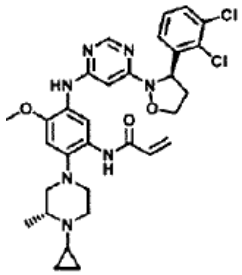
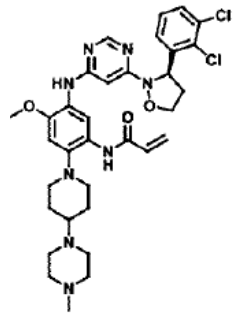
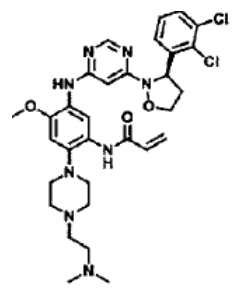
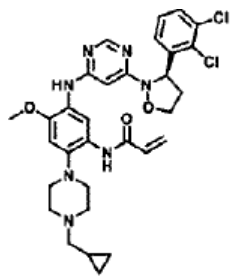
[574]

553		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.84 (s, 1H), 8.40 (s, 1H), 8.35 (d, J = 1.0 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.21 (td, J = 8.0, 5.3 Hz, 1H), 7.13 (s, 1H), 7.05 (td, J = 8.5, 1.5 Hz, 1H), 6.73 (s, 1H), 6.36 (d, J = 2.9 Hz, 1H), 6.33 - 6.11 (m, 1H), 5.95 (dd, J = 8.8, 4.4 Hz, 1H), 5.73 (ddd, J = 20.7, 9.5, 2.5 Hz, 1H), 4.16 - 4.03 (m, 3H), 3.85 (s, 3H), 3.13 (d, J = 11.7 Hz, 2H), 2.94 (dtd, J = 12.3, 8.0, 4.3 Hz, 1H), 2.87 - 2.70 (m, 3H), 2.63 (s, 6H), 2.29 - 2.14 (m, 3H), 2.00 - 1.84 (m, 2H).; 506.4[M+H]$^+$	1.24
554		N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.06 (s, 1H), 8.25 (s, 1H), 8.05 (s, 1H), 7.95 - 7.88 (m, 4H), 7.56 - 7.48 (m, 3H), 6.85 (s, 1H), 6.64 (dd, J = 17.0, 10.2 Hz, 1H), 6.24 (dd, J = 17.1, 1.9 Hz, 2H), 5.79 - 5.64 (m, 2H), 4.28 (dd, J = 7.0, 4.0 Hz, 1H), 4.01 (d, J = 8.2 Hz, 1H), 3.79 (s, 3H), 3.61 (s, 2H), 3.17 (d, J = 12.0 Hz, 4H), 3.01 - 2.91 (m, 1H), 2.87 (s, 3H), 2.75 (t, J = 11.6 Hz, 4H), 2.45 - 2.31 (m, 1H), 2.05 (s, 4H), 1.90 (d, J = 10.8 Hz, 4H). ; 649.5[M+H]+	1.13
555		N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.07 (s, 1H), 8.24 (s, 1H), 8.04 (s, 1H), 7.97 - 7.88 (m, 4H), 7.59 - 7.48 (m, 3H), 6.84 (s, 1H), 6.64 (dd, J = 17.0, 10.2 Hz, 1H), 6.24 (dd, J = 17.0, 1.9 Hz, 2H), 5.80 - 5.64 (m, 2H), 4.54 (d, J = 13.4 Hz, 1H), 4.34 - 4.21 (m, 1H), 4.03 (dt, J = 16.1, 10.8 Hz, 2H), 3.79 (s, 3H), 3.57 (d, J = 35.8 Hz, 2H), 3.47 - 3.34 (m, 2H), 3.18 (d, J = 11.7 Hz, 2H), 2.93 (d, J = 9.3 Hz, 2H), 2.75 (t, J = 11.7 Hz, 2H), 2.39 (dt, J = 13.0, 3.8 Hz, 1H), 2.07 (s, 5H), 2.02 - 1.87 (m, 2H) ; 636.5[M+H]+	1.25
556		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.08 (s, 1H), 8.24 (d, J = 3.6 Hz, 1H), 8.03 (s, 1H), 7.96 - 7.87 (m, 4H), 7.52 (qd, J = 7.5, 3.7 Hz, 3H), 6.85 (s, 1H), 6.62 (dd, J = 17.0, 10.2 Hz, 1H), 6.24 (dd, J = 17.1, 1.9 Hz, 2H), 5.71 (ddd, J = 29.2, 9.4, 3.8 Hz, 2H), 4.29 (s, 1H), 4.02 (td, J = 16.2, 14.9, 9.8 Hz, 4H), 3.79 (s, 3H), 3.72 (t, J = 12.3 Hz, 3H), 3.49 (d, J = 12.1 Hz, 2H), 3.33 (s, 1H), 3.18 (d, J = 11.3 Hz, 4H), 2.93 (s, 1H), 2.75 (t, J = 11.8 Hz, 4H), 2.39 (dq, J = 13.1, 7.5 Hz, 1H), 2.22 - 2.09 (m, 2H), 2.02 - 1.84 (m, 2H). ; 677.5[M+H]+	1.23
557		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.09 (d, J = 16.6 Hz, 1H), 8.03 (s, 1H), 8.21 (s, 1H), 8.08 (s, 1H), 7.92 (dt, J = 8.6, 4.3 Hz, 4H), 7.50 - 7.46 (m, 3H), 6.83 (s, 1H), 6.54 (dt, J = 17.0, 10.2 Hz, 1H), 6.33 (s, 1H), 6.23 (dd, J = 16.4, 3.3 Hz, 1H), 5.72 (ddd, J = 19.7, 9.5, 4.5 Hz, 2H), 4.72 (s, 1H), 4.66 (d, J = 7.0 Hz, 1H), 4.23 (dd, J = 8.6, 4.6 Hz, 2H), 3.93 (t, J = 7.9 Hz, 1H), 3.81 (s, 3H), 3.75 (t, J = 10.1 Hz, 2H), 3.57 - 3.43 (m, 2H), 3.15 (t, J = 9.9 Hz, 2H), 2.92 - 2.73 (m, 3H), 2.36 (ddd, J = 12.8, 8.5, 4.1 Hz, 2H), 2.18 - 2.02 (m, 3H), 1.83 (s, 2H). ; 648.5[M+H]$^+$	1.24

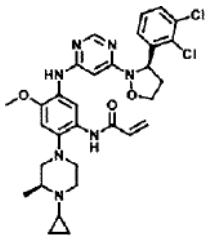
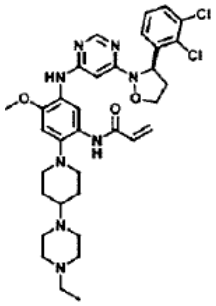
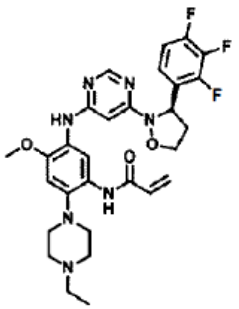
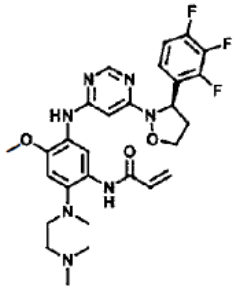
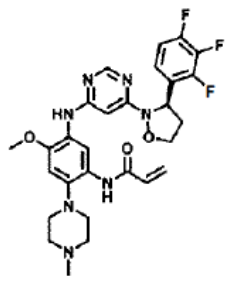
[575]

558		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.94 (s, 1H), 9.33 (s, 1H), 8.86 (s, 1H), 8.18 (s, 1H), 7.62 (s, 1H), 7.38 - 7.35 (m, 2H), 6.65 (s, 1H), 6.51 (dd, J = 17.0, 10.2 Hz, 1H), 6.31 - 6.16 (m, 2H), 5.78 (dd, J = 8.8, 4.0 Hz, 1H), 5.73 (dd, J = 10.2, 2.0 Hz, 1H), 4.17 (td, J = 7.9, 3.8 Hz, 1H), 3.92 - 3.87 (m, 1H), 3.83 (s, 3H), 3.46 - 3.30 (m, 2H), 3.37 - 3.29 (m, 1H), 3.22 (q, J = 8.3 Hz, 1H), 2.92 (dt, J = 8.4, 4.0 Hz, 1H), 2.84 (d, J = 5.6 Hz, 6H), 2.40 - 2.29 (m, 2H), 2.11 (ddd, J = 12.3, 8.3, 3.5 Hz, 2H). : 582.4[M+H]$^+$	1.22
559		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.69 (s, 1H), 9.07 (s, 1H), 8.81 (s, 1H), 8.28 (s, 1H), 8.19 (s, 1H), 7.41 - 7.37 (m, 2H), 6.85 (s, 1H), 6.66 (dd, J = 17.0, 10.1 Hz, 1H), 6.43 (s, 1H), 6.24 (dd, J = 17.0, 2.0 Hz, 1H), 5.78 (ddd, J = 16.5, 9.4, 3.4 Hz, 2H), 4.17 (td, J = 7.9, 3.8 Hz, 1H), 3.91 (t, J = 8.1 Hz, 1H), 3.84 (s, 3H), 3.58 (d, J = 11.7 Hz, 2H), 3.29 - 3.16 (m, 6H), 3.05 (t, J = 12.2 Hz, 2H), 2.90 (qd, J = 8.3, 4.0 Hz, 1H), 2.12 (dtd, J = 12.8, 8.2, 5.0 Hz, 1H), 1.28 (t, J = 7.3 Hz, 3H). : 582.4[M+H]$^+$	1.26
560		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.10 (d, J = 30.3 Hz, 2H), 8.22 (s, 1H), 8.09 (s, 1H), 7.45 - 7.31 (m, 3H), 6.86 (s, 1H), 6.63 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 - 6.18 (m, 2H), 5.85 - 5.68 (m, 2H), 4.20 (td, J = 7.9, 4.0 Hz, 1H), 3.96 (q, J = 8.0 Hz, 1H), 3.81 (s, 3H), 3.74 - 3.27 (m, 7H), 3.17 (d, J = 11.9 Hz, 4H), 2.95 (qt, J = 7.6, 3.8 Hz, 1H), 2.87 (s, 3H), 2.76 (t, J = 11.7 Hz, 2H), 2.15 (dp, J = 11.6, 3.9, 3.0 Hz, 1H), 2.07 (d, J = 11.5 Hz, 2H), 1.89 (d, J = 15.3 Hz, 2H). : 651.5[M+H]$^+$	1.20
561		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.90 (s, 1H), 8.54 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.62 - 7.57 (m, 1H), 7.37 (dd, J = 8.0, 1.6 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.96 (s, 1H), 6.82 (s, 1H), 6.76 (s, 1H), 6.40 - 6.31 (m, 1H), 6.26 (dd, J = 17.0, 9.9 Hz, 1H), 5.97 (dd, J = 8.8, 4.4 Hz, 1H), 5.75 (dd, J = 9.9, 1.6 Hz, 1H), 4.14 - 4.03 (m, 4H), 3.83 (s, 3H), 3.47 - 3.37 (m, 2H), 2.93 (s, 4H), 2.76 (s, 4H), 2.23 (dtd, J = 12.5, 8.2, 4.5 Hz, 1H), 1.84 (d, J = 12.6 Hz, 2H), 1.64 (ddd, J = 23.0, 13.6, 7.7 Hz, 4H).: 654.4[M+H]	1.35
562		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.48 (s, 1H), 8.35 (dd, J = 8.0, 1.0 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.37 (ddd, J = 8.0, 4.1, 1.5 Hz, 1H), 7.20 (dt, J = 7.9, 4.0 Hz, 1H), 7.03 - 6.94 (m, 2H), 6.81 - 6.75 (m, 1H), 6.55 (d, J = 1.0 Hz, 1H), 6.30 - 6.22 (m, 1H), 5.95 (td, J = 8.8, 4.5 Hz, 1H), 5.75 (dd, J = 10.0, 1.6 Hz, 1H), 5.55 (s, 1H), 4.10 (q, J = 7.0 Hz, 2H), 3.96 (q, J = 8.1 Hz, 1H), 3.85 (d, J = 3.0 Hz, 4H), 3.30 (s, 3H), 3.26 (d, J = 7.2 Hz, 2H), 3.23 (s, 3H), 3.20 - 3.18 (m, 2H), 3.16 (s, 2H), 3.04 (t, J = 6.7 Hz, 4H), 1.99 - 1.95 (m, 4H).: 667.4[M+H]	1.19

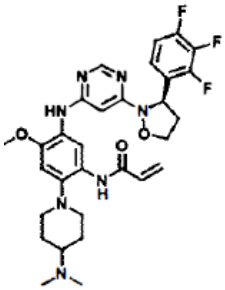
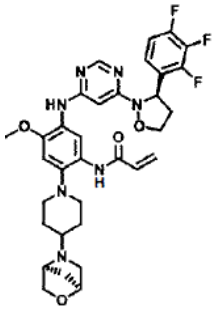
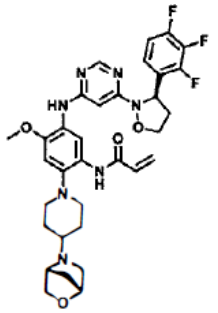
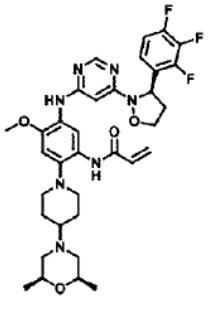
[576]

563		N-(2-(4-cyclopentylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.90 (s, 1H), 8.50 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.60 (dd, J = 7.9, 1.6 Hz, 1H), 7.37 (dd, J = 8.0, 1.6 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.95 (s, 1H), 6.83 (s, 1H), 6.76 (s, 1H), 6.40 - 6.21 (m, 2H), 5.07 (dd, J = 8.8, 4.4 Hz, 1H), 5.75 (dd, J = 9.8, 1.7 Hz, 1H), 4.15 - 4.04 (m, 2H), 3.82 (s, 3H), 3.00 - 2.91 (m, 4H), 2.70 (s, 2H), 2.59 (p, J = 7.8 Hz, 2H), 2.23 (dtd, J = 12.6, 8.2, 4.4 Hz, 1H), 1.93 (s, 2H), 1.79 - 1.70 (m, 2H), 1.60 (d, J = 6.9 Hz, 4H), 1.47 (q, J = 11.4, 9.8 Hz, 2H). : 638.4[M+H]	1.39
564		N-(2-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.90 (s, 1H), 8.60 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.63 - 7.57 (m, 1H), 7.37 (dd, J = 7.9, 1.6 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.94 (s, 1H), 6.78 (d, J = 9.8 Hz, 2H), 6.41 - 6.22 (m, 2H), 5.07 (dd, J = 8.7, 4.4 Hz, 1H), 5.75 (dd, J = 9.9, 1.7 Hz, 1H), 4.15 - 4.04 (m, 2H), 3.82 (s, 3H), 3.13 (d, J = 11.8 Hz, 1H), 2.96 (ddt, J = 12.1, 7.9, 4.1 Hz, 1H), 2.90 (d, J = 9.1 Hz, 1H), 2.83 (d, J = 10.3 Hz, 1H), 2.63 - 2.55 (m, 2H), 2.23 (dp, J = 12.1, 4.1 Hz, 1H), 1.56 (s, 3H), 1.26 (d, J = 6.2 Hz, 3H), 0.66 (ddt, J = 28.0, 10.2, 5.5 Hz, 2H), 0.49 (dq, J = 10.9, 5.9 Hz, 1H), 0.37 (dt, J = 10.5, 5.4 Hz, 1H). 624.4[M+H]	1.38
565		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.43 (s, 1H), 8.36 (s, 1H), 7.60 (d, J = 7.6 Hz, 1H),7.37 (d, J = 7.8 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.92 (s, 1H), 6.75 (s, 2H), 6.36 (d, J = 16.8 Hz, 1H),6.25 (dd, J = 16.9, 9.9 Hz, 1H), 5.96 (dd, J = 8.8, 4.5 Hz, 1H), 5.74 (d, J = 10.1 Hz, 1H), 4.17 - 4.04 (m,2H), 3.85 (s, 3H), 3.40 - 3.33 (m, 2H), 3.29 - 3.16 (m, 3H), 3.07 (d, J = 11.6 Hz, 2H), 3.00 - 2.88 (m, 3H), 2.80 - 2.70 (m, 4H), 2.46 - 2.38 (m, 4H), 2.26 - 2.16 (m, 2H), 2.09 (d, J = 12.4 Hz, 2H).: 667.4 [M+H]$^+$	1.28
566		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.90 (s, 1H), 8.36 (d, J = 5.3 Hz, 1H), 7.61 - 7.57 (m, 1H), 7.36(d, J = 3.3 Hz, 1H), 7.21 - 7.19 (m, 1H), 7.00 (s, 1H), 6.80 (d, J = 5.0 Hz, 1H), 6.74 (s, 1H), 6.55 (s, 1H),6.47 - 6.39 (m, 1H), 6.35 - 6.26 (m, 1H), 5.99 - 5.92 (m, 1H), 5.78 - 5.71 (m, 1H), 4.09 (q, J = 8.0 Hz,2H), 3.85 (s, 3H), 3.36 (t, J = 6.1 Hz, 3H), 3.21 - 3.16 (m, 5H), 3.13 (s, 2H), 3.04 (t, J = 6.4 Hz, 4H), 2.75(s, 6H).641.51 [M+H]$^+$	1.26
567		N-(2-(4-(cyclopropylmethyl)piperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.91 (s, 1H), 8.56 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.64 - 7.58 (m, 1H), 7.37 (dd, J = 7.9, 1.6 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.95 (s, 1H), 6.84 (s, 1H), 6.76 (s, 1H), 6.41- 6.34 (m, 1H), 6.32 - 6.22 (m, 1H), 5.07 (dd, J = 8.8, 4.4 Hz, 1H), 5.74 (dd, J = 9.9, 1.6 Hz, 1H), 4.16 -4.04 (m, 2H), 3.84 (s, 3H), 3.04 - 2.89 (m, 5H), 2.74 (s, 3H), 2.54 (s, 1H), 2.38 (s, 1H), 2.32 - 2.16 (m,2H), 1.56 - 1.50 (m, 1H), 0.64 - 0.58 (m, 2H), 0.23 - 0.15 (m, 2H).: 624.39 [M+H]$^+$	1.38

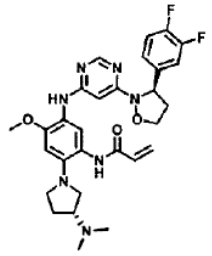
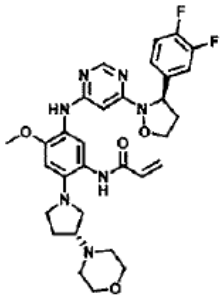
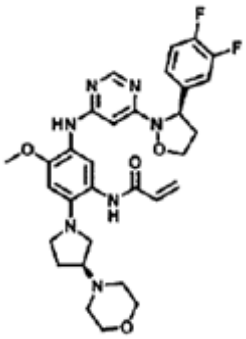
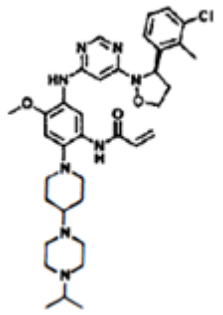
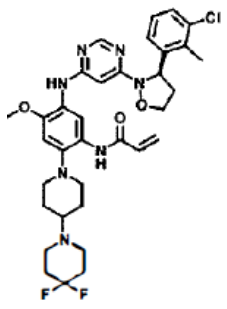
[577]

568		N-(2-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.89 (s, 1H), 8.60 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.60 (dd, J =7.1, 1.1 Hz, 1H), 7.37 (dd, J = 8.0, 1.6 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.94 (s, 1H), 6.79 (s, 1H), 6.77(s, 1H), 6.41 - 6.34 (m, 1H), 6.27 (dd, J = 17.0, 9.9 Hz, 1H), 5.97 (dd, J = 8.8, 4.4 Hz, 1H), 5.75 (dd, J =10.0, 1.6 Hz, 1H), 4.15 - 4.05 (m, 2H), 3.82 (s, 3H), 3.17 - 3.09 (m, 1H), 3.00 - 2.92 (m, 1H), 2.90 - 2.87(m, 1H), 2.82 (d, J = 11.1 Hz, 1H), 2.70 (s, 1H), 2.64 - 2.57 (m, 2H), 2.30 - 2.19 (m, 1H), 1.56 (s, 2H),1.26 (d, J = 6.2 Hz, 3H), 0.74 - 0.60 (m, 2H), 0.54 - 0.45 (m, 1H), 0.44 - 0.35 (m, 1H).: 624.4 [M+H]$^+$	1.38
569		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.40 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.60 (dd, J =7.6, 1.6 Hz, 1H), 7.37 (dd, J = 8.0, 1.6 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.94 (s, 1H), 6.77 - 6.72 (m, 2H),6.40 - 6.32 (m, 1H), 6.25 (dd, J = 16.9, 10.1 Hz, 1H), 5.96 (dd, J = 8.8, 4.4 Hz, 1H), 5.74 (dd, J = 9.9, 1.6Hz, 1H), 4.16 - 4.05 (m, 2H), 3.85 (s, 3H), 3.46 - 3.38 (m, 1H), 3.35 - 3.28 (m, 2H), 3.08 (d, J = 11.7 Hz,2H), 3.00 - 2.85 (m, 5H), 2.74 (q, J = 12.4 Hz, 5H), 2.40 (s, 2H), 2.30 - 2.18 (m, 2H), 2.00 (d, J = 12.1Hz, 2H), 1.10 (t, J = 7.3 Hz, 3H).: 681.4 [M+H]$^+$	1.28
570		N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.72 (s, 1H), 8.45 (s, 1H), 8.29 (s, 1H), 7.70 (s, 1H), 7.32 - 7.26 (m, 1H), 6.93 (tdd, J = 9.2, 6.8, 2.0 Hz, 1H), 6.84 (s, 1H), 6.64 (s, 1H), 6.40 - 6.28 (m, 2H), 5.83 (dd, J = 8.8, 4.7 Hz, 1H), 5.75 (dd, J = 8.6, 2.9 Hz, 1H), 4.13 (td, J = 8.1, 4.2 Hz, 1H), 4.03 (q, J = 8.0 Hz, 1H), 3.86 (s, 3H), 3.15 - 3.06 (m, 4H), 3.07 - 2.93 (m, 4H), 2.85 (dq, J = 8.7, 5.5, 4.6 Hz, 3H), 2.28 (dtd, J = 12.6, 8.1, 4.6 Hz, 1H), 1.28 (t, J = 7.3 Hz, 3H): 584.3[M+H]$^+$	1.25
571		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 9.38 (s, 1H), 8.78 (s, 1H), 8.28 (d, J = 1.0 Hz, 1H), 7.79 (s, 1H), 7.29 (q, J = 6.1, 5.2 Hz, 1H), 6.97 - 6.90 (m, 1H), 6.82 - 6.77 (m, 1H), 6.75 (s, 1H), 6.72 - 6.71 (m, 1H), 6.41 (dd, J = 16.9, 1.7 Hz, 1H), 5.85 (dd, J = 8.8, 4.6 Hz, 1H), 5.72 (dd, J = 10.3, 1.7 Hz, 1H), 4.15 (td, J = 7.0, 5.9, 3.1 Hz, 1H), 4.07 (q, J = 8.1 Hz, 1H), 3.85 (s, 3H), 3.16 (t, J = 5.9 Hz, 2H), 2.93 (t, J = 5.9 Hz, 2H), 2.84 (ddd, J = 10.1, 7.1, 3.2 Hz, 1H), 2.66 (s, 3H), 2.61 (s, 6H), 2.29 (dt, J = 12.5, 4.0 Hz, 1H): 572.4[M+H]$^+$	1.30
572		N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.75 (s, 1H), 8.42 (s, 1H), 8.29 (s, 1H), 7.71 (s, 1H), 7.33 - 7.27 (m, 1H), 6.96 - 6.90 (m, 1H), 6.82 (s, 1H), 6.66 (s, 1H), 6.37 (d, J = 16.7 Hz, 1H), 6.28 (dd, J = 16.8, 9.9 Hz, 1H), 5.84 (dd, J = 8.3, 4.5 Hz, 1H), 5.76 (dd, J = 9.8, 1.7 Hz, 1H), 4.13 (td, J = 8.0, 4.1 Hz, 1H), 4.04 (q, J = 8.1 Hz, 1H), 3.86 (s, 3H), 3.01 (q, J = 4.1 Hz, 4H), 2.84 (dq, J = 8.4, 4.2 Hz, 5H), 2.49 (s, 3H), 2.28 (dtd, J = 12.7, 8.2, 4.7 Hz, 1H): 570.4[M+H]$^+$	1.27

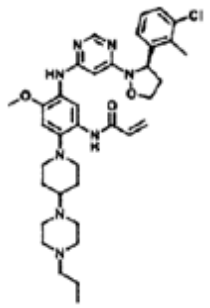
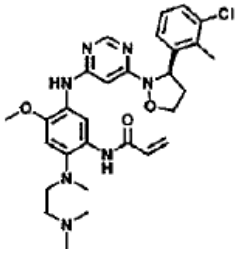
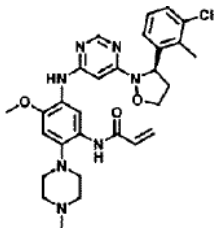
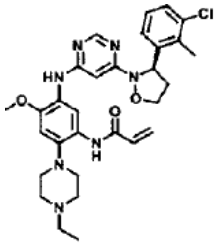
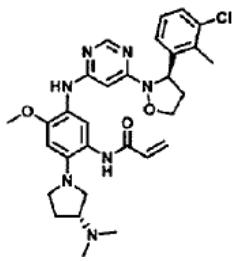
[578]

573		N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.75 (s, 1H), 8.46 (s, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.50 (s, 1H), 7.33 - 7.28 (m, 1H), 6.93 (tdd, J = 9.2, 6.9, 2.1 Hz, 1H), 6.74 (s, 1H), 6.60 (s, 1H), 6.40 - 6.34 (m, 2H), 5.85 (dd, J = 8.8, 4.6 Hz, 1H), 5.75 (dd, J = 7.3, 4.2 Hz, 1H), 4.13 (td, J = 8.0, 4.2 Hz, 1H), 4.05 (q, J = 8.0 Hz, 1H), 3.85 (s, 3H), 3.12 (d, J = 11.8 Hz, 2H), 2.87 - 2.70 (m, 4H), 2.60 (s, 6H), 2.28 (dq, J = 8.7, 4.7, 4.0 Hz, 1H), 2.17 - 2.10 (m, 2H), 1.80 (qd, J = 10.8, 9.6, 5.9 Hz, 2H): 598.5[M+H]$^+$	1.28
574		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.14 (s, 1H), 9.31 (d, J = 35.5 Hz, 1H), 8.33 (s, 1H), 7.87 (d, J = 12.0 Hz, 1H), 7.37 - 7.20 (m, 2H), 6.94 (d, J = 10.8 Hz, 1H), 6.62 (ddd, J = 21.3, 17.0, 10.2 Hz, 1H), 6.28 - 6.15 (m, 2H), 5.78 (s, 1H), 5.70 (dd, J = 8.6, 5.6 Hz, 1H), 4.73 - 4.68 (m, 1H), 4.61 (d, J = 29.7 Hz, 1H), 4.36 - 4.29 (m, 1H), 4.21 (d, J = 10.3 Hz, 1H), 4.10 - 4.01 (m, 1H), 3.83 (d, J = 2.3 Hz, 3H), 3.70 (dd, J = 9.3, 5.0 Hz, 1H), 3.53 - 3.41 (m, 2H), 3.25 (d, J = 13.0 Hz, 3H), 3.10 - 3.10 (m, 1H), 2.90 (ddd, J = 26.1, 15.2, 7.3 Hz, 3H), 2.37 - 2.28 (m, 2H), 2.19 (d, J = 11.5 Hz, 1H), 2.14 - 2.03 (m, 3H).: 652.3[M+H]$^+$	1.28
575		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.72 (s, 1H), 9.23 (d, J = 32.9 Hz, 1H), 8.29 (s, 1H), 7.92 (d, J = 12.2 Hz, 1H), 7.29 (dt, J = 20.3, 8.0 Hz, 2H), 6.90 (d, J = 7.4 Hz, 1H), 6.58 (dt, J = 16.2, 8.1 Hz, 1H), 6.28 - 6.19 (m, 2H), 5.78 - 5.65 (m, 2H), 4.68 (d, J = 22.6 Hz, 2H), 4.58 (s, 1H), 4.01 (d, J = 7.0 Hz, 2H), 3.82 (d, J = 2.0 Hz, 3H), 3.70 (d, J = 9.6 Hz, 1H), 3.45 (d, J = 8.0 Hz, 2H), 3.37 - 3.13 (m, 4H), 2.94 - 2.68 (m, 4H), 2.31 (dt, J = 13.6, 5.6 Hz, 2H), 2.08 (d, J = 11.4 Hz, 3H).: 652.3[M+H]$^+$	1.26
576		N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.16 (s, 1H), 9.23 (s, 1H), 8.33 (s, 1H), 7.89 (s, 1H), 7.32 (ddd, J = 9.4, 7.2, 1.9 Hz, 1H), 7.25 (dd, J = 11.3, 4.7 Hz, 1H), 6.94 (s, 1H), 6.70 (dd, J = 17.0, 10.2 Hz, 1H), 6.20 - 6.22 (m, 1H), 6.18 (s, 1H), 5.75 (d, J = 5.1 Hz, 1H), 5.72 - 5.68 (m, 1H), 4.33 (q, J = 3.7 Hz, 1H), 4.10 - 4.11 (m, 2H), 4.06 (d, J = 7.6 Hz, 2H), 3.82 (s, 3H), 3.46 (d, J = 11.7 Hz, 2H), 3.30 - 3.21 (m, 3H), 3.01 - 2.90 (m, 1H), 2.85 - 2.76 (m, 2H), 2.60 (d, J = 10.7 Hz, 3H), 2.33 (d, J = 7.7 Hz, 1H), 2.24 (d, J = 10.4 Hz, 2H), 2.00 (d, J = 12.6 Hz, 2H), 1.17 (d, J = 6.3 Hz, 6H).: 668.3[M+H]$^+$	1.35

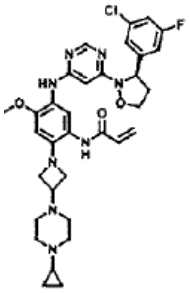
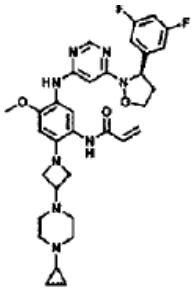
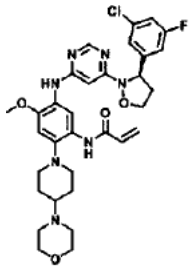
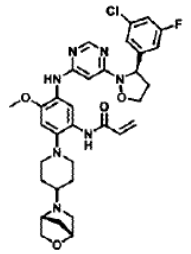
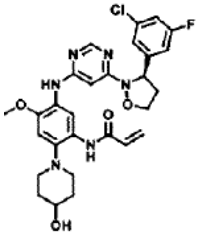
[579]

577		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.04 (s, 1H), 7.86 (s, 1H), 7.25 - 7.17 (m, 1H), 7.12 - 7.08 (m, 2H), 6.64 (s, 1H), 6.31 - 6.20 (m, 2H), 5.68 - 5.64 (m, 1H), 5.38 (dd, *J* = 8.4, 4.7 Hz, 1H), 4.00 (td, *J* = 7.8, 4.3 Hz, 1H), 3.84 - 3.77 (m, 2H), 3.75 (s, 3H), 3.47 (dd, *J* = 10.7, 4.4 Hz, 1H), 3.34 - 3.23 (m, 2H), 3.23 - 3.16 (m, 1H), 3.01 (d, *J* = 2.2 Hz, 2H), 2.78 (s, 5H), 2.60 - 2.56 (m, 2H), 2.32 (ddd, *J* = 10.2, 9.4, 5.4 Hz, 1H), 2.22 - 2.03 (m, 2H) ; 566.4 [M+H]$^+$	1.20
578		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.02 (s, 1H), 7.69 (s, 1H), 7.25 - 7.17 (m, 1H), 7.12 - 7.04 (m, 2H), 6.55 - 6.42 (m, 2H), 6.22 (td, *J* = 4.1, 1.8 Hz, 2H), 5.64 (dd, *J* = 10.3, 1.4 Hz, 1H), 5.38 (dd, *J* = 8.5, 4.6 Hz, 1H), 3.99 (td, *J* = 7.8, 4.3 Hz, 1H), 3.84 - 3.75 (m, 1H), 3.72 (s, 3H), 3.67 (t, *J* = 4.6 Hz, 4H), 3.28 (dd, *J* = 9.4, 6.5 Hz, 1H), 3.21 - 3.12 (m, 3H), 2.72 - 2.55 (m, 5H), 2.55 (d, *J* = 8.4 Hz, 9H), 2.23 - 2.07 (m, 2H), 1.86 (dq, *J* = 12.2, 8.5 Hz, 1H) ; 608.4[M+H]$^+$	1.18
579		N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.14 (s, 1H), 7.69 (s, 1H), 7.39 - 7.32 (m, 1H), 7.27 - 7.19 (m, 2H), 6.66 (s, 1H), 6.53 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.40 - 6.30 (m, 2H), 5.79 (dd, *J* = 10.2, 1.5 Hz, 1H), 5.53 (dd, *J* = 8.5, 4.7 Hz, 1H), 4.13 (td, *J* = 7.9, 4.2 Hz, 1H), 3.95 (d, *J* = 7.9 Hz, 1H), 3.86 (s, 3H), 3.75 (t, *J* = 4.6 Hz, 4H), 3.30 - 3.24 (m, 8H), 3.01 - 2.91 (m, 1H), 2.84 - 2.73 (m, 1H), 2.68 (s, 1H), 2.66 - 2.49 (m, 4H), 2.38 - 2.27 (m, 1H), 2.27 - 2.18 (m, 1H), 1.91 (dq, *J* = 17.6, 8.8 Hz, 1H) ; 608.4 [M+H]$^+$	1.17
580		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.59 (s, 1H), 8.14 (s, 1H), 7.40 (d, *J* = 7.7 Hz, 2H), 7.34 (d, *J* = 7.9 Hz, 2H), 7.20 (t, *J* = 7.9 Hz, 2H), 6.82 (s, 1H), 6.65 (dd, *J* = 16.8, 10.2 Hz, 2H), 6.34 (s, 1H), 6.20 (dd, *J* = 17.0, 2.0 Hz, 1H), 5.69 (dd, *J* = 9.2, 5.0 Hz, 2H), 4.19 - 4.10 (m, 2H), 3.79 (s, 3H), 3.15 (s, 4H), 3.09 (s, 3H), 3.00 (s, 2H), 2.43 (d, *J* = 8.1 Hz, 9H), 1.84 (d, *J* = 12.1 Hz, 3H), 1.68 (s, 6H), 0.96 (d, *J* = 6.5 Hz, 7H).; 675.5[M+H]$^+$	1.25
581		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.59 (s, 1H), 8.17 - 8.12 (m, 2H), 7.40 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.34 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 6.82 (s, 1H), 6.66 (dd, *J* = 16.9, 10.2 Hz, 1H), 6.35 (s, 1H), 6.21 (dd, *J* = 17.0, 2.0 Hz, 1H), 5.75 - 5.67 (m, 2H), 4.15 (td, *J* = 7.9, 3.9 Hz, 1H), 3.79 (s, 3H), 3.32 (s, 4H), 3.06 (d, *J* = 11.2 Hz, 2H), 2.82 (tq, *J* = 8.1, 4.1 Hz, 1H), 2.66 (t, *J* = 5.7 Hz, 5H), 2.42 (s, 4H), 2.08 (ddt, *J* = 11.7, 7.8, 4.1 Hz, 1H), 2.00 (s, 1H), 1.95 (td, *J* = 13.2, 12.4, 6.2 Hz, 5H), 1.77 (dd, *J* = 14.2, 8.5 Hz, 5H).; 668.5[M+H]$^+$	1.36

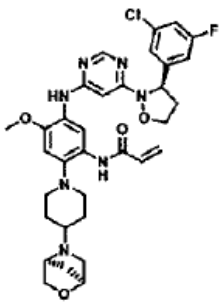
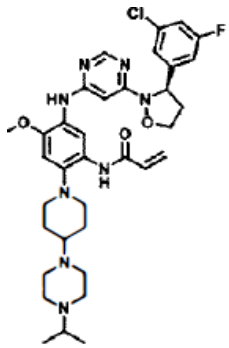
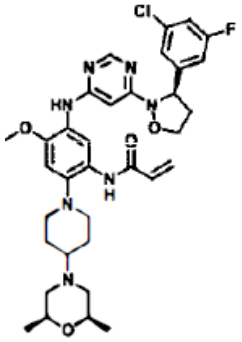
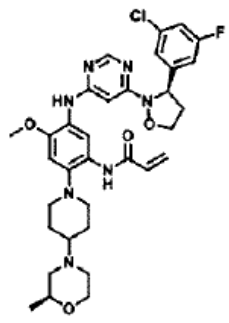
[580]

582		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.59 (s, 1H), 8.16 - 8.12 (m, 2H), 7.40 (dd, J = 7.8, 1.3 Hz, 1H), 7.34 (dd, J = 8.0, 1.4 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.82 (s, 1H), 6.65 (dd, J = 17.0, 10.2 Hz, 1H), 6.35 (s, 1H), 6.20 (dd, J = 16.9, 2.0 Hz, 1H), 5.74 - 5.66 (m, 2H), 4.14 (td, J = 7.9, 3.8 Hz, 1H), 3.79 (s, 3H), 3.04 (d, J = 10.7 Hz, 3H), 2.83 (dtd, J = 11.9, 8.0, 3.8 Hz, 2H), 2.66 (t, J = 11.6 Hz, 3H), 2.54 (s, 2H), 2.42 (s, 4H), 2.37 (d, J = 7.9 Hz, 4H), 2.24 - 2.17 (m, 3H), 2.13 - 2.01 (m, 2H), 1.84 (d, J = 13.9 Hz, 3H), 1.78 (s, 3H), 1.71 (t, J = 11.8 Hz, 3H), 1.42 (h, J = 7.3 Hz, 3H), 0.85 (t, J = 7.4 Hz, 4H).; 675.6[M+H]$^+$	1.26
583		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.06 (s, 1H), 8.47 (s, 1H), 8.16 (d, J = 1.0 Hz, 1H), 7.40 (dd, J = 7.9, 1.3 Hz, 1H), 7.34 (dd, J = 8.0, 1.4 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.99 (s, 1H), 6.43 - 6.33 (m, 2H), 6.21 (dd, J = 17.0, 2.2 Hz, 1H), 5.74 - 5.67 (m, 2H), 4.15 (td, J = 7.9, 3.8 Hz, 1H), 3.80 (s, 3H), 2.84 (dt, J = 12.0, 4.8 Hz, 4H), 2.71 (s, 3H), 2.43 (s, 4H), 2.32 (t, J = 5.8 Hz, 2H), 2.20 (s, 7H), 2.08 (tdd, J = 11.5, 8.3, 4.1 Hz, 2H), 1.86 (s, 4H).; 566.4[M+H]$^+$	1.31
584		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.97 (s, 1H), 8.60 (s, 1H), 8.15 (d, J = 0.9 Hz, 1H), 7.40 (dd, J = 7.7, 1.3 Hz, 1H), 7.34 (dd, J = 8.0, 1.4 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.84 (s, 1H), 6.59 (dd, J = 17.0, 10.2 Hz, 1H), 6.36 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.71 (td, J = 9.0, 8.3, 3.5 Hz, 2H), 4.15 (td, J = 7.9, 3.9 Hz, 1H), 3.81 (s, 3H), 2.90 - 2.76 (m, 6H), 2.42 (s, 4H), 2.25 (s, 3H), 2.14 - 2.00 (m, 2H), 1.82 (s, 4H).; 564.4[M+H]$^+$	1.25
585		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (s, 1H), 8.60 (s, 1H), 8.15 (d, J = 1.0 Hz, 1H), 7.40 (dd, J = 7.8, 1.4 Hz, 1H), 7.34 (dd, J = 8.0, 1.4 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.86 (s, 1H), 6.59 (dd, J = 17.0, 10.1 Hz, 1H), 6.36 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.71 (td, J = 8.6, 7.5, 3.4 Hz, 2H), 4.15 (td, J = 7.8, 3.8 Hz, 1H), 3.81 (s, 4H), 2.91 - 2.77 (m, 6H), 2.41 (d, J = 13.2 Hz, 6H), 2.07 (dtd, J = 10.3, 7.4, 6.6, 4.5 Hz, 2H), 1.87 (s, 4H), 1.03 (t, J = 7.2 Hz, 4H).; 578.4[M+H]$^+$	1.26
586		N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.37 (s, 1H), 8.46 (s, 1H), 8.11 (d, J = 0.9 Hz, 1H), 7.39 (dd, J = 7.8, 1.3 Hz, 1H), 7.34 (dd, J = 7.9, 1.3 Hz, 2H), 7.19 (t, J = 7.8 Hz, 2H), 6.53 - 6.41 (m, 2H), 6.18 (dd, J = 17.0, 2.1 Hz, 2H), 5.71 - 5.68 (m, 1H), 4.13 (td, J = 7.9, 3.8 Hz, 2H), 3.79 (s, 4H), 3.37 (td, J = 9.5, 6.4 Hz, 2H), 3.26 - 3.16 (m, 4H), 2.81 (dtd, J = 12.0, 8.0, 3.8 Hz, 2H), 2.42 (s, 4H), 2.16 (s, 7H), 2.07 (tdt, J = 10.8, 7.0, 3.4 Hz, 4H), 1.71 (p, J = 10.6, 10.0 Hz, 2H).; 578.4[M+H]$^+$	1.22

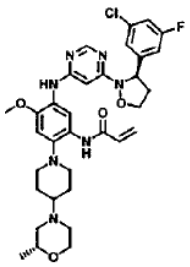
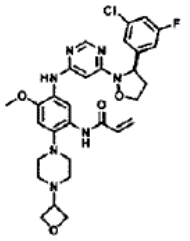
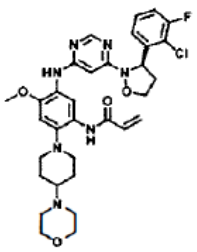
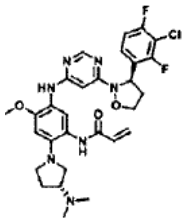
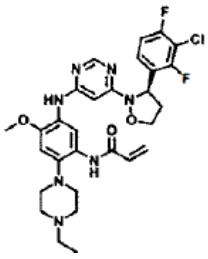
[581]

587		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(3-(4-cyclopropylpiperazine-1-yl)azetidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.04 (s, 1H), 7.13 - 7.05 (m, 2H), 7.00 - 6.93 (m, 1H), 6.75 - 6.66 (m, 1H), 6.49 (s, 1H), 6.42 - 6.36 (m, 1H), 6.36 - 6.22 (m, 2H), 5.81 - 5.71 (m, 1H), 5.64 (dd, J = 8.6, 4.6 Hz, 1H), 4.17 - 3.90 (m, 4H), 3.85 (s, 3H), 3.83 - 3.65 (m, 3H), 3.20 - 3.10 (m, 1H), 2.80 - 2.57 (m, 5H), 2.55 - 2.23 (m, 5H), 0.50 - 0.37 (m, 4H); 649.40[M+H]$^+$	1.24
588		N-(2-(3-(4-cyclopropylpiperazine-1-yl)azetidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.03 (s, 1H), 7.08 (s, 1H), 7.04 - 6.93 (m, 2H), 6.75 - 6.63 (m, 2H), 6.48 (s, 1H), 6.44 - 6.35 (m, 1H), 6.35 - 6.19 (m, 2H), 5.80 - 5.71 (m, 1H), 5.65 (dd, J = 8.6, 4.4 Hz, 1H), 4.16 - 3.80 (m, 4H), 3.85 (s, 3H), 3.80 - 3.55 (m, 3H), 3.20 - 3.10 (m, 1H), 2.85 - 2.57 (m, 5H), 2.40 - 2.27 (m, 5H), 0.52 - 0.35 (m, 4H); 633.48[M+H]$^+$	1.18
589		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.10 (d, J = 9.4 Hz, 1H), 7.00 - 6.91 (m, 2H), 6.75 (s, 1H), 6.72 (s, 1H), 6.40 - 6.18 (m, 2H), 5.74 (dd, J = 10.1, 1.0 Hz, 1H), 5.66 (dd, J = 8.7, 4.5 Hz, 1H), 4.16 (td, J = 8.0, 4.2 Hz, 1H), 4.06 (q, J = 8.1 Hz, 1H), 3.85 (s, 3H), 3.82 - 3.74 (m, 4H), 3.12 - 3.02 (m, J = 10.2 Hz, 2H), 2.82 - 2.67 (m, 3H), 2.67 - 2.56 (m, 4H), 2.38 - 2.24 (m, 2H), 2.13 - 2.04 (m, 2H), 1.75 - 1.56 (m, 2H); 638.42[M+H]$^+$	1.30
590		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.49 (s, 1H), 8.35 (s, 1H), 7.14 - 7.06 (m, 2H), 6.97 (d, J = 8.3 Hz, 1H), 6.75 (s, 1H), 6.71 (s, 1H), 6.44 - 6.12 (m, 3H), 5.76 - 5.70 (m, 1H), 5.65 (dd, J = 8.7, 4.5 Hz, 1H), 4.47 (s, 1H), 4.19 - 4.01 (m, 3H), 3.91 - 3.82 (m, 4H), 3.72 - 3.65 (m, 1H), 3.27 - 3.17 (m, 1H), 3.08 - 3.00 (m, 2H), 2.82 - 2.70 (m, 3H), 2.70 - 2.60 (m, 1H), 2.59 - 2.51 (m, 1H), 2.38 - 2.28 (m, 1H), 2.07 - 1.93 (m, 3H), 1.90 - 1.74 (m, 3H); 650.42[M+H]$^+$	1.30
591		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-hydroxypiperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.50 (s, 1H), 8.36 (s, 1H), 7.10 (d, J = 9.4 Hz, 1H), 7.04 - 6.98 (m, 1H), 6.99 - 6.94 (m, 1H), 6.77 (s, 1H), 6.71 (s, 1H), 6.40 - 6.22 (m, 2H), 5.75 (dd, J = 9.9, 1.4 Hz, 1H), 5.66 (dd, J = 8.7, 4.6 Hz, 1H), 4.16 (td, J = 8.1, 4.2 Hz, 1H), 4.06 (q, J = 8.1 Hz, 1H), 3.98 - 3.89 (m, 1H), 3.85 (s, 3H), 3.09 - 3.00 (m, 2H), 2.82 - 2.71 (m, 3H), 2.30 - 2.28 (m, 1H), 2.12 - 2.02 (m, 2H), 1.82 - 1.71 (m, 2H); 569.32[M+H]$^+$	1.47

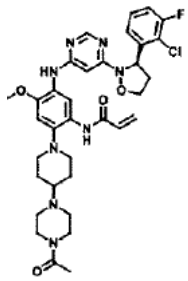
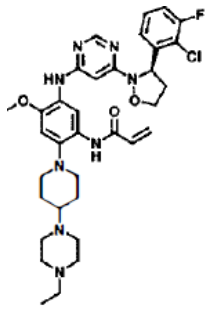
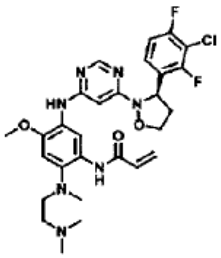
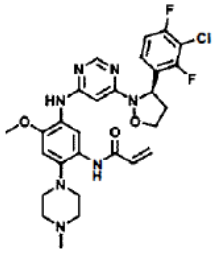
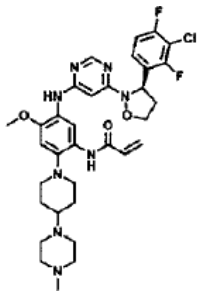
[582]

592		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.87 (s, 1H), 8.48 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.10 (dt, J = 9.5, 2.2 Hz, 1H), 7.00 - 6.92 (m, 2H), 6.76 (s, 1H), 6.72 (d, J = 1.0 Hz, 1H), 6.35 (dd, J = 17.0, 1.5 Hz, 1H), 6.23 (dd, J = 16.9, 10.1 Hz, 1H), 5.73 (dd, J = 10.0, 1.5 Hz, 1H), 5.66 (dd, J = 8.8, 4.6 Hz, 1H), 4.44 (t, J = 2.0 Hz, 1H), 4.20 - 4.00 (m, 3H), 3.85 (s, 3H), 3.77 (s, 1H), 3.66 (dd, J = 7.9, 1.6 Hz, 1H), 3.14 (dd, J = 9.9, 1.7 Hz, 1H), 3.07 - 2.99 (m, 2H), 2.84 - 2.71 (m, 3H), 2.63 - 2.54 (m, 1H), 2.51 (d, J = 9.9 Hz, 1H), 2.40 - 2.27 (m, 1H), 2.08 - 2.00 (m, 1H), 1.99 - 1.88 (m, 2H), 1.86 - 1.79 (m, 1H), 1.75 - 1.70 (m, 1H), 1.70 - 1.63 (m, 2H), : 650.4 [M+H]$^+$	1.26
593		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.86 (s, 1H), 8.46 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.10 (dt, J = 9.4, 2.1 Hz, 1H), 7.00 - 6.88 (m, 2H), 6.78 - 6.69 (m, 2H), 6.35 (dd, J = 17.0, 1.5 Hz, 1H), 6.24 (dd, J = 16.9, 10.0 Hz, 1H), 5.74 (dd, J = 10.0, 1.5 Hz, 1H), 5.66 (dd, J = 8.7, 4.6 Hz, 1H), 4.20 - 4.11 (m, 1H), 4.11 - 4.00 (m, 1H), 3.84 (s, 3H), 3.00 - 3.02 (m, 2H), 2.82 - 2.55 (m, 12H), 2.37 - 2.27 (m, 2H), 2.14 - 2.06 (m, 2H), 1.74 - 1.70 (m, 1H), 1.69 - 1.60 (m, 2H), 1.08 (d, J = 6.5 Hz, 6H), : 679.4 [M+H]$^+$	1.23
594		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.86 (s, 1H), 8.43 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.10 (dt, J = 9.5, 2.1 Hz, 1H), 7.00 - 6.93 (m, 2H), 6.73 (d, J = 14.5 Hz, 2H), 6.37 (dd, J = 16.9, 1.5 Hz, 1H), 6.25 (dd, J = 17.0, 10.0 Hz, 1H), 5.75 (dd, J = 10.0, 1.6 Hz, 1H), 5.66 (dd, J = 8.7, 4.6 Hz, 1H), 4.20 - 4.11 (m, 1H), 4.11 - 4.00 (m, 1H), 3.85 (s, 3H), 3.77 - 3.65 (m, 2H), 3.10 - 3.03 (m, 2H), 2.88 (d, J = 10.8 Hz, 2H), 2.82 - 2.76 (m, 1H), 2.76 - 2.66 (m, 2H), 2.40 - 2.25 (m, 2H), 2.11 - 2.02 (m, 2H), 1.90 (t, J = 10.6 Hz, 2H), 1.83 - 1.72 (m, 1H), 1.70 - 1.59 (m, 2H), 1.21 (d, 6H), : 666.4 [M+H]$^+$	1.33
595		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.10 (dt, J = 9.6, 2.1 Hz, 1H), 7.01 - 6.88 (m, 2H), 6.77 - 6.68 (m, 2H), 6.37 (dd, J = 16.9, 1.5 Hz, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.74 (dd, J = 10.0, 1.5 Hz, 1H), 5.66 (dd, J = 8.7, 4.6 Hz, 1H), 4.20 - 4.11 (m, 1H), 4.11 - 3.99 (m, 1H), 3.97 - 3.88 (m, 1H), 3.85 (s, 3H), 3.76 - 3.69 (m, 1H), 3.69 - 3.61 (m, 1H), 3.07 (d, J = 11.3 Hz, 2H), 2.87 (dd, J = 22.0, 11.1 Hz, 2H), 2.82 - 2.67 (m, 3H), 2.38 - 2.26 (m, 3H), 2.11 - 2.04 (m, 2H), 2.02 - 1.92 (m, 1H), 1.72 - 1.65 (m, 2H), 1.65 - 1.62 (m, 1H), 1.19 (d, 3H), : 652.4 [M+H]$^+$	1.30

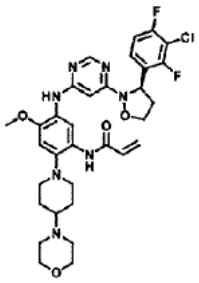
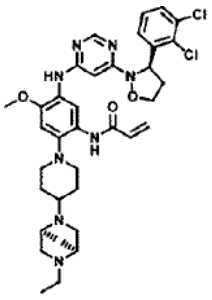
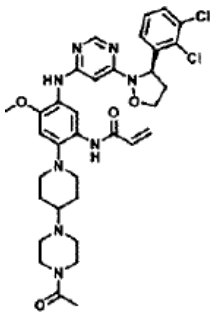
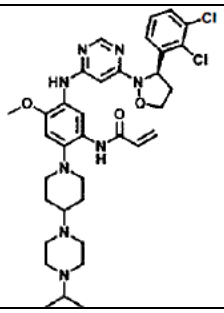
[583]

596		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.10 (dt, *J* = 9.4, 2.1 Hz, 1H), 7.01 - 6.93 (m, 2H), 6.73 (d, *J* = 14.4 Hz, 2H), 6.37 (dd, *J* = 17.0, 1.5 Hz, 1H), 6.25 (dd, *J* = 16.9, 10.1 Hz, 1H), 5.74 (dd, *J* = 10.0, 1.5 Hz, 1H), 5.66 (dd, *J* = 8.8, 4.6 Hz, 1H), 4.20 - 4.13 (m, 1H), 4.13 - 4.00 (m, 1H), 3.97 - 3.88 (m, 1H), 3.85 (s, 3H), 3.77 - 3.60 (m, 1H), 3.69 - 3.61 (m, 1H), 3.11 - 3.03 (m, 2H), 2.94 - 2.81 (m, 2H), 2.81 - 2.76 (m, 1H), 2.76 - 2.66 (m, 2H), 2.40 - 2.16 (m, 3H), 2.11 - 2.02 (m, 2H), 2.01 - 1.92 (m, 1H), 1.73 - 1.59 (m, 3H), 1.19 (d, 3H). : 652.4 $[M+H]^+$	1.28
597		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.91 (s, 1H), 8.49 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 7.10 (dt, *J* = 9.5, 2.0 Hz, 1H), 7.02 - 6.93 (m, 2H), 6.82 (s, 1H), 6.72 (s, 1H), 6.36 (dd, *J* = 16.9, 1.5 Hz, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.75 (dd, *J* = 10.0, 1.5 Hz, 1H), 5.66 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.69 (dt, *J* = 21.2, 6.3 Hz, 4H), 4.21 - 4.11 (m, 1H), 4.11 - 4.00 (m, 1H), 3.85 (s, 3H), 3.61 (p, *J* = 6.4 Hz, 1H), 3.01 - 2.89 (m, 4H), 2.84 - 2.71 (m, 1H), 2.64 - 2.42 (m, 4H), 2.40 - 2.27 (m, 1H), 1.76 - 1.68 (m, 1H). : 610.4 $[M+H]^+$	1.25
598		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.04 (s, 1H), 9.06 (s, 1H), 8.08 (s, 1H), 8.21 (s, 1H), 8.11 (s, 1H), 7.37 (td, *J* = 7.9, 2.4 Hz, 2H), 6.86 (s, 1H), 6.61 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.34 (s, 1H), 6.23 (dd, *J* = 17.0, 1.9 Hz, 1H), 5.83 - 5.69 (m, 2H), 4.18 (td, *J* = 7.8, 3.8 Hz, 1H), 4.08 - 4.01 (m, 2H), 3.93 (q, *J* = 8.0 Hz, 1H), 3.82 (s, 3H), 3.72 (t, *J* = 12.2 Hz, 2H), 3.49 (d, *J* = 12.1 Hz, 2H), 3.34 (d, *J* = 12.5 Hz, 1H), 3.25 - 3.10 (m, 4H), 2.93 (dtd, *J* = 12.1, 8.0, 3.9 Hz, 1H), 2.75 (t, *J* = 11.8 Hz, 2H), 2.13 (ddq, *J* = 12.0, 8.2, 4.0 Hz, 3H), 1.91 (s, 2H). : 638.5$[M+H]^+$	1.25
599		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.31 (s, 1H), 8.64 (s, 1H), 8.15 (s, 1H), 7.66 (s, 1H), 7.48 (td, *J* = 8.5, 6.2 Hz, 1H), 7.31 (td, *J* = 8.8, 1.7 Hz, 1H), 6.65 (s, 1H), 6.50 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.31 (s, 1H), 6.21 (dd, *J* = 17.0, 2.1 Hz, 1H), 5.71 (td, *J* = 9.5, 3.6 Hz, 2H), 4.17 (td, *J* = 7.9, 3.7 Hz, 1H), 3.93 (d, *J* = 6.5 Hz, 1H), 3.82 (s, 4H), 3.37 (s, 2H), 3.32 (d, *J* = 3.6 Hz, 1H), 3.20 (q, *J* = 10.8, 9.5 Hz, 1H), 2.83 (d, *J* = 5.3 Hz, 7H), 2.34 (d, *J* = 11.0 Hz, 1H), 2.27 - 2.17 (m, 1H), 2.15 - 2.06 (m, 1H). : 600.4$[M+H]^+$	1.28
600		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.06 (s, 1H), 8.81 (s, 1H), 8.27 (s, 1H), 8.19 (s, 1H), 7.48 (td, *J* = 8.5, 6.2 Hz, 1H), 7.32 (td, *J* = 8.8, 1.7 Hz, 1H), 6.84 (s, 1H), 6.66 (dd, *J* = 17.0, 10.1 Hz, 1H), 6.41 (s, 1H), 6.24 (dd, *J* = 17.0, 2.0 Hz, 1H), 5.73 (ddd, *J* = 10.1, 9.4, 3.6 Hz, 2H), 4.20 (td, *J* = 7.8, 3.6 Hz, 1H), 3.89 (q, *J* = 7.8 Hz, 1H), 3.83 (s, 3H), 3.58 (d, *J* = 11.5 Hz, 2H), 3.31 - 3.18 (m, 6H), 3.04 (t, *J* = 12.3 Hz, 2H), 2.80 (tt, *J* = 8.0, 4.0 Hz, 1H), 2.28 - 2.16 (m, 1H), 1.28 (t, *J* = 7.2 Hz, 3H). : 600.4$[M+H]^+$	1.31

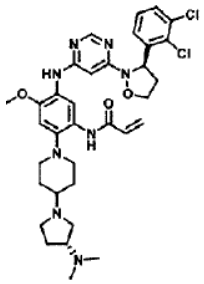
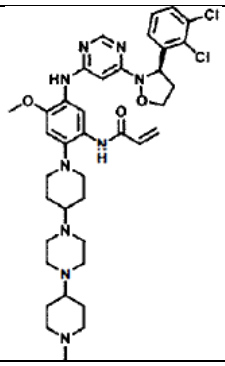
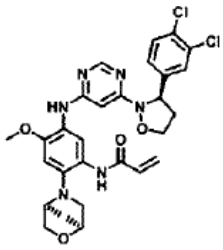
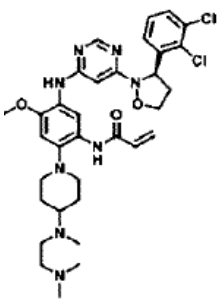
[584]

601		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.04 (s, 1H), 8.76 (s, 1H), 8.16 (d, J = 13.4 Hz, 2H), 7.43 - 7.30 (m, 3H), 6.84 (s, 1H), 6.61 (dd, J = 17.3, 9.8 Hz, 1H), 6.39 (s, 1H), 6.23 (d, J = 17.0 Hz, 1H), 5.84 - 5.68 (m, 2H), 4.53 (d, J = 13.7 Hz, 1H), 4.20 - 4.12 (m, 1H), 4.06 (d, J = 13.5 Hz, 1H), 3.90 (d, J = 8.4 Hz, 1H), 3.82 (s, 3H), 3.52 (s, 2H), 3.45 - 3.32 (m, 2H), 3.17 (s, 3H), 3.02 (s, 1H), 2.91 (d, J = 10.7 Hz, 2H), 2.73 (d, J = 12.1 Hz, 2H), 2.08 (d, J = 7.1 Hz, 6H), 1.91 (s, 2H). : 670.4[M+H]$^+$	1.23
602		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.14 (d, J = 1.0 Hz, 1H), 7.43 (d, J = 7.9 Hz, 1H), 7.30 (td, J = 8.1, 5.3 Hz, 1H), 7.15 (td, J = 8.8, 8.2, 1.5 Hz, 1H), 6.90 (s, 1H), 6.54 (dd, J = 16.9, 10.3 Hz, 1H), 6.37 (ddd, J = 25.3, 16.8, 1.7 Hz, 1H), 6.17 - 6.12 (m, 1H), 5.89 - 5.75 (m, 2H), 4.12 (td, J = 8.0, 4.1 Hz, 1H), 3.98 (q, J = 8.0 Hz, 1H), 3.86 (s, 4H), 3.72 (hept, J = 6.3 Hz, 2H), 3.22 (d, J = 7.4 Hz, 2H), 3.18 - 3.10 (m, 3H), 3.02 - 2.88 (m, 6H), 2.86 - 2.76 (m, 4H), 2.61 - 2.54 (m, 1H), 2.19 (ddd, J = 16.2, 8.1, 4.3 Hz, 1H), 2.04 (d, J = 12.3 Hz, 2H), 1.84 - 1.74 (m, 2H), 1.18 (tt, J = 7.4, 1.3 Hz, 1H).: 665.5[M+H]$^+$	1.19
603		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.93 (s, 1H), 8.71 (d, J = 9.5 Hz, 1H), 8.35 (s, 1H), 7.50 (td, J = 8.5, 6.2 Hz, 1H), 7.32 (td, J = 8.8, 1.7 Hz, 1H), 6.95 (s, 1H), 6.46 (d, J = 25.1 Hz, 1H), 6.23 (ddd, J = 17.1, 5.5, 2.1 Hz, 1H), 6.09 (dd, J = 17.3, 10.1 Hz, 1H), 5.77 - 5.65 (m, 2H), 4.19 (tt, J = 7.9, 3.9 Hz, 1H), 3.93 - 3.78 (m, 4H), 3.62 - 3.47 (m, 3H), 3.16 (d, J = 5.3 Hz, 1H), 3.06 (dd, J = 14.9, 7.5 Hz, 4H), 2.96 (s, 1H), 2.81 (dp, J = 12.6, 3.9 Hz, 1H), 2.68 - 2.60 (m, 3H), 2.51 (p, J = 1.9 Hz, 2H), 2.23 (ddd, J = 12.9, 8.5, 5.1 Hz, 1H).: 588.3[M+H]$^+$	1.36
604		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.43 (d, J = 31.7 Hz, 1H), 8.18 (dd, J = 3.3, 1.0 Hz, 1H), 7.50 (td, J = 8.6, 6.1 Hz, 1H), 7.19 - 6.91 (m, 2H), 6.53 (dd, J = 7.6, 1.1 Hz, 1H), 6.40 - 6.05 (m, 2H), 5.84 - 5.70 (m, 2H), 4.15 (td, J = 7.9, 4.0 Hz, 1H), 3.99 (td, J = 8.0, 2.1 Hz, 1H), 3.91 (d, J = 9.9 Hz, 3H), 3.81 (t, J = 7.6 Hz, 1H), 3.66 (t, J = 7.9 Hz, 1H), 3.34 (s, 3H), 3.17 (t, J = 4.9 Hz, 1H), 2.86 (d, J = 8.4 Hz, 2H), 2.75 (t, J = 7.6 Hz, 1H), 2.26 (ddd, J = 12.8, 8.5, 4.8 Hz, 1H), 1.38 (s, 6H).: 586.3[M+H]$^+$	1.30
605		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 8.4 Hz, 1H), 8.68 (d, J = 4.5 Hz, 1H), 8.59 (d, J = 8.3 Hz, 1H), 8.44 (d, J = 2.2 Hz, 1H), 8.12 (t, J = 7.7 Hz, 1H), 8.00 (dq, J = 8.1, 5.6, 3.8 Hz, 3H), 7.95 - 7.82 (m, 4H), 5.07 (p, J = 7.2 Hz, 1H), 3.67 (s, 4H), 3.48 (d, J = 7.3 Hz, 2H), 3.20 (s, 4H), 3.11 (dtd, J = 15.2, 8.4, 8.0, 3.7 Hz, 2H), 2.07 (dd, J = 13.4, 2.8 Hz, 1H), 2.01 (dd, J = 15.3, 3.5 Hz, 2H), 1.91 (qd, J = 13.2, 10.6, 5.1 Hz, 5H), 1.79 (td, J = 13.1, 12.7, 5.4 Hz, 2H), 1.60 (td, J = 13.6, 4.3 Hz, 2H), 1.48 (d, J = 7.0 Hz, 4H).: 669.4[M+H]+	1.28

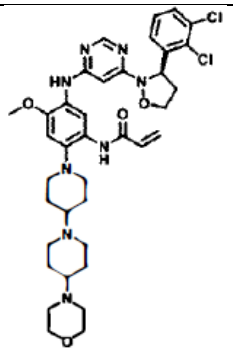
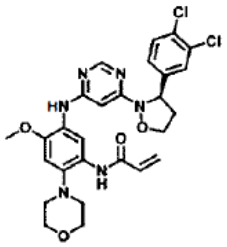
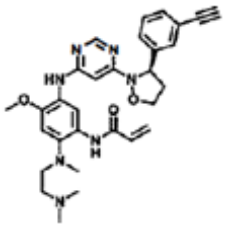
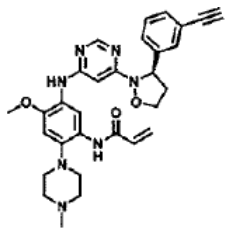
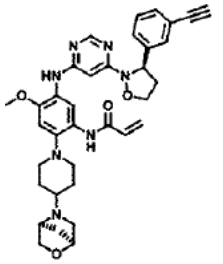
[585]

606		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.04 (s, 1H), 8.21 (s, 1H), 8.11 (s, 1H), 7.47 (td, J = 8.5, 6.2 Hz, 1H), 7.32 (td, J = 8.8, 1.7 Hz, 1H), 6.85 (s, 1H), 6.62 (dd, J = 17.0, 10.2 Hz, 1H), 6.33 (s, 1H), 6.23 (dd, J = 16.9, 2.0 Hz, 1H), 5.77 - 5.67 (m, 2H), 4.21 (td, J = 7.9, 3.7 Hz, 1H), 3.91 (q, J = 8.2 Hz, 1H), 3.81 (s, 3H), 3.68 - 3.34 (m, 4H), 3.16 (d, J = 10.9 Hz, 4H), 2.85 (s, 4H), 2.74 (t, J = 11.7 Hz, 3H), 2.30 - 2.19 (m, 1H), 2.03 (s, 2H), 1.88 (d, J = 20.1 Hz, 2H). : 656.4[M+H]+	1.35
607		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.88 (s, 1H), 8.47 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.60 (dd, J = 8.1, 1.6 Hz, 1H), 7.37 (dd, J = 7.9, 1.6 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.94 (s, 1H), 6.76 (d, J = 3.0 Hz, 2H), 6.40 - 6.32 (m, 1H), 6.25 (dd, J = 17.4, 10.5 Hz, 1H), 5.96 (dd, J = 8.9, 4.4 Hz, 1H), 5.73 (dd, J = 9.9, 1.6 Hz, 1H), 4.14 - 4.04 (m, 2H), 3.85 (s, 3H), 3.31 (dd, J = 10.3, 4.4 Hz, 1H), 3.22 - 3.15 (m, 1H), 3.01 (s, 2H), 2.94 (dq, J = 8.1, 4.0 Hz, 1H), 2.79 (d, J = 11.9 Hz, 2H), 2.50 (s, 1H), 2.28 - 2.16 (m, 2H), 2.05 (d, J = 9.7 Hz, 3H), 1.90 (t, J = 12.4 Hz, 2H), 1.86 - 1.80 (m, 1H), 1.76 - 1.66 (m, 2H), 1.36 (s, 2H), 1.32 - 1.23 (m, 4H).: 603.4[M+H]	1.22
608		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 11.33 (s, 1H), 8.85 (s, 1H), 8.42 - 8.22 (m, 2H), 7.62 - 7.54 (m, 1H), 7.37 (dd, J = 8.0, 1.6 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.74 (d, J = 3.6 Hz, 2H), 6.42 - 6.23 (m, 2H), 5.96 (dd, J = 8.8, 4.4 Hz, 1H), 5.76 (dd, J = 9.8, 1.7 Hz, 1H), 4.16 - 4.04 (m, 2H), 3.85 (s, 3H), 3.66 (td, J = 6.7, 4.0 Hz, 2H), 3.09 (qd, J = 7.5, 4.1 Hz, 4H), 2.99 - 2.92 (m, 1H), 2.12 (s, 3H), 1.56 (dd, J = 12.2, 7.1 Hz, 8H), 1.45 (d, J = 6.6 Hz, 4H).: 695.4[M+H]	1.31
609		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.37 (dd, J = 8.0, 1.6 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.92 (s, 1H), 6.75 (s, 2H), 6.40 - 6.31 (m, 1H), 6.24 (dd, J = 17.0, 9.9 Hz, 1H), 5.96 (dd, J = 8.8, 4.4 Hz, 1H), 5.74 (dd, J = 9.9, 1.6 Hz, 1H), 4.17 - 4.04 (m, 2H), 3.85 (s, 3H), 3.31 (dd, J = 7.3, 5.3 Hz, 1H), 3.06 (d, J = 11.6 Hz, 2H), 2.98 - 2.88 (m, 2H), 2.74 (q, J = 12.5 Hz, 8H), 2.33 (s, 2H), 2.25 (s, 2H), 2.09 (d, J = 12.4 Hz, 2H), 1.84 (t, J = 6.9 Hz, 1H), 1.67 (d, J = 12.3 Hz, 6H).: 605.5[M+H]	1.28

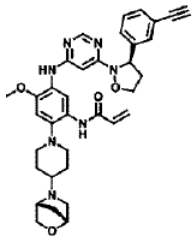
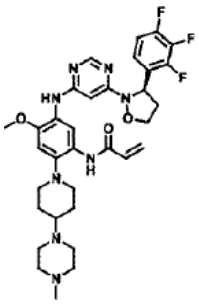
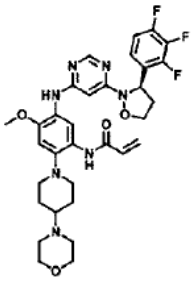
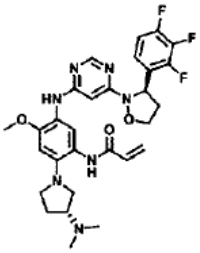
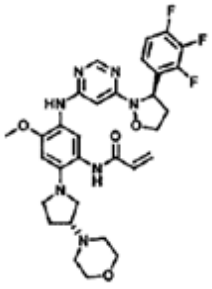
[586]

610		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.86 (s, 1H), 8.46 (s, 1H), 8.37 - 8.32 (m, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.37 (dd, J = 8.0, 1.6 Hz, 1H), 7.19 (td, J = 7.9, 3.3 Hz, 1H), 6.94 (s, 1H), 6.76 (s, 1H), 6.61 (d, J = 54.6 Hz, 1H), 6.43 - 6.17 (m, 2H), 5.96 (dt, J = 10.8, 5.3 Hz, 1H), 5.74 (dd, J = 9.9, 1.6 Hz, 1H), 4.17 - 4.02 (m, 2H), 3.85 (s, 3H), 3.27 (d, J = 7.4 Hz, 2H), 3.19 (q, J = 5.9 Hz, 2H), 3.04 (d, J = 11.0 Hz, 2H), 2.95 (dd, J = 8.5, 4.5 Hz, 1H), 2.79 - 2.70 (m, 2H), 2.62 (s, 6H), 2.37 (d, J = 8.1 Hz, 4H), 2.08 (d, J = 13.2 Hz, 2H), 1.94 - 1.83 (m, 2H), 1.47 (d, J = 6.5 Hz, 1H).; 681.4[M+H]	1.19
611		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.86 (s, 1H), 8.34 (d, J = 8.5 Hz, 1H), 7.58 (t, J = 8.3 Hz, 1H), 7.41 - 7.32 (m, 1H), 7.19 (td, J = 7.9, 4.5 Hz, 1H), 6.96 (dd, J = 17.1, 11.1 Hz, 2H), 6.75 (s, 1H), 6.43 - 6.17 (m, 2H), 5.95 (t, J = 9.9 Hz, 1H), 5.74 (d, J = 9.4 Hz, 1H), 5.35 (s, 1H), 4.12 - 4.06 (m, 1H), 3.95 - 3.80 (m, 2H), 3.85 (d, J = 1.2 Hz, 2H), 3.30 - 3.32 (m, 4H), 3.30 (s, 3H), 3.21 - 3.16 (m, 4H), 3.05 (t, J = 12.1 Hz, 4H), 2.79 (d, J = 6.7 Hz, 2H), 2.73 (d, J = 17.7 Hz, 4H), 2.56 (s, 3H), 2.21 (d, J = 4.3 Hz, 1H), 2.09 (d, J = 12.7 Hz, 2H), 2.02 (d, J = 10.0 Hz, 2H), 1.85 (t, J = 6.2 Hz, 2H). : 750.5[M+H]	1.19
612		N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.68 (s, 1H), 8.35 (s, 1H), 7.96 (s, 1H), 7.58 (d, J = 2.1 Hz, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.32 - 7.28 (m, 1H), 6.88 (s, 1H), 6.71 (s, 1H), 6.64 (s, 1H), 6.39 (d, J = 16.9 Hz, 1H), 6.28 (dd, J = 16.8, 10.0 Hz, 1H), 5.76 (d, J = 10.0 Hz, 1H), 5.64 (dd, J = 8.7, 4.6 Hz, 1H), 4.65 (s, 1H), 4.18 - 4.10 (m, 1H), 4.03 (dd, J = 14.8, 7.9 Hz, 2H), 3.86 (s, 3H), 3.75 (d, J = 7.8 Hz, 1H), 3.43 (d, J = 10.2 Hz, 1H), 3.23 (d, J = 10.1 Hz, 1H), 2.81 - 2.70 (m, 1H), 2.61 (s, 1H), 2.37 - 2.27 (m, 1H), 2.08 (d, J = 10.0 Hz, 1H), 1.99 (d, J = 10.1 Hz, 1H).; 583.2[M+H]	1.46
613		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2-(dimethylamino)ethyl)(methyl)amino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.40 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.60 (d, J =7.9 Hz, 1H), 7.37 (dd, J = 8.0, 1.5 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.94 (s, 1H), 6.75 (s, 2H), 6.38 - 6.32(m, 2H), 6.00 - 5.95 (m, 1H), 5.76 (dd, J = 8.6, 3.0 Hz, 1H), 4.17 - 4.04 (m, 3H), 3.85 (s, 3H), 3.12 - 3.04(m, 4H), 3.00 - 2.92 (m, 3H), 2.72 (s, 6H), 2.43 (s, 3H), 2.27 - 2.17 (m, 2H), 2.04 - 1.97 (m, 3H), 1.83 -1.77 (m, 2H).; 660.4 [M+H]$^+$	1.21

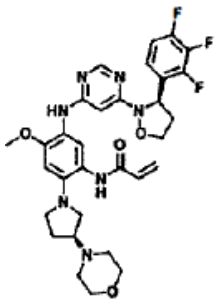
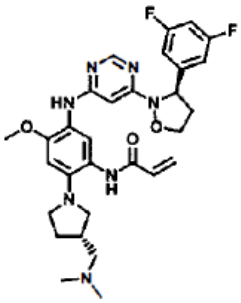
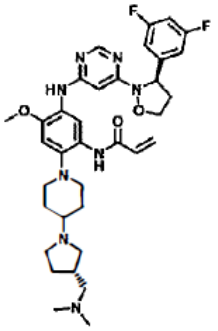
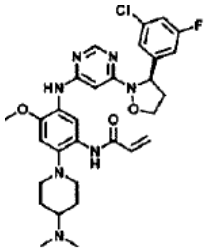
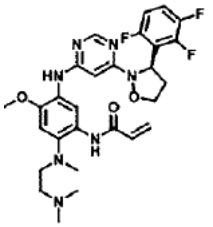
[587]

614		N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholino-[1,4'-bipiperidine]-1'-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.35 (s, 1H), 7.50 (d, J = 7.9 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 6.95 (s, 1H), 6.75 (s, 2H), 6.40 - 6.31 (m, 1H), 6.25 (dd, J = 16.8, 10.0 Hz, 1H), 5.96 (dd, J = 8.7, 4.4 Hz, 1H), 5.74 (dd, J = 9.9, 1.6 Hz, 1H), 4.16 - 4.03 (m, 2H), 3.85 (s, 3H), 3.73 (t, J = 4.6 Hz, 4H), 3.10 (dd, J = 26.9, 11.1 Hz, 4H), 2.99 - 2.90 (m, 1H), 2.72 (q, J = 12.3 Hz, 2H), 2.57 (t, J = 4.7 Hz, 4H), 2.40 (s, 1H), 2.25 - 2.19 (m, 3H), 2.05 (d, J = 12.3 Hz, 2H), 1.88 (d, J = 12.6 Hz, 3H), 1.72 - 1.57 (m, 4H).; 737.47 $[M+H]^+$	1.22
615		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.92 (s, 1H), 8.51 (s, 1H), 8.37 (s, 1H), 7.58 (d, J = 2.1 Hz, 1H), 7.41 (d, J = 8.2 Hz, 1H), 7.30 (dd, J = 8.2, 2.1 Hz, 1H), 6.97 (s, 1H), 6.78 (s, 1H), 6.72 (s, 1H), 6.37 (d, J = 16.9 Hz, 1H), 6.27 (dd, J = 16.9, 10.0 Hz, 1H), 5.76 (d, J = 10.0 Hz, 1H), 5.65 (dd, J = 8.7, 4.6 Hz, 1H), 4.21 - 4.13 (m, 1H), 4.06 (q, J = 8.0 Hz, 1H), 3.91 - 3.87 (m, 4H), 3.87 (s, 3H), 2.94 - 2.84 (m, 4H), 2.82 - 2.72 (m, 1H), 2.38 - 2.28 (m, 1H).; 571.2 $[M+H]^+$	1.62
616		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, Chloroform-d) δ 9.59 (s, 1H), 8.80 (s, 1H), 8.32 (s, 1H), 7.60 (s, 1H), 7.46 (d, J = 7.4 Hz, 2H), 7.38 (d, J = 7.6 Hz, 1H), 7.29 (t, J = 7.8 Hz, 1H), 6.76 (s, 1H), 6.70 (s, 1H), 6.56 (dd, J = 16.9, 10.1 Hz, 1H), 6.41 (dd, J = 16.9, 1.9 Hz, 1H), 5.69 (td, J = 10.1, 3.2 Hz, 2H), 4.15 (dd, J = 8.0, 4.4 Hz, 1H), 4.00 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.05 (s, 1H), 3.03 (t, J = 5.9 Hz, 2H), 2.78 (dq, J = 12.0, 3.7 Hz, 1H), 2.67 (s, 3H), 2.63 (t, J = 6.0 Hz, 2H), 2.43 (s, 6H), 2.36 (dt, J = 12.2, 4.0 Hz, 1H); 542.4[M+H]+	1.20
617		N-(5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, Chloroform-d) δ 8.87 - 8.66 (m, 1H), 8.48 - 8.37 (m, 1H), 8.35 - 8.26 (m, 1H), 7.59 (d, J = 1.8 Hz, 1H), 7.55 (s, 1H), 7.45 (d, J = 7.7 Hz, 1H), 7.37 (dt, J = 7.8, 1.4 Hz, 1H), 7.32 - 7.27 (m, 1H), 6.80 (d, J = 2.4 Hz, 1H), 6.63 (d, J = 6.7 Hz, 1H), 6.42 - 6.31 (m, 1H), 6.27 (dd, J = 16.9, 9.9 Hz, 1H), 5.75 (dd, J = 9.9, 1.6 Hz, 1H), 5.66 (dd, J = 8.7, 4.6 Hz, 1H), 4.14 (td, J = 8.0, 4.3 Hz, 1H), 4.04 (q, J = 8.2 Hz, 1H), 3.85 (s, 3H), 3.05 (s, 1H), 3.04 - 2.89 (m, 4H), 2.84 (td, J = 6.2, 2.2 Hz, 1H), 2.76 (dq, J = 7.7, 3.8, 3.3 Hz, 4H), 2.45 (d, J = 2.9 Hz, 3H), 2.35 (dtd, J = 12.5, 8.1, 4.6 Hz, 1H); 540.4[M+H]+	1.13
618		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.98 (s, 1H), 9.24 (d, J = 30.9 Hz, 1H), 8.31 (s, 1H), 7.86 (d, J = 13.3 Hz, 1H), 7.49 - 7.37 (m, 4H), 6.90 (d, J = 6.6 Hz, 1H), 6.60 (dt, J = 17.7, 8.9 Hz, 1H), 6.26 - 6.21 (m, 1H), 6.08 (s, 1H), 5.79 - 5.73 (m, 1H), 5.51 (t, J = 7.3 Hz, 1H), 4.72 - 4.62 (m, 2H), 4.57 (s, 1H), 4.44 (d, J = 9.2 Hz, 1H), 4.31 (d, J = 4.3 Hz, 2H), 4.24 (s, 2H), 4.04 (d, J = 7.8 Hz, 1H), 3.81 (s, 3H), 3.70 (d, J = 10.1 Hz, 1H), 3.49 - 3.43 (m, 1H), 3.20 (d, J = 22.6 Hz, 3H), 2.93 (dd, J = 7.9, 4.1 Hz, 1H), 2.82 (s, 2H), 2.38 - 2.26 (m, 2H), 2.08 (d, J = 8.7 Hz, 3H).; 622.3$[M+H]^+$	1.11

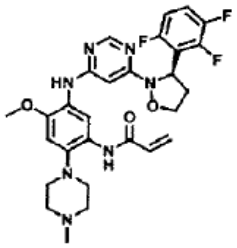
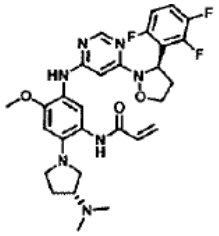
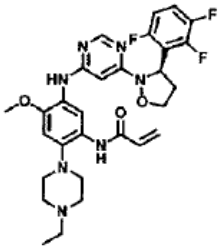
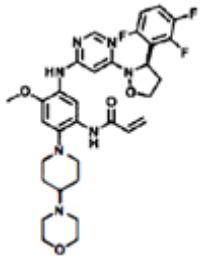
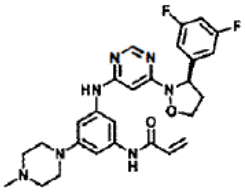
[588]

619		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.88 (s, 1H), 9.23 (d, J = 30.8 Hz, 1H), 8.30 (s, 1H), 7.88 (d, J = 12.9 Hz, 1H), 7.48 - 7.36 (m, 4H), 6.90 (d, J = 6.7 Hz, 1H), 6.61 (td, J = 17.4, 10.2 Hz, 1H), 6.28 - 6.22 (m, 1H), 6.10 (s, 1H), 5.76 (t, J = 5.2 Hz, 1H), 5.55 - 5.46 (m, 1H), 4.73 - 4.62 (m, 2H), 4.57 (s, 1H), 4.30 (d, J = 4.3 Hz, 2H), 4.24 (s, 1H), 4.20 (d, J = 10.4 Hz, 1H), 4.03 (d, J = 7.8 Hz, 2H), 3.81 (d, J = 2.1 Hz, 3H), 3.70 (d, J = 9.9 Hz, 1H), 3.51 - 3.41 (m, 2H), 3.29 - 3.13 (m, 3H), 2.92 (d, J = 7.8 Hz, 1H), 2.83 - 2.67 (m, 2H), 2.30 (dd, J = 13.1, 5.1 Hz, 2H), 2.08 (d, J = 10.3 Hz, 2H).; 622.3[M+H]$^+$	1.11
620		N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	653.5[M+H]+	1.18
621		N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	640.5[M+H]+	1.27
622		N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	584.5 [M+H]$^+$	1.18
623		N-(4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 7.77 (s, 1H), 7.33 (td, J = 8.2, 2.0 Hz, 1H), 7.09 (td, J = 9.3, 1.8 Hz, 1H), 6.68 (s, 1H), 6.59 (dd, J = 17.0, 10.3 Hz, 1H), 6.41 - 6.32 (m, 2H), 5.81 - 5.72 (m, 2H), 4.15 (td, J = 7.9, 4.1 Hz, 1H), 3.98 (d, J = 8.0 Hz, 1H), 3.87 (s, 3H), 3.81 (t, J = 4.4 Hz, 4H), 3.41 (dd, J = 9.3, 6.7 Hz, 1H), 3.31 (ddd, J = 16.1, 7.6, 3.3 Hz, 5H), 2.89 - 2.69 (m, 5H), 2.67 (s, 8H), 2.33 - 2.21 (m, 2H), 2.01 (td, J = 16.9, 8.4 Hz, 1H), 1.43 - 1.35 (m, 4H) ; 626.4 [M+H]$^+$	1.25

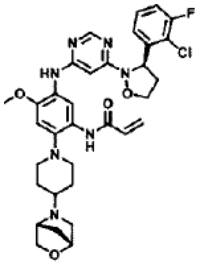
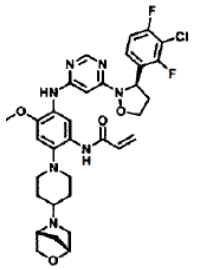
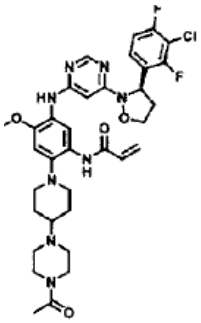
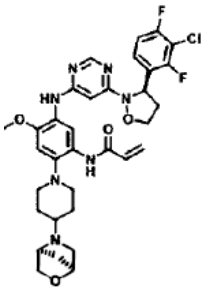
[589]

624		N-(4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	626.4 $[M+H]^+$	1.22
625		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-((dimethylamino)methyl)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.33 (s, 1H), 8.53 (s, 1H), 8.13 (d, J = 1.0 Hz, 1H), 7.37 (s, 1H), 7.13 - 7.09 (m, 3H), 6.53 - 6.43 (m, 2H), 6.20 (d, J = 2.1 Hz, 1H), 5.68 (dd, J = 10.2, 2.1 Hz, 1H), 5.55 (dd, J = 8.7, 5.0 Hz, 1H), 4.11 (td, J = 7.8, 3.8 Hz, 1H), 3.79 (s, 3H), 3.30 - 3.16 (m, 5H), 3.00 (dd, J = 9.3, 6.6 Hz, 1H), 2.75 (dtd, J = 12.0, 7.8, 3.8 Hz, 1H), 2.24 (dd, J = 7.7, 5.2 Hz, 2H), 2.14 (s, 7H), 2.05 - 1.93 (m, 1H), 1.56 (dq, J = 12.1, 7.8 Hz, 1H).: 580.4[M+H]$^+$	1.14
626		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-((dimethylamino)methyl)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.96 (s, 1H), 8.66 (s, 1H), 8.17 (s, 1H), 7.13 (td, J = 7.8, 7.2, 3.1 Hz, 4H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.1 Hz, 1H), 6.35 (s, 1H), 6.21 (dd, J = 16.9, 2.0 Hz, 1H), 5.72 (dd, J = 10.2, 2.0 Hz, 1H), 5.56 (dd, J = 8.7, 5.0 Hz, 1H), 4.13 (td, J = 7.9, 3.9 Hz, 1H), 3.80 (s, 3H), 3.01 - 2.97 (m, 2H), 2.81 - 2.61 (m, 5H), 2.54 (d, J = 7.3 Hz, 2H), 2.25 (ddd, J = 12.8, 8.5, 4.8 Hz, 4H), 2.11 (d, J = 7.3 Hz, 14H), 1.95 - 1.87 (m, 2H), 1.68 (h, J = 8.7, 7.8 Hz, 2H), 1.36 (h, J = 6.9 Hz, 1H).:663.5[M+H]$^+$	1.05
627		N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.86 (s, 1H), 8.50 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.10 (dt, J = 9.4, 2.2 Hz, 1H), 7.00 - 6.88 (m, 2H), 6.78 - 6.69 (m, 2H), 6.35 (dd, J = 17.0, 1.5 Hz, 1H), 6.25 (dd, J = 17.0, 10.0 Hz, 1H), 5.74 (dd, J = 9.0, 1.6 Hz, 1H), 5.66 (dd, J = 8.7, 4.6 Hz, 1H), 4.20 - 4.11 (m, 1H), 4.11 - 4.00 (m, 1H), 3.85 (s, 3H), 3.00 - 3.02 (m, 2H), 2.84 - 2.77 (m, 1H), 2.76 - 2.66 (m, 2H), 2.35 (s, 6H), 2.34 - 2.28 (m, 1H), 2.27 - 2.17 (m, 1H), 2.09 - 2.01 (m, 2H), 1.70 - 1.61 (m, 2H), 1.62 - 1.53 (m, 1H). : 596.4 $[M+H]^+$	1.27
628		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 10.09 (s, 1H), 8.94 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.05 (qd, J = 9.1, 4.9 Hz, 1H), 6.88 (s, 1H), 6.86 - 6.80 (m, 1H), 6.79 (s, 1H), 6.68 (d, J = 1.1 Hz, 1H), 6.40 (dd, J = 17.0, 1.9 Hz, 1H), 6.27 (dd, J = 17.0, 10.0 Hz, 1H), 5.91 (dd, J = 9.1, 6.5 Hz, 1H), 5.67 (dd, J = 10.0, 1.9 Hz, 1H), 4.42 - 4.33 (m, 1H), 4.07 - 3.96 (m, 1H), 3.82 (s, 3H), 2.93 - 2.81 (m, 2H), 2.81 - 2.74 (m, 1H), 2.71 (s, 3H), 2.63 - 2.50 (m, 1H), 2.35 - 2.28 (m, 2H), 2.27 (s, 6H). : 572.4 $[M+H]^+$	1.19

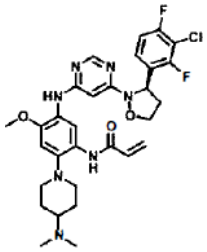
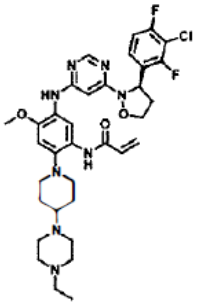
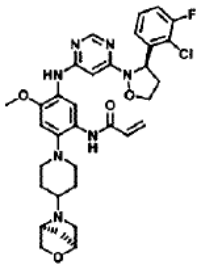
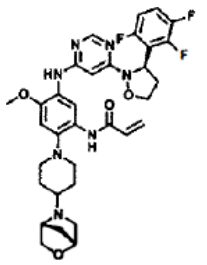
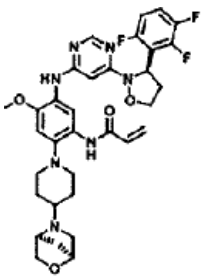
[590]

629		N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.88 (s, 1H), 8.52 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.06 (qd, J = 9.1, 4.8 Hz, 1H), 6.88 (s, 1H), 6.87 - 6.79 (m, 1H), 6.78 (s, 1H), 6.64 (s, 1H), 6.37 (dd, J = 17.0, 1.6 Hz, 1H), 6.26 (dd, J = 16.9, 9.9 Hz, 1H), 5.90 (dd, J = 9.1, 6.5 Hz, 1H), 5.75 (dd, J = 9.9, 1.6 Hz, 1H), 4.41 - 4.32 (m, 1H), 4.04 - 3.94 (m, 1H), 3.82 (s, 3H), 2.97 - 2.85 (m, 4H), 2.80 - 2.72 (m, 1H), 2.71 - 2.47 (m, 5H), 2.30 (s, 3H). ; 570.4 [M+H]$^+$	1.14
630		N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.61 (s, 1H), 8.35 (s, 1H), 8.11 (s, 1H), 7.06 (qd, J = 9.1, 4.8 Hz, 1H), 6.89 - 6.78 (m, 2H), 6.73 (s, 1H), 6.60 (s, 1H), 6.38 (dd, J = 16.9, 1.7 Hz, 1H), 6.28 (dd, J = 16.9, 10.0 Hz, 1H), 5.90 (dd, J = 9.0, 6.6 Hz, 1H), 5.73 (dd, J = 10.0, 1.7 Hz, 1H), 4.41 - 4.32 (m, 1H), 4.03 - 3.92 (m, 1H), 3.82 (s, 3H), 3.24 - 3.17 (m, 1H), 3.17 - 3.04 (m, 3H), 2.92 - 2.81 (m, 1H), 2.81 - 2.69 (m, 1H), 2.63 - 2.49 (m, 1H), 2.29 (s, 6H), 2.24 - 2.11 (m, 1H), 1.99 - 1.85 (m, 1H). ; 584.4 [M+H]$^+$	1.11
631		N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.88 (s, 1H), 8.56 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.06 (qd, J = 9.1, 4.8 Hz, 1H), 6.90 - 6.79 (m, 3H), 6.64 (s, 1H), 6.37 (dd, J = 17.0, 1.6 Hz, 1H), 6.26 (dd, J = 17.0, 9.9 Hz, 1H), 5.90 (dd, J = 9.0, 6.6 Hz, 1H), 5.75 (dd, J = 10.0, 1.6 Hz, 1H), 4.42 - 4.33 (m, 1H), 4.04 - 3.94 (m, 1H), 3.81 (s, 3H), 2.99 - 2.88 (m, 4H), 2.80 - 2.72 (m, 2H), 2.78 - 2.58 (m, 4H), 2.62 - 2.56 (m, 1H), 2.52 (q, J = 7.2 Hz, 2H), 1.16 (t, J = 7.8, 7.2 Hz, 3H). ; 584.3 [M+H]$^+$	1.14
632		N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.85 (s, 1H), 8.42 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.12 - 7.00 (m, 1H), 6.89 - 6.79 (m, 2H), 6.74 (s, 1H), 6.66 - 6.61 (m, 1H), 6.36 (dd, J = 16.9, 1.5 Hz, 1H), 6.24 (dd, J = 16.9, 10.1 Hz, 1H), 5.90 (dd, J = 9.0, 6.6 Hz, 1H), 5.74 (dd, J = 10.1, 1.5 Hz, 1H), 4.41 - 4.32 (m, 1H), 3.99 (q, J = 8.3 Hz, 1H), 3.83 (s, 3H), 3.78 (t, J = 4.6 Hz, 4H), 3.10 - 3.03 (m, 2H), 2.80 - 2.68 (m, 3H), 2.65 - 2.50 (m, 5H), 2.35 - 2.24 (m, 1H), 2.13 - 2.03 (m, 2H), 1.72 - 1.64 (m, 2H). ; 640.4 [M+H]$^+$	1.15
633		N-(3-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-5-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.24 (s, 1H), 7.39 (s, 1H), 7.16 (s, 1H), 7.07 (d, J = 7.1 Hz, 2H), 6.95 (s, 1H), 6.88 - 6.80 (m, 1H), 6.56 (s, 1H), 6.49 - 6.32 (m, 2H), 5.79 (dd, J = 2.1, 9.7 Hz, 1H), 5.61 - 5.52 (m, 1H), 4.20 - 4.12 (m, 1H), 3.97 (q, J = 7.9 Hz, 1H), 3.38 - 3.34 (m, 4H), 2.98 - 2.91 (m, 4H), 2.89 - 2.82 (m, 1H), 2.60 (s, 3H), 2.39 - 2.31 (m, 1H) ; 522.3[M+H]$^+$	1.19

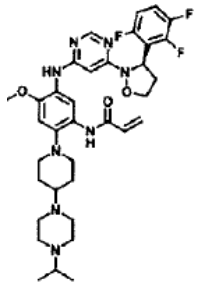
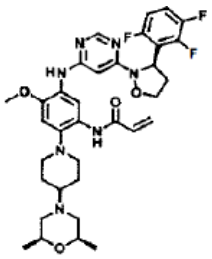
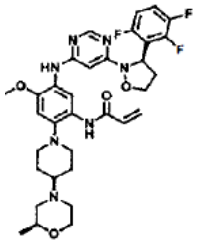
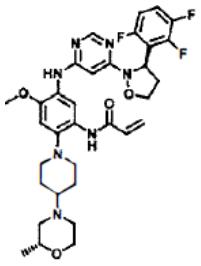
[591]

634		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (s, 1H), 8.65 (s, 1H), 8.15 (d, J = 6.0 Hz, 2H), 7.45 - 7.31 (m, 3H), 6.84 (s, 1H), 6.61 (s, 1H), 6.39 (s, 1H), 6.21 (d, J = 16.9 Hz, 1H), 5.86 - 5.66 (m, 2H), 4.36 (s, 1H), 4.18 - 4.11 (m, 1H), 3.88 (q, J = 8.0 Hz, 2H), 3.81 (s, 3H), 3.54 (s, 1H), 3.02 (s, 3H), 2.95 - 2.82 (m, 2H), 2.73 (t, J = 10.9 Hz, 3H), 2.10 (d, J = 8.5 Hz, 2H), 1.91 (s, 2H), 1.66 (s, 4H). : 650.4[M+H]$^+$	1.25
635		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.64 (s, 1H), 8.15 (d, J = 3.7 Hz, 2H), 7.49 (td, J = 8.6, 6.2 Hz, 1H), 7.31 (td, J = 8.8, 1.7 Hz, 1H), 6.84 (s, 1H), 6.64 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (s, 1E), 6.20 (dd, J = 16.9, 2.0 Hz, 1H), 5.71 (dd, J = 9.0, 5.2 Hz, 2H), 4.33 (s, 1H), 4.17 (td, J = 7.9, 3.7 Hz, 1H), 3.87 (dd, J = 11.7, 7.8 Hz, 2H), 3.80 (s, 3H), 3.70 (s, 1H), 3.51 (d, J = 7.3 Hz, 1H), 3.03 - 2.92 (m, 3H), 2.79 (dt, J = 8.1, 3.9 Hz, 1H), 2.75 - 2.65 (m, 2H), 2.44 (d, J = 10.2 Hz, 1H), 2.34 (d, J = 9.6 Hz, 1H), 2.25 - 2.15 (m, 1H), 1.87 (s, 2H), 1.72 - 1.56 (m, 4H). : 668.4[M+H]$^+$	1.32
636		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 11.26 (s, 1H), 8.82 (s, 1H), 8.37 - 8.27 (m, 2H), 7.46 (td, J = 8.4, 6.0 Hz, 1H), 6.95 (td, J = 8.5, 1.8 Hz, 1H), 6.72 (s, 2H), 6.48 - 6.27 (m, 2H), 5.80 - 5.82 (m, 1H), 5.77 (dd, J = 9.3, 2.2 Hz, 1H), 4.15 (td, J = 8.0, 4.1 Hz, 1H), 4.07 (q, J = 8.1 Hz, 1H), 3.85 (s, 4H), 3.70 - 3.62 (m, 1H), 3.16 (d, J = 11.7 Hz, 1H), 3.08 (dd, J = 8.9, 6.5 Hz, 1H), 2.90 - 2.83 (m, 1H), 2.83 - 2.71 (m, 1H), 2.34 - 2.19 (m, 4H), 2.13 (s, 3H), 2.06 (d, J = 14.5 Hz, 2H), 1.58 - 1.52 (m, 4H), 1.45 (d, J = 6.6 Hz, 3H). : 607.4[M+H]$^+$	1.31
637		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.64 (s, 1H), 8.15 (d, J = 3.8 Hz, 2H), 7.49 (td, J = 8.5, 6.2 Hz, 1H), 7.31 (td, J = 8.8, 1.6 Hz, 1H), 6.84 (s, 1H), 6.64 (dd, J = 17.0, 10.2 Hz, 1H), 6.35 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.71 (dd, J = 9.3, 5.4 Hz, 2H), 4.33 (s, 1H), 4.16 (dd, J = 8.0, 3.8 Hz, 1H), 3.92 - 3.83 (m, 2H), 3.80 (s, 3H), 3.70 (s, 1H), 3.51 (d, J = 7.3 Hz, 1H), 3.02 - 2.92 (m, 3H), 2.79 (dt, J = 8.1, 4.0 Hz, 1H), 2.71 (t, J = 12.1 Hz, 2H), 2.34 (d, J = 9.5 Hz, 1H), 2.26 - 2.16 (m, 1H), 1.85 (s, 3H), 1.74 - 1.56 (m, 4H). : 668.5[M+H]$^+$	1.33

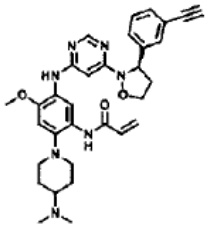
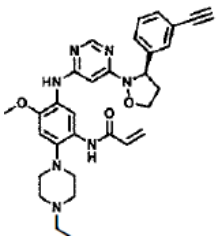
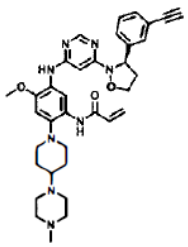
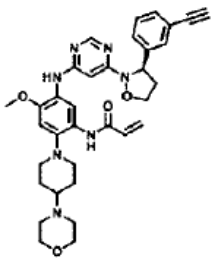
[592]

638		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (s, 1H), 8.65 (s, 1H), 8.27 - 8.06 (m, 2H), 7.49 (td, J = 8.6, 6.2 Hz, 1H), 7.31 (td, J = 8.8, 1.7 Hz, 1H), 6.83 (s, 1H), 6.65 (dd, J = 17.0, 10.2 Hz, 1H), 6.38 (d, J = 12.7 Hz, 1H), 6.28 - 6.15 (m, 1H), 5.72 (ddd, J = 8.7, 5.8, 3.3 Hz, 2H), 4.17 (td, J = 7.9, 3.7 Hz, 1H), 3.93 - 3.75 (m, 4H), 3.15 - 3.00 (m, 3H), 2.79 (qd, J = 7.5, 3.4 Hz, 1H), 2.72 - 2.60 (m, 2H), 2.34 - 2.16 (m, 7H), 1.80 - 1.60 (m, 4H).; 614.4[M+H]$^+$	1.31
639		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (s, 1H), 8.66 (s, 1H), 8.16 (d, J = 6.4 Hz, 1H), 7.49 (td, J = 8.5, 6.2 Hz, 1H), 7.31 (t, J = 8.8 Hz, 1H), 6.83 (s, 1H), 6.68 (ddd, J = 10.1, 16.6, 10.2 Hz, 1H), 6.22 - 6.03 (m, 2H), 5.81 - 5.66 (m, 3H), 3.80 (s, 3H), 3.27 - 3.12 (m, 2H), 3.04 (d, J = 24.7 Hz, 5H), 2.62 (dd, J = 11.1, 5.5 Hz, 4H), 2.43 (dd, J = 14.5, 7.1 Hz, 3H), 1.97 - 1.65 (m, 6H), 1.13 - 1.01 (m, 6H).; 683.4[M+H]$^+$	1.25
640		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.13 (s, 1H), 8.68 (s, 1H), 8.16 (s, 1H), 7.46 - 7.28 (m, 3H), 6.85 (s, 1H), 6.60 (t, J = 13.6 Hz, 1H), 6.42 (s, 1H), 6.24 (ddd, J = 17.0, 11.6, 1.9 Hz, 1H), 5.84 - 5.70 (m, 2H), 4.15 (td, J = 7.9, 3.8 Hz, 1H), 3.88 (q, J = 8.0 Hz, 1H), 3.82 (s, 3H), 3.72 - 3.64 (m, 2H), 3.50 (d, J = 6.6 Hz, 5H), 2.80 (dtd, J = 12.4, 8.3, 4.3 Hz, 2H), 2.73 (d, J = 12.2 Hz, 2H), 2.32 - 1.94 (m, 7H), 1.06 (t, J = 7.0 Hz, 2H).; 650.4[M+H]$^+$	1.23
641		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.84 (s, 1H), 8.46 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.12 - 6.99 (m, 1H), 6.87 - 6.78 (m, 2H), 6.75 (s, 1H), 6.66 - 6.61 (m, 1H), 6.35 (dd, J = 17.0, 1.5 Hz, 1H), 6.23 (dd, J = 16.9, 10.1 Hz, 1H), 5.90 (dd, J = 9.1, 6.5 Hz, 1H), 5.73 (dd, J = 10.1, 1.5 Hz, 1H), 4.44 (t, J = 2.0 Hz, 1H), 4.36 (td, J = 8.1, 2.5 Hz, 1H), 4.11 (dd, J = 12.7, 7.5 Hz, 1H), 4.07 - 3.94 (m, 1H), 3.83 (s, 3H), 3.79 - 3.74 (m, 1H), 3.66 (dd, J = 8.0, 1.6 Hz, 1H), 3.13 (dd, J = 10.0, 1.8 Hz, 1H), 3.06 - 2.98 (m, 2H), 2.83 - 2.69 (m, 3H), 2.63 - 2.51 (m, 2H), 2.51 - 2.46 (m, 1H), 2.04 - 2.00 (m, 1H), 1.99 - 1.86 (m, 2H), 1.86 - 1.79 (m, 1H), 1.72 - 1.59 (m, 2H). ; 652.5 [M+H]$^+$	1.18
642		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.84 (s, 1H), 8.46 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.12 - 6.99 (m, 1H), 6.91 - 6.78 (m, 2H), 6.75 (s, 1H), 6.63 (d, J = 1.0 Hz, 1H), 6.35 (dd, J = 17.0, 1.5 Hz, 1H), 6.23 (dd, J = 16.9, 10.1 Hz, 1H), 5.90 (dd, J = 9.1, 6.5 Hz, 1H), 5.72 (dd, J = 10.1, 1.5 Hz, 1H), 4.44 (t, J = 2.0 Hz, 1H), 4.36 (td, J = 8.1, 2.5 Hz, 1H), 4.10 (dd, J = 13.3, 7.5 Hz, 1H), 4.04 - 3.93 (m, 1H), 3.83 (s, 3H), 3.79 - 3.74 (m, 1H), 3.66 (dd, J = 8.0, 1.7 Hz, 1H), 3.13 (dd, J = 9.9, 1.8 Hz, 1H), 3.07 - 2.97 (m, 2H), 2.82 - 2.60 (m, 3H), 2.63 - 2.54 (m, 2H), 2.50 (dd, J = 9.9, 1.5 Hz, 1H), 2.08 - 2.00 (m, 1H), 1.98 - 1.89 (m, 2H), 1.84 - 1.80 (m, 1H), 1.72 - 1.60 (m, 2H). ; 652.5 [M+H]$^+$	1.19

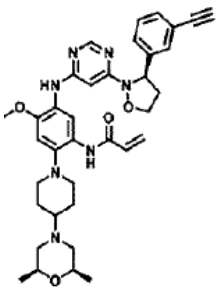
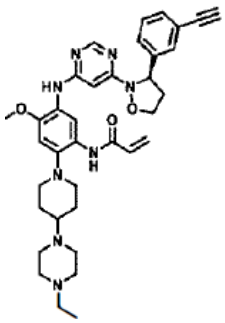
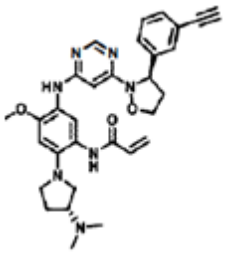
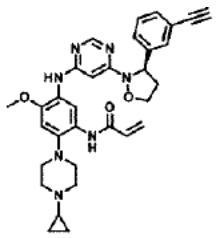
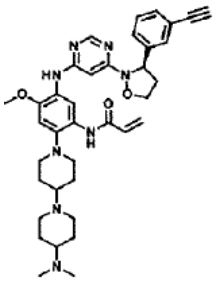
[593]

643		N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl) acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.84 (s, 1H), 8.44 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.12 - 6.99 (m, 1H), 6.88 - 6.78 (m, 2H), 6.74 (s, 1H), 6.63 (s, 1H), 6.35 (dd, J = 16.9, 1.6 Hz, 1H), 6.23 (dd, J = 16.9, 10.0 Hz, 1H), 5.90 (dd, J = 9.0, 6.5 Hz, 1H), 5.73 (dd, J = 10.0, 1.6 Hz, 1H), 4.36 (td, J = 8.1, 2.5 Hz, 1H), 3.99 (q, J = 8.3 Hz, 1H), 3.82 (s, 3H), 3.05 (d, J = 11.3 Hz, 2H), 2.82 - 2.49 (m, 13H), 2.37 - 2.25 (m, 1H), 2.07 (dd, J = 14.4, 10.7 Hz, 2H), 1.73 - 1.59 (m, 2H), 1.08 (d, J = 6.5 Hz, 6H). ; 681.5 [M+H]$^+$	1.16
644		N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl) acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.84 (s, 1H), 8.41 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.12 - 6.99 (m, 1H), 6.89 (s, 1H), 6.88 - 6.78 (m, 1H), 6.74 (s, 1H), 6.63 (s, 1H), 6.37 (dd, J = 16.9, 1.5 Hz, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.90 (dd, J = 9.1, 6.6 Hz, 1H), 5.74 (dd, J = 10.0, 1.5 Hz, 1H), 4.36 (td, J = 8.1, 2.5 Hz, 1H), 3.99 (q, J = 8.5 Hz, 1H), 3.83 (s, 3H), 3.77 - 3.65 (m, 2H), 3.10 - 3.02 (m, 2H), 2.88 (d, J = 10.8 Hz, 2H), 2.82 - 2.64 (m, 3H), 2.63 - 2.49 (m, 1H), 2.35 - 2.23 (m, 1H), 2.10 - 2.02 (m, 2H), 1.90 (t, J = 10.6 Hz, 2H), 1.73 - 1.58 (m, 2H), 1.20 (d, J = 6.3 Hz, 6H). ; 668.5 [M+H]$^+$	1.25
645		N-(4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl) acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.84 (s, 1H), 8.42 (s, 1H), 8.36 (d, J = 1.1 Hz, 1H), 7.12 - 6.99 (m, 1H), 6.88 - 6.78 (m, 2H), 6.74 (s, 1H), 6.63 (s, 1H), 6.36 (dd, J = 16.9, 1.5 Hz, 1H), 6.25 (dd, J = 16.9, 10.1 Hz, 1H), 5.90 (dd, J = 9.1, 6.6 Hz, 1H), 5.74 (dd, J = 10.1, 1.5 Hz, 1H), 4.41 - 4.32 (m, 1H), 4.04 - 3.86 (m, 2H), 3.83 (s, 3H), 3.76 - 3.60 (m, 2H), 3.10 - 3.02 (m, 2H), 2.90 (d, J = 11.3 Hz, 1H), 2.84 (d, J = 11.3 Hz, 1H), 2.81 - 2.66 (m, 3H), 2.63 - 2.50 (m, 1H), 2.35 - 2.23 (m, 2H), 2.11 - 2.02 (m, 2H), 1.97 (t, J = 10.5 Hz, 1H), 1.72 - 1.60 (m, 2H), 1.19 (d, J = 6.3 Hz, 3H). ; 654.5 [M+H]$^+$	1.21
646		N-(4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl) acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.84 (s, 1H), 8.42 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.12 - 6.99 (m, 1H), 6.89 (s, 1H), 6.88 - 6.78 (m, 1H), 6.74 (s, 1H), 6.63 (s, 1H), 6.36 (dd, J = 16.9, 1.6 Hz, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.90 (dd, J = 9.1, 6.6 Hz, 1H), 5.74 (dd, J = 10.0, 1.5 Hz, 1H), 4.41 - 4.32 (m, 1H), 4.04 - 3.86 (m, 2H), 3.83 (s, 3H), 3.74 - 3.62 (m, 2H), 3.10 - 3.02 (m, 2H), 2.91 (d, 1H), 2.84 (d, J = 11.2 Hz, 1H), 2.81 - 2.65 (m, 3H), 2.63 - 2.50 (m, 1H), 2.35 - 2.24 (m, 2H), 2.11 - 2.02 (m, 2H), 1.97 (t, J = 10.5 Hz, 1H), 1.73 - 1.58 (m, 2H), 1.19 (d, J = 6.3 Hz, 3H). ; 654.5 [M+H]$^+$	1.22

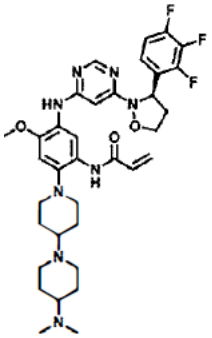
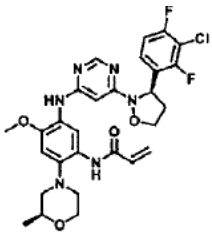
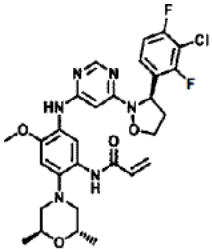
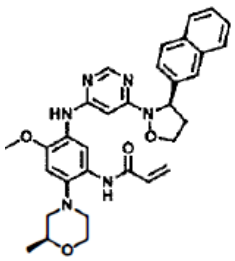
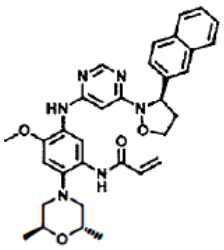
[594]

647		N-(2-(4-(dimethylamino)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.87 (s, 1H), 8.49 (s, 1H), 8.40 - 8.33 (m, 1H), 7.61 (d, *J* = 1.8 Hz, 1H), 7.46 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.37 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.30 (d, *J* = 7.7 Hz, 1H), 6.96 (s, 1H), 6.75 (s, 1H), 6.70 (s, 1H), 6.35 (dd, *J* = 17.1, 1.7 Hz, 1H), 6.25 (dd, *J* = 17.0, 9.9 Hz, 1H), 5.73 (dd, *J* = 9.9, 1.7 Hz, 1H), 5.67 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.15 (td, *J* = 7.9, 4.3 Hz, 1H), 4.06 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.09 - 3.00 (m, 3H), 2.74 (tt, *J* = 12.3, 7.1 Hz, 4H), 2.36 (s, 6H), 2.34 - 2.29 (m, 1H), 2.05 (d, *J* = 12.8 Hz, 2H), 1.64 (td, *J* = 12.1, 3.7 Hz, 2H): 568.4[M+H]$^+$	1.18
648		N-(2-(4-ethylpiperazine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.91 (s, 1H), 8.56 (s, 1H), 8.37 (s, 1H), 7.61 (d, *J* = 1.8 Hz, 1H), 7.46 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.37 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.32 - 7.27 (m, 1H), 7.01 (d, *J* = 3.8 Hz, 1H), 6.81 (s, 1H), 6.70 (s, 1H), 6.36 (dd, *J* = 16.9, 1.7 Hz, 1H), 6.27 (dd, *J* = 17.0, 10.0 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.7 Hz, 1H), 5.68 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.15 (td, *J* = 8.0, 4.3 Hz, 1H), 4.06 (q, *J* = 8.0 Hz, 1H), 3.82 (s, 3H), 3.05 (s, 1H), 2.94 (t, *J* = 5.0 Hz, 4H), 2.79 - 2.73 (m, 1H), 2.74 - 2.54 (m, 4H), 2.52 (q, *J* = 7.2 Hz, 2H), 2.35 (dtd, *J* = 12.4, 8.1, 4.5 Hz, 1H), 1.15 (t, *J* = 7.2 Hz, 3H): 554.4[M+H]$^+$	1.17
649		N-(5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.87 (s, 1H), 8.46 (s, 1H), 8.36 (s, 1H), 7.61 (d, *J* = 1.8 Hz, 1H), 7.46 (dt, *J* = 7.8, 1.6 Hz, 1H), 7.37 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.31 - 7.27 (m, 1H), 7.02 (s, 1H), 6.75 (s, 1H), 6.69 (s, 1H), 6.38 - 6.32 (m, 1H), 6.25 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.75 - 5.71 (m, 1H), 5.67 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.14 (td, *J* = 7.9, 4.3 Hz, 1H), 4.06 (q, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.05 (d, *J* = 6.6 Hz, 3H), 2.83 - 2.59 (m, 7H), 2.51 (s, 4H), 2.36 (d, *J* = 4.3 Hz, 1H), 2.32 (d, *J* = 2.5 Hz, 3H), 2.30 (d, *J* = 6.5 Hz, 1H), 2.08 (d, *J* = 12.2 Hz, 2H), 1.66 (tt, *J* = 12.1, 7.2 Hz, 2H): 623.5[M+H]$^+$	1.10
650		N-(5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.87 (s, 1H), 8.44 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.60 (d, *J* = 1.8 Hz, 1H), 7.46 (dt, *J* = 7.8, 1.7 Hz, 1H), 7.37 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.29 (t, *J* = 7.7 Hz, 1H), 6.98 (s, 1H), 6.75 (s, 1H), 6.69 (s, 1H), 6.36 (dd, *J* = 17.0, 1.5 Hz, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.74 (dd, *J* = 10.0, 1.6 Hz, 1H), 5.67 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.15 (td, *J* = 8.0, 4.3 Hz, 1H), 4.06 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.77 (t, *J* = 4.6 Hz, 4H), 3.13 - 2.99 (m, 3H), 2.81 - 2.67 (m, 3H), 2.66 - 2.57 (m, 4H), 2.41 - 2.25 (m, 2H), 2.07 (d, *J* = 12.5 Hz, 2H), 1.65 (qd, *J* = 12.0, 3.9 Hz, 2H): 610.5[M+H]$^+$	1.19

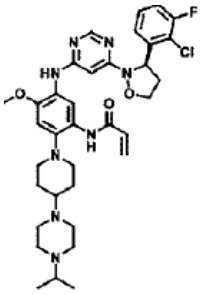
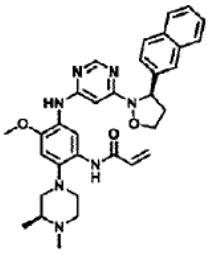
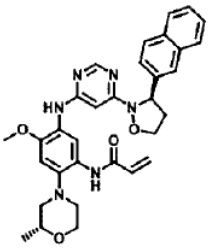
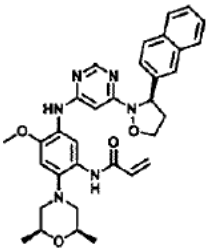
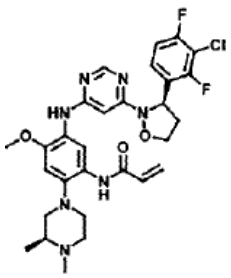
[595]

651		N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (s, 1H), 7.94 (s, 1H), 7.46 (s, 1H), 7.39 - 7.36 (m, 2H), 6.94 (s, 1H), 6.60 (dd, *J* = 16.9, 10.2 Hz, 1H), 6.40 (dd, *J* = 16.9, 1.3 Hz, 1H), 5.96 (s, 1H), 5.86 - 5.80 (m, 1H), 5.62 - 5.45 (m, 1H), 4.43 (td, *J* = 7.6, 4.3 Hz, 1H), 4.18 (dd, *J* = 15.0, 8.2 Hz, 1H), 4.00 (s, 2H), 3.84 (s, 3H), 3.58 (t, *J* = 5.8 Hz, 3H), 3.33 (dt, *J* = 3.2, 1.6 Hz, 5H), 3.08 - 2.98 (m, 1H), 2.90 - 2.75 (m, 4H), 2.45 (dt, *J* = 13.0, 7.2 Hz, 1H), 2.29 (d, *J* = 11.2 Hz, 2H), 2.12 - 2.03 (m, 2H), 1.30 (d, *J* = 6.3 Hz, 6H) ; 638.5 [M+H]$^+$	1.19
652		N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 7.97 (s, 1H), 7.46 (s, 1H), 7.42 - 7.33 (m, 3H), 6.93 (s, 1H), 6.50 (dd, *J* = 16.9, 10.2 Hz, 1H), 6.30 (dd, *J* = 17.0, 1.1 Hz, 1H), 5.82 (d, *J* = 11.1 Hz, 1H), 5.50 (d, *J* = 4.5 Hz, 1H), 4.41 (s, 1H), 4.17 (s, 1H), 3.84 (s, 2H), 3.56 (s, 1H), 3.35 - 3.30 (m, 5H), 3.24 (dd, *J* = 14.6, 7.4 Hz, 3H), 2.87 (q, *J* = 11.1 Hz, 2H), 2.44 (s, 1H), 2.17 (d, *J* = 11.2 Hz, 2H), 2.01 (s, 2H), 1.37 (t, *J* = 7.2 Hz, 3H) ; 637.5 [M+H]$^+$	1.11
653		N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.16 (s, 1H), 7.84 (s, 1H), 7.55 (s, 1H), 7.45 (d, *J* = 7.3 Hz, 1H), 7.37 - 7.33 (m, 2H), 6.75 (s, 1H), 6.55 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.41 - 6.34 (m, 2H), 5.81 (dd, *J* = 10.2, 1.2 Hz, 1H), 5.53 (dd, *J* = 8.5, 4.8 Hz, 1H), 4.15 (td, *J* = 7.8, 4.3 Hz, 1H), 4.00 - 3.91 (m, 2H), 3.80 (s, 3H), 3.56 - 3.30 (m, 4H), 3.33 (dd, *J* = 3.2, 1.6 Hz, 3H), 3.23 (dd, *J* = 16.7, 8.0 Hz, 1H), 2.94 (s, 6H), 2.80 (tdd, *J* = 13.8, 9.0, 5.1 Hz, 1H), 2.47 (dtd, *J* = 11.6, 7.7, 3.7 Hz, 1H), 2.38 - 2.28 (m, 1H), 2.21 (dt, *J* = 14.7, 8.0 Hz, 1H) ; 554.4 [M+H]$^+$	1.11
654		N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.09 (s, 1H), 9.27 (s, 1H), 8.31 (s, 1H), 8.01 (s, 1H), 7.46 (s, 1H), 7.40 (d, *J* = 1.3 Hz, 3H), 6.84 (d, *J* = 5.0 Hz, 2H), 6.25 (dd, *J* = 16.9, 2.0 Hz, 1H), 6.08 (s, 1H), 5.78 - 5.74 (m, 1H), 5.52 (dd, *J* = 8.5, 5.5 Hz, 1H), 4.31 (d, *J* = 4.3 Hz, 1H), 4.26 (s, 1H), 4.05 (d, *J* = 7.8 Hz, 1H), 3.80 (s, 3H), 3.56 (t, *J* = 16.1 Hz, 4H), 3.25 (t, *J* = 7.9 Hz, 4H), 2.92 (td, *J* = 7.8, 4.2 Hz, 2H), 2.36 - 2.27 (m, 1H), 1.28 - 1.19 (m, 2H), 0.83 (d, *J* = 7.0 Hz, 2H).; 566.3[M+H]$^+$	1.19
655		N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.39 (s, 1H), 9.33 (s, 1H), 8.34 (s, 1H), 7.86 (s, 1H), 7.45 (s, 1H), 7.40 (s, 3H), 6.92 (s, 1H), 6.79 (dd, *J* = 16.9, 10.2 Hz, 1H), 6.26 (dd, *J* = 17.0, 1.9 Hz, 1H), 6.07 (s, 1H), 5.76 (dd, *J* = 8.7, 3.0 Hz, 1H), 5.53 (d, *J* = 2.9 Hz, 1H), 4.33 (d, *J* = 4.4 Hz, 1H), 4.25 (s, 1H), 4.08 (d, *J* = 7.7 Hz, 1H), 3.81 (s, 3H), 3.62 (d, *J* = 11.5 Hz, 2H), 3.53 (s, 1H), 3.37 (s, 1H), 3.25 (d, *J* = 11.1 Hz, 2H), 3.16 (d, *J* = 7.5 Hz, 2H), 3.00 - 2.93 (m, 1H), 2.85 (d, *J* = 11.9 Hz, 2H), 2.71 (d, *J* = 4.8 Hz, 6H), 2.35 - 2.27 (m, 5H), 2.22 - 2.08 (m, 4H).; 651.4[M+H]$^+$	1.04

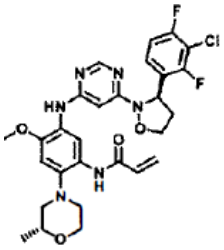
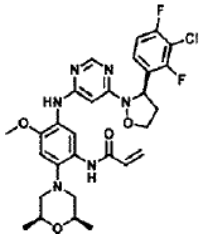
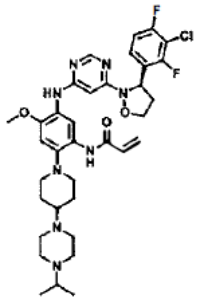
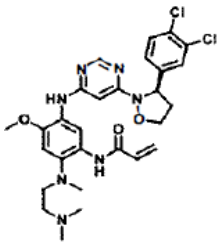
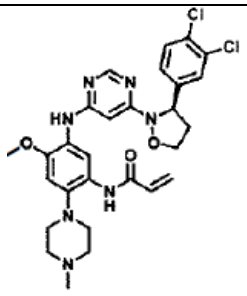
[596]

656		N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.22 (s, 1H), 9.27 (s, 1H), 8.34 (s, 1H), 7.80 (s, 1H), 7.32 (ddd, *J* = 9.6, 7.2, 1.9 Hz, 1H), 7.24 (t, *J* = 6.8 Hz, 1H), 6.92 (s, 1H), 6.79 - 6.72 (m, 1H), 6.25 (dd, *J* = 17.0, 1.9 Hz, 1H), 6.18 (s, 1H), 5.76 (dd, *J* = 10.1, 2.0 Hz, 1H), 5.70 (dd, *J* = 8.6, 5.6 Hz, 1H), 4.32 (dd, *J* = 7.7, 4.0 Hz, 1H), 4.06 (d, *J* = 8.0 Hz, 1H), 3.82 (s, 3H), 3.62 (d, *J* = 11.7 Hz, 2H), 3.51 (s, 1H), 3.36 (s, 1H), 3.24 (d, *J* = 11.2 Hz, 2H), 3.17 - 3.09 (m, 2H), 2.96 (d, *J* = 3.8 Hz, 1H), 2.85 - 2.78 (m, 2H), 2.71 (d, *J* = 4.8 Hz, 6H), 2.35 - 2.28 (m, 5H), 2.17 (s, 2H), 2.00 (d, *J* = 11.6 Hz, 2H). :681.3[M+H]$^+$	1.12
657		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-2-methylmorpholino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.11 (s, 1H), 8.24 (d, *J* = 4.1 Hz, 1H), 8.05 (s, 1H), 7.45 (q, *J* = 7.8 Hz, 1H), 7.32 (td, *J* = 8.8, 1.7 Hz, 1H), 6.80 (s, 1H), 6.63 (dd, *J* = 16.0, 10.2 Hz, 1H), 6.29 - 6.17 (m, 2H), 5.71 (ddd, *J* = 14.9, 9.4, 3.6 Hz, 2H), 4.24 (dd, *J* = 7.9, 4.2 Hz, 1H), 3.96 (d, *J* = 8.2 Hz, 1H), 3.90 - 3.73 (m, 6H), 2.96 - 2.74 (m, 4H), 2.57 - 2.51 (m, 2H), 2.26 (dd, *J* = 12.7, 6.1 Hz, 1H), 1.11 (d, *J* = 6.3 Hz, 3H).: 587.3[M+H]+	1.68
658		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2S,6S)-2,6-dimethylmorpholino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.06 (s, 1H), 8.24 (s, 1H), 7.91 (s, 1H), 7.45 (td, *J* = 8.5, 6.1 Hz, 1H), 7.32 (td, *J* = 8.8, 1.6 Hz, 1H), 6.86 (s, 1H), 6.51 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.31 - 6.13 (m, 2H), 5.72 (ddd, *J* = 20.1, 9.4, 3.7 Hz, 2H), 4.25 (td, *J* = 7.8, 3.8 Hz, 1H), 4.06 (tt, *J* = 9.7, 4.7 Hz, 2H), 3.96 (dp, *J* = 8.1, 4.4, 3.9 Hz, 1H), 3.82 (s, 3H), 2.85 (dt, *J* = 11.5, 5.6 Hz, 4H), 2.64 (dd, *J* = 11.4, 5.7 Hz, 2H), 2.34 - 2.18 (m, 1H), 1.26 (d, *J* = 6.4 Hz, 6H).: 601.4[M+H]+	1.72
659		N-(4-methoxy-2-((S)-2-methylmorpholino)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.12 (s, 1H), 8.25 (d, *J* = 3.7 Hz, 1H), 8.02 (s, 1H), 7.97 - 7.85 (m, 4H), 7.52 (td, *J* = 6.3, 5.7, 3.4 Hz, 3H), 6.87 (s, 1H), 6.64 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.28 - 6.13 (m, 2H), 5.71 (ddd, *J* = 27.0, 9.4, 3.7 Hz, 2H), 4.32 (td, *J* = 7.6, 4.0 Hz, 1H), 4.04 (d, *J* = 7.9 Hz, 1H), 3.85 (td, *J* = 8.0, 8.1, 3.2 Hz, 2H), 3.79 (s, 4H), 3.00 - 2.72 (m, 4H), 2.60 - 2.51 (m, 2H), 2.39 (dq, *J* = 8.6, 5.1, 3.8 Hz, 1H), 1.12 (d, *J* = 6.3 Hz, 3H).: 567.4[M+H]+	1.56
660		N-(2-((2S,6S)-2,6-dimethylmorpholino)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.06 (s, 1H), 8.25 (s, 1H), 7.91 (dd, *J* = 15.3, 7.8 Hz, 5H), 7.52 (ddt, *J* = 10.7, 6.9, 3.4 Hz, 3H), 6.85 (d, *J* = 2.6 Hz, 1H), 6.51 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.30 - 6.13 (m, 2H), 5.71 (ddd, *J* = 20.8, 9.4, 3.8 Hz, 2H), 4.37 - 4.25 (m, 1H), 4.12 - 3.95 (m, 4H), 3.79 (d, *J* = 2.8 Hz, 3H), 2.94 (d, *J* = 9.5 Hz, 1H), 2.84 (dd, *J* = 11.6, 3.1 Hz, 2H), 2.64 (dd, *J* = 11.4, 5.6 Hz, 2H), 2.39 (dt, *J* = 13.0, 3.7 Hz, 1H), 1.27 (d, *J* = 6.4 Hz, 6H). : 581.5[M+H]+	1.59

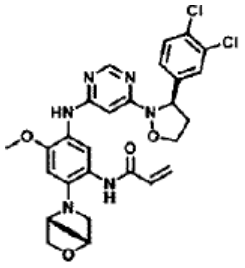
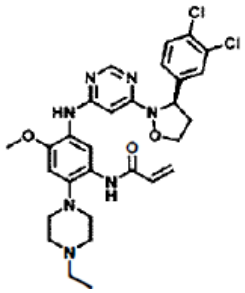
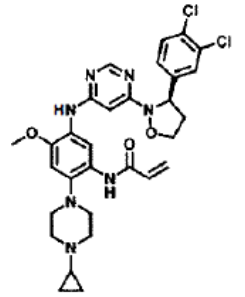
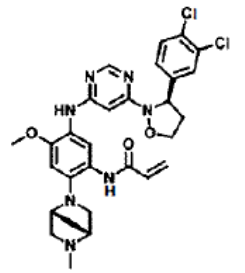
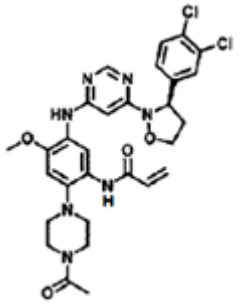
[597]

661		N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.15 (d, J = 1.1 Hz, 1H), 7.43 (d, J = 7.9 Hz, 1H), 7.30 (td, J = 8.1, 5.3 Hz, 1H), 7.20 - 7.10 (m, 1H), 6.84 - 6.70 (m, 1H), 6.54 (dd, J = 17.0, 10.3 Hz, 1H), 6.43 - 6.34 (m, 2H), 5.91 - 5.82 (m, 2H), 5.60 (ddd, J = 8.0, 5.6, 2.6 Hz, 1H), 4.12 (td, J = 8.0, 4.2 Hz, 1H), 3.85 (d, J = 12.7 Hz, 6H), 3.68 (s, 2H), 3.37 (dq, J = 6.4, 3.5 Hz, 2H), 3.17 - 3.11 (m, 4H), 2.99 - 2.93 (m, 4H), 2.57 (dt, J = 11.1, 7.3 Hz, 3H), 2.07 - 2.00 (m, 2H), 1.99 - 1.90 (m, 2H), 1.26 (d, J = 6.5 Hz, 6H).; 679.5[M+H]$^+$	1.20
662		N-(2-((S)-3,4-dimethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.02 (s, 1H), 8.64 (s, 1H), 8.18 (s, 1H), 7.95 - 7.85 (m, 4H), 7.57 (dd, J = 8.6, 1.7 Hz, 1H), 7.54 - 7.45 (m, 2H), 6.86 (s, 1H), 6.61 (dd, J = 17.0, 10.2 Hz, 1H), 6.43 (s, 1H), 6.23 (dd, J = 17.0, 2.0 Hz, 1H), 5.72 (ddd, J = 15.8, 9.3, 3.6 Hz, 2H), 4.20 (td, J = 7.8, 3.7 Hz, 1H), 3.86 (d, J = 24.8 Hz, 4H), 3.17 (s, 4H), 3.04 (s, 4H), 2.84 (dtd, J = 11.9, 7.9, 3.6 Hz, 2H), 2.41 - 2.29 (m, 1H), 1.91 (s, 2H), 1.21 (d, J = 20.2 Hz, 3H).; 580.5[M+H]$^+$	1.23
663		N-(4-methoxy-2-((R)-2-methylmorpholino)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.07 (s, 1H), 8.61 (s, 1H), 8.19 (d, J = 11.6 Hz, 2H), 7.96 - 7.85 (m, 4H), 7.57 (dd, J = 8.6, 1.7 Hz, 1H), 7.49 (ddt, J = 9.6, 7.1, 3.5 Hz, 2H), 6.86 (s, 1H), 6.62 (dd, J = 17.0, 10.2 Hz, 1H), 6.41 (s, 1H), 6.21 (dd, J = 16.9, 2.0 Hz, 1H), 5.71 (td, J = 8.9, 8.1, 3.4 Hz, 2H), 4.19 (td, J = 7.9, 3.8 Hz, 1H), 3.98 - 3.72 (m, 7H), 2.94 - 2.74 (m, 4H), 2.34 (dtd, J = 12.9, 8.2, 5.0 Hz, 1H), 1.91 (s, 1H), 1.11 (d, J = 6.3 Hz, 3H).; 567.4[M+H]$^+$	1.54
664		N-(2-((2S,6R)-2,6-dimethylmorpholino)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.06 (s, 1H), 8.61 (s, 1H), 8.27 - 8.10 (m, 2H), 7.97 - 7.85 (m, 4H), 7.57 (dd, J = 8.6, 1.7 Hz, 1H), 7.54 - 7.44 (m, 2H), 6.86 (s, 1H), 6.61 (dd, J = 17.0, 10.2 Hz, 1H), 6.40 (s, 1H), 6.21 (dd, J = 16.9, 2.0 Hz, 1H), 5.80 - 5.63 (m, 2H), 4.19 (td, J = 7.8, 3.8 Hz, 1H), 3.90 - 3.80 (m, 5H), 2.94 - 2.77 (m, 3H), 2.48 - 2.27 (m, 3H), 1.86 (s, 1H), 1.10 (d, J = 6.2 Hz, 6H).; 581.4[M+H]$^+$	1.60
665		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.05 (s, 1H), 8.82 (s, 1H), 8.27 (s, 1H), 8.19 (s, 1H), 7.48 (q, J = 7.9 Hz, 1H), 7.31 (t, J = 8.8 Hz, 1H), 6.85 (s, 1H), 6.63 (dd, J = 16.9, 10.3 Hz, 1H), 6.40 (s, 1H), 6.24 (d, J = 16.9 Hz, 1H), 5.79 - 5.66 (m, 2H), 4.19 (dd, J = 8.0, 3.7 Hz, 1H), 3.90 (t, J = 8.0 Hz, 1H), 3.83 (s, 3H), 3.57 (d, J = 12.0 Hz, 1H), 3.47 (s, 1H), 3.38 (q, J = 7.8, 7.3 Hz, 1H), 3.26 - 3.15 (m, 2H), 3.02 (t, J = 11.0 Hz, 1H), 2.90 (d, J = 4.2 Hz, 3H), 2.83 (q, J = 9.8, 9.4 Hz, 2H), 2.23 (dq, J = 13.4, 7.7 Hz, 1H), 1.32 (d, J = 6.5 Hz, 3H). : 600.4[M+H]$^+$	1.35

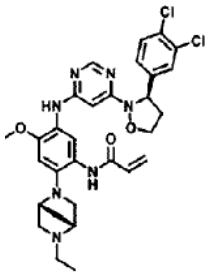
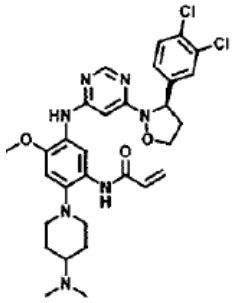
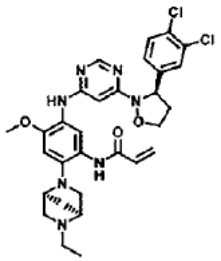
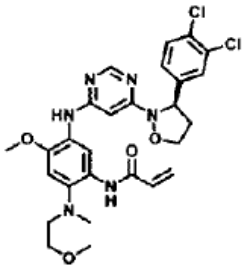
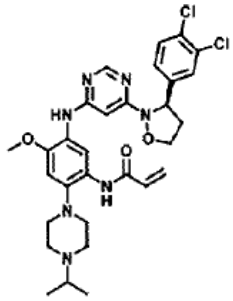
[598]

666		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-2-methylmorpholino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.07 (s, 1H), 8.80 (s, 1H), 8.17 (d, J = 14.1 Hz, 2H), 7.48 (q, J = 8.0 Hz, 1H), 7.31 (t, J = 8.8 Hz, 1H), 6.87 (s, 1H), 6.62 (dd, J = 17.1, 10.2 Hz, 1H), 6.36 (s, 1H), 6.21 (d, J = 17.3 Hz, 1H), 5.71 (t, J = 9.4 Hz, 2H), 4.19 (td, J = 8.0, 3.6 Hz, 1H), 3.92 - 3.75 (m, 8H), 2.92 - 2.76 (m, 4H), 2.27 - 2.16 (m, 1H), 1.11 (d, J = 6.2 Hz, 3H). : 587.4[M+H]$^+$	1.70
667		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2S,6R)-2,6-dimethylmorpholino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.05 (s, 1H), 8.66 (s, 1H), 8.18 (d, J = 7.0 Hz, 2H), 7.40 (td, J = 8.6, 6.2 Hz, 1H), 7.31 (td, J = 8.8, 1.7 Hz, 1H), 6.85 (s, 1H), 6.61 (dd, J = 17.0, 10.2 Hz, 1H), 6.38 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.71 (dt, J = 8.4, 4.2 Hz, 2H), 4.17 (td, J = 8.0, 3.7 Hz, 1H), 3.87 (q, J = 6.8, 5.0 Hz, 3H), 3.81 (s, 3H), 2.87 (d, J = 11.2 Hz, 2H), 2.79 (qd, J = 8.2, 3.9 Hz, 1H), 2.42 (td, J = 10.7, 4.8 Hz, 2H), 2.20 (tt, J = 8.2, 4.9 Hz, 1H), 1.10 (d, J = 6.3 Hz, 6H). : 601.4[M+H]$^+$	1.77
668		N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (s, 1H), 8.66 (s, 1H), 8.16 (d, J = 3.7 Hz, 2H), 7.40 (td, J = 8.5, 6.2 Hz, 1H), 7.31 (t, J = 8.8 Hz, 1H), 6.82 (s, 1H), 6.64 (dd, J = 16.9, 10.3 Hz, 1H), 6.38 (s, 1H), 6.22 (d, J = 17.0 Hz, 1H), 5.72 (td, J = 10.6, 8.7, 6.1 Hz, 2H), 4.17 (q, J = 7.1, 6.4 Hz, 1H), 3.86 (q, J = 8.0 Hz, 2H), 3.80 (s, 3H), 3.42 - 3.35 (m, 2H), 3.14 (d, J = 25.2 Hz, 5H), 2.86 - 2.64 (m, 11H), 2.22 (dt, J = 9.3, 6.7 Hz, 2H), 1.75 (s, 5H). : 697.5[M+H]$^+$	1.23
669		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 12.67 - 12.39 (m, 1H), 9.46 (s, 1H), 8.89 (d, J = 12.7 Hz, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.59 (d, J = 2.1 Hz, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.30 (dd, J = 8.4, 2.1 Hz, 1H), 6.93 (s, 1H), 6.78 (s, 1H), 6.71 (s, 1H), 6.41 (d, J = 16.8 Hz, 1H), 5.71 (d, J = 10.2 Hz, 1H), 5.65 (dd, J = 8.6, 4.6 Hz, 1H), 4.17 (dd, J = 8.0, 4.2 Hz, 1H), 4.10 (q, J = 8.1 Hz, 1H), 3.85 (s, 3H), 3.36 - 3.23 (m, 2H), 3.12 (s, 2H), 2.79 (dt, J = 8.2, 3.9 Hz, 4H), 2.74 (s, 3H), 2.33 (dtd, J = 12.6, 8.2, 4.6 Hz, 4H).:586.3 [M+H]$^+$	1.35
670		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.92 (s, 1H), 8.37 (s, 1H), 8.33 (s, 1H), 7.57 (d, J = 2.1 Hz, 1H),7.41 (d, J = 8.3 Hz, 1H), 7.30 (dd, J = 8.3, 2.1 Hz, 1H), 7.04 - 6.98 (m, 1H), 6.81 (s, 1H), 6.69 (s, 1H),6.43 - 6.32 (m, 2H), 5.76 (dd, J = 9.6, 1.9 Hz, 1H), 5.64 (dd, J = 8.7, 4.7 Hz, 1H), 4.22 - 4.13 (m, 2H),4.04 (q, J = 8.0 Hz, 2H), 3.87 (s, 3H), 3.70 - 3.60 (m, 4H), 3.13 - 3.02 (m, 5H), 2.33 (dt, J = 8.5, 4.5 Hz,2H).: 584.3 [M+H]$^+$	1.31

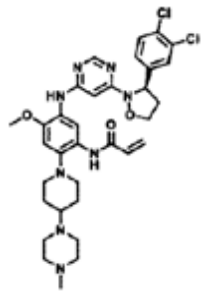
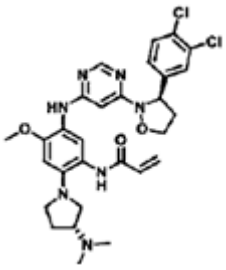
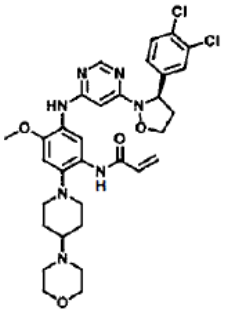
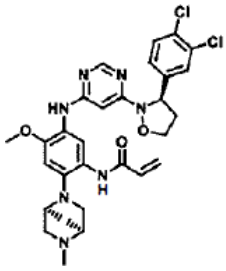
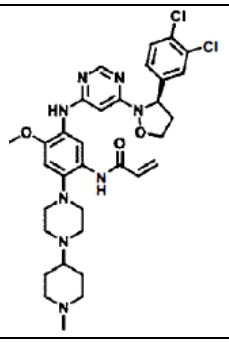
[599]

671		N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.64 (s, 1H), 8.35 (s, 1H), 7.96 (s, 1H), 7.58 (d, *J* = 2.1 Hz, 1H),7.41 (d, *J* = 8.3 Hz, 1H), 7.30 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.89 (s, 1H), 6.71 (d, *J* = 13.5 Hz, 2H), 6.38 (d, *J*= 16.8 Hz, 1H), 6.28 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.79 - 5.74 (m, 1H), 5.65 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.67 -4.62 (m, 1H), 4.21 - 4.13 (m, 1H), 4.08 - 4.02 (m, 2H), 3.88 - 3.85 (m, 4H), 3.75 (d, *J* = 7.9 Hz, 1H), 3.45(d, *J* = 10.2 Hz, 1H), 3.20 (d, *J* = 10.1 Hz, 1H), 2.77 (ddt, *J* = 12.1, 8.1, 4.0 Hz, 1H), 2.33 (ddt, *J* = 11.8,7.9, 4.0 Hz, 1H), 2.09 (d, *J* = 9.9 Hz, 1H), 2.00 (d, *J* = 9.9 Hz, 1H).: 583.3 $[M+H]^+$	1.44
672		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.92 (s, 1H), 8.45 (s, 1H), 8.37 (s, 1H), 7.58 (s, 1H), 7.41 (d, *J* =8.3 Hz, 1H), 7.30 (d, *J* = 10.2 Hz, 1H), 6.98 (s, 1H), 6.83 (s, 1H), 6.70 (s, 1H), 6.38 (d, *J* = 16.5 Hz, 1H), 6.32 - 6.21 (m, 1H), 5.76 (d, *J* = 10.0 Hz, 1H), 5.68 - 5.61 (m, 1H), 4.20 - 4.13 (m, 1H), 4.09 - 4.01 (m, 1H), 3.85 (s, 3H), 3.70 - 3.62 (m, 1H), 3.37 - 3.29 (m, 1H), 3.14 - 3.03 (m, 3H), 2.85 - 2.67 (m, 4H), 2.42 - 2.25 (m, 2H), 1.54 (t, 2H), 1.45 (d, *J* = 6.5 Hz, 2H).: 598.3 $[M+H]^+$	1.32
673		N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.60 (s, 1H), 8.36 (s, 1H), 7.58 (s, 1H), 7.41 (d, *J* =8.3 Hz, 1H), 7.30 (d, *J* = 10.3 Hz, 1H), 6.92 (s, 1H), 6.79 (s, 1H), 6.72 (s, 1H), 6.40 - 6.33 (m, 1H), 6.32 -6.24 (m, 1H), 5.76 (d, *J* = 9.8 Hz, 1H), 5.67 - 5.63 (m, 1H), 4.19 - 4.13 (m, 1H), 4.11 - 4.03 (m, 1H), 3.81(s, 3H), 2.93 - 2.86 (m, 4H), 2.84 - 2.73 (m, 3H), 2.37 - 2.27 (m, 2H), 1.77 - 1.68 (m, 2H), 0.52 (d, *J* =6.5 Hz, 2H), 0.47 (d, *J* = 3.3 Hz, 2H).: 610.4 $[M+H]^+$	1.47
674		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((1R,4R)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.68 (s, 1H), 8.34 (s, 1H), 8.13 (s, 1H), 7.58 (s, 1H), 7.41 (d, *J* =8.3 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 6.96 (s, 1H), 6.85 (s, 1H), 6.62 (s, 1H), 6.30 (d, *J* = 15.4 Hz, 1H),6.21 - 6.13 (m, 1H), 5.77 - 5.70 (m, 1H), 5.66 - 5.60 (m, 1H), 4.18 - 4.10 (m, 2H), 4.05 - 3.97 (m, 2H),3.89 (s, 3H), 3.82 (s, 2H), 3.61 (s, 2H), 3.20 - 3.12 (m, 1H), 2.80 - 2.73 (m, 1H), 2.70 (s, 3H), 2.38 - 2.27(m, 1H), 2.13 (s, 1H).: 596.3 $[M+H]^+$	1.25
675		N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.94 (s, 1H), 8.44 (s, 1H), 8.38 (d, *J* = 1.0 Hz, 1H), 7.58 (d, *J* = 2.0 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.30 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.97 (s, 1H), 6.72 (s, 2H), 6.38 (d, *J* = 16.9 Hz, 1H), 6.26 (dd, *J* = 16.9, 10.1 Hz, 1H), 5.77 (dd, *J* = 10.0, 1.5 Hz, 1H), 5.65 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.17 (td, *J* = 8.0, 4.2 Hz, 1H), 4.06 (q, *J* = 8.1 Hz, 1H), 3.85 (s, 3H), 3.65 (s, 2H), 2.88 (d, *J* = 5.3 Hz, 4H), 2.78 (ddt, *J* = 12.1, 8.0, 4.0 Hz, 1H), 2.34 (ddd, *J* = 12.4, 8.3, 4.6 Hz, 1H), 2.17 (s, 3H), 1.25 (s, 2H).: 612.3[M+H]	1.51

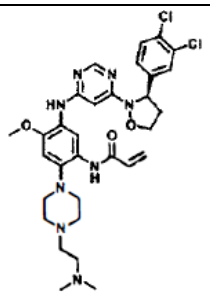
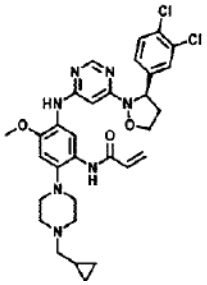
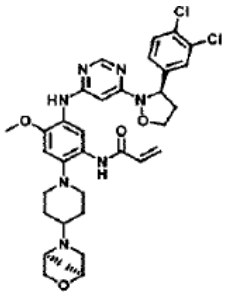
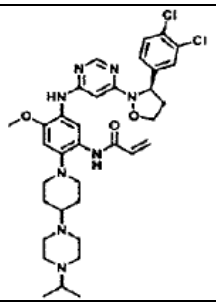
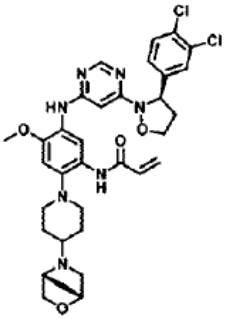
[600]

676		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.59 (s, 1H), 8.33 (s, 1H), 8.12 (s, 1H), 7.58 (d, J = 2.0 Hz, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.30 (dd, J = 8.3, 2.2 Hz, 1H), 6.90 (s, 1H), 6.76 (s, 1H), 6.67 (s, 1H), 6.40 (s, 1H), 6.25 - 6.18 (m, 1H), 5.75 - 5.70 (m, 1H), 5.64 (dd, J = 8.4, 5.2 Hz, 1H), 4.19 - 4.12 (m, 1H), 4.05 (q, J = 8.0 Hz, 1H), 3.86 (s, 3H), 3.37 - 3.23 (m, 2H), 3.08 (d, J = 10.1 Hz, 1H), 2.94 (s, 2H), 2.82 - 2.60 (m, 4H), 2.33 - 2.26 (m, 2H), 2.03 (s, 3H), 1.82 (dt, J = 23.4, 7.2 Hz, 1H).: 610.3[M+H]	1.27
677		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.42 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.58 (d, J = 2.1 Hz, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.30 (dd, J = 8.4, 2.1 Hz, 1H), 6.96 (s, 1H), 6.73 (d, J = 13.2 Hz, 2H), 6.41 - 6.33 (m, 1H), 6.28 (dd, J = 17.0, 9.7 Hz, 1H), 5.75 (dd, J = 9.8, 1.7 Hz, 1H), 5.65 (dd, J = 8.7, 4.6 Hz, 1H), 4.16 (td, J = 8.0, 4.2 Hz, 1H), 4.06 (q, J = 8.1 Hz, 1H), 3.85 (s, 3H), 3.34 - 3.27 (m, 1H), 3.10 (d, J = 11.7 Hz, 2H), 2.75 (q, J = 11.5 Hz, 4H), 2.51 (s, 6H), 2.37 - 2.30 (m, 2H), 2.14 (d, J = 12.5 Hz, 2H).: 612.4[M+H]	1.32
678		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 9.36 (s, 1H), 8.66 (s, 1H), 8.35 (s, 1H), 8.03 (s, 1H), 7.58 (d, J = 2.0 Hz, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.30 (dd, J = 8.2, 2.1 Hz, 1H), 6.88 (s, 1H), 6.63 (s, 1H), 6.40 (q, J = 7.6, 6.2 Hz, 2H), 5.75 (d, J = 11.3 Hz, 1H), 5.64 (dd, J = 8.7, 4.6 Hz, 1H), 4.14 (td, J = 7.9, 4.1 Hz, 1H), 4.02 (q, J = 8.0 Hz, 1H), 3.89 (s, 3H), 3.39 - 3.27 (m, 1H), 3.13 (d, J = 10.2 Hz, 1H), 2.76 (dtd, J = 12.2, 8.1, 4.2 Hz, 2H), 2.38 - 2.28 (m, 2H), 2.04 (s, 2H), 1.83 (dd, J = 18.7, 11.5 Hz, 2H), 1.48 (d, J = 24.4 Hz, 2H), 1.26 (d, J = 6.0 Hz, 3H).: 610.3[M+H]	1.28
679		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 9.14 (s, 1H), 8.98 (s, 1H), 8.36 (d, J = 1.1 Hz, 1H), 7.58 (d, J = 2.1 Hz, 1H), 7.40 (d, J = 8.3 Hz, 1H), 7.30 (dd, J = 8.4, 2.1 Hz, 1H), 6.92 (s, 1H), 6.81 - 6.71 (m, 2H), 6.40 (dd, J = 17.0, 2.0 Hz, 1H), 6.30 (dd, J = 17.0, 9.8 Hz, 1H), 5.67 (ddd, J = 18.7, 9.3, 3.3 Hz, 2H), 4.10 - 4.04 (m, 2H), 3.84 (s, 3H), 3.45 (d, J = 15.5 Hz, 5H), 2.97 (dt, J = 7.4, 3.2 Hz, 2H), 2.75 (s, 4H), 2.32 (dtd, J = 12.4, 8.1, 4.6 Hz, 1H).: 573.3[M+H]	1.69
680		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.92 (s, 1H), 8.55 (s, 1H), 8.37 (s, 1H), 7.58 (s, 1H), 7.41 (d, J =8.3 Hz, 1H), 7.30 (d, J = 10.1 Hz, 1H), 6.96 (s, 1H), 6.85 (s, 1H), 6.71 (s, 1H), 6.38 (d, J = 17.1 Hz, 1H).6.33 - 6.26 (m, 1H), 5.76 (d, J = 11.2 Hz, 1H), 5.60 - 5.62 (m, 1H), 4.19 - 4.11 (m, 2H), 4.10 - 4.01 (m,2H), 3.84 (s, 3H), 3.72 - 3.61 (m, 1H), 3.37 - 3.27 (m, 2H), 3.12 - 3.05 (m, 1H), 2.96 (s, 5H), 2.82 - 2.73(m, 3H), 2.62 (s, 1H), 2.38 - 2.28 (m, 2H).: 612.4 $[M+H]^+$	1.47

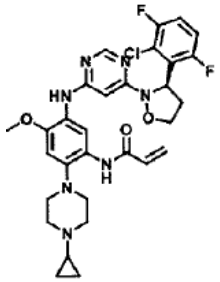
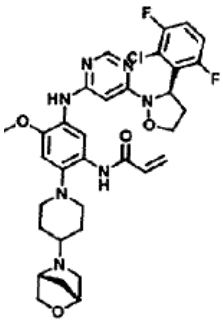
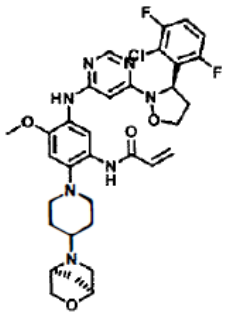
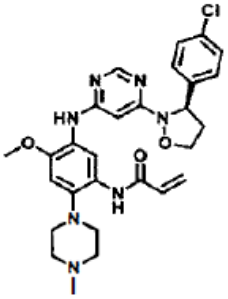
[601]

681		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 7.58 (s, 1H), 7.40 (d, *J* =8.3 Hz, 1H), 7.30 (d, *J* = 8.3 Hz, 1H), 6.92 (s, 1H), 6.75 (s, 1H), 6.71 (s, 1H), 6.36 (d, *J* = 16.9 Hz, 1H),6.29 - 6.25 (m, 1H), 5.74 (d, *J* = 10.0 Hz, 1H), 5.67 - 5.62 (m, 1H), 4.18 - 4.12 (m, 1H), 4.10 - 4.03 (m, 1H), 3.84 (s, 3H), 3.40 - 3.27 (m, 2H), 3.22 - 3.15 (m, 1H), 3.11 - 3.02 (m, 2H), 2.80 - 2.65 (m, 6H), 2.50 - 2.40 (m, 3H), 2.38 - 2.29 (m, 6H), 2.08 (d, *J* = 14.7 Hz, 2H).: 667.4 $[M+H]^+$	1.25
682		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 11.35 (s, 1H), 8.57 (s, 1H), 8.33 (s, 1H), 7.58 (s, 1H), 7.40 (d, *J* =8.3 Hz, 1H), 7.30 (d, *J* = 7.5 Hz, 1H), 6.86 (s, 1H), 6.68 (d, *J* = 6.6 Hz, 2H), 6.40 (d, *J* = 16.7 Hz, 2H), 5.74 (s, 1H), 5.67 - 5.61 (m, 1H), 4.21 - 4.13 (m, 1H), 4.05 (q, *J* = 8.1 Hz, 1H), 3.83 (s, 3H), 3.70 - 3.60(m, 1H), 3.37 - 3.27 (m, 1H), 3.13 - 2.98 (m, 3H), 2.82 - 2.70 (m, 2H), 2.63 (s, 6H), 2.37 - 2.24 (m, 2H).: 508.4 $[M+H]^+$	1.27
683		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.58 (s, 1H), 7.41 (d, *J* =8.3 Hz, 1H), 7.29 (d, *J* = 1.7 Hz, 1H), 6.92 (s, 1H), 6.75 (s, 1H), 6.71 (s, 1H), 6.36 (d, *J* = 15.9 Hz, 1H),6.29 - 6.20 (m, 1H), 5.74 (d, *J* = 10.1 Hz, 1H), 5.68 - 5.61 (m, 1H), 4.19 - 4.12 (m, 1H), 4.11 - 4.03 (m,1H), 3.85 (s, 3H), 3.79 - 3.75 (m, 4H), 3.36 - 3.28 (m, 1H), 3.22 - 3.16 (m, 1H), 3.12 - 3.04 (m, 2H), 2.75(t, *J* = 11.0 Hz, 3H), 2.62 (s, 4H), 2.37 - 2.25 (m, 3H), 2.08 (d, *J* = 13.9 Hz, 2H).: 654.4 $[M+H]^+$	1.33
684		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.67 (s, 1H), 8.35 (s, 1H), 8.10 (s, 1H), 7.58 (d, *J* = 2.0 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.33 - 7.28 (m, 1H), 6.93 (s, 1H), 6.86 (s, 1H), 6.62 (s, 1H), 6.42 (d, *J* = 10.1 Hz, 2H), 5.77 - 5.72 (m, 1H), 5.64 (dd, *J* = 8.7, 4.7 Hz, 1H), 4.14 (td, *J* = 7.8, 4.0 Hz, 1H), 4.01 (q, *J* = 8.0 Hz, 1H), 3.80 (s, 3H), 3.77 (s, 1H), 3.67 - 3.59 (m, 1H), 3.33 - 3.27 (m, 1H), 3.21 - 3.13 (m, 2H), 3.06 (s, 1H), 2.92 - 2.85 (m, 1H), 2.76 (dt, *J* = 8.4, 4.3 Hz, 2H), 2.68 (s, 3H), 2.33 (dt, *J* = 12.4, 4.0 Hz, 1H):, 506.3[M+H]	1.26
685		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.56 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.58 (d, *J* = 2.1 Hz, 1H), 7.40 (d, *J* = 8.3 Hz, 1H), 7.30 (dd, *J* = 8.5, 2.1 Hz, 1H), 6.93 (s, 1H), 6.82 (s, 1H), 6.72 (s, 1H), 6.41 - 6.32 (m, 1H), 6.26 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.75 (dd, *J* = 9.9, 1.6 Hz, 1H), 5.65 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.15 (td, *J* = 8.1, 4.2 Hz, 1H), 4.06 (q, *J* = 8.1 Hz, 1H), 3.83 (s, 3H), 2.95 - 2.88 (m, 4H), 2.79 - 2.69 (m, 4H), 2.31 (d, *J* = 14.6 Hz, 4H), 1.99 (t, *J* = 11.7 Hz, 2H), 1.86 (d, *J* = 12.6 Hz, 2H), 1.66 (s, 4H), 1.25 (s, 2H).: 667.4[M+H]	1.15

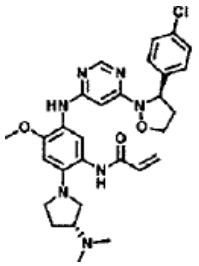
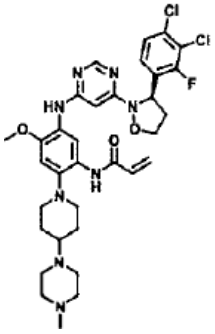
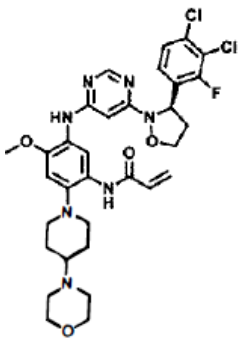
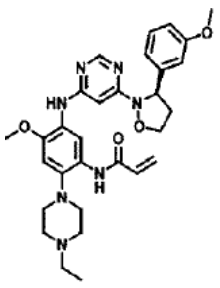
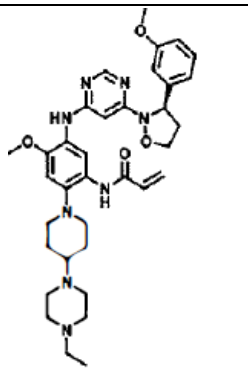
[602]

686		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.89 (s, 1H), 8.56 (s, 1H), 8.39 - 8.20 (m, 1H), 7.57 (d, *J* = 5.8 Hz, 1H), 7.45 - 7.37 (m, 1H), 7.30 (d, *J* = 7.1 Hz, 1H), 7.07 - 6.92 (m, 2H), 6.83 - 6.70 (m, 1H), 6.53 (d, *J* = 9.1 Hz, 1H), 6.37 (d, *J* = 17.0 Hz, 1H), 5.75 (d, *J* = 10.5 Hz, 1H), 5.64 (dd, *J* = 12.9, 7.8 Hz, 1H), 4.15 (s, 1H), 4.06 (d, *J* = 8.2 Hz, 1H), 3.84 (s, 3H), 3.43 (s, 2H), 3.33 (d, *J* = 6.4 Hz, 4H), 3.28 (s, 3H), 3.21 (d, *J* = 1.8 Hz, 2H), 2.95 (d, *J* = 7.0 Hz, 2H), 2.68 (s, 3H).; 641.4[M+H]	1.26
687		N-(2-(4-(cyclopropylmethyl)piperazine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.58 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.58 (d, *J* = 2.1 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.30 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.94 (s, 1H), 6.83 (s, 1H), 6.72 (s, 1H), 6.40 - 6.32 (m, 1H), 6.26 (dd, *J* = 16.9, 10.1 Hz, 1H), 5.75 (dd, *J* = 9.9, 1.6 Hz, 1H), 5.65 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.16 (td, *J* = 8.1, 4.2 Hz, 1H), 4.06 (q, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 2.95 (t, *J* = 4.7 Hz, 4H), 2.76 (ddt, *J* = 12.3, 8.1, 4.2 Hz, 2H), 2.36 (d, *J* = 6.7 Hz, 2H), 2.30 (ddd, *J* = 13.7, 8.8, 5.0 Hz, 1H), 1.60 (s, 4H), 0.61 - 0.53 (m, 2H), 0.16 (q, *J* = 5.1 Hz, 2H).; 624.4[M+H]	1.37
688		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 11.35 (s, 1H), 8.87 (s, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 7.58 (s, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 6.93 (s, 1H), 6.75 - 6.70 (m, 1H), 6.43 - 6.32 (m, 2H), 5.82 - 5.73 (m, 1H), 5.69 - 5.63 (m, 1H), 4.20 - 4.13 (m, 2H), 4.10 - 4.03 (m, 1H), 3.85 (s, 3H), 3.70 - 3.61 (m, 2H), 3.52 - 3.45 (m, 1H), 3.34 - 3.28 (m, 1H), 3.13 - 3.05 (m, 3H), 2.82 - 2.70 (m, 4H), 2.38 - 2.27 (m, 2H), 2.11 - 1.95 (m, 3H), 1.24 - 1.17 (m, 2H).; 666.4 [M+H]$^+$	1.30
689		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.43 (s, 1H), 8.36 (s, 1H), 7.58 (s, 1H), 7.40 (d, *J* =8.3 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 1H), 6.92 (s, 1H), 6.74 (s, 1H), 6.71 (s, 1H), 6.36 (d, *J* = 17.4 Hz, 1H),6.28 - 6.24 (m, 1H), 5.74 (d, *J* = 11.0 Hz, 1H), 5.68 - 5.62 (m, 1H), 4.19 - 4.12 (m, 2H), 4.10 - 4.02 (m,2H), 3.84 (s, 3H), 3.35 - 3.26 (m, 1H), 3.06 (d, *J* = 14.2 Hz, 3H), 2.82 - 2.57 (m, 9H), 2.37 - 2.28 (m,2H), 2.13 - 2.02 (m, 3H), 1.09 (s, 6H).; 605.5 [M+H]$^+$	1.29
690		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.58 (s, 1H), 7.41 (d, *J* =8.3 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 6.93 (s, 1H), 6.73 (s, 2H), 6.37 (s, 2H), 5.79 - 5.74 (m, 1H), 5.69 -5.61 (m, 1H), 4.20 - 4.11 (m, 2H), 4.11 - 4.03 (m, 2H), 3.93 - 3.88 (m, 1H), 3.85 (s, 3H), 3.45 - 3.39 (m,1H), 3.37 - 3.29 (m, 1H), 3.00 (s, 2H), 2.83 - 2.70 (m, 4H), 2.38 - 2.27 (m, 2H), 2.10 - 1.95 (m, 3H), 1.55(d, *J* = 11.7 Hz, 2H), 1.45 (d, *J* = 6.6 Hz, 1H).; 666.4 [M+H]$^+$	1.32

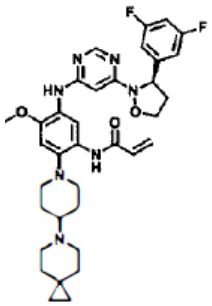
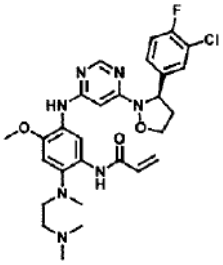
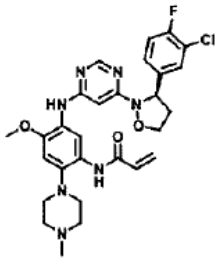
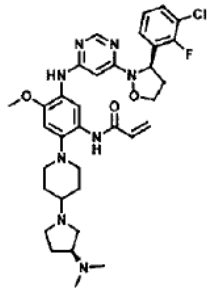
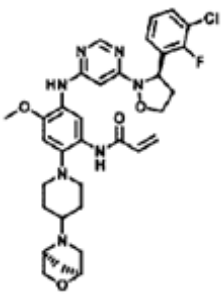
[603]

691		N-(5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.87 (s, 1H), 8.58 (s, 1H), 8.34 (d, *J* = 1.0 Hz, 1H), 7.10 - 7.01 (m, 1H), 7.01 - 6.92 (m, 1H), 6.87 (s, 1H), 6.78 (s, 1H), 6.62 (s, 1H), 6.37 (dd, *J* = 16.9, 1.7 Hz, 1H), 6.28 (dd, *J* = 17.0, 0.8 Hz, 1H), 5.93 (t, *J* = 8.3 Hz, 1H), 5.75 (dd, *J* = 9.8, 1.8 Hz, 1H), 4.38 (td, *J* = 8.0, 1.9 Hz, 1H), 4.02 - 3.91 (m, 1H), 3.79 (s, 3H), 2.89 - 2.74 (m, 9H), 2.61 - 2.47 (m, 1H), 1.77 - 1.67 (m, 1H), 0.57 - 0.42 (m, 4H). : 612.4 [M+H]$^+$	1.18
692		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.83 (s, 1H), 8.46 (s, 1H), 8.33 (d, *J* = 1.1 Hz, 1H), 7.10 - 7.01 (m, 1H), 7.01 - 6.92 (m, 1H), 6.85 (s, 1H), 6.75 (s, 1H), 6.65 - 6.60 (m, 1H), 6.35 (dd, *J* = 17.0, 1.5 Hz, 1H), 6.23 (dd, *J* = 16.9, 10.1 Hz, 1H), 5.93 (t, *J* = 8.3 Hz, 1H), 5.72 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.44 (t, *J* = 2.0 Hz, 1H), 4.37 (td, *J* = 8.0, 1.9 Hz, 1H), 4.00 (d, *J* = 7.9 Hz, 1H), 3.97 (td, *J* = 9.0, 8.6, 6.0 Hz, 1H), 3.83 (s, 3H), 3.77 (d, *J* = 2.2 Hz, 1H), 3.66 (dd, *J* = 8.0, 1.6 Hz, 1H), 3.14 (dd, *J* = 9.9, 1.8 Hz, 1H), 3.06 - 2.97 (m, 2H), 2.83 - 2.75 (m, 2H), 2.73 (dd, *J* = 12.0, 2.5 Hz, 1H), 2.62 - 2.46 (m, 3H), 2.04 (d, *J* = 13.0 Hz, 1H), 1.99 - 1.88 (m, 2H), 1.86 - 1.79 (m, 1H), 1.73 - 1.60 (m, 2H). : 668.4 [M+H]$^+$	1.17
693		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.84 (s, 1H), 8.46 (s, 1H), 8.33 (d, *J* = 1.0 Hz, 1H), 7.10 - 7.00 (m, 1H), 7.00 - 6.92 (m, 1H), 6.84 (s, 1H), 6.75 (s, 1H), 6.66 - 6.60 (m, 1H), 6.35 (dd, *J* = 17.0, 1.5 Hz, 1H), 6.23 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.93 (t, *J* = 8.3 Hz, 1H), 5.72 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.44 (t, *J* = 2.1 Hz, 1H), 4.37 (td, *J* = 8.0, 1.8 Hz, 1H), 4.00 (d, *J* = 7.9 Hz, 1H), 4.01 - 3.86 (m, 1H), 3.83 (s, 3H), 3.76 (s, 1H), 3.66 (dd, *J* = 8.0, 1.6 Hz, 1H), 3.14 (dd, *J* = 9.9, 1.8 Hz, 1H), 3.06 - 2.98 (m, 2H), 2.83 - 2.60 (m, 3H), 2.62 - 2.52 (m, 2H), 2.50 (d, *J* = 10.2 Hz, 1H), 2.04 (d, *J* = 12.9 Hz, 1H), 1.99 - 1.88 (m, 2H), 1.82 (d, *J* = 10.9 Hz, 1H), 1.72 - 1.60 (m, 2H). : 668.4 [M+H]$^+$	1.16
694		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.38 (s, 1H), 8.18 (s, 1H), 7.45 - 7.31 (m, 4H), 6.95 (s, 1H), 6.49 - 6.33 (m, 2H), 5.82 (d, *J* = 10.9 Hz, 1H), 5.54 - 5.49 (m, 1H), 4.14 (td, *J* = 7.7, 4.5 Hz, 1H), 4.00 - 3.94 (m, 1H), 3.89 (s, 3H), 3.33 (dd, *J* = 3.2, 1.6 Hz, 2H), 3.25 - 3.18 (m, 4H), 3.15 (d, *J* = 13.0 Hz, 5H), 2.84 (s, 1H), 2.76 (d, *J* = 14.0 Hz, 3H) : 550.5 [M+H]$^+$	1.41

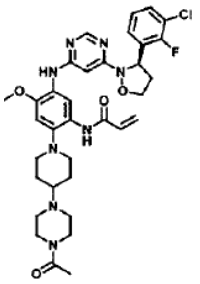
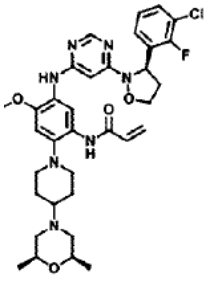
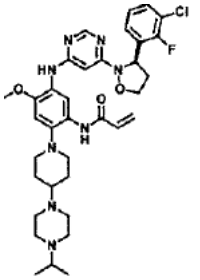
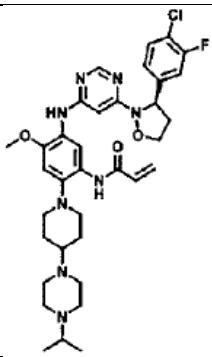
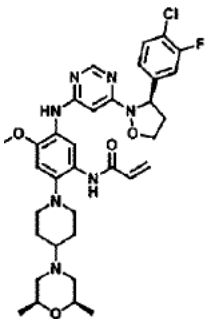
[604]

695		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	N/A : 564.5 $[M+H]^+$	1.18
696		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.77 (s, 1H), 8.42 (s, 1H), 8.30 (s, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.44 (d, J = 7.9 Hz, 1H), 7.23 (dd, J = 8.5, 1.6 Hz, 1H), 6.75 (s, 1H), 6.70 (s, 1H), 6.40 - 6.32 (m, 1H), 6.27 (dd, J = 16.9, 9.8 Hz, 1H), 5.85 (dd, J = 9.0, 4.7 Hz, 1H), 5.75 (dd, J = 9.8, 1.7 Hz, 1H), 4.13 (dt, J = 8.1, 4.1 Hz, 1H), 4.05 (q, J = 8.0 Hz, 1H), 3.85 (s, 3H), 3.07 (d, J = 11.9 Hz, 2H), 2.83 (dd, J = 8.5, 4.5 Hz, 7H), 2.73 (q, J = 12.3 Hz, 4H), 2.55 - 2.48 (m, 1H), 2.45 (s, 3H), 2.29 - 2.24 (m, 1H), 2.08 (s, 2H), 1.71 (h, J = 7.8 Hz, 2H); 685.5[M+H]$^+$	1.59
697		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.85 (s, 1H), 8.43 (s, 1H), 8.34 (s, 1H), 7.46 (t, J = 8.0 Hz, 1H), 7.23 (d, J = 8.7 Hz, 1H), 6.75 (d, J = 4.1 Hz, 2H), 6.36 (d, J = 16.7 Hz, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.87 (dd, J = 9.0, 4.7 Hz, 1H), 5.74 (d, J = 9.8 Hz, 1H), 4.14 - 4.11 (m, 1H), 4.06 (d, J = 8.1 Hz, 1H), 3.85 (s, 3H), 3.78 (t, J = 4.6 Hz, 4H), 3.07 (d, J = 11.5 Hz, 2H), 2.85 (d, J = 9.7 Hz, 1H), 2.73 (d, J = 12.3 Hz, 2H), 2.63 (t, J = 4.5 Hz, 4H), 2.28 (d, J = 7.7 Hz, 2H), 2.08 (d, J = 10.9 Hz, 2H), 1.66 (d, J = 11.0 Hz, 2H); 672.4[M+H]$^+$	1.59
698		N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.33 (s, 1H), 8.15 (s, 1H), 7.24 (t, J = 8.1 Hz, 1H), 7.01 - 6.98 (m, 2H), 6.92 (s, 1H), 6.83 - 6.77 (m, 1H), 6.55 (dd, J = 17.0, 10.2 Hz, 1H), 6.43 (s, 1H), 6.36 (dd, J = 17.0, 1.6 Hz, 1H), 5.80 (dd, J = 10.2, 1.6 Hz, 1H), 5.49 (dd, J = 8.5, 4.7 Hz, 1H), 4.13 (td, J = 7.9, 4.4 Hz, 1H), 3.96 (q, J = 7.0 Hz, 1H), 3.88 (s, 3H), 3.78 (s, 3H), 3.10 (s, 4H), 2.93 (q, J = 7.3 Hz, 2H), 2.78 (dtd, J = 12.2, 7.9, 4.3 Hz, 1H), 2.37 - 2.28 (m, 1H), 1.97 (s, 4H), 1.29 (t, J = 7.3 Hz, 3H); 560.5[M+H]$^+$	1.03
699		N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d6) δ 10.24 (s, 2H), 10.01 (s, 1H), 9.19 (s, 1H), 8.30 (s, 1H), 7.28 (t, J = 7.9 Hz, 1H), 6.94 - 6.83 (m, 4H), 6.71 (t, J = 13.8 Hz, 1H), 6.25 (dd, J = 16.9, 1.9 Hz, 1H), 6.04 (s, 1H), 5.76 (d, J = 11.3 Hz, 1H), 5.47 (s, 1H), 4.29 (d, J = 7.6 Hz, 2H), 4.04 (t, J = 7.6 Hz, 2H), 3.79 (s, 2H), 3.78 - 3.76 (m, 2H), 3.75 (s, 3H), 3.65 (d, J = 14.4 Hz, 2H), 3.57 (s, 3H), 3.23 (s, 1H), 3.21 - 3.18 (m, 2H), 2.95 - 2.85 (m, 1H), 2.79 (t, J = 11.5 Hz, 2H), 2.31 (dd, J = 12.8, 5.6 Hz, 1H), 2.19 (d, J = 11.1 Hz, 2H), 2.13 - 2.04 (m, 2H), 1.29 (dd, J = 11.1, 3.3 Hz, 5H); 643.6[M+H]$^+$	1.27

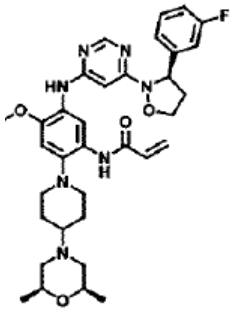
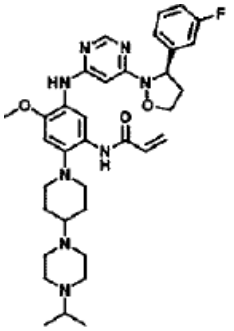
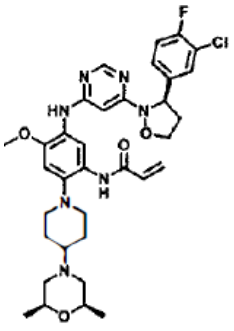
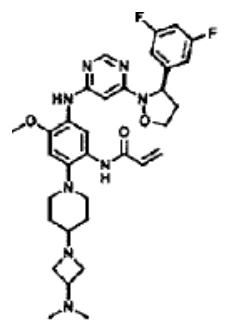
[605]

700		N-(2-(4-(6-azaspiro[2.5]octan-6-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.19 (s, 1H), 8.07 (s, 1H), 7.00 - 6.89 (m, 2H), 6.81 (s, 1H), 6.73 (tt, J = 2.5, 9.1 Hz, 1H), 6.52 - 6.40 (m, 1H), 6.36 (s, 1H), 6.33 - 6.20 (m, 1H), 5.70 (d, J = 10.3 Hz, 1H), 5.45 (dd, J = 4.8, 8.7 Hz, 1H), 4.04 (td, J = 4.2, 7.9 Hz, 1H), 3.86 (q, J = 7.9 Hz, 1H), 3.78 (s, 3H), 3.17 - 3.09 (m, 6H), 2.80 - 2.67 (m, 3H), 2.26 - 2.17 (m, 1H), 2.12 - 2.05 (m, 2H), 1.96 - 1.87 (m, 2H), 1.67 - 1.55 (m, 3H), 0.83 - 0.74 (m, 2H), 0.30 (s, 4H) ; 646.3[M+H]$^+$	1.59
701		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.19 (s, 1H), 7.99 (s, 1H), 7.56 (dd, J = 7.1, 2.1 Hz, 1H), 7.45 - 7.37 (m, 1H), 7.24 (t, J = 8.9 Hz, 1H), 6.06 (s, 1H), 6.62 - 6.39 (m, 3H), 5.87 (dd, J = 10.1, 1.6 Hz, 1H), 5.54 (dd, J = 8.5, 4.8 Hz, 1H), 4.18 (td, J = 7.9, 4.2 Hz, 1H), 3.98 (dd, J = 16.0, 8.0 Hz, 1H), 3.93 (s, 3H), 3.43 (t, J = 5.8 Hz, 2H), 3.19 (dd, J = 7.1, 4.2 Hz, 2H), 2.84 (dd, J = 8.1, 4.0 Hz, 1H), 2.80 (s, 6H), 2.73 (s, 3H), 2.30 - 2.20 (m, 1H). ; 570.5 [M+H]$^+$	1.11
702		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.28 (s, 1H), 8.18 (s, 1H), 7.56 (dd, J = 7.1, 2.1 Hz, 1H), 7.44 - 7.38 (m, 1H), 7.23 (t, J = 8.9 Hz, 1H), 6.05 (s, 1H), 6.57 (dd, J = 17.1, 10.3 Hz, 1H), 6.48 - 6.34 (m, 2H), 5.84 (d, J = 10.3 Hz, 1H), 5.53 (dd, J = 8.4, 4.7 Hz, 1H), 4.17 (td, J = 7.9, 4.3 Hz, 1H), 3.98 (dd, J = 16.0, 8.0 Hz, 1H), 3.90 (s, 3H), 3.10 (d, J = 15.7 Hz, 8H), 2.83 (dt, J = 16.1, 6.0 Hz, 1H), 2.72 (s, 3H), 2.35 (dt, J = 8.7, 6.4 Hz, 1H).; 568.4 [M+H]$^+$	1.25
703		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.01 (d, J = 4.4 Hz, 1H), 7.71 (s, 1H), 7.34 - 7.17 (m, 1H), 7.13 (t, J = 7.5 Hz, 1H), 7.06 - 6.85 (m, 2H), 6.48 (dd, J = 16.9, 10.3 Hz, 1H), 6.26 (dd, J = 16.9, 1.6 Hz, 1H), 5.94 (s, 1H), 5.68 (dd, J = 10.2, 1.6 Hz, 1H), 5.63 - 5.47 (m, 1H), 4.25 (td, J = 7.7, 4.1 Hz, 1H), 4.02 (q, J = 7.9 Hz, 2H), 3.72 (d, J = 3.9 Hz, 4H), 3.64 - 3.37 (m, 4H), 3.36 - 3.23 (m, 2H), 3.17 (s, 1H), 2.82 - 2.61 (m, 2H), 2.29 - 2.15 (m, 3H), 2.09 (d, J = 14.0 Hz, 2H), 1.20 (dd, J = 6.7, 5.1 Hz, 7H), 1.11 (d, J = 2.9 Hz, 2H).; 665.56[M+H]	1.38
704		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.06 (s, 1H), 7.76 (s, 1H), 7.34 (t, J = 7.6 Hz, 1H), 7.21 (t, J = 7.1 Hz, 1H), 7.07 (t, J = 7.9 Hz, 1H), 6.88 (d, J = 17.8 Hz, 1H), 6.51 (d, J = 10.8 Hz, 1H), 6.30 (d, J = 17.1 Hz, 1H), 6.00 (s, 1H), 5.70 (dd, J = 26.0, 9.1 Hz, 2H), 4.66 (s, 1H), 4.58 (d, J = 14.4 Hz, 1H), 4.38 - 4.29 (m, 1H), 4.22 (d, J = 10.7 Hz, 1H), 4.00 (q, J = 7.9 Hz, 1H), 3.78 (t, J = 3.0 Hz, 4H), 3.54 (d, J = 11.5 Hz, 2H), 3.42 - 3.23 (m, 2H), 3.09 - 2.68 (m, 4H), 2.34 (dq, J = 13.6, 7.2 Hz, 2H), 2.23 - 1.81 (m, 6H), 1.19 (s, 2H).; 650.5[M+H]	1.53

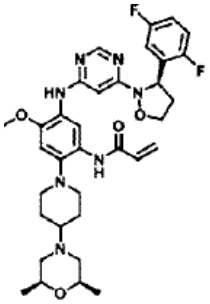
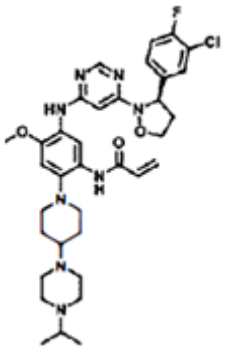
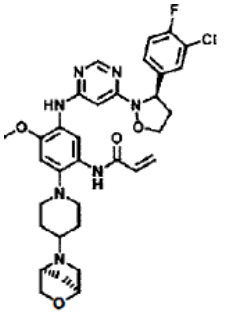
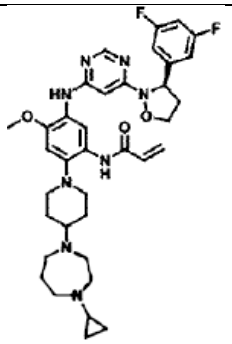
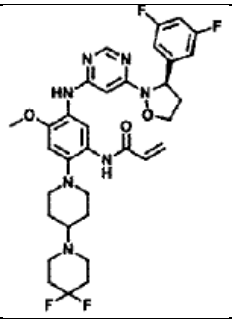
[606]

705		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.19 (d, J = 7.2 Hz, 1H), 7.91 (d, J = 6.5 Hz, 1H), 7.50 - 7.42 (m, 1H), 7.33 (t, J = 7.2 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 7.08 (s, 1H), 6.66 (s, 1H), 6.43 (dd, J = 16.6, 7.6 Hz, 1H), 6.12 (s, 1H), 5.78 (s, 1H), 4.76 (s, 1H), 4.45 (s, 1H), 4.21 (q, J = 7.3 Hz, 2H), 3.90 (d, J = 7.1 Hz, 5H), 3.75 (s, 3H), 3.67 (s, 2H), 3.42 (s, 2H), 3.11 (s, 5H), 2.47 (dt, J = 13.0, 6.6 Hz, 1H), 2.36 (s, 3H), 2.20 (s, 2H), 2.03 (d, J = 12.5 Hz, 1H), 1.31 (s, 1H).: 679.6[M+H]	1.51
706		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	: 666.5[M+H]+	1.52
707		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.15 (s, 1H), 8.26 (s, 1H), 8.01 (s, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.38 (t, J = 7.3 Hz, 1H), 7.24 (t, J = 7.9 Hz, 1H), 6.80 (s, 1H), 6.74 - 6.63 (m, 1H), 6.30 - 6.17 (m, 2H), 5.85 - 5.67 (m, 2H), 4.27 (d, J = 9.0 Hz, 1H), 4.00 (q, J = 7.7 Hz, 1H), 3.81 (s, 3H), 3.26 - 3.18 (m, 4H), 2.73 (d, J = 4.7 Hz, 4H), 1.34 - 1.30 (m, 7H), 1.30 - 1.22 (m, 8H), 1.09 (p, J = 7.2, 6.6 Hz, 4H). : 679.5[M+H]+	1.29
708		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.62 (s, 1H), 8.16 (d, J = 0.9 Hz, 1H), 7.56 (t, J = 8.1 Hz, 1H), 7.41 (dd, J = 10.6, 2.0 Hz, 1H), 7.29 (dd, J = 8.4, 2.0 Hz, 1H), 6.82 (s, 1H), 6.74 - 6.57 (m, 1H), 6.34 (s, 1H), 6.20 (dd, J = 16.9, 2.0 Hz, 1H), 5.73 (ddd, J = 10.4, 8.7, 2.2 Hz, 1H), 5.55 (dd, J = 8.7, 5.0 Hz, 1H), 4.13 (td, J = 7.9, 3.9 Hz, 1H), 3.93 - 3.72 (m, 4H), 3.04 (d, J = 10.8 Hz, 2H), 2.67 (dddd, J = 47.8, 24.7, 12.0, 6.5 Hz, 5H), 2.45 (s, 3H), 2.35 - 2.16 (m, 2H), 1.90 (s, 7H), 1.69 (q, J = 13.6 Hz, 2H), 0.97 (d, J = 6.5 Hz, 6H).: 679.5[M+H]$^+$	1.23
709		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.20 (d, J = 0.6 Hz, 1H), 7.91 (s, 1H), 7.50 (t, J = 7.9 Hz, 1H), 7.26 (dd, J = 32.3, 9.2 Hz, 2H), 7.07 (d, J = 34.4 Hz, 1H), 6.68 (dd, J = 17.3, 10.6 Hz, 1H), 6.53 - 6.36 (m, 1H), 6.07 (s, 1H), 5.88 (d, J = 8.8 Hz, 1H), 5.53 (s, 1H), 4.44 (td, J = 7.7, 4.1 Hz, 1H), 4.19 (q, J = 7.7 Hz, 1H), 4.03 (s, 2H), 3.90 (d, J = 6.2 Hz, 3H), 3.61 (d, J = 12.1 Hz, 2H), 3.39 (d, J = 40.6 Hz, 4H), 3.19 - 2.95 (m, 3H), 2.81 (t, J = 11.5 Hz, 2H), 2.55 - 1.98 (m, 5H), 1.30 (d, J = 6.3 Hz, 6H).: 666.5[M+H]$^+$	1.34

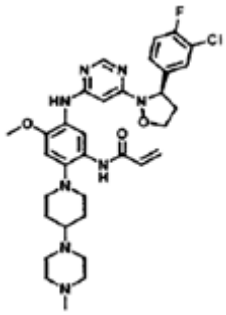
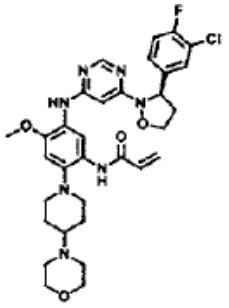
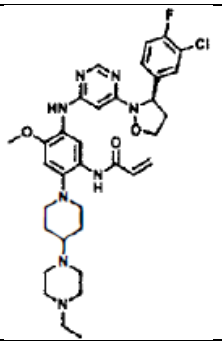
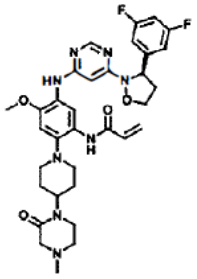
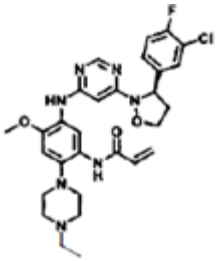
[607]

710		N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.61 (s, 1H), 9.94 (s, 1H), 9.16 (s, 1H), 8.31 (s, 1H), 7.90 (s, 1H), 7.42 (td, J = 8.1, 6.2 Hz, 1H), 7.23 - 7.16 (m, 2H), 7.13 (td, J = 8.6, 8.0, 2.5 Hz, 1H), 6.91 (s, 1H), 6.68 (dd, J = 16.9, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.00 (s, 1H), 5.76 (dd, J = 10.2, 1.9 Hz, 1H), 5.54 (t, J = 7.1 Hz, 1H), 4.29 (dd, J = 7.6, 4.4 Hz, 1H), 4.18 - 4.08 (m, 2H), 4.04 (q, J = 7.7 Hz, 1H), 3.81 (s, 3H), 3.46 (d, J = 11.8 Hz, 2H), 3.22 (q, J = 15.5 Hz, 3H), 3.00 - 2.86 (m, 1H), 2.72 (dq, J = 21.6, 11.3, 10.7 Hz, 4H), 2.37 - 2.27 (m, 1H), 2.23 (d, J = 11.5 Hz, 2H), 2.06 (d, J = 10.2 Hz, 2H), 1.17 (d, J = 6.3 Hz, 6H). ; 632.5[M+H]$^+$	1.21
711		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.22 (s, 1H), 11.88 (s, 1H), 9.69 (s, 1H), 9.15 (s, 1H), 8.28 (s, 1H), 7.98 (s, 1H), 7.42 (td, J = 8.0, 6.1 Hz, 1H), 7.28 - 7.16 (m, 2H), 7.12 (td, J = 8.7, 2.6 Hz, 1H), 6.89 (s, 1H), 6.60 (dd, J = 16.8, 10.3 Hz, 1H), 6.25 (dd, J = 16.8, 1.9 Hz, 1H), 6.14 (s, 1H), 5.76 (d, J = 10.3 Hz, 1H), 5.59 - 5.44 (m, 1H), 4.27 (s, 1H), 4.00 (s, 3H), 3.80 (s, 3H), 3.77 (s, 1H), 3.68 (s, 4H), 3.61 (d, J = 7.0 Hz, 1H), 3.46 (s, 1H), 3.21 (d, J = 11.9 Hz, 2H), 2.89 (s, 1H), 2.78 (dd, J = 19.8, 8.6 Hz, 2H), 2.31 (dd, J = 12.1, 5.0 Hz, 1H), 2.15 (s, 2H), 2.05 (s, 2H), 1.31 (d, J = 6.6 Hz, 6H). ; 645.6[M+H]$^+$	1.11
712		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.61 - 7.51 (m, 1H), 7.46 - 7.36 (m, 1H), 7.23 (t, J = 8.9 Hz, 1H), 6.92 (s, 1H), 6.57 (dd, J = 10.2, 17.0 Hz, 1H), 6.45 (s, 1H), 6.42 - 6.31 (m, 1H), 5.82 (d, J = 10.3 Hz, 1H), 5.57 - 5.49 (m, 1H), 4.18 - 4.12 (m, 1H), 3.98 (q, J = 8.0 Hz, 1H), 3.88 (s, 3H), 3.81 - 3.74 (m, 2H), 3.21 - 3.09 (m, 4H), 2.84 - 2.78 (m, 2H), 2.64 - 2.57 (m, 1H), 2.40 - 2.28 (m, 1H), 2.15 - 2.00 (m, 3H), 1.86 - 1.76 (m, 2H), 1.23 (s, 3H), 1.21 (s, 3H) ; 665.3[M+H]$^+$	1.66
713		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(3-(dimethylamino)azetidine-1-yl)piperidine-1-yl)-4-methoxyphenyl) acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.17 (s, 1H), 7.11 - 7.04 (m, 2H), 6.92 (s, 1H), 6.88 - 6.80 (m, 1H), 6.61 - 6.43 (m, 2H), 6.41 - 6.29 (m, 1H), 5.84 - 5.75 (m, 1H), 5.60 - 5.51 (m, 1H), 4.18 - 4.12 (m, 1H), 3.88 (s, 3H), 3.26 - 3.16 (m, 3H), 3.16 - 3.03 (m, 5H), 2.88 - 2.73 (m, 4H), 2.37 - 2.29 (m, 1H), 2.25 - 2.19 (m, 7H), 1.63 - 1.50 (m, 2H) ; 665.3[M+H]$^+$	1.73

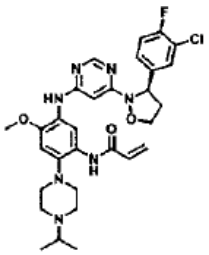
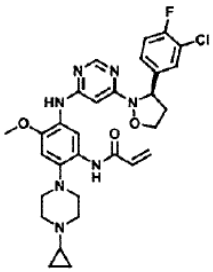
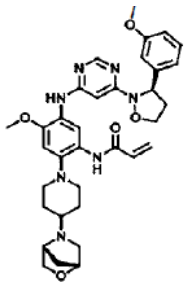
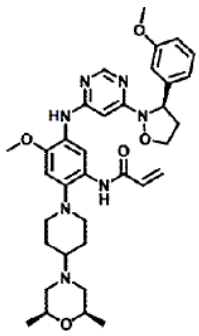
[608]

714		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.28 - 7.21 (m, 1H), 7.20 - 7.11 (m, 1H), 7.00 - 6.90 (m, 1H), 6.92 (s, 1H), 6.62 - 6.48 (m, 2H), 6.42 - 6.32 (m, 1H), 5.86 - 5.72 (m, 2H), 4.18 - 4.11 (m, 1H), 4.03 - 3.94 (m, 1H), 3.80 (s, 3H), 3.80 - 3.72 (m, 2H), 3.21 - 3.14 (m, 2H), 3.10 - 3.05 (m, 2H), 2.87 - 2.77 (m, 2H), 2.59 - 2.51 (m, 1H), 2.35 - 2.20 (m, 1H), 2.12 - 2.06 (m, 3H), 1.85 - 1.72 (m, 2H), 1.22 (s, 3H), 1.20 (s, 3H) ; 650.3[M+H]$^+$	1.82
715		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.18 (s, 1H), 7.59 - 7.53 (m, 1H), 7.44 - 7.37 (m, 1H), 7.23 (t, J = 8.8 Hz, 1H), 6.92 (s, 1H), 6.62 - 6.50 (m, 1H), 6.45 (s, 1H), 6.42 - 6.30 (m, 1H), 5.86 - 5.76 (m, 1H), 5.56 - 5.40 (m, 1H), 4.18 - 4.13 (m, 1H), 3.98 (q, J = 8.0 Hz, 1H), 3.88 (s, 3H), 3.20 - 3.14 (m, 3H), 3.09 - 3.00 (m, 4H), 2.98 - 2.90 (m, 3H), 2.86 - 2.76 (m, 4H), 2.62 - 2.54 (m, 1H), 2.38 - 2.29 (m, 1H), 2.10 - 2.02 (m, 2H), 1.86 - 1.73 (m, 2H), 1.29 (s, 3H), 1.27 (s, 2H) ; 679.3[M+H]$^+$	1.54
716		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.18 (s, 1H), 7.59 - 7.50 (m, 1H), 7.40 - 7.35 (m, 1H), 7.23 (t, J = 8.8 Hz, 1H), 6.93 (s, 1H), 6.64 - 6.50 (m, 1H), 6.45 (s, 1H), 6.42 - 6.30 (m, 1H), 5.81 (d, J = 10.3 Hz, 1H), 5.58 - 5.48 (m, 1H), 4.18 - 4.13 (m, 3H), 3.98 (q, J = 8.0 Hz, 1H), 3.80 (s, 3H), 3.77 - 3.70 (m, 1H), 3.29 - 3.22 (m, 1H), 3.19 - 3.12 (m, 2H), 2.90 - 2.79 (m, 4H), 2.30 - 2.28 (m, 1H), 2.21 - 2.00 (m, 1H), 2.00 - 2.00 (m, 3H), 1.82 - 1.76 (m, 1H) ; 650.3[M+H]$^+$	2.27
717		N-(2-(4-(4-cyclopropyl-1,4-diazepane-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.25 (s, 1H), 8.11 (s, 1H), 7.04 - 6.94 (m, 2H), 6.84 (s, 1H), 6.77 (tt, J = 2.5, 9.1 Hz, 1H), 6.51 (dd, J = 10.2, 17.0 Hz, 1H), 6.40 (s, 1H), 6.31 (d, J = 16.8 Hz, 1H), 5.75 (d, J = 10.3 Hz, 1H), 5.50 (dd, J = 4.8, 8.7 Hz, 1H), 4.00 (td, J = 4.2, 7.0 Hz, 1H), 3.93 - 3.85 (m, 1H), 3.82 (s, 3H), 3.21 (d, J = 5.4 Hz, 2H), 3.13 (ddq, J = 4.4, 8.7, 12.6 Hz, 4H), 3.04 (q, J = 5.1 Hz, 3H), 2.91 (t, J = 5.8 Hz, 2H), 2.76 (ddt, J = 5.1, 9.9, 14.4 Hz, 4H), 2.33 - 2.20 (m, 1H), 2.00 - 1.98 (m, 3H), 1.94 (dt, J = 5.3, 11.1 Hz, 3H), 0.51 (dd, J = 4.3, 6.4 Hz, 2H), 0.49 - 0.40 (m, 2H) ; 675.4[M+H]$^+$	2.07
718		N-(2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.10 (s, 1H), 9.20 (s, 1H), 8.32 (s, 1H), 7.90 (s, 1H), 7.17 (tt, J = 9.2, 2.4 Hz, 1H), 7.10 (h, J = 4.7 Hz, 2H), 6.90 (s, 1H), 6.71 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 17.1, 1.9 Hz, 1H), 6.13 (s, 1H), 5.70 - 5.71 (m, 1H), 5.55 (dd, J = 8.6, 5.4 Hz, 1H), 4.04 (q, J = 7.7 Hz, 3H), 3.81 (s, 4H), 3.65 (d, J = 12.2 Hz, 3H), 3.41 (d, J = 21.8 Hz, 2H), 3.28 - 3.11 (m, 4H), 2.93 (tq, J = 12.0, 6.8, 5.7 Hz, 2H), 2.84 - 2.57 (m, 5H), 2.44 - 2.28 (m, 4H), 2.23 (d, J = 10.2 Hz, 2H), 2.08 (d, J = 9.8 Hz, 2H). : 656.5[M+H]$^+$	1.52

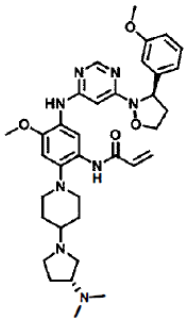
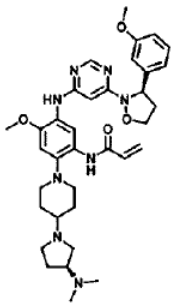
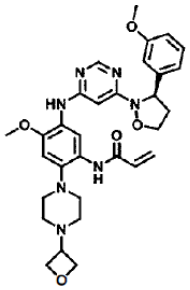
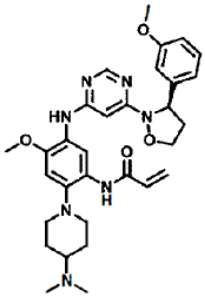
[609]

719		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.75 (s, 1H), 8.41 (s, 1H), 8.29 (d, J = 1.0 Hz, 1H), 7.50 (dd, J = 7.0, 2.2 Hz, 1H), 7.30 (ddd, J = 8.6, 4.6, 2.3 Hz, 1H), 7.00 (t, J = 8.7 Hz, 2H), 6.73 (s, 1H), 6.64 (s, 1H), 6.27 (dd, J = 16.9, 9.8 Hz, 1H), 5.74 (dd, J = 9.8, 1.8 Hz, 1H), 5.62 (dd, J = 8.7, 4.6 Hz, 1H), 5.29 (s, 1H), 4.14 (td, J = 8.0, 4.2 Hz, 1H), 3.83 (s, 4H), 3.10 - 3.00 (m, 3H), 2.80 - 2.67 (m, 5H), 2.56 - 2.46 (m, 2H), 2.46 (s, 3H), 2.31 (dtd, J = 12.5, 8.1, 4.6 Hz, 2H), 2.03 (s, 8H), 1.76 - 1.63 (m, 3H).; 651.5[M+H]$^+$	1.51
720		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	638.5[M+H]$^+$	1.58
721		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.05 (s, 1H), 9.22 (s, 1H), 8.31 (s, 1H), 7.58 (dd, J = 7.1, 2.0 Hz, 1H), 7.46 - 7.36 (m, 3H), 6.89 (d, J = 12.7 Hz, 1H), 6.72 (dd, J = 16.8, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.13 (s, 1H), 5.80 - 5.72 (m, 1H), 5.54 (dd, J = 8.5, 5.4 Hz, 1H), 4.04 (q, J = 7.7 Hz, 5H), 3.81 (s, 3H), 3.67 (s, 4H), 3.57 (d, J = 4.7 Hz, 3H), 3.46 (d, J = 9.0 Hz, 1H), 3.31 - 3.15 (m, 5H), 2.98 - 2.74 (m, 5H), 2.39 - 2.24 (m, 2H), 2.24 - 2.01 (m, 5H), 1.29 (t, J = 7.2 Hz, 4H).; 665.6[M+H]$^+$	1.52
722		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methyl-2-oxopiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 10.15 (s, 1H), 8.34 (s, 1H), 7.97 (s, 1H), 7.16 (tt, J = 9.3, 2.4 Hz, 1H), 7.12 - 6.99 (m, 3H), 6.75 (dd, J = 16.9, 10.3 Hz, 1H), 6.30 - 6.21 (m, 1H), 5.80 - 5.74 (m, 1H), 5.56 (dd, J = 8.6, 5.4 Hz, 1H), 4.04 (q, J = 7.7 Hz, 1H), 3.83 (s, 4H), 3.77 - 3.66 (m, 2H), 3.60 (s, 1H), 3.56 (s, 2H), 3.38 (s, 2H), 3.22 (s, 3H), 3.08 (d, J = 10.2 Hz, 2H), 2.94 (ttd, J = 12.2, 7.5, 4.6 Hz, 2H), 2.81 (s, 3H), 2.37 - 2.08 (m, 3H), 1.65 (s, 2H).; 649.5[M+H]$^+$	1.59
723		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.34 (s, 1H), 8.18 (s, 1H), 7.57 (dd, J = 7.1, 2.1 Hz, 1H), 7.44 - 7.37 (m, 1H), 7.23 (t, J = 8.9 Hz, 1H), 6.96 (s, 1H), 6.50 - 6.43 (m, 2H), 6.36 (dd, J = 17.0, 1.5 Hz, 1H), 5.81 (d, J = 10.3 Hz, 1H), 5.55 (dd, J = 8.3, 4.7 Hz, 1H), 4.16 (td, J = 7.8, 4.1 Hz, 1H), 4.03 - 3.93 (m, 1H), 3.90 (s, 3H), 3.00 (t, J = 4.7 Hz, 4H), 2.81 (ddd, J = 25.7, 16.6, 12.7 Hz, 5H), 2.59 (q, J = 7.2 Hz, 2H), 2.41 - 2.27 (m, 1H), 1.20 (t, J = 7.2 Hz, 3H). ; 582.2 [M+H]$^+$	1.16

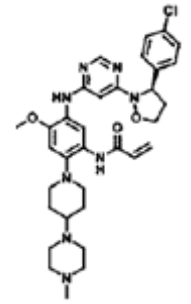
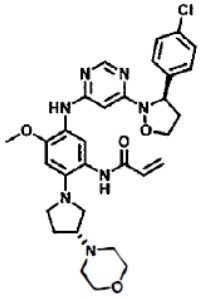
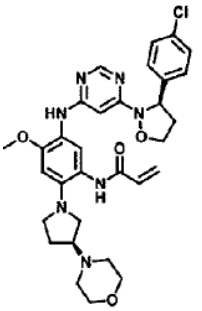
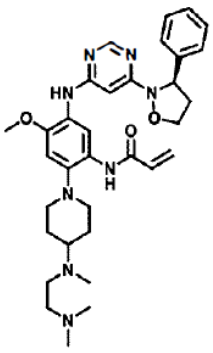
[610]

724		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.34 (s, 1H), 8.18 (s, 1H), 7.57 (dd, J = 7.1, 2.1 Hz, 1H), 7.44 - 7.37 (m, 1H), 7.23 (t, J = 8.9 Hz, 1H), 6.95 (s, 1H), 6.59 - 6.43 (m, 2H), 6.36 (dd, J = 17.0, 1.5 Hz, 1H), 5.81 (d, J = 10.2 Hz, 1H), 5.55 (dd, J = 8.4, 4.7 Hz, 1H), 4.16 (td, J = 7.0, 4.3 Hz, 1H), 4.01 - 3.94 (m, 1H), 3.89 (d, J = 5.2 Hz, 3H), 3.07 - 2.95 (m, 4H), 2.82 (p, J = 12.5 Hz, 6H), 2.34 (ddd, J = 15.6, 7.0, 4.1 Hz, 1H), 1.17 (t, J = 10.7 Hz, 6H). ; 596.4 [M+H]$^+$	1.25
725		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.34 (s, 1H), 8.18 (d, J = 0.7 Hz, 1H), 7.57 (dd, J = 7.1, 2.1 Hz, 1H), 7.45 - 7.38 (m, 1H), 7.23 (t, J = 8.8 Hz, 1H), 6.02 (s, 1H), 6.60 - 6.44 (m, 2H), 6.37 (dd, J = 17.0, 1.5 Hz, 1H), 5.82 (dd, J = 10.2, 1.3 Hz, 1H), 5.55 (dd, J = 8.5, 4.7 Hz, 1H), 4.16 (td, J = 7.0, 4.2 Hz, 1H), 3.98 (dd, J = 16.1, 8.1 Hz, 1H), 3.89 (s, 3H), 2.98 - 2.75 (m, 9H), 2.39 - 2.27 (m, 1H), 1.85 - 1.76 (m, 1H), 0.61 - 0.44 (m, 4H). ; 594.3 [M+H]$^+$	1.30
726		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d6) δ 9.75 (s, 1H), 9.20 (d, J = 20.0 Hz, 1H), 8.28 (s, 1H), 7.88 (d, J = 12.0 Hz, 1H), 7.28 (t, J = 7.9 Hz, 1H), 6.95 - 6.83 (m, 4H), 6.65 - 6.53 (m, 1H), 6.28 - 6.20 (m, 1H), 6.06 (s, 1H), 5.76 (d, J = 10.3 Hz, 1H), 5.51 - 5.42 (m, 1H), 4.71 (s, 1H), 4.62 (d, J = 27.3 Hz, 1H), 4.28 (d, J = 5.5 Hz, 1H), 4.21 (d, J = 10.2 Hz, 1H), 4.02 (s, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 3.71 (d, J = 9.7 Hz, 1H), 3.47 (t, J = 9.4 Hz, 2H), 3.26 - 3.16 (m, 2H), 2.91 - 2.76 (m, 2H), 2.76 - 2.65 (m, 1H), 2.36 - 2.24 (m, 2H), 2.09 (d, J = 14.7 Hz, 4H); 628.6[M+H]$^+$	1.41
727		N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d6) δ 9.79 (s, 1H), 9.13 (s, 1H), 8.28 (s, 1H), 7.91 (s, 1H), 7.28 (t, J = 7.9 Hz, 1H), 6.94 - 6.85 (m, 4H), 6.67 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.04 (s, 1H), 5.76 (d, J = 10.2 Hz, 1H), 5.51 - 5.42 (m, 1H), 4.28 (t, J = 6.1 Hz, 2H), 4.00 (s, 2H), 3.79 (s, 3H), 3.75 (s, 3H), 3.47 (d, J = 11.7 Hz, 2H), 3.27 (s, 1H), 3.21 (d, J = 12.0 Hz, 2H), 2.95 - 2.86 (m, 1H), 2.72 (dt, J = 30.7, 11.2 Hz, 4H), 2.35 - 2.27 (m, 1H), 2.22 (d, J = 11.6 Hz, 2H), 2.10 - 1.98 (m, 2H), 1.18 (s, 3H), 1.16 (s, 3H); 644.6[M+H]$^+$	1.55

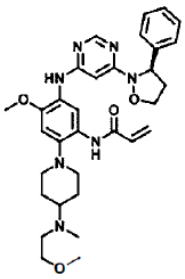
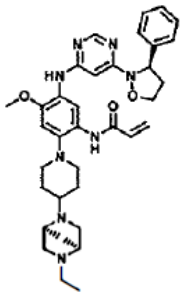
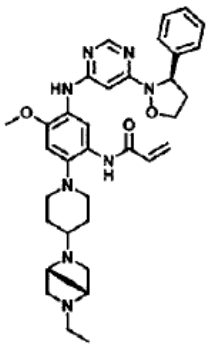
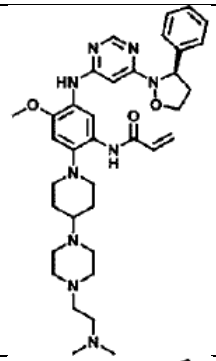
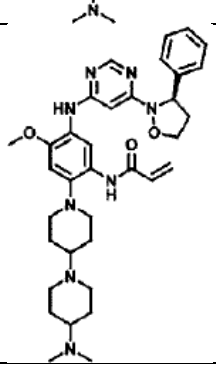
[611]

728		N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d6) δ 9.51 (s, 1H), 9.21 (s, 1H), 8.26 (s, 1H), 7.95 (s, 1H), 7.28 (t, *J* = 7.9 Hz, 1H), 6.95 - 6.89 (m, 3H), 6.85 (dd, *J* = 8.3, 2.6 Hz, 1H), 6.64 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.24 (dd, *J* = 17.0, 1.9 Hz, 1H), 6.13 (s, 1H), 5.75 (d, *J* = 10.3 Hz, 1H), 5.48 (t, *J* = 6.8 Hz, 1H), 4.30 - 4.20 (m, 1H), 3.98 (s, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 3.63 (d, *J* = 4.1 Hz, 2H), 3.37 (s, 2H), 3.23 - 3.18 (m, 2H), 2.84 (s, 8H), 2.78 - 2.70 (m, 2H), 2.39 (dd, *J* = 9.7, 7.5 Hz, 1H), 2.29 (dd, *J* = 12.7, 5.0 Hz, 1H), 2.22 - 2.13 (m, 2H), 2.12 - 2.00 (m, 2H): 643.6[M+H]$^+$	1.36
729		N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d6) δ 9.69 (s, 1H), 9.22 (s, 1H), 8.27 (s, 1H), 7.91 (s, 1H), 7.28 (t, *J* = 7.9 Hz, 1H), 6.92 (t, *J* = 6.3 Hz, 3H), 6.85 (dd, *J* = 8.3, 2.6 Hz, 1H), 6.64 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.24 (dd, *J* = 16.9, 1.9 Hz, 1H), 6.08 (s, 1H), 5.76 (d, *J* = 10.3 Hz, 1H), 5.52 - 5.42 (m, 1H), 4.30 - 4.24 (m, 1H), 4.01 - 3.99 (m, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 3.57 - 3.48 (m, 2H), 3.44 - 3.28 (m, 2H), 3.25 - 3.19 (m, 2H), 2.84 (s, 8H), 2.80 - 2.69 (m, 2H), 2.45 - 2.36 (m, 1H), 2.34 - 2.27 (m, 1H), 2.16 (d, *J* = 19.9 Hz, 2H), 2.07 (d, *J* = 16.0 Hz, 2H): 643.6[M+H]$^+$	1.36
730		N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, Methanol-d4) δ 8.29 (s, 1H), 8.14 (s, 1H), 7.24 (t, J = 8.1 Hz, 1H), 6.99 (dd, J = 5.0, 2.9 Hz, 2H), 6.92 (d, J = 8.1 Hz, 1H), 6.82 - 6.78 (m, 1H), 6.56 - 6.46 (m, 1H), 6.39 (s, 1H), 6.37 - 6.30 (m, 1H), 5.81 - 5.76 (m, 1H), 5.49 - 5.45 (m, 1H), 4.74 (t, J = 6.7 Hz, 2H), 4.66 (t, J = 6.2 Hz, 2H), 4.13 (td, J = 7.8, 4.4 Hz, 1H), 3.96 (q, J = 7.9 Hz, 1H), 3.90 (s, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 3.69 - 3.61 (m, 1H), 2.99 (t, J = 4.8 Hz, 4H), 2.78 (dtd, J = 12.3, 8.0, 4.4 Hz, 1H), 2.60 (s, 3H), 2.37 - 2.28 (m, 1H): 588.5[M+H]+	1.11
731		N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, Chloroform-d) δ 8.82 (s, 1H), 8.44 (s, 1H), 8.33 (s, 1H), 7.24 (d, J = 7.9 Hz, 2H), 7.06 - 7.01 (m, 2H), 6.79 (dd, J = 8.1, 2.5 Hz, 1H), 6.73 (s, 1H), 6.66 (s, 1H), 6.37 (d, J = 16.4 Hz, 1H), 6.30 (dd, J = 16.5, 9.8 Hz, 1H), 5.75 (dd, J = 9.5, 2.0 Hz, 1H), 5.66 (dd, J = 8.7, 4.4 Hz, 1H), 4.15 (td, J = 8.0, 4.4 Hz, 1H), 4.05 (q, J = 8.2 Hz, 1H), 3.84 (s, 3H), 3.80 (s, 3H), 3.09 (d, J = 11.4 Hz, 2H), 2.82 - 2.70 (m, 4H), 2.49 (s, 6H), 2.41 - 2.35 (m, 1H), 2.12 (s, 2H), 1.80 (dd, J = 12.0, 4.0 Hz, 2H): 574.5[M+H]+	1.23

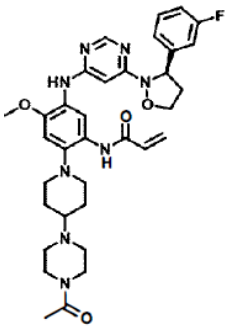
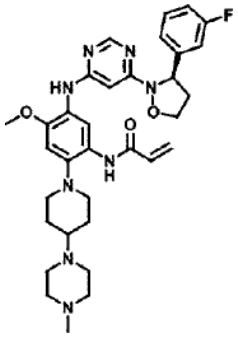
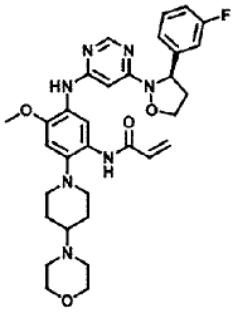
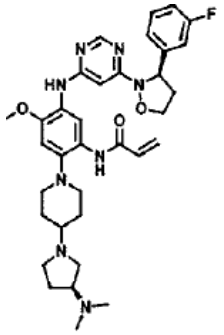
[612]

732		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.23 (s, 1H), 8.06 (s, 1H), 7.26 (dd, J = 37.4, 8.4 Hz, 4H), 6.77 (s, 1H), 6.35 (d, J = 16.7 Hz, 1H), 5.41 (dd, J = 8.4, 4.6 Hz, 1H), 4.01 (dd, J = 11.9, 7.6 Hz, 1H), 3.86 (d, J = 7.9 Hz, 1H), 3.74 (s, 3H), 3.44 (s, 1H), 3.21 (dt, J = 3.2, 1.6 Hz, 2H), 3.09 - 2.80 (m, 8H), 2.71 - 2.60 (m, 4H), 2.54 (s, 1H), 2.19 (ddd, J = 17.9, 12.7, 6.7 Hz, 1H), 1.91 (d, J = 11.7 Hz, 2H) ; 633.6 [M+H]$^+$	1.20
733		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.35 (s, 1H), 8.12 (s, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.5 Hz, 2H), 6.90 (s, 1H), 6.75 (s, 1H), 6.67 (s, 1H), 6.31 (dt, J = 16.9, 13.3 Hz, 2H), 5.74 (d, J = 10.8 Hz, 1H), 5.66 (dd, J = 8.5, 4.5 Hz, 1H), 4.18 - 4.10 (m, 1H), 4.06 (dd, J = 15.7, 7.8 Hz, 1H), 3.83 (s, 3H), 3.76 (t, J = 4.5 Hz, 4H), 3.26 - 3.04 (m, 4H), 3.03 - 2.93 (m, 1H), 2.74 (ddd, J = 16.3, 7.9, 4.0 Hz, 1H), 2.63 - 2.43 (m, 4H), 2.38 - 2.28 (m, 1H), 2.18 (dd, J = 12.1, 7.5 Hz, 1H), 1.94 (dt, J = 19.8, 7.8 Hz, 1H), 1.25 (s, 1H) ; 606.4 [M+H]$^+$	1.17
734		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.00 (s, 1H), 7.55 (s, 1H), 7.27 (dd, J = 36.0, 8.5 Hz, 4H), 6.54 (s, 1H), 6.41 (dd, J = 17.0, 10.2 Hz, 1H), 6.24 (dd, J = 17.0, 1.4 Hz, 1H), 6.18 (s, 1H), 5.67 (dd, J = 10.2, 1.4 Hz, 1H), 5.40 (dd, J = 8.4, 4.6 Hz, 1H), 4.00 (dt, J = 7.8, 3.9 Hz, 1H), 3.81 (q, J = 7.9 Hz, 1H), 3.74 (s, 3H), 3.63 (t, J = 4.6 Hz, 4H), 3.27 - 3.12 (m, 11H), 2.88 - 2.79 (m, 1H), 2.72 - 2.61 (m, 1H), 2.56 - 2.36 (m, 4H), 2.25 - 2.15 (m, 1H), 2.14 - 2.05 (m, 1H), 1.84 - 1.72 (m, 1H) ; 606.5 [M+H]$^+$	1.18
735		N-(2-(4-((2-(dimethylamino)ethyl)(methyl)amino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.88 (s, 1H), δ 8.47 (s, 1H), 8.36 (s, 1H), 7.46 (d, J = 7.6 Hz, 2H), 7.33 (t, J = 7.5 Hz, 2H), 7.25 (d, J = 7.3 Hz, 1H), 6.95 (s, 1H), 6.75 (s, 1H), 6.68 (d, J = 6.9 Hz, 1H), 6.34 (d, J = 1.8 Hz, 1H), 6.29 (d, J = 9.8 Hz, 1H), 5.75 (dd, J = 9.7, 1.8 Hz, 1H), 5.70 (dd, J = 8.7, 4.5 Hz, 1H), 4.14 (dd, J = 8.0, 4.5 Hz, 1H), 4.07 (d, J = 7.9 Hz, 1H), 3.83 (s, 3H), 3.57 (s, 2H), 3.05 (d, J = 11.7 Hz, 2H), 2.78 - 2.65 (m, 4H), 2.51 (q, J = 8.1, 7.0 Hz, 3H), 2.35 (d, J = 14.5 Hz, 9H), 1.98 (d, J = 12.7 Hz, 2H), 1.75 - 1.64 (m, 2H).; 601.6 [M+H]$^+$	1.35

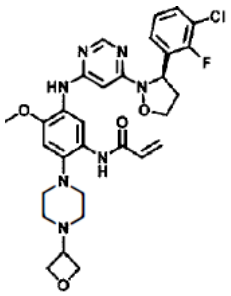
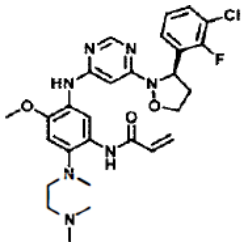
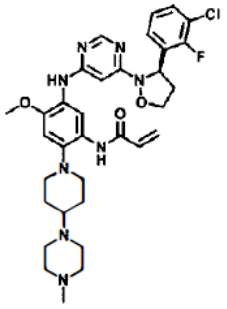
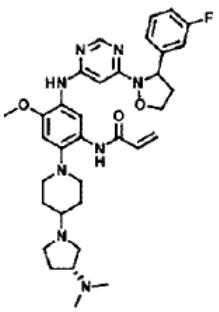
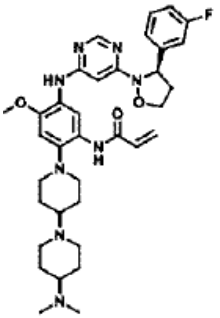
[613]

736		N-(4-methoxy-2-(4-((2-methoxyethyl)(methyl)amino)piperidine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.01 (s, 1H), 9.17 (s, 1H), 8.30 (s, 1H), 7.93 (s, 1H), 7.37 (m, 4H), 7.30 (m, 1H), 6.87 (m, 1H), 6.76 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 2.0 Hz, 1H), 6.04 (s, 1H), 5.76 (dd, J = 10.1, 2.0 Hz, 1H), 5.54 - 5.48 (m, 1H), 4.30 (dd, J = 7.7, 4.6 Hz, 1H), 4.06 (q, J = 7.7 Hz, 2H), 3.79 (s, 3H), 3.60 (m, 6H), 3.34 (s, 3H), 3.17 (s, 3H), 3.11 (m, 4H), 2.78 (m, 3H), 2.72 (m, 1H).; 588.6 $[M+H]^+$	1.87
737		N-(2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 9.24 (s, 1H), 8.28 (s, 1H), 7.86 (s, 1H), 7.37(m, 4H), 7.33 - 7.25 (m, 1H), 6.90 (d, J = 16.8 Hz, 1H), 6.66 - 6.51 (m, 1H), 6.24 (dd, J =17.0, 1.8 Hz, 1H), 6.07 (m, 1H), 5.76 (d, J = 10.3 Hz, 1H), 5.51 (m, 1H), 4.56 (s, 1H), 4.29 (s, 1H), 4.04 (dd, J = 15.3, 7.5 Hz, 2H), 3.80 (s, 3H), 3.13 (m, 1H), 3.01 (m, 2H), 2.90 (m, 2H),2.73 (m, 4H), 2.37 - 2.24 (m, 2H), 2.18 - 1.95 (m, 4H), 1.78 - 1.68 (m, 1H), 1.33 - 1.21 (m,6H).; 625.7 $[M+H]^+$	1.76
738		N-(2-(4-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.76 (s, 1H), 9.25 (s, 1H), 8.28 (s, 1H), 7.86 (s, 1H), 7.37 (m, 4H),7.29 (m, 1H), 6.89 (d, J = 17.2 Hz, 1H), 6.57 (m, 1H), 6.24 (dd, J = 17.1, 1.8 Hz, 1H), 6.06 (m, 1H), 5.76(d, J = 10.3 Hz, 1H), 5.50 (s, 1H), 4.61 - 4.51 (m, 1H), 4.34 - 4.25 (m, 1H), 4.04 (m, 2H), 3.80 (s, 3H),3.17 (m, 1H), 3.02 (m, 2H), 2.91 (m, 2H), 2.74 (m, 4H), 2.34 - 2.20 (m, 2H), 2.06 (m, 4H), 1.73 (dt, J =14.0, 6.5 Hz, 1H), 1.28 (m, 6H).; 625.7 $[M+H]^+$	1.80
739		N-(2-(4-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.46 (d, J = 7.5 Hz, 2H), 7.34 (t, J = 7.6 Hz, 2H), 7.24 (t, J = 7.3 Hz, 1H), 6.95 (s, 1H), 6.74 (s, 1H), 6.68 (s, 1H), 6.34 (s, 1H), 6.27 (s, 1H), 5.75 (s, 1H), 5.68 (s, 1H), 4.16 (s, 1H), 4.07 (s, 1H), 3.84 (s, 3H), 3.58 (s, 1H), 3.30 (t, J = 6.1 Hz, 1H), 3.23 - 3.13 (m, 1H), 3.04 (s, 2H), 2.95 (t, J = 6.9 Hz, 1H), 2.74 (m, 6H), 2.65 (m, 7H), 2.45 (s, 6H), 2.40 (s, 2H), 2.08 (d, J = 12.5 Hz, 2H).; 656.7 $[M+H]^+$	1.72
740		N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.86 (s, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 7.46 (d, J = 7.4 Hz, 2H), 7.34 (t, J = 7.5 Hz, 2H), 7.24 (t, J = 7.4 Hz, 1H), 6.94 (s, 1H), 6.74 (s, 1H), 6.60 (s, 1H), 6.36 (dd, J = 17.0, 1.6 Hz, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.74 (dd, J = 9.9, 1.6 Hz, 1H), 5.70 (dd, J = 8.6, 4.5 Hz, 1H), 4.14 (dd, J = 7.9, 4.5 Hz, 1H), 4.07 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.23 (t, J = 6.2 Hz, 2H), 2.75 - 2.70 (m, 2H), 2.33 (s, 6H), 2.28 (s, 3H), 2.08 - 2.02 (m, 2H), 1.80 (d, J = 12.4 Hz, 2H), 1.67 (t, J = 6.2 Hz, 2H), 1.58 (dd, J = 11.9, 3.5 Hz, 2H), 1.26 (s, 3H), 1.12 (t, J = 7.2 Hz, 2H).; 627.6[M+H]	1.02

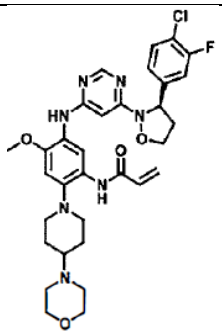
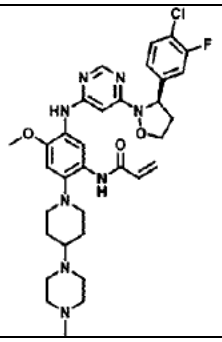
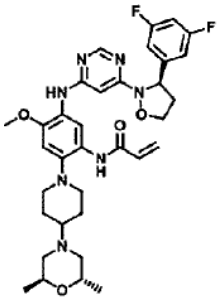
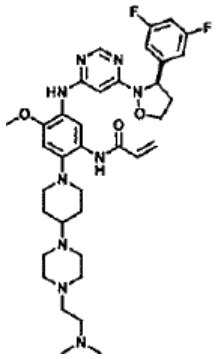
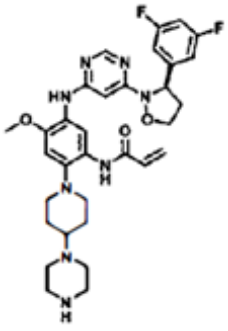
[614]

741		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.60 (d, J = 51.9 Hz, 1H), 9.95 (s, 1H), 9.19 (s, 1H), 8.31 (d, J = 3.5 Hz, 1H), 7.90 (s, 1H), 7.42 (q, J = 7.3 Hz, 1H), 7.20 (t, J = 9.5 Hz, 2H), 7.13 (t, J = 8.7 Hz, 1H), 6.89 (s, 1H), 6.77 - 6.59 (m, 1H), 6.25 (d, J = 16.9 Hz, 1H), 6.00 (s, 1H), 5.76 (d, J = 10.2 Hz, 1H), 5.54 (t, J = 7.0 Hz, 1H), 4.50 (d, J = 13.8 Hz, 1H), 4.30 (s, 2H), 4.03 (d, J = 15.2 Hz, 3H), 3.80 (s, 3H), 3.71 (s, 1H), 3.49 (s, 2H), 3.37 (d, J = 16.8 Hz, 1H), 3.22 (d, J = 12.1 Hz, 3H), 2.97 (d, J = 28.0 Hz, 2H), 2.78 (s, 2H), 2.32 (q, J = 6.0 Hz, 1H), 2.19 (s, 2H), 2.06 (s, 3H).; 645.6[M+H]$^+$	1.44
742		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.88 (s, 1H), 9.18 (s, 1H), 8.30 (s, 1H), 7.92 (d, J = 15.7 Hz, 1H), 7.42 (td, J = 8.1, 6.2 Hz, 1H), 7.24 - 7.16 (m, 2H), 7.13 (td, J = 8.8, 2.6 Hz, 1H), 6.89 (s, 1H), 6.69 (dd, J = 16.9, 10.1 Hz, 1H), 6.25 (dd, J = 17.0, 2.0 Hz, 1H), 6.10 (s, 1H), 5.80 - 5.71 (m, 1H), 5.54 (dd, J = 8.5, 5.6 Hz, 1H), 4.28 (dd, J = 7.7, 4.2 Hz, 2H), 4.07 - 4.00 (m, 4H), 3.80 (s, 3H), 3.75 (d, J = 9.1 Hz, 2H), 3.57 (s, 2H), 3.22 (d, J = 11.9 Hz, 2H), 2.97 - 2.80 (m, 1H), 2.83 (d, J = 13.2 Hz, 3H), 2.80 - 2.70 (m, 2H), 2.32 (h, J = 7.5 Hz, 2H), 2.18 (s, 2H), 2.06 (d, J = 11.9 Hz, 2H). ; 617.6[M+H]$^+$	1.10
743		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.34 (s, 1H), 9.84 (s, 1H), 9.17 (s, 1H), 8.30 (s, 1H), 7.92 (s, 1H), 7.42 (td, J = 7.9, 6.1 Hz, 1H), 7.24 - 7.16 (m, 2H), 7.13 (td, J = 8.6, 2.7 Hz, 1H), 6.90 (s, 1H), 6.66 (dd, J = 17.0, 10.3 Hz, 1H), 6.25 (dd, J = 16.9, 1.9 Hz, 1H), 6.11 (s, 1H), 5.80 - 5.70 (m, 1H), 5.54 (t, J = 7.1 Hz, 1H), 4.31 - 4.26 (m, 2H), 4.03 - 3.94 (m, 4H), 3.81 (s, 3H), 3.45 (d, J = 12.0 Hz, 2H), 3.30 (s, 1H), 3.22 (d, J = 11.5 Hz, 2H), 3.14 (d, J = 11.6 Hz, 2H), 2.97 - 2.87 (m, 1H), 2.77 (t, J = 11.8 Hz, 2H), 2.32 (td, J = 13.0, 7.7 Hz, 1H), 2.20 (d, J = 11.7 Hz, 2H), 2.02 (d, J = 9.9 Hz, 2H). ; 604.6[M+H]$^+$	1.13
744		N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.21 (d, J = 8.8 Hz, 1H), 8.26 (d, J = 7.9 Hz, 1H), 7.95 (s, 1H), 7.42 (q, J = 7.6 Hz, 1H), 7.26 - 7.15 (m, 2H), 7.12 (t, J = 8.8 Hz, 1H), 6.91 (s, 1H), 6.63 (s, 1H), 6.28 - 6.10 (m, 2H), 5.75 (d, J = 10.5 Hz, 1H), 5.54 (dd, J = 8.7, 5.4 Hz, 1H), 4.25 (s, 1H), 3.99 (s, 3H), 3.81 (s, 3H), 3.22 (s, 3H), 2.84 (s, 8H), 2.78 - 2.70 (m, 3H), 2.31 (d, J = 15.1 Hz, 3H), 2.18 (s, 3H), 2.06 (d, J = 22.5 Hz, 3H).; 631.6[M+H]+	1.38

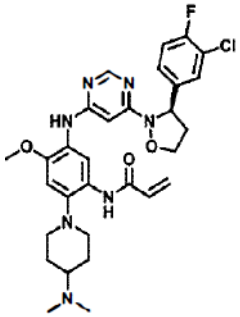
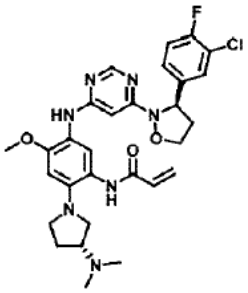
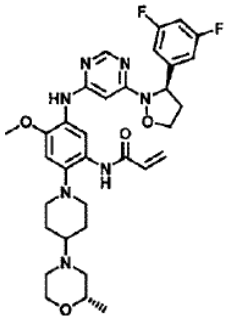
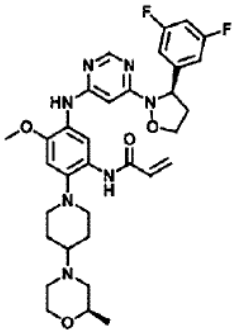
[615]

745		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.05 (s, 1H), 8.92 (s, 1H), 8.25 (d, J = 11.3 Hz, 1H), 8.20 (s, 1H), 7.57 - 7.47 (m, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.23 (t, J = 7.9 Hz, 1H), 6.84 (d, J = 8.6 Hz, 1H), 6.66 (dd, J = 17.1, 10.0 Hz, 1H), 6.37 (s, 1H), 6.24 (dd, J = 16.8, 2.0 Hz, 1H), 5.81 - 5.67 (m, 2H), 4.21 (q, J = 7.2, 6.8 Hz, 1H), 3.90 (d, J = 8.1 Hz, 2H), 3.83 (s, 3H), 3.36 (t, J = 5.6 Hz, 4H), 3.24 - 3.07 (m, 8H), 2.86 (t, J = 11.7 Hz, 1H), 2.28 - 2.17 (m, 1H).: 610.5[M+H]+	1.27
746		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.89 (s, 1H), 8.29 (s, 1H), 8.07 (s, 1H), 7.54 (td, J = 7.6, 1.7 Hz, 1H), 7.37 (t, J = 7.3 Hz, 1H), 7.24 (t, J = 7.9 Hz, 2H), 6.96 (s, 1H), 6.27 - 6.18 (m, 2H), 5.75 - 5.67 (m, 2H), 4.31 (s, 2H), 4.05 (d, J = 8.2 Hz, 2H), 3.82 (s, 4H), 2.97 (d, J = 10.4 Hz, 1H), 2.72 (d, J = 4.8 Hz, 7H), 2.61 (s, 4H), 2.30 (tt, J = 13.1, 6.1 Hz, 1H). : 570.5[M+H]+	1.34
747		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.15 (s, 1H), 8.26 (d, J = 4.1 Hz, 1H), 7.99 (s, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.44 - 7.34 (m, 1H), 7.24 (t, J = 7.9 Hz, 1H), 6.80 (s, 1H), 6.67 (dd, J = 17.4, 9.9 Hz, 1H), 6.28 - 6.18 (m, 2H), 5.79 - 5.67 (m, 2H), 4.33 - 4.22 (m, 1H), 4.01 (d, J = 9.9 Hz, 2H), 3.83 - 3.78 (m, 3H), 3.78 - 3.70 (m, 4H), 3.21 (d, J = 12.0 Hz, 3H), 2.93 (d, J = 8.0 Hz, 2H), 2.86 (s, 3H), 2.83 - 2.71 (m, 4H), 2.28 (d, J = 12.7 Hz, 2H), 2.17 (s, 2H), 2.03 (s, 2H). : 651.6[M+H]+	1.24
748		N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-(3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, MeOD) δ 8.21 (s, 1H), 7.92 (s, 1H), 7.41 (td, J = 7.9, 5.7 Hz, 1H), 7.21 (d, J = 7.7 Hz, 1H), 7.17 - 6.97 (m, 3H), 6.68 (dd, J = 16.9, 10.1 Hz, 1H), 6.46 (d, J = 16.8 Hz, 1H), 6.02 (s, 1H), 5.88 (d, J = 10.3 Hz, 1H), 5.52 (s, 1H), 4.51 - 4.39 (m, 1H), 4.21 (q, J = 7.7 Hz, 3H), 3.90 (s, 6H), 3.70 - 3.50 (m, 2H), 3.43 (s, 2H), 3.05 (s, 9H), 2.62 - 2.11 (m, 6H), 1.31 (s, 1H).: 632.5[M+H]+	1.07
749		N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, MeOD) δ 8.13 (s, 1H), 7.80 (s, 1H), 7.40 - 7.10 (m, 1H), 7.10 - 6.84 (m, 4H), 6.68 - 6.47 (m, 1H), 6.37 (d, J = 16.5 Hz, 1H), 6.10 - 5.83 (m, 1H), 5.83 - 5.70 (m, 1H), 5.41 (s, 1H), 4.34 (d, J = 5.3 Hz, 1H), 4.11 (t, J = 7.6 Hz, 1H), 3.81 (s, 6H), 3.56 - 3.23 (m, 6H), 3.06 - 2.80 (m, 2H), 2.85 (s, 6H), 2.37 (d, J = 14.1 Hz, 4H), 2.20 (s, 4H), 1.33 - 1.13 (m, 2H).: 646.5[M+H]+	1.06

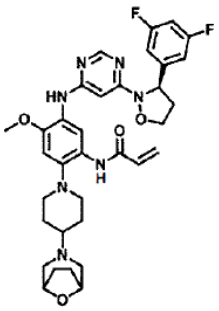
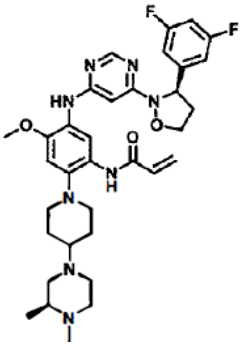
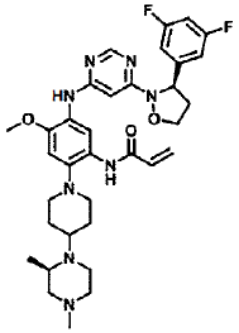
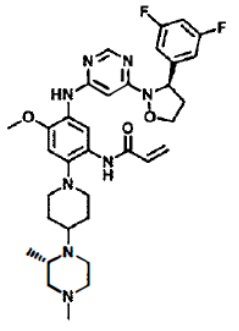
[616]

750		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.11 (s, 1H), 7.79 (s, 1H), 7.39 (t, J = 7.9 Hz, 1H), 7.26 - 6.94 (m, 3H), 6.56 (dd, J = 16.9, 10.2 Hz, 1H), 6.35 (dd, J = 16.9, 1.6 Hz, 1H), 5.97 (s, 1H), 5.78 (dd, J = 10.1, 1.6 Hz, 1H), 5.41 (t, J = 7.2 Hz, 1H), 4.33 (td, J = 7.6, 4.1 Hz, 1H), 4.05 (ddd, J = 30.5, 10.7, 4.9 Hz, 3H), 3.81 (d, J = 6.0 Hz, 5H), 3.60 - 3.49 (m, 2H), 3.47 - 3.27 (m, 3H), 3.23 (d, J = 12.2 Hz, 2H), 3.15 (dd, J = 13.9, 5.1 Hz, 3H), 3.00 - 2.85 (m, 1H), 2.45 - 2.21 (m, 3H), 2.18 - 1.99 (m, 2H).: 630.4[M+H]$^+$	1.28
751		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.22 (s, 1H), 7.93 (s, 1H), 7.50 (t, J = 7.9 Hz, 1H), 7.31 (dd, J = 10.0, 2.0 Hz, 1H), 7.23 (dd, J = 8.3, 2.0 Hz, 1H), 7.13 (s, 1H), 6.60 (dd, J = 16.9, 10.2 Hz, 1H), 6.46 (dd, J = 16.9, 1.6 Hz, 1H), 6.08 (s, 1H), 5.88 (dd, J = 10.2, 1.6 Hz, 1H), 5.54 (t, J = 7.3 Hz, 1H), 4.44 (td, J = 7.6, 4.1 Hz, 1H), 4.20 (td, J = 8.3, 6.5 Hz, 1H), 4.16 - 3.55 (m, 12H), 3.54 - 3.30 (m, 2H), 3.32 - 3.11 (m, 3H), 3.08 (s, 4H), 2.56 - 2.37 (m, 3H), 2.35 - 2.20 (m, 2H).: 652.4[M+H]$^+$	1.23
752		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6S)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.11 - 7.04 (m, 2H), 6.92 (s, 1H), 6.80 - 6.79 (m, 1H), 6.50 - 6.50 (m, 1H), 6.45 (s, 1H), 6.41 - 6.30 (m, 1H), 5.82 (d, J = 10.3 Hz, 1H), 5.61 - 5.51 (m, 1H), 4.19 - 4.04 (m, 4H), 3.98 (q, J = 7.9 Hz, 1H), 3.88 (s, 3H), 3.20 - 3.10 (m, 3H), 2.84 - 2.72 (m, 5H), 2.50 - 2.43 (m, 3H), 2.38 - 2.28 (m, 1H), 1.84 - 1.73 (m, 2H), 1.20 (s, 3H), 1.28 (s, 3H) : 650.3[M+H]$^+$	1.28
753		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.17 (s, 1H), 8.09 - 8.03 (m, 1H), 6.98 - 6.91 (m, 2H), 6.82 - 6.77 (m, 1H), 6.75 - 6.68 (m, 1H), 6.50 - 6.37 (m, 1H), 6.34 (s, 1H), 6.30 - 6.20 (m, 1H), 5.69 (d, J = 10.3 Hz, 1H), 5.50 - 5.41 (m, 1H), 4.06 - 4.01 (m, 1H), 3.90 - 3.81 (m, 2H), 3.77 (s, 3H), 3.15 - 3.00 (m, 3H), 3.00 - 3.00 (m, 6H), 2.99 - 2.93 (m, 2H), 2.73 - 2.70 (m, 8H), 2.68 - 2.53 (m, 9H), 2.25 - 2.20 (m, 1H), 2.03 - 1.95 (m, 2H) : 692.4[M+H]$^+$	1.13
754		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.17 (s, 0H), 8.08 - 8.04 (m, 1H), 6.98 - 6.90 (m, 2H), 6.81 - 6.68 (m, 2H), 6.47 - 6.37 (m, 1H), 6.37 - 6.30 (m, 1H), 6.28 - 6.19 (m, 1H), 5.74 - 5.61 (m, 1H), 5.48 - 5.43 (m, 1H), 4.05 - 4.00 (m, 1H), 3.88 - 3.81 (m, 1H), 3.76 (s, 3H), 3.18 - 2.96 (m, 5H), 2.81 - 2.56 (m, 10H), 2.50 - 2.39 (m, 1H), 2.20 - 2.16 (m, 1H), 1.73 - 1.62 (m, 2H) : 621.3[M+H]$^+$	1.09

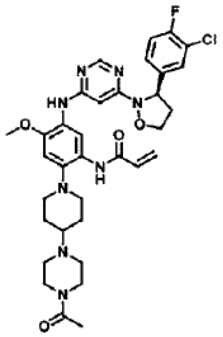
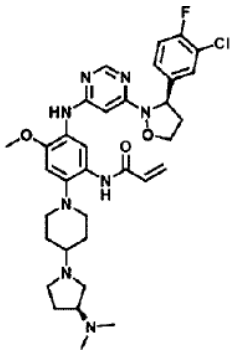
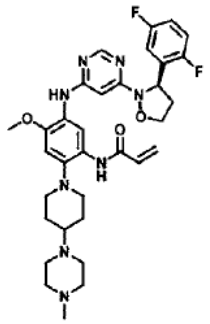
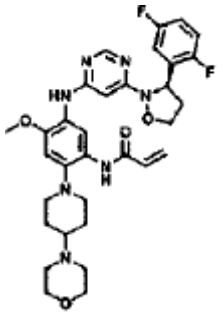
[617]

755		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.32 (s, 1H), 8.18 (d, J = 0.8 Hz, 1H), 7.57 (dd, J = 7.1, 2.1 Hz, 1H), 7.41 (ddd, J = 8.4, 4.5, 2.2 Hz, 1H), 7.23 (t, J = 8.9 Hz, 1H), 6.92 (s, 1H), 6.58 (dd, J = 16.9, 10.3 Hz, 1H), 6.46 (d, J = 0.8 Hz, 1H), 6.37 (dd, J = 17.0, 1.5 Hz, 1H), 5.81 (dd, J = 10.3, 1.3 Hz, 1H), 5.55 (dd, J = 8.5, 4.7 Hz, 1H), 4.16 (td, J = 7.8, 4.2 Hz, 1H), 3.98 (q, J = 8.0 Hz, 1H), 3.88 (s, 3H), 3.19 - 3.09 (m, 2H), 2.88 - 2.73 (m, 3H), 2.43 - 2.27 (m, 8H), 2.05 (d, J = 10.7 Hz, 2H), 1.75 (dt, J = 11.8, 8.3 Hz, 2H). ; 596.4 $[M+H]^+$	1.27
756		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.14 (s, 1H), 7.68 (s, 1H), 7.56 (dd, J = 7.2, 2.1 Hz, 1H), 7.44 - 7.37 (m, 1H), 7.22 (t, J = 8.9 Hz, 1H), 6.67 (s, 1H), 6.54 (dd, J = 17.0, 10.2 Hz, 1H), 6.42 - 6.30 (m, 2H), 5.79 (dd, J = 10.2, 1.6 Hz, 1H), 5.53 (dd, J = 8.5, 4.5 Hz, 1H), 4.14 (td, J = 7.8, 4.2 Hz, 1H), 3.95 (q, J = 7.0 Hz, 1H), 3.88 (s, 3H), 3.26 (m, J = 9.3 Hz, 3H), 2.95 - 2.86 (m, 1H), 2.86 - 2.75 (m, 1H), 2.39 - 2.16 (m, 9H), 1.97 - 1.84 (m, 1H). ; 582.4 $[M+H]^+$	1.25
757		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.85 (s, 1H), 8.44 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.07 - 6.89 (m, 3H), 6.75 (s, 1H), 6.73 - 6.63 (m, 2H), 6.37 (dd, J = 17.0, 1.5 Hz, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.75 (dd, J = 10.0, 1.5 Hz, 1H), 5.66 (dd, J = 8.8, 4.6 Hz, 1H), 4.15 (td, J = 8.1, 4.2 Hz, 1H), 4.06 (q, J = 8.1 Hz, 1H), 3.97 - 3.88 (m, 1H), 3.85 (s, 3H), 3.77 - 3.63 (m, 2H), 3.07 (d, J = 11.4 Hz, 2H), 2.91 (d, J = 11.1 Hz, 1H), 2.85 (d, J = 11.2 Hz, 1H), 2.82 - 2.73 (m, 2H), 2.73 - 2.67 (m, 1H), 2.40 - 2.25 (m, 3H), 2.12 - 2.02 (m, 2H), 1.97 (t, J = 10.5 Hz, 1H), 1.70 - 1.65 (m, 2H), 1.19 (d, J = 6.3 Hz, 3H). ; 636.5 $[M+H]^+$	1.23
758		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.06 - 6.98 (m, 2H), 6.96 (s, 1H), 6.75 (s, 1H), 6.73 - 6.63 (m, 2H), 6.37 (dd, J = 17.0, 1.5 Hz, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.74 (dd, J = 10.0, 1.6 Hz, 1H), 5.67 (dd, J = 8.7, 4.5 Hz, 1H), 4.15 (td, J = 8.1, 4.2 Hz, 1H), 4.06 (q, J = 8.1 Hz, 1H), 3.93 (dd, J = 11.4, 3.4, 1.5 Hz, 1H), 3.85 (s, 3H), 3.76 - 3.60 (m, 2H), 3.11 - 3.02 (m, 2H), 2.94 - 2.66 (m, 5H), 2.40 - 2.24 (m, 3H), 2.08 (d, J = 12.3 Hz, 2H), 1.97 (t, J = 10.5 Hz, 1H), 1.68 - 1.63 (m, 2H), 1.19 (d, J = 6.2 Hz, 3H). ; 636.5 $[M+H]^+$	1.20

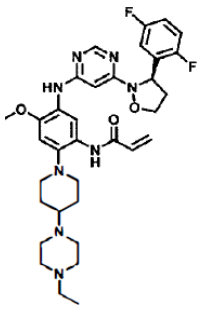
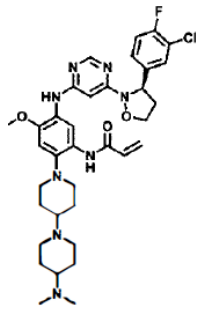
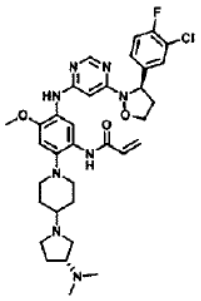
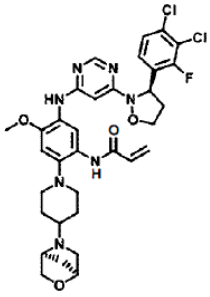
[618]

759		N-(2-(4-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.86 (s, 1H), 8.45 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.06 - 6.97 (m, 2H), 6.96 (s, 1H), 6.75 (s, 1H), 6.72 - 6.63 (m, 2H), 6.38 (dd, J = 16.9, 1.7 Hz, 1H), 6.28 (dd, J = 16.9, 9.9 Hz, 1H), 5.75 (dd, J = 9.8, 1.7 Hz, 1H), 5.67 (dd, J = 8.7, 4.5 Hz, 1H), 4.33 (dt, J = 4.5, 2.3 Hz, 2H), 4.20 - 4.10 (m, 1H), 4.06 (q, J = 8.1 Hz, 1H), 3.84 (s, 3H), 3.00 - 2.98 (m, 2H), 2.82 - 2.65 (m, 5H), 2.48 (dd, J = 10.0, 2.2 Hz, 2H), 2.40 - 2.21 (m, 2H), 1.96 - 1.93 (m, 2H), 1.91 - 1.84 (m, 2H), 1.77 - 1.68 (m, 1H), 1.67 - 1.55 (m, 3H), 1.55 - 1.47 (m, 1H). : 648.5 [M+H]$^+$	1.15
760		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.86 (s, 1H), 8.45 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.06 - 6.98 (m, 2H), 6.96 (s, 1H), 6.75 (s, 1H), 6.73 - 6.61 (m, 2H), 6.36 (dd, J = 17.0, 1.6 Hz, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.74 (dd, J = 10.0, 1.6 Hz, 1H), 5.66 (dd, J = 8.7, 4.6 Hz, 1H), 4.15 (td, J = 8.0, 4.2 Hz, 1H), 4.06 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.06 (d, J = 10.4 Hz, 2H), 3.01 - 2.96 (m, 1H), 2.94 - 2.84 (m, 2H), 2.82 - 2.68 (m, 3H), 2.44 - 2.34 (m, 3H), 2.32 (s, 3H), 2.31 - 2.27 (m, 1H), 2.13 - 2.00 (m, 4H), 1.74 - 1.59 (m, 2H), 1.11 (d, J = 6.2 Hz, 3H). : 649.5 [M+H]$^+$	1.15
761		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-2,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.87 (s, 1H), 8.45 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.04 - 6.98 (m, 2H), 6.96 (s, 1H), 6.76 (s, 1H), 6.74 - 6.63 (m, 2H), 6.37 (dd, J = 16.9, 1.7 Hz, 1H), 6.27 (dd, J = 16.9, 9.9 Hz, 1H), 5.75 (dd, J = 9.9, 1.7 Hz, 1H), 5.67 (dd, J = 8.8, 4.6 Hz, 1H), 4.15 (td, J = 8.1, 4.2 Hz, 1H), 4.06 (q, J = 8.0 Hz, 1H), 3.85 (s, 3H), 3.07 (dt, J = 11.3, 5.1 Hz, 2H), 2.99 - 2.84 (m, 3H), 2.83 - 2.59 (m, 6H), 2.40 - 2.30 (m, 2H), 2.30 (s, 3H), 2.09 - 2.03 (m, 1H), 1.95 - 1.80 (m, 3H), 1.63 (qd, J = 12.0, 3.9 Hz, 1H), 1.11 (d, J = 6.3 Hz, 3H). : 649.5 [M+H]$^+$	1.15
762		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-2,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.87 (s, 1H), 8.44 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.06 - 6.96 (m, 2H), 6.94 (s, 1H), 6.76 (s, 1H), 6.76 - 6.63 (m, 2H), 6.37 (dd, J = 16.9, 1.6 Hz, 1H), 6.27 (dd, J = 16.9, 9.9 Hz, 1H), 5.75 (dd, J = 9.9, 1.6 Hz, 1H), 5.67 (dd, J = 8.8, 4.5 Hz, 1H), 4.15 (td, J = 8.1, 4.2 Hz, 1H), 4.06 (q, J = 8.1 Hz, 1H), 3.85 (s, 3H), 3.07 (d, J = 11.5 Hz, 2H), 2.99 - 2.84 (m, 3H), 2.84 - 2.73 (m, 3H), 2.73 - 2.60 (m, 3H), 2.40 - 2.31 (m, 2H), 2.30 (s, 3H), 2.10 - 2.06 (m, 1H), 1.89 (dd, J = 22.0, 9.7 Hz, 3H), 1.63 (q, J = 12.2, 11.7 Hz, 1H), 1.12 (d, J = 6.3 Hz, 3H). : 649.5 [M+H]$^+$	1.16

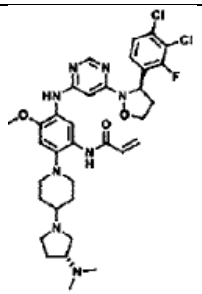
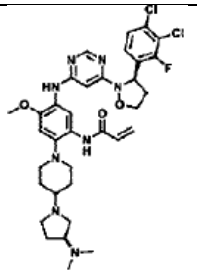
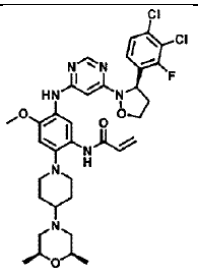
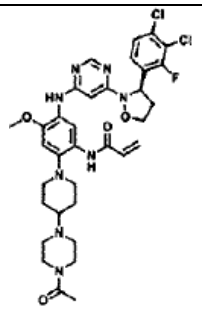
[619]

763		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.26 (s, 1H), 9.27 (s, 1H), 8.33 (s, 1H), 7.86 (s, 1H), 7.58 (dd, J = 7.1, 2.1 Hz, 1H), 7.42 (t, J = 8.8 Hz, 1H), 7.40 - 7.35 (m, 1H), 6.90 (d, J = 11.0 Hz, 1H), 6.72 (dd, J = 17.0, 10.2 Hz, 1H), 6.24 (dd, J = 17.0, 1.9 Hz, 1H), 6.11 (s, 1H), 5.70 - 5.71 (m, 1H), 5.54 (dd, J = 8.5, 5.5 Hz, 2H), 3.89 (t, J = 6.1 Hz, 1H), 3.80 (d, J = 2.6 Hz, 4H), 3.56 (s, 6H), 3.48 (s, 3H), 3.36 (dd, J = 16.4, 10.4 Hz, 2H), 3.20 (d, J = 28.8 Hz, 5H), 3.04 - 2.87 (m, 4H), 2.81 (s, 3H), 2.39 - 2.27 (m, 2H), 2.06 (s, 4H).; 679.5[M+H]$^+$	1.25
764		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.12 (s, 1H), 9.31 (s, 1H), 8.32 (s, 1H), 7.86 (s, 1H), 7.58 (dd, J = 7.1, 2.2 Hz, 1H), 7.47 - 7.34 (m, 3H), 6.96 (s, 1H), 6.67 (dd, J = 16.7, 10.6 Hz, 1H), 6.24 (dd, J = 17.1, 1.9 Hz, 1H), 6.10 (d, J = 9.8 Hz, 1H), 5.75 (dd, J = 7.7, 3.8 Hz, 1H), 5.53 (dd, J = 8.5, 5.5 Hz, 2H), 4.02 (dq, J = 18.8, 10.0, 8.8 Hz, 6H), 3.81 (s, 5H), 3.56 (s, 5H), 3.25 (s, 6H), 3.17 - 3.06 (m, 2H), 2.92 (t, J = 6.4 Hz, 2H), 2.89 - 2.69 (m, 9H), 2.47 - 2.26 (m, 3H), 2.27 - 2.02 (m, 5H).; 665.6[M+H]$^+$	1.13
765		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.38 (s, 1H), 9.29 (s, 1H), 8.34 (s, 1H), 7.32 (td, J = 9.3, 4.5 Hz, 1H), 7.26 - 7.10 (m, 3H), 6.93 (s, 1H), 6.74 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.16 (s, 1H), 5.79 - 5.71 (m, 1H), 5.66 (dd, J = 8.7, 5.6 Hz, 2H), 4.07 (q, J = 7.8 Hz, 2H), 3.81 (d, J = 2.5 Hz, 5H), 3.45 (s, 2H), 3.35 - 3.14 (m, 4H), 2.95 (dq, J = 12.0, 6.0 Hz, 3H), 2.84 (s, 6H), 2.71 (d, J = 4.9 Hz, 1H), 2.36 - 2.09 (m, 6H), 1.35 - 1.24 (m, 3H).; 635.5[M+H]$^+$	1.33
766		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	622.5[M+H]$^+$	1.36

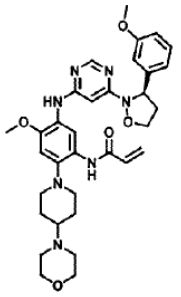
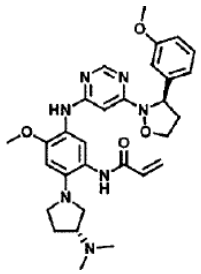
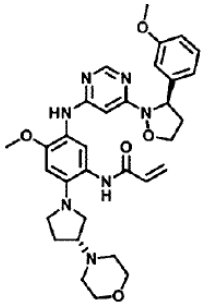
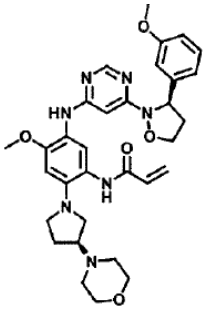
[620]

767		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.79 (s, 1H), 8.41 (d, J = 9.0 Hz, 2H), 8.32 (d, J = 1.2 Hz, 2H), 7.40 (s, 2H), 7.30 (ddd, J = 9.3, 5.8, 3.3 Hz, 2H), 6.99 (td, J = 9.2, 4.3 Hz, 2H), 6.89 (ddd, J = 8.7, 6.3, 3.6 Hz, 2H), 6.26 (dd, J = 16.9, 9.8 Hz, 1H), 5.74 (dt, J = 9.9, 1.9 Hz, 1H), 4.07 - 3.99 (m, 2H), 3.84 (d, J = 1.5 Hz, 5H), 3.42 (s, 3H), 3.08 (dd, J = 15.5, 10.3 Hz, 5H), 2.80 - 2.62 (m, 10H), 2.55 (d, J = 3.3 Hz, 3H), 2.44 (s, 2H), 2.29 (ddd, J = 12.3, 9.8, 3.9 Hz, 2H), 2.03 (s, 12H), 1.70 (q, J = 10.8, 10.3 Hz, 3H).; 649.5[M+H]$^+$	1.36
768		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.16 (s, 1H), 8.05 (s, 1H), 7.47 - 7.41 (m, 1H), 7.33 - 7.25 (m, 1H), 7.16 - 7.05 (m, 1H), 6.80 (s, 1H), 6.50 - 6.37 (m, 1H), 6.36 - 6.30 (m, 1H), 6.30 - 6.19 (m, 1H), 5.73 - 5.64 (m, 1H), 5.47 - 5.39 (m, 1H), 4.06 - 4.00 (m, 1H), 3.89 - 3.82 (m, 1H), 3.76 (s, 3H), 3.13 - 3.08 (m, 3H), 3.08 - 2.99 (m, 6H), 2.95 - 2.88 (m, 2H), 2.75 - 2.64 (m, 8H), 2.43 - 2.37 (m, 1H), 2.26 - 2.18 (m, 1H), 1.98 - 1.91 (m, 2H), 1.80 - 1.70 (m, 3H) ; 679.3[M+H]$^+$	1.33
769		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.16 (s, 1H), 8.06 (s, 1H), 7.48 - 7.40 (m, 1H), 7.31 - 7.25 (m, 1H), 7.14 - 7.04 (m, 1H), 6.80 (s, 1H), 6.51 - 6.38 (m, 1H), 6.33 (s, 1H), 6.31 - 6.18 (m, 1H), 5.74 - 5.63 (m, 1H), 5.48 - 5.36 (m, 1H), 4.07 - 4.01 (m, 1H), 3.89 - 3.81 (m, 1H), 3.77 (s, 3H), 3.11 (s, 1H), 3.05 - 3.00 (m, 3H), 2.93 - 2.85 (m, 2H), 2.77 - 2.64 (m, 5H), 2.45 (s, 6H), 2.27 - 2.10 (m, 3H), 2.05 - 1.98 (m, 2H), 1.73 - 1.64 (m, 2H) ; 665.3[M+H]$^+$	1.33
770		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.73 (s, 1H), 9.24 (d, J = 31.7 Hz, 1H), 8.28 (s, 1H), 7.93 (d, J = 12.1 Hz, 1H), 7.53 (dd, J = 8.7, 1.5 Hz, 1H), 7.41 (t, J = 8.1 Hz, 1H), 6.90 (d, J = 7.6 Hz, 1H), 6.58 (dd, J = 17.4, 10.3 Hz, 1H), 6.27 - 6.19 (m, 2H), 5.79 - 5.65 (m, 2H), 4.74 - 4.53 (m, 3H), 4.29 (d, J = 4.6 Hz, 1H), 4.20 (d, J = 10.3 Hz, 1H), 4.01 (d, J = 7.9 Hz, 1H), 3.82 (d, J = 1.7 Hz, 3H), 3.60 (s, 2H), 3.47 (d, J = 8.6 Hz, 2H), 3.38 (d, J = 6.0 Hz, 1H), 3.22 (d, J = 10.8 Hz, 2H), 2.92 - 2.72 (m, 3H), 2.31 (d, J = 11.5 Hz, 2H), 2.08 (d, J = 10.5 Hz, 3H). 684.2[M+H]$^+$	1.54

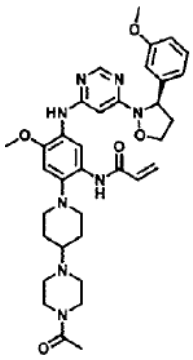
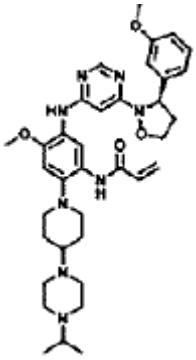
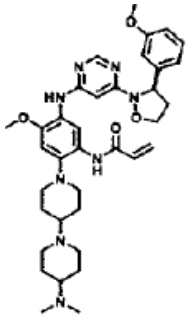
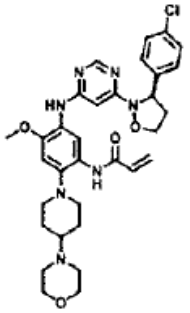
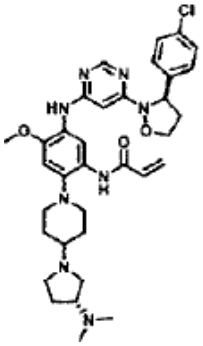
[621]

771		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	699.5[M+H]$^+$	1.47
772		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	699.3 [M+H]$^+$	1.49
773		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.61 (s, 1H), 9.13 (s, 1H), 8.27 (s, 1H), 7.97 (s, 1H), 7.53 (dd, J = 8.6, 1.5 Hz, 1H), 7.41 (t, J = 8.1 Hz, 1H), 6.90 (s, 1H), 6.66 (dd, J = 17.0, 10.3 Hz, 1H), 6.29 - 6.17 (m, 2H), 5.78 - 5.64 (m, 2H), 4.28 (d, J = 4.3 Hz, 1H), 4.11 (s, 2H), 4.00 (d, J = 8.0 Hz, 1H), 3.82 (s, 3H), 3.48 (s, 2H), 3.21 (d, J = 11.6 Hz, 3H), 2.95 - 2.88 (m, 1H), 2.72 (dd, J = 22.5, 11.6 Hz, 4H), 2.33 - 2.27 (m, 1H), 2.22 (d, J = 11.7 Hz, 2H), 2.03 (d, J = 11.5 Hz, 2H), 1.17 (d, J = 6.2 Hz, 6H). 700.5 [M+H]$^+$	1.62
774		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	713.3 [M+H]$^+$	1.54

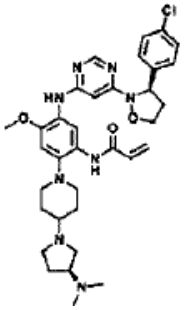
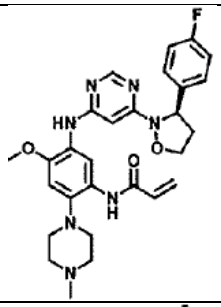
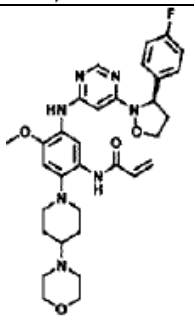
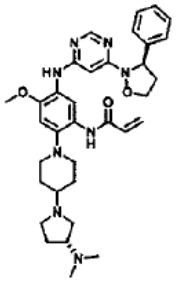
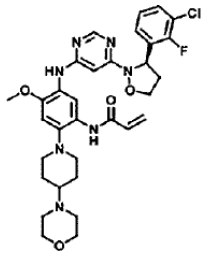
[622]

775		N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, Methanol-d4) δ 8.28 (s, 1H), 8.14 (s, 1H), 7.24 (t, J = 8.0 Hz, 1H), 6.99 (dd, J = 5.0, 3.0 Hz, 2H), 6.89 (s, 1H), 6.82 - 6.78 (m, 1H), 6.55 (dd, J = 17.0, 10.3 Hz, 1H), 6.40 - 6.32 (m, 2H), 5.79 (dd, J = 10.3, 1.5 Hz, 1H), 5.48 (dd, J = 8.5, 4.7 Hz, 1H), 4.13 (td, J = 7.8, 4.4 Hz, 1H), 3.96 (q, J = 7.9 Hz, 1H), 3.85 (s, 3H), 3.79 (d, J = 4.7 Hz, 7H), 3.17 - 3.11 (m, 2H), 2.82 - 2.74 (m, 7H), 2.56 (tt, J = 11.6, 4.0 Hz, 1H), 2.37 - 2.28 (m, 1H), 2.12 - 2.06 (m, 2H), 1.80 - 1.74 (m, 2H); 616.5[M+H]+	1.03
776		N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, Methanol-d4) δ 8.11 (s, 1H), 7.70 (s, 1H), 7.24 (t, J = 8.0 Hz, 1H), 6.99 (dd, J = 5.0, 3.0 Hz, 2H), 6.83 - 6.78 (m, 1H), 6.68 (s, 1H), 6.52 (dd, J = 17.0, 10.2 Hz, 1H), 6.36 (dd, J = 17.1, 1.7 Hz, 1H), 6.30 (s, 1H), 5.79 (dd, J = 10.1, 1.7 Hz, 1H), 5.50 - 5.46 (m, 1H), 4.12 (td, J = 7.8, 4.4 Hz, 1H), 3.93 (q, J = 7.9 Hz, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 3.42 - 3.32 (m, 5H), 2.81 - 2.73 (m, 1H), 2.59 (s, 6H), 2.37 - 2.28 (m, 2H), 2.07 - 2.01 (m, 1H); 560.5[M+H]+	1.00
777		N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, Methanol-d4) δ 8.10 (s, 1H), 7.64 (s, 1H), 7.24 (t, J = 8.0 Hz, 1H), 6.99 (dd, J = 5.1, 3.1 Hz, 2H), 6.82 - 6.78 (m, 1H), 6.64 (s, 1H), 6.52 (dd, J = 17.0, 10.2 Hz, 1H), 6.34 (dd, J = 17.0, 1.7 Hz, 1H), 6.27 (s, 1H), 5.77 (dd, J = 10.3, 1.7 Hz, 1H), 5.49 - 5.45 (m, 1H), 4.11 (td, J = 7.8, 4.4 Hz, 1H), 3.93 (q, J = 7.9 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.74 (t, J = 4.8 Hz, 4H), 3.30 - 3.32 (m, 2H), 3.30 - 3.26 (m, 2H), 2.98 (p, J = 7.3 Hz, 1H), 2.76 (tq, J = 8.0, 4.5, 4.0 Hz, 1H), 2.64 (dt, J = 10.2, 4.8 Hz, 2H), 2.55 (dt, J = 11.8, 5.1 Hz, 2H), 2.32 (ddt, J = 11.6, 7.7, 3.9 Hz, 1H), 2.23 (dtd, J = 13.8, 6.7, 2.7 Hz, 1H), 1.94 - 1.86 (m, 1H); 602.5[M+H]+	1.06
778		N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, Methanol-d4) δ 8.10 (s, 1H), 7.63 (s, 1H), 7.24 (t, J = 8.1 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.82 - 6.78 (m, 1H), 6.64 (s, 1H), 6.52 (dd, J = 17.0, 10.2 Hz, 1H), 6.30 - 6.21 (m, 2H), 5.78 (dd, J = 10.2, 1.7 Hz, 1H), 5.46 (dd, J = 8.5, 4.7 Hz, 1H), 4.11 (td, J = 7.8, 4.4 Hz, 1H), 3.92 (q, J = 7.8 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.74 (t, J = 4.8 Hz, 4H), 3.36 - 3.32 (m, 2H), 3.27 (dt, J = 9.3, 4.4 Hz, 2H), 3.00 (p, J = 7.2 Hz, 1H), 2.76 (ddt, J = 12.3, 8.0, 3.9 Hz, 1H), 2.66 (dt, J = 9.7, 4.6 Hz, 2H), 2.56 (dt, J = 11.3, 4.8 Hz, 2H), 2.32 (ddt, J = 11.7, 7.8, 3.9 Hz, 1H), 2.23 (dtd, J = 13.7, 6.8, 2.9 Hz, 1H), 1.94 - 1.87 (m, 1H); 602.5[M+H]+	1.02

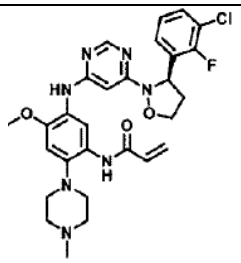
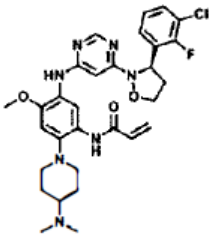
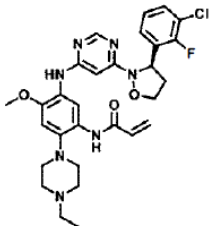
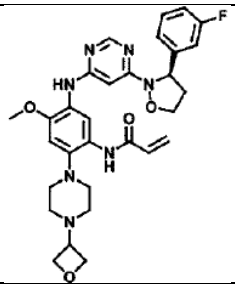
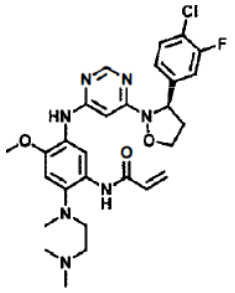
[623]

779		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, Methanol-d4) δ 8.27 (s, 1H), 8.14 (s, 1H), 7.24 (t, J = 8.1 Hz, 1H), 6.99 (dd, J = 5.0, 2.9 Hz, 2H), 6.80 (s, 1H), 6.83 - 6.78 (m, 1H), 6.54 (dd, J = 17.0, 10.3 Hz, 1H), 6.41 - 6.30 (m, 2H), 5.79 (d, J = 10.3 Hz, 1H), 5.51 - 5.45 (m, 1H), 4.13 (td, J = 7.8, 4.3 Hz, 1H), 3.96 (q, J = 7.9 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.63 (dt, J = 15.5, 5.3 Hz, 4H), 3.13 (d, J = 11.3 Hz, 2H), 2.83 - 2.72 (m, 5H), 2.60 (t, J = 5.2 Hz, 2H), 2.53 (tt, J = 11.5, 3.9 Hz, 1H), 2.38 - 2.28 (m, 1H), 2.11 (s, 3H), 2.06 - 2.00 (m, 2H), 1.83 - 1.73 (m, 2H): 657.6[M+H]+	1.12
780		N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	657.6[M+H]+	1.12
781		N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	657.7[M+H]+	1.04
782		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	620.5 [M+H]+	1.38
783		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	647.6 [M+H]+	1.12

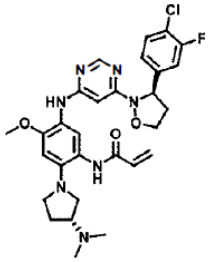
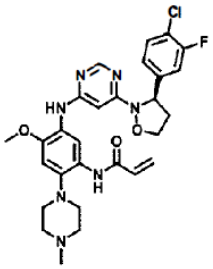
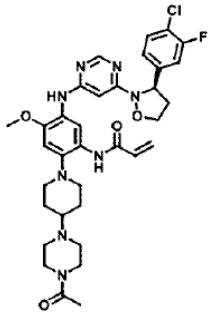
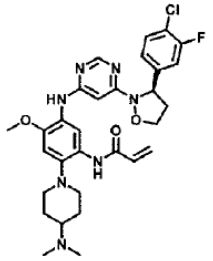
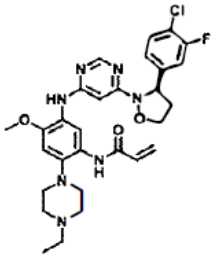
[624]

784		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	647.6 $[M+H]^+$	1.13
785		N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (s, 1H), 9.11 (s, 1H), 8.25 (s, 1H), 8.13 (s, 1H), 7.42 (dd, J = 8.6, 5.6 Hz, 2H), 7.10 (t, J = 8.8 Hz, 2H), 6.87 (s, 1H), 6.74 (dd, J = 17.0, 10.3 Hz, 1H), 6.28 - 6.15 (m, 2H), 5.76 (dd, J = 10.3, 2.0 Hz, 1H), 5.52 (dd, J = 8.6, 5.2 Hz, 1H), 4.25 - 4.21 (m, 1H), 3.97 (d, J = 7.8 Hz, 1H), 3.82 (s, 3H), 3.33 (d, J = 10.5 Hz, 3H), 3.18 (d, J = 5.9 Hz, 4H), 2.87 (d, J = 14.9 Hz, 1H), 2.83 (d, J = 4.7 Hz, 3H), 2.34 - 2.24 (m, 2H).; 534.4 $[M+H]^+$	1.28
786		N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	604.5 $[M+H]^+$	1.3
787		N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-$d6$) δ 9.71 (s, 1H), 9.23 (s, 1H), 8.27 (s, 1H), 7.90 (s, 1H), 7.37 (m, 4H), 7.29 (td, J = 5.3, 3.0 Hz, 1H), 6.91 (m, 1H), 6.64 (dd, J = 17.0, 10.2 Hz, 1H), 6.24 (dd, J = 17.1, 1.9 Hz, 1H), 6.07 (s, 1H), 5.82 - 5.70 (m, 1H), 5.51 (d, J = 9.1 Hz, 1H), 4.29 (m, 2H), 4.03 (m, 4H), 3.80 (s, 3H), 3.23 (m, 3H), 2.95 - 2.60 (m, 12H), 2.36 - 2.26 (m, 1H), 2.18 (m, 2H), 2.06 (m, 2H). ; 613.6 $[M+H]^+$	1.00
788		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.20 (s, 1H), 8.29 (d, J = 4.6 Hz, 1H), 7.92 (s, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.36 (t, J = 7.3 Hz, 1H), 7.24 (t, J = 7.9 Hz, 1H), 6.91 (s, 1H), 6.67 (dd, J = 17.3, 10.5 Hz, 1H), 6.25 (d, J = 16.6 Hz, 1H), 6.17 (s, 1H), 5.81 - 5.66 (m, 2H), 4.31 (t, J = 6.0 Hz, 1H), 4.04 (dt, J = 10.7, 5.9 Hz, 1H), 4.01 - 3.90 (m, 4H), 3.81 (s, 3H), 3.22 (d, J = 11.4 Hz, 3H), 3.18 - 3.10 (m, 3H), 3.01 - 2.90 (m, 2H), 2.78 (t, J = 12.0 Hz, 2H), 2.30 (dt, J = 12.9, 6.5 Hz, 1H), 2.21 (d, J = 11.7 Hz, 3H), 2.05 (t, J = 12.4 Hz, 2H).; 638.5[M+H]+	1.28

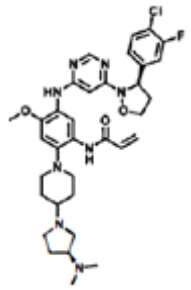
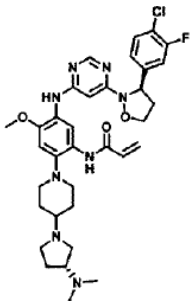
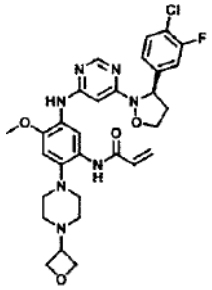
[625]

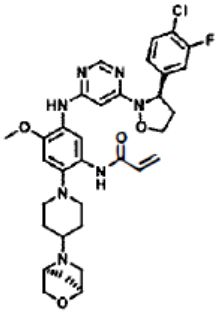
789		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d_6) δ 9.15 (d, J = 11.3 Hz, 1H), 8.26 (q, J = 5.7 Hz, 1H), 7.58 - 7.50 (m, 1H), 7.42 - 7.34 (m, 1H), 7.24 (t, J = 7.9 Hz, 1H), 6.86 (d, J = 15.2 Hz, 1H), 6.29 - 6.18 (m, 2H), 5.74 (dt, J = 13.0, 5.2 Hz, 2H), 4.32 - 4.23 (m, 1H), 4.00 (d, J = 7.6 Hz, 2H), 3.83 (d, J = 2.7 Hz, 3H), 3.80 - 3.71 (m, 4H), 3.31 (d, J = 12.4 Hz, 1H), 3.19 (dd, J = 10.3, 6.1 Hz, 4H), 3.16 - 3.07 (m, 3H), 2.82 (d, J = 4.6 Hz, 2H), 2.27 (s, 1H).: 568.5[M+H]+	1.41
790		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	: 596.5[M+H]+	1.41
791		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 9.57 (d, J = 11.0 Hz, 1H), 8.25 (d, J = 5.0 Hz, 1H), 7.54 (t, J = 7.9 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.24 (t, J = 7.9 Hz, 1H), 6.82 (t, J = 8.8 Hz, 1H), 6.66 (d, J = 20.8 Hz, 1H), 6.23 (ddd, J = 16.5, 14.4, 2.0 Hz, 1H), 6.08 (dd, J = 17.3, 10.2 Hz, 1H), 5.78 - 5.67 (m, 2H), 4.34 - 4.22 (m, 1H), 4.06 - 3.93 (m, 1H), 3.81 (d, J = 3.4 Hz, 3H), 3.75 (q, J = 6.1 Hz, 1H), 3.61 (td, J = 6.6, 3.9 Hz, 3H), 3.16 - 3.10 (m, 4H), 2.80 (dd, J = 8.1, 4.6 Hz, 6H), 2.73 (dd, J = 6.0, 3.8 Hz, 1H), 2.34 - 2.23 (m, 2H). : 596.5[M+H]+	1.39
792		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-$d6$) δ 10.64 (s, 1H), 9.68 (s, 1H), 9.16 (d, J = 10.0 Hz, 1H), 8.29 (s, 1H), 8.06 (s, 1H), 7.42 (td, J = 7.9, 6.1 Hz, 1H), 7.20 (t, J = 10.1 Hz, 2H), 7.17 - 7.08 (m, 1H), 6.88 (s, 1H), 6.67 (dd, J = 16.9, 10.0 Hz, 1H), 6.25 (dd, J = 17.0, 2.3 Hz, 1H), 5.81 - 5.69 (m, 1H), 5.53 (t, J = 7.0 Hz, 1H), 4.81 (d, J = 6.5 Hz, 3H), 4.66 (t, J = 5.3 Hz, 2H), 4.52 (s, 1H), 4.28 (s, 1H), 4.02 (s, 1H), 3.82 (d, J = 2.3 Hz, 3H), 3.57 (d, J = 24.1 Hz, 3H), 3.36 (s, 1H), 3.24 (s, 3H), 3.12 (d, J = 11.4 Hz, 1H), 2.91 (s, 1H). : 576.5[M+H]+	1.29
793		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.09 (s, 1H), 7.57 (s, 1H), 7.38 (t, J = 7.9 Hz, 1H), 7.18 (dd, J = 10.1, 2.0 Hz, 1H), 7.10 (dd, J = 8.3, 2.0 Hz, 1H), 6.92 (s, 1H), 6.71 (dd, J = 16.9, 10.2 Hz, 1H), 6.32 (dd, J = 16.9, 1.6 Hz, 1H), 5.97 (s, 1H), 5.73 (dd, J = 10.3, 1.6 Hz, 1H), 5.44 (t, J = 7.1 Hz, 1H), 4.32 (td, J = 7.5, 3.9 Hz, 1H), 4.07 (q, J = 7.7 Hz, 1H), 3.80 (s, 3H), 3.44 (t, J = 5.7 Hz, 2H), 3.27 (t, J = 5.6 Hz, 2H), 3.20 (s, 1H), 2.94 (q, J = 8.9, 7.3 Hz, 1H), 2.85 - 2.73 (m, 6H), 2.67 (s, 3H), 2.41 - 2.28 (m, 1H).: 571.3[M+H]+	1.31

[626]

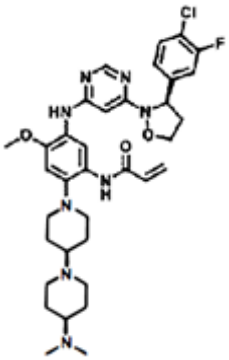
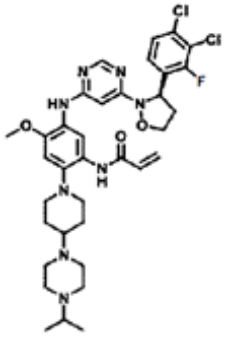
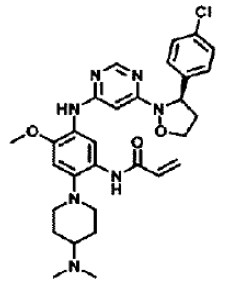
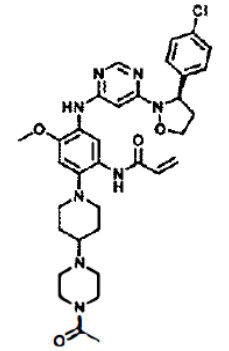
794		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, MeOD) δ 8.04 (s, 1H), 7.45 - 7.27 (m, 2H), 7.17 (dd, J = 10.1, 2.1 Hz, 1H), 7.00 (dd, J = 8.3, 2.0 Hz, 1H), 6.65 (s, 1H), 6.60 (dd, J = 17.0, 10.3 Hz, 1H), 6.28 (dd, J = 17.0, 1.7 Hz, 1H), 5.95 (s, 1H), 5.72 (dd, J = 10.3, 1.7 Hz, 1H), 5.43 (d, J = 7.3 Hz, 1H), 4.30 (td, J = 7.6, 4.2 Hz, 1H), 4.06 (td, J = 8.2, 6.6 Hz, 1H), 3.91 (q, J = 6.5 Hz, 1H), 3.77 (s, 3H), 3.50 (dd, J = 10.9, 4.8 Hz, 1H), 3.54 - 3.43 (m, 2H), 3.20 (s, 1H), 3.19 - 3.13 (m, 1H), 2.97 - 2.90 (m, 1H), 2.86 (d, J = 10.8 Hz, 6H), 2.47 - 2.30 (m, 2H), 2.22 (dd, J = 13.0, 6.7 Hz, 1H).; 583.4[M+H]+	1.24
795		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, MeOD) δ 8.08 (s, 1H), 7.87 (s, 1H), 7.38 (t, J = 7.9 Hz, 1H), 7.18 (dd, J = 10.1, 2.0 Hz, 1H), 7.10 (dd, J = 8.3, 2.0 Hz, 1H), 6.91 (s, 1H), 6.59 (dd, J = 16.9, 10.2 Hz, 1H), 6.30 (dd, J = 17.0, 1.6 Hz, 1H), 5.95 (s, 1H), 5.73 (dd, J = 10.2, 1.6 Hz, 1H), 5.42 (d, J = 7.7 Hz, 1H), 4.31 (td, J = 7.6, 4.1 Hz, 1H), 4.07 (q, J = 7.9 Hz, 1H), 3.78 (s, 3H), 3.53 (d, J = 11.9 Hz, 2H), 3.42 - 3.31 (m, 2H), 3.22 - 3.17 (m, 6H), 2.90 (s, 3H), 2.41 - 2.29 (m, 1H).; 568.3[M+H]+	1.27
796		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, MeOD) δ 8.20 (s, 1H), 8.06 (s, 1H), 7.33 (t, J = 8.0 Hz, 1H), 7.22 (dd, J = 10.5, 2.0 Hz, 1H), 7.15 (dd, J = 8.5, 2.0 Hz, 1H), 6.80 (s, 1H), 6.44 (dd, J = 17.0, 10.3 Hz, 1H), 6.34 (s, 1H), 6.24 (dd, J = 17.0, 1.6 Hz, 1H), 5.60 (dd, J = 10.2, 1.6 Hz, 1H), 5.44 (dd, J = 8.7, 4.7 Hz, 1H), 4.10 - 3.98 (m, 1H), 3.86 (d, J = 8.0 Hz, 1H), 3.76 (s, 3H), 3.50 (dt, J = 16.1, 5.4 Hz, 4H), 3.03 (d, J = 11.4 Hz, 2H), 2.76 - 2.61 (m, 3H), 2.60 - 2.45 (m, 4H), 2.35 (s, 1H), 2.28 - 2.13 (m, 1H), 2.01 (s, 3H), 1.91 (d, J = 11.7 Hz, 2H), 1.74 - 1.60 (m, 2H).; 679.4[M+H]+	1.28
797		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, MeOD) δ 8.24 (s, 1H), 7.92 (s, 1H), 7.51 (t, J = 7.9 Hz, 1H), 7.31 (dd, J = 10.0, 2.0 Hz, 1H), 7.26 - 7.05 (m, 2H), 6.70 (dd, J = 17.0, 10.2 Hz, 1H), 6.47 (dd, J = 16.8, 1.5 Hz, 1H), 6.10 (s, 1H), 5.99 - 5.80 (m, 1H), 5.54 (t, J = 7.1 Hz, 1H), 4.45 (td, J = 7.5, 3.9 Hz, 1H), 4.20 (q, J = 7.7 Hz, 1H), 3.93 (s, 3H), 3.75 (p, J = 6.6 Hz, 1H), 3.65 - 3.34 (m, 4H), 3.13 - 3.05 (m, 1H), 2.98 (s, 6H), 2.91 (d, J = 3.1 Hz, 1H), 2.48 (dd, J = 13.0, 6.6 Hz, 1H), 2.35 (d, J = 12.3 Hz, 2H), 2.27 - 2.12 (m, 2H).; 597.4[M+H]+	1.28
798		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, MeOD) δ 8.08 (s, 1H), 7.88 (s, 1H), 7.38 (t, J = 7.9 Hz, 1H), 7.18 (dd, J = 10.1, 2.0 Hz, 1H), 7.10 (dd, J = 8.3, 2.0 Hz, 1H), 6.92 (s, 1H), 6.60 (dd, J = 16.9, 10.3 Hz, 1H), 6.29 (dd, J = 16.9, 1.6 Hz, 1H), 5.96 (s, 1H), 5.73 (dd, J = 10.2, 1.6 Hz, 1H), 5.42 (d, J = 7.4 Hz, 1H), 4.31 (td, J = 7.6, 4.2 Hz, 1H), 4.07 (q, J = 7.9 Hz, 1H), 3.78 (s, 3H), 3.58 (d, J = 11.9 Hz, 2H), 3.41 - 3.27 (m, 2H), 3.21 (tt, J = 4.4, 2.1 Hz, 7H), 3.00 - 2.84 (m, 1H), 2.42 - 2.23 (m, 1H), 1.34 (t, J = 7.3 Hz, 3H).; 582.3[M+H]+	1.28

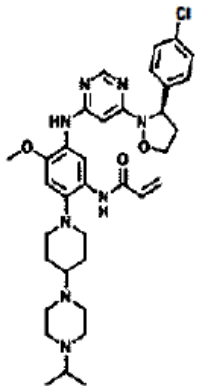
[627]

799		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.09 (s, 1H), 7.80 (s, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.14 (ddd, *J* = 31.8, 9.2, 2.0 Hz, 2H), 6.98 (s, 1H), 6.56 (dd, *J* = 16.9, 10.2 Hz, 1H), 6.33 (dd, *J* = 17.0, 1.6 Hz, 1H), 5.95 (s, 1H), 5.75 (dd, *J* = 10.2, 1.6 Hz, 1H), 5.41 (s, 1H), 4.32 (td, *J* = 7.5, 4.1 Hz, 1H), 4.08 (td, *J* = 8.3, 6.6 Hz, 2H), 3.79 (s, 5H), 3.66 - 3.40 (m, 3H), 3.38 - 3.24 (m, 3H), 3.06 - 2.77 (m, 9H), 2.60 (s, 1H), 2.33 (ddd, *J* = 37.1, 18.9, 9.9 Hz, 4H), 2.13 (s, 2H).; 666.5[M+H]$^+$	1.17
800		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-*d6*) δ 10.36 (s, 1H), 9.39 (s, 1H), 8.35 (s, 1H), 7.85 (s, 1H), 7.60 (t, *J* = 8.1 Hz, 1H), 7.42 (dd, *J* = 10.4, 2.0 Hz, 1H), 7.25 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.98 (d, *J* = 7.0 Hz, 1H), 6.72 (dt, *J* = 17.1, 8.4 Hz, 1H), 6.25 (dd, *J* = 17.0, 1.9 Hz, 1H), 6.13 (s, 1H), 5.81 - 5.73 (m, 1H), 5.56 (dd, *J* = 8.5, 5.4 Hz, 1H), 4.32 (td, *J* = 7.6, 4.4 Hz, 2H), 4.21 (s, 1H), 4.05 (dq, *J* = 26.8, 9.7, 8.7 Hz, 3H), 3.70 - 3.50 (m, 2H), 3.40 (s, 1H), 3.28 (d, *J* = 12.1 Hz, 2H), 2.95 (tq, *J* = 12.2, 7.3, 5.0 Hz, 1H), 2.88 - 2.75 (m, 8H), 2.48 - 2.40 (m, 1H), 2.33 (dtd, *J* = 12.7, 7.5, 5.2 Hz, 1H), 2.15 (dd, *J* = 30.8, 18.7 Hz, 4H).: 665.5[M+H]$^+$	1.37
801		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.22 (dd, *J* = 15.0, 7.8 Hz, 1H), 8.32 (d, *J* = 4.0 Hz, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.42 (dd, *J* = 10.4, 2.0 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 6.93 (d, *J* = 3.9 Hz, 1H), 6.73 (dt, *J* = 17.2, 8.5 Hz, 1H), 6.25 (dt, *J* = 17.1, 2.5 Hz, 1H), 6.08 (d, *J* = 8.3 Hz, 1H), 5.83 - 5.71 (m, 1H), 5.54 (dd, *J* = 8.5, 5.5 Hz, 1H), 4.81 (q, *J* = 7.8 Hz, 2H), 4.69 (h, *J* = 7.8, 6.3 Hz, 1H), 4.56 (s, 1H), 4.31 (tt, *J* = 7.5, 3.8 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 1H), 3.83 (s, 3H), 3.63 (s, 1H), 3.56 - 3.47 (m, 1H), 2.98 - 2.87 (m, 1H), 2.40 (d, *J* = 7.2 Hz, 7H).: 610.4[M+H]$^+$	1.46

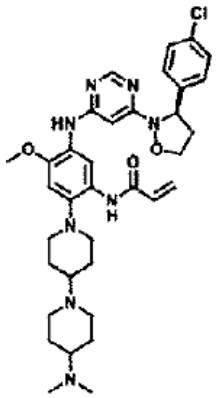
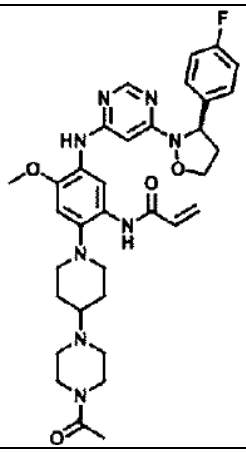
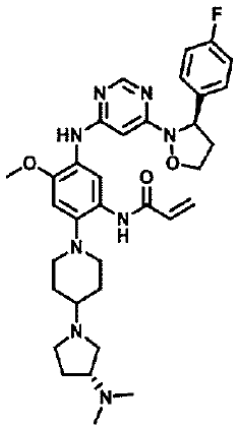
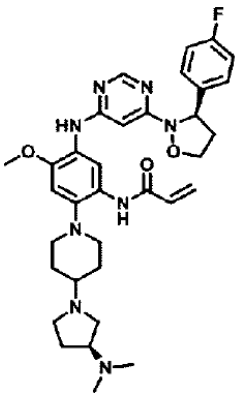
802		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.17 (s, 1H), 9.30 (d, J = 32.5 Hz, 1H), 8.33 (t, J = 2.0 Hz, 1H), 7.85 (d, J = 12.8 Hz, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.42 (dd, J = 10.4, 2.0 Hz, 1H), 7.30 - 7.16 (m, 1H), 6.92 (d, J = 7.2 Hz, 1H), 6.61 (dt, J = 17.7, 10.2 Hz, 1H), 6.25 (dt, J = 17.1, 2.2 Hz, 1H), 6.13 (s, 1H), 5.76 (dd, J = 10.1, 1.8 Hz, 2H), 5.55 (dd, J = 8.6, 5.5 Hz, 1H), 4.80 - 4.40 (m, 3H), 4.30 (q, J = 6.9 Hz, 1H), 4.21 (d, J = 10.3 Hz, 1H), 4.06 (q, J = 5.4, 3.2 Hz, 1H), 3.82 (d, J = 2.2 Hz, 3H), 3.70 (dd, J = 9.6, 5.2 Hz, 1H), 3.57 - 3.08 (m, 5H), 3.02 - 2.63 (m, 3H), 2.32 (dtd, J = 12.8, 7.5, 5.0 Hz, 2H), 2.20 - 1.91 (m, 5H).; 650.4[M+H]$^+$	1.46

[628]

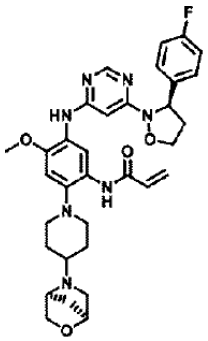
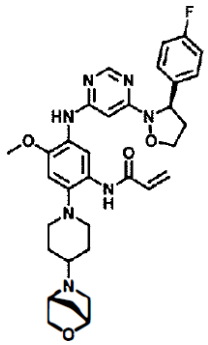
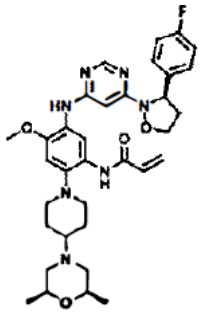
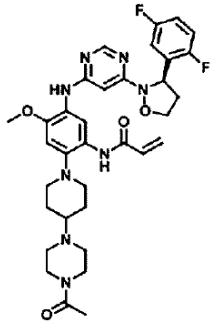
803		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.37 - 9.18 (m, 1H), 8.34 (s, 1H), 7.87 (s, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.42 (dd, *J* = 10.4, 2.0 Hz, 1H), 7.24 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.92 (s, 1H), 6.78 (dd, *J* = 16.9, 10.2 Hz, 1H), 6.25 (dd, *J* = 16.9, 2.0 Hz, 1H), 6.18 - 6.03 (m, 1H), 5.76 (dd, *J* = 10.1, 2.1 Hz, 1H), 5.55 (dd, *J* = 8.5, 5.4 Hz, 1H), 4.31 (td, *J* = 7.6, 4.4 Hz, 1H), 4.07 (q, *J* = 7.7 Hz, 1H), 3.81 (s, 3H), 3.62 (d, *J* = 11.6 Hz, 2H), 3.52 (s, 1H), 3.38 (d, *J* = 12.2 Hz, 1H), 3.24 (d, *J* = 11.3 Hz, 2H), 3.20 - 3.08 (m, 2H), 3.07 - 2.90 (m, 2H), 2.81 (d, *J* = 13.2 Hz, 2H), 2.71 (d, *J* = 4.8 Hz, 6H), 2.33 (dd, *J* = 12.2, 5.7 Hz, 5H), 2.22 - 2.03 (m, 4H).: 679.6[M+H]$^+$	1.34
804		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.87 (s, 1H), 9.19 (s, 1H), 8.29 (s, 1H), 7.98 (s, 1H), 7.53 (dd, *J* = 8.6, 1.5 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 6.90 (s, 1H), 6.71 (dd, *J* = 16.9, 10.2 Hz, 1H), 6.25 (dd, *J* = 17.0, 2.0 Hz, 2H), 5.73 (ddd, *J* = 25.8, 9.3, 3.8 Hz, 2H), 4.30 (d, *J* = 4.1 Hz, 1H), 4.03 (d, *J* = 7.9 Hz, 3H), 3.82 (s, 3H), 3.60 (t, *J* = 6.4 Hz, 2H), 3.48 (d, *J* = 7.0 Hz, 2H), 3.22 (d, *J* = 11.3 Hz, 3H), 3.00 - 2.88 (m, 2H), 2.85 - 2.76 (m, 2H), 2.31 (dd, *J* = 13.2, 6.0 Hz, 2H), 2.21 - 2.02 (m, 5H), 1.32 (d, *J* = 6.6 Hz, 6H).: 713.6 [M+H]$^+$	1.53
805		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, Chloroform-d) δ 8.78 (s, 1H), 8.43 (s, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.47 (s, 1H), 7.39 (d, J = 8.5 Hz, 2H), 7.30 (d, J = 8.5 Hz, 2H), 6.73 (s, 1H), 6.64 (s, 1H), 6.43 - 6.28 (m, 2H), 5.75 (dd, J = 8.9, 2.7 Hz, 1H), 5.65 (dd, J = 8.6, 4.5 Hz, 1H), 4.14 (td, J = 8.0, 4.4 Hz, 1H), 4.05 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.11 (d, J = 11.4 Hz, 2H), 2.82 - 2.71 (m, 4H), 2.57 (s, 6H), 2.33 (dp, J = 12.4, 4.4, 3.9 Hz, 1H), 2.12 (d, J = 12.4 Hz, 2H), 1.86 (tt, J = 13.0, 7.6 Hz, 2H): 578.5[M+H]+	1.21
806		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-	1H NMR (400 MHz, Methanol-d4) δ 8.26 (d, J = 3.5 Hz, 1H), 8.14 (s, 1H), 7.42 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.5 Hz, 2H), 6.90 (s, 1H), 6.54 (dd, J = 17.0, 10.2 Hz, 1H), 6.41 - 6.31 (m, 2H), 5.79 (d, J = 10.3 Hz, 1H), 5.52 (dd, J = 8.6, 4.7 Hz, 1H), 4.13 (td, J = 7.9, 4.3 Hz, 1H), 3.96 (q, J = 7.9 Hz, 1H), 3.85 (s, 3H), 3.62 (dt, J = 14.9, 5.0 Hz, 4H), 3.17 - 3.10 (m, 2H), 2.78 (ddd, J = 11.9, 7.8, 4.2 Hz, 3H), 2.70 (dt, J = 21.8, 5.2 Hz, 4H), 2.50 (tt, J = 11.4, 3.8 Hz, 1H), 2.35 - 2.28 (m, 1H), 2.11 (s, 3H), 2.06 - 2.00 (m, 2H), 1.78 (dd, J = 12.4, 4.0 Hz, 2H): 661.5[M+H]+	1.22

		methoxyphenyl)acrylamide		
807		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	661.6[M+H]+	1.18

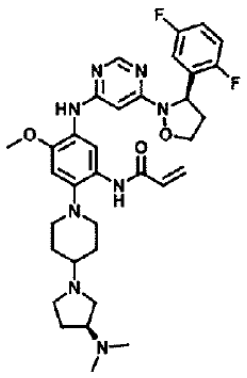
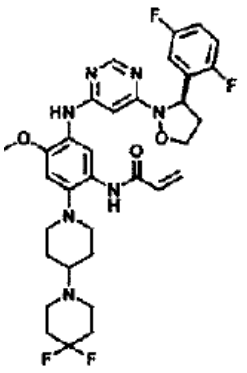
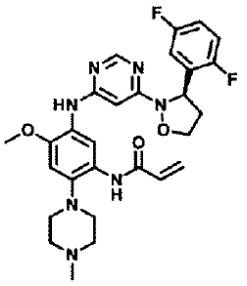
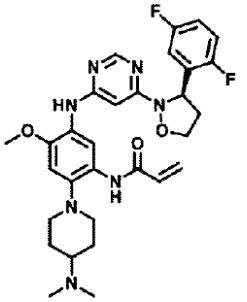
[629]

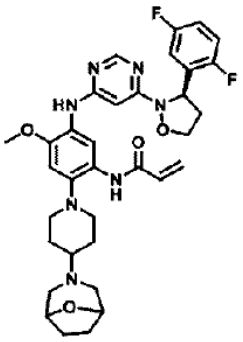
808		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide	661.6[M+H]+	1.13
809		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.00 (s, 1H), 9.21 (s, 1H), 8.30 (s, 1H), 7.80 (s, 1H), 7.41 (dt, J = 6.5, 2.7 Hz, 2H), 7.18 (d, J = 8.8 Hz, 2H), 6.90 (s, 1H), 6.70 (dd, J = 17.0, 10.1 Hz, 1H), 6.25 (dd, J = 17.0, 1.9 Hz, 1H), 6.08 (s, 1H), 5.75 (dd, J = 10.0, 2.0 Hz, 1H), 5.53 (dd, J = 8.5, 5.2 Hz, 1H), 4.49 (d, J = 13.6 Hz, 1H), 4.33 - 4.28 (m, 1H), 4.04 (s, 1H), 3.80 (s, 3H), 3.48 (d, J = 5.1 Hz, 2H), 3.19 (d, J = 17.9 Hz, 6H), 3.04 - 2.88 (m, 4H), 2.78 (s, 2H), 2.30 (d, J = 7.6 Hz, 2H), 2.20 (d, J = 11.7 Hz, 2H), 2.06 (s, 3H).; 645.6 [M+H]$^+$	1.12
810		N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H), 9.34 (s, 1H), 8.33 (s, 1H), 7.83 (s, 1H), 7.40 (dd, J = 8.6, 5.5 Hz, 2H), 7.20 (t, J = 8.8 Hz, 2H), 6.96 (d, J = 7.6 Hz, 1H), 6.69 (dd, J = 17.0, 10.0 Hz, 1H), 6.29 - 6.23 (m, 1H), 6.06 (s, 1H), 5.79 - 5.72 (m, 1H), 5.53 (dd, J = 8.4, 5.4 Hz, 1H), 4.33 (s, 1H), 4.08 (d, J = 7.6 Hz, 2H), 4.00 (d, J = 3.7 Hz, 2H), 3.80 (d, J = 5.9 Hz, 1H), 3.75 (s, 1H), 3.64 (d, J = 8.8 Hz, 1H), 3.59 - 3.51 (m, 1H), 3.39 (s, 1H), 3.28 - 3.21 (m, 2H), 2.95 (td, J = 7.5, 4.1 Hz, 1H), 2.85 - 2.75 (m, 8H), 2.46 - 2.38 (m, 1H), 2.31 (d, J = 7.6 Hz, 1H), 2.23 - 2.08 (m, 4H), 1.65 - 1.56 (m, 1H), 1.47 - 1.37 (m, 1H).; 631.3 [M+H]$^+$	1.04
811		N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.87 (s, 1H), 9.26 (s, 1H), 8.29 (s, 1H), 7.89 (s, 1H), 7.46 - 7.37 (m, 2H), 7.20 (t, J = 8.8 Hz, 2H), 6.93 (d, J = 7.6 Hz, 1H), 6.66 (dd, J = 17.0, 10.2 Hz, 1H), 6.24 (dd, J = 16.9, 1.9 Hz, 1H), 6.11 - 5.97 (m, 1H), 5.76 (d, J = 10.7 Hz, 1H), 5.52 (t, J = 7.0 Hz, 1H), 4.29 (d, J = 4.8 Hz, 1H), 4.06 - 3.96 (m, 3H), 3.93 (s, 2H), 3.81 (s, 3H), 3.30 (s, 1H), 3.20 (d, J = 25.1 Hz, 4H), 3.07 - 2.99 (m, 1H), 2.87 - 2.81 (m, 6H), 2.72 (d, J = 4.9 Hz, 2H), 2.33 - 2.26 (m, 2H), 2.20 - 2.01 (m, 4H).; 631.3 [M+H]$^+$	1.03

[630]

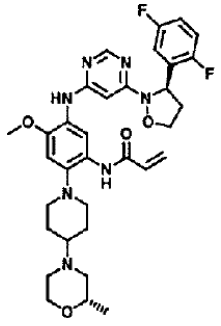
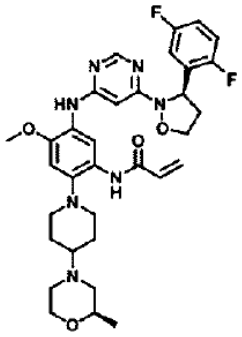
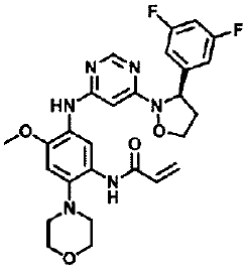
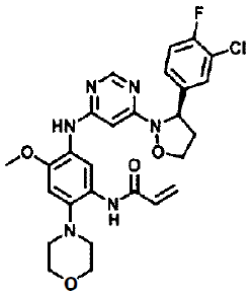
812		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	616.3 $[M+H]^+$	1.11
813		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.08 (s, 1H), 9.28 (d, J = 30.5 Hz, 1H), 8.32 (s, 1H), 7.85 (d, J = 13.4 Hz, 1H), 7.44 - 7.36 (m, 2H), 7.20 (t, J = 8.8 Hz, 2H), 6.91 (d, J = 7.5 Hz, 1H), 6.69 - 6.54 (m, 1H), 6.24 (dd, J = 17.0, 2.1 Hz, 1H), 6.07 (s, 1H), 5.79 - 5.71 (m, 1H), 5.53 (dd, J = 8.5, 5.3 Hz, 1H), 4.73 - 4.53 (m, 3H), 4.31 (d, J = 4.5 Hz, 1H), 4.19 (s, 1H), 4.05 (s, 1H), 3.81 (s, 3H), 3.73 - 3.67 (m, 2H), 3.52 - 3.42 (m, 2H), 3.23 (d, J = 10.8 Hz, 2H), 2.95 - 2.71 (m, 4H), 2.32 (t, J = 3.9 Hz, 2H), 2.11 - 2.01 (m, 3H).; 616.3 $[M+H]^+$	1.13
814		N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	632.3 $[M+H]^+$	1.18
815		N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.75 (s, 1H), 10.12 (s, 1H), 9.24 (s, 1H), 8.32 (s, 1H), 7.89 (s, 1H), 7.32 (td, J = 9.4, 4.4 Hz, 1H), 7.24 - 7.19 (m, 1H), 7.16 (ddt, J = 9.1, 5.9, 2.7 Hz, 1H), 6.91 (s, 1H), 6.70 (dd, J = 17.0, 10.1 Hz, 1H), 6.24 (dd, J = 17.0, 1.9 Hz, 1H), 5.75 (dd, J = 10.2, 1.9 Hz, 1H), 5.66 (dd, J = 8.7, 5.6 Hz, 1H), 4.53 - 4.46 (m, 2H), 4.32 (td, J = 7.6, 4.0 Hz, 3H), 4.09 - 3.96 (m, 4H), 3.81 (s, 4H), 3.73 (t, J = 13.0 Hz, 2H), 3.35 (t, J = 13.1 Hz, 2H), 3.29 - 3.17 (m, 4H), 2.96 (dtd, J = 19.3, 11.7, 9.7, 4.7 Hz, 3H), 2.80 (s, 2H), 2.06 (s, 4H).; 663.6$[M+H]^+$	1.18

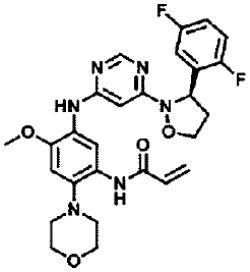
[631]

816		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.77 (s, 1H), 9.14 (s, 1H), 8.29 (s, 1H), 7.96 (s, 1H), 7.32 (td, J = 9.3, 4.4 Hz, 1H), 7.26 - 7.13 (m, 2H), 6.88 (d, J = 13.3 Hz, 1H), 6.68 (dd, J = 16.9, 10.2 Hz, 1H), 6.26 (d, J = 1.9 Hz, 1H), 5.78 - 5.72 (m, 1H), 5.67 (dd, J = 8.7, 5.5 Hz, 1H), 4.01 (q, J = 7.8 Hz, 6H), 3.81 (s, 5H), 3.71 - 3.60 (m, 3H), 3.43 (s, 2H), 3.20 (t, J = 12.0 Hz, 5H), 2.91 (dt, J = 11.8, 4.7 Hz, 2H), 2.83 - 2.55 (m, 5H), 2.44 - 2.16 (m, 6H), 2.05 (d, J = 11.9 Hz, 2H).; 640.5[M+H]$^+$	1.10
817		N-(2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	656.5[M+H]$^+$	1.27
818		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.91 (s, 1H), 8.53 (s, 1H), 8.38 (d, J = 1.0 Hz, 1H), 7.37 - 7.28 (m, 1H), 7.03 - 6.94 (m, 2H), 6.93 - 6.86 (m, 1H), 6.78 (d, J = 16.4 Hz, 2H), 6.37 (dd, J = 17.0, 1.6 Hz, 1H), 6.27 (dd, J = 16.9, 10.0 Hz, 1H), 5.90 (dd, J = 8.8, 4.4 Hz, 1H), 5.75 (dd, J = 10.0, 1.6 Hz, 1H), 4.16 - 4.02 (m, 2H), 3.85 (s, 3H), 2.95 - 2.89 (m, 4H), 2.87 - 2.79 (m, 1H), 2.40 (s, 3H), 2.34 - 2.25 (m, 1H), 1.66 - 1.62 (m, 4H). ; 552.4 [M+H]$^+$	1.18
819		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-	^{1}H NMR (400 MHz, Chloroform-d) δ 8.88 (s, 1H), 8.46 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.37 - 7.28 (m, 1H), 7.03 - 6.97 (m, 1H), 6.95 (s, 1H), 6.93 - 6.87 (m, 1H), 6.76 (d, J = 2.4 Hz, 2H), 6.41 - 6.32 (m, 1H), 6.26 (dd, J = 16.9, 9.9 Hz, 1H), 5.90 (dd, J = 8.8, 4.4 Hz, 1H), 5.74 (dd, J = 9.9, 1.6 Hz, 1H), 4.16 - 4.05 (m, 2H), 3.85 (s, 3H), 3.08 (d, J = 11.5 Hz, 2H), 2.88 - 2.80 (m, 1H), 2.79 - 2.70 (m, 2H), 2.43 (s, 6H), 2.32 - 2.25 (m, 2H), 2.09 (d, J = 12.6 Hz, 2H), 1.74 - 1.70 (m, 2H). ; 580.4 [M+H]$^+$	1.19

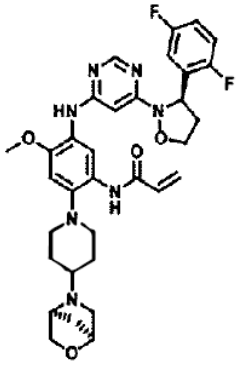
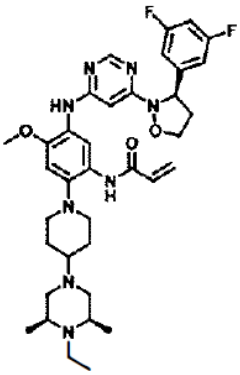
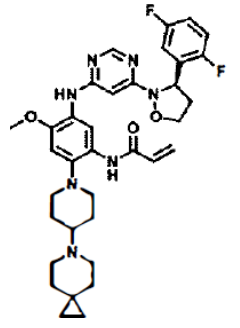
		methoxyphenyl)acrylamide		
820		N-(2-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	: 648.5 $[M+H]^+$	1.25

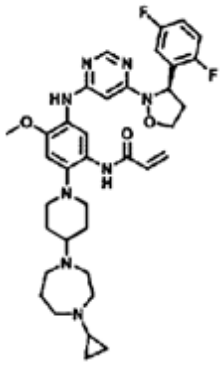
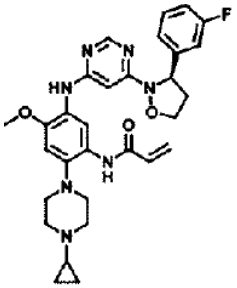
[632]

821		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	636.5 $[M+H]^+$	1.23
822		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	636.5 $[M+H]^+$	1.22
823		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.34 (s, 1H), 8.19 (s, 1H), 7.07 (d, J = 6.7 Hz, 2H), 6.95 (s, 1H), 6.87 - 6.80 (m, 1H), 6.56 (dd, J = 16.9, 10.2 Hz, 1H), 6.48 (s, 1H), 6.36 (dd, J = 17.0, 1.5 Hz, 1H), 5.81 (d, J = 11.5 Hz, 1H), 5.59 - 5.54 (m, 1H), 4.15 (td, J = 7.9, 4.3 Hz, 1H), 3.98 (dd, J = 16.0, 8.0 Hz, 1H), 3.90 (d, J = 5.9 Hz, 7H), 2.98 - 2.91 (m, 4H), 2.88 - 2.79 (m, 1H), 2.41 - 2.29 (m, 1H), : 539.4 $[M+H]^+$	1.46
824		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.34 (s, 1H), 8.18 (s, 1H), 7.58 - 7.54 (m, 1H), 7.45 - 7.37 (m, 1H), 7.22 (d, J = 8.8 Hz, 1H), 6.95 (s, 1H), 6.60 - 6.53 (m, 1H), 6.48 (s, 1H), 6.36 (dd, J = 17.0, 1.5 Hz, 1H), 5.81 (d, J = 10.3 Hz, 1H), 5.55 (dd, J = 8.4, 4.9 Hz, 1H), 4.16 (td, J = 7.8, 4.1 Hz, 1H), 3.98 (q, J = 8.0 Hz, 1H), 3.90 (d, J = 5.5 Hz, 7H), 2.98 - 2.91 (m, 4H), 2.82 (dtd, J = 12.2, 8.0, 4.2 Hz, 1H), 2.34 (ddd, J = 16.4, 10.4, 6.5 Hz, 1H), : 555.4 $[M+H]^+$	1.50

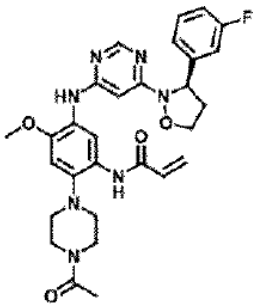
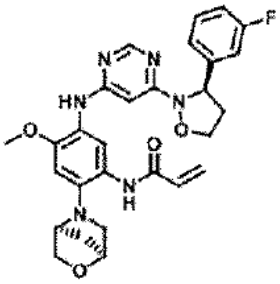
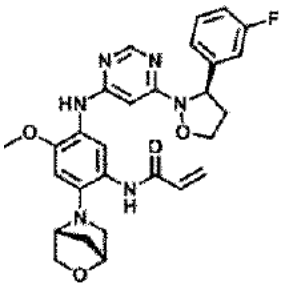
825		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.35 (s, 1H), 8.19 (s, 1H), 7.26 (ddd, *J* = 9.1, 5.8, 3.2 Hz, 1H), 7.15 (td, *J* = 9.3, 4.3 Hz, 1H), 7.07 - 7.00 (m, 1H), 6.95 (s, 1H), 6.61 - 6.49 (m, 2H), 6.36 (dd, *J* = 17.0, 1.5 Hz, 1H), 5.84 - 5.73 (m, 2H), 4.15 (td, *J* = 7.9, 4.2 Hz, 1H), 4.00 (q, *J* = 8.0 Hz, 1H), 3.92 - 3.86 (m, 7H), 2.98 - 2.93 (m, 4H), 2.86 (ddd, *J* = 16.7, 8.2, 4.2 Hz, 1H), 2.34 - 2.22 (m, 1H). ; 539.4 [M+H]$^+$	1.46

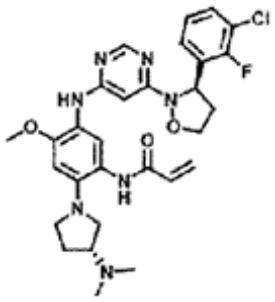
[633]

826		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.29 - 7.21 (m, 1H), 7.20 - 7.10 (m, 1H), 7.08 - 7.00 (m, 1H), 6.94 (s, 1H), 6.62 - 6.46 (m, 2H), 6.41 - 6.31 (m, 1H), 5.87 - 5.70 (m, 2H), 4.21 - 4.13 (m, 3H), 4.02 - 3.96 (m, 1H), 3.90 (s, 3H), 3.80 - 3.72 (m, 1H), 3.19 - 3.13 (m, 2H), 3.02 - 2.91 (m, 2H), 2.90 - 2.80 (m, 3H), 2.32 - 2.23 (m, 1H), 2.20 - 2.13 (m, 1H), 2.13 - 2.07 (m, 1H), 2.07 - 2.02 (m, 2H), 1.86 - 1.76 (m, 2H) ; 634.3[M+H]$^+$	1.22
827		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((3S,5R)-4-ethyl-3,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.18 (s, 1H), 7.11 - 7.01 (m, 2H), 6.92 (s, 1H), 6.90 - 6.78 (m, 1H), 6.64 - 6.50 (m, 1H), 6.46 (s, 1H), 6.41 - 6.31 (m, 1H), 5.86 - 5.78 (m, 1H), 5.61 - 5.51 (m, 1H), 4.18 - 4.13 (m, 1H), 4.00 - 3.94 (m, 1H), 3.88 (s, 3H), 3.30 - 3.27 (m, 3H), 3.24 - 3.13 (m, 6H), 2.86 - 2.76 (m, 4H), 2.60 - 2.52 (m, 1H), 2.43 - 2.32 (m, 3H), 1.84 - 1.76 (m, 2H), 1.35 - 1.33 (m, 6H), 1.25 - 1.21 (m, 3H) ; 677.4[M+H]$^+$	1.23
828		N-(2-(4-(6-azaspiro[2.5]octan-6-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.31 (s, 1H), 8.19 (s, 1H), 7.31 - 7.21 (m, 1H), 7.21 - 7.10 (m, 1H), 7.08 - 7.00 (m, 1H), 6.93 (s, 1H), 6.65 - 6.48 (m, 2H), 6.41 - 6.33 (m, 1H), 5.86 - 5.72 (m, 2H), 4.19 - 4.12 (m, 1H), 4.01 - 3.96 (m, 1H), 3.90 (s, 3H), 3.31 - 3.21 (m, 5H), 2.96 - 2.79 (m, 4H), 2.36 - 2.15 (m, 4H), 2.12 - 1.99 (m, 3H), 1.82 - 1.68 (m, 3H), 0.53 (s, 4H) ; 646.3[M+H]$^+$	1.33

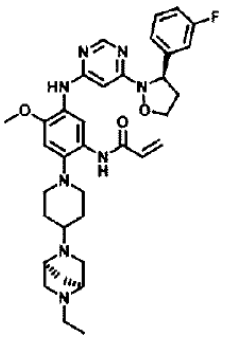
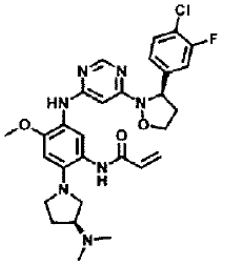
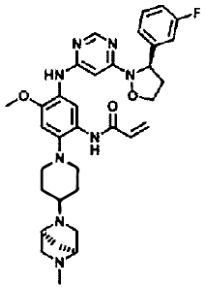
829		N-(2-(4-(4-cyclopropyl-1,4-diazepane-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.25 (d, J = 3.8 Hz, 1H), 8.11 (s, 1H), 7.18 (ddd, J = 3.2, 5.8, 9.2 Hz, 1H), 7.08 (td, J = 4.3, 9.3 Hz, 1H), 6.97 (dt, J = 4.2, 8.7 Hz, 1H), 6.85 (s, 1H), 6.57 - 6.41 (m, 2H), 6.31 (d, J = 16.9 Hz, 1H), 5.80 - 5.64 (m, 2H), 4.07 (dd, J = 4.2, 8.0 Hz, 1H), 3.92 (q, J = 8.0 Hz, 1H), 3.82 (s, 3H), 3.34 - 3.27 (m, 3H), 3.15 (d, J = 12.1 Hz, 3H), 3.08 - 3.04 (m, 2H), 2.93 (q, J = 5.8, 6.2 Hz, 3H), 2.79 (ddd, J = 6.2, 9.9, 15.1 Hz, 3H), 2.21 (dtd, J = 4.5, 8.0, 12.6 Hz, 1H), 2.11 - 1.92 (m, 7H), 0.52 (dd, J = 4.3, 6.4 Hz, 2H), 0.49 - 0.42 (m, 2H) ; 675.4[M+H]$^+$	1.14
830		N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.84 (s, 1H), 9.45 (s, 1H), 9.13 (s, 1H), 8.26 (s, 1H), 8.13 (s, 1H), 7.42 (td, J = 7.9, 6.0 Hz, 1H), 7.31 - 7.17 (m, 2H), 7.11 (td, J = 8.5, 2.7 Hz, 1H), 6.84 (s, 1H), 6.74 (dd, J = 17.0, 10.2 Hz, 1H), 6.33 - 6.12 (m, 2H), 5.77 (dd, J = 10.1, 2.0 Hz, 1H), 5.54 (dd, J = 8.5, 5.3 Hz, 1H), 4.25 (q, J = 7.2, 6.7 Hz, 1H), 3.97 (q, J = 7.8 Hz, 1H), 3.82 (s, 3H), 3.55 (s, 3H), 3.21 (d, J = 4.7 Hz, 4H), 2.96 - 2.81 (m, 2H), 2.36 - 2.22 (m, 2H), 1.22 - 1.11 (m, 2H), 0.85 (d, J = 7.1 Hz, 2H). ; 560.4[M+H]$^+$	1.14

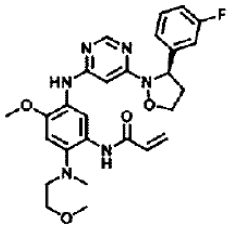
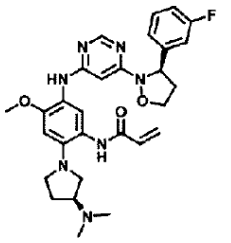
[634]

831		N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.80 (s, 1H), 9.18 (s, 1H), 8.29 (s, 1H), 8.00 (s, 1H), 7.42 (td, J = 8.0, 6.1 Hz, 1H), 7.20 (dd, J = 14.6, 5.3 Hz, 2H), 7.12 (td, J = 8.6, 2.6 Hz, 1H), 6.92 (s, 1H), 6.60 (dd, J = 17.0, 10.1 Hz, 1H), 6.24 (dd, J = 17.0, 2.0 Hz, 1H), 6.12 (s, 1H), 5.75 (dd, J = 10.2, 2.0 Hz, 1H), 5.59 - 5.47 (m, 1H), 4.29 (dt, J = 7.9, 3.9 Hz, 1H), 4.03 (d, J = 7.7 Hz, 1H), 3.79 (s, 3H), 3.66 (d, J = 4.8 Hz, 4H), 2.87 (dt, J = 16.2, 4.9 Hz, 5H), 2.32 (h, J = 7.4 Hz, 1H), 2.05 (s, 3H). ; 562.4[M+H]$^+$	1.30
832		N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.77 (s, 1H), 9.37 (s, 1H), 8.27 (s, 1H), 7.42 (td, J = 8.0, 6.2 Hz, 1H), 7.24 - 7.08 (m, 4H), 6.52 - 6.30 (m, 2H), 6.10 (dd, J = 17.1, 2.1 Hz, 1H), 6.01 (s, 1H), 5.70 (dd, J = 10.2, 2.1 Hz, 1H), 5.54 (t, J = 7.0 Hz, 1H), 4.53 (d, J = 21.0 Hz, 2H), 4.29 (t, J = 6.2 Hz, 1H), 4.05 - 4.01 (m, 1H), 3.95 (d, J = 7.7 Hz, 1H), 3.79 (s, 4H), 3.56 (d, J = 9.3 Hz, 1H), 2.93 (d, J = 9.9 Hz, 2H), 2.32 (q, J = 5.4 Hz, 1H), 1.85 (q, J = 9.8 Hz, 2H). ; 533.4[M+H]$^+$	1.29
833		N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.92 (s, 1H), 9.40 (s, 1H), 8.29 (s, 1H), 7.42 (td, J = 8.1, 6.2 Hz, 1H), 7.28 - 7.04 (m, 4H), 6.54 - 6.41 (m, 2H), 6.19 (dd, J = 17.1, 2.1 Hz, 1H), 5.99 (s, 1H), 5.70 (dd, J = 10.1, 2.1 Hz, 1H), 5.54 (dd, J = 8.5, 5.4 Hz, 1H), 4.53 (d, J = 18.2 Hz, 2H), 4.31 (q, J = 3.2 Hz, 1H), 4.05 (q, J = 7.7 Hz, 1H), 3.95 (d, J = 7.6 Hz, 1H), 3.77 (d, J = 9.2 Hz, 4H), 3.56 (d, J = 9.4 Hz, 1H), 2.92 (t, J = 10.6 Hz, 2H), 2.32 (dq, J = 12.8, 7.3, 6.5 Hz, 1H), 1.88 (dd, J = 17.8, 8.3 Hz, 2H). ; 533.5[M+H]$^+$	1.29

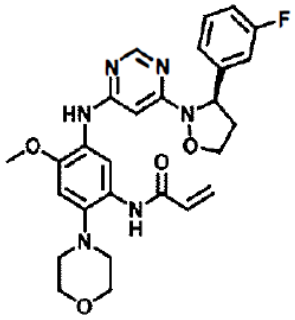
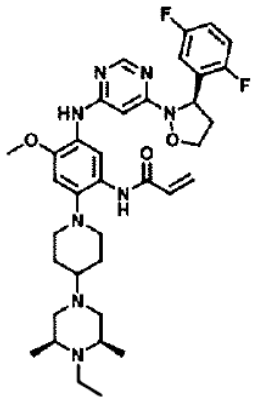
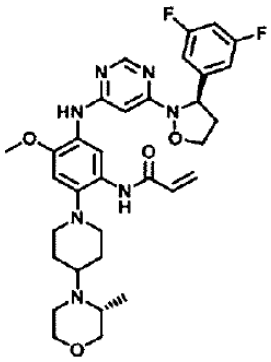
834		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 9.57 (d, J = 0.7 Hz, 1H), 8.24 (d, J = 4.4 Hz, 1H), 7.63 (s, 1H), 7.59 - 7.50 (m, 1H), 7.37 (t, J = 7.1 Hz, 1H), 7.23 (t, J = 7.9 Hz, 1H), 6.89 - 6.76 (m, 1H), 6.71 (d, J = 21.2 Hz, 1H), 6.26 - 6.10 (m, 2H), 5.71 (td, J = 6.0, 2.6 Hz, 2H), 4.32 - 4.21 (m, 1H), 3.98 (d, J = 7.5 Hz, 1H), 3.92 - 3.86 (m, 1H), 3.83 (d, J = 7.8 Hz, 3H), 3.13 (dt, J = 11.7, 4.1 Hz, 2H), 3.07 (t, J = 7.8 Hz, 2H), 2.91 (t, J = 8.1 Hz, 2H), 2.80 (dd, J = 8.0, 4.7 Hz, 6H), 2.38 - 2.20 (m, 3H). : 582.4[M+H]+	1.21

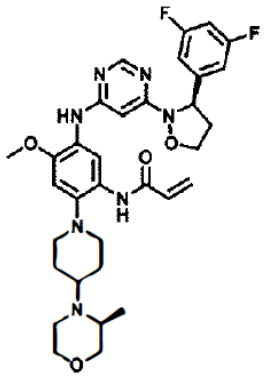
[635]

835		N-(2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 9.24 (d, J = 12.7 Hz, 1H), 8.28 (s, 1H), 7.90 (s, 1H), 7.42 (td, J = 8.0, 6.1 Hz, 1H), 7.26 - 7.17 (m, 2H), 7.12 (td, J = 8.7, 2.7 Hz, 1H), 6.90 (d, J = 17.0 Hz, 1H), 6.58 (t, J = 13.9 Hz, 1H), 6.25 (ddd, J = 17.1, 4.8, 1.9 Hz, 1H), 6.19 - 6.01 (m, 1H), 5.76 (d, J = 10.5 Hz, 1H), 5.54 (dd, J = 8.5, 5.3 Hz, 1H), 4.56 (s, 1H), 4.27 (td, J = 7.9, 7.4, 4.7 Hz, 1H), 4.01 (q, J = 7.8 Hz, 2H), 3.82 (s, 3H), 3.76 (t, J = 6.3 Hz, 1H), 3.61 (dqd, J = 13.2, 6.6, 3.7 Hz, 8H), 3.12 (qd, J = 7.4, 4.2 Hz, 7H), 2.90 (d, J = 7.7 Hz, 1H), 2.77 - 2.67 (m, 2H), 2.31 (tdd, J = 12.7, 8.8, 5.3 Hz, 2H), 2.19 - 1.95 (m, 2H). ; 643.6[M+H]+	1.05
836		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.54 (s, 1H), 8.24 (d, J = 4.6 Hz, 1H), 7.68 - 7.55 (m, 2H), 7.41 (dd, J = 10.5, 2.0 Hz, 1H), 7.26 (d, J = 8.5 Hz, 1H), 6.81 (s, 1H), 6.68 (s, 1H), 6.30 - 6.04 (m, 2H), 5.79 - 5.67 (m, 1H), 5.54 (dd, J = 8.8, 5.4 Hz, 1H), 3.82 (d, J = 7.8 Hz, 3H), 3.39 (t, J = 6.9 Hz, 2H), 3.19 - 3.13 (m, 4H), 3.08 (s, 4H), 2.80 (dd, J = 8.1, 4.7 Hz, 6H), 2.39 - 2.22 (m, 2H). ; 585.2[M+H]+	1.23
837		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-	1H NMR (400 MHz, DMSO-d6) δ 9.26 (s, 1H), 8.30 (s, 1H), 7.87 (s, 1H), 7.42 (td, J = 8.0, 6.0 Hz, 1H), 7.25 - 7.16 (m, 2H), 7.12 (td, J = 8.6, 2.7 Hz, 1H), 6.91 (d, J = 23.6 Hz, 1H), 6.67 - 6.50 (m, 1H), 6.24 (dd, J = 17.3, 1.7 Hz, 1H), 6.12 (s, 1H), 5.81 - 5.71 (m, 1H), 5.50 - 5.40 (m, 1H), 4.47 (s, 1H), 4.28 (s, 2H), 3.66 (d, J = 4.3 Hz, 3H), 3.55 - 3.47 (m, 1H), 3.38 (q, J = 7.1 Hz, 2H), 3.27 (t, J = 8.4 Hz, 4H), 3.05 - 2.98 (m, 5H), 2.88 (t, J = 3.9 Hz, 2H), 2.72 (d, J = 5.0 Hz, 2H), 2.33 (dq, J = 13.3, 5.9 Hz, 2H), 2.19 - 2.00 (m, 2H), 1.77 (ddd, J = 22.2, 15.4, 8.2 Hz, 2H). ; 620.6[M+H]+	1.04

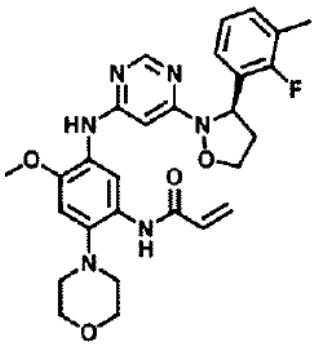
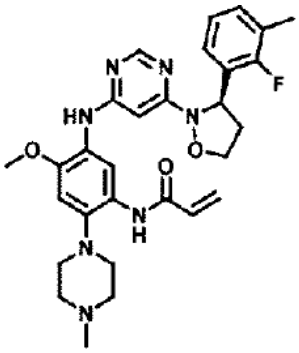
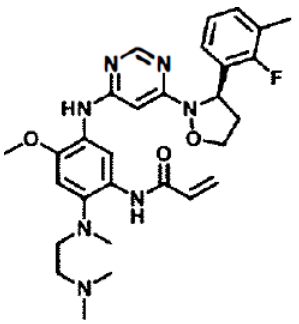
		yl)piperidine-1-yl)phenyl)acrylamide		
838		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d_6) δ 10.38 (s, 1H), 8.37 (s, 1H), 8.08 (d, J = 8.3 Hz, 1H), 7.43 (td, J = 8.0, 5.9 Hz, 1H), 7.32 (s, 1H), 7.25 - 7.17 (m, 2H), 7.13 (td, J = 8.7, 2.6 Hz, 1H), 6.58 (dd, J = 17.1, 10.1 Hz, 1H), 6.33 - 6.15 (m, 2H), 5.81 (dd, J = 10.1, 1.9 Hz, 1H), 5.57 (dd, J = 8.5, 5.4 Hz, 1H), 4.32 (td, J = 7.6, 4.3 Hz, 1H), 4.07 (q, J = 7.7 Hz, 1H), 3.86 (s, 3H), 3.49 (t, J = 5.0 Hz, 2H), 3.05 (s, 2H), 2.94 (ddd, J = 12.3, 8.0, 4.6 Hz, 1H), 2.33 (dtd, J = 12.8, 7.7, 5.3 Hz, 1H), 1.26 (dd, J = 10.5, 4.3 Hz, 2H), 0.85 (q, J = 5.2, 4.0 Hz, 2H).; 523.4[M+H]$^+$	1.49
839		N-(2-((S)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.33 (s, 1H), 9.99 (s, 1H), 9.66 (d, J = 6.9 Hz, 1H), 8.30 (d, J = 2.4 Hz, 1H), 7.58 (d, J = 2.7 Hz, 1H), 7.42 (td, J = 8.2, 6.3 Hz, 1H), 7.24 - 7.09 (m, 3H), 6.90 (ddd, J = 17.1, 10.2, 3.1 Hz, 1H), 6.69 (s, 1H), 6.22 (dd, J = 17.0, 2.1 Hz, 1H), 6.13 - 5.97 (m, 1H), 5.71 (dd, J = 10.1, 2.1 Hz, 1H), 5.55 (dd, J = 8.5, 5.3 Hz, 1H), 4.29 (td, J = 7.6, 4.4 Hz, 2H), 4.04 (q, J = 7.7 Hz, 1H), 3.89 (q, J = 6.1 Hz, 1H), 3.63 (dd, J = 11.1, 4.2 Hz, 1H), 3.52 (q, J = 7.6, 7.0 Hz, 1H), 3.41 (dd, J = 11.2, 6.4 Hz, 1H), 3.04 (q, J = 8.2 Hz, 1H), 2.92 (dtd, J = 12.6, 7.7, 4.6 Hz, 1H), 2.80 (dd, J = 7.4, 4.8 Hz, 6H), 2.38 - 2.24 (m, 3H).548.5[M+H]$^+$	1.07

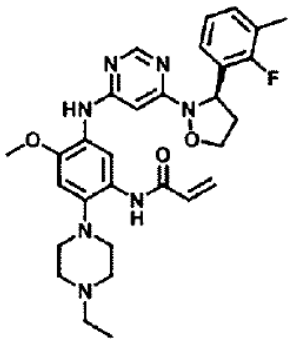
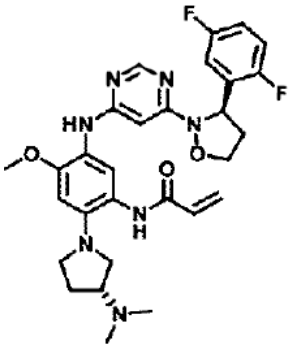
[636]

840		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide	1H NMR (400 MHz, DMSO-d_6) δ 10.39 (s, 1H), 9.36 - 9.24 (m, 1H), 8.35 (s, 1H), 7.86 (s, 1H), 7.43 (td, J = 8.0, 5.9 Hz, 1H), 7.24 - 7.09 (m, 3H), 6.94 (s, 1H), 6.69 (dd, J = 17.0, 10.2 Hz, 1H), 6.24 (dd, J = 16.9, 2.0 Hz, 1H), 6.08 (s, 1H), 5.75 (dd, J = 10.1, 2.0 Hz, 1H), 5.55 (dd, J = 8.5, 5.4 Hz, 1H), 4.33 (td, J = 7.5, 4.3 Hz, 1H), 4.09 (q, J = 7.7 Hz, 1H), 3.82 (d, J = 5.1 Hz, 7H), 3.00 - 2.88 (m, 5H), 2.33 (dtd, J = 12.7, 7.6, 5.3 Hz, 1H).; 521.4[M+H]$^+$	1.41
841		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((3S,5R)-4-ethyl-3,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.29 - 7.21 (m, 1H), 7.21 - 7.10 (m, 1H), 7.10 - 6.99 (m, 1H), 6.92 (s, 1H), 6.61 - 6.46 (m, 2H), 6.41 - 6.31 (m, 1H), 5.89 - 5.72 (m, 2H), 4.17 - 4.12 (m, 1H), 4.03 - 3.96 (m, 1H), 3.89 (s, 3H), 3.30 - 3.26 (m, 3H), 3.26 - 3.11 (m, 5H), 2.89 - 2.76 (m, 3H), 2.60 - 2.51 (m, 1H), 2.43 - 2.35 (m, 2H), 2.32 - 2.23 (m, 1H), 2.07 - 2.00 (m, 2H), 1.87 - 1.73 (m, 2H), 1.34 (s, 3H), 1.33 (s, 3H), 1.22 (t, J = 7.3 Hz, 3H) ; 677.4[M+H]$^+$	1.36
842		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-3-methylmorpholino)piperidine-1-	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.12 - 7.02 (m, 2H), 6.94 (s, 1H), 6.87 - 6.78 (m, 1H), 6.57 (dd, J = 10.2, 17.0 Hz, 1H), 6.46 (s, 1H), 6.42 - 6.31 (m, 1H), 5.82 (d, J = 10.2 Hz, 1H), 5.60 - 5.51 (m, 1H), 4.19 - 4.13 (m, 1H), 3.98 (q, J = 8.0 Hz, 1H), 3.89 (s, 4H), 3.83 - 3.71 (m, 2H), 3.51 - 3.41 (m, 1H), 3.23 - 3.04 (m, 5H), 3.03 - 2.92 (m, 1H), 2.92 - 2.75 (m, 5H), 2.38 - 2.29 (m, 1H), 1.93 - 1.84 (m, 1H), 1.84 - 1.75 (m, 1H), 1.16 (d, J = 6.4 Hz, 3H) ; 636.3[M+H]$^+$	1.24

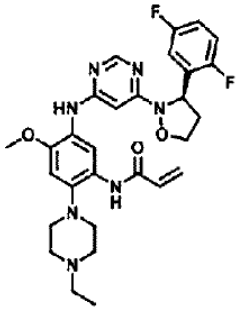
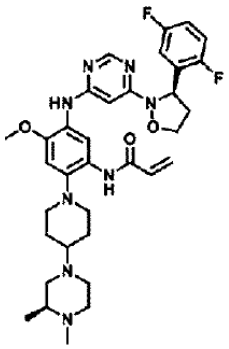
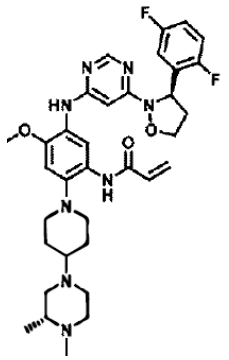
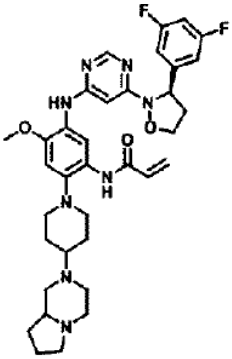
		yl)phenyl)acrylamide		
843		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-3-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.18 (s, 1H), 7.12 - 7.02 (m, 2H), 6.94 (s, 1H), 6.89 - 6.78 (m, 1H), 6.63 - 6.50 (m, 1H), 6.46 (s, 1H), 6.42 - 6.31 (m, 1H), 5.82 (d, J = 10.2 Hz, 1H), 5.62 - 5.50 (m, 1H), 4.18 - 4.12 (m, 1H), 3.98 (q, J = 8.0 Hz, 1H), 3.80 (s, 4H), 3.82 - 3.71 (m, 2H), 3.48 - 3.40 (m, 1H), 3.22 - 3.05 (m, 5H), 2.98 - 2.91 (m, 1H), 2.92 - 2.73 (m, 5H), 2.38 - 2.30 (m, 1H), 1.93 - 1.86 (m, 1H), 1.84 - 1.76 (m, 1H), 1.15 (d, J = 6.4 Hz, 3H) ; 636.3[M+H]$^+$	1.24

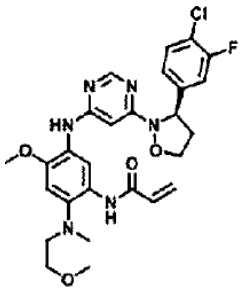
[637]

844		N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.34 (s, 1H), 8.16 (s, 1H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.15 (t, *J* = 7.3 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.95 (s, 1H), 6.56 (dd, *J* = 17.0, 10.3 Hz, 1H), 6.49 (s, 1H), 6.36 (d, *J* = 17.0 Hz, 1H), 5.79 (dd, *J* = 15.2, 7.2 Hz, 2H), 4.13 (td, *J* = 7.7, 4.3 Hz, 1H), 3.99 (q, *J* = 7.9 Hz, 1H), 3.93 - 3.79 (m, 7H), 2.99 - 2.90 (m, 4H), 2.88 - 2.80 (m, 1H), 2.32 - 2.22 (m, 4H). ; 535.5 $[M+H]^+$	1.64
845		N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.34 (s, 1H), 8.16 (s, 1H), 7.35 (t, *J* = 7.0 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.95 (s, 1H), 6.58 - 6.47 (m, 2H), 6.36 (d, *J* = 17.0 Hz, 1H), 5.84 - 5.74 (m, 2H), 4.13 (td, *J* = 7.8, 4.5 Hz, 1H), 3.99 (dd, *J* = 16.4, 8.5 Hz, 1H), 3.90 (s, 3H), 2.99 (t, *J* = 4.5 Hz, 4H), 2.84 (dt, *J* = 16.4, 6.3 Hz, 1H), 2.70 (s, 4H), 2.41 (s, 3H), 2.31 - 2.22 (m, 4H). ; 548.5 $[M+H]^+$	1.37
846		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.34 (s, 1H), 8.16 (s, 1H), 7.35 (t, *J* = 7.0 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.95 (s, 1H), 6.58 - 6.47 (m, 2H), 6.36 (d, *J* = 17.0 Hz, 1H), 5.84 - 5.74 (m, 2H), 4.13 (td, *J* = 7.8, 4.5 Hz, 1H), 3.99 (dd, *J* = 16.4, 8.5 Hz, 1H), 3.90 (s, 3H), 2.99 (t, *J* = 4.5 Hz, 4H), 2.84 (dt, *J* = 16.4, 6.3 Hz, 1H), 2.70 (s, 4H), 2.41 (s, 3H), 2.31 - 2.22 (m, 4H). ; 550.5 $[M+H]^+$	1.38

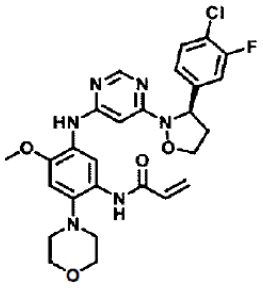
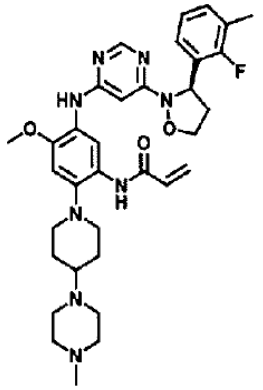
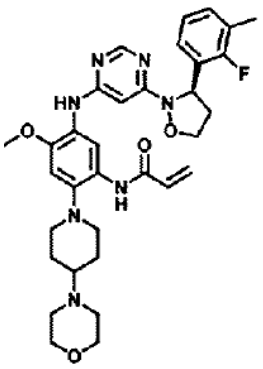
847		N-(2-(4-ethylpiperazine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.34 (s, 1H), 8.16 (s, 1H), 7.35 (t, *J* = 7.1 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.96 (s, 1H), 6.58 - 6.46 (m, 2H), 6.36 (d, *J* = 15.7 Hz, 1H), 5.85 - 5.74 (m, 2H), 4.13 (td, *J* = 7.9, 4.6 Hz, 1H), 3.99 (dd, *J* = 16.0, 8.1 Hz, 1H), 3.90 (s, 3H), 3.00 (t, *J* = 4.7 Hz, 4H), 2.90 - 2.81 (m, 1H), 2.74 (s, 4H), 2.58 (q, *J* = 7.3 Hz, 2H), 2.33 - 2.20 (m, 4H), 1.19 (t, *J* = 7.2 Hz, 3H). : 562.5 [M+H]$^+$	1.23
848		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-*d*6) δ 11.06 (s, 1H), 9.74 (s, 1H), 9.58 (s, 1H), 8.27 (s, 1H), 7.59 (s, 1H), 7.37 - 7.27 (m, 1H), 7.26 - 7.12 (m, 2H), 6.83 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.69 (s, 1H), 6.22 (dd, *J* = 17.0, 2.1 Hz, 1H), 6.12 (s, 1H), 5.78 - 5.62 (m, 2H), 4.33 - 4.26 (m, 1H), 4.06 - 3.98 (m, 1H), 3.82 (s, 3H), 3.60 (s, 6H), 3.30 - 3.37 (m, 1H), 3.10 - 3.04 (m, 1H), 2.95 - 2.88 (m, 1H), 2.82 - 2.78 (m, 4H), 2.30 - 2.27 (m, 1H). : 566.5 [M+H]$^+$	1.16

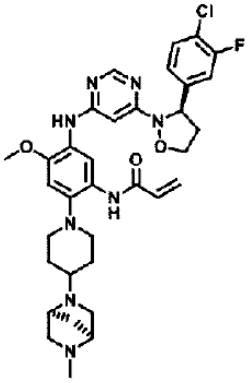
[638]

849		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.72 (s, 1H), 9.57 (s, 1H), 9.15 (d, J = 5.6 Hz, 1H), 8.27 (d, J = 3.0 Hz, 1H), 8.11 (s, 1H), 7.37 - 7.27 (m, 1H), 7.26 - 7.13 (m, 2H), 6.85 (d, J = 13.3 Hz, 1H), 6.74 (dd, J = 17.0, 10.2 Hz, 1H), 6.29 - 6.18 (m, 2H), 5.80 - 5.72 (m, 1H), 5.67 (dd, J = 8.7, 5.4 Hz, 1H), 4.33 - 4.23 (m, 1H), 4.04 - 3.95 (m, 1H), 3.83 (s, 3H), 3.40 - 3.37 (m, 2H), 3.30 - 3.25 (m, 2H), 3.21 - 3.16 (m, 4H), 2.90 - 2.82 (m, 2H), 2.31 - 2.21 (m, 1H), 1.31 (t, J = 7.3 Hz, 3H). ; 566.5 [M+H]$^+$	1.22
850		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.87 (s, 1H), 8.44 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.36 - 7.27 (m, 1H), 7.00 (td, J = 9.2, 4.4 Hz, 1H), 6.94 (s, 1H), 6.93 - 6.84 (m, 1H), 6.76 (d, J = 1.4 Hz, 2H), 6.36 (dd, J = 17.0, 1.6 Hz, 1H), 6.25 (dd, J = 16.9, 9.9 Hz, 1H), 5.90 (dd, J = 8.9, 4.3 Hz, 1H), 5.74 (dd, J = 10.0, 1.6 Hz, 1H), 4.17 - 4.02 (m, 2H), 3.85 (s, 3H), 3.06 (d, J = 11.4 Hz, 2H), 3.02 - 2.95 (m, 1H), 2.93 - 2.78 (m, 3H), 2.78 - 2.66 (m, 2H), 2.44 - 2.34 (m, 2H), 2.32 (s, 3H), 2.31 - 2.26 (m, 2H), 2.17 (s, 1H), 2.13 - 2.04 (m, 2H), 2.03 - 1.96 (m, 1H), 1.69 - 1.63 (m, 2H), 1.10 (d, J = 6.1 Hz, 3H). ; 649.5 [M+H]$^+$	1.17
851		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.87 (s, 1H), 8.44 (s, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.36 - 7.27 (m, 1H), 7.00 (td, J = 9.2, 4.4 Hz, 1H), 6.95 (s, 1H), 6.94 - 6.84 (m, 1H), 6.79 - 6.72 (m, 2H), 6.41 - 6.32 (m, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.90 (dd, J = 8.8, 4.3 Hz, 1H), 5.74 (dd, J = 10.0, 1.6 Hz, 1H), 4.17 - 4.02 (m, 2H), 3.85 (s, 3H), 3.06 (d, J = 11.6 Hz, 2H), 3.02 - 2.96 (m, 1H), 2.95 - 2.87 (m, 2H), 2.87 - 2.70 (m, 1H), 2.73 (q, J = 12.1 Hz, 2H), 2.41 (s, 2H), 2.34 (s, 3H), 2.32 - 2.25 (m, 2H), 2.21 (d, J = 23.1 Hz, 1H), 2.12 - 2.02 (m, 3H), 1.69 - 1.64 (m, 2H), 1.12 (d, J = 6.2 Hz, 3H). ; 649.5 [M+H]$^+$	1.18
852		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(hexahydropyrrolo[1,2-a]pyrazine-2(1H)-yl)piperidine-	^{1}H NMR (400 MHz, Chloroform-d) δ 8.86 (s, 1H), 8.45 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.06 - 6.96 (m, 2H), 6.94 (s, 1H), 6.75 (s, 1H), 6.74 - 6.63 (m, 2H), 6.36 (dd, J = 16.9, 1.5 Hz, 1H), 6.25 (dd, J = 16.9, 10.0 Hz, 1H), 5.74 (dd, J = 10.0, 1.6 Hz, 1H), 5.67 (dd, J = 8.8, 4.6 Hz, 1H), 4.15 (td, J = 8.1, 4.2 Hz, 1H), 4.06 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.19 - 3.13 (m, 1H), 3.13 - 3.03 (m, 4H), 3.03 - 2.96 (m, 1H), 2.84 - 2.68 (m, 3H), 2.52 - 2.39 (m, 2H), 2.39 - 2.27 (m, 2H), 2.20 - 2.14 (m, 1H), 2.10 - 2.06 (m, 2H), 1.88 - 1.66 (m, 8H). ; 661.6 [M+H]$^+$	1.18

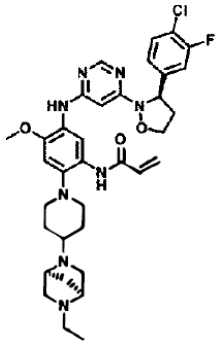
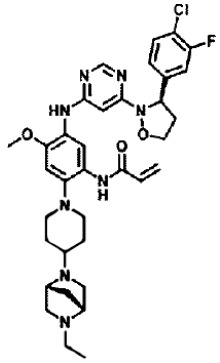
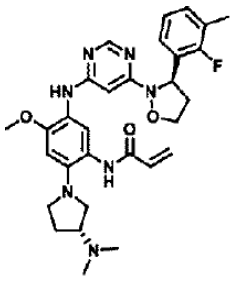
		1-yl)-4-methoxyphenyl)acrylamide		
853		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.34 (s, 1H), 8.37 - 8.20 (m, 1H), 7.58 (t, J = 8.1 Hz, 1H), 7.42 (dd, J = 10.5, 2.0 Hz, 1H), 7.27 (d, J = 8.3 Hz, 1H), 7.03 (s, 1H), 6.44 (dd, J = 16.9, 10.1 Hz, 1H), 6.23 (d, J = 17.2 Hz, 2H), 5.77 (d, J = 10.2 Hz, 1H), 5.54 (dd, J = 8.6, 5.2 Hz, 1H), 4.22 (td, J = 8.0, 4.1 Hz, 1H), 3.95 (q, J = 7.8 Hz, 1H), 3.81 (s, 3H), 3.40 (t, J = 5.2 Hz, 2H), 3.32 (s, 2H), 3.04 (s, 1H), 2.82 (s, 2H), 2.50 (p, J = 1.9 Hz, 6H), 2.35 - 2.21 (m, 1H). ; 557.4[M+H]+	1.63

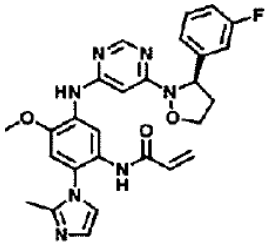
[639]

854		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.11 (s, 1H), 8.22 (s, 1H), 8.06 (s, 1H), 7.58 (t, J = 8.0 Hz, 1H), 7.41 (dd, J = 10.5, 2.0 Hz, 1H), 7.27 (dd, J = 8.4, 2.0 Hz, 1H), 6.89 (s, 1H), 6.64 (dd, J = 16.9, 10.2 Hz, 1H), 6.24 (d, J = 2.0 Hz, 1H), 6.19 (d, J = 2.0 Hz, 1H), 5.73 (dd, J = 10.2, 2.0 Hz, 1H), 5.54 (dd, J = 8.6, 5.2 Hz, 1H), 4.21 (td, J = 7.7, 4.1 Hz, 2H), 3.93 (q, J = 7.9 Hz, 1H), 3.81 (d, J = 6.5 Hz, 7H), 2.87 (t, J = 4.6 Hz, 4H), 2.82 (td, J = 7.7, 3.9 Hz, 1H), 2.29 (ddd, J = 12.6, 8.4, 5.1 Hz, 1H). : 555.4[M+H]+	1.55
855		N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 9.07 (s, 1H), 8.81 (s, 1H), 8.13 (d, J = 31.2 Hz, 1H), 7.26 (t, J = 7.4 Hz, 1H), 7.23 - 7.15 (m, 1H), 7.07 (t, J = 7.5 Hz, 1H), 6.90 (d, J = 38.3 Hz, 1H), 6.72 - 6.59 (m, 1H), 6.40 - 6.17 (m, 2H), 5.80 - 5.64 (m, 2H), 4.21 - 4.12 (m, 1H), 3.85 - 3.79 (m, 3H), 3.59 (dh, J = 9.7, 3.2 Hz, 3H), 3.13 (dh, J = 11.0, 3.6 Hz, 4H), 3.03 (d, J = 12.9 Hz, 1H), 2.91 (s, 1H), 2.87 - 2.76 (m, 3H), 2.26 (d, J = 2.2 Hz, 3H), 2.21 - 2.10 (m, 2H), 1.28 (ddd, J = 8.4, 6.4, 3.0 Hz, 8H), 1.18 - 1.03 (m, 2H). : 555.4[M+H]+	1.17
856		N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.49 (s, 1H), 9.14 (s, 1H), 8.23 (s, 1H), 8.03 (s, 1H), 7.27 - 7.16 (m, 2H), 7.07 (t, J = 7.6 Hz, 1H), 6.89 (s, 1H), 6.66 (dd, J = 16.9, 10.2 Hz, 1H), 6.31 - 6.18 (m, 2H), 5.72 (ddd, J = 17.5, 9.4, 3.6 Hz, 2H), 4.23 (td, J = 7.7, 4.0 Hz, 1H), 4.06 - 3.92 (m, 7H), 3.81 (s, 3H), 3.59 (pd, J = 6.6, 3.9 Hz, 4H), 3.44 (d, J = 12.1 Hz, 3H), 3.11 (dq, J = 7.4, 3.2 Hz, 5H), 2.26 (d, J = 2.0 Hz, 4H).: 618.5[M+H]+	1.27

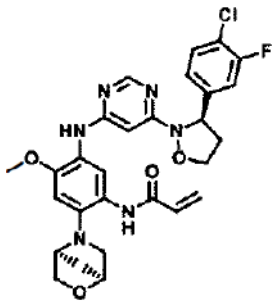
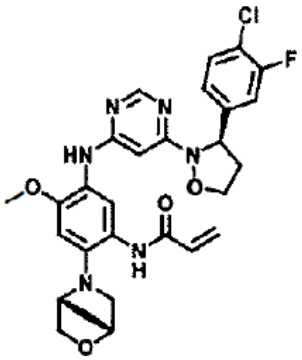
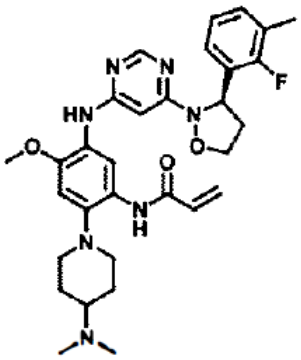
857		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)phenyl) acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.41 (s, 1H), 9.37 (s, 1H), 8.35 (s, 1H), 7.81 (s, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.42 (dd, J = 10.3, 2.0 Hz, 1H), 7.24 (dd, J = 8.4, 2.0 Hz, 1H), 6.96 (d, J = 20.1 Hz, 1H), 6.75 - 6.52 (m, 1H), 6.25 (dd, J = 17.0, 1.8 Hz, 1H), 6.12 (s, 1H), 5.82 - 5.70 (m, 1H), 5.56 (dd, J = 8.5, 5.4 Hz, 1H), 4.82 (s, 1H), 4.71 (s, 1H), 4.49 (s, 2H), 4.32 (td, J = 7.5, 4.3 Hz, 1H), 4.08 (q, J = 7.6 Hz, 2H), 3.83 (s, 3H), 3.79 - 3.61 (m, 2H), 3.36 - 3.16 (m, 3H), 3.01 - 2.63 (m, 7H), 2.42 - 1.98 (m, 6H).; 663.5[M+H]$^+$	1.17

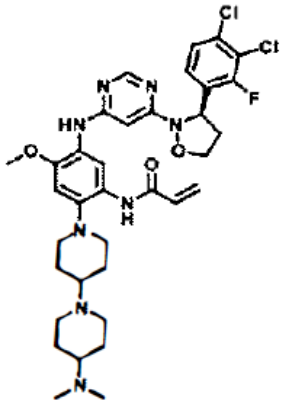
[640]

858		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.37 (s, 1H), 9.36 (s, 1H), 8.35 (s, 1H), 7.81 (s, 1H), 7.60 (t, J = 8.1 Hz, 1H), 7.42 (dd, J = 10.4, 2.0 Hz, 1H), 7.25 (dd, J = 8.4, 2.0 Hz, 1H), 6.95 (d, J = 15.4 Hz, 1H), 6.64 (ddd, J = 27.1, 16.8, 10.5 Hz, 1H), 6.25 (dd, J = 16.9, 1.8 Hz, 1H), 6.12 (s, 1H), 5.83 - 5.69 (m, 1H), 5.56 (dd, J = 8.5, 5.4 Hz, 1H), 4.84 (s, 1H), 4.71 (s, 1H), 4.58 (d, J = 8.9 Hz, 2H), 4.32 (td, J = 7.6, 4.4 Hz, 2H), 4.08 (q, J = 7.5 Hz, 2H), 3.83 (s, 3H), 3.72 - 3.55 (m, 2H), 3.46 - 3.14 (m, 5H), 2.95 (ddp, J = 12.2, 7.3, 4.4 Hz, 1H), 2.77 (p, J = 13.6, 12.9 Hz, 2H), 2.58 (d, J = 12.5 Hz, 1H), 2.33 (dtd, J = 12.7, 7.5, 5.1 Hz, 1H), 2.09 (d, J = 38.9 Hz, 3H), 1.30 (dd, J = 8.7, 5.0 Hz, 3H).; 677.5[M+H]$^+$	1.15
859		N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.41 (s, 1H), 9.38 (s, 1H), 8.35 (s, 1H), 7.81 (s, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.42 (dd, J = 10.4, 2.0 Hz, 1H), 7.25 (dd, J = 8.3, 2.0 Hz, 1H), 6.96 (d, J = 14.3 Hz, 1H), 6.63 (td, J = 16.3, 8.2 Hz, 1H), 6.25 (dd, J = 17.1, 1.8 Hz, 1H), 6.12 (d, J = 9.8 Hz, 1H), 5.77 (d, J = 10.5 Hz, 1H), 5.56 (dd, J = 8.5, 5.4 Hz, 1H), 4.84 (s, 1H), 4.71 (s, 1H), 4.58 (d, J = 9.9 Hz, 2H), 4.32 (td, J = 7.6, 4.4 Hz, 1H), 4.08 (q, J = 7.5 Hz, 2H), 3.83 (s, 3H), 3.71 - 3.58 (m, 1H), 3.45 - 3.12 (m, 5H), 2.96 (ddp, J = 12.3, 7.4, 4.6 Hz, 1H), 2.77 (ddd, J = 23.2, 16.4, 8.4 Hz, 2H), 2.40 - 2.26 (m, 2H), 2.21 - 2.02 (m, 3H), 1.36 - 1.22 (m, 4H).; 677.5[M+H]$^+$	1.17
860		N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, MeOD) δ 8.06 - 7.93 (m, 1H), 7.56 (s, 1H), 7.27 - 7.15 (m, 1H), 7.08 - 6.96 (m, 1H), 6.90 (t, J = 7.6 Hz, 1H), 6.54 (s, 1H), 6.42 (dd, J = 17.0, 10.2 Hz, 1H), 6.29 - 6.17 (m, 2H), 5.72 - 5.57 (m, 2H), 3.98 (td, J = 7.9, 4.4 Hz, 1H), 3.83 (q, J = 7.9 Hz, 1H), 3.75 (s, 3H), 3.20 - 3.08 (m, 4H), 2.83 - 2.61 (m, 2H), 2.55 (s, 1H), 2.19 (d, J = 13.3 Hz, 9H), 2.10 (ddd, J = 12.3, 7.9, 4.4 Hz, 2H), 1.84 - 1.72 (m, 1H).; 562.4[M+H]$^+$	1.19

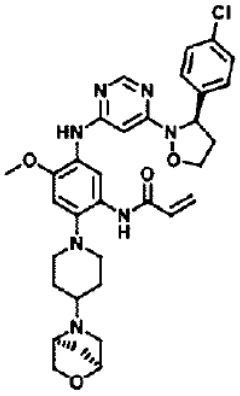
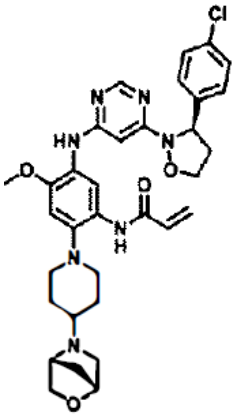
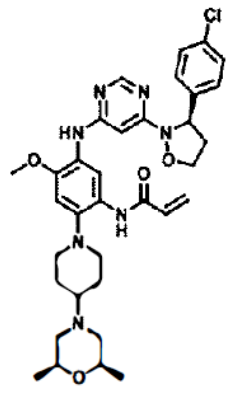
861		N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(2-methyl-1H-imidazole-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 14.80 (s, 1H), 10.08 (s, 1H), 9.23 (s, 1H), 8.36 (d, J = 8.6 Hz, 2H), 7.60 (dd, J = 46.0, 2.1 Hz, 2H), 7.47 - 7.34 (m, 2H), 7.30 - 7.20 (m, 2H), 7.11 (td, J = 8.7, 2.8 Hz, 1H), 6.78 (s, 1H), 6.31 (dd, J = 17.1, 10.2 Hz, 1H), 6.09 (dd, J = 17.1, 1.9 Hz, 1H), 5.68 (dd, J = 10.2, 2.0 Hz, 1H), 5.56 (dd, J = 8.7, 5.2 Hz, 1H), 4.24 (td, J = 7.8, 3.7 Hz, 1H), 3.80 (s, 4H), 2.83 (tq, J = 8.3, 4.3 Hz, 1H), 2.54 (s, 3H), 2.30 (ddt, J = 11.8, 7.8, 3.7 Hz, 1H). ; 516.4[M+H]$^+$	1.31

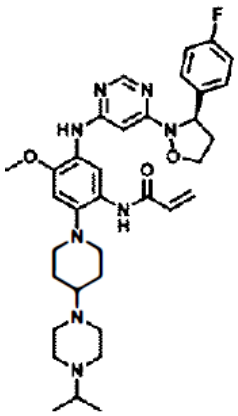
[641]

862		N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.93 (s, 1H), 9.40 (s, 1H), 8.28 (s, 1H), 7.59 (t, J = 8.0 Hz, 1H), 7.41 (dd, J = 10.4, 2.0 Hz, 1H), 7.24 (dd, J = 8.5, 2.0 Hz, 1H), 7.15 (s, 1H), 6.54 - 6.40 (m, 2H), 6.19 (dd, J = 17.1, 2.1 Hz, 1H), 6.12 - 5.94 (m, 1H), 5.70 (dd, J = 10.2, 2.1 Hz, 1H), 5.54 (dd, J = 8.5, 5.4 Hz, 1H), 4.51 (s, 2H), 4.32 - 4.20 (m, 1H), 4.05 (q, J = 7.7 Hz, 1H), 3.95 (d, J = 7.7 Hz, 1H), 3.78 (d, J = 7.3 Hz, 4H), 3.57 (d, J = 9.3 Hz, 1H), 2.93 (dd, J = 11.3, 5.7 Hz, 2H), 2.37 - 2.26 (m, 1H), 1.87 (p, J = 10.2, 9.5 Hz, 2H). ; 567.4[M+H]$^+$	1.44
863		N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.88 (s, 1H), 9.39 (s, 1H), 8.28 (s, 1H), 7.59 (t, J = 8.0 Hz, 1H), 7.41 (dd, J = 10.4, 2.1 Hz, 1H), 7.24 (dd, J = 8.3, 2.0 Hz, 1H), 7.16 (s, 1H), 6.52 - 6.42 (m, 2H), 6.19 (dd, J = 17.1, 2.1 Hz, 1H), 6.02 (s, 1H), 5.70 (dd, J = 10.1, 2.1 Hz, 1H), 5.53 (dd, J = 8.6, 5.4 Hz, 1H), 4.51 (s, 2H), 4.32 - 4.28 (m, 1H), 4.04 (q, J = 7.6 Hz, 1H), 3.95 (d, J = 7.7 Hz, 1H), 3.78 (d, J = 5.1 Hz, 4H), 3.60 - 3.51 (m, 1H), 2.93 (t, J = 8.2 Hz, 2H), 2.32 (td, J = 12.9, 7.5 Hz, 1H), 1.85 (q, J = 9.4 Hz, 2H). ; 567.4[M+H]$^+$	1.45
864		N-(2-(4-(dimethylamino)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.96 (s, 1H), 9.92 (s, 1H), 9.17 (s, 1H), 8.20 (s, 1H), 7.94 (s, 1H), 7.20 (dt, J = 22.2, 7.1 Hz, 2H), 7.08 (t, J = 7.6 Hz, 1H), 6.90 (s, 1H), 6.72 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 16.9, 2.0 Hz, 1H), 6.13 (s, 1H), 5.76 (dd, J = 10.1, 2.0 Hz, 1H), 5.68 (t, J = 7.2 Hz, 1H), 4.30 (td, J = 7.7, 4.2 Hz, 2H), 4.05 (d, J = 7.8 Hz, 2H), 3.81 (s, 3H), 3.28 (d, J = 3.8 Hz, 1H), 3.20 (d, J = 11.4 Hz, 2H), 2.92 (dd, J = 8.4, 4.3 Hz, 1H), 2.75 (d, J = 4.9 Hz, 6H), 2.26 (d, J = 1.9 Hz, 4H), 2.11 (d, J = 9.6 Hz, 2H), 2.01 (t, J = 12.0 Hz, 2H). ; 576.5[M+H]$^+$	1.27

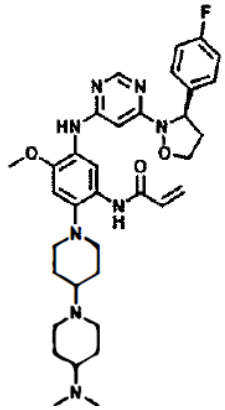
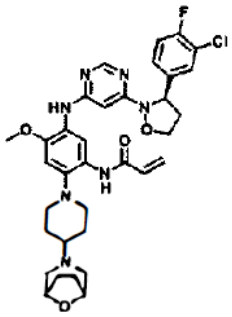
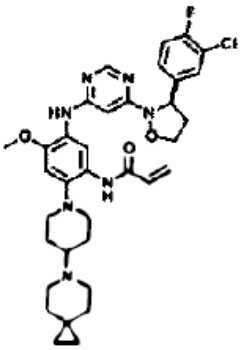
865		N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.04 (s, 1H), 9.23 (s, 1H), 8.31 (s, 1H), 7.92 (s, 1H), 7.53 (dd, J = 8.6, 1.5 Hz, 1H), 7.39 (t, J = 8.1 Hz, 1H), 6.90 (s, 1H), 6.74 (dd, J = 17.0, 10.3 Hz, 1H), 6.31 - 6.12 (m, 2H), 5.77 - 5.60 (m, 2H), 4.32 (d, J = 4.0 Hz, 1H), 4.05 (d, J = 7.9 Hz, 1H), 3.82 (s, 3H), 3.61 (s, 1H), 3.50 (s, 1H), 3.35 (d, J = 3.4 Hz, 1H), 3.23 (d, J = 11.1 Hz, 2H), 3.13 (s, 1H), 3.00 - 2.89 (m, 1H), 2.86 - 2.76 (m, 2H), 2.72 (d, J = 4.8 Hz, 6H), 2.35 - 2.26 (m, 5H), 2.17 (d, J = 9.4 Hz, 2H), 2.12 - 2.02 (m, 2H), 1.62 (d, J = 2.7 Hz, 1H), 1.49 - 1.36 (m, 1H). ; 613.3 $[M+H]^+$	1.27

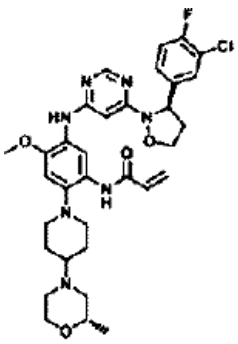
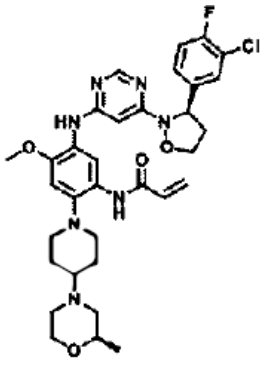
[642]

866		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.48 (s, 1H), 8.36 (s, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 6.96 (s, 1H), 6.75 (s, 1H), 6.69 (s, 1H), 6.29 (dt, J = 17.0, 13.1 Hz, 2H), 5.74 (d, J = 11.0 Hz, 1H), 5.66 (dd, J = 8.5, 4.5 Hz, 1H), 4.47 (s, 1H), 4.18 - 4.01 (m, 3H), 3.85 (s, 3H), 3.69 (d, J = 7.9 Hz, 1H), 3.21 (d, J = 10.2 Hz, 1H), 3.04 (dd, J = 10.6, 5.0 Hz, 2H), 2.81 - 2.71 (m, 4H), 2.67 (d, J = 10.6 Hz, 1H), 2.57 (d, J = 10.0 Hz, 1H), 2.38 - 2.27 (m, 1H), 2.09 - 1.90 (m, 4H), 1.83 (dd, J = 33.8, 9.8 Hz, 3H), 1.26 (s, 1H) ; 632.5 $[M+H]^+$	1.23
867		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.48 (s, 1H), 8.35 (s, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.5 Hz, 2H), 6.97 (s, 1H), 6.76 (s, 1H), 6.70 (s, 1H), 6.35 (d, J = 16.3 Hz, 1H), 6.24 (dd, J = 16.9, 10.0 Hz, 1H), 5.73 (d, J = 11.1 Hz, 1H), 5.66 (dd, J = 8.6, 4.5 Hz, 1H), 4.44 (s, 1H), 4.18 - 4.03 (m, 3H), 3.85 (s, 3H), 3.77 (s, 1H), 3.66 (d, J = 7.4 Hz, 1H), 3.14 (d, J = 9.0 Hz, 1H), 3.02 (d, J = 11.7 Hz, 2H), 2.76 (ddd, J = 12.1, 9.6, 3.3 Hz, 3H), 2.63 - 2.54 (m, 1H), 2.51 (d, J = 9.9 Hz, 1H), 2.38 - 2.26 (m, 1H), 2.04 (d, J = 12.4 Hz, 1H), 1.92 (d, J = 10.0 Hz, 2H), 1.83 (d, J = 9.8 Hz, 1H), 1.74 - 1.60 (m, 2H), 1.25 (s, 1H) ; 632.4 $[M+H]^+$	1.38
868		N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.43 (s, 1H), 8.36 (s, 1H), 7.40 (d, J = 8.5 Hz, 2H), 7.30 (d, J = 8.4 Hz, 1H), 6.94 (s, 1H), 6.72 (d, J = 10.8 Hz, 2H), 6.29 (dt, J = 16.9, 13.2 Hz, 2H), 5.74 (d, J = 11.0 Hz, 1H), 5.66 (dd, J = 8.6, 4.5 Hz, 1H), 4.18 - 4.02 (m, 2H), 3.84 (s, 3H), 3.77 - 3.65 (m, 2H), 3.06 (d, J = 11.0 Hz, 2H), 2.88 (d, J = 10.8 Hz, 2H), 2.80 - 2.66 (m, 3H), 2.39 - 2.24 (m, 2H), 2.07 (d, J = 12.5 Hz, 2H), 1.90 (t, J = 10.6 Hz, 2H), 1.66 (dd, J = 21.1, 11.0 Hz, 2H), 1.26 (s, 1H), 1.20 (d, J = 6.3 Hz, 6H) ; 648.4 $[M+H]^+$	1.21

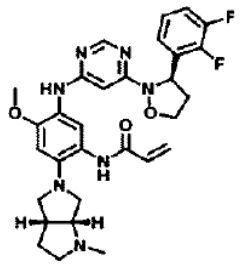
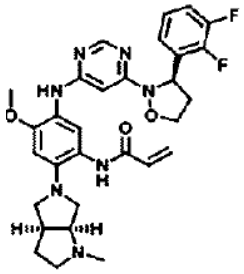
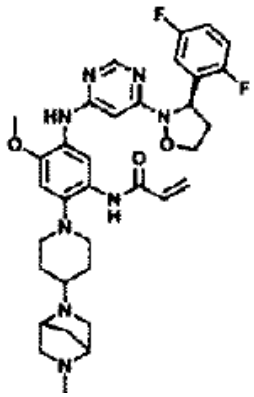
869		N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.97 (s, 1H), 9.10 (s, 1H), 8.30 (s, 1H), 7.93 (s, 1H), 7.43 - 7.37 (m, 2H), 7.20 (t, *J* = 8.8 Hz, 2H), 6.90 (s, 1H), 6.72 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.25 (dd, *J* = 17.0, 2.0 Hz, 1H), 6.07 (s, 1H), 5.76 (dd, *J* = 10.1, 2.0 Hz, 1H), 5.52 (t, *J* = 6.9 Hz, 1H), 4.31 (d, *J* = 4.5 Hz, 1H), 4.05 (d, *J* = 7.7 Hz, 2H), 3.80 (s, 3H), 3.77 (s, 2H), 3.69 (s, 4H), 3.62 - 3.58 (m, 1H), 3.47 (d, *J* = 5.4 Hz, 2H), 3.22 (d, *J* = 11.5 Hz, 2H), 2.91 (d, *J* = 7.6 Hz, 1H), 2.80 (t, *J* = 11.5 Hz, 2H), 2.35 - 2.28 (m, 1H), 2.21 - 2.04 (m, 4H), 1.32 (d, *J* = 6.5 Hz, 6H). 645.4 $[M+H]^+$	1.08

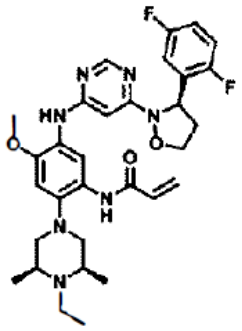
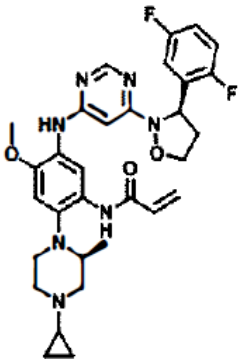
[643]

870		N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.34 (s, 1H), 9.31 (s, 1H), 8.34 (s, 1H), 7.85 (s, 1H), 7.40 (dd, J = 8.5, 5.4 Hz, 2H), 7.20 (t, J = 8.8 Hz, 2H), 6.91 (s, 1H), 6.79 (dd, J = 17.0, 10.2 Hz, 1H), 6.25 (dd, J = 16.9, 1.9 Hz, 1H), 6.06 (s, 1H), 5.76 (dd, J = 9.4, 2.5 Hz, 1H), 5.54 (dd, J = 8.4, 5.3 Hz, 1H), 4.35 - 4.30 (m, 1H), 4.08 (d, J = 7.7 Hz, 1H), 3.81 (s, 3H), 3.62 (d, J = 11.6 Hz, 2H), 3.53 (s, 1H), 3.37 (t, J = 3.5 Hz, 1H), 3.24 (d, J = 11.1 Hz, 2H), 3.18 - 3.08 (m, 2H), 2.98 - 2.80 (m, 1H), 2.86 - 2.77 (m, 2H), 2.71 (d, J = 4.8 Hz, 6H), 2.37 - 2.24 (m, 5H), 2.15 (d, J = 17.8 Hz, 4H).; 645.4 [M+H]$^+$	1.01
871		N-(2-(4-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.23 (s, 1H), 7.89 (s, 1H), 7.52 (dd, J = 6.9, 1.8 Hz, 1H), 7.39 - 7.32 (m, 1H), 7.26 (t, J = 8.8 Hz, 1H), 7.19 (s, 1H), 6.68 (dd, J = 16.9, 10.2 Hz, 1H), 6.48 (d, J = 16.7 Hz, 1H), 6.09 (s, 1H), 5.89 (d, J = 10.7 Hz, 1H), 5.50 (t, J = 6.9 Hz, 1H), 4.57 (s, 2H), 4.44 (td, J = 7.6, 4.1 Hz, 1H), 4.18 (dd, J = 15.1, 8.2 Hz, 1H), 3.92 (s, 3H), 3.54 (d, J = 12.3 Hz, 4H), 3.31 (s, 5H), 3.05 (q, J = 12.1 Hz, 1H), 2.49 - 2.23 (m, 7H), 2.17 - 2.11 (m, 2H).; 664.5 [M+H]$^+$	1.27
872		N-(2-(4-(6-azaspiro[2.5]octan-6-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	662.6 [M+H]$^+$	1.37

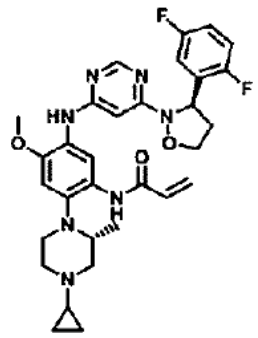
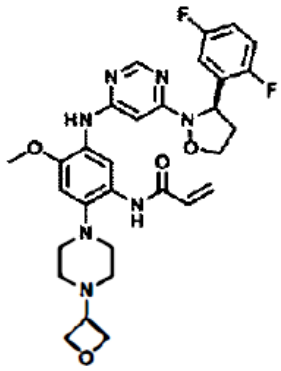
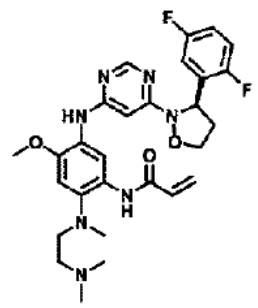
873		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 9.88 (s, 1H), 8.20 (s, 1H), 7.85 (s, 1H), 7.34 (d, *J* = 6.7 Hz, 1H), 7.14 (d, *J* = 11.8 Hz, 2H), 6.62 (s, 1H), 6.38 (d, *J* = 15.6 Hz, 1H), 6.03 (s, 1H), 5.76 (d, *J* = 8.5 Hz, 1H), 5.57 (s, 1H), 4.36 (s, 4H), 4.00 (d, *J* = 48.1 Hz, 4H), 3.54 - 3.32 (m, 3H), 2.91 (d, *J* = 20.6 Hz, 4H), 2.72 (s, 2H), 2.43 (s, 2H), 1.77 (s, 2H), 1.57 (s, 1H), 1.27 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 1H).; 652.3 $[M+H]^+$	1.26
874		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	652.3 $[M+H]^+$	1.3

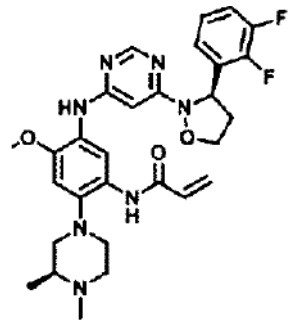
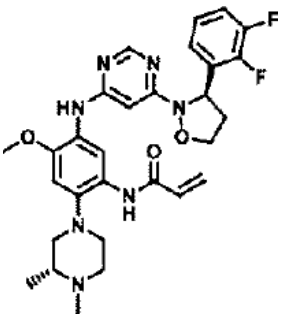
[644]

875		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.72 (s, 1H), 8.35 (s, 1H), 7.36 (t, J = 6.6 Hz, 1H), 7.09 - 6.99 (m, 2H), 6.86 (s, 1H), 6.73 (s, 1H), 6.68 (s, 1H), 6.42 (d, J = 16.9 Hz, 1H), 6.34 - 6.23 (m, 1H), 5.93 (dd, J = 8.6, 4.4 Hz, 1H), 5.74 - 5.67 (m, 1H), 4.17 - 4.03 (m, 2H), 3.83 (s, 3H), 3.24 - 3.14 (m, 1H), 3.11 - 2.99 (m, 2H), 2.94 - 2.80 (m, 4H), 2.61 - 2.50 (m, 1H), 2.43 (s, 3H), 2.35 - 2.25 (m, 2H), 2.21 - 2.13 (m, 1H), 1.65 - 1.53 (m, 1H); 578.46[M+H]$^+$	1.22
876		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.72 (s, 1H), 8.35 (s, 1H), 7.36 (t, J = 6.0 Hz, 1H), 7.10 - 6.98 (m, 2H), 6.88 (s, 1H), 6.71 (s, 1H), 6.69 (s, 1H), 6.42 (d, J = 16.0 Hz, 1H), 6.35 - 6.24 (m, 1H), 5.93 (dd, J = 8.6, 4.5 Hz, 1H), 5.74 - 5.67 (m, 1H), 4.13 (td, J = 8.0, 4.3 Hz, 1H), 4.05 (q, J = 8.1 Hz, 1H), 3.83 (s, 3H), 3.22 - 3.05 (m, 2H), 2.98 - 2.80 (m, 5H), 2.68 - 2.58 (m, 1H), 2.45 (s, 3H), 2.36 - 2.27 (m, 2H), 2.24 - 2.14 (m, 1H), 1.76 - 1.66 (m, 1H); 578.46[M+H]$^+$	1.22
877		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.47 (s, 1H), 8.37 (s, 1H), 7.35 - 7.29 (m, 1H), 7.03 - 6.86 (m, 3H), 6.76 (s, 2H), 6.35 (d, J = 16.3 Hz, 1H), 6.24 (dd, J = 16.9, 10.0 Hz, 1H), 5.90 (dd, J = 8.6, 4.2 Hz, 1H), 5.75 - 5.69 (m, 1H), 4.16 - 4.03 (m, 2H), 3.86 (s, 3H), 3.08 - 2.99 (m, 3H), 2.87 - 2.71 (m, 4H), 2.64 - 2.56 (m, 2H), 2.49 (s, 3H), 2.34 - 2.24 (m, 2H), 2.07 - 2.02 (m, 1H), 1.94 - 1.83 (m, 3H), 1.72 - 1.63 (m, 2H); 647.56[M+H]$^+$	1.14

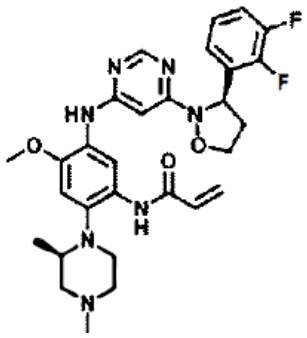
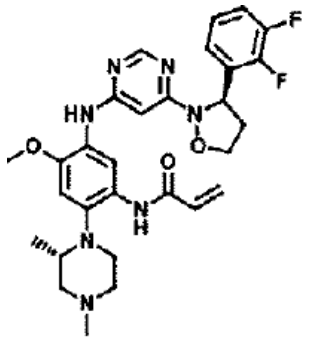
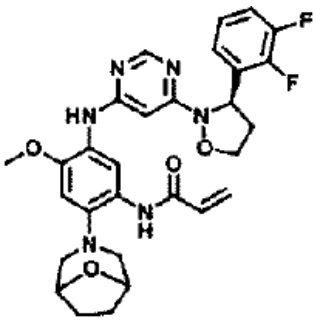
		yl)phenyl)acrylamide		
878		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((3S,5R)-4-ethyl-3,5-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.57 (s, 1H), 8.37 (s, 1H), 7.35 - 7.29 (m, 1H), 7.03 - 6.95 (m, 2H), 6.93 - 6.86 (m, 1H), 6.79 (s, 1H), 6.77 (s, 1H), 6.37 (d, *J* = 16.2 Hz, 1H), 6.27 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.90 (dd, *J* = 8.7, 4.2 Hz, 1H), 5.75 (dd, *J* = 10.0, 1.2 Hz, 1H), 4.16 - 4.04 (m, 2H), 3.84 (s, 3H), 3.06 - 2.96 (m, 2H), 2.88 - 2.78 (m, 5H), 2.70 - 2.59 (m, 1H), 2.34 - 2.23 (m, 1H), 1.18 - 1.10 (m, 7H), 1.00 (t, *J* = 6.9 Hz, 3H); 504.52[M+H]$^+$	1.26
879		N-(2-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.97 (s, 1H), 8.39 (s, 1H), 7.36 - 7.28 (m, 1H), 7.06 (s, 1H), 7.04 - 6.96 (m, 1H), 6.94 - 6.85 (m, 1H), 6.82 (s, 1H), 6.80 (s, 1H), 6.38 - 6.24 (m, 2H), 5.90 (dd, *J* = 8.6, 4.2 Hz, 1H), 5.74 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.17 - 4.07 (m, 2H), 3.80 (s, 3H), 3.14 - 3.00 (m, 3H), 2.90 - 2.78 (m, 3H), 2.52 - 2.44 (m, 1H), 2.34 - 2.25 (m, 1H), 2.23 - 2.16 (m, 1H), 1.72 - 1.66 (m, 1H), 0.82 (d, *J* = 6.2 Hz, 3H), 0.56 - 0.44 (m, 4H); 502.45[M+H]$^+$	1.30

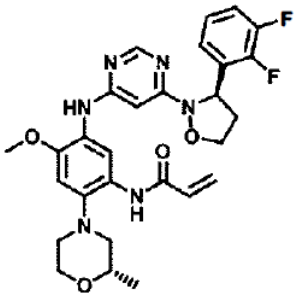
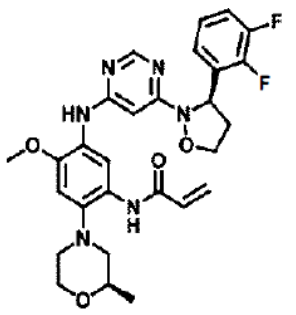
[645]

880		N-(2-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.98 (s, 1H), 8.39 (s, 1H), 7.36 - 7.28 (m, 1H), 7.06 (s, 1H), 7.03 - 6.97 (m, 1H), 6.93 - 6.87 (m, 1H), 6.82 (s, 2H), 6.38 - 6.24 (m, 2H), 5.91 (dd, *J* = 8.7, 4.2 Hz, 1H), 5.74 (dd, *J* = 9.7, 1.8 Hz, 1H), 4.18 - 4.06 (m, 2H), 3.81 (s, 3H), 3.15 - 2.99 (m, 3H), 2.91 - 2.77 (m, 3H), 2.52 - 2.45 (m, 1H), 2.35 - 2.25 (m, 1H), 2.23 - 2.16 (m, 1H), 1.73 - 1.66 (m, 1H), 0.83 (d, *J* = 6.2 Hz, 3H), 0.57 - 0.44 (m, 4H); 592.45[M+H]$^+$	1.31
881		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.92 (s, 1H), 8.49 (s, 1H), 8.38 (d, *J* = 0.9 Hz, 1H), 7.32 (ddd, *J* = 9.1, 5.9, 3.2 Hz, 1H), 7.05 - 6.95 (m, 2H), 6.90 (ddd, *J* = 8.8, 7.3, 3.6 Hz, 1H), 6.82 (s, 1H), 6.77 (s, 1H), 6.36 (dd, *J* = 17.0, 1.6 Hz, 1H), 6.25 (dd, *J* = 17.0, 10.0 Hz, 1H), 5.90 (dd, *J* = 8.7, 4.4 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.5 Hz, 1H), 4.72 (t, *J* = 6.5 Hz, 2H), 4.67 (t, *J* = 6.2 Hz, 2H), 4.18 - 4.02 (m, 2H), 3.85 (s, 3H), 3.66 - 3.55 (m, 1H), 3.03 - 2.90 (m, 4H), 2.89 - 2.76 (m, 1H), 2.64 - 2.43 (m, 4H), 2.36 - 2.23 (m, 1H). ; 594.4 [M+H]$^+$	1.24
882		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethyl	^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.00 (s, 1H), 8.96 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 7.33 (ddd, *J* = 9.1, 5.0, 3.2 Hz, 1H), 7.05 - 6.95 (m, 2H), 6.95 - 6.84 (m, 1H), 6.83 - 6.78 (m, 2H), 6.40 (dd, *J* = 16.9, 2.1 Hz, 1H), 6.34 (d, *J* = 9.6 Hz, 1H), 5.90 (dd, *J* = 8.9, 4.3 Hz, 1H), 5.71 - 5.64 (m, 1H), 4.19 - 4.07 (m, 2H), 3.85 (s, 3H), 2.93 - 2.85 (m, 2H), 2.85 - 2.77 (m, 1H), 2.72 (s, 3H), 2.41 - 2.33 (m, 2H), 2.30 (s, 6H), 2.28 - 2.24 (m, 1H). ; 554.4 [M+H]$^+$	1.25

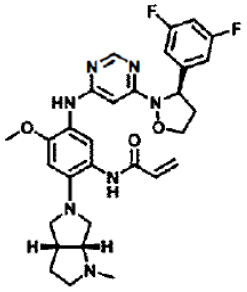
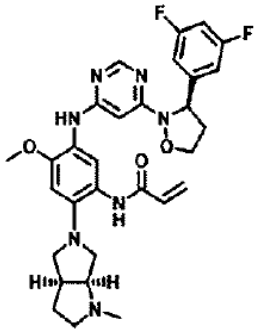
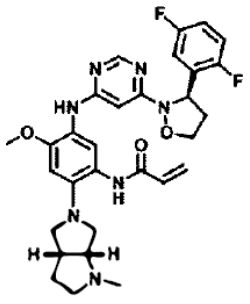
		amino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide		
883		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (s, 1H), 8.54 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 7.40 - 7.32 (m, 1H), 7.12 - 6.99 (m, 2H), 6.97 (s, 1H), 6.77 (d, *J* = 16.1 Hz, 2H), 6.37 (dd, *J* = 17.0, 1.6 Hz, 1H), 6.26 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.93 (dd, *J* = 8.9, 4.5 Hz, 1H), 5.75 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.19 - 4.11 (m, 1H), 4.07 (q, *J* = 8.1 Hz, 1H), 3.85 (s, 3H), 3.03 - 2.78 (m, 5H), 2.64 (dd, *J* = 11.4, 9.5 Hz, 1H), 2.52 - 2.42 (m, 1H), 2.39 (s, 3H), 2.38 - 2.25 (m, 2H), 1.14 (d, *J* = 6.3 Hz, 3H). ; 566.4 $[M+H]^+$	1.22
884		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (s, 1H), 8.54 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 7.40 - 7.31 (m, 1H), 7.12 - 6.99 (m, 2H), 6.97 (s, 1H), 6.77 (d, *J* = 14.8 Hz, 2H), 6.37 (dd, *J* = 17.0, 1.5 Hz, 1H), 6.26 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.93 (dd, *J* = 8.9, 4.6 Hz, 1H), 5.75 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.19 - 4.02 (m, 2H), 3.84 (s, 3H), 3.06 - 2.93 (m, 2H), 2.93 - 2.79 (m, 3H), 2.61 (dd, *J* = 11.5, 9.5 Hz, 1H), 2.47 (td, *J* = 11.5, 11.0, 3.0 Hz, 1H), 2.40 (s, 3H), 2.38 - 2.25 (m, 2H), 1.14 (d, *J* = 6.3 Hz, 3H). ; 566.4 $[M+H]^+$	1.23

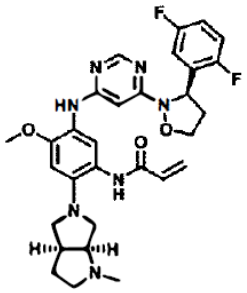
[646]

885		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-2,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 9.05 (s, 1H), 8.92 (s, 1H), 8.39 (d, J = 1.0 Hz, 1H), 7.40 - 7.32 (m, 1H), 7.12 - 6.99 (m, 3H), 6.85 - 6.77 (m, 2H), 6.35 (dd, J = 16.9, 1.7 Hz, 1H), 6.26 (dd, J = 17.0, 9.8 Hz, 1H), 5.94 (dd, J = 8.8, 4.5 Hz, 1H), 5.74 (dd, J = 9.8, 1.7 Hz, 1H), 4.16 (td, J = 8.1, 4.3 Hz, 1H), 4.09 (q, J = 8.0 Hz, 1H), 3.83 (s, 3H), 3.19 - 3.06 (m, 1H), 3.02 - 2.92 (m, 2H), 2.91 - 2.77 (m, 3H), 2.39 (s, 3H), 2.37 - 2.21 (m, 2H), 1.98 (t, J = 10.4 Hz, 1H), 0.83 (d, J = 6.2 Hz, 3H). : 566.4 $[M+H]^+$	1.27
886		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-2,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 9.03 (s, 1H), 8.91 (s, 1H), 8.39 (d, J = 1.0 Hz, 1H), 7.40 - 7.32 (m, 1H), 7.12 - 6.99 (m, 3H), 6.85 - 6.77 (m, 2H), 6.35 (dd, J = 16.9, 1.7 Hz, 1H), 6.26 (dd, J = 16.9, 9.8 Hz, 1H), 5.94 (dd, J = 8.8, 4.5 Hz, 1H), 5.74 (dd, J = 9.8, 1.8 Hz, 1H), 4.21 - 4.04 (m, 2H), 3.83 (s, 3H), 3.19 - 3.07 (m, 1H), 3.01 - 2.78 (m, 5H), 2.38 (s, 3H), 2.37 - 2.21 (m, 2H), 1.98 (t, J = 10.4 Hz, 1H), 0.82 (d, J = 6.2 Hz, 3H). : 566.4 $[M+H]^+$	1.24
887		N-(2-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-	^{1}H NMR (400 MHz, Chloroform-d) δ 8.92 (s, 1H), 8.60 (s, 1H), 8.38 (d, J = 1.0 Hz, 1H), 7.39 - 7.31 (m, 1H), 7.12 - 6.99 (m, 2H), 6.98 (s, 1H), 6.82 (s, 1H), 6.76 (s, 1H), 6.41 (dd, J = 16.9, 1.4 Hz, 1H), 6.26 (dd, J = 16.9, 10.2 Hz, 1H), 5.93 (dd, J = 8.7, 4.6 Hz, 1H), 5.77 (dd, J = 10.1, 1.4 Hz, 1H), 4.49 - 4.44 (m, 2H), 4.15 (td, J = 8.0, 4.2 Hz, 1H), 4.07 (q, J = 8.0 Hz, 1H), 3.85 (s, 3H), 3.12 (td, J = 11.2, 2.1 Hz, 2H), 2.86 (dtd, J = 12.5, 8.1, 4.1 Hz, 1H), 2.65 (d, J = 11.2 Hz, 2H), 2.32 (dtd, J = 12.7, 8.4, 5.3 Hz, 1H), 2.17 - 2.10 (m, 2H), 2.10 - 2.02 (m, 2H). : 565.4 $[M+H]^+$	1.55

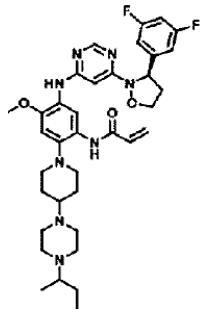
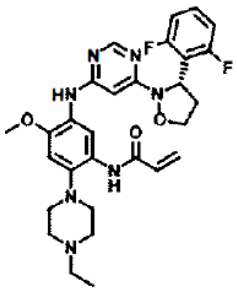
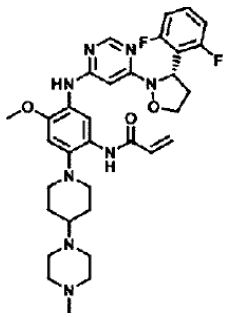
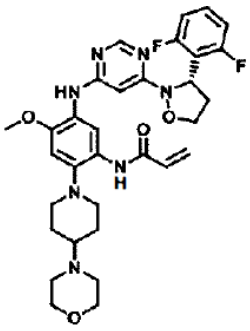
		yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide		
888		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-2-methylmorpholino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.92 (s, 1H), 8.51 (s, 1H), 8.38 (d, *J* = 1.0 Hz, 1H), 7.40 - 7.31 (m, 1H), 7.12 - 7.00 (m, 2H), 6.98 (s, 1H), 6.76 (d, *J* = 1.6 Hz, 2H), 6.37 (dd, *J* = 17.0, 1.5 Hz, 1H), 6.26 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.93 (dd, *J* = 8.7, 4.6 Hz, 1H), 5.76 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.20 - 4.12 (m, 1H), 4.12 - 4.00 (m, 2H), 3.87 (s, 3H), 3.83 - 3.72 (m, 2H), 2.94 - 2.75 (m, 4H), 2.60 (dd, *J* = 11.4, 9.7 Hz, 1H), 2.38 - 2.25 (m, 1H), 1.24 (d, *J* = 6.3 Hz, 3H). : 553.4 [M+H]$^+$	1.58
889		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-2-methylmorpholino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.92 (s, 1H), 8.51 (s, 1H), 8.38 (d, *J* = 1.0 Hz, 1H), 7.40 - 7.31 (m, 1H), 7.12 - 7.01 (m, 2H), 6.99 (s, 1H), 6.76 (d, *J* = 2.5 Hz, 2H), 6.37 (dd, *J* = 16.9, 1.5 Hz, 1H), 6.26 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.93 (dd, *J* = 8.8, 4.6 Hz, 1H), 5.76 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.20 - 4.11 (m, 1H), 4.11 - 4.00 (m, 2H), 3.87 (s, 3H), 3.85 - 3.74 (m, 2H), 2.97 - 2.74 (m, 4H), 2.57 (dd, *J* = 11.6, 9.8 Hz, 1H), 2.38 - 2.25 (m, 1H), 1.24 (d, *J* = 6.3 Hz, 3H). : 553.4 [M+H]$^+$	1.58

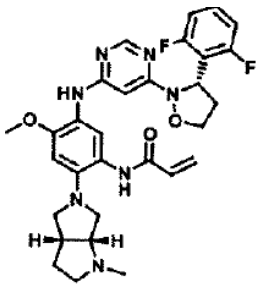
[647]

890		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.18 (s, 1H), 8.58 (s, 1H), 8.15 (s, 1H), 7.80 (s, 1H), 7.15 - 7.07 (m, 3H), 6.67 (s, 1H), 6.43 (dd, J = 17.1, 10.2 Hz, 1H), 6.21 (dd, J = 17.0, 2.0 Hz, 1H), 5.72 (dd, J = 10.1, 2.0 Hz, 1H), 5.55 (dd, J = 8.7, 5.0 Hz, 1H), 4.12 (td, J = 7.9, 3.9 Hz, 1H), 3.79 (s, 4H), 2.99 - 2.82 (m, 4H), 2.76 (ddp, J = 11.9, 7.7, 3.7 Hz, 3H), 2.36 - 2.17 (m, 6H), 2.06 - 1.95 (m, 1H), 1.84 (s, 1H), 1.63 (tt, J = 12.3, 6.9 Hz, 2H), 1.23 (s, 1H).; 578.4[M+H]$^+$	1.24
891		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.19 (s, 1H), 8.58 (s, 1H), 8.15 (d, J = 0.9 Hz, 1H), 7.80 (s, 1H), 7.15 - 7.06 (m, 5H), 6.67 (s, 1H), 6.44 (dd, J = 17.1, 10.2 Hz, 1H), 6.21 (dd, J = 17.1, 1.9 Hz, 2H), 5.72 (dd, J = 10.2, 2.0 Hz, 1H), 5.55 (dd, J = 8.7, 5.0 Hz, 2H), 4.12 (td, J = 7.9, 3.9 Hz, 2H), 3.79 (s, 4H), 3.00 - 2.88 (m, 4H), 2.76 (dp, J = 8.4, 4.2 Hz, 4H), 2.31 - 2.21 (m, 8H), 2.00 (q, J = 9.5, 6.8 Hz, 2H), 1.87 (s, 5H), 1.63 (tt, J = 12.4, 6.9 Hz, 2H), 1.23 (s, 2H).; 578.5[M+H]$^+$	1.25
892		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.19 (s, 1H), 8.60 (s, 1H), 8.14 (s, 1H), 7.79 (s, 1H), 7.29 (td, J = 9.3, 4.5 Hz, 2H), 7.18 (tdt, J = 11.9, 7.4, 3.3 Hz, 3H), 6.67 (s, 1H), 6.44 (dd, J = 17.1, 10.2 Hz, 1H), 6.21 (dd, J = 17.1, 1.9 Hz, 1H), 5.71 (td, J = 9.6, 9.1, 3.5 Hz, 2H), 4.16 (td, J = 7.9, 3.8 Hz, 1H), 3.79 (s, 3H), 3.00 - 2.82 (m, 5H), 2.77 (tt, J = 8.4, 4.2 Hz, 3H), 2.37 - 2.20 (m, 6H), 2.00 (q, J = 9.4, 7.2 Hz, 2H), 1.78 (s, 3H), 1.63 (tt, J = 11.4, 6.9 Hz, 2H), 1.23 (s, 3H).; 578.4[M+H]$^+$	1.24

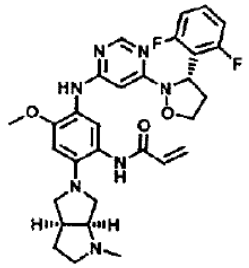
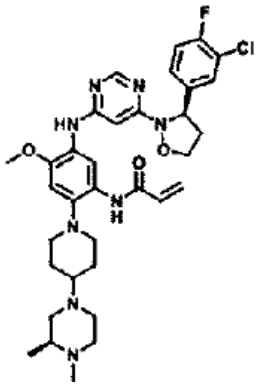
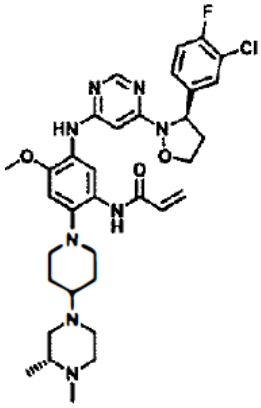
		methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide		
893		N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.20 (s, 1H), 8.60 (s, 1H), 8.14 (d, J = 0.9 Hz, 1H), 7.80 (s, 1H), 7.29 (td, J = 9.2, 4.4 Hz, 1H), 7.24 - 7.13 (m, 3H), 6.67 (s, 1H), 6.44 (dd, J = 17.1, 10.2 Hz, 1H), 6.21 (dd, J = 17.1, 1.9 Hz, 1H), 5.71 (td, J = 9.7, 3.5 Hz, 2H), 4.16 (td, J = 7.9, 3.9 Hz, 2H), 3.79 (s, 3H), 3.01 - 2.83 (m, 5H), 2.78 (qd, J = 8.2, 4.0 Hz, 3H), 2.35 - 2.11 (m, 7H), 2.00 (q, J = 9.6, 6.8 Hz, 1H), 1.89 (s, 4H), 1.63 (tt, J = 11.9, 6.9 Hz, 1H), 1.23 (s, 1H).: 578.4[M+H]$^+$	1.23

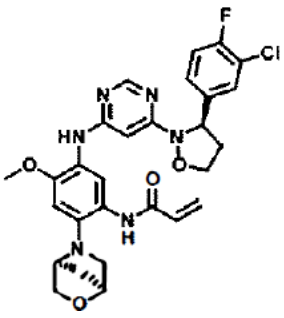
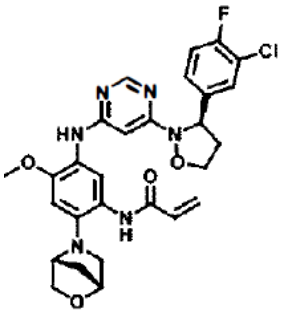
[648]

894		N-(2-(4-(4-(sec-butyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.81 (s, 1H), 8.43 (s, 1H), 8.33 (d, *J* = 1.0 Hz, 1H), 7.17 (s, 1H), 6.99 (h, *J* = 4.4 Hz, 2H), 6.74 (s, 1H), 6.68 (s, 1H), 6.33 (d, *J* = 1.7 Hz, 1H), 6.25 (dd, *J* = 16.9, 9.9 Hz, 2H), 5.73 (dd, *J* = 9.8, 1.7 Hz, 1H), 5.65 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.07 - 4.00 (m, 1H), 3.83 (s, 3H), 3.05 (d, *J* = 11.2 Hz, 2H), 2.77 (d, *J* = 3.0 Hz, 8H), 2.67 - 2.58 (m, 1H), 2.42 (td, *J* = 11.9, 11.4, 6.2 Hz, 1H), 2.33 (q, *J* = 4.2 Hz, 2H), 2.11 - 2.05 (m, 2H), 1.72 - 1.64 (m, 3H), 1.28 (d, *J* = 6.7 Hz, 5H), 1.07 (d, *J* = 6.5 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H).; 677.6[M+H]$^+$	1.23
895		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, Methanol-d4) δ 8.31 (s, 1H), 8.16 (s, 1H), 7.34 (tt, J = 8.5, 6.2 Hz, 1H), 6.96 (dd, J = 15.5, 7.2 Hz, 3H), 6.56 (dd, J = 17.0, 10.3 Hz, 1H), 6.42 - 6.31 (m, 2H), 5.81 (dd, J = 10.2, 1.6 Hz, 1H), 5.76 (dd, J = 8.9, 7.0 Hz, 1H), 4.34 (td, J = 7.9, 2.5 Hz, 1H), 3.97 - 3.90 (m, 1H), 3.89 (s, 3H), 3.11 (s, 4H), 2.93 (q, J = 7.3 Hz, 2H), 2.80 (dddd, J = 11.9, 9.1, 6.5, 2.5 Hz, 1H), 2.59 - 2.48 (m, 1H), 1.98 (s, 4H), 1.30 (t, J = 7.3 Hz, 3H); 566.4[M+H]+	1.12
896		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, Methanol-d4) δ 8.28 (s, 1H), 8.16 (s, 1H), 7.34 (tt, J = 8.5, 6.2 Hz, 1H), 6.97 (t, J = 8.4 Hz, 2H), 6.92 (s, 1H), 6.53 (dd, J = 17.0, 10.2 Hz, 1H), 6.41 - 6.31 (m, 2H), 5.81 (d, J = 10.3 Hz, 1H), 5.76 (dd, J = 8.9, 7.0 Hz, 1H), 4.34 (td, J = 7.9, 2.4 Hz, 1H), 3.95 - 3.89 (m, 1H), 3.88 (s, 3H), 3.40 - 3.36 (m, 2H), 3.00 (t, J = 4.8 Hz, 4H), 2.85 (qq, J = 6.1, 2.9 Hz, 6H), 2.78 (dt, J = 9.9, 3.0 Hz, 1H), 2.74 (s, 3H), 2.63 (tq, J = 11.7, 4.2 Hz, 1H), 2.57 - 2.48 (m, 1H), 2.15 (dd, J = 12.8, 3.1 Hz, 2H), 1.84 (td, J = 13.8, 13.2, 6.9 Hz, 2H); 635.5[M+H]+	1.00
897		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopi	1H NMR (400 MHz, Methanol-d4) δ 8.15 (s, 1H), 8.03 (s, 1H), 7.22 (tt, J = 8.4, 6.2 Hz, 1H), 6.85 (t, J = 8.4 Hz, 2H), 6.78 (s, 1H), 6.44 (dd, J = 17.0, 10.3 Hz, 1H), 6.31 - 6.17 (m, 2H), 5.72 - 5.66 (m, 1H), 5.63 (dd, J = 8.9, 7.0 Hz, 1H), 4.22 (td, J = 7.9, 2.4 Hz, 1H), 3.79 (td, J = 9.0, 8.3, 6.6 Hz, 1H), 3.74 (s, 3H), 3.70 (t, J = 4.7 Hz, 4H), 3.04 (d, J = 11.7 Hz, 2H), 2.83 - 2.60 (m, 7H), 2.44 (ttd, J = 16.8, 11.3, 9.5, 5.7 Hz, 2H), 1.99 (dd, J = 12.6, 3.5 Hz, 2H), 1.72 - 1.62 (m, 2H); 622.4[M+H]+	1.14

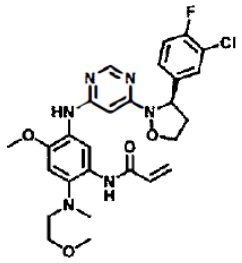
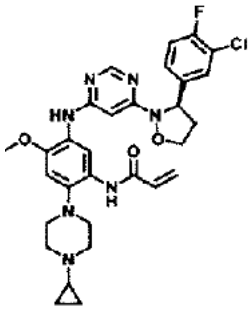
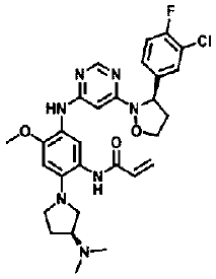
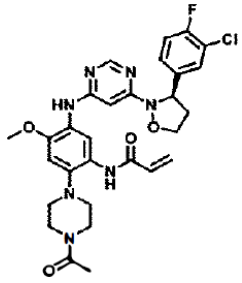
		peridine-1-yl)phenyl)acrylamide		
898		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.04 (s, 1H), 9.94 (s, 1H), 8.25 (s, 1H), 7.71 (s, 1H), 7.46 - 7.36 (m, 1H), 7.17 - 7.03 (m, 3H), 6.86 (s, 1H), 6.27 - 6.21 (m, 1H), 5.98 (s, 1H), 5.74 - 5.64 (m, 2H), 4.47 (d, J = 2.2 Hz, 1H), 4.06 - 3.99 (m, 2H), 3.78 (s, 3H), 3.60 (d, J = 11.7 Hz, 1H), 3.53 (d, J = 6.7 Hz, 1H), 3.15 - 3.01 (m, 4H), 2.86 (d, J = 5.0 Hz, 5H), 2.44 (dd, J = 12.1, 7.8 Hz, 2H), 1.83 (dd, J = 13.5, 6.5 Hz, 1H), ; 578.5 [M+H]$^+$	1.14

[649]

899		N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.04 (s, 1H), 9.97 (s, 1H), 8.26 (s, 1H), 7.71 (s, 1H), 7.42 (tt, J = 8.3, 6.3 Hz, 1H), 7.17 - 7.00 (m, 2H), 7.08 - 7.01 (m, 1H), 6.86 (s, 1H), 6.25 (dd, J = 17.0, 2.1 Hz, 1H), 5.96 (s, 1H), 5.72 (dt, J = 11.8, 8.7 Hz, 2H), 4.47 (d, J = 2.3 Hz, 1H), 4.04 - 3.90 (m, 2H), 3.78 (s, 3H), 3.69 (d, J = 11.7 Hz, 1H), 3.55 - 3.40 (m, 1H), 3.39 (s, 1H), 3.16 - 2.98 (m, 5H), 2.95 - 2.80 (m, 1H), 2.86 (d, J = 4.9 Hz, 2H), 2.47 - 2.35 (m, 2H), 1.88 - 1.77 (m, 1H).; 578.5 [M+H]$^+$	1.13
900		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.32 (s, 1H), 8.02 (s, 1H), 7.35 (d, J = 6.8 Hz, 1H), 7.19 - 7.10 (m, 2H), 6.80 (s, 2H), 6.40 (d, J = 16.1 Hz, 1H), 6.24 (s, 1H), 5.81 (d, J = 9.1 Hz, 1H), 5.56 (s, 1H), 4.24 (d, J = 62.7 Hz, 6H), 3.75 (s, 4H), 3.48 (d, J = 7.3 Hz, 3H), 2.92 (s, 4H), 2.68 (s, 3H), 2.41 (s, 3H), 1.31 - 1.13 (m, 6H).; 665.6 [M+H]$^+$	1.23
901		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.18 (s, 1H), 7.96 (s, 1H), 7.35 (d, J = 6.8 Hz, 1H), 7.21 - 7.10 (m, 3H), 6.69 (dd, J = 16.9, 10.2 Hz, 1H), 6.42 (d, J = 17.0 Hz, 1H), 6.14 (s, 1H), 5.81 (d, J = 10.2 Hz, 1H), 5.55 (d, J = 7.7 Hz, 1H), 4.36 (s, 1H), 4.29 (s, 2H), 4.19 (d, J = 7.6 Hz, 2H), 3.98 (s, 1H), 3.86 (s, 3H), 3.65 (s, 4H), 3.49 (s, 2H), 2.92 (s, 3H), 2.60 (s, 3H), 2.46 - 2.40 (m, 1H), 1.77 (s, 1H), 1.62 (d, J = 6.3 Hz, 3H), 1.27 - 1.18 (m, 3H).; 665.6 [M+H]$^+$	1.24

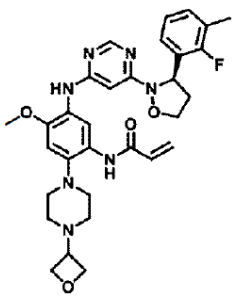
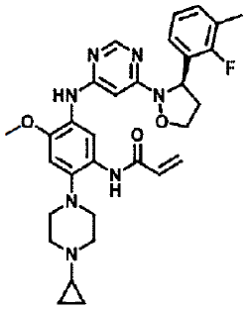
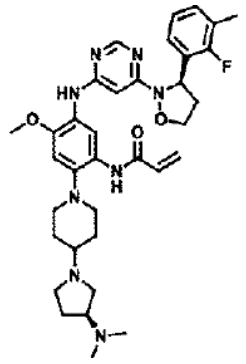
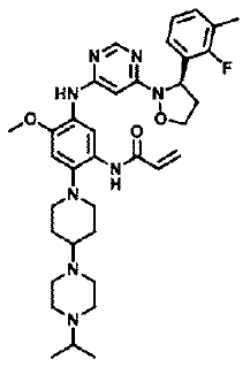
902		N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.11 (s, 1H), 7.54 (dd, J = 7.1, 2.2 Hz, 1H), 7.47 (s, 1H), 7.38 (ddd, J = 7.3, 4.5, 2.2 Hz, 1H), 7.20 (t, J = 8.8 Hz, 1H), 6.54 (s, 1H), 6.46 (dd, J = 17.0, 10.1 Hz, 1H), 6.34 (dd, J = 17.1, 1.8 Hz, 1H), 6.20 (s, 1H), 5.77 (dd, J = 10.1, 1.8 Hz, 1H), 5.53 - 5.48 (m, 1H), 4.58 (s, 1H), 4.36 (s, 1H), 4.14 (dd, J = 8.0, 4.3 Hz, 1H), 4.10 (d, J = 7.6 Hz, 1H), 3.93 (q, J = 8.0 Hz, 1H), 3.85 (s, 4H), 3.51 (d, J = 9.6 Hz, 1H), 3.10 (d, J = 9.6 Hz, 1H), 2.78 (dtd, J = 12.3, 8.0, 4.2 Hz, 1H), 2.31 (ddt, J = 11.8, 7.8, 4.1 Hz, 1H), 2.04 (dd, J = 9.9, 2.2 Hz, 1H), 1.92 (dd, J = 9.8, 2.5 Hz, 1H); 567.3[M+H]$^+$	1.41
903		N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.11 (s, 1H), 7.53 (dd, J = 7.1, 2.2 Hz, 1H), 7.47 (s, 1H), 7.38 (ddd, J = 8.6, 4.6, 2.3 Hz, 1H), 7.20 (t, J = 8.8 Hz, 1H), 6.54 (s, 1H), 6.46 (dd, J = 17.0, 10.1 Hz, 1H), 6.34 (dd, J = 17.1, 1.8 Hz, 1H), 6.20 (s, 1H), 5.77 (dd, J = 10.1, 1.8 Hz, 1H), 5.51 - 5.47 (m, 1H), 4.58 (t, J = 1.9 Hz, 1H), 4.35 (s, 1H), 4.13 (dt, J = 7.9, 3.9 Hz, 1H), 4.09 (d, J = 7.5 Hz, 1H), 3.91 (q, J = 7.9 Hz, 1H), 3.84 (s, 4H), 3.49 (dd, J = 9.7, 1.7 Hz, 1H), 3.12 (d, J = 9.7 Hz, 1H), 2.78 (dtd, J = 12.3, 8.0, 4.2 Hz, 1H), 2.35 - 2.25 (m, 1H), 2.03 (dd, J = 9.9, 2.3 Hz, 1H), 1.91 (dd, J = 9.4, 2.6 Hz, 1H); 567.3[M+H]$^+$	1.40

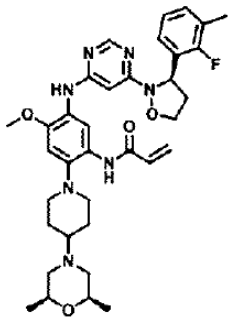
[650]

904		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.50 (s, 1H), 8.06 (s, 1H), 7.44 (dd, J = 7.1, 2.2 Hz, 1H), 7.28 (ddd, J = 8.7, 4.6, 2.3 Hz, 1H), 7.10 (t, J = 8.8 Hz, 1H), 6.87 (s, 1H), 6.41 - 6.29 (m, 2H), 6.23 (dd, J = 17.0, 1.8 Hz, 1H), 5.68 (dd, J = 10.0, 1.8 Hz, 1H), 5.41 (dd, J = 8.6, 4.8 Hz, 1H), 4.04 (td, J = 7.9, 4.2 Hz, 1H), 3.87 (q, J = 7.9 Hz, 1H), 3.75 (s, 3H), 3.43 (t, J = 4.9 Hz, 2H), 3.32 (s, 3H), 2.93 (t, J = 4.9 Hz, 2H), 2.72 (td, J = 8.0, 4.0 Hz, 1H), 2.67 (s, 3H), 2.26 - 2.16 (m, 1H); 557.4[M+H]$^+$	1.65
905		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	504.4[M+H]$^+$	1.28
906		N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.69 (s, 1H), 8.35 (s, 1H), 8.22 (s, 1H), 7.53 (dd, J = 7.0, 2.3 Hz, 1H), 7.32 (ddd, J = 8.6, 4.6, 2.3 Hz, 1H), 7.10 (t, J = 8.7 Hz, 1H), 6.92 (s, 1H), 6.75 (s, 1H), 6.67 (s, 1H), 6.43 - 6.35 (m, 1H), 6.30 (dd, J = 16.9, 9.7 Hz, 1H), 5.73 (dd, J = 9.7, 2.0 Hz, 1H), 5.64 (dd, J = 8.7, 4.5 Hz, 1H), 4.15 (td, J = 8.0, 4.2 Hz, 1H), 4.04 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.13 (q, J = 8.4, 7.8 Hz, 4H), 2.91 (t, J = 7.2 Hz, 1H), 2.79 - 2.71 (m, 1H), 2.31 (s, 7H), 2.22 - 2.14 (m, 1H), 2.02 - 1.94 (m, 1H); 582.4[M+H]$^+$	1.23
907		N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.33 (s, 1H), 8.17 (s, 1H), 7.54 (dd, J = 7.1, 2.2 Hz, 1H), 7.30 (ddd, J = 7.3, 4.6, 2.2 Hz, 1H), 7.20 (t, J = 8.8 Hz, 1H), 6.90 (s, 1H), 6.57 (dd, J = 17.0, 10.3 Hz, 1H), 6.45 (s, 1H), 6.36 (dd, J = 17.0, 1.5 Hz, 1H), 5.80 (d, J = 10.4 Hz, 1H), 5.52 (dd, J = 8.6, 4.7 Hz, 1H), 4.14 (td, J = 7.9, 4.2 Hz, 1H), 3.96 (q, J = 8.0 Hz, 1H), 3.86 (s, 3H), 3.78 (t, J = 5.1 Hz, 2H), 3.73 (t, J = 5.0 Hz, 2H), 2.95 (t, J = 5.0 Hz, 2H), 2.90 (t, J = 5.1 Hz, 2H), 2.80 (dtd, J = 12.3, 8.0, 4.2 Hz, 1H), 2.36 - 2.26 (m, 1H), 2.16 (s, 3H); 596.3[M+H]$^+$	1.41

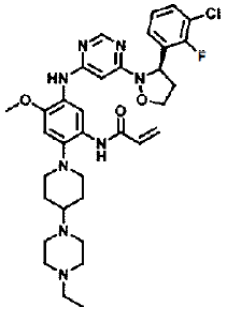
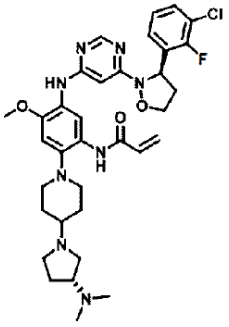
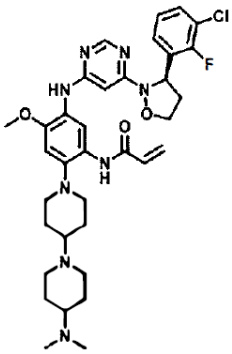
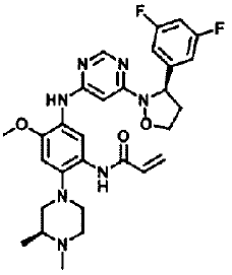
		yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide		

[651]

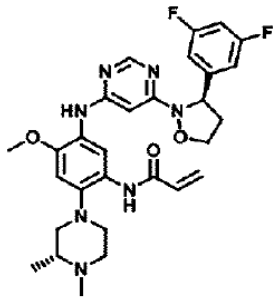
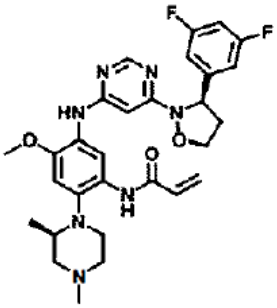
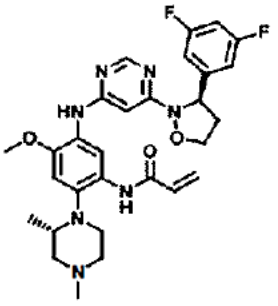
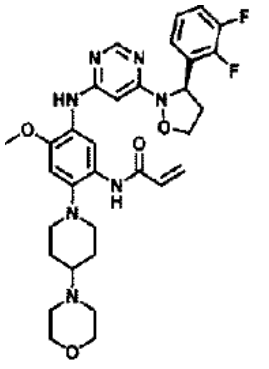
908		N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.10 (s, 1H), 9.05 (s, 1H), 8.21 (s, 1H), 7.23 (dt, J = 15.8, 7.3 Hz, 2H), 7.07 (t, J = 7.6 Hz, 1H), 6.86 (s, 1H), 6.65 (dd, J = 17.0, 10.1 Hz, 1H), 6.32 (s, 1H), 6.24 (dd, J = 17.0, 2.0 Hz, 1H), 5.78 - 5.73 (m, 1H), 5.71 (dd, J = 8.7, 5.2 Hz, 1H), 4.80 (d, J = 6.4 Hz, 4H), 4.47 (t, J = 6.6 Hz, 1H), 4.20 (td, J = 7.8, 3.0 Hz, 2H), 3.84 (s, 7H), 3.17 (s, 5H), 2.83 (dq, J = 8.1, 4.2 Hz, 1H), 2.26 (d, J = 1.9 Hz, 3H), 2.19 (ddt, J = 11.6, 7.7, 3.9 Hz, 1H). ; 590.4[M+H]+	1.25
909		N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 8.99 (s, 1H), 8.60 (s, 1H), 8.15 (d, J = 2.9 Hz, 2H), 7.28 (t, J = 7.4 Hz, 1H), 7.19 (t, J = 7.3 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.85 (s, 1H), 6.61 (dd, J = 17.0, 10.2 Hz, 1H), 6.37 (s, 1H), 6.27 - 6.16 (m, 2H), 6.13 - 5.81 (m, 1H), 5.72 (dd, J = 9.2, 4.4 Hz, 2H), 4.14 (td, J = 7.9, 3.8 Hz, 1H), 3.85 (q, J = 7.9 Hz, 1H), 3.79 (s, 3H), 2.88 - 2.60 (m, 10H), 2.54 (s, 1H), 2.26 (d, J = 2.0 Hz, 3H), 2.13 (ddt, J = 12.8, 8.2, 4.1 Hz, 1H), 1.71 (dq, J = 6.8, 3.4 Hz, 1H). ; 574.5[M+H]+	1.29
910		N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 8.95 (s, 1H), 8.60 (s, 1H), 8.14 (s, 1H), 7.28 (t, J = 7.1 Hz, 1H), 7.19 (t, J = 7.0 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.82 (s, 1H), 6.60 - 6.59 (m, 1H), 6.35 (s, 1H), 6.20 (dt, J = 17.3, 2.4 Hz, 2H), 5.72 (dd, J = 9.1, 4.9 Hz, 2H), 4.14 (td, J = 7.9, 3.9 Hz, 1H), 3.85 (t, J = 8.0 Hz, 2H), 3.80 (d, J = 2.1 Hz, 3H), 3.46 (q, J = 8.9, 8.0 Hz, 2H), 3.06 - 2.93 (m, 8H), 2.78 (dt, J = 9.8, 6.0 Hz, 2H), 2.71 - 2.62 (m, 4H), 2.36 - 2.30 (m, 1H), 2.26 (d, J = 2.0 Hz, 3H), 2.12 (d, J = 4.0 Hz, 6H). ; 645.6[M+H]+	1.12
911		N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-	1H NMR (400 MHz,DMSO-d6) δ 8.95 (s, 1H), 8.60 (s, 1H), 8.14 (s, 1H), 7.28 (t, J = 7.3 Hz, 1H), 7.19 (t, J = 7.2 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.82 (s, 1H), 6.60 (ddt, J = 21.3, 16.9, 6.5 Hz, 1H), 6.35 (s, 1H), 6.27 - 6.00 (m, 1H), 5.73 (ddd, J = 9.7, 6.9, 3.3 Hz, 2H), 4.14 (td, J = 7.9, 3.9 Hz, 1H), 3.85 (t, J = 8.0 Hz, 1H), 3.80 (s, 3H), 3.65 (t, J = 7.0 Hz, 2H), 3.45 (t, J = 7.8 Hz, 2H), 3.23 (t, J = 6.3 Hz, 3H), 3.17 (ddt, J = 12.6, 10.3, 6.4 Hz, 4H), 3.05 (d, J = 10.4 Hz, 3H), 2.98 (dd, J = 11.5, 3.6 Hz, 4H), 2.78 (dd, J = 8.1, 4.2 Hz, 2H), 2.71 - 2.61 (m, 2H), 2.26 (d, J = 2.0 Hz, 2H), 2.12 (s, 6H). ; 659.6[M+H]+	1.23

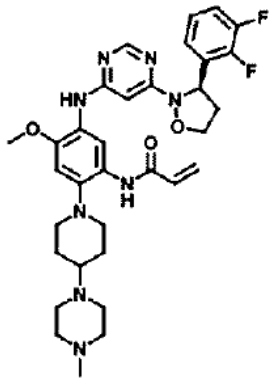
		methoxyphenyl)acrylamide		
912		N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 8.91 (s, 1H), 8.62 (s, 1H), 8.15 (s, 1H), 7.31 - 7.25 (m, 1H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.83 (s, 1H), 6.63 (d, *J* = 11.6 Hz, 1H), 6.37 (s, 1H), 6.28 - 6.19 (m, 1H), 5.72 (dd, *J* = 9.1, 5.4 Hz, 2H), 4.14 (td, *J* = 7.9, 3.8 Hz, 1H), 3.86 (t, *J* = 8.0 Hz, 1H), 3.81 (s, 3H), 3.60 (ddt, *J* = 13.0, 9.8, 4.8 Hz, 4H), 3.13 (qd, *J* = 7.1, 3.4 Hz, 4H), 2.77 (dq, *J* = 8.2, 4.1 Hz, 2H), 2.74 - 2.63 (m, 4H), 2.26 (d, *J* = 2.0 Hz, 3H), 2.20 - 2.08 (m, 2H), 1.83 (s, 2H), 1.13 (s, 6H). ; 630.4[M+H]+	1.32

[652]

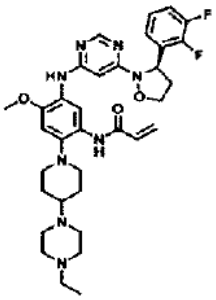
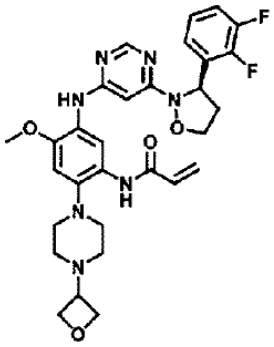
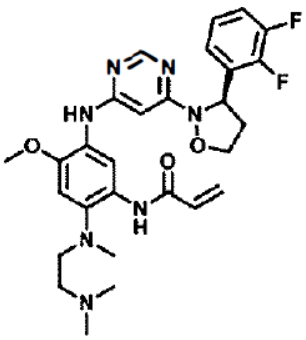
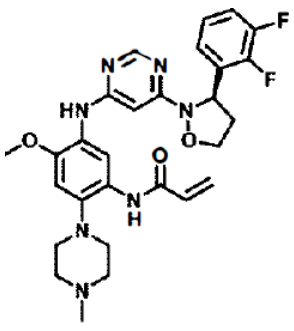
913		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 8.95 (s, 1H), 8.63 (s, 1H), 8.14 (d, J = 6.5 Hz, 2H), 7.55 - 7.48 (m, 1H), 7.48 - 7.40 (m, 1H), 7.22 (t, J = 7.9 Hz, 1H), 6.82 (s, 1H), 6.76 - 6.58 (m, 1H), 6.36 (s, 1H), 6.22 (td, J = 16.7, 16.1, 2.0 Hz, 2H), 5.87 (dt, J = 10.3, 1.5 Hz, 1H), 4.16 (dt, J = 8.1, 4.0 Hz, 1H), 3.85 (q, J = 8.0 Hz, 1H), 3.80 (s, 3H), 3.67 (q, J = 7.9, 7.3 Hz, 1H), 3.22 (dd, J = 12.7, 6.3 Hz, 3H), 3.19 - 3.12 (m, 2H), 3.05 (d, J = 10.7 Hz, 3H), 3.00 (s, 1H), 2.81 (dq, J = 8.3, 4.2 Hz, 1H), 2.67 (t, J = 11.9 Hz, 4H), 2.37 - 2.20 (m, 2H), 2.20 (dq, J = 12.9, 4.9, 4.4 Hz, 3H), 1.85 (d, J = 12.1 Hz, 2H), 1.71 (d, J = 11.6 Hz, 2H).; 665.5[M+H]+	1.25
914		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz,DMSO-d6) δ 8.95 (s, 1H), 8.63 (s, 1H), 8.15 (s, 1H), 7.55 - 7.48 (m, 1H), 7.48 - 7.40 (m, 1H), 7.22 (t, J = 7.9 Hz, 1H), 6.82 (s, 1H), 6.64 (dd, J = 16.8, 10.1 Hz, 1H), 6.35 (s, 1H), 6.24 - 6.17 (m, 1H), 5.72 (dt, J = 9.3, 5.0 Hz, 2H), 4.17 (td, J = 7.9, 3.7 Hz, 1H), 3.85 (q, J = 8.1 Hz, 1H), 3.80 (s, 3H), 3.20 - 3.13 (m, 1H), 3.01 (td, J = 15.7, 14.1, 6.8 Hz, 4H), 2.82 (dq, J = 8.3, 4.8 Hz, 2H), 2.73 - 2.62 (m, 4H), 2.37 (t, J = 7.6 Hz, 1H), 2.14 (s, 7H), 1.87 (d, J = 28.6 Hz, 3H), 1.73 - 1.57 (m, 3H). ; 665.5[M+H]+	1.19
915		N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide	1H NMR (400 MHz, DMSO-d6) δ 9.08 (d, J = 11.8 Hz, 1H), 8.65 (s, 1H), 8.15 (d, J = 5.0 Hz, 1H), 8.05 (d, J = 3.7 Hz, 1H), 7.55 - 7.48 (m, 1H), 7.44 (t, J = 7.2 Hz, 1H), 7.23 (t, J = 7.9 Hz, 1H), 6.82 (s, 1H), 6.38 (s, 1H), 6.30 - 6.16 (m, 1H), 6.04 (dq, J = 30.3, 6.5 Hz, 1H), 5.72 (dd, J = 8.8, 5.1 Hz, 1H), 4.18 (td, J = 8.0, 3.6 Hz, 1H), 3.85 (q, J = 7.9 Hz, 1H), 3.80 (s, 3H), 3.62 (t, J = 7.6 Hz, 1H), 3.07 (d, J = 2.9 Hz, 4H), 3.01 (dt, J = 13.1, 6.2 Hz, 5H), 2.91 (t, J = 7.7 Hz, 4H), 2.66 (s, 6H), 2.25 - 2.14 (m, 1H), 1.75 - 1.66 (m, 6H).; 679.5[M+H]+	1.20
916		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.01 (s, 1H), 8.66 (s, 1H), 8.17 (d, J = 4.8 Hz, 2H), 7.12 (dp, J = 7.7, 2.5, 2.1 Hz, 3H), 6.83 (s, 1H), 6.61 (dd, J = 17.0, 10.2 Hz, 1H), 6.38 (s, 1H), 6.21 (dd, J = 17.0, 2.0 Hz, 1H), 5.77 - 5.68 (m, 1H), 5.56 (dd, J = 8.7, 5.0 Hz, 1H), 4.13 (td, J = 7.9, 3.9 Hz, 1H), 3.82 (s, 3H), 3.34 (s, 3H), 2.95 (d, J = 13.0 Hz, 4H), 2.76 (dtd, J = 12.1, 7.9, 3.8 Hz, 2H), 2.40 (s, 2H), 2.30 - 2.18 (m, 1H), 1.32 - 1.21 (m, 2H), 1.11 (d, J = 7.4 Hz, 3H).; 566.4[M+H]$^+$	1.21

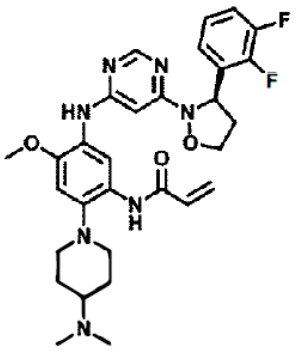
[653]

917		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.99 (s, 1H), 8.64 (s, 1H), 8.17 (s, 1H), 8.13 (s, 1H), 7.12 (dq, J = 9.4, 3.2 Hz, 3H), 6.83 (s, 1H), 6.58 (dd, J = 17.0, 10.2 Hz, 1H), 6.36 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.72 (dd, J = 10.2, 2.0 Hz, 1H), 5.56 (dd, J = 8.7, 5.0 Hz, 1H), 4.13 (td, J = 7.9, 3.9 Hz, 1H), 3.81 (s, 4H), 3.32 (s, 10H), 2.98 - 2.71 (m, 5H), 2.24 (ddd, J = 20.7, 10.1, 6.2 Hz, 4H), 1.32 - 1.19 (m, 3H), 1.09 - 0.97 (m, 3H).; 566.4[M+H]$^+$	1.23
918		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-2,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	566.5[M+H]$^+$	1.27
919		N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-2,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	566.5[M+H]$^+$	1.27
920		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.63 (s, 1H), 8.16 (s, 1H), 7.35 (ddd, J = 10.4, 6.3, 1.9 Hz, 1H), 7.32 - 7.26 (m, 1H), 7.23 - 7.15 (m, 1H), 6.83 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.36 (s, 1H), 6.21 (dd, J = 17.0, 2.0 Hz, 1H), 5.70 - 5.68 (m, 2H), 3.86 (d, J = 8.2 Hz, 1H), 3.80 (s, 3H), 3.59 (t, J = 4.5 Hz, 4H), 3.33 (s, 4H), 3.05 (d, J = 11.1 Hz, 2H), 2.81 (dtd, J = 12.0, 7.9, 3.7 Hz, 1H), 2.66 (tt, J = 11.7, 2.5 Hz, 2H), 2.22 (dddq, J = 16.8, 12.9, 8.2, 5.0, 4.3 Hz, 2H), 1.91 - 1.81 (m, 2H), 1.69 (tdd, J = 15.1, 9.1, 3.4 Hz, 2H), 1.30 - 1.20 (m, 2H), 0.85 (td, J = 7.9, 7.3, 3.1 Hz, 1H).; 622.4[M+H]$^+$	1.21

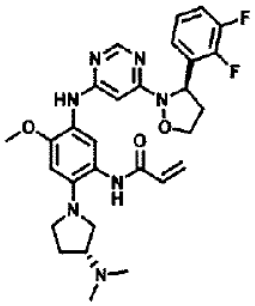
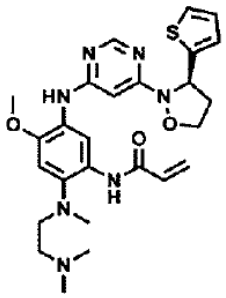
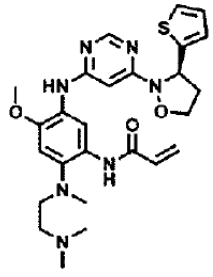
921		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.97 (s, 1H), 8.64 (s, 1H), 8.16 (s, 1H), 7.40 - 7.25 (m, 2H), 7.26 - 7.15 (m, 1H), 6.82 (s, 1H), 6.68 (ddd, J = 19.3, 17.0, 10.3 Hz, 1H), 6.36 (s, 1H), 6.29 - 6.16 (m, 2H), 5.78 - 5.68 (m, 3H), 4.17 (td, J = 8.0, 3.8 Hz, 1H), 3.80 (s, 3H), 3.07 (d, J = 11.0 Hz, 3H), 2.87 - 2.61 (m, 11H), 2.56 (s, 1H), 1.92 - 1.66 (m, 5H), 1.31 - 1.20 (m, 5H).:635.5[M+H]$^+$	1.16

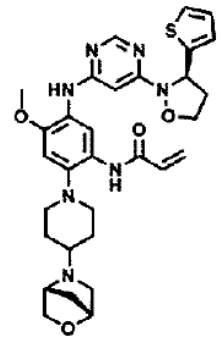
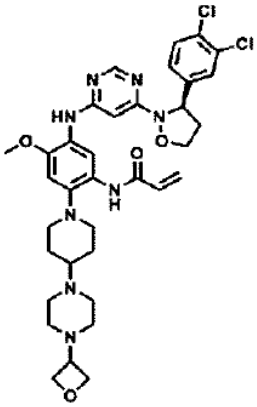
[654]

922		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	649.5[M+H]$^+$	1.17
923		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.91 (s, 1H), 8.49 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 7.39 - 7.31 (m, 1H), 7.12 - 7.00 (m, 2H), 7.00 (s, 1H), 6.82 (s, 1H), 6.75 (s, 1H), 6.36 (dd, *J* = 17.0, 1.6 Hz, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.93 (dd, *J* = 8.8, 4.6 Hz, 1H), 5.74 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.72 (t, *J* = 6.5 Hz, 2H), 4.67 (t, *J* = 6.2 Hz, 2H), 4.14 (td, *J* = 8.1, 4.2 Hz, 1H), 4.06 (q, *J* = 8.1 Hz, 1H), 3.85 (s, 3H), 3.61 (p, *J* = 6.4 Hz, 1H), 3.03 - 2.91 (m, 4H), 2.91 - 2.79 (m, 1H), 2.63 - 2.41 (m, 4H), 2.38 - 2.25 (m, 1H). : 504.5 [M+H]$^+$	1.26
924		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.10 (s, 1H), 8.95 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 7.41 - 7.32 (m, 1H), 7.12 - 6.99 (m, 2H), 6.98 (s, 1H), 6.80 (d, *J* = 1.3 Hz, 2H), 6.40 (dd, *J* = 17.0, 2.0 Hz, 1H), 6.29 (dd, *J* = 17.0, 9.8 Hz, 1H), 5.94 (dd, *J* = 8.8, 4.5 Hz, 1H), 5.68 (dd, *J* = 9.8, 2.0 Hz, 1H), 4.20 - 4.05 (m, 2H), 3.85 (s, 3H), 2.94 - 2.80 (m, 3H), 2.72 (s, 3H), 2.37 - 2.31 (m, 3H), 2.28 (s, 6H). : 554.4 [M+H]$^+$	1.21
925		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (s, 1H), 8.53 (s, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 7.40 - 7.31 (m, 1H), 7.12 - 7.00 (m, 2H), 6.98 (s, 1H), 6.80 (s, 1H), 6.75 (s, 1H), 6.37 (dd, *J* = 16.9, 1.6 Hz, 1H), 6.27 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.93 (dd, *J* = 8.9, 4.5 Hz, 1H), 5.75 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.14 (td, *J* = 8.1, 4.2 Hz, 1H), 4.07 (q, *J* = 8.1 Hz, 1H), 3.84 (s, 3H), 2.99 - 2.88 (m, 4H), 2.88 - 2.79 (m, 1H), 2.73 - 2.49 (m, 4H), 2.40 (s, 3H), 2.34 - 2.25 (m, 1H). : 552.4 [M+H]$^+$	1.17

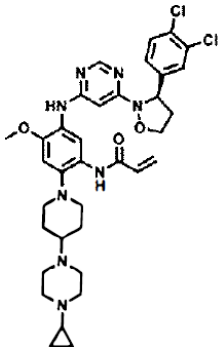
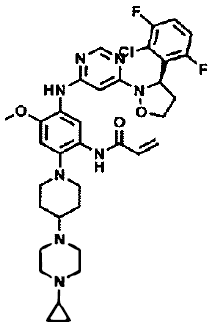
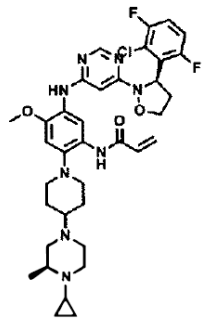
926		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.87 (s, 1H), 8.46 (s, 1H), 8.36 (d, *J* = 1.0 Hz, 1H), 7.36 (dt, *J* = 9.7, 3.5 Hz, 1H), 7.12 - 6.99 (m, 2H), 6.96 (s, 1H), 6.75 (d, *J* = 3.5 Hz, 2H), 6.36 (dd, *J* = 16.9, 1.6 Hz, 1H), 6.26 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.93 (dd, *J* = 8.9, 4.6 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.14 (td, *J* = 8.1, 4.3 Hz, 1H), 4.07 (q, *J* = 8.0 Hz, 1H), 3.85 (s, 3H), 3.11 - 3.04 (m, 2H), 2.86 (dtd, *J* = 12.4, 8.1, 4.2 Hz, 1H), 2.77 (dd, *J* = 12.3, 2.3 Hz, 1H), 2.71 (dd, *J* = 12.1, 2.3 Hz, 1H), 2.42 (s, 6H), 2.36 - 2.26 (m, 2H), 2.09 (d, *J* = 12.6 Hz, 2H), 1.71 (dtd, *J* = 14.7, 12.0, 4.0 Hz, 2H), ; 580.5 $[M+H]^+$	1.20

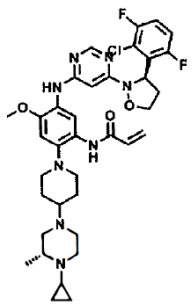
[655]

927		N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.65 (s, 1H), 8.35 (s, 1H), 8.17 (s, 1H), 7.40 - 7.31 (m, 1H), 7.12 - 6.98 (m, 2H), 6.91 (s, 1H), 6.73 (d, J = 11.0 Hz, 2H), 6.38 (dd, J = 17.0, 1.9 Hz, 1H), 6.30 (dd, J = 16.9, 9.7 Hz, 1H), 5.93 (dd, J = 8.8, 4.5 Hz, 1H), 5.73 (dd, J = 9.7, 1.9 Hz, 1H), 4.14 (td, J = 8.0, 4.2 Hz, 1H), 4.06 (q, J = 8.1 Hz, 1H), 3.84 (s, 3H), 3.23 - 3.14 (m, 1H), 3.14 - 3.06 (m, 3H), 2.94 - 2.78 (m, 2H), 2.37 - 2.31 (m, 1H), 2.30 (s, 6H), 2.24 - 2.12 (m, 1H), 2.00 - 1.92 (m, 1H). : 566.4 $[M+H]^+$	1.13
928		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(thiophene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 10.06 (s, 1H), 8.96 (s, 1H), 8.41 (s, 1H), 7.20 (dd, J = 5.1, 1.1 Hz, 1H), 7.07 (d, J = 3.5 Hz, 1H), 6.98 - 6.91 (m, 2H), 6.79 (s, 1H), 6.71 (s, 1H), 6.43 - 6.24 (m, 2H), 6.01 (dd, J = 8.2, 3.3 Hz, 1H), 5.68 (dd, J = 9.8, 2.0 Hz, 1H), 4.26 - 4.12 (m, 2H), 3.84 (s, 3H), 2.92 - 2.83 (m, 2H), 2.75 - 2.62 (m, 4H), 2.55 - 2.45 (m, 1H), 2.38 - 2.31 (m, 2H), 2.29 (s, 6H); 524.36$[M+H]^+$	1.16
929		N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(thiophene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.52 (s, 1H), 8.41 (s, 1H), 7.20 (dd, J = 5.1, 1.0 Hz, 1H), 7.07 (d, J = 3.5 Hz, 1H), 6.98 - 6.91 (m, 2H), 6.79 (s, 1H), 6.67 (s, 1H), 6.40 - 6.22 (m, 2H), 6.00 (dd, J = 8.2, 3.3 Hz, 1H), 5.75 (dd, J = 10.0, 1.3 Hz, 1H), 4.21 (td, J = 8.0, 5.5 Hz, 1H), 4.13 (q, J = 7.9 Hz, 1H), 3.83 (s, 3H), 2.97 - 2.87 (m, 4H), 2.73 - 2.63 (m, 1H), 2.57 - 2.46 (m, 1H), 2.30 (s, 3H); 522.33$[M+H]^+$	1.13

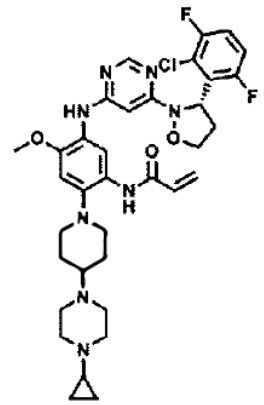
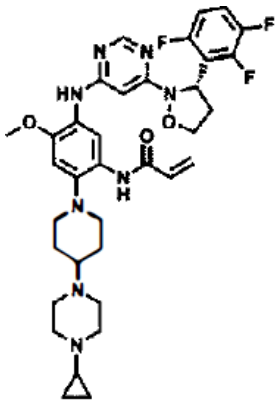
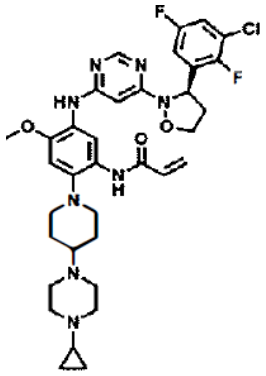
930		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(thiophene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.48 (s, 1H), 8.40 (s, 1H), 7.20 (dd, *J* = 5.1, 1.0 Hz, 1H), 7.07 (d, *J* = 3.5 Hz, 1H), 6.98 - 6.93 (m, 2H), 6.75 (s, 1H), 6.67 (s, 1H), 6.38 - 6.20 (m, 2H), 6.00 (dd, *J* = 8.3, 3.3 Hz, 1H), 5.73 (dd, *J* = 10.0, 1.3 Hz, 1H), 4.45 (s, 1H), 4.24 - 4.07 (m, 3H), 3.84 (s, 3H), 3.80 (s, 1H), 3.60 - 3.63 (m, 1H), 3.19 - 3.14 (m, 1H), 3.06 - 2.99 (m, 2H), 2.81 - 2.65 (m, 3H), 2.64 - 2.56 (m, 1H), 2.56 - 2.46 (m, 2H), 2.08 - 1.65 (m, 6H): 604.45[M+H]$^+$	1.16
931		N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.36 (s, 1H), 7.58 (s, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.30 (d, *J* = 8.6 Hz, 1H), 6.93 (s, 1H), 6.71 (s, 2H), 6.38 (d, *J* = 16.1 Hz, 3H), 5.76 (d, *J* = 11.1 Hz, 1H), 5.65 (s, 1H), 4.70 (t, *J* = 6.6 Hz, 2H), 4.66 - 4.56 (m, 2H), 4.16 (d, *J* = 4.3 Hz, 1H), 4.06 (d, *J* = 8.2 Hz, 1H), 3.92 (s, 1H), 3.85 (s, 3H), 3.61 (d, *J* = 33.0 Hz, 2H), 3.45 - 3.29 (m, 4H), 3.26 - 3.06 (m, 4H), 2.86 (s, 1H), 2.78 (d, *J* = 18.0 Hz, 5H), 2.39 - 2.26 (m, 3H). : 709.4 [M+H]$^+$	1.31

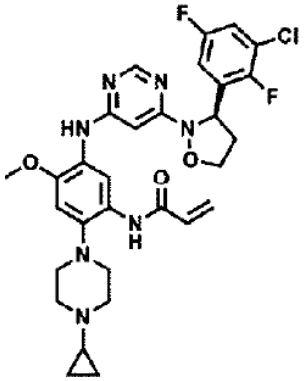
[656]

932		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 9.13 (s, 1H), 8.84 (s, 1H), 8.35 (s, 1H), 8.31 (s, 1H), 7.57 (s, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.29 (dd, *J* = 8.8, 2.2 Hz, 1H), 6.70 (m, 2H), 6.38 (s, 2H), 5.80 - 5.73 (m, 1H), 5.64 (dd, *J* = 8.8, 4.6 Hz, 1H), 4.17 (td, *J* = 7.9, 4.2 Hz, 1H), 4.06 (q, *J* = 8.2 Hz, 1H), 3.95 - 3.90 (m, 2H), 3.84 (s, 3H), 3.66 (d, *J* = 17.4 Hz, 4H), 3.33 (t, *J* = 6.3 Hz, 4H), 3.13 - 3.04 (m, 6H), 2.33 (dd, *J* = 12.3, 4.3 Hz, 2H), 2.29 - 2.22 (m, 2H), 0.55 (s, 2H), 0.30 (s, 2H).; 603.5 $[M+H]^+$	1.38
933		N-(5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.82 (s, 1H), 8.43 (s, 1H), 8.33 (d, *J* = 1.0 Hz, 1H), 7.08 - 7.01 (m, 1H), 7.00 - 6.93 (m, 1H), 6.84 (s, 1H), 6.73 (s, 1H), 6.62 (s, 1H), 6.37 - 6.20 (m, 2H), 5.94 (d, *J* = 8.3 Hz, 1H), 5.75 - 5.71 (m, 1H), 4.39 - 4.35 (m, 1H), 3.99 - 3.93 (m, 1H), 3.82 (s, 3H), 3.05 (d, *J* = 11.4 Hz, 2H), 2.78 - 2.59 (m, 11H), 2.56 - 2.40 (m, 1H), 2.32 (td, *J* = 7.5, 3.8 Hz, 1H), 2.07 (d, *J* = 12.6 Hz, 2H), 1.72 - 1.65 (m, 2H), 1.64 - 1.60 (m, 1H), 0.48 - 0.41 (m, 4H). ; 695.5 $[M+H]^+$	1.20
934		N-(5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.83 (s, 1H), 8.42 (s, 1H), 8.33 (d, *J* = 1.1 Hz, 1H), 7.05 (ddd, *J* = 9.0, 7.9, 4.5 Hz, 1H), 6.97 (td, *J* = 9.5, 4.3 Hz, 1H), 6.83 (s, 1H), 6.73 (s, 1H), 6.62 (s, 1H), 6.35 (dd, *J* = 17.0, 1.5 Hz, 1H), 6.24 (dd, *J* = 17.0, 10.1 Hz, 1H), 5.93 (t, *J* = 8.3 Hz, 1H), 5.79 - 5.70 (m, 1H), 4.42 - 4.33 (m, 1H), 3.96 (td, *J* = 8.9, 6.0 Hz, 1H), 3.82 (s, 3H), 3.08 - 2.99 (m, 3H), 2.96 (d, *J* = 10.7 Hz, 1H), 2.87 (d, *J* = 10.8 Hz, 1H), 2.83 - 2.65 (m, 3H), 2.60 - 2.42 (m, 3H), 2.36 - 2.24 (m, 2H), 2.07 (d, *J* = 12.1 Hz, 2H), 2.00 (t, *J* = 10.4 Hz, 1H), 1.72 - 1.62 (m, 2H), 1.58 - 1.48 (m, 1H), 1.21 (d, 3H), 0.70 - 0.55 (m, 2H), 0.40 - 0.38 (m, 1H), 0.37 - 0.26 (m, 1H). ; 709.5 $[M+H]^+$	1.22

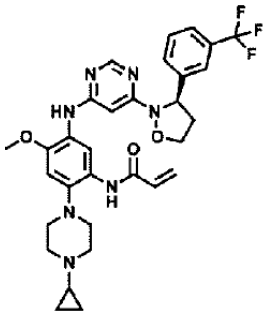
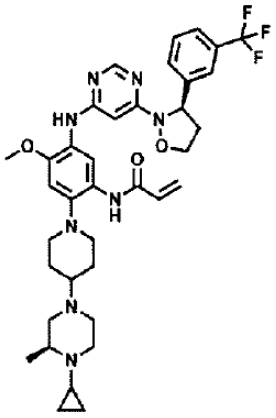
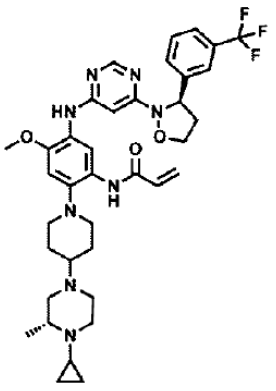
935		N-(5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.80 (s, 1H), 8.43 (s, 1H), 8.32 (d, *J* = 1.0 Hz, 1H), 7.05 (ddd, *J* = 9.1, 7.9, 4.5 Hz, 1H), 6.97 (td, *J* = 9.5, 4.4 Hz, 1H), 6.87 (s, 1H), 6.73 (s, 1H), 6.62 (s, 1H), 6.36 (dd, *J* = 16.9, 1.5 Hz, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.93 (t, *J* = 8.3 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.5 Hz, 1H), 4.37 (td, *J* = 8.0, 1.9 Hz, 1H), 4.01 - 3.90 (m, 1H), 3.82 (s, 3H), 3.03 (td, *J* = 11.3, 10.8, 5.1 Hz, 3H), 2.96 (d, *J* = 10.8 Hz, 1H), 2.92 - 2.84 (m, 1H), 2.84 - 2.64 (m, 3H), 2.60 - 2.42 (m, 3H), 2.36 - 2.23 (m, 2H), 2.11 - 1.95 (m, 3H), 1.73 - 1.58 (m, 2H), 1.58 - 1.49 (m, 1H), 1.21 (d, 3H), 0.71 - 0.55 (m, 2H), 0.49 - 0.38 (m, 1H), 0.37 - 0.26 (m, 1H). ; 709.5 $[M+H]^+$	1.22

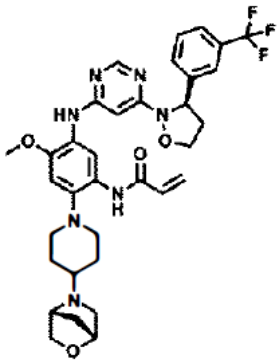
[657]

936		N-(5-((6-((S)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.04 (s, 2H), 8.16 (s, 1H), 8.04 (s, 1H), 7.44 (td, J = 8.9, 4.4 Hz, 1H), 7.30 (td, J = 9.7, 4.4 Hz, 1H), 6.84 (s, 1H), 6.62 (dd, J = 16.9, 10.2 Hz, 1H), 6.28 - 6.06 (m, 3H), 5.78 - 5.68 (m, 3H), 4.39 (t, J = 7.6 Hz, 1H), 3.79 (s, 3H), 3.46 (s, 2H), 3.27 (s, 2H), 3.15 (d, J = 11.5 Hz, 4H), 3.02 (d, J = 24.8 Hz, 3H), 2.89 - 2.66 (m, 6H), 2.41 (ddd, J = 10.2, 11.3, 7.8 Hz, 2H), 2.08 (d, J = 3.5 Hz, 3H), 1.91 (s, 3H), 0.55 (d, J = 6.9 Hz, 2H), 0.48 (s, 2H).; 605.5[M+H]$^+$	1.15
937		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.97 (s, 1H), 8.58 (s, 1H), 8.14 (s, 1H), 7.45 (qd, J = 9.4, 4.8 Hz, 1H), 7.13 (tdd, J = 9.5, 3.9, 2.0 Hz, 1H), 6.81 (s, 1H), 6.65 (dd, J = 17.0, 10.2 Hz, 1H), 6.27 (d, J = 5.4 Hz, 1H), 6.22 (t, J = 1.7 Hz, 1H), 5.74 - 5.64 (m, 2H), 4.32 (td, J = 8.1, 2.2 Hz, 1H), 3.78 (s, 3H), 3.56 (p, J = 6.6 Hz, 2H), 3.07 (q, J = 7.5 Hz, 4H), 2.79 (ddt, J = 13.9, 10.4, 5.6 Hz, 2H), 2.65 (d, J = 9.6 Hz, 10H), 2.41 (ddd, J = 18.7, 11.0, 7.8 Hz, 2H), 1.95 - 1.85 (m, 2H), 1.76 (q, J = 12.5, 11.3 Hz, 2H), 0.41 (dt, J = 6.2, 3.0 Hz, 2H), 0.31 (p, J = 3.9 Hz, 2H).; 679.5[M+H]$^+$	1.18
938		N-(5-((6-((R)-3-(3-chloro-2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyph	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.66 (s, 1H), 8.16 (s, 1H), 7.57 (ddd, J = 8.4, 5.5, 3.2 Hz, 1H), 7.22 (ddd, J = 8.7, 5.3, 3.2 Hz, 1H), 6.82 (s, 1H), 6.65 (dd, J = 16.9, 10.2 Hz, 1H), 6.36 (s, 1H), 6.20 (dd, J = 17.0, 2.0 Hz, 1H), 5.71 (dd, J = 9.2, 3.8 Hz, 2H), 4.18 (td, J = 7.9, 3.7 Hz, 1H), 3.79 (s, 3H), 3.04 (d, J = 11.2 Hz, 2H), 2.81 (dtd, J = 12.1, 8.0, 3.6 Hz, 1H), 2.66 (t, J = 11.7 Hz, 2H), 2.54 (s, 2H), 2.32 - 2.14 (m, 3H), 2.00 (s, 2H), 1.86 (s, 8H), 1.76 - 1.62 (m, 3H), 1.58 (tt, J = 6.7, 3.6 Hz, 2H), 0.39 (dt, J = 6.2, 3.0 Hz, 2H), 0.27 (p, J = 3.9 Hz, 2H).; 605.5[M+H]$^+$	1.37

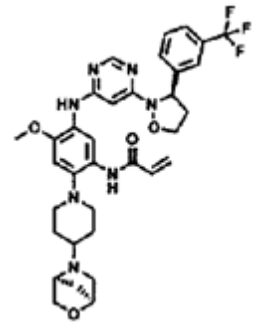
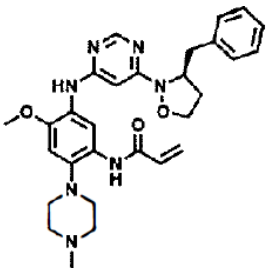
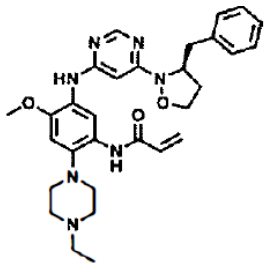
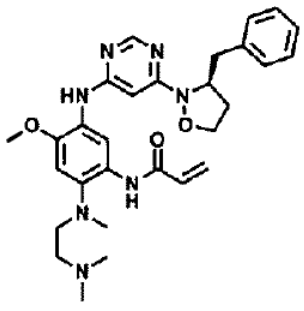
		enyl)acrylamide		
939		N-(5-((6-((R)-3-(3-chloro-2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.99 (s, 1H), 8.67 (s, 1H), 8.17 (s, 1H), 7.57 (ddd, J = 8.4, 5.6, 3.2 Hz, 1H), 7.22 (ddd, J = 8.7, 5.2, 3.2 Hz, 1H), 6.85 (s, 1H), 6.61 (dd, J = 17.0, 10.2 Hz, 1H), 6.38 (s, 1H), 6.20 (dd, J = 17.0, 1.9 Hz, 1H), 5.76 - 5.67 (m, 2H), 4.18 (td, J = 7.9, 3.7 Hz, 1H), 3.79 (s, 3H), 2.78 (dt, J = 34.1, 4.9 Hz, 10H), 2.21 (dtd, J = 13.0, 8.2, 4.9 Hz, 1H), 1.76 (s, 1H), 1.70 (dq, J = 6.9, 3.7, 3.3 Hz, 1H), 0.44 (dt, J = 6.3, 3.0 Hz, 2H), 0.32 (p, J = 4.0 Hz, 2H).: 612.3[M+H]$^+$	1.35

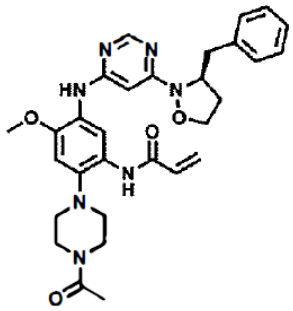
[658]

940		N-(2-(4-cyclopropylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (s, 1H), 8.60 (s, 1H), 8.37 (s, 1H), 7.73 (s, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.52 - 7.43 (m, 2H), 7.03 (s, 1H), 6.79 (s, 1H), 6.74 (s, 1H), 6.37 (dd, *J* = 16.9, 1.7 Hz, 1H), 6.29 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.80 - 5.73 (m, 2H), 4.23 - 4.14 (m, 1H), 4.14 - 4.02 (m, 1H), 3.81 (s, 3H), 2.92 - 2.75 (m, 9H), 2.43 - 2.30 (m, 1H), 1.77 - 1.68 (m, 1H), 0.57 - 0.42 (m, 4H). ; 610.4 $[M+H]^+$	1.31
941		N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.86 (s, 1H), 8.45 (s, 1H), 8.30 - 8.20 (m, 1H), 7.73 (s, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.54 - 7.47 (m, 1H), 7.47 - 7.41 (m, 1H), 6.96 (s, 1H), 6.74 (d, *J* = 6.4 Hz, 2H), 6.36 (dd, *J* = 16.9, 1.6 Hz, 1H), 6.25 (dd, *J* = 17.0, 10.0 Hz, 1H), 5.80 - 5.69 (m, 2H), 4.16 (td, *J* = 8.0, 4.2 Hz, 1H), 4.09 (q, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.00 - 3.00 (m, 3H), 2.97 (d, *J* = 10.8 Hz, 1H), 2.92 - 2.66 (m, 4H), 2.58 - 2.43 (m, 2H), 2.42 - 2.24 (m, 3H), 2.12 - 1.96 (m, 3H), 1.74 - 1.59 (m, 2H), 1.59 - 1.49 (m, 1H), 1.21 (d, 3H), 0.71 - 0.55 (m, 2H), 0.49 - 0.38 (m, 1H), 0.37 - 0.27 (m, 1H). ; 707.5 $[M+H]^+$	1.34
942		N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.86 (s, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 7.73 (s, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.54 - 7.48 (m, 1H), 7.48 - 7.41 (m, 1H), 6.98 (s, 1H), 6.74 (d, *J* = 6.4 Hz, 2H), 6.36 (dd, *J* = 17.1, 1.6 Hz, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.81 - 5.70 (m, 2H), 4.21 - 4.12 (m, 1H), 4.12 - 4.03 (m, 1H), 3.84 (s, 3H), 3.00 - 2.99 (m, 3H), 2.96 (d, *J* = 10.8 Hz, 1H), 2.88 (dd, *J* = 10.8, 2.7 Hz, 1H), 2.84 - 2.65 (m, 3H), 2.59 - 2.42 (m, 2H), 2.42 - 2.23 (m, 3H), 2.10 - 1.96 (m, 3H), 1.66 (qt, *J* = 12.1, 3.3 Hz, 2H), 1.58 - 1.48 (m, 1H), 1.21 (d, 3H), 0.70 - 0.55 (m, 2H), 0.49 - 0.38 (m, 1H), 0.37 - 0.26 (m, 1H). ; 707.5 $[M+H]^+$	1.33

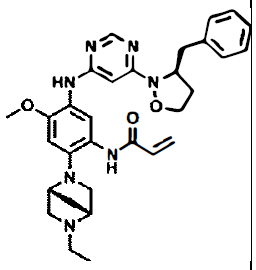
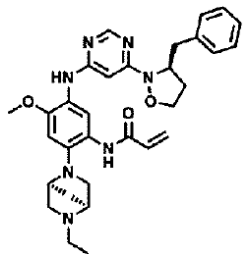
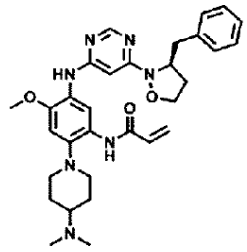
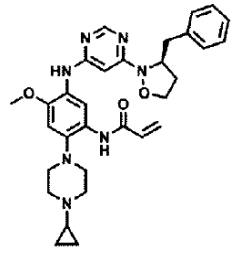
943		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.87 (s, 1H), 8.48 (s, 1H), 8.30 - 8.34 (m, 1H), 7.73 (s, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.54 - 7.43 (m, 2H), 6.98 (s, 1H), 6.75 (d, *J* = 9.5 Hz, 2H), 6.35 (dd, *J* = 16.9, 1.5 Hz, 1H), 6.24 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.80 - 5.69 (m, 2H), 4.44 (t, *J* = 2.0 Hz, 1H), 4.21 - 4.12 (m, 1H), 4.12 - 4.04 (m, 2H), 3.85 (s, 3H), 3.77 (s, 1H), 3.66 (dd, *J* = 8.0, 1.6 Hz, 1H), 3.14 (dd, *J* = 9.9, 1.8 Hz, 1H), 3.07 - 2.98 (m, 2H), 2.87 - 2.77 (m, 2H), 2.77 - 2.69 (m, 1H), 2.64 - 2.54 (m, 1H), 2.51 (d, *J* = 9.9 Hz, 1H), 2.43 - 2.30 (m, 1H), 2.04 (d, *J* = 12.7 Hz, 1H), 1.99 - 1.88 (m, 2H), 1.83 (d, *J* = 9.9 Hz, 1H), 1.75 - 1.62 (m, 2H). : 666.5 $[M+H]^+$	1.28

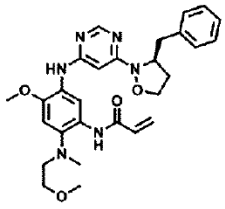
[659]

944		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.87 (s, 1H), 8.49 (s, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.73 (s, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.54 - 7.43 (m, 2H), 7.00 (s, 1H), 6.75 (d, J = 11.5 Hz, 2H), 6.35 (dd, J = 17.0, 1.5 Hz, 1H), 6.24 (dd, J = 16.9, 10.0 Hz, 1H), 5.80 - 5.69 (m, 2H), 4.44 (t, J = 2.0 Hz, 1H), 4.21 - 4.13 (m, 1H), 4.13 - 4.03 (m, 2H), 3.85 (s, 3H), 3.77 (s, 1H), 3.66 (dd, J = 7.9, 1.7 Hz, 1H), 3.14 (dd, J = 9.9, 1.7 Hz, 1H), 3.08 - 2.97 (m, 2H), 2.87 - 2.70 (m, 3H), 2.64 - 2.56 (m, 1H), 2.56 - 2.47 (m, 1H), 2.42 - 2.30 (m, 1H), 2.04 (d, J = 12.8 Hz, 1H), 1.99 - 1.88 (m, 2H), 1.86 - 1.79 (m, 1H), 1.75 - 1.62 (m, 2H). : 666.5 [M+H]$^+$	1.28
945		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.88 (s, 1H), 8.42 (s, 1H), 8.38 (s, 1H), 7.34 - 7.28 (m, 4H), 7.24- 7.20 (m, 1H), 7.01 (m, 1H), 6.79 (s, 1H), 6.57 (s, 1H), 6.47 - 6.23 (m, 2H), 5.75 (dd, J = 9.8, 1.7 Hz,1H), 4.02 - 4.84 (m, 1H), 4.06 (td, J = 8.1, 4.7 Hz, 1H), 3.95 (q, J = 8.1 Hz, 1H), 3.84 (s, 3H), 3.66 (p, J =6.7 Hz, 1H), 3.26 (dd, J = 13.7, 5.8 Hz, 1H), 3.07 (dd, J = 16.9, 9.4 Hz, 4H), 2.80 (d, J = 4.8 Hz, 2H),2.53 (s, 3H), 2.21 - 2.14 (m, 4H).: 530.5 [M+H]$^+$	1.11
946		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.87 (s, 1H), 8.50 (s, 1H), 8.37 (s, 1H), 7.36 - 7.29 (m, 4H), 7.23(dd, J = 5.9, 2.7 Hz, 1H), 7.03 (s, 1H), 6.81 (s, 1H), 6.57 (s, 1H), 6.40 - 6.11 (m, 2H), 5.76 (m, 1H), 4.88(m, 1H), 4.06 (td, J = 8.0, 4.6 Hz, 1H), 3.96 (q, J = 8.1 Hz, 1H), 3.83 (s, 3H), 3.65 (m, 2H), 3.26 (m, 1H),3.08 (t, J = 7.4 Hz, 2H), 3.04 - 2.06 (m, 4H), 2.80 (m, 3H), 2.18 (dtd, J = 12.6, 8.1, 4.7 Hz, 1H), 2.06(dtd, J = 11.9, 7.9, 3.9 Hz, 1H), 1.54 (d, J = 7.4 Hz, 3H).: 544.5 [M+H]$^+$	1.07
947		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d6) δ 9.85 (s, 1H), 8.55 (s, 1H), 8.30 (s, 1H), 8.19 (s,1H), 7.30 (d, J = 4.4 Hz, 4H), 7.24 - 7.17 (m, 1H), 6.93 (s, 1H), 6.32 (s, 1H), 6.27 -6.15 (m, 2H), 5.71 (dd, J = 10.1, 2.2 Hz, 1H), 4.75 (td, J = 7.4, 3.7 Hz, 1H), 4.05 (m,1H), 3.86 - 3.72 (m, 4H), 3.62 - 3.53 (m, 1H), 3.16 - 3.01 (m, 4H), 2.75 (dd, J = 13.7,7.9 Hz, 1H), 2.62 (s, 3H), 2.52 - 2.49 (m, 6H), 2.19 - 2.08 (m, 1H), 2.05 - 1.94 (m, 1H).: 532.5 [M+H]$^+$	1.15

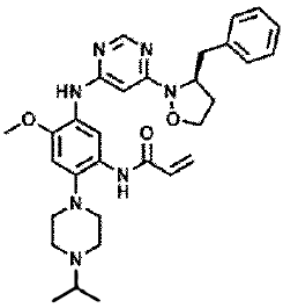
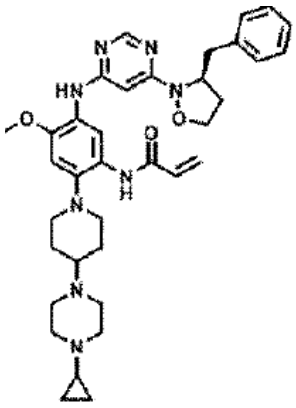
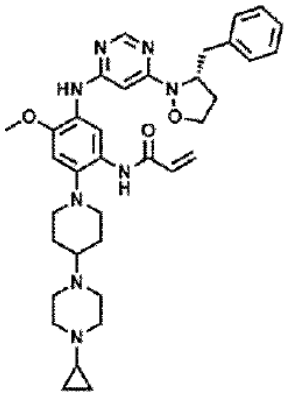
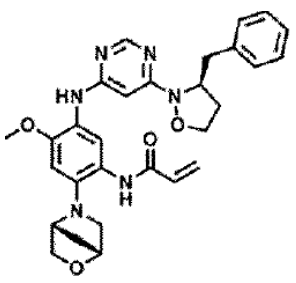
948		N-(2-(4-acetylpiperazine-1-yl)-5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-d) δ 8.93 (s, 1H), 8.43 (s, 1H), 8.40 (s, 1H), 7.35 - 7.28 (m, 4H), 7.24- 7.19 (m, 1H), 6.90 (s, 1H), 6.71 (s, 1H), 6.60 (s, 1H), 6.41 - 6.20 (m, 2H), 5.76 (dd, J = 10.1, 1.5 Hz,1H), 4.03 - 4.84 (m, 1H), 4.07 (m, 1H), 3.96 (q, J = 8.0 Hz, 1H), 3.84 - 3.80 (m, 4H), 3.64 (m, 2H), 3.26(dd, J = 13.7, 5.8 Hz, 1H), 3.08 (d, J = 6.6 Hz, 1H), 2.91 - 2.85 (m, 4H), 2.80 (dd, J = 13.7, 8.9 Hz, 1H), 2.17 (m, 4H), 2.12 - 2.02 (m, 1H).; 558.5 $[M+H]^+$	1.28

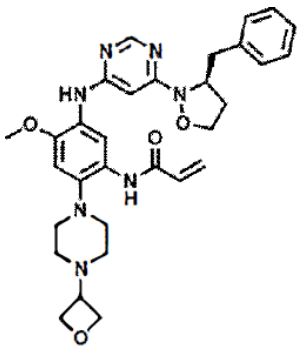
[660]

949		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.58 (s, 1H), 8.35 (s, 1H), 8.13 (s, 1H), 7.37 - 7.28 (m, 4H), 7.24 - 7.18 (m, 1H), 6.80 (s, 1H), 6.79 (s, 1H), 6.54 (s, 1H), 6.32 - 6.11 (m, 2H), 5.72 (dd, *J* = 9.7, 1.9 Hz, 1H), 4.88 (m, 1H), 4.07 (m, 1H), 3.99 - 3.80 (m, 4H), 3.86 (s, 3H), 3.26 (dd, *J* = 13.7, 5.7 Hz, 1H), 3.14 - 2.98 (m, 3H), 2.81 (m, 2H), 2.22 - 2.13 (m, 1H), 2.07 (m, 4H), 1.31 (t, *J* = 7.3 Hz, 3H).; 556.5 [M+H]$^+$	0.96
950		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.61 (s, 1H), 8.36 (s, 1H), 8.10 (s, 1H), 7.31 (m, 4H), 7.23 (m, 1H), 6.86 (s, 1H), 6.74 (s, 1H), 6.50 (s, 1H), 6.30 - 6.13 (m, 2H), 5.75 - 5.70 (m, 1H), 4.88 (m, 1H), 4.03 (m, 1H), 3.95 - 2.85 (s, 7H), 3.26 (dd, *J* = 13.7, 5.7 Hz, 1H), 2.97 (m, 3H), 2.84 - 2.77 (m, 2H), 2.15 (m, 1H), 2.05 (m, 4H), 1.26 (t, *J* = 7.5 Hz, 3H).; 556.5 [M+H]$^+$	1.10
951		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.45 (s, 1H), 8.38 (s, 1H), 7.35 - 7.29 (m, 4H), 7.21 (d, *J* = 6.8 Hz, 1H), 6.88 (s, 1H), 6.74 (s, 1H), 6.50 (s, 1H), 6.33 - 6.13 (m, 2H), 5.73 (dd, *J* = 9.8, 1.7 Hz, 1H), 4.93 - 4.84 (m, 1H), 4.06 (td, *J* = 8.1, 4.8 Hz, 1H), 3.96 (q, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.26 (dd, *J* = 13.7, 5.8 Hz, 1H), 3.07 (m, 2H), 2.84 - 2.68 (m, 4H), 2.43 (s, 6H), 2.23 - 2.13 (m, 2H), 2.13 - 2.02 (m, 4H).; 558.5 [M+H]$^+$	1.11
952		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.89 (s, 1H), 8.59 (s, 1H), 8.38 (s, 1H), 7.36 - 7.27 (m, 4H), 7.24 - 7.18 (m, 1H), 6.86 (s, 1H), 6.78 (s, 1H), 6.59 (s, 1H), 6.40 - 6.23 (m, 2H), 5.75 (dd, *J* = 9.8, 1.7 Hz, 1H), 4.93 - 4.85 (m, 1H), 4.06 (td, *J* = 8.1, 4.7 Hz, 1H), 3.97 (q, *J* = 8.0 Hz, 1H), 3.80 (s, 3H), 3.26 (dd, *J* = 13.7, 5.7 Hz, 1H), 2.90 - 2.75 (m, 9H), 2.23 - 2.13 (m, 1H), 2.07 (m, 1H), 1.72 (mz, 1H), 0.52 (m, 2H), 0.47 (m, 2H).; 556.5 [M+H]$^+$	1.15

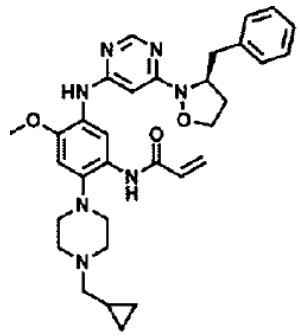
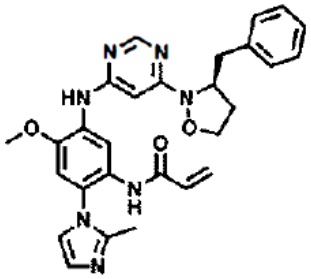
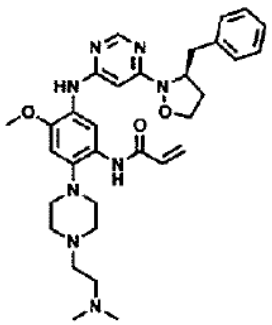
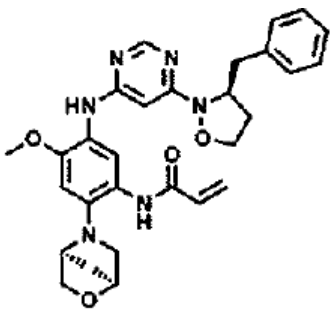
953		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 9.12 (s, 1H), 8.97 (s, 1H), 8.38 (s, 1H), 7.35 - 7.27 (m, 4H), 7.23 - 7.17 (m, 1H), 6.86 (s, 1H), 6.76 (s, 1H), 6.61 (s, 1H), 6.45 - 6.24 (m, 2H), 5.68 (dd, *J* = 9.8, 2.0 Hz, 1H), 4.89 (m, 1H), 4.10 - 3.94 (m, 2H), 3.83 (s, 3H), 3.45 (t, *J* = 4.9 Hz, 2H), 3.42 (s, 3H), 3.26 (dd, *J* = 13.6, 5.7 Hz, 1H), 2.96 (m, 2H), 2.80 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.75 (s, 3H), 2.23 - 2.13 (m, 1H), 2.06 (m, 1H).; 510.47 $[M+H]^+$	1.51

[661]

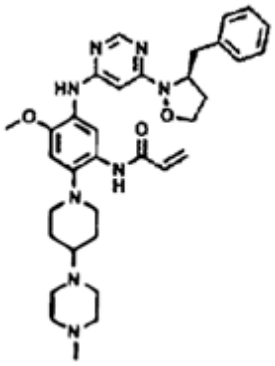
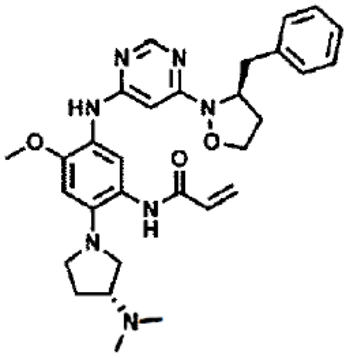
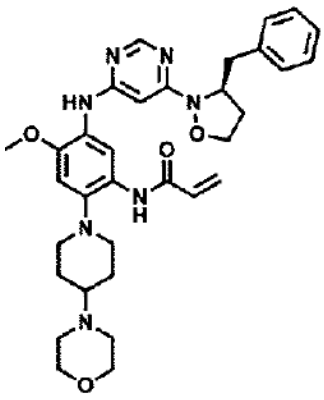
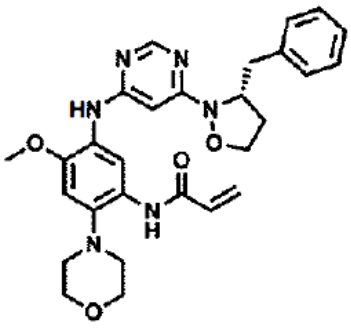
954		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.89 (s, 1H), 8.57 (s, 1H), 8.38 (d, *J* = 1.0 Hz, 1H), 7.36 - 7.27 (m, 4H), 7.25 - 7.19 (m, 1H), 6.86 (s, 1H), 6.82 (s, 1H), 6.59 (s, 1H), 6.30 - 6.22 (m, 2H), 5.74 (dd, *J* = 9.9, 1.7 Hz, 1H), 4.88 (m, 1H), 4.06 (td, *J* = 8.1, 4.7 Hz, 1H), 3.97 (q, *J* = 8.0 Hz, 1H), 3.81 (s, 3H), 3.26 (dd, *J* = 13.7, 5.8 Hz, 1H), 2.92 (m, 4H), 2.84 - 2.75 (m, 2H), 2.72 (m, 4H), 2.17 (m, 1H), 2.07 (m, 1H), 1.12 (d, *J* = 6.5 Hz, 6H).; 558.5 [M+H]$^+$	1.15
955		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.85 (s, 1H), 8.44 (s, 1H), 8.38 (s, 1H), 7.33 - 7.20 (m, 4H), 7.24 - 7.21 (m, 1H), 6.84 (s, 1H), 6.73 (s, 1H), 6.59 (s, 1H), 6.37 - 6.31 (m, 1H), 6.23 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.73 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.91 - 4.85 (m, 1H), 4.04 (dd, *J* = 8.1, 4.7 Hz, 1H), 3.96 (q, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.26 (dd, *J* = 13.7, 5.8 Hz, 1H), 3.05 (d, *J* = 11.5 Hz, 2H), 2.83 - 2.75 (m, 2H), 2.63 (s, 4H), 2.32 (s, 1H), 2.16 (dt, *J* = 7.8, 3.8 Hz, 1H), 2.10 - 2.05 (m, 3H), 1.64 (s, 4H), 1.26 (d, *J* = 4.3 Hz, 3H), 0.89 - 0.85 (m, 1H), 0.48 - 0.41 (m, 4H) ; 630.6[M+H]$^+$	1.18
956		N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.85 (s, 1H), 8.43 (s, 1H), 8.38 (s, 1H), 7.33 - 7.28 (m, 4H), 7.24 - 7.19 (m, 1H), 6.84 (s, 1H), 6.73 (s, 1H), 6.58 (s, 1H), 6.38 - 6.31 (m, 1H), 6.24 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.73 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.95 - 4.79 (m, 1H), 4.05 (td, *J* = 8.1, 4.7 Hz, 1H), 3.96 (q, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.26 (dd, *J* = 13.7, 5.7 Hz, 1H), 3.05 (d, *J* = 11.5 Hz, 2H), 2.85 - 2.76 (m, 2H), 2.64 (s, 4H), 2.33 (s, 1H), 2.17 (tq, *J* = 8.2, 4.8, 4.0 Hz, 1H), 2.07 (tt, *J* = 8.0, 3.9 Hz, 3H), 1.63 (s, 4H), 1.26 (s, 3H), 0.88 - 0.85 (m, 1H), 0.49 - 0.41 (m, 4H) ; 630.6[M+H]$^+$	1.18
957		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.63 (s, 1H), 8.37 (s, 1H), 7.95 (s, 1H), 7.35 - 7.31 (m, 4H), 7.24 - 7.18 (m, 1H), 6.81 (s, 1H), 6.71 (s, 1H), 6.56 (s, 1H), 6.38 (d, *J* = 17.0 Hz, 1H), 6.27 (dd, *J* = 16.8, 10.0 Hz, 1H), 5.75 (d, *J* = 9.8 Hz, 1H), 4.93 - 4.83 (m, 1H), 4.65 (s, 1H), 4.09 - 4.02 (m, 2H), 4.00 - 3.92 (m, 1H), 3.89 - 3.86 (m, 1H), 3.85 (s, 3H), 3.74 (d, *J* = 8.0 Hz, 1H), 3.44 (d, *J* = 10.2 Hz, 1H), 3.20 - 3.18 (m, 2H), 2.80 (dd, *J* = 13.7, 9.0 Hz, 1H), 2.12 - 1.96 (m, 4H).; 529.4 [M+H]$^+$	1.28

		methoxyphenyl)acrylamide		
958		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.48 (s, 1H), 8.30 (d, *J* = 0.9 Hz, 1H), 7.34 - 7.27 (m, 4H), 7.22 (t, *J* = 6.6 Hz, 1H), 6.88 (s, 1H), 6.80 (s, 1H), 6.60 (s, 1H), 6.35 (dd, *J* = 16.9, 1.5 Hz, 1H), 6.24 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.74 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.89 (tt, *J* = 9.1, 4.4 Hz, 1H), 4.72 (t, *J* = 6.5 Hz, 2H), 4.66 (t, *J* = 6.2 Hz, 2H), 4.06 (td, *J* = 8.1, 4.7 Hz, 1H), 3.96 (q, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.60 (p, *J* = 6.4 Hz, 1H), 3.26 (dd, *J* = 13.7, 5.8 Hz, 1H), 2.95 (t, *J* = 4.8 Hz, 4H), 2.80 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.53 (s, 3H), 2.18 (dtd, *J* = 12.6, 8.2, 4.8 Hz, 1H), 2.06 (dtd, *J* = 12.3, 8.1, 4.1 Hz, 1H), 1.25 (s, 1H). : 572.4 [M+H]$^+$	1.15

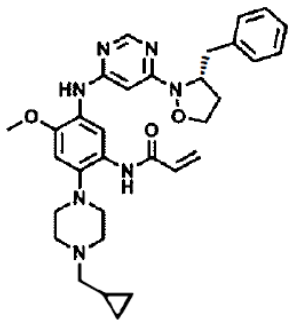
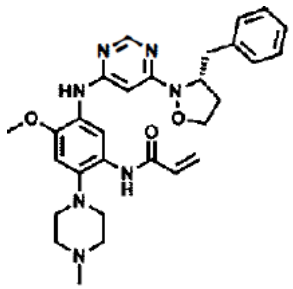
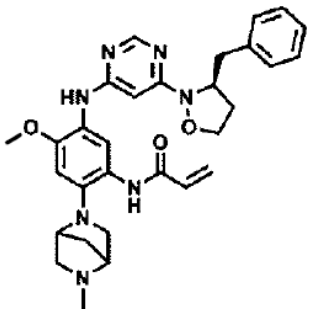
[662]

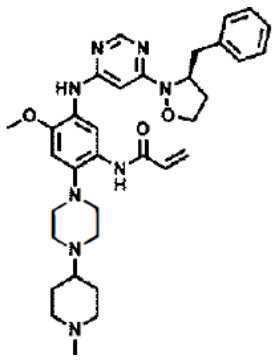
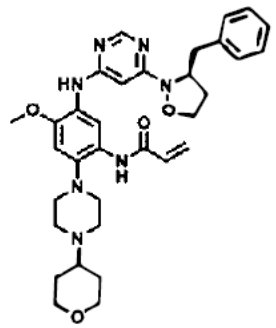
959		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(cyclopropylmethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.57 (s, 1H), 8.38 (s, 1H), 7.34 - 7.20 (m, 4H), 7.22 (t, *J* = 6.6 Hz, 1H), 6.86 (s, 1H), 6.82 (s, 1H), 6.60 (s, 1H), 6.36 (d, *J* = 16.4 Hz, 1H), 6.25 (dd, *J* = 17.0, 9.9 Hz, 1H), 5.73 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.93 - 4.85 (m, 1H), 4.06 (td, *J* = 8.1, 4.7 Hz, 1H), 3.97 (q, *J* = 8.1 Hz, 1H), 3.82 (s, 3H), 3.26 (dd, *J* = 13.7, 5.7 Hz, 1H), 2.93 (d, *J* = 5.6 Hz, 4H), 2.80 (dd, *J* = 13.7, 8.9 Hz, 2H), 2.72 (s, 3H), 2.35 (d, *J* = 6.6 Hz, 2H), 2.17 (ddt, *J* = 12.5, 8.0, 3.9 Hz, 1H), 2.07 (tt, *J* = 8.0, 4.0 Hz, 1H), 0.98 - 0.81 (m, 1H), 0.60 - 0.53 (m, 2H), 0.16 (q, *J* = 4.9 Hz, 2H).: 570.5 [M+H]$^+$	1.18
960		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(2-methyl-1H-imidazole-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 9.10 (s, 1H), 8.46 (s, 1H), 7.32 (d, *J* = 6.3 Hz, 4H), 7.23 (s, 1H), 7.14 (d, *J* = 5.9 Hz, 2H), 6.94 (s, 1H), 6.73 (s, 1H), 6.70 (s, 1H), 6.65 (s, 1H), 6.27 (d, *J* = 16.9 Hz, 1H), 6.04 (dd, *J* = 16.7, 10.2 Hz, 1H), 5.70 (d, *J* = 10.4 Hz, 1H), 4.80 (s, 1H), 4.11 (d, *J* = 8.1 Hz, 1H), 3.94 (d, *J* = 8.0 Hz, 1H), 3.88 (s, 3H), 3.29 (dd, *J* = 13.6, 5.7 Hz, 1H), 2.82 (dd, *J* = 13.6, 8.9 Hz, 1H), 2.24 (s, 3H), 2.20 (s, 1H), 2.12 (s, 1H); 512.5 [M+H]$^+$	1.38
961		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.88 (s, 1H), 8.49 (s, 1H), 8.38 (s, 1H), 7.32 (m, 4H), 7.22 (s, 1H),6.90 (s, 1H), 6.79 (s, 1H), 6.59 (s, 1H), 6.35 (d, *J* = 17.2 Hz, 1H), 6.26 (s, 1H), 5.74 (d, *J* = 11.2 Hz, 1H),4.88 (d, *J* = 13.0 Hz, 1H), 4.05 (d, *J* = 3.2 Hz, 1H), 3.96 (d, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.36 (d, *J* =15.0 Hz, 2H), 3.26 (dd, *J* = 13.6, 5.7 Hz, 2H), 2.93 (s, 4H), 2.83 - 2.76 (m, 4H), 2.72 (s, 3H), 2.57 (s, 3H),2.16 (d, *J* = 4.5 Hz, 2H), 2.06 (d, *J* = 8.1 Hz, 2H).: 587.5 [M+H]$^+$	1.07
962		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.66 (s, 1H), 8.37 (s, 1H), 7.95 (s, 1H), 7.32 - 7.20 (m, 4H), 7.23 (dd, *J* = 6.0, 2.7 Hz, 1H), 6.81 (s, 1H), 6.70 (s, 1H), 6.52 (s, 1H), 6.38 (d, *J* = 16.8 Hz, 1H), 6.27 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.75 (d, *J* = 10.0 Hz, 1H), 4.87 (dd, *J* = 11.4, 6.2 Hz, 1H), 4.65 (s, 1H), 4.05 (d, *J* = 7.8 Hz, 2H), 3.94 - 3.88 (m, 1H), 3.85 (s, 3H), 3.75 (d, *J* = 7.8 Hz, 1H), 3.42 (d, *J* = 10.2 Hz, 1H), 3.20 - 3.21 (m, 2H), 2.79 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.61 (s, 1H), 2.18 - 2.13 (m, 1H), 2.07 (ddd, *J* = 11.9, 7.8, 3.7 Hz, 2H), 1.90 (d, *J* = 9.9 Hz, 1H).: 520.4[M+H]	1.29

[663]

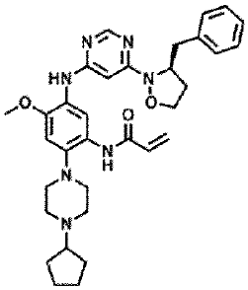
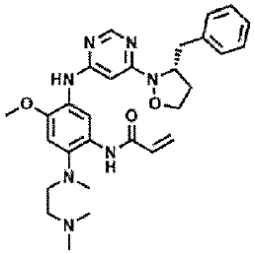
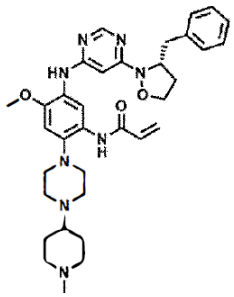
963		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.84 (s, 1H), 8.39 (d, *J* = 10.9 Hz, 2H), 7.31 (d, *J* = 6.7 Hz, 4H), 7.24 - 7.21 (m, 1H), 6.93 (s, 1H), 6.73 (s, 1H), 6.58 (s, 1H), 6.39 - 6.33 (m, 1H), 6.25 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.76 - 5.71 (m, 1H), 4.87 (dd, *J* = 11.2, 6.2 Hz, 1H), 4.05 (dd, *J* = 8.1, 4.7 Hz, 1H), 3.96 (d, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.65 (p, *J* = 6.7 Hz, 2H), 3.24 (d, *J* = 5.7 Hz, 1H), 3.08 (d, *J* = 7.4 Hz, 2H), 2.83 - 2.71 (m, 6H), 2.48 (s, 3H), 2.16 (tt, *J* = 8.1, 4.5 Hz, 3H), 2.07 (dt, *J* = 7.8, 4.2 Hz, 3H), 1.71 (d, *J* = 12.6 Hz, 2H), 1.55 (t, *J* = 7.4 Hz, 2H).; 613.6[M+H]	1.09
964		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.68 (s, 1H), 8.53 (s, 1H), 8.35 (d, *J* = 0.9 Hz, 1H), 7.34 - 7.27 (m, 4H), 7.24 - 7.20 (m, 1H), 6.92 (s, 1H), 6.65 (s, 1H), 6.54 (s, 1H), 6.43 - 6.28 (m, 2H), 5.71 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.91 - 4.82 (m, 1H), 4.05 (dd, *J* = 8.1, 4.8 Hz, 1H), 3.95 (q, *J* = 8.0 Hz, 1H), 3.82 (s, 3H), 3.65 (p, *J* = 6.7 Hz, 2H), 3.28 - 3.23 (m, 1H), 3.09 (q, *J* = 7.5 Hz, 2H), 2.79 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.62 (s, 3H), 2.30 (s, 2H), 2.16 (ddt, *J* = 12.6, 8.1, 4.5 Hz, 2H), 2.06 (dq, *J* = 8.0, 4.0 Hz, 2H), 1.55 (t, *J* = 7.4 Hz, 2H), 544.5[M+H]	1.13
965		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.86 (s, 1H), 8.43 (s, 1H), 8.38 (d, *J* = 1.0 Hz, 1H), 7.34 - 7.27 (m, 4H), 7.24 - 7.20 (m, 1H), 6.85 (s, 1H), 6.74 (s, 1H), 6.59 (s, 1H), 6.39 - 6.32 (m, 1H), 6.24 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.73 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.92 - 4.85 (m, 1H), 4.06 (td, *J* = 8.0, 4.7 Hz, 1H), 3.96 (q, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 3.29 - 3.24 (m, 1H), 3.07 (d, *J* = 11.5 Hz, 2H), 2.80 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.72 (dd, *J* = 12.0, 9.5 Hz, 2H), 2.63 (s, 3H), 2.21 - 2.14 (m, 1H), 2.07 (tt, *J* = 8.0, 3.8 Hz, 3H), 1.57 - 1.53 (m, 3H), 1.45 (d, *J* = 6.7 Hz, 2H).; 600.5[M+H]	1.15
966		N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.92 (s, 1H), 8.50 (s, 1H), 8.39 (d, *J* = 0.9 Hz, 1H), 7.34 - 7.28 (m, 4H), 7.24 - 7.20 (m, 1H), 6.80 (s, 1H), 6.76 (s, 1H), 6.60 (s, 1H), 6.40 - 6.31 (m, 1H), 6.26 (dd, *J* = 17.0, 9.9 Hz, 1H), 5.75 (dd, *J* = 9.9, 1.5 Hz, 1H), 4.89 (tq, *J* = 8.9, 4.1 Hz, 1H), 4.06 (td, *J* = 8.1, 4.7 Hz, 1H), 3.97 (t, *J* = 8.0 Hz, 1H), 3.88 (t, *J* = 4.6 Hz, 3H), 3.85 (s, 2H), 3.26 (dd, *J* = 13.7, 5.8 Hz, 1H), 2.88 (dd, *J* = 6.0, 3.5 Hz, 3H), 2.80 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.23 - 2.13 (m, 1H), 2.07 (dtd, *J* = 12.0, 7.9, 3.9 Hz, 1H), 1.50 (s, 3H).; 517.4[M+H]	1.53

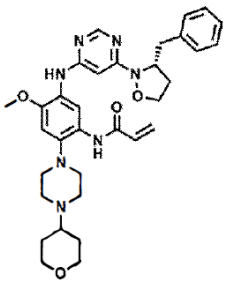
[664]

967		N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(cyclopropylmethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.89 (s, 1H), 8.52 (s, 1H), 8.38 (d, *J* = 1.0 Hz, 1H), 7.34 - 7.27 (m, 4H), 7.24 - 7.20 (m, 1H), 6.89 (s, 1H), 6.79 (s, 1H), 6.59 (s, 1H), 6.36 (dd, *J* = 17.0, 1.6 Hz, 1H), 6.26 (dd, *J* = 17.2, 9.6 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.88 (tt, *J* = 8.9, 4.9 Hz, 1H), 4.06 (td, *J* = 8.0, 4.7 Hz, 1H), 3.96 (q, *J* = 8.1 Hz, 1H), 3.83 (s, 3H), 3.62 - 3.57 (m, 1H), 3.26 (dd, *J* = 13.7, 5.9 Hz, 1H), 3.03 (d, *J* = 7.7 Hz, 1H), 2.92 (t, *J* = 4.9 Hz, 4H), 2.80 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.62 (s, 3H), 2.40 (s, 3H), 2.27 (s, 1H), 2.19 - 2.12 (m, 1H), 2.10 - 2.01 (m, 2H), 1.85 (p, *J* = 6.9 Hz, 1H).: 570.5[M+H]	1.30
968		N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.90 (s, 1H), 8.56 (s, 1H), 8.39 (d, *J* = 0.9 Hz, 1H), 7.34 - 7.28 (m, 4H), 7.24 - 7.19 (m, 1H), 6.87 (s, 1H), 6.82 (s, 1H), 6.50 (s, 1H), 6.30 - 6.32 (m, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.88 (dp, *J* = 9.0, 4.4 Hz, 1H), 4.06 (td, *J* = 8.1, 4.7 Hz, 1H), 3.96 (q, *J* = 8.1 Hz, 1H), 3.82 (s, 3H), 3.26 (dd, *J* = 13.7, 5.8 Hz, 1H), 2.95 (s, 3H), 2.80 (dd, *J* = 13.6, 8.9 Hz, 2H), 2.37 (d, *J* = 6.5 Hz, 2H), 2.17 (h, *J* = 3.9, 3.4 Hz, 1H), 2.09 - 2.03 (m, 1H), 1.63 (s, 3H), 1.54 (d, *J* = 7.6 Hz, 2H).: 530.5[M+H]	1.26
969		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.24 (s, 1H), 8.37 (s, 1H), 8.13 (s, 1H), 7.30 (d, *J* = 4.4 Hz, 5H), 7.21 (h, *J* = 4.2 Hz, 1H), 6.44 (dd, *J* = 17.1, 10.2 Hz, 1H), 6.37 (s, 1H), 6.23 - 6.07 (m, 2H), 5.67 (dd, *J* = 10.2, 2.1 Hz, 1H), 4.74 (qd, *J* = 7.6, 3.6 Hz, 1H), 4.16 (s, 1H), 4.04 (td, *J* = 8.0, 4.7 Hz, 1H), 3.76 (s, 4H), 3.11 - 2.98 (m, 2H), 2.80 - 2.60 (m, 3H), 2.10 (dq, *J* = 7.8, 3.9, 3.5 Hz, 1H), 1.98 (ddd, *J* = 11.8, 7.8, 3.7 Hz, 1H), 1.80 (d, *J* = 9.3 Hz, 1H), 1.68 (d, *J* = 9.2 Hz, 1H), 1.24 (s, 3H), 0.92 - 0.76 (m, 2H).:542.5 [M+H]$^+$	1.12

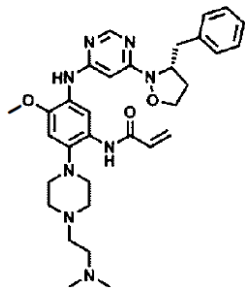
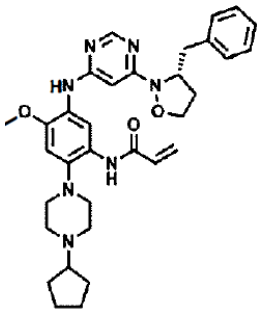
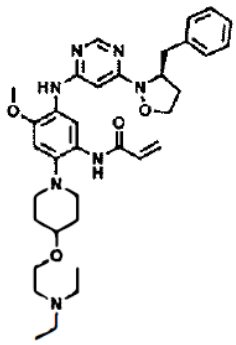
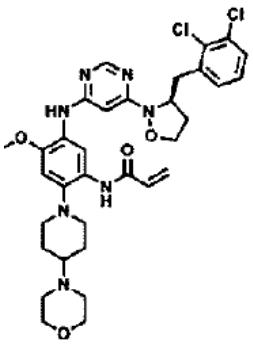
970		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide	1H NMR (400 MHz, chloroform-*d*) δ 8.89 (s, 1H), 8.54 (s, 1H), 8.38 (s, 1H), 7.34 - 7.27 (m, 4H), 7.22 (t, *J* = 6.6 Hz, 1H), 6.86 (s, 1H), 6.80 (s, 1H), 6.59 (s, 1H), 6.39 - 6.32 (m, 1H), 6.25 (dd, *J* = 17.0, 9.9 Hz, 1H), 5.74 (dd, *J* = 9.9, 1.7 Hz, 1H), 4.92 - 4.83 (m, 1H), 4.06 (td, *J* = 8.0, 4.7 Hz, 1H), 3.96 (q, *J* = 7.9 Hz, 1H), 3.81 (s, 3H), 3.26 (dd, *J* = 13.6, 5.8 Hz, 2H), 3.00 (d, *J* = 11.6 Hz, 2H), 2.93 - 2.80 (m, 4H), 2.83 - 2.77 (m, 2H), 2.75 (s, 2H), 2.34 (s, 3H), 2.17 (s, 2H), 2.06 (d, *J* = 8.1 Hz, 3H), 1.88 (d, *J* = 13.7 Hz, 2H), 1.46 (s, 2H).; 613.6 $[M+H]^+$	1.03
971		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.89 (s, 1H), 8.54 (s, 1H), 8.39 (s, 1H), 7.32 (s, 4H), 7.23 (d, *J* = 6.7 Hz, 1H), 6.87 (s, 1H), 6.80 (s, 1H), 6.59 (s, 1H), 6.36 (d, *J* = 16.1 Hz, 1H), 6.30 - 6.20 (m, 1H), 5.74 (d, *J* = 11.4 Hz, 1H), 4.90 (s, 1H), 4.06 (d, *J* = 4.4 Hz, 3H), 3.96 (d, *J* = 8.1 Hz, 1H), 3.82 (s, 3H), 3.42 (t, *J* = 11.1 Hz, 2H), 3.26 (dd, *J* = 13.7, 5.8 Hz, 1H), 2.93 (s, 4H), 2.84 - 2.69 (m, 5H), 2.52 (s, 1H), 2.17 (s, 2H), 2.06 (s, 2H), 1.83 (d, *J* = 10.8 Hz, 2H).; 600.5 $[M+H]^+$	1.16

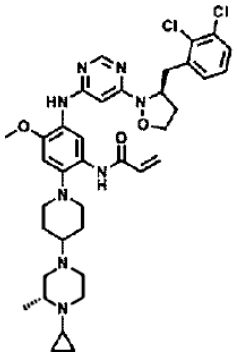
[665]

972		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopentylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.80 (s, 1H), 8.58 (s, 1H), 8.38 (s, 1H), 7.31 (s, 4H), 7.22 (s, 1H), 6.87 (s, 1H), 6.81 (s, 1H), 6.59 (s, 1H), 6.35 (d, *J* = 16.0 Hz, 1H), 6.26 (dd, *J* = 16.9, 9.8 Hz, 1H), 5.74 (d, *J* = 9.9 Hz, 1H), 4.87 (s, 1H), 4.03 (s, 1H), 3.95 (s, 1H), 3.81 (s, 3H), 3.26 (dd, *J* = 13.7, 5.8 Hz, 1H), 2.93 (s, 4H), 2.80 (dd, *J* = 13.7, 8.9 Hz, 2H), 2.70 (s, 2H), 2.62 - 2.55 (m, 2H), 2.17 (s, 3H), 2.10 - 2.03 (m, 1H), 1.92 (s, 2H), 1.74 (s, 2H), 1.52 - 1.40 (m, 2H).; 584.5 [M+H]$^+$	1.22
973		N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 10.08 (s, 1H), 8.04 (s, 1H), 8.38 (s, 1H), 7.36 - 7.27 (m, 4H), 7.24 - 7.19 (m, 1H), 6.87 (s, 1H), 6.78 (s, 1H), 6.63 (s, 1H), 6.39 (dd, *J* = 16.9, 1.9 Hz, 1H), 6.20 (d, *J* = 11.0 Hz, 1H), 5.67 (dd, *J* = 9.8, 2.0 Hz, 1H), 4.93 - 4.85 (m, 1H), 4.10 - 3.96 (m, 2H), 3.83 (s, 3H), 3.26 (dd, *J* = 13.7, 5.8 Hz, 1H), 2.87 (s, 2H), 2.83 (s, 1H), 2.71 (s, 3H), 2.27 (s, 8H), 2.20 - 2.14 (m, 1H), 2.06 (dtd, *J* = 11.6, 7.8, 3.6 Hz, 1H).; 532.5[M+H]	1.17
974		N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.88 (s, 1H), 8.47 (s, 1H), 8.38 (s, 1H), 7.31 (d, *J* = 6.9 Hz, 4H), 7.22 (t, *J* = 6.6 Hz, 1H), 6.88 (s, 1H), 6.78 (s, 1H), 6.59 (s, 1H), 6.36 (d, *J* = 17.1 Hz, 1H), 6.25 (dd, *J* = 17.0, 9.9 Hz, 1H), 5.77 - 5.72 (m, 1H), 4.91 - 4.85 (m, 1H), 4.05 (dd, *J* = 8.0, 4.8 Hz, 1H), 3.96 (q, *J* = 8.1 Hz, 1H), 3.83 (s, 3H), 3.37 - 3.33 (m, 1H), 3.28 (d, *J* = 5.8 Hz, 1H), 3.24 (d, *J* = 5.7 Hz, 1H), 3.22 - 3.18 (m, 2H), 3.17 (s, 1H), 3.00 (t, *J* = 6.4 Hz, 1H), 2.92 (s, 3H), 2.72 (s, 2H), 2.56 (s, 2H), 2.17 (s, 2H), 1.26 (s, 3H), 1.12 (t, *J* = 7.2 Hz, 1H), 1.07 (t, *J* = 7.2 Hz, 1H), 0.97 (d, *J* = 6.6 Hz, 1H), 0.90 - 0.86 (m, 2H).; 613.6[M+H]	1.04

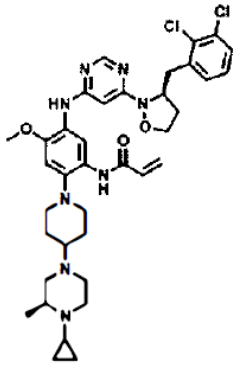
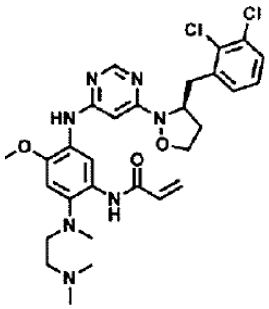
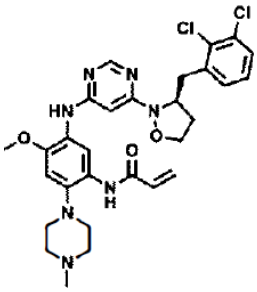
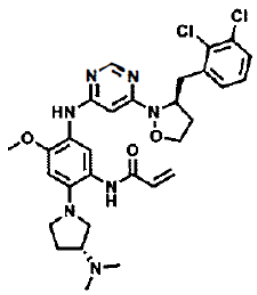
975		N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.89 (s, 1H), 8.53 (s, 1H), 8.38 (s, 1H), 7.31 (d, *J* = 6.8 Hz, 4H), 7.24 - 7.20 (m, 1H), 6.88 (s, 1H), 6.80 (s, 1H), 6.59 (s, 1H), 6.36 (d, *J* = 16.8 Hz, 1H), 6.25 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.77 - 5.71 (m, 1H), 4.93 - 4.85 (m, 1H), 4.09 - 4.04 (m, 2H), 3.96 (q, *J* = 8.1 Hz, 1H), 3.82 (s, 2H), 3.42 (t, *J* = 11.6 Hz, 2H), 3.26 (dd, *J* = 13.7, 5.7 Hz, 1H), 2.92 (d, *J* = 4.8 Hz, 3H), 2.76 (d, *J* = 5.9 Hz, 2H), 2.50 (d, *J* = 11.7 Hz, 1H), 2.17 (td, *J* = 8.6, 7.7, 3.8 Hz, 1H), 2.09 - 2.03 (m, 1H), 1.84 (d, *J* = 12.4 Hz, 2H), 1.69 - 1.63 (m, 2H), 1.26 (s, 4H), 0.90 - 0.83 (m, 2H).; 600.5[M+H]	1.18

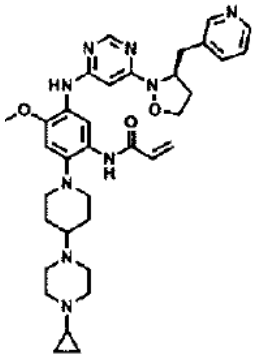
[666]

976		N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.88 (s, 1H), 8.50 (s, 1H), 8.38 (s, 1H), 7.31 (d, *J* = 6.8 Hz, 4H), 7.23 (d, *J* = 6.5 Hz, 1H), 6.89 (s, 1H), 6.79 (s, 1H), 6.59 (s, 1H), 6.33 (s, 1H), 6.27 (d, *J* = 10.1 Hz, 1H), 5.74 (d, *J* = 10.0 Hz, 1H), 4.88 (s, 1H), 4.05 (dd, *J* = 8.1, 4.7 Hz, 2H), 3.96 (d, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.37 - 3.32 (m, 3H), 3.28 (d, *J* = 5.8 Hz, 1H), 3.24 (d, *J* = 5.7 Hz, 1H), 2.93 (d, *J* = 4.9 Hz, 3H), 2.71 (s, 3H), 2.54 (s, 4H), 2.17 (s, 3H), 1.25 (s, 3H).: 587.5[M+H]	1.08
977		N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopentylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, chloroform-*d*) δ 8.89 (s, 1H), 8.58 (s, 1H), 8.38 (d, *J* = 1.0 Hz, 1H), 7.35 - 7.27 (m, 4H), 7.24 - 7.19 (m, 1H), 6.86 (s, 1H), 6.81 (s, 1H), 6.59 (s, 1H), 6.39 - 6.32 (m, 1H), 6.26 (dd, *J* = 17.0, 0.9 Hz, 1H), 5.74 (dd, *J* = 9.8, 1.7 Hz, 1H), 4.87 (dd, *J* = 11.4, 6.2 Hz, 1H), 4.06 (td, *J* = 8.1, 4.6 Hz, 1H), 3.97 (q, *J* = 6.7, 5.5 Hz, 1H), 3.81 (s, 3H), 3.26 (dd, *J* = 13.7, 5.8 Hz, 1H), 2.92 (d, *J* = 5.1 Hz, 3H), 2.80 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.62 (s, 1H), 2.17 (s, 2H), 2.02 (s, 1H), 1.92 (s, 2H), 1.74 (s, 2H), 1.58 (s, 8H).: 584.5[M+H]	1.23
978		N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(diethylamino)ethoxy)piperidine-1-yl)-4-methoxyphenyl)acrylamide	630.57[M+H]$^+$	1.23
979		N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	668.4[M+H]$^+$	1.25

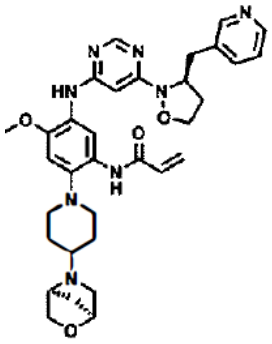
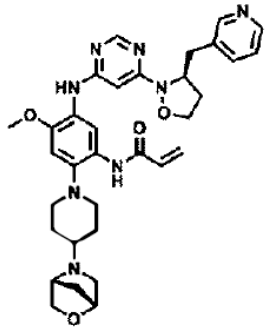
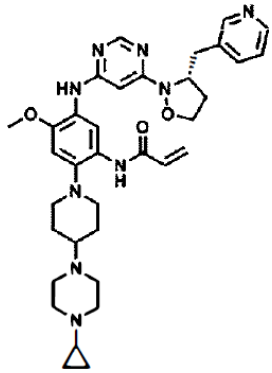
980		N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (s, 1H), 8.56 (s, 1H), 8.12 (s, 1H), 7.48 (ddd, J = 21.1, 7.9, 1.6 Hz, 2H), 7.20 (t, J = 7.8 Hz, 1H), 6.79 (s, 1H), 6.66 (dd, J = 16.9, 10.2 Hz, 1H), 6.30 - 6.14 (m, 2H), 5.71 (dd, J = 10.2, 2.0 Hz, 1H), 4.92 (qd, J = 8.0, 3.1 Hz, 1H), 3.77 (s, 3H), 3.35 (s, 1H), 3.13 - 2.91 (m, 5H), 2.84 (dt, J = 10.8, 2.8 Hz, 1H), 2.73 (t, J = 11.5 Hz, 2H), 2.63 (qd, J = 9.8, 9.4, 5.2 Hz, 2H), 2.45 - 2.35 (m, 1H), 2.35 - 2.13 (m, 5H), 2.02 (dtd, J = 11.6, 8.0, 3.0 Hz, 1H), 1.96 - 1.86 (m, 1H), 1.86 - 1.77 (m, 2H), 1.69 (tq, J = 11.9, 8.3, 6.1 Hz, 3H), 1.49 (dh, J = 7.6, 3.6 Hz, 2H), 1.09 (d, J = 6.3 Hz, 3H), 0.57 (dtd, J = 10.1, 6.6, 4.1 Hz, 1H), 0.44 - 0.30 (m, 2H), 0.17 (dq, J = 9.2, 3.9 Hz, 1H).; 721.5[M+H]$^+$	1.29

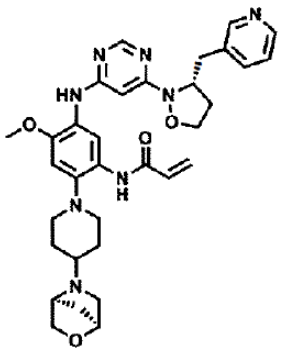
[667]

981		N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.01 (s, 1H), 8.59 (s, 1H), 8.13 (s, 2H), 7.48 (ddd, J = 21.8, 7.9, 1.6 Hz, 2H), 7.29 (t, J = 7.8 Hz, 1H), 6.81 (s, 1H), 6.62 (dd, J = 17.0, 10.2 Hz, 1H), 6.29 (s, 1H), 6.21 (dd, J = 16.9, 1.9 Hz, 1H), 5.74 - 5.69 (m, 1H), 4.02 (qd, J = 8.0, 3.1 Hz, 1H), 3.79 (s, 4H), 3.37 (s, 2H), 3.09 (dt, J = 18.5, 9.2 Hz, 5H), 2.96 (dd, J = 14.1, 6.4 Hz, 2H), 2.70 (t, J = 11.6 Hz, 4H), 2.59 (s, 2H), 2.25 - 1.96 (m, 5H), 1.91 (s, 5H), 1.74 - 1.41 (m, 2H), 1.19 (s, 3H), 0.65 (s, 1H), 0.45 (s, 2H), 0.25 (s, 1H).:721.4[M+H]$^+$	1.45
982		N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 10.04 (s, 1H), 8.42 (s, 1H), 8.13 (d, J = 1.0 Hz, 1H), 7.51 (dd, J = 8.0, 1.6 Hz, 1H), 7.45 (dd, J = 7.8, 1.6 Hz, 1H), 7.29 (t, J = 7.8 Hz, 1H), 6.97 (s, 1H), 6.39 (dd, J = 16.9, 10.1 Hz, 1H), 6.30 (s, 1H), 6.21 (dd, J = 16.9, 2.1 Hz, 1H), 5.78 - 5.71 (m, 1H), 4.03 (dq, J = 11.9, 5.1, 4.0 Hz, 1H), 3.78 (s, 3H), 2.96 (dd, J = 14.1, 6.5 Hz, 2H), 2.88 (t, J = 5.8 Hz, 3H), 2.60 (s, 4H), 2.38 (t, J = 5.8 Hz, 2H), 2.18 (dt, J = 8.2, 4.4 Hz, 1H), 2.02 (dtd, J = 11.6, 8.0, 3.0 Hz, 2H), 1.00 (s, 6H), 1.00 - 0.91 (m, 1H), 0.85 (td, J = 8.0, 7.3, 3.1 Hz, 1H).: 600.3[M+H]$^+$	1.31
983		N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (s, 1H), 8.58 (s, 1H), 8.12 (s, 1H), 7.51 (dd, J = 8.0, 1.6 Hz, 2H), 7.45 (dd, J = 7.8, 1.6 Hz, 2H), 7.29 (t, J = 7.8 Hz, 2H), 6.82 (s, 1H), 6.59 (dd, J = 17.0, 10.2 Hz, 1H), 6.28 (s, 1H), 6.19 (dd, J = 16.9, 1.9 Hz, 1H), 5.71 (dd, J = 10.2, 1.9 Hz, 1H), 4.02 (qd, J = 8.0, 3.0 Hz, 2H), 3.79 (s, 3H), 3.16 - 2.90 (m, 6H), 2.85 (t, J = 4.8 Hz, 4H), 2.24 (s, 4H), 2.10 (dddd, J = 60.6, 11.6, 7.9, 3.3 Hz, 5H).: 508.3[M+H]$^+$	1.25
984		N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.26 (s, 1H), 9.58 (s, 1H), 8.57 (s, 1H), 8.12 (s, 1H), 7.81 (s, 1H), 7.51 (dd, J = 8.0, 1.5 Hz, 1H), 7.47 - 7.43 (m, 1H), 7.30 (t, J = 7.8 Hz, 1H), 6.90 (dd, J = 17.0, 10.2 Hz, 1H), 6.68 (s, 1H), 6.24 - 6.14 (m, 2H), 5.68 (dd, J = 10.2, 2.1 Hz, 1H), 4.02 (qd, J = 7.9, 3.0 Hz, 1H), 3.80 (s, 3H), 3.60 (dt, J = 9.4, 2.7 Hz, 2H), 3.48 - 3.39 (m, 1H), 3.37 (s, 2H), 3.32 (dd, J = 11.0, 6.4 Hz, 1H), 3.11 (dd, J = 7.5, 4.4 Hz, 3H), 2.96 (dd, J = 14.2, 6.7 Hz, 2H), 2.78 (d, J = 4.7 Hz, 6H), 2.29 (dq, J = 12.7, 7.3, 5.6 Hz, 2H), 2.19 (dtd, J = 12.9, 8.3, 5.0 Hz, 1H), 2.02 (dtd, J = 11.6, 7.9, 3.0 Hz, 1H).: 612.3[M+H]$^+$	1.24

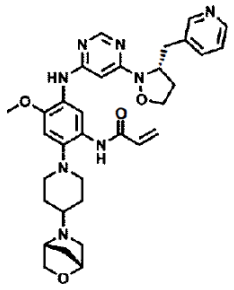
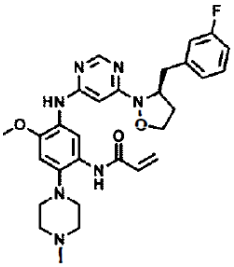
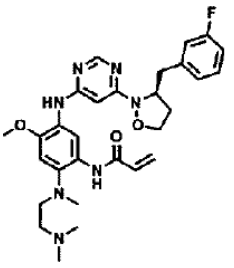
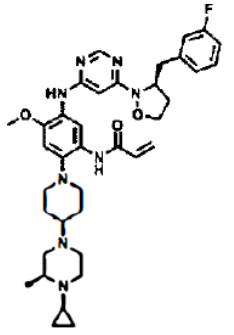
985		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.79 (s, 1H), 8.52 (d, *J* = 2.3 Hz, 1H), 8.45 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.31 (s, 1H), 7.70 (dt, *J* = 7.9, 2.1 Hz, 1H), 7.22 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.01 (s, 1H), 6.69 (s, 1H), 6.57 (s, 1H), 6.39 - 6.30 (m, 2H), 5.74 (td, *J* = 9.6, 9.2, 2.1 Hz, 2H), 4.88 (qd, *J* = 7.3, 3.8 Hz, 1H), 3.81 (s, 3H), 3.17 - 3.02 (m, 5H), 2.72 (q, *J* = 11.6 Hz, 4H), 2.62 (s, 1H), 2.26 (dtd, *J* = 12.2, 8.1, 4.2 Hz, 2H), 2.17 (d, *J* = 12.0 Hz, 2H), 2.12 - 1.99 (m, 2H), 1.98 - 1.85 (m, 3H), 1.79 (t, *J* = 5.1 Hz, 1H), 1.47 (d, *J* = 6.7 Hz, 3H), 1.24 (s, 4H), 0.51 (t, *J* = 7.0 Hz, 5H).; 640.5[M+H]$^+$	1.09

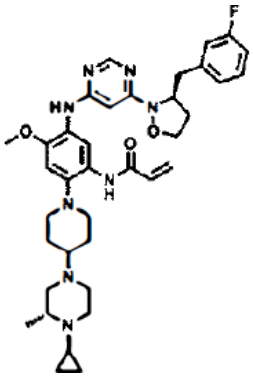
[668]

986		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.81 (s, 1H), 8.53 (d, J = 2.2 Hz, 1H), 8.46 (q, J = 1.8 Hz, 2H), 8.32 (s, 1H), 7.70 (dt, J = 7.9, 2.0 Hz, 1H), 7.22 (dd, J = 7.8, 4.8 Hz, 1H), 6.94 (s, 1H), 6.73 (s, 1H), 6.50 (s, 1H), 6.35 - 6.25 (m, 2H), 5.72 (dd, J = 9.7, 1.9 Hz, 1H), 4.89 (qd, J = 7.2, 3.8 Hz, 1H), 3.83 (s, 3H), 3.73 - 3.66 (m, 2H), 3.39 (q, J = 6.5 Hz, 1H), 3.30 (td, J = 7.3, 5.2 Hz, 1H), 3.23 (d, J = 10.1 Hz, 2H), 3.14 (dd, J = 14.0, 6.7 Hz, 2H), 2.81 - 2.59 (m, 6H), 2.45 (s, 1H), 2.27 (dtd, J = 12.3, 8.2, 4.3 Hz, 2H), 2.09 - 1.99 (m, 4H), 1.99 - 1.91 (m, 2H), 1.88 (d, J = 9.9 Hz, 2H), 1.25 (s, 2H).; 613.3[M+H]$^+$	1.03
987		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.81 (s, 1H), 8.50 - 8.42 (m, 2H), 8.32 (s, 1H), 7.69 (d, J = 7.9 Hz, 1H), 7.21 (dd, J = 7.8, 4.8 Hz, 1H), 6.92 (s, 1H), 6.72 (s, 1H), 6.58 (s, 1H), 6.34 - 6.23 (m, 2H), 5.72 (dd, J = 9.6, 1.9 Hz, 1H), 4.88 (qd, J = 7.3, 3.8 Hz, 1H), 3.99 - 3.88 (m, 2H), 3.82 (s, 3H), 3.69 (d, J = 8.4 Hz, 1H), 3.13 (dd, J = 14.0, 6.8 Hz, 1H), 3.09 - 2.97 (m, 3H), 2.74 (tdd, J = 12.1, 6.9, 3.3 Hz, 4H), 2.61 (d, J = 10.3 Hz, 2H), 2.49 (s, 1H), 2.26 (dtd, J = 12.5, 8.2, 4.3 Hz, 2H), 2.03 (dq, J = 11.6, 3.8 Hz, 4H), 1.89 (d, J = 10.3 Hz, 2H), 1.34 - 1.21 (m, 4H).; 613.5[M+H]$^+$	1.05
988		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-	^{1}H NMR (400 MHz, Chloroform-d) δ 8.77 (s, 1H), 8.33 (s, 1H), 8.30 (s, 1H), 7.70 (d, J = 7.7 Hz, 1H), 7.09 (s, 1H), 6.67 (s, 1H), 6.55 (s, 1H), 6.36 (d, J = 5.7 Hz, 2H), 5.74 (t, J = 5.8 Hz, 1H), 5.29 (s, 1H), 4.88 (dq, J = 7.5, 3.5 Hz, 1H), 4.52 (t, J = 16.1 Hz, 1H), 3.81 (s, 4H), 3.64 (h, J = 6.7 Hz, 2H), 3.32 - 3.27 (m, 1H), 3.10 - 3.03 (m, 3H), 2.90 - 2.66 (m, 8H), 2.27 (dhept, J = 11.9, 3.9 Hz, 5H), 2.04 (dtt, J = 14.7, 10.5, 5.1 Hz, 2H), 1.92 (s, 2H), 0.86 - 0.80 (m, 5H), 0.57 (d, J = 6.4 Hz, 4H).; 640.5[M+H]$^+$	1.09

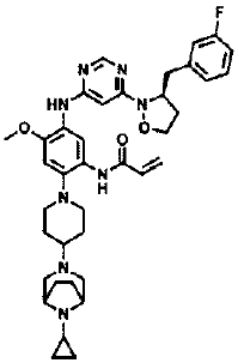
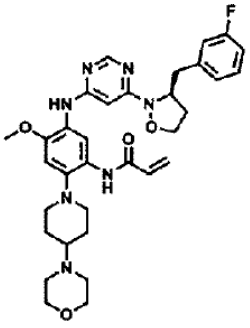
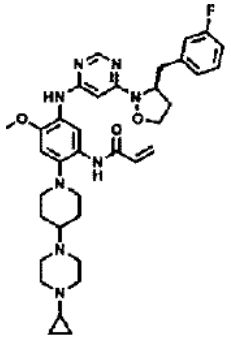
		yl)amino)phenyl)acrylamide		
989		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.80 (s, 1H), 8.43 (s, 1H), 8.32 (s, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 6.99 (s, 1H), 6.71 (d, *J* = 4.0 Hz, 1H), 6.59 (s, 1H), 6.39 - 6.32 (m, 2H), 5.77 - 5.72 (m, 1H), 5.29 (s, 1H), 4.89 (tt, *J* = 11.1, 5.5 Hz, 1H), 4.57 (s, 1H), 3.99 - 3.86 (m, 3H), 3.82 (s, 3H), 3.65 (p, *J* = 6.7 Hz, 2H), 3.31 (td, *J* = 7.3, 5.3 Hz, 2H), 3.11 (ddd, *J* = 25.4, 14.4, 7.1 Hz, 5H), 2.99 (dt, *J* = 15.0, 7.8 Hz, 2H), 2.27 (dtd, *J* = 12.4, 8.1, 4.2 Hz, 3H), 2.17 (dt, *J* = 14.9, 7.4 Hz, 2H), 1.55 (t, *J* = 7.4 Hz, 2H), 1.50 - 1.46 (m, 5H), 0.90 - 0.78 (m, 2H).; 613.4[M+H]$^+$	1.02

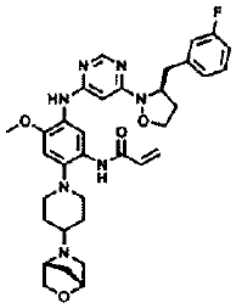
[669]

990		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.81 (s, 1H), 8.43 (s, 1H), 8.32 (s, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.23 (s, 1H), 6.92 (s, 1H), 6.70 (s, 1H), 6.60 (s, 1H), 6.37 - 6.32 (m, 2H), 5.74 (dd, J = 7.2, 4.3 Hz, 1H), 4.80 (qd, J = 7.3, 3.8 Hz, 1H), 4.56 (s, 1H), 3.95 (q, J = 8.1 Hz, 1H), 3.87 (dt, J = 13.9, 7.1 Hz, 2H), 3.82 (s, 3H), 3.77 (d, J = 9.2 Hz, 1H), 3.43 (p, J = 7.4, 6.4 Hz, 2H), 3.37 - 3.25 (m, 2H), 3.11 (ddd, J = 25.4, 14.5, 7.2 Hz, 4H), 2.96 (dt, J = 22.6, 7.8 Hz, 2H), 2.86 (dd, J = 14.1, 7.3 Hz, 2H), 2.26 (ddd, J = 12.9, 8.5, 4.5 Hz, 2H), 2.15 (td, J = 15.7, 14.2, 6.7 Hz, 2H), 1.48 (s, 3H), 1.29 - 1.22 (m, 4H), 1.19 (t, J = 7.3 Hz, 2H).; 613.5[M+H]$^+$	1.03
991		N-(5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.51 (s, 1H), 8.37 (s, 1H), 7.29 - 7.22 (m, 1H), 7.10 (d, J = 7.6 Hz, 1H), 7.04 (d, J = 9.9 Hz, 1H), 6.94 - 6.87 (m, 2H), 6.79 (s, 1H), 6.59 (s, 1H), 6.39 - 6.21 (m, 2H), 5.74 (dd, J = 9.9, 1.4 Hz, 1H), 4.92 - 4.83 (m, 1H), 4.07 (td, J = 8.1, 4.6 Hz, 1H), 3.96 (q, J = 8.1 Hz, 1H), 3.83 (s, 3H), 3.23 (dd, J = 13.8, 6.2 Hz, 1H), 2.97 - 2.88 (m, 4H), 2.80 (dd, J = 13.8, 8.3 Hz, 1H), 2.70 - 2.56 (m, 3H), 2.41 (s, 3H), 2.27 - 2.17 (m, 1H), 2.09 - 1.99 (m, 1H), 1.77 - 1.62 (m, 2H); 548.32[M+H]$^+$	1.14
992		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.47 (s, 1H), 8.81 (s, 1H), 8.36 (s, 1H), 7.29 - 7.21 (m, 1H), 7.10 (d, J = 7.7 Hz, 1H), 7.04 (d, J = 9.9 Hz, 1H), 7.00 - 6.87 (m, 2H), 6.68 (s, 1H), 6.63 (s, 1H), 6.40 (dd, J = 16.8, 1.9 Hz, 1H), 5.70 (dd, J = 10.2, 1.9 Hz, 1H), 4.94 - 4.80 (m, 1H), 4.09 (td, J = 8.1, 4.6 Hz, 1H), 3.99 (q, J = 8.1 Hz, 1H), 3.84 (s, 3H), 3.49 (s, 3H), 3.33 - 3.25 (m, 2H), 3.22 (dd, J = 13.8, 6.3 Hz, 1H), 2.85 - 2.77 (m, 6H), 2.74 (s, 3H), 2.31 - 2.17 (m, 1H), 2.10 - 2.01 (m, 1H); 550.30[M+H]$^+$	1.18
993		N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.42 (s, 1H), 8.37 (s, 1H), 7.29 - 7.21 (m, 5H), 7.10 (d, J = 7.7 Hz, 1H), 7.04 (d, J = 9.8 Hz, 1H), 6.90 (td, J = 8.5, 2.2 Hz, 1H), 6.86 (s, 1H), 6.73 (s, 1H), 6.59 (s, 1H), 6.38 - 6.20 (m, 2H), 5.76 - 5.71 (m, 1H), 4.92 - 4.83 (m, 1H), 4.06 (td, J = 8.1, 4.5 Hz, 1H), 3.96 (q, J = 8.1 Hz, 1H), 3.83 (s, 3H), 3.22 (dd, J = 13.8, 6.2 Hz, 1H), 3.10 - 2.86 (m, 5H), 2.83 - 2.49 (m, 5H), 2.43 - 2.16 (m, 3H), 2.14 - 1.99 (m, 4H), 1.77 - 1.52 (m, 3H), 1.22 (d, J = 5.9 Hz, 3H), 0.71 - 0.55 (m, 2H), 0.50 - 0.28 (m, 2H); 671.61[M+H]$^+$	1.19

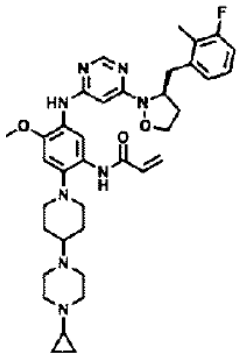
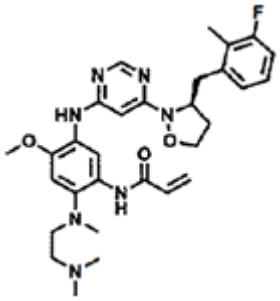
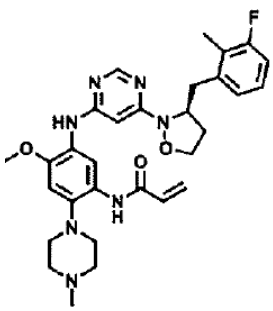
		2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide		
994		N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.42 (s, 1H), 8.37 (s, 1H), 7.28 - 7.22 (m, 1H), 7.10 (d, *J* = 7.7 Hz, 1H), 7.04 (d, *J* = 9.9 Hz, 1H), 6.91 (td, *J* = 8.5, 2.1 Hz, 1H), 6.85 (s, 1H), 6.73 (s, 1H), 6.59 (s, 1H), 6.38 - 6.19 (m, 2H), 5.77 - 5.70 (m, 1H), 4.92 - 4.83 (m, 1H), 4.06 (td, *J* = 8.1, 4.6 Hz, 1H), 3.96 (q, *J* = 8.1 Hz, 1H), 3.83 (s, 3H), 3.22 (dd, *J* = 13.8, 6.2 Hz, 1H), 3.09 - 2.85 (m, 5H), 2.83 - 2.67 (m, 3H), 2.64 - 2.42 (m, 2H), 2.41 - 2.17 (m, 3H), 2.13 - 1.97 (m, 4H), 1.73 - 1.50 (m, 3H), 1.22 (d, *J* = 6.1 Hz, 3H), 0.71 - 0.54 (m, 2H), 0.49 - 0.20 (m, 2H): 671.51[M+H]$^+$	1.19

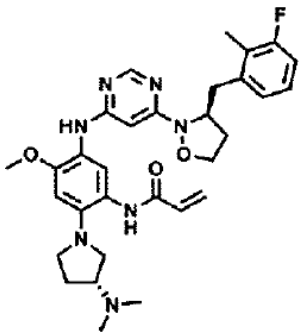
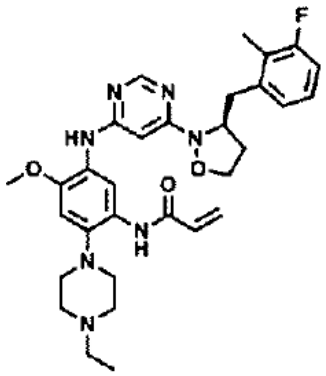
[670]

995		N-(2-(4-((1R,5S)-8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.45 (s, 1H), 8.36 (s, 1H), 7.28 - 7.21 (m, 1H), 7.10 (d, J = 7.6 Hz, 1H), 7.04 (d, J = 9.8 Hz, 1H), 6.90 (td, J = 8.4, 2.1 Hz, 1H), 6.85 (s, 1H), 6.73 (s, 1H), 6.59 (s, 1H), 6.39 - 6.21 (m, 2H), 5.74 (dd, J = 9.8, 1.6 Hz, 1H), 4.93 - 4.83 (m, 1H), 4.06 (td, J = 8.1, 4.6 Hz, 1H), 3.96 (q, J = 8.1 Hz, 1H), 3.83 (s, 3H), 3.35 - 3.17 (m, 3H), 3.06 - 2.96 (m, 2H), 2.80 (dd, J = 13.8, 8.3 Hz, 1H), 2.73 - 2.63 (m, 4H), 2.47 - 2.17 (m, 4H), 2.09 - 1.80 (m, 8H), 1.73 - 1.54 (m, 2H), 0.50 - 0.27 (m, 4H): 683.47[M+H]$^+$	1.22
996		N-(5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (s, 1H), 8.42 (s, 1H), 8.37 (s, 1H), 7.29 - 7.20 (m, 1H), 7.10 (d, J = 7.6 Hz, 1H), 7.04 (d, J = 9.9 Hz, 1H), 6.94 - 6.85 (m, 2H), 6.74 (s, 1H), 6.59 (s, 1H), 6.39 - 6.20 (m, 2H), 5.73 (dd, J = 10.0, 1.3 Hz, 1H), 4.92 - 4.83 (m, 1H), 4.06 (td, J = 8.1, 4.6 Hz, 1H), 3.96 (q, J = 8.1 Hz, 1H), 3.83 (s, 3H), 3.83 - 3.73 (m, 4H), 3.22 (dd, J = 13.8, 6.2 Hz, 1H), 3.12 - 3.02 (m, 2H), 2.84 - 2.60 (m, 7H), 2.41 - 2.28 (m, 1H), 2.26 - 2.17 (m, 1H), 2.13 - 2.00 (m, 3H), 1.73 - 1.57 (m, 2H): 618.48[M+H]$^+$	1.14
997		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	: 657.44[M+H]$^+$	1.21

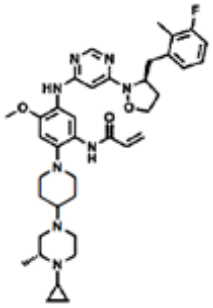
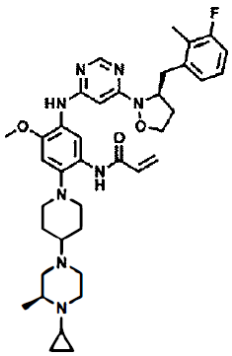
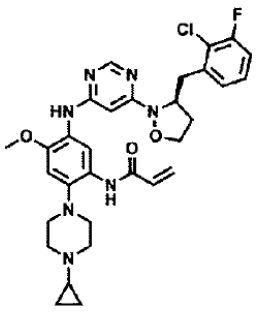
998		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	: 630.53[M+H]$^+$	1.17

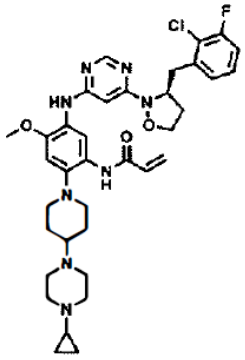
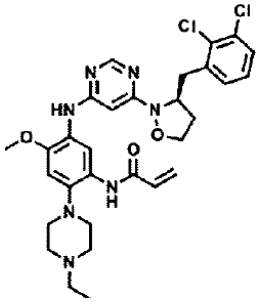
[671]

999		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.25 (s, 1H), 8.16 (s, 1H), 7.13 - 7.08 (m, 2H), 6.95 - 6.87 (m, 2H), 6.61 - 6.48 (m, 1H), 6.40 - 6.32 (m, 1H), 6.29 (s, 1H), 5.81 (d, J = 10.2 Hz, 1H), 4.14 - 4.09 (m, 1H), 3.93 - 3.86 (m, 5H), 3.22 - 3.17 (m, 3H), 3.04 - 2.97 (m, 3H), 2.91 - 2.80 (m, 8H), 2.33 (d, 3H), 2.27 - 2.21 (m, 1H), 2.17 - 2.11 (m, 3H), 1.90 - 1.78 (m, 4H), 0.60 - 0.53 (m, 2H), 0.53 - 0.43 (m, 2H) ; 671.4[M+H]$^+$	1.22
1000		N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (s, 1H), 7.98 (s, 1H), 7.14 - 7.09 (m, 2H), 6.97 - 6.86 (m, 2H), 6.60 - 6.49 (m, 1H), 6.47 - 6.36 (m, 2H), 5.91 - 5.81 (m, 1H), 4.17 - 4.11 (m, 1H), 3.95 - 3.84 (m, 5H), 3.45 - 3.38 (m, 2H), 3.25 - 3.19 (m, 1H), 3.16 - 3.12 (m, 2H), 2.90 - 2.82 (m, 1H), 2.77 (s, 6H), 2.73 (s, 3H), 2.34 (d, J = 2.2 Hz, 3H), 2.20 - 2.20 (m, 1H), 2.20 - 2.09 (m, 1H) ; 564.3[M+H]$^+$	1.23
1001		N-(5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.30 (s, 1H), 8.17 (s, 1H), 7.15 - 7.05 (m, 2H), 6.97 - 6.84 (m, 2H), 6.63 - 6.44 (m, 1H), 6.40 - 6.29 (m, 2H), 5.82 (d, J = 10.3 Hz, 1H), 4.16 - 4.09 (m, 1H), 3.95 - 3.83 (m, 5H), 3.24 - 3.17 (m, 1H), 3.10 - 3.04 (m, 4H), 3.04 - 2.93 (m, 4H), 2.89 - 2.81 (m, 1H), 2.62 (s, 3H), 2.33 (s, 3H), 2.30 - 2.19 (m, 1H), 2.19 - 2.09 (m, 1H) ; 645.3[M+H]$^+$	1.16

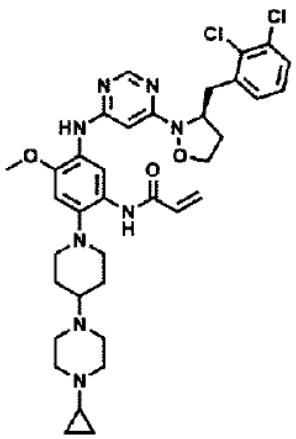
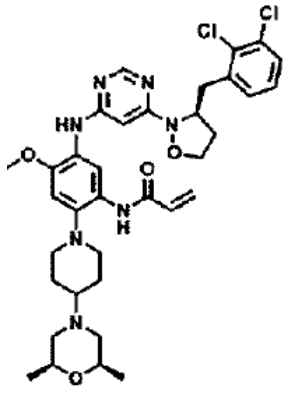
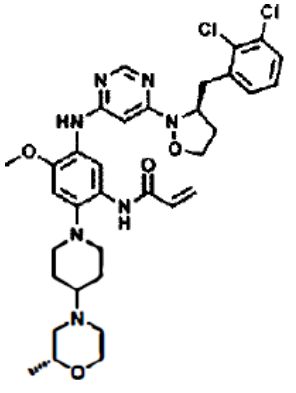
1002		N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.14 (s, 1H), 7.70 (s, 1H), 7.15 - 7.06 (m, 2H), 6.95 - 6.86 (m, 1H), 6.71 (s, 1H), 6.62 - 6.48 (m, 1H), 6.42 - 6.30 (m, 1H), 6.20 (s, 1H), 5.81 (dd, J = 1.7, 10.2 Hz, 1H), 4.14 - 4.06 (m, 1H), 3.94 - 3.81 (m, 4H), 3.78 - 3.70 (m, 1H), 3.47 - 3.34 (m, 4H), 3.32 - 3.16 (m, 3H), 2.89 - 2.80 (m, 1H), 2.32 (d, J = 2.2 Hz, 3H), 2.27 - 2.18 (m, 1H), 2.18 - 2.04 (m, 2H), 1.43 - 1.35 (m, 6H) ; 576.3[M+H]$^+$	1.15
1003		N-(2-(4-ethylpiperazine-1-yl)-5-((6-(S)-(3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.31 (s, 1H), 8.17 (s, 1H), 7.17 - 7.05 (m, 2H), 6.98 - 6.83 (m, 2H), 6.64 - 6.49 (m, 1H), 6.42 - 6.28 (m, 2H), 5.82 (d, J = 10.4 Hz, 1H), 4.13 (td, J = 4.5, 7.9 Hz, 1H), 4.00 - 3.79 (m, 5H), 3.23 - 3.17 (m, 1H), 3.17 - 3.06 (m, 8H), 2.99 - 2.93 (m, 2H), 2.89 - 2.80 (m, 1H), 2.33 (d, J = 2.8 Hz, 3H), 2.26 - 2.20 (m, 1H), 2.17 - 2.09 (m, 1H), 1.33 - 1.30 (m, 3H) ; 576.3[M+H]$^+$	1.19

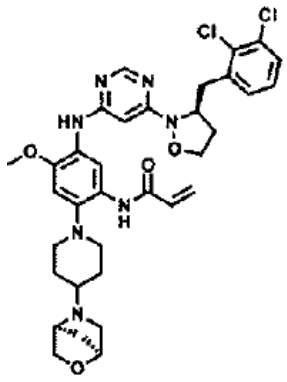
[672]

1004		N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.26 (s, 1H), 8.16 (s, 1H), 7.17 - 7.04 (m, 2H), 6.96 - 6.84 (m, 2H), 6.56 (dd, J = 10.2, 17.0 Hz, 1H), 6.40 - 6.26 (m, 2H), 5.81 (d, J = 10.3 Hz, 1H), 4.15 - 4.00 (m, 1H), 3.96 - 3.79 (m, 5H), 3.23 - 3.17 (m, 4H), 2.88 - 2.70 (m, 6H), 2.69 - 2.50 (m, 2H), 2.46 - 2.37 (m, 1H), 2.33 (d, J = 2.2 Hz, 3H), 2.30 - 2.18 (m, 1H), 2.18 - 2.09 (m, 3H), 1.92 - 1.82 (m, 2H), 1.77 - 1.71 (m, 1H), 1.30 (d, J = 6.2 Hz, 3H), 0.81 - 0.72 (m, 1H), 0.72 - 0.62 (m, 1H), 0.62 - 0.52 (m, 1H), 0.45 - 0.32 (m, 1H) ; 685.4[M+H]$^+$	1.23
1005		N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.27 (s, 1H), 8.16 (s, 1H), 7.16 - 7.03 (m, 2H), 6.95 - 6.84 (m, 2H), 6.64 - 6.47 (m, 1H), 6.41 - 6.23 (m, 2H), 5.87 - 5.74 (m, 1H), 4.15 - 4.08 (m, 1H), 3.93 - 3.84 (m, 4H), 3.30 - 3.23 (m, 1H), 3.22 - 3.12 (m, 5H), 2.88 - 2.61 (m, 7H), 2.47 - 2.37 (m, 1H), 2.32 (d, J = 2.2 Hz, 3H), 2.30 - 2.19 (m, 1H), 2.19 - 2.10 (m, 3H), 1.93 - 1.81 (m, 2H), 1.76 - 1.72 (m, 1H), 1.30 (d, J = 6.3 Hz, 3H), 0.80 - 0.70 (m, 1H), 0.70 - 0.62 (m, 1H), 0.62 - 0.51 (m, 1H), 0.44 - 0.36 (m, 1H) ; 685.4[M+H]$^+$	1.23
1006		N-(5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.28 (s, 1H), 8.14 (s, 1H), 7.32 - 7.20 (m, 2H), 7.17 - 7.04 (m, 1H), 6.92 (s, 1H), 6.54 (dd, J = 10.2, 17.0 Hz, 1H), 6.39 - 6.25 (m, 2H), 5.82 (d, J = 10.2 Hz, 1H), 4.14 (td, J = 4.7, 8.0 Hz, 1H), 3.96 - 3.83 (m, 4H), 3.39 - 3.34 (m, 1H), 3.23 - 3.16 (m, 1H), 3.11 - 3.04 (m, 1H), 3.01 - 2.87 (m, 8H), 2.33 - 2.23 (m, 1H), 2.18 - 2.07 (m, 1H), 1.92 - 1.85 (m, 1H), 0.63 - 0.56 (m, 2H), 0.56 - 0.49 (m, 2H) ; 608.3[M+H]$^+$	1.21

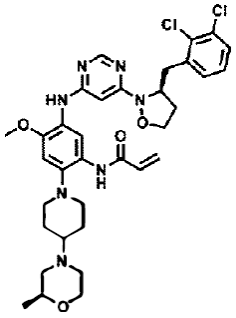
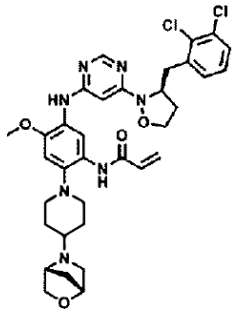
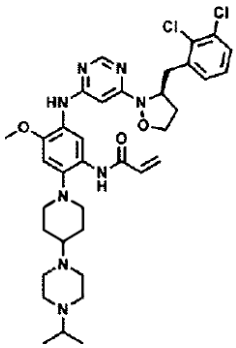
1007		N-(5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.26 (s, 1H), 8.14 (s, 1H), 7.33 - 7.20 (m, 2H), 7.17 - 7.04 (m, 1H), 6.91 (s, 1H), 6.56 (dd, J = 10.2, 17.0 Hz, 1H), 6.44 - 6.23 (m, 2H), 5.81 (d, J = 10.2 Hz, 1H), 4.17 - 4.10 (m, 1H), 3.97 - 3.80 (m, 5H), 3.24 - 3.14 (m, 3H), 3.14 - 3.03 (m, 2H), 3.03 - 2.92 (m, 3H), 2.92 - 2.76 (m, 7H), 2.33 - 2.22 (m, 1H), 2.18 - 2.07 (m, 3H), 1.90 - 1.78 (m, 3H), 0.60 - 0.50 (m, 2H), 0.50 - 0.43 (m, 2H) ; 691.3[M+H]$^+$	1.19
1008		N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.85 (s, 1H), 8.55 (s, 1H), 8.32 (s, 1H), 7.34 (ddd, J = 13.6, 7.8, 1.6 Hz, 2H), 7.12 (t, J = 7.8 Hz, 1H), 6.92 (s, 1H), 6.80 (s, 1H), 6.59 (s, 1H), 6.25 (dd, J = 16.9, 9.9 Hz, 1H), 5.73 (dd, J = 9.8, 1.7 Hz, 1H), 5.00 (qd, J = 7.4, 3.3 Hz, 1H), 3.80 (s, 3H), 3.24 (dd, J = 14.2, 7.4 Hz, 1H), 3.07 (dd, J = 14.2, 7.1 Hz, 1H), 2.92 (t, J = 4.9 Hz, 5H), 2.76 - 2.56 (m, 4H), 2.51 (q, J = 7.2 Hz, 3H), 2.25 (dtd, J = 12.9, 8.3, 4.9 Hz, 2H), 2.07 (dtd, J = 11.8, 7.8, 3.4 Hz, 1H), 1.25 (d, J = 2.9 Hz, 2H), 1.14 (t, J = 7.2 Hz, 4H).; 612.3[M+H]$^+$	1.41

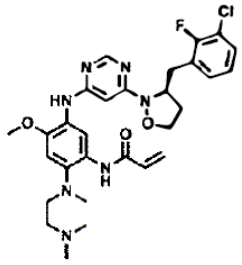
[673]

1009		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.81 (s, 1H), 8.42 (s, 1H), 8.32 (s, 1H), 7.34 (ddd, *J* = 12.7, 7.8, 1.6 Hz, 2H), 7.12 (t, *J* = 7.8 Hz, 1H), 6.89 (s, 1H), 6.72 (s, 1H), 6.58 (s, 1H), 6.24 (dd, *J* = 16.9, 9.9 Hz, 1H), 5.72 (dd, *J* = 9.9, 1.7 Hz, 1H), 5.00 (qd, *J* = 7.5, 3.4 Hz, 1H), 3.81 (s, 3H), 3.24 (dd, *J* = 14.2, 7.4 Hz, 1H), 3.06 (dt, *J* = 13.6, 5.4 Hz, 4H), 2.78 - 2.62 (m, 10H), 2.38 (s, 1H), 2.25 (dtd, *J* = 12.8, 8.3, 4.8 Hz, 2H), 2.07 (tt, *J* = 11.8, 3.4 Hz, 3H), 1.77 - 1.64 (m, 4H), 1.31 - 1.21 (m, 4H), 0.86 (dtd, *J* = 12.7, 6.5, 1.9 Hz, 3H), 0.51 - 0.40 (m, 4H).; 707.4[M+H]$^+$	1.31
1010		N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.82 (s, 1H), 8.41 (s, 1H), 8.32 (d, *J* = 1.0 Hz, 1H), 7.34 (ddd, *J* = 12.9, 7.9, 1.6 Hz, 2H), 7.12 (t, *J* = 7.8 Hz, 1H), 6.88 (s, 1H), 6.73 (s, 1H), 6.58 (s, 1H), 6.24 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.73 (dd, *J* = 10.0, 1.6 Hz, 1H), 5.00 (qd, *J* = 7.4, 3.4 Hz, 1H), 3.82 (s, 3H), 3.70 (dqd, *J* = 12.4, 6.2, 1.9 Hz, 2H), 3.24 (dd, *J* = 14.2, 7.4 Hz, 1H), 3.11 - 3.02 (m, 3H), 2.87 (d, *J* = 10.8 Hz, 2H), 2.76 - 2.65 (m, 2H), 2.32 - 2.19 (m, 2H), 2.07 (dtd, *J* = 12.0, 7.4, 7.0, 3.1 Hz, 4H), 1.89 (t, *J* = 10.6 Hz, 3H), 1.65 (qd, *J* = 12.1, 3.9 Hz, 2H), 1.20 (d, *J* = 6.3 Hz, 6H).; 606.4[M+H]$^+$	1.27
1011		N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.82 (s, 1H), 8.42 (s, 1H), 8.32 (d, *J* = 1.0 Hz, 1H), 7.34 (ddd, *J* = 12.9, 7.9, 1.6 Hz, 2H), 7.12 (t, *J* = 7.8 Hz, 1H), 6.88 (s, 1H), 6.73 (s, 1H), 6.58 (s, 1H), 6.23 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.72 (dd, *J* = 9.9, 1.6 Hz, 1H), 5.00 (qd, *J* = 7.4, 3.3 Hz, 1H), 4.11 (td, *J* = 8.1, 4.8 Hz, 1H), 4.00 (q, *J* = 8.1 Hz, 1H), 3.92 (ddd, *J* = 11.3, 3.4, 1.5 Hz, 1H), 3.82 (s, 3H), 3.75 - 3.60 (m, 2H), 3.24 (dd, *J* = 14.2, 7.4 Hz, 1H), 3.06 (dt, *J* = 15.4, 6.0 Hz, 3H), 2.92 - 2.79 (m, 2H), 2.76 - 2.66 (m, 2H), 2.27 (ddt, *J* = 25.5, 12.9, 4.5 Hz, 4H), 2.17 - 2.01 (m, 4H), 1.96 (t, *J* = 10.5 Hz, 2H), 1.64 (qt, *J* = 12.1, 3.6 Hz, 2H), 1.18 (d, *J* = 6.3 Hz, 4H).; 682.4[M+H]$^+$	1.26

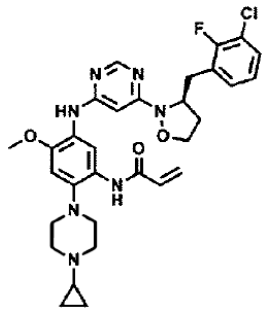
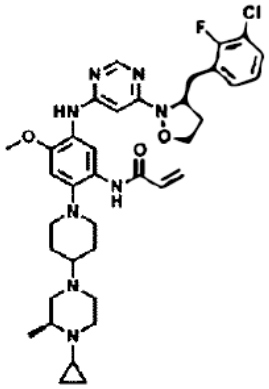
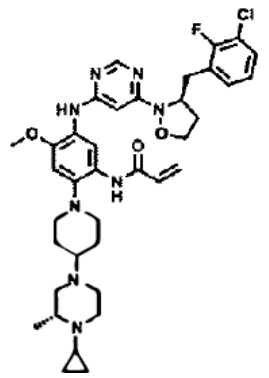
1012		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	680.4[M+H]$^+$	1.24

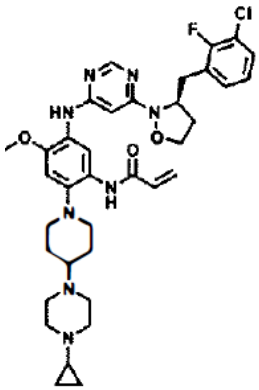
[674]

1013		N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.83 (s, 1H), 8.43 (s, 1H), 8.33 (d, J = 1.0 Hz, 1H), 7.35 (ddd, J = 12.6, 7.8, 1.5 Hz, 2H), 7.13 (t, J = 7.8 Hz, 1H), 6.85 (s, 1H), 6.74 (d, J = 4.6 Hz, 1H), 6.59 (s, 1H), 6.24 (dd, J = 16.9, 10.0 Hz, 1H), 5.73 (dd, J = 10.0, 1.5 Hz, 1H), 5.01 (qd, J = 7.4, 3.4 Hz, 1H), 3.83 (s, 4H), 3.74 - 3.61 (m, 3H), 3.25 (dd, J = 14.2, 7.4 Hz, 1H), 3.08 (dd, J = 15.0, 8.5 Hz, 4H), 2.87 (dd, J = 22.8, 11.2 Hz, 2H), 2.72 (q, J = 11.3 Hz, 3H), 2.29 (ddt, J = 13.8, 8.6, 3.8 Hz, 4H), 2.08 - 2.04 (m, 2H), 1.96 (t, J = 10.5 Hz, 1H), 1.25 (s, 3H), 1.21 - 1.15 (m, 4H).: 684.2[M+H]$^+$	1.31
1014		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.82 (s, 1H), 8.46 (s, 1H), 8.32 (d, J = 1.0 Hz, 1H), 7.34 (ddd, J = 13.4, 7.8, 1.6 Hz, 2H), 7.12 (t, J = 7.8 Hz, 1H), 6.89 (s, 1H), 6.74 (s, 1H), 6.58 (d, J = 1.1 Hz, 1H), 6.21 (dd, J = 17.0, 10.0 Hz, 1H), 5.71 (dd, J = 10.0, 1.5 Hz, 1H), 5.00 (qd, J = 7.4, 3.4 Hz, 1H), 4.09 (td, J = 8.1, 3.3 Hz, 2H), 3.82 (s, 3H), 3.77 - 3.73 (m, 1H), 3.65 (dd, J = 7.9, 1.6 Hz, 1H), 3.27 - 2.97 (m, 7H), 2.75 (qd, J = 11.4, 2.5 Hz, 2H), 2.56 (tt, J = 10.1, 3.9 Hz, 1H), 2.49 (dd, J = 10.0, 1.4 Hz, 1H), 2.24 - 2.19 (m, 2H), 2.07 (ddd, J = 16.4, 8.1, 3.8 Hz, 2H), 2.02 - 1.94 (m, 1H), 1.94 - 1.87 (m, 2H), 1.84 - 1.77 (m, 1H), 1.72 - 1.58 (m, 3H).: 680.4[M+H]$^+$	1.25
1015		N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.80 (s, 1H), 8.37 (s, 1H), 8.31 (s, 1H), 7.30 - 7.31 (m, 2H), 7.14 (d, J = 7.9 Hz, 1H), 6.72 (s, 1H), 6.57 (s, 1H), 6.36 (ddd, J = 17.0, 6.6, 1.8 Hz, 2H), 6.26 (dd, J = 16.9, 9.8 Hz, 1H), 5.74 (dd, J = 9.8, 1.7 Hz, 1H), 5.00 (qd, J = 7.4, 3.4 Hz, 1H), 3.83 (s, 3H), 3.65 (h, J = 6.7 Hz, 3H), 3.33 (qd, J = 7.2, 5.1 Hz, 2H), 3.23 (d, J = 7.4 Hz, 1H), 3.16 (s, 4H), 3.09 (qd, J = 7.1, 5.2 Hz, 8H), 2.72 (s, 2H), 2.26 (qd, J = 8.0, 4.1 Hz, 1H), 2.00 (ddt, J = 12.2, 8.2, 4.0 Hz, 4H), 1.76 - 1.67 (m, 3H), 1.56 (t, J = 7.5 Hz, 5H), 1.41 (d, J = 6.6 Hz, 6H).: 709.5[M+H]$^+$	1.23

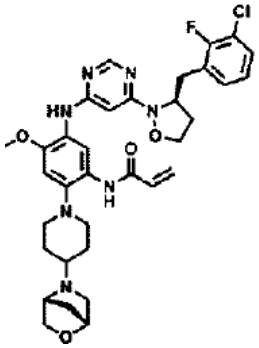
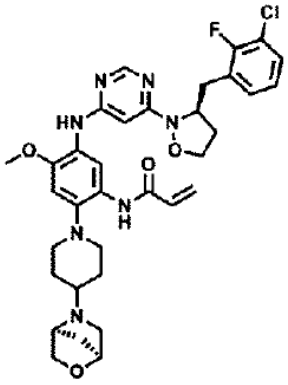
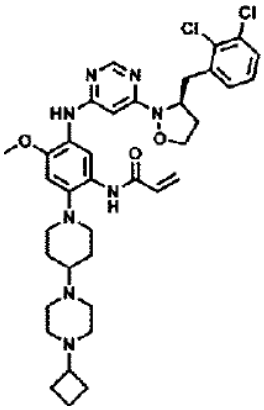
1016		N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	: 584.41[M+H]$^+$	1.32

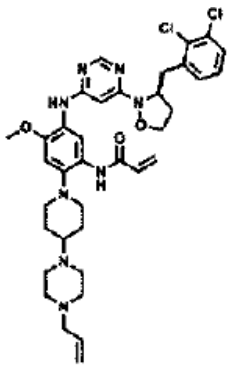
[675]

1017		N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.58 (s, 1H), 8.34 (s, 1H), 7.30 (t, *J* = 7.1 Hz, 1H), 7.28 - 7.23 (m, 1H), 7.01 (t, *J* = 7.8 Hz, 1H), 6.91 (s, 1H), 6.78 (s, 1H), 6.60 (s, 1H), 6.39 - 6.22 (m, 2H), 5.74 (dd, *J* = 9.8, 1.5 Hz, 1H), 4.96 - 4.88 (m, 1H), 4.09 (td, *J* = 8.1, 4.7 Hz, 1H), 3.98 (q, *J* = 8.1 Hz, 1H), 3.80 (s, 3H), 3.15 (dd, *J* = 14.0, 6.6 Hz, 1H), 2.98 (dd, *J* = 13.9, 7.6 Hz, 1H), 2.89 - 2.84 (m, 4H), 2.31 - 2.20 (m, 1H), 2.10 - 2.00 (m, 1H), 1.75 - 1.69 (m, 1H), 0.56 - 0.50 (m, 2H), 0.50 - 0.44 (m, 2H); 608.42[M+H]$^+$	1.31
1018		N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.43 (s, 1H), 8.34 (s, 1H), 7.30 (t, *J* = 7.1 Hz, 1H), 7.28 - 7.23 (m, 1H), 7.01 (t, *J* = 7.8 Hz, 1H), 6.85 (d, *J* = 4.6 Hz, 1H), 6.73 (s, 1H), 6.59 (s, 1H), 6.38 - 6.19 (m, 2H), 5.73 (dd, *J* = 10.0, 1.2 Hz, 1H), 4.96 - 4.88 (m, 1H), 4.08 (td, *J* = 8.1, 4.7 Hz, 1H), 3.97 (q, *J* = 8.0 Hz, 1H), 3.82 (s, 3H), 3.15 (dd, *J* = 14.0, 7.0 Hz, 1H), 3.08 - 2.93 (m, 5H), 2.91 - 2.84 (m, 1H), 2.77 - 2.66 (m, 2H), 2.58 - 2.43 (m, 2H), 2.34 - 2.21 (m, 3H), 2.10 - 1.97 (m, 4H), 1.71 - 1.50 (m, 3H), 1.21 (d, *J* = 6.3 Hz, 3H), 0.60 - 0.56 (m, 2H), 0.48 - 0.40 (m, 1H), 0.36 - 0.28 (m, 1H); 705.53[M+H]$^+$	1.33
1019		N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyph	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.43 (s, 1H), 8.34 (s, 1H), 7.30 (t, *J* = 7.1 Hz, 1H), 7.28 - 7.23 (m, 1H), 7.01 (t, *J* = 7.8 Hz, 1H), 6.85 (s, 1H), 6.73 (s, 1H), 6.59 (s, 1H), 6.37 - 6.18 (m, 2H), 5.73 (dd, *J* = 10.1, 1.1 Hz, 1H), 4.96 - 4.87 (m, 1H), 4.08 (td, *J* = 8.1, 4.7 Hz, 1H), 3.97 (q, *J* = 7.9 Hz, 1H), 3.82 (s, 3H), 3.15 (dd, *J* = 14.0, 6.7 Hz, 1H), 3.08 - 2.93 (m, 5H), 2.91 - 2.84 (m, 1H), 2.76 - 2.65 (m, 2H), 2.57 - 2.43 (m, 2H), 2.35 - 2.20 (m, 3H), 2.10 - 1.96 (m, 4H), 1.76 - 1.50 (m, 3H), 1.21 (d, *J* = 6.3 Hz, 3H), 0.60 - 0.56 (m, 2H), 0.47 - 0.39 (m, 1H), 0.36 - 0.28 (m, 1H); 705.53[M+H]$^+$	1.34

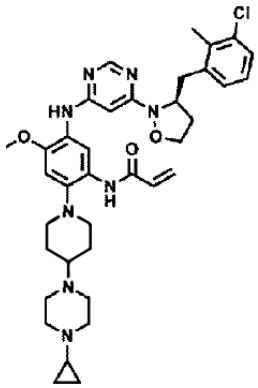
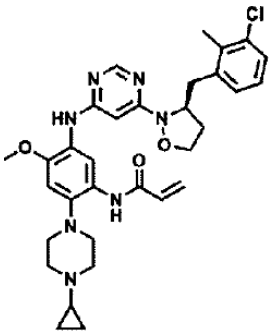
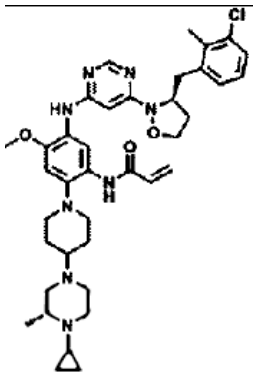
		enyl)acrylamide		
1020		N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.43 (s, 1H), 8.34 (s, 1H), 7.30 (t, *J* = 7.1 Hz, 1H), 7.28 - 7.23 (m, 1H), 7.01 (t, *J* = 7.8 Hz, 1H), 6.85 (s, 1H), 6.73 (s, 1H), 6.50 (s, 1H), 6.37 - 6.19 (m, 2H), 5.73 (dd, *J* = 10.0, 1.3 Hz, 1H), 4.96 - 4.87 (m, 1H), 4.08 (td, *J* = 8.1, 4.7 Hz, 1H), 3.97 (q, *J* = 8.0 Hz, 1H), 3.82 (s, 3H), 3.15 (dd, *J* = 14.2, 6.5 Hz, 1H), 3.08 - 3.01 (m, 2H), 2.98 (dd, *J* = 14.0, 7.6 Hz, 1H), 2.78 - 2.58 (m, 9H), 2.37 - 2.20 (m, 2H), 2.11 - 2.01 (m, 3H), 1.73 - 1.54 (m, 4H), 0.50 - 0.30 (m, 4H); 691.50[M+H]$^+$	1.31

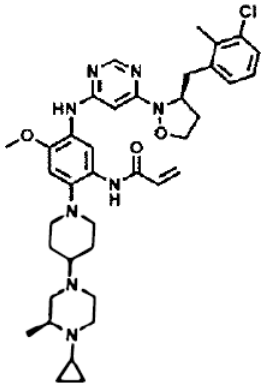
[676]

1021		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.47 (s, 1H), 8.34 (s, 1H), 7.30 (t, J = 7.1 Hz, 1H), 7.28 - 7.23 (m, 1H), 7.01 (t, J = 7.8 Hz, 1H), 6.93 (s, 1H), 6.74 (s, 1H), 6.59 (s, 1H), 6.36 - 6.19 (m, 2H), 5.75 - 5.69 (m, 1H), 4.97 - 4.87 (m, 1H), 4.45 (s, 1H), 4.12 - 4.04 (m, 2H), 3.98 (q, J = 8.0 Hz, 1H), 3.85 - 3.78 (m, 4H), 3.71 - 3.64 (m, 1H), 3.21 - 3.10 (m, 2H), 3.06 - 2.94 (m, 3H), 2.81 - 2.69 (m, 2H), 2.66 - 2.57 (m, 1H), 2.57 - 2.49 (m, 1H), 2.31 - 2.20 (m, 1H), 2.09 - 1.82 (m, 5H), 1.78 - 1.66 (m, 2H); 664.45[M+H]$^+$	1.24
1022		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.47 (s, 1H), 8.34 (s, 1H), 7.30 (t, J = 7.1 Hz, 1H), 7.28 - 7.23 (m, 1H), 7.01 (t, J = 7.8 Hz, 1H), 6.86 (s, 1H), 6.75 (s, 1H), 6.60 (s, 1H), 6.37 - 6.18 (m, 2H), 5.72 (dd, J = 10.1, 1.3 Hz, 1H), 4.96 - 4.88 (m, 1H), 4.44 (s, 1H), 4.12 - 4.05 (m, 2H), 3.98 (q, J = 8.1 Hz, 1H), 3.84 (s, 3H), 3.77 (s, 1H), 3.66 (d, J = 7.5 Hz, 1H), 3.20 - 3.11 (m, 2H), 3.06 - 2.94 (m, 3H), 2.81 - 2.70 (m, 2H), 2.63 - 2.54 (m, 1H), 2.53 - 2.47 (m, 1H), 2.31 - 2.21 (m, 1H), 2.10 - 2.01 (m, 2H), 1.98 - 1.89 (m, 2H), 1.86 - 1.80 (m, 1H), 1.73 - 1.66 (m, 2H); 664.45[M+H]$^+$	1.23
1023		N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphe	^{1}H NMR (400 MHz, Chloroform-d) δ 8.82 (s, 1H), 8.43 (s, 1H), 8.32 (d, J = 1.0 Hz, 1H), 7.34 (ddd, J = 12.8, 7.9, 1.6 Hz, 2H), 7.12 (t, J = 7.8 Hz, 1H), 6.86 (s, 1H), 6.73 (s, 1H), 6.58 (s, 1H), 6.23 (dd, J = 16.9, 10.0 Hz, 1H), 5.72 (dd, J = 10.0, 1.6 Hz, 1H), 5.00 (qd, J = 7.4, 3.4 Hz, 1H), 4.00 (q, J = 8.1 Hz, 1H), 3.82 (s, 3H), 3.24 (dd, J = 14.2, 7.4 Hz, 1H), 3.11 - 3.00 (m, 3H), 2.83 - 2.54 (m, 8H), 2.44 (s, 2H), 2.38 - 2.20 (m, 2H), 2.25 (dt, J = 12.0, 3.0 Hz, 2H), 2.05 (ddt, J = 15.8, 9.5, 3.2 Hz, 7H), 1.91 (t, J = 9.8 Hz, 3H), 1.68 (dtd, J = 27.2, 12.0, 11.0, 5.5 Hz, 5H).; 721.5[M+H]$^+$	1.27

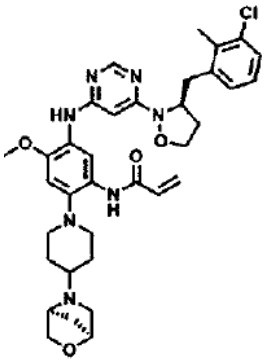
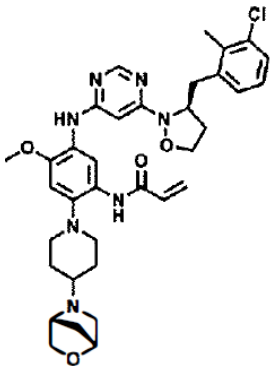
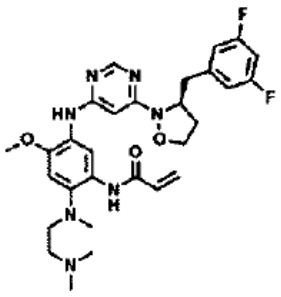
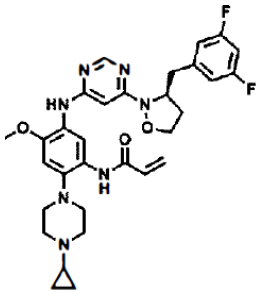
		nyl)acrylamide		
1024		N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	707.3[M+H]$^+$	1.40

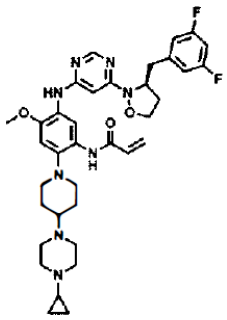
[677]

1025		N-(5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 10.67 (s, 1H), 8.27 (d, J = 6.4 Hz, 2H), 8.13 (s, 1H), 7.10 - 7.00 (m, 2H), 6.67 (s, 1H), 6.48 - 6.30 (m, 2H), 5.98 (s, 1H), 5.77 (dd, J = 9.7, 1.8 Hz, 1H), 4.74 (tt, J = 9.2, 5.0 Hz, 1H), 4.00 (q, J = 7.6 Hz, 1H), 3.77 (s, 4H), 3.72 (s, 8H), 3.37 (dd, J = 13.8, 5.5 Hz, 1H), 3.24 (d, J = 11.9 Hz, 1H), 3.16 (d, J = 11.6 Hz, 2H), 2.76 (dt, J = 11.1, 8.5 Hz, 3H), 2.53 (td, J = 7.1, 3.5 Hz, 1H), 2.45 (s, 3H), 2.34 (dtd, J = 13.4, 7.9, 5.6 Hz, 1H), 2.20 (dt, J = 11.7, 6.2 Hz, 3H), 2.16 - 2.01 (m, 3H), 1.17 (d, J = 4.0 Hz, 2H), 0.98 - 0.78 (m, 4H).: 687.5	1.34
1026		N-(5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.65 (s, 1H), 8.46 (s, 1H), 8.24 - 8.22 (m, 1H), 7.23 (d, J = 1.4 Hz, 1H), 7.13 (dd, J = 7.8, 1.4 Hz, 1H), 7.05 (t, J = 7.8 Hz, 1H), 6.77 (s, 1H), 6.40 - 6.23 (m, 3H), 5.75 (dd, J = 9.6, 2.0 Hz, 1H), 4.84 - 4.74 (m, 1H), 3.80 (s, 3H), 2.96 (s, 6H), 2.80 (dd, J = 14.0, 8.7 Hz, 2H), 2.47 (s, 3H), 2.22 (dtd, J = 12.4, 7.9, 4.6 Hz, 1H), 2.14 - 2.07 (m, 1H), 2.06 (s, 4H), 1.91 (d, J = 10.0 Hz, 1H), 1.26 (d, J = 2.6 Hz, 1H), 0.91 - 0.80 (m, 1H), 0.71 (s, 2H), 0.61 (d, J = 6.6 Hz, 2H).: 604.4[M+H]$^+$	1.33
1027		N-(5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyp	701.6[M+H]$^+$	1.32

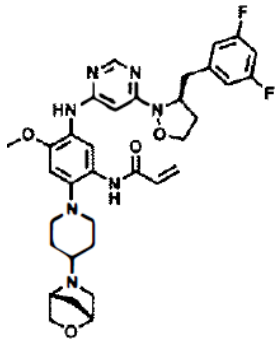
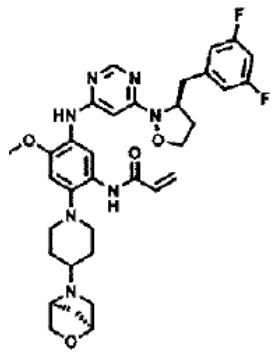
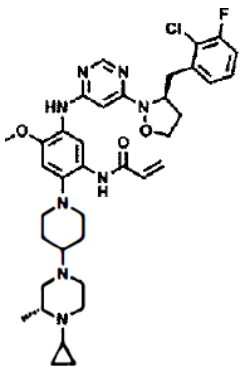
		henyl)acrylamide		
1028		N-(5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.72 (s, 1H), 8.45 (s, 1H), 8.28 (d, *J* = 1.0 Hz, 1H), 7.22 (d, *J* = 1.3 Hz, 1H), 7.15 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.04 (t, *J* = 7.7 Hz, 1H), 6.67 (s, 1H), 6.52 - 6.47 (m, 1H), 6.42 - 6.26 (m, 2H), 5.73 (dd, *J* = 9.3, 2.2 Hz, 1H), 4.81 (tdd, *J* = 8.3, 6.1, 4.1 Hz, 1H), 4.09 (td, *J* = 8.0, 4.5 Hz, 1H), 3.96 (q, *J* = 8.1 Hz, 1H), 3.80 (s, 3H), 3.57 (d, *J* = 10.6 Hz, 1H), 3.29 (dd, *J* = 14.0, 6.1 Hz, 1H), 3.12 - 3.02 (m, 3H), 2.97 (s, 1H), 2.88 (d, *J* = 10.2 Hz, 1H), 2.84 - 2.62 (m, 4H), 2.47 (s, 3H), 2.30 - 2.11 (m, 4H), 2.11 - 2.06 (m, 2H), 1.33 - 1.22 (m, 2H), 0.92 - 0.77 (m, 2H).; 701.6[M+H]$^+$	1.36

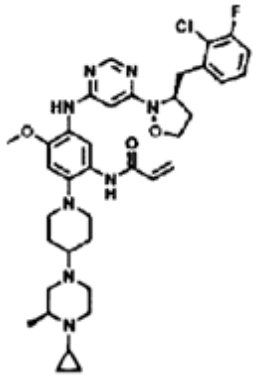
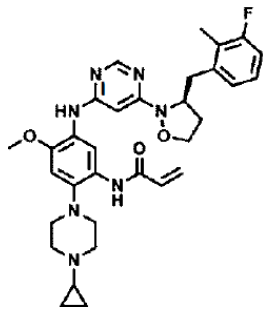
[678]

1029		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.72 (s, 1H), 8.45 (s, 1H), 8.28 (d, *J* = 1.0 Hz, 1H), 7.22 (d, *J* = 1.3 Hz, 1H), 7.15 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.04 (t, *J* = 7.7 Hz, 1H), 6.67 (s, 1H), 6.52 - 6.47 (m, 1H), 6.42 - 6.26 (m, 2H), 5.73 (dd, *J* = 9.3, 2.2 Hz, 1H), 4.81 (tdd, *J* = 8.3, 6.1, 4.1 Hz, 1H), 4.09 (td, *J* = 8.0, 4.5 Hz, 1H), 3.96 (q, *J* = 8.1 Hz, 1H), 3.80 (s, 3H), 3.57 (d, *J* = 10.6 Hz, 1H), 3.29 (dd, *J* = 14.0, 6.1 Hz, 1H), 3.12 - 3.02 (m, 3H), 2.97 (s, 1H), 2.88 (d, *J* = 10.2 Hz, 1H), 2.84 - 2.62 (m, 4H), 2.47 (s, 3H), 2.30 - 2.11 (m, 4H), 2.11 - 2.06 (m, 2H), 1.33 - 1.22 (m, 2H), 0.92 - 0.77 (m, 2H).: 660.4[M+H]$^+$	1.23
1030		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.74 (s, 1H), 8.48 (s, 1H), 8.29 (d, *J* = 1.0 Hz, 1H), 7.24 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.16 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.05 (t, *J* = 7.8 Hz, 1H), 6.72 (s, 1H), 6.53 (s, 1H), 6.34 (s, 1H), 6.32 (d, *J* = 2.1 Hz, 1H), 5.73 (dd, *J* = 6.9, 4.7 Hz, 1H), 4.87 - 4.77 (m, 1H), 4.11 - 4.04 (m, 2H), 3.83 (s, 3H), 3.75 - 3.71 (m, 1H), 3.39 (d, *J* = 10.4 Hz, 1H), 3.30 (dd, *J* = 14.0, 6.1 Hz, 1H), 3.06 (d, *J* = 11.8 Hz, 2H), 2.85 - 2.62 (m, 6H), 2.48 (s, 3H), 2.20 (dtd, *J* = 12.4, 8.1, 4.6 Hz, 2H), 2.06 (s, 5H), 1.94 (d, *J* = 11.2 Hz, 5H), 1.34 - 1.22 (m, 2H).: 660.4[M+H]$^+$	1.25
1031		N-(5-((6-((S)-3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide	: 568.40[M+H]$^+$	1.24
1032		N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-(S)-(3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.59 (s, 1H), 8.36 (s, 1H), 6.91 - 6.83 (m, 3H), 6.78 (s, 1H), 6.70 - 6.62 (m, 1H), 6.61 (s, 1H), 6.30 - 6.23 (m, 2H), 5.75 (dd, *J* = 9.8, 1.6 Hz, 1H), 4.88 (qd, *J* = 7.5, 3.0 Hz, 1H), 4.08 (td, *J* = 8.2, 4.4 Hz, 1H), 3.97 (q, *J* = 8.2 Hz, 1H), 3.80 (s, 3H), 3.18 (dd, *J* = 13.9, 6.7 Hz, 1H), 2.94 - 2.72 (m, 9H), 2.32 - 2.20 (m, 1H), 2.08 - 1.98 (m, 1H), 1.75 - 1.68 (m, 1H), 0.56 - 0.49 (m, 2H), 0.49 - 0.43 (m, 2H): 502.45[M+H]$^+$	1.22

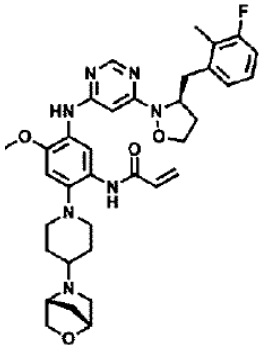
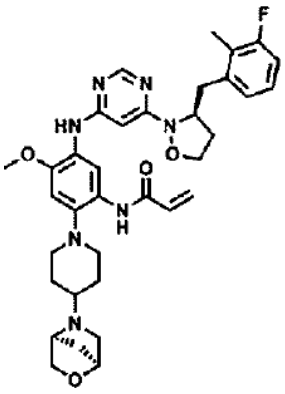
		4-yl)amino)-4-methoxyphenyl)acrylamide		
1033		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 6.90 - 6.82 (m, 3H), 6.73 (s, 1H), 6.60 - 6.62 (m, 1H), 6.60 (s, 1H), 6.38 - 6.10 (m, 2H), 5.73 (dd, *J* = 10.0, 1.3 Hz, 1H), 4.92 - 4.83 (m, 1H), 4.07 (td, *J* = 8.2, 4.5 Hz, 1H), 3.97 (q, *J* = 8.1 Hz, 1H), 3.83 (s, 3H), 3.17 (dd, *J* = 14.0, 6.7 Hz, 1H), 3.10 - 3.00 (m, 2H), 2.83 - 2.58 (m, 10H), 2.38 - 2.21 (m, 2H), 2.11 - 1.97 (m, 3H), 1.72 - 1.62 (m, 4H), 0.51 - 0.38 (m, 4H); 675.53[M+H]$^+$	1.23

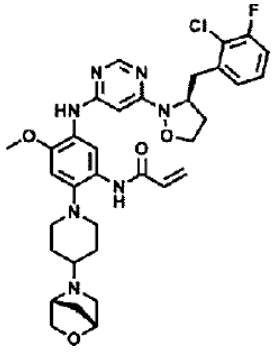
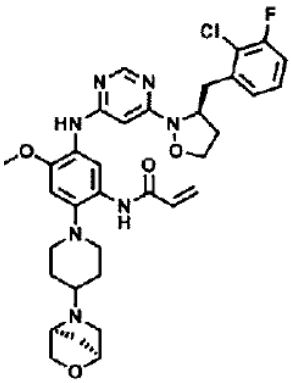
[679]

1034		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.47 (s, 1H), 8.36 (s, 1H), 6.91 - 6.83 (m, 3H), 6.75 (s, 1H), 6.70 - 6.62 (m, 1H), 6.61 (s, 1H), 6.38 - 6.18 (m, 2H), 5.72 (dd, J = 10.0, 1.3 Hz, 1H), 4.88 (qd, J = 7.6, 3.0 Hz, 1H), 4.44 (s, 1H), 4.12 - 4.03 (m, 2H), 3.97 (q, J = 8.1 Hz, 1H), 3.84 (s, 3H), 3.81 - 3.74 (m, 1H), 3.70 - 3.63 (m, 1H), 3.21 - 3.11 (m, 2H), 3.07 - 2.97 (m, 2H), 2.83 - 2.70 (m, 3H), 2.63 - 2.54 (m, 1H), 2.54 - 2.47 (m, 1H), 2.31 - 2.19 (m, 1H), 2.07 - 1.99 (m, 2H), 1.98 - 1.80 (m, 2H), 1.87 - 1.79 (m, 1H), 1.75 - 1.67 (m, 2H); 648.44[M+H]$^+$	1.20
1035		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.47 (s, 1H), 8.36 (s, 1H), 6.91 - 6.84 (m, 3H), 6.75 (s, 1H), 6.69 - 6.62 (m, 1H), 6.60 (s, 1H), 6.37 - 6.19 (m, 2H), 5.72 (dd, J = 10.0, 1.2 Hz, 1H), 4.88 (qd, J = 7.6, 3.0 Hz, 1H), 4.45 (s, 1H), 4.13 - 4.04 (m, 2H), 3.97 (q, J = 8.1 Hz, 1H), 3.84 (s, 3H), 3.82 - 3.74 (m, 1H), 3.71 - 3.63 (m, 1H), 3.22 - 3.12 (m, 2H), 3.07 - 2.98 (m, 2H), 2.83 - 2.70 (m, 3H), 2.64 - 2.55 (m, 1H), 2.55 - 2.48 (m, 1H), 2.30 - 2.20 (m, 1H), 2.09 - 1.99 (m, 2H), 1.99 - 1.80 (m, 2H), 1.88 - 1.80 (m, 1H), 1.77 - 1.68 (m, 2H); 648.44[M+H]$^+$	1.19
1036		N-(5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.27 (s, 1H), 8.14 (s, 1H), 7.32 - 7.19 (m, 2H), 7.15 - 7.07 (m, 1H), 6.91 (s, 1H), 6.63 - 6.49 (m, 1H), 6.39 - 6.27 (m, 2H), 5.81 (dd, J = 1.5, 10.2 Hz, 1H), 4.17 - 4.11 (m, 1H), 3.97 - 3.82 (m, 4H), 3.30 - 3.25 (m, 1H), 3.24 - 3.13 (m, 5H), 3.11 - 3.02 (m, 1H), 2.86 - 2.60 (m, 6H), 2.44 - 2.37 (m, 1H), 2.33 - 2.23 (m, 1H), 2.17 - 2.10 (m, 3H), 1.94 - 1.79 (m, 2H), 1.79 - 1.67 (m, 1H), 1.30 (d, J = 6.3 Hz, 3H), 0.81 - 0.70 (m, 1H), 0.70 - 0.62 (m, 1H), 0.62 - 0.51 (m, 1H), 0.45 - 0.35 (m, 1H) ; 705.3[M+H]$^+$	1.23

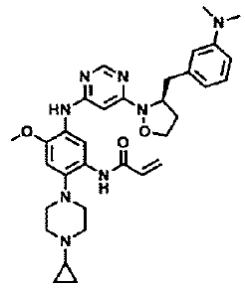
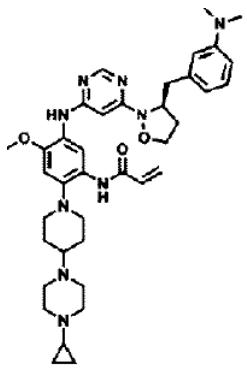
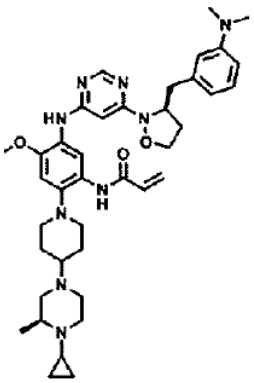
		methoxyphenyl)acrylamide		
1037		N-(5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.27 (s, 1H), 8.15 (s, 1H), 7.33 - 7.20 (m, 2H), 7.18 - 7.06 (m, 1H), 6.91 (s, 1H), 6.63 - 6.48 (m, 1H), 6.41 - 6.25 (m, 2H), 5.84 - 5.76 (m, 1H), 4.17 - 4.10 (m, 1H), 3.94 - 3.84 (m, 4H), 3.30 - 3.25 (m, 1H), 3.25 - 3.15 (m, 5H), 3.10 - 3.03 (m, 1H), 2.85 - 2.64 (m, 6H), 2.47 - 2.38 (m, 1H), 2.33 - 2.24 (m, 1H), 2.17 - 2.08 (m, 3H), 1.93 - 1.81 (m, 2H), 1.77 - 1.69 (m, 1H), 1.30 (d, J = 6.2 Hz, 3H), 0.80 - 0.71 (m, 1H), 0.70 - 0.62 (m, 1H), 0.60 - 0.52 (m, 1H), 0.43 - 0.35 (m, 1H) ; 705.3[M+H]$^+$	1.24
1038		N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.29 (s, 1H), 8.16 (s, 1H), 7.15 - 7.02 (m, 2H), 6.96 - 6.81 (m, 2H), 6.60 - 6.49 (m, 1H), 6.40 - 6.25 (m, 2H), 5.82 (dd, J = 1.5, 10.2 Hz, 1H), 4.15 - 4.07 (m, 1H), 3.93 - 3.85 (m, 4H), 3.24 - 3.16 (m, 1H), 3.01 - 2.90 (m, 8H), 2.88 - 2.81 (m, 1H), 2.32 (d, J = 2.2 Hz, 3H), 2.27 - 2.20 (m, 1H), 2.17 - 2.09 (m, 1H), 1.94 - 1.88 (m, 1H), 0.64 - 0.57 (m, 2H), 0.57 - 0.50 (m, 2H) ; 588.3[M+H]$^+$	1.19

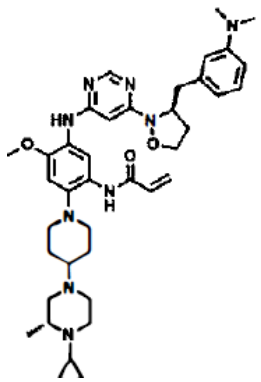
[680]

1039		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.26 (s, 1H), 8.17 (s, 1H), 7.17 - 7.04 (m, 2H), 6.97 - 6.83 (m, 2H), 6.63 - 6.49 (m, 1H), 6.41 - 6.25 (m, 2H), 5.81 (d, J = 10.2 Hz, 1H), 4.61 - 4.58 (m, 1H), 4.29 - 4.24 (m, 1H), 4.20 - 4.09 (m, 2H), 3.95 - 3.84 (m, 4H), 3.81 - 3.75 (m, 1H), 3.32 - 3.28 (m, 1H), 3.24 - 3.12 (m, 3H), 3.07 - 2.95 (m, 2H), 2.90 - 2.78 (m, 3H), 2.32 (d, J = 2.2 Hz, 3H), 2.29 - 2.02 (m, 7H), 1.89 - 1.77 (m, 2H) ; 644.3[M+H]$^+$	1.18
1040		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.26 (s, 1H), 8.17 (s, 1H), 7.16 - 7.04 (m, 2H), 6.97 - 6.84 (m, 2H), 6.63 - 6.47 (m, 1H), 6.42 - 6.26 (m, 2H), 5.86 - 5.75 (m, 1H), 4.59 (s, 1H), 4.27 (s, 1H), 4.20 - 4.08 (m, 2H), 3.95 - 3.84 (m, 4H), 3.82 - 3.74 (m, 1H), 3.32 (d, J = 3.0 Hz, 1H), 3.24 - 3.11 (m, 3H), 3.08 - 2.96 (m, 2H), 2.89 - 2.78 (m, 3H), 2.32 (d, J = 2.2 Hz, 3H), 2.30 - 2.01 (m, 7H), 1.90 - 1.76 (m, 2H) ; 644.3[M+H]$^+$	1.18

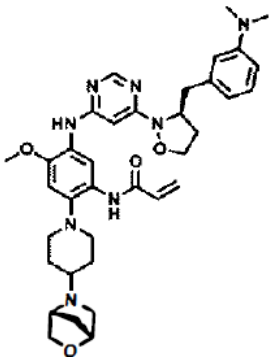
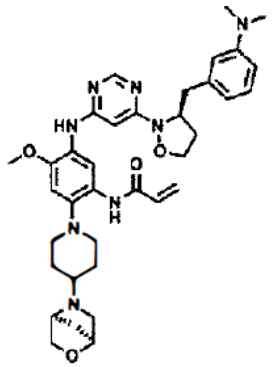
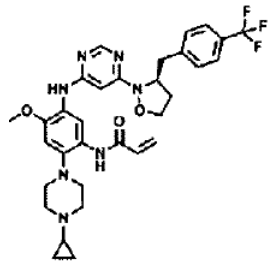
1041		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.26 (s, 1H), 8.15 (s, 1H), 7.29 - 7.22 (m, 2H), 7.14 - 7.08 (m, 1H), 6.92 (s, 1H), 6.55 (dd, J = 10.3, 17.0 Hz, 1H), 6.38 - 6.30 (m, 2H), 5.81 (d, J = 10.4 Hz, 1H), 4.60 - 4.58 (m, 1H), 4.28 - 4.24 (m, 1H), 4.19 - 4.11 (m, 2H), 3.95 - 3.89 (m, 1H), 3.87 (s, 3H), 3.80 - 3.75 (m, 1H), 3.31 - 3.30 (m, 1H), 3.22 - 3.14 (m, 3H), 3.10 - 2.97 (m, 3H), 2.89 - 2.80 (m, 2H), 2.32 - 2.24 (m, 1H), 2.21 - 2.04 (m, 6H), 1.87 - 1.79 (m, 2H) ; 663.3[M+H]$^+$	1.18
1042		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.26 (s, 1H), 8.15 (s, 1H), 7.31 - 7.21 (m, 2H), 7.14 - 7.07 (m, 1H), 6.92 (s, 1H), 6.55 (dd, J = 10.2, 17.0 Hz, 1H), 6.40 - 6.28 (m, 2H), 5.81 (d, J = 10.2 Hz, 1H), 4.60 - 4.58 (m, 1H), 4.27 - 4.25 (m, 1H), 4.19 - 4.11 (m, 2H), 3.96 - 3.89 (m, 1H), 3.87 (s, 3H), 3.80 - 3.75 (m, 1H), 3.31 - 3.29 (m, 1H), 3.22 - 3.14 (m, 3H), 3.10 - 2.97 (m, 3H), 2.89 - 2.81 (m, 2H), 2.33 - 2.24 (m, 1H), 2.23 - 2.01 (m, 6H), 1.88 - 1.76 (m, 2H) ; 663.3[M+H]$^+$	1.18

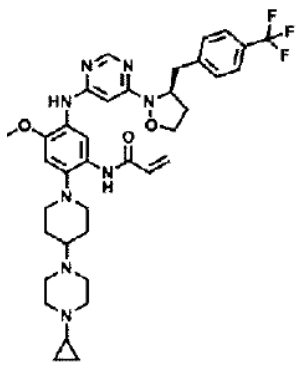
[681]

1043		N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.91 (s, 1H), 8.59 (s, 1H), 8.40 (d, *J* = 1.0 Hz, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 6.88 (s, 1H), 6.78 (s, 1H), 6.75 - 6.65 (m, 2H), 6.65 - 6.57 (m, 2H), 6.36 (dd, *J* = 17.0, 1.7 Hz, 1H), 6.27 (dd, *J* = 17.0, 9.8 Hz, 1H), 5.74 (dd, *J* = 9.8, 1.7 Hz, 1H), 4.96 - 4.85 (m, 1H), 4.07 (td, *J* = 8.0, 5.0 Hz, 1H), 3.98 (q, *J* = 8.0 Hz, 1H), 3.80 (s, 3H), 3.27 (dd, *J* = 13.7, 5.6 Hz, 1H), 2.95 (s, 6H), 2.89 - 2.85 (m, 4H), 2.85 - 2.75 (m, 4H), 2.75 - 2.67 (m, 1H), 2.22 - 2.03 (m, 2H), 1.77 - 1.67 (m, 1H), 0.57 - 0.42 (m, 4H). : 599.5 $[M+H]^+$	1.12
1044		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.86 (s, 1H), 8.46 - 8.37 (m, 2H), 7.17 (t, *J* = 7.8 Hz, 1H), 6.85 (s, 1H), 6.76 - 6.57 (m, 5H), 6.34 (dd, *J* = 17.0, 1.6 Hz, 1H), 6.23 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.72 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.91 (ddt, *J* = 13.4, 9.6, 5.2 Hz, 1H), 4.07 (td, *J* = 8.0, 5.0 Hz, 1H), 3.98 (q, *J* = 7.9 Hz, 1H), 3.83 (s, 3H), 3.26 (dd, *J* = 13.7, 5.6 Hz, 1H), 3.05 (d, *J* = 11.6 Hz, 2H), 2.95 (s, 6H), 2.78 - 2.68 (m, 6H), 2.68 - 2.53 (m, 4H), 2.37 - 2.27 (m, 1H), 2.22 - 2.03 (m, 4H), 1.71 - 1.61 (m, 3H), 0.51 - 0.38 (m, 4H). : 682.5 $[M+H]^+$	1.14
1045		N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.86 (s, 1H), 8.43 (s, 1H), 8.39 (d, *J* = 1.0 Hz, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 6.87 (s, 1H), 6.75 - 6.71 (m, 2H), 6.68 (d, *J* = 7.4 Hz, 1H), 6.65 - 6.57 (m, 2H), 6.35 (dd, *J* = 17.0, 1.6 Hz, 1H), 6.24 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.73 (dd, *J* = 10.0, 1.6 Hz, 1H), 4.96 - 4.85 (m, 1H), 4.07 (td, *J* = 8.0, 5.0 Hz, 1H), 3.98 (q, *J* = 7.9 Hz, 1H), 3.83 (s, 3H), 3.26 (dd, *J* = 13.6, 5.6 Hz, 1H), 3.08 - 2.95 (m, 4H), 2.94 (s, 6H), 2.87 (d, *J* = 10.8 Hz, 1H), 2.77 - 2.65 (m, 3H), 2.59 - 2.42 (m, 2H), 2.30 (tt, *J* = 11.5, 4.7 Hz, 2H), 2.22 - 2.03 (m, 4H), 2.00 (t, *J* = 10.3 Hz, 1H), 1.66 (qd, *J* = 11.8, 5.9 Hz, 2H), 1.58 - 1.48 (m, 1H), 1.21 (d, *J* = 6.4 Hz, 3H), 0.70 - 0.55 (m, 2H), 0.49 - 0.38 (m, 1H), 0.37 - 0.26 (m, 1H). : 606.5 $[M+H]^+$	1.17

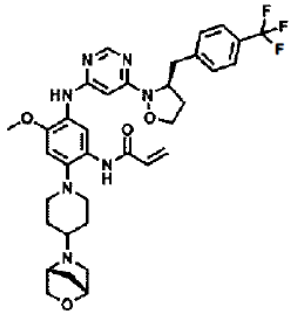
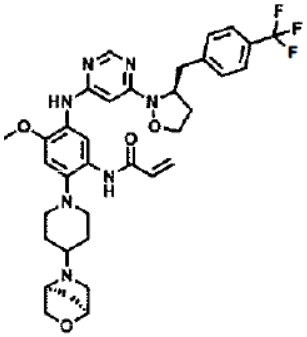
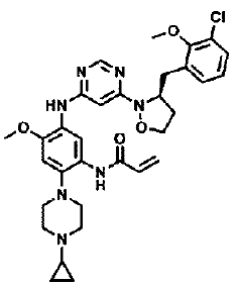
		yl)amino)-4-methoxyphenyl)acrylamide		
1046		N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.86 (s, 1H), 8.44 (s, 1H), 8.40 - 8.37 (m, 1H), 7.16 (t, *J* = 7.8 Hz, 1H), 6.90 (s, 1H), 6.75 - 6.71 (m, 2H), 6.68 (d, *J* = 7.4 Hz, 1H), 6.62 (d, *J* = 2.6 Hz, 1H), 6.59 (d, *J* = 2.6 Hz, 1H), 6.35 (dd, *J* = 16.9, 1.6 Hz, 1H), 6.24 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.72 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.90 (tt, *J* = 9.1, 5.0 Hz, 1H), 4.07 (td, *J* = 8.0, 5.0 Hz, 1H), 3.98 (q, *J* = 7.9 Hz, 1H), 3.82 (s, 3H), 3.26 (dd, *J* = 13.7, 5.6 Hz, 1H), 3.08 - 2.96 (m, 4H), 2.94 (s, 6H), 2.87 (d, *J* = 10.9 Hz, 1H), 2.78 - 2.65 (m, 3H), 2.57 - 2.42 (m, 2H), 2.35 - 2.23 (m, 2H), 2.21 - 2.03 (m, 4H), 2.00 (t, *J* = 10.4 Hz, 1H), 1.73 - 1.58 (m, 2H), 1.57 - 1.48 (m, 1H), 1.22 - 1.10 (m, 3H), 0.70 - 0.54 (m, 2H), 0.40 - 0.38 (m, 1H), 0.37 - 0.26 (m, 1H). ; 606.5 $[M+H]^+$	1.17

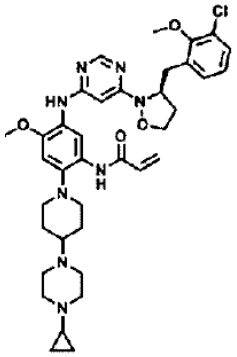
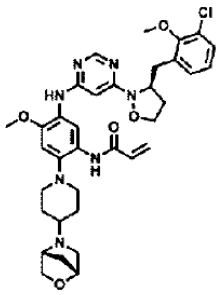
[682]

1047		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.87 (s, 1H), 8.47 (s, 1H), 8.40 (d, J = 1.0 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 6.88 (s, 1H), 6.77 - 6.65 (m, 3H), 6.65 - 6.57 (m, 2H), 6.34 (dd, J = 16.9, 1.5 Hz, 1H), 6.22 (dd, J = 16.9, 10.0 Hz, 1H), 5.72 (dd, J = 10.0, 1.5 Hz, 1H), 4.96 - 4.85 (m, 1H), 4.46 - 4.41 (m, 1H), 4.07 (td, J = 7.9, 5.0 Hz, 2H), 3.98 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.79 - 3.73 (m, 1H), 3.66 (dd, J = 7.9, 1.6 Hz, 1H), 3.26 (dd, J = 13.6, 5.6 Hz, 1H), 3.13 (dd, J = 10.0, 1.8 Hz, 1H), 3.10 - 2.97 (m, 2H), 2.95 (s, 6H), 2.82 - 2.73 (m, 2H), 2.72 - 2.66 (m, 1H), 2.63 - 2.46 (m, 2H), 2.22 - 2.00 (m, 3H), 1.99 - 1.89 (m, 2H), 1.84 - 1.80 (m, 1H), 1.74 - 1.59 (m, 2H). ; 655.5 [M+H]$^+$	1.13
1048		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.87 (s, 1H), 8.47 (s, 1H), 8.40 (d, J = 1.0 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 6.89 (s, 1H), 6.77 - 6.70 (m, 2H), 6.68 (d, J = 7.4 Hz, 1H), 6.65 - 6.57 (m, 2H), 6.34 (dd, J = 16.9, 1.6 Hz, 1H), 6.22 (dd, J = 17.0, 10.0 Hz, 1H), 5.72 (dd, J = 10.0, 1.5 Hz, 1H), 4.96 - 4.85 (m, 1H), 4.44 (t, J = 2.0 Hz, 1H), 4.12 - 4.04 (m, 2H), 3.98 (q, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.76 (s, 1H), 3.66 (dd, J = 7.9, 1.6 Hz, 1H), 3.26 (dd, J = 13.7, 5.6 Hz, 1H), 3.13 (dd, J = 9.9, 1.8 Hz, 1H), 3.02 (dd, J = 12.0, 4.5 Hz, 2H), 2.94 (s, 6H), 2.82 - 2.66 (m, 3H), 2.62 - 2.54 (m, 1H), 2.50 (d, J = 9.9 Hz, 1H), 2.22 - 2.00 (m, 3H), 1.97 - 1.87 (m, 2H), 1.86 - 1.78 (m, 1H), 1.72 - 1.60 (m, 2H). ; 655.5 [M+H]$^+$	1.11
1049		N-(2-(4-cyclopropylpiperazine-1-yl)-4-methoxy-5-((6-((S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.59 (s, 1H), 8.37 (d, J = 5.7 Hz, 1H), 7.54 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 6.88 (s, 1H), 6.78 (s, 1H), 6.59 (s, 1H), 6.39 - 6.23 (m, 2H), 5.75 (dd, J = 9.8, 1.6 Hz, 1H), 4.02 (qd, J = 7.5, 3.9 Hz, 1H), 4.06 (td, J = 8.1, 4.5 Hz, 1H), 3.97 (q, J = 8.2 Hz, 1H), 3.80 (s, 3H), 3.25 (dd, J = 13.8, 6.6 Hz, 1H), 2.93 - 2.71 (m, 9H), 2.29 - 2.19 (m, 1H), 2.09 - 1.99 (m, 1H), 1.75 - 1.60 (m, 1H), 0.55 - 0.42 (m, 4H); 624.48[M+H]$^+$	1.29

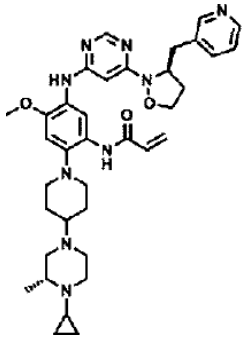
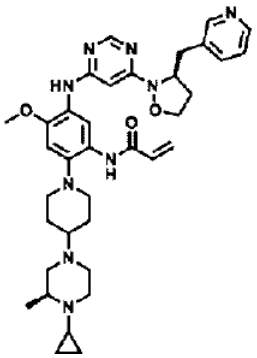
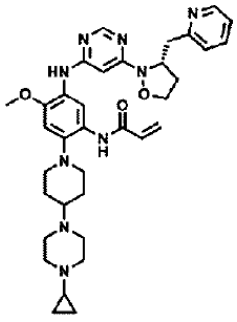
1050		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.44 (s, 1H), 8.35 (s, 1H), 7.54 (d, *J* = 8.1 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 6.86 (s, 1H), 6.73 (s, 1H), 6.50 (s, 1H), 6.38 - 6.10 (m, 2H), 5.73 (dd, *J* = 10.0, 1.3 Hz, 1H), 4.95 - 4.86 (m, 1H), 4.06 (td, *J* = 8.1, 4.5 Hz, 1H), 3.96 (q, *J* = 8.1 Hz, 1H), 3.83 (s, 3H), 3.24 (dd, *J* = 13.8, 6.6 Hz, 1H), 3.08 - 3.01 (m, 2H), 2.89 (dd, *J* = 13.8, 7.7 Hz, 1H), 2.79 - 2.58 (m, 9H), 2.37 - 2.29 (m, 1H), 2.27 - 2.21 (m, 1H), 2.11 - 1.99 (m, 3H), 1.72 - 1.64 (m, 4H), 0.51 - 0.39 (m, 4H); 707.52[M+H]$^+$	1.30

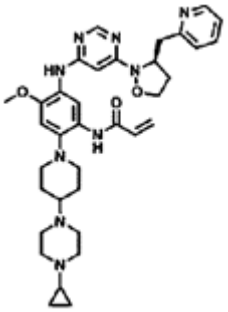
[683]
[684]

1051		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.47 (s, 1H), 8.35 (s, 1H), 7.54 (d, J = 7.9 Hz, 2H), 7.44 (d, J = 7.9 Hz, 2H), 6.89 (d, J = 9.4 Hz, 1H), 6.75 (s, 1H), 6.59 (s, 1H), 6.38 - 6.19 (m, 2H), 5.76 - 5.70 (m, 1H), 4.96 - 4.85 (m, 1H), 4.45 (s, 1H), 4.12 - 4.02 (m, 2H), 3.97 (q, J = 8.0 Hz, 1H), 3.86 - 3.76 (m, 4H), 3.70 - 3.64 (m, 1H), 3.24 (dd, J = 13.8, 6.6 Hz, 1H), 3.20 - 3.12 (m, 1H), 3.07 - 2.99 (m, 2H), 2.89 (dd, J = 13.8, 7.7 Hz, 1H), 2.80 - 2.69 (m, 2H), 2.65 - 2.49 (m, 2H), 2.30 - 2.19 (m, 1H), 2.08 - 2.00 (m, 2H), 2.00 - 1.90 (m, 2H), 1.88 - 1.81 (m, 1H), 1.76 - 1.66 (m, 2H): 680.47[M+H]$^+$	1.25
1052		N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.47 (s, 1H), 8.35 (s, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 6.88 (s, 1H), 6.75 (s, 1H), 6.59 (s, 1H), 6.37 - 6.19 (m, 2H), 5.75 - 5.69 (m, 1H), 4.96 - 4.86 (m, 1H), 4.45 (s, 1H), 4.12 - 4.03 (m, 2H), 3.97 (q, J = 8.1 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 1H), 3.70 - 3.63 (m, 1H), 3.24 (dd, J = 13.8, 6.6 Hz, 1H), 3.19 - 3.11 (m, 1H), 3.06 - 2.98 (m, 2H), 2.89 (dd, J = 13.8, 7.7 Hz, 1H), 2.81 - 2.70 (m, 2H), 2.63 - 2.49 (m, 2H), 2.29 - 2.20 (m, 1H), 2.08 - 1.99 (m, 2H), 1.99 - 1.90 (m, 2H), 1.85 - 1.80 (m, 1H), 1.73 - 1.66 (m, 2H): 680.47[M+H]$^+$	1.25
1053		N-(5-((6-((S)-3-(3-chloro-2-methoxybenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (s, 1H), 8.05 (s, 1H), 7.19 (dd, J = 7.7, 20.0 Hz, 2H), 6.93 (t, J = 7.8 Hz, 1H), 6.81 (s, 1H), 6.42 (dd, J = 10.2, 17.0 Hz, 1H), 6.24 (d, J = 15.2 Hz, 2H), 5.70 (d, J = 10.3 Hz, 1H), 4.02 - 3.96 (m, 1H), 3.83 - 3.73 (m, 7H), 3.07 - 2.98 (m, 1H), 2.87 - 2.76 (m, 9H), 2.15 - 2.06 (m, 1H), 2.06 - 1.97 (m, 1H), 1.80 - 1.74 (m, 1H), 0.82 - 0.77 (m, 1H), 0.51 - 0.45 (m, 2H), 0.45 - 0.39 (m, 2H) ; 620.3[M+H]$^+$	1.2

1054		N-(5-((6-((S)-3-(3-chloro-2-methoxybenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 8.05 (s, 1H), 7.25 - 7.14 (m, 2H), 6.93 (t, J = 7.8 Hz, 1H), 6.80 (s, 1H), 6.43 (dd, J = 10.2, 16.9 Hz, 1H), 6.30 - 6.18 (m, 2H), 5.69 (d, J = 9.9 Hz, 1H), 4.01 - 3.96 (m, 1H), 3.81 - 3.75 (m, 7H), 3.09 - 3.01 (m, 3H), 2.93 - 2.85 (m, 3H), 2.82 - 2.62 (m, 8H), 2.13 - 2.07 (m, 1H), 2.06 - 1.96 (m, 3H), 1.95 - 1.92 (m, 1H), 1.79 - 1.67 (m, 3H), 1.54 - 1.47 (m, 1H), 0.49 - 0.40 (m, 2H), 0.40 - 0.31 (m, 2H) ; 703.3[M+H]$^+$	1.21
1055		N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-methoxybenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.14 (s, 1H), 8.05 (s, 1H), 7.25 - 7.19 (m, 1H), 7.19 - 7.14 (m, 1H), 6.93 (t, J = 7.8 Hz, 1H), 6.81 (s, 1H), 6.42 (dd, J = 10.3, 17.0 Hz, 1H), 6.28 - 6.20 (m, 2H), 5.69 (d, J = 10.2 Hz, 1H), 4.18 - 4.13 (m, 1H), 4.07 - 4.03 (m, 1H), 4.02 - 3.96 (m, 1H), 3.81 - 3.74 (m, 7H), 3.68 - 3.65 (m, 1H), 3.08 - 3.01 (m, 3H), 2.96 - 2.86 (m, 2H), 2.83 - 2.71 (m, 3H), 2.13 - 2.06 (m, 2H), 2.01 - 1.94 (m, 4H), 1.73 - 1.67 (m, 2H), 0.82 - 0.74 (m, 3H) ; 676.3[M+H]$^+$	1.18

[685]

1056		N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.72 (s, 1H), 8.52 (d, J = 2.3 Hz, 2H), 8.46 (dd, J = 4.9, 1.6 Hz, 2H), 8.40 (s, 2H), 8.27 (s, 1H), 7.73 (dt, J = 7.8, 2.0 Hz, 2H), 7.25 - 7.22 (m, 1H), 6.72 (s, 2H), 6.53 (s, 1H), 6.33 - 6.25 (m, 3H), 5.73 (dd, J = 9.5, 2.1 Hz, 2H), 4.87 (qd, J = 7.2, 3.8 Hz, 2H), 3.81 (s, 4H), 3.43 (s, 1H), 3.17 - 3.10 (m, 4H), 3.10 - 2.99 (m, 7H), 2.86 (dd, J = 14.1, 7.1 Hz, 2H), 2.72 (q, J = 11.0, 10.5 Hz, 6H), 2.27 (dtd, J = 12.4, 8.2, 4.3 Hz, 2H), 2.09 (d, J = 12.6 Hz, 4H), 1.77 (qd, J = 12.2, 3.9 Hz, 4H), 1.60 (tt, J = 6.8, 3.9 Hz, 2H), 0.65 (dp, J = 15.3, 5.5, 4.8 Hz, 4H), 0.45 (td, J = 10.6, 9.0, 5.9 Hz, 2H), 0.37 (p, J = 4.8 Hz, 2H).; 654.6[M+H]$^+$	0.87
1057		N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Chloroform-d) δ 8.75 (s, 1H), 8.53 (d, J = 2.2 Hz, 1H), 8.46 (dd, J = 4.9, 1.6 Hz, 2H), 8.41 (s, 1H), 8.28 (d, J = 0.9 Hz, 1H), 7.72 (dt, J = 7.9, 1.9 Hz, 1H), 7.25 - 7.21 (m, 1H), 6.72 (s, 1H), 6.55 (s, 1H), 6.37 - 6.20 (m, 3H), 5.73 (dd, J = 9.7, 1.9 Hz, 1H), 4.87 (dt, J = 11.2, 5.5 Hz, 2H), 3.82 (s, 4H), 3.14 (dd, J = 14.1, 6.7 Hz, 3H), 3.10 - 3.02 (m, 5H), 2.86 (dd, J = 14.0, 7.3 Hz, 2H), 2.78 - 2.63 (m, 5H), 2.63 - 2.50 (m, 3H), 2.45 (dd, J = 12.5, 9.6 Hz, 2H), 2.27 (dtd, J = 12.4, 8.3, 4.4 Hz, 2H), 2.19 - 2.06 (m, 5H), 1.75 (q, J = 11.9 Hz, 3H), 1.60 (dd, J = 6.9, 3.4 Hz, 2H), 1.23 (d, J = 6.3 Hz, 4H), 0.71 - 0.59 (m, 3H), 0.46 (p, J = 6.1 Hz, 1H), 0.36 (d, J = 8.2 Hz, 1H).; 654.6[M+H]$^+$	0.92
1058		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(pyridine-2-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.51 - 8.42 (m, 1H), 8.26 (s, 1H), 8.14 (s, 1H), 7.83 - 7.71 (m, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.29 (dd, J = 5.1, 7.5 Hz, 1H), 6.91 (s, 1H), 6.56 (dd, J = 10.2, 17.0 Hz, 1H), 6.36 (d, J = 18.2 Hz, 2H), 5.81 (d, J = 10.2 Hz, 1H), 4.09 (dd, J = 4.7, 8.2 Hz, 1H), 3.94 - 3.84 (m, 4H), 3.32 - 3.30 (m, 1H), 3.20 - 3.23 (m, 1H), 3.23 - 3.14 (m, 2H), 3.06 - 2.96 (m, 4H), 2.92 - 2.76 (m, 7H), 2.32 - 2.26 (m, 1H), 2.21 - 2.11 (m, 3H), 1.92 - 1.77 (m, 3H), 0.94 - 0.88 (m, 1H), 0.60 - 0.53 (m, 2H), 0.52 - 0.45 (m, 2H) ; 640.4[M+H]$^+$	0.85

1059		N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-2-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide.	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.49 - 8.42 (m, 1H), 8.26 (s, 1H), 8.14 (s, 1H), 7.79 - 7.74 (m, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.31 - 7.27 (m, 1H), 6.91 (s, 1H), 6.55 (dd, J = 10.2, 17.0 Hz, 1H), 6.40 - 6.30 (m, 2H), 5.81 (d, J = 10.3 Hz, 1H), 4.12 - 4.07 (m, 1H), 3.92 - 3.85 (m, 4H), 3.28 - 3.24 (m, 1H), 3.22 - 3.17 (m, 2H), 3.06 - 2.98 (m, 4H), 2.93 - 2.75 (m, 8H), 2.33 - 2.25 (m, 1H), 2.21 - 2.12 (m, 3H), 1.91 - 1.80 (m, 3H), 0.93 - 0.89 (m, 1H), 0.61 - 0.55 (m, 2H), 0.53 - 0.45 (m, 2H) ; 640.4[M+H]$^+$	0.86

[686] **<Experimental Example 1>** Evaluation of Ba/F3 and lung cancer cell proliferation suppression activity

[687] The following experiment was carried out to evaluate the suppression activity of the compounds according to the present invention against proliferation of Ba/F3 and lung cancer cells which express EGFR mutations.

[688] Of the cancer cell lines expressing the EGFR gene, A549 was cultured after adding 10% FBS (HyClone) to DMEM (Invitrogen), and RPMI-1640 (Invitrogen) with 10% FBS was used for the other cancer cells. For the Ba/F3 cells, RPMI-1640 with 10% FBS and 5ng/ml IL-3 (R&D Systems) was used. The transduced Ba/F3 cells were cultured by adding 1ug/ml puromycin (Invitrogen) to the same medium.

[689] 24 hours before treatment with the compounds, 3000 to 5000 cells were distributed into each well of a white clear bottom 96 well plate (Corning). The compounds were diluted in dimethylsulfoxide (dilution ratio 3:1; 12 concentrations total) and injected 0.5ul each for a final concentration of 0.3nM to 50um. As for measurement of live cells, 72 hours after treatment with the compounds, a CellTiter-Glo luminescent cell-viability reagent (Promega) was used to store the cells at room temperature for 10 minutes, followed by measurement of luminescence using a reader (SynergyNeo, Biotek). Each test was repeated three times.

[690] The result was calculated as a cell growth ratio (%) compared to a control. The program GraphPad Prism version 5.0 was used to draw the graphs and calculate the GI_{50} values.

[691] Table 2 below shows the results of proliferation suppression for Ba/F3 cells which express EGFR (HER2) mutations.

[692] [Table 2]

[693]

Example Compound	Ba/F3 cell (GI_{50} (μM))									
	EGFR L858R/ T790M	EGFR Del19/T 790M	EGFR L858R	EGFR Exon20 ins NPH	EGFR Exon20 ins SVD	EGFR Exon20 ins FQEA	EGFR Exon20 ins H	EGFR Exon20 ins ASV	HER2 Exon20 ins YVMA	naive
1	B	B	A	-	-	-	-	-	-	D
2	C	C	B	-	-	-	-	-	-	D
3	C	B	-	B	B	A	C	B	B	D
4	A	A	A	A	A	A	A	A	A	D
5	B	B	A	-	-	-	-	-	-	D
6	A	A	A	A	A	A	A	A	A	D
7	B	A	-	-	-	-	-	-	-	D
8	B	B	-	-	-	-	-	-	-	C
9	A	A	A	A	A	A	A	A	A	D
10	A	A	A	A	A	A	A	A	A	D
12	A	A	A	A	A	A	A	A	A	D
13	A	A	A	A	A	A	A	A	A	D
15	A	A	A	A	A	A	A	A	A	D
26	A	-	-	A	A	-	-	-	A	D
28	A	A	A	A	A	A	A	A	A	C
29	A	A	A	A	A	A	A	A	A	D
30	A	A	A	A	A	A	-	A	A	D
57	A	A	A	A	A	A	-	A	A	D
236	A	A	A	A	A	A	-	A	A	C
237	A	-	-	A	-	-	-	A	-	D
238	A	A	A	A	A	A	-	A	A	C
239	A	A	A	A	A	A	-	A	A	D
240	A	-	-	A	-	-	-	A	-	D
241	A	A	A	A	A	A	-	A	A	C
242	A	B	A	A	A	A	-	A	A	C
249	A	-	-	A	-	-	-	-	-	D
250	A	-	-	A	-	-	-	-	-	D
251	A	-	-	A	-	-	-	-	-	D
252	A	-	-	A	-	-	-	-	-	C
253	A	-	-	A	-	-	-	-	-	C

[694] A: GI_{50} < 50nM; B;50nM ≤ GI_{50} < 500nM;

[695] C: 500nM ≤ GI_{50} < 5000 nM; D: 5000nM ≤ GI_{50}

[696] Additionally, Table 3 below shows the activity of the respective example compounds against the Ba/F3 cell line wherein NPH has been inserted (ins) at Exon20 of EGFR.

[697] [Table 3]

[698]

Example Compound	Ba/F3 (NPH) Activity	Example Compound	Ba/F3 (NPH) Activity	Example Compound	Ba/F3 (NPH) Activity	Example Compound	Ba/F3 (NPH) Activity	Example Compound	Ba/F3 (NPH) Activity	Example Compound	Ba/F3 (NPH) Activity
1		178	A	355	A	532	A	709	A	886	A
2		179	A	356	A	533	A	710		887	A
3	B	180	A	357	A	534	A	711		888	A
4	A	181	A	358	A	535	A	712	A	889	A
5		182	A	359	A	536	A	713	A	890	A
6	A	183	A	360	A	537	A	714	A	891	A
7		184	B	361	A	538	A	715	A	892	A
8		185	A	362	A	539	A	716	A	893	A
9	A	186	A	363	A	540	A	717	A	894	A
10	A	187	A	364	A	541	A	718	A	895	C
11	A	188	A	365	B	542	B	719	A	896	C
12	A	189	A	366		543	A	720	A	897	C
13	A	190	B	367		544	A	721	A	898	C
14		191	A	368		545	A	722	B	899	C
15	A	192	A	369	C	546	A	723	A	900	A
16		193	A	370	A	547	A	724	A	901	A
17		194	A	371	A	548	A	725	A	902	A
18	A	195	A	372	A	549	A	726	A	903	A
19		196	A	373	A	550	B	727	A	904	A
20		197	A	374	A	551	A	728	A	905	A
21		198	A	375	A	552	A	729	A	906	A
22		199	A	376	A	553	A	730	B	907	A
23		200	B	377	B	554	B	731	B	908	A
24	A	201	A	378	A	555	B	732	A	909	A
25	B	202	A	379	A	556	B	733	A	910	A
26	A	203	A	380	A	557	B	734	B	911	A
27	A	204	A	381	A	558	A	735	A	912	A
28	A	205	A	382	A	559	A	736	A	913	A
29	A	206	B	383	A	560	A	737	A	914	A
30	A	207	A	384	A	561	A	738	A	915	B
31	A	208	A	385	A	562	B	739	A	916	A
32		209	A	386	B	563	A	740	B	917	A
33	A	210	A	387	A	564	A	741	A	918	A
34		211	A	388	A	565	A	742	A	919	A
35	B	212	A	389	A	566	B	743	A	920	A
36	A	213	A	390	B	567	A	744	A	921	A
37		214	A	391	B	568	A	745	A	922	A
38	A	215	C	392	A	569	A	746	A	923	A
39	A	216	A	393	B	570	A	747	A	924	A
40	B	217		394	A	571	A	748	A	925	A
41	B	218	B	395	B	572	A	749	A	926	A
42	B	219	B	396	B	573	A	750	A	927	A
43	B	220	B	397	A	574	A	751	A	928	A
44	B	221	B	398	A	575	A	752	A	929	A
45	B	222	B	399	B	576	A	753	A	930	A
46	C	223	B	400	A	577	A	754	B	931	A
47	B	224	C	401	A	578	B	755	A	932	B
48	B	225	B	402	A	579	C	756	A	933	A
49	C	226	C	403	A	580	A	757	A	934	A

[699]

50	B	227	B	404	B	581	A	758	B	935	A
51	C	228	A	405	B	582	A	759	B	936	B
52	A	229	B	406	A	583	A	760	A	937	B
53	A	230	B	407	B	584	A	761	A	938	A
54	A	231	B	408	A	585	A	762	A	939	B
55	A	232	B	409	A	586	A	763	A	940	B
56	A	233	C	410	B	587	B	764	A	941	A
57	A	234	C	411	A	588	B	765	A	942	A
58	A	235	B	412	A	589	A	766	A	943	A
59	A	236	A	413	A	590	A	767	A	944	A
60	A	237	A	414	A	591	A	768	A	945	A
61	A	238	A	415	A	592	A	769	A	946	A
62	A	239	A	416	A	593	A	770	A	947	A
63	A	240	A	417	A	594	A	771	B	948	A
64	A	241	A	418	A	595	A	772	B	949	A
65	A	242	A	419	A	596	A	773	B	950	A
66	A	243	A	420	A	597	A	774	B	951	A
67	B	244	A	421	A	598	A	775	A	952	A
68	A	245	A	422	A	599	A	776	A	953	B
69		246	A	423	A	600	A	777	B	954	A
70	_	247	A	424	A	601	A	778	B	955	A
71	A	248	A	425	A	602	A	779	A	956	C
72	_	249	A	426	A	603	A	780	B	957	A
73	A	250	A	427	A	604	A	781	B	958	A
74	B	251	A	428	A	605	A	782	A	959	A
75	A	252	A	429	A	606	A	783	A	960	B
76	A	253	A	430	A	607	A	784	A	961	A
77	A	254	A	431	A	608	A	785	A	962	A
78	A	255	A	432	A	609	A	786	A	963	A
79	A	256	A	433	A	610	B	787	A	964	A
80	A	257	A	434	A	611	B	788	A	965	A
81	B	258	A	435	B	612	A	789	A	966	C
82	A	259	A	436	B	613	B	790	A	967	C
83	A	260	A	437	B	614	B	791	B	968	C
84	B	261	C	438	A	615	A	792	A	969	A
85	A	262	A	439	A	616	A	793	A	970	A
86	A	263	A	440	A	617	A	794	B	971	A
87	A	264	A	441	B	618	A	795	B	972	A
88	A	265	A	442	A	619	A	796	A	973	B
89	A	266	A	443	A	620	A	797	A	974	C
90	A	267	A	444	B	621	A	798	A	975	C
91	A	268	A	445	A	622	C	799	A	976	C
92	A	269	C	446	A	623	C	800	A	977	C
93	A	270	B	447	A	624	C	801	A	978	C
94	A	271	B	448	A	625	A	802	A	979	A
95	C	272	B	449	A	626	A	803	A	980	A
96	A	273	B	450	A	627	A	804	A	981	A
97	A	274	_	451	A	628	A	805	A	982	A
98	A	275	_	452	A	629	B	806	A	983	A
99	A	276		453	A	630	B	807	A	984	A
100	A	277	A	454	A	631	B	808	B	985	C
101	A	278	A	455	A	632	A	809	A	986	
102	A	279	A	456	A	633	B	810	A	987	C
103	A	280		457	A	634	A	811	A	988	B
104		281		458	A	635	A	812	A	989	B

[700]

105	A	282		459	A	636	A	813	A	990	B
106	A	283	A	460	A	637	A	814	A	991	A
107	A	284	A	461	A	638	A	815	A	992	A
108	A	285	A	462	A	639	A	816	A	993	A
109	A	286	A	463	B	640	A	817	A	994	A
110	A	287		464	A	641	A	818	A	995	A
111	A	288		465	A	642	A	819	A	996	A
112	A	289		466	B	643	A	820	A	997	A
113	A	290		467	A	644	A	821	A	998	A
114	A	291	B	468	A	645	A	822	A	999	A
115	A	292		469	A	646	A	823	A	1000	A
116	C	293		470	A	647	A	824	A	1001	A
117	A	294	B	471	A	648	A	825	A	1002	A
118	C	295	C	472	A	649	A	826	A	1003	A
119	A	296		473	A	650	A	827	A	1004	A
120	C	297	A	474	A	651	A	828	A	1005	A
121	A	298	A	475	A	652	B	829	A	1006	A
122	A	299	A	476	A	653	A	830	A	1007	A
123	A	300	A	477	A	654	B	831	A	1008	A
124	A	301	A	478	A	655	B	832	A	1009	A
125	A	302	B	479	A	656	B	833	A	1010	A
126	A	303	A	480	A	657	A	834	A	1011	A
127	A	304	A	481	A	658	B	835	A	1012	A
128	A	305	A	482	A	659	B	836	A	1013	A
129	C	306	B	483	A	660	C	837	A	1014	A
130	A	307	C	484	B	661	A	838	A	1015	A
131	A	308	C	485	A	662	B	839	A	1016	A
132	B	309	C	486	A	663	B	840	A	1017	A
133	B	310	C	487	A	664	C	841	A	1018	A
134	A	311	C	488	A	665	B	842	A	1019	A
135	A	312	C	489	A	666	B	843	A	1020	A
136	B	313	C	490	B	667	B	844	A	1021	A
137	B	314	C	491	B	668	B	845	A	1022	A
138	A	315	C	492	B	669	A	846	A	1023	
139	A	316	A	493	A	670	A	847	A	1024	A
140	A	317	A	494	A	671	A	848	A	1025	A
141	A	318	A	495	C	672	A	849	A	1026	B
142	A	319	B	496	B	673	A	850	A	1027	A
143	A	320	A	497	A	674	A	851	A	1028	A
144	A	321	B	498	A	675	A	852	A	1029	A
145	A	322	A	499	A	676	A	853	B	1030	A
146	B	323	A	500	A	677	A	854	A	1031	A
147	A	324	A	501	A	678	A	855	A	1032	B
148	A	325	A	502	A	679	B	856	A	1033	A
149	A	326	A	503	A	680	A	857	A	1034	A
150	A	327	B	504	A	681	A	858	A	1035	A
151	B	328	A	505	A	682	A	859	A	1036	A
152	A	329	A	506	A	683	A	860	A	1037	A
153	A	330	A	507	B	684	A	861	B	1038	A
154	A	331	A	508	A	685	A	862	A	1039	A
155	A	332	A	509	B	686	B	863	A	1040	A
156	A	333	A	510	B	687	A	864	A	1041	A
157	A	334	A	511	A	688	A	865	B	1042	A
158	A	335	A	512	A	689	B	866	A	1043	C
159	A	336	A	513	B	690	A	867	A	1044	B

[701]

160	A	337	B	514	B	691	B	868	A	1045	B
161	A	338	B	515	B	692	A	869	A	1046	B
162	A	339	A	516	A	693	A	870	A	1047	B
163	A	340	A	517	A	694		871	A	1048	B
164	A	341	A	518	A	695	B	872	A	1049	C
165	A	342	A	519	A	696		873	A	1050	B
166	A	343	A	520	A	697		874	A	1051	A
167	A	344	A	521	A	698		875	A	1052	A
168	A	345	A	522	B	699		876	A	1053	A
169	A	346	A	523	A	700	A	877	A	1054	A
170	A	347	A	524	A	701	A	878	A	1055	A
171	A	348	A	525	A	702	A	879	A	1056	B
172	A	349	A	526	A	703		880	A	1057	B
173	A	350	A	527	A	704		881	A	1058	C
174	A	351	A	528	A	705		882	A	1059	A
175	A	352	A	529	A	706	A	883	A		
176	A	353	A	530	A	707	A	884	A		
177	A	354	A	531	A	708	A	885	A		

[702] A: GI_{50} < 50nM; B: 50nM ≤ GI_{50} < 500nM;

[703] C: 500nM ≤ GI_{50} < 5000nM; D: 5000nM ≤ GI_{50}

[704] As shown in Table 2 and Table 3 above, the example compounds of the present invention exhibit high suppression activity against EGFR single or double mutations or ERBB2 mutations in the Ba/F3 cell line.

[705] Table 4 below shows the results of evaluating proliferation suppression activity (GI_{50})against the EGFR mutant lung cancer cell lines PC9, PC9GR and H1975.

[706] [Table 4]

[707]

Example Compound	cancer cell (GI_{50}(nM))			
	PC9GR	H1975	PC9	A549
4	20	28	1	>15000
6	32	60	1	>15000
9	4	6	1	>15000
10	10	13	14	>15000
11	7	9	2	>15000
12	5	8	12	>15000
13	64	63	12	>15000
15	6	13	7	>15000
30	6	1	1	-
57	4	1	1	-
236	7	1	1	-
238	4	1	1	-
239	5	1	1	-
241	12	1	1	-
242	23	4	1	-
Poziotinib	20	34	1	>15000
Osimertinib	16	36	7	2414
Lazertinib	14	24	5	4819

[708] In Table 4, it can be seen that the example compounds of the present invention exhibit good proliferation suppression activity against the EGFR mutant lung cancer cell lines PC9, PC9GR and H1975.

[709] FIG. 1 shows experimental data results examining whether or not cancer was suppressed when the example compounds were orally administered to a PDX (Exon20ins V769_D770ins ASV) cell line xenograft in vivo model for 28

days, then observed for 21 days without administration. (Testing consigned to Champions Oncology, Inc.)

[710] Referring to FIG. 1, it can be seen that the example compounds of the present invention reduce tumor size in an animal model, thereby exhibiting effective suppression of cancer.

[711] [Table 5]

[712]

% inhibition of scanMAX Kinase profiling										
Protein \ Example Compound	4	6	9	30	57	236	238	239	241	242
EGFR(E746-A750del)	100	100	100	95	98	89	100	96	100	50
EGFR(G719C)	100	100	100	100	100	100	100	100	100	100
EGFR(G719S)	100	100	100	100	100	100	100	99	99	100
EGFR(L747-E749del, A750P)	97	100	100	100	98	98	91	95	98	99
EGFR(L747-T751del,Sins)	100	100	100	96	100	100	92	93	96	100
EGFR(L858R)	100	100	100	100	100	100	99	100	100	100
EGFR(L858R,T790M)	96	85	96	97	96	98	98	98	98	96
EGFR(L861Q)	100	100	100	100	100	98	98	97	98	100
EGFR(S752-I759del)	100	96	100	99	98	89	91	82	95	100
EGFR(T790M)	99	100	99	100	100	100	100	100	100	100
ERBB2	100	100	100	100	100	100	100	100	100	100
ERBB4	100	100	100	100	100	100	100	100	94	100

[713] Table 5 above shows the results of DiscoverX (eurofin) KINOMEscan (scanMAX platform) kinase profiling testing on compounds 4, 6, 9, 30, 57, 236, 238, 239, 241 and 242. As can be seen in Table 5, high suppression activity was exhibited against the EGFR mutant and ERBB2 and ERBB4. It was confirmed that the above example compounds had high selectivity against EGFR series genes. Accordingly, these can be useful in the treating of cancers wherein this kinase is expressed. In particular, as they have substantially outstanding lung cancer cell line proliferation suppression, they can be useful in the treatment of lung cancer, breast cancer, and brain cancer.

[714] Whereas the present invention has been explained in detail in the above through preferred preparation examples, example compounds and experimental examples, the scope of the present invention is not limited to these specific example compounds and shall be defined by the appended claims. Further, it shall be understood that a person having ordinary skill in the art may make various modifications and changes without departing from the scope of the present invention.

What is claimed is…

[Claim 1] A compound selected from any one of the compounds 1 through 1059 below, or pharmaceutically acceptable salts of the same:

1) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((S)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
2) N-(4-methoxy-2-morpholino-5-((6-((S)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
3) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((S)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
4) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
5) N-(4-methoxy-2-morpholino-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
6) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
7) N-(2-(4-cyclopropylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
8) N-(2-(2-(dimethylamino)ethoxy)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
9) N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
10) N-(4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
11) N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
12) N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
13) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
14) N-(2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
15) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
16) N-(2-(4-acetylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
17) N-(4-methoxy-2-((2-methoxyethyl)(methyl)amino)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
18) N-(4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
19) N-(4-methoxy-2-(2-methyl-1H-imidazole-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
20) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
21) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
22) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
23) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;

24) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
25) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
26) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
27) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
28) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
29) N-(2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
30) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
31) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
32) N-(4-methoxy-2-(5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
33) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
34) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
35) N-(4-methoxy-2-(3-methyl-3,6-diazabicyclo[3.1.1]heptane-6-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
36) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
37) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
38) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
39) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
40) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
41) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
42) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
43) N-(4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-morpholinophenyl)acrylamide;
44) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
45) N-(4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
46) N-(2-(4-cyclopropylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
47) N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
48) N-(4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

49) N-(2-(4-acetylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
50) N-(2-(4-dimethylaminopiperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
51) N-(2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
52) N-(4-methoxy-2-(4-(5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
53) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
54) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
55) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
56) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
57) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
58) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
59) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
60) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
61) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
62) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
63) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
64) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
65) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
66) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
67) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
68) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-

difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
69) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
70) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
71) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
72) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
73) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
74) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
75) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
76) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
77) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
78) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
79) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
80) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
81) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
82) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
83) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
84) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
85) N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
86) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
87) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-

methoxyphenyl)acrylamide;
88) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
89) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
90) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
91) N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
92) N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
93) N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
94) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
95) N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
96) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
97) N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
98) N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
99) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
100) N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
101) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
102) N-(4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
103) N-(2-(4-(2-oxa-6-azaspiro[3.3]heptane-6-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
104) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(5-ethylhexahydropyrrolo[3,4-c]pyrrole-2(1H)-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
105) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aS)-tetrahydro-1H-puro[3,4-c]pyrrole-5(3H)-yl)piperidine-

1-yl)phenyl)acrylamide;
106) N-(2-(4-(4-cyclopropyl-3,3-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
107) N-(2-(4-((2R,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
108) N-(2-(4-((2S,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
109) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
110) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
111) N-(2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
112) N-(2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
113) N-(2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
114) N-(2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
115) N-(2-(4-((1R,5S)-8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
116) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-ethoxyphenyl)acrylamide;
117) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)-(E)-4-(dimethylamino)but-2-enamide;
118) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
119) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-(((R)-1,1,1-trifluoropropane-2-yl)oxy)phenyl)acrylamide;
120) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)-2-fluoroacrylamide;
121) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
122) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

123) N-(2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
124) N-(2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
125) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
126) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
127) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
128) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
129) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
130) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
131) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
132) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
133) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
134) N-(2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
135) N-(2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
136) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
137) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
138) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
139) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
140) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-

methoxyphenyl)acrylamide;
141) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
142) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
143) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
144) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
145) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
146) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
147) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(thiophene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
148) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
149) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
150) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
151) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
152) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
153) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
154) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
155) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
156) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
157) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
158) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
159) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-

yl)amino)-2-(4-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
160) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
161) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
162) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
163) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
164) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
165) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
166) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
167) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
168) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
169) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
170) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
171) N-(2-(4-((2S,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
172) N-(2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
173) N-(2-(4-((2R,5S)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
174) N-(2-(4-((2S,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
175) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
176) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-

methoxyphenyl)acrylamide;
177) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
178) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2R,5R)-4-cyclopropyl-2,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
179) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
180) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
181) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropyl-3,3-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
182) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
183) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
184) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
185) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
186) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
187) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
188) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
189) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
190) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
191) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
192) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
193) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
194) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
195) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;

196) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
197) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
198) N-(4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
199) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
200) N-(4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
201) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
202) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
203) N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
204) N-(2-(4-(4-(cyclopropylmethyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
205) N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
206) N-(2-(4-(4-cyclopentylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
207) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
208) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
209) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
210) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
211) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
212) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
213) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
214) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-

methoxyphenyl)acrylamide;
215) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
216) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
217) N-(2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
218) N-(4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
219) N-(2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
220) N-(2-(4-isopropylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
221) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
222) N-(2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
223) N-(4-methoxy-2-((2-methoxyethyl)(methyl)amino)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
224) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
225) N-(2-(4-cyclopentylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
226) N-(2-(4-cyclopentylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
227) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
228) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
229) N-(4-methoxy-2-(4-((2-methoxyethyl)(methyl)amino)piperidine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
230) N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
231) N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
232) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
233) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
234) N-(4-methoxy-2-(4-((1R,4R)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
235) N-(4-methoxy-5-((6-((R)-3-(6-methylpyridine-3-yl)isoxazolidine-2-

yl)pyrimidine-4-yl)amino)-2-(4-morpholino-[1,4'-bipiperidine]-1'-yl)phenyl)acrylamide;
236) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
237) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
238) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
239) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
240) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
241) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
242) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
243) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
244) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
245) N-(2-(4-(dimethylamino)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
246) N-(2-(4-ethylpiperazine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
247) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
248) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
249) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(3-ethyl-3,6-diazabicyclo[3.1.1]heptane-6-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
250) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
251) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
252) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(6-ethyl-3,6-diazabicyclo[3.1.1]heptane-3-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
253) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-4-(dimethylamino)-1,4'-bipiperidine-1'-yl)-4-methoxyphenyl)acrylamide;
254) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

255) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
256) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
257) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
258) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
259) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
260) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)phenyl)acrylamide;
261) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-(3-methyl-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
262) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
263) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
264) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
265) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
266) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
267) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
268) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
269) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-methyl-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
270) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-methyl-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
271) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
272) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
273) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
274) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

4-methoxy-2-(4-(4-methyl-3-oxopiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
275) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1-isopropylpiperidine-4-yl)amino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
276) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2-(dimethylamino)ethyl)(methyl)amino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
277) N-(2-(4-(cyclopropylmethyl)piperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
278) N-(2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
279) N-(2-(4-cyclopentylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
280) N-(2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
281) N-(2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
282) N-(4-methoxy-2-(4-methyl-1H-imidazole-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
283) N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
284) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
285) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
286) N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
287) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
288) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
289) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
290) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
291) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
292) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
293) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
294) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
295) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
296) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
297) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
298) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-

2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
299) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
300) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-propylpiperazine-1-yl)phenyl)acrylamide;
301) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
302) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
303) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
304) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
305) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-(1,4'-bipiperidine)-1'-yl)-4-methoxyphenyl)acrylamide;
306) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
307) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
308) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
309) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
310) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
311) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
312) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
313) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
314) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
315) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
316) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
317) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
318) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
319) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-

yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
320) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
321) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
322) N-(2-(4-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
323) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
324) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
325) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
326) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
327) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
328) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
329) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
330) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(2-methyl-1H-imidazole-1-yl)phenyl)acrylamide;
331) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
332) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
333) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
334) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
335) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
336) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
337) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-2-methylmorpholino)phenyl)acrylamide;
338) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-2-methylmorpholino)phenyl)acrylamide;
339) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;

340) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
341) N-(2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
342) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
343) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
344) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
345) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide;
346) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
347) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
348) N-(2-(4-cyclopentylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
349) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
350) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
351) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
352) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
353) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
354) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
355) N-(2-(4-(6-azaspiro[2.5]octan-6-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
356) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
357) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
358) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropyl-1,4-diazepane-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
359) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
360) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;

361) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
362) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
363) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
364) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
365) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
366) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
367) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
368) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
369) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
370) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((3S,5R)-4-ethyl-3,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
371) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
372) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
373) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
374) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
375) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
376) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
377) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(5-methyl-1H-imidazole-1-yl)phenyl)acrylamide;
378) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
379) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)phenyl)acrylamide;
380) N-(2-(4-(cyclopropylmethyl)piperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
381) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
382) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
383) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
384) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
385) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
386) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methyl-1H-imidazole-1-yl)phenyl)acrylamide;
387) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((2-methoxyethyl)(methyl)amino)piperidine-1-yl)phenyl)acrylamide;
388) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-3-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
389) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
390) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-hydroxypiperidine-1-yl)-4-methoxyphenyl)acrylamide;
391) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
392) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
393) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
394) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
395) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
396) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
397) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)-(E)-4-(dimethylamino)but-2-enamide;
398) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
399) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
400) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
401) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
402) N-(1-(2-acrylamido-4-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-5-methoxyphenyl)piperidine-4-yl)-N-(1-isopropylpiperidine-4-yl)acrylamide;
403) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
404) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
405) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-

yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
406) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
407) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
408) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
409) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
410) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
411) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
412) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
413) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
414) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
415) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
416) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
417) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
418) N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
419) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
420) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
421) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
422) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2-(dimethylamino)ethyl)(methyl)amino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
423) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
424) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
425) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

426) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholino-[1,4'-bipiperidine]-1'-yl)phenyl)acrylamide;
427) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
428) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
429) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
430) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
431) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
432) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
433) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
434) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
435) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
436) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
437) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
438) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
439) N-(4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
440) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
441) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
442) N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
443) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
444) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
445) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
446) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-

yl)piperidine-1-yl)phenyl)acrylamide;
447) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
448) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
449) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
450) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
451) N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
452) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
453) N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
454) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
455) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
456) N-(5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
457) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
458) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
459) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
460) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
461) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
462) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
463) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
464) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
465) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
466) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
467) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-

methoxy-2-morpholinophenyl)acrylamide;
468) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
469) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
470) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
471) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
472) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
473) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((1R,4R)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)phenyl)acrylamide;
474) N-(2-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
475) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
476) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
477) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)-[1,4'-bipiperidine]-1'-yl)phenyl)acrylamide;
478) N-(5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
479) N-(2-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)-5-((6-((R)-3-(2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
480) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
481) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
482) N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
483) N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
484) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
485) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
486) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
487) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
488) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

489) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
490) N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
491) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
492) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
493) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
494) N-(5-((6-((R)-3-(3-cyanophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
495) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(3-methoxy-3-methylbutoxy)phenyl)acrylamide;
496) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(3-methoxy-3-methylbutoxy)phenyl)-(E)-4-(dimethylamino)but-2-enamide;
497) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
498) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
499) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
500) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
501) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
502) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
503) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
504) N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
505) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
506) N-(4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
507) N-(4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
508) N-(5-((6-((R)-3-(3-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-

(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
509) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
510) N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
511) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
512) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
513) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
514) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
515) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
516) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
517) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
518) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
519) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
520) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
521) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
522) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
523) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
524) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
525) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
526) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
527) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methyl-1H-imidazole-1-yl)phenyl)acrylamide;
528) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
529) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-

yl)phenyl)acrylamide;
530) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
531) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
532) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
533) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-fluorophenyl)acrylamide;
534) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methylphenyl)acrylamide;
535) N-(4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
536) N-(4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(naphthalene-1-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
537) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
538) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
539) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
540) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
541) N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)piperidine-1-yl)phenyl)acrylamide;
542) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(3-methyl-3,6-diazabicyclo[3.1.1]heptane-6-yl)phenyl)acrylamide;
543) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
544) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
545) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
546) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
547) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
548) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
549) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-

4-yl)amino)-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
550) N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
551) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
552) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
553) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
554) N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
555) N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
556) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
557) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
558) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
559) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
560) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
561) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)phenyl)acrylamide;
562) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide;
563) N-(2-(4-cyclopentylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
564) N-(2-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
565) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
566) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
567) N-(2-(4-(cyclopropylmethyl)piperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
568) N-(2-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
569) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-

methoxyphenyl)acrylamide;
570) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
571) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
572) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
573) N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
574) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
575) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
576) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
577) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
578) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
579) N-(5-((6-((R)-3-(3,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
580) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
581) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
582) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-propylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
583) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
584) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
585) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
586) N-(5-((6-((R)-3-(3-chloro-2-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
587) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(3-(4-cyclopropylpiperazine-1-yl)azetidine-1-yl)-4-methoxyphenyl)acrylamide;
588) N-(2-(3-(4-cyclopropylpiperazine-1-yl)azetidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
589) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
590) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;

591) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-hydroxypiperidine-1-yl)-4-methoxyphenyl)acrylamide;
592) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
593) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
594) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
595) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
596) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
597) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
598) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
599) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
600) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
601) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
602) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
603) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
604) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
605) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
606) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
607) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
608) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
609) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
610) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-

methoxyphenyl)acrylamide;
611) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
612) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
613) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2-(dimethylamino)ethyl)(methyl)amino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
614) N-(5-((6-((R)-3-(2,3-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholino-[1,4'-bipiperidine]-1'-yl)phenyl)acrylamide;
615) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
616) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
617) N-(5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
618) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
619) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
620) N-(4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
621) N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
622) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
623) N-(4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
624) N-(4-methoxy-2-((S)-3-morpholinopyrolidine-1-yl)-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
625) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-((dimethylamino)methyl)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
626) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-((dimethylamino)methyl)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
627) N-(5-((6-((R)-3-(3-chloro-5-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
628) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
629) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
630) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
631) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
632) N-(4-methoxy-2-(4-morpholinopiperidine-1-yl)-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;

633) N-(3-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-5-(4-methylpiperazine-1-yl)phenyl)acrylamide;
634) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
635) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
636) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
637) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
638) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
639) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
640) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
641) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
642) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
643) N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
644) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
645) N-(4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
646) N-(4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
647) N-(2-(4-(dimethylamino)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
648) N-(2-(4-ethylpiperazine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
649) N-(5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
650) N-(5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
651) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
652) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;

653) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
654) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
655) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(3-ethynylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
656) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxy-5-((6-((R)-3-(2,3,4-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
657) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-2-methylmorpholino)phenyl)acrylamide;
658) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2S,6S)-2,6-dimethylmorpholino)-4-methoxyphenyl)acrylamide;
659) N-(4-methoxy-2-((S)-2-methylmorpholino)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
660) N-(2-((2S,6S)-2,6-dimethylmorpholino)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
661) N-(5-((6-((R)-3-(2-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
662) N-(2-((S)-3,4-dimethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
663) N-(4-methoxy-2-((R)-2-methylmorpholino)-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
664) N-(2-((2S,6R)-2,6-dimethylmorpholino)-4-methoxy-5-((6-((R)-3-(naphthalene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
665) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
666) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-2-methylmorpholino)phenyl)acrylamide;
667) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2S,6R)-2,6-dimethylmorpholino)-4-methoxyphenyl)acrylamide;
668) N-(5-((6-((R)-3-(3-chloro-2,4-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
669) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
670) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
671) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
672) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
673) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
674) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((1R,4R)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-

yl)phenyl)acrylamide;
675) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
676) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
677) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
678) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
679) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
680) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
681) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
682) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
683) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
684) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)phenyl)acrylamide;
685) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide;
686) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
687) N-(2-(4-(cyclopropylmethyl)piperazine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
688) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
689) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
690) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
691) N-(5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
692) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
693) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
694) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-

methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
695) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
696) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
697) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
698) N-(2-(4-ethylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
699) N-(2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
700) N-(2-(4-(6-azaspiro[2.5]octan-6-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
701) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
702) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
703) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
704) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
705) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
706) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
707) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
708) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
709) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
710) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
711) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
712) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
713) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(3-(dimethylamino)azetidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

714) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
715) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
716) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
717) N-(2-(4-(4-cyclopropyl-1,4-diazepane-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
718) N-(2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
719) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
720) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
721) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
722) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methyl-2-oxopiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
723) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
724) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
725) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
726) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
727) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
728) N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
729) N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
730) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
731) N-(2-(4-(dimethylamino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
732) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
733) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
734) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-

methoxy-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
735) N-(2-(4-((2-(dimethylamino)ethyl)(methyl)amino)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
736) N-(4-methoxy-2-(4-((2-methoxyethyl)(methyl)amino)piperidine-1-yl)-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
737) N-(2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
738) N-(2-(4-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
739) N-(2-(4-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
740) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
741) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
742) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
743) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
744) N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
745) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
746) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
747) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
748) N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-(3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
749) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
750) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
751) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
752) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6S)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
753) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
754) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

4-methoxy-2-(4-(piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
755) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
756) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
757) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
758) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
759) N-(2-(4-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
760) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
761) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-2,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
762) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-2,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
763) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
764) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
765) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
766) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
767) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
768) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
769) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
770) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
771) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
772) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
773) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
774) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichloro-2-

fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
775) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
776) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
777) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
778) N-(4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-morpholinopyrolidine-1-yl)phenyl)acrylamide;
779) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
780) N-(2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
781) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxy-5-((6-((R)-3-(3-methoxyphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
782) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
783) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
784) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
785) N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
786) N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
787) N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-phenylisoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
788) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
789) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
790) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
791) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
792) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
793) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
794) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
795) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
796) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
797) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

798) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
799) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
800) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
801) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
802) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
803) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
804) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
805) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
806) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
807) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
808) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
809) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
810) N-(2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
811) N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
812) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
813) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
814) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
815) N-(2-(4-(4-acetylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
816) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

817) N-(2-(4,4-difluoro-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
818) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
819) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
820) N-(2-(4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
821) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
822) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
823) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
824) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
825) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
826) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
827) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((3S,5R)-4-ethyl-3,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
828) N-(2-(4-(6-azaspiro[2.5]octan-6-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
829) N-(2-(4-(4-cyclopropyl-1,4-diazepane-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
830) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
831) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
832) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
833) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
834) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
835) N-(2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
836) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
837) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-

yl)phenyl)acrylamide;
838) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
839) N-(2-((S)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
840) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
841) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((3S,5R)-4-ethyl-3,5-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
842) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-3-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
843) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-3-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
844) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
845) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
846) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
847) N-(2-(4-ethylpiperazine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
848) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
849) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
850) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
851) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
852) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(hexahydropyrrolo[1,2-a]pyrazine-2(1H)-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
853) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
854) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
855) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
856) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
857) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)phenyl)acrylamide;
858) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-

yl)-4-methoxyphenyl)acrylamide;
859) N-(5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
860) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
861) N-(5-((6-((R)-3-(3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(2-methyl-1H-imidazole-1-yl)phenyl)acrylamide;
862) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
863) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(4-chloro-3-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
864) N-(2-(4-(dimethylamino)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
865) N-(5-((6-((R)-3-(3,4-dichloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
866) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
867) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
868) N-(5-((6-((R)-3-(4-chlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
869) N-(5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
870) N-(2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-5-((6-((R)-3-(4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
871) N-(2-(4-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
872) N-(2-(4-(6-azaspiro[2.5]octan-6-yl)piperidine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
873) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
874) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
875) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
876) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;

877) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)piperidine-1-yl)phenyl)acrylamide;
878) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((3S,5R)-4-ethyl-3,5-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
879) N-(2-((S)-4-cyclopropyl-2-methylpiperazine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
880) N-(2-((R)-4-cyclopropyl-2-methylpiperazine-1-yl)-5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
881) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
882) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
883) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
884) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
885) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-2,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
886) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-2,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
887) N-(2-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
888) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((S)-2-methylmorpholino)phenyl)acrylamide;
889) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((R)-2-methylmorpholino)phenyl)acrylamide;
890) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
891) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
892) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
893) N-(5-((6-((R)-3-(2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
894) N-(2-(4-(4-(sec-butyl)piperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
895) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
896) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
897) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
898) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

4-methoxy-2-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
899) N-(5-((6-((S)-3-(2,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrole-5(1H)-yl)phenyl)acrylamide;
900) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
901) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3,4-dimethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
902) N-(2-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
903) N-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
904) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
905) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
906) N-(5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
907) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((R)-3-(3-chloro-4-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
908) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
909) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
910) N-(2-(4-((S)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
911) N-(5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
912) N-(2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-5-((6-((R)-3-(2-fluoro-3-methylphenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
913) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
914) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-3-(dimethylamino)pyrolidine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
915) N-(5-((6-((R)-3-(3-chloro-2-fluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)-[1,4'-bipiperidine]-1'-yl)-4-methoxyphenyl)acrylamide;
916) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
917) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-

2-((R)-3,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
918) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-2,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
919) N-(5-((6-((R)-3-(3,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((S)-2,4-dimethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
920) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
921) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
922) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-ethylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
923) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
924) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
925) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
926) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
927) N-(5-((6-((R)-3-(2,3-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
928) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxy-5-((6-((R)-3-(thiophene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
929) N-(4-methoxy-2-(4-methylpiperazine-1-yl)-5-((6-((R)-3-(thiophene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
930) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(thiophene-2-yl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
931) N-(5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-(oxetane-3-yl)piperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
932) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((R)-3-(3,4-dichlorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
933) N-(5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
934) N-(5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
935) N-(5-((6-((R)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
936) N-(5-((6-((S)-3-(2-chloro-3,6-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
937) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(2,3,6-trifluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
938) N-(5-((6-((R)-3-(3-chloro-2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;

939) N-(5-((6-((R)-3-(3-chloro-2,5-difluorophenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
940) N-(2-(4-cyclopropylpiperazine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
941) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
942) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
943) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
944) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(3-(trifluoromethyl)phenyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
945) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
946) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
947) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
948) N-(2-(4-acetylpiperazine-1-yl)-5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
949) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
950) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)-4-methoxyphenyl)acrylamide;
951) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(dimethylamino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
952) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
953) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-((2-methoxyethyl)(methyl)amino)phenyl)acrylamide;
954) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-isopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
955) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
956) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
957) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxyphenyl)acrylamide;
958) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(oxetane-3-yl)piperazine-1-yl)phenyl)acrylamide;
959) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(cyclopropylmethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
960) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(2-methyl-1H-imidazole-1-yl)phenyl)acrylamide;
961) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
962) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((1S,4S)-2-

oxa-5-azabicyclo[2.2.1]heptane-5-yl)-4-methoxyphenyl)acrylamide;
963) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(4-methylpiperazine-1-yl)piperidine-1-yl)phenyl)acrylamide;
964) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
965) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
966) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-morpholinophenyl)acrylamide;
967) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(cyclopropylmethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
968) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
969) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(5-methyl-2,5-diazabicyclo[2.2.1]heptane-2-yl)phenyl)acrylamide;
970) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide;
971) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)phenyl)acrylamide;
972) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopentylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
973) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
974) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(1-methylpiperidine-4-yl)piperazine-1-yl)phenyl)acrylamide;
975) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-(tetrahydro-2H-pyran-4-yl)piperazine-1-yl)phenyl)acrylamide;
976) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(dimethylamino)ethyl)piperazine-1-yl)-4-methoxyphenyl)acrylamide;
977) N-(5-((6-((R)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopentylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
978) N-(5-((6-((S)-3-benzylisoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(2-(diethylamino)ethoxy)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
979) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
980) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
981) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
982) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
983) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
984) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((R)-3-(dimethylamino)pyrolidine-1-yl)-4-methoxyphenyl)acrylamide;
985) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
986) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-

yl)amino)phenyl)acrylamide;
987) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
988) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
989) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
990) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
991) N-(5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
992) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
993) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
994) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
995) N-(2-(4-((1R,5S)-8-cyclopropyl-3,8-diazabicyclo[3.2.1]octan-3-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
996) N-(5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-morpholinopiperidine-1-yl)phenyl)acrylamide;
997) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
998) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
999) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1000) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1001) N-(5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-methylpiperazine-1-yl)phenyl)acrylamide;
1002) N-(2-((R)-3-(dimethylamino)pyrolidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1003) N-(2-(4-ethylpiperazine-1-yl)-5-((6-(S)-(3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1004) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;

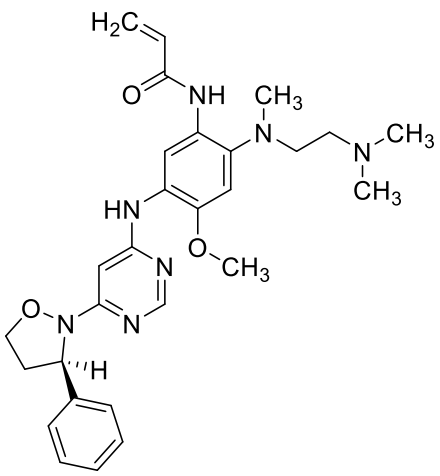
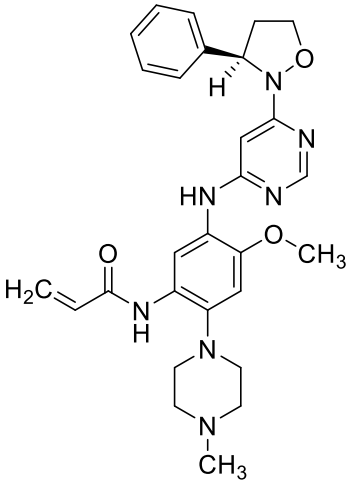
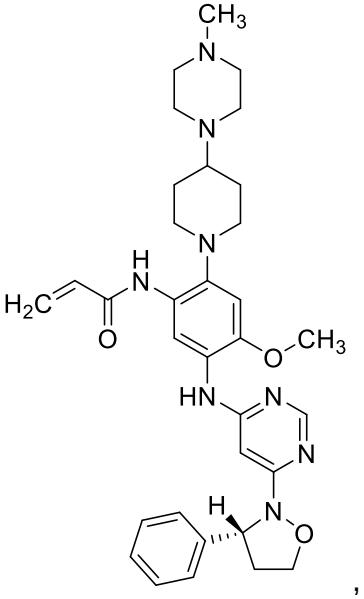
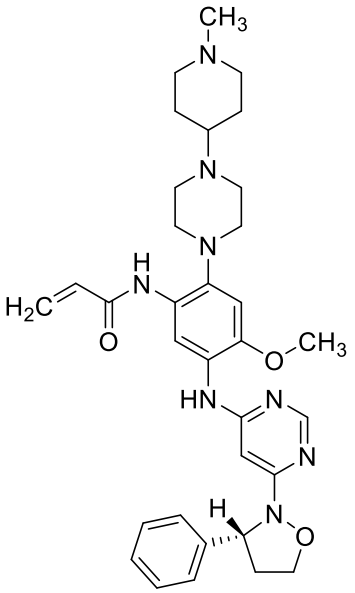
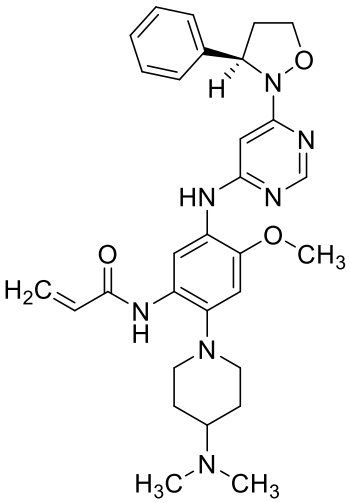
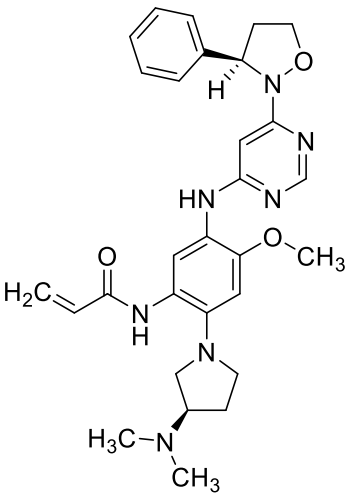
1005) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1006) N-(5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
1007) N-(5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1008) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-ethylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
1009) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1010) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((2S,6R)-2,6-dimethylmorpholino)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1011) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((R)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
1012) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1013) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxy-2-(4-((S)-2-methylmorpholino)piperidine-1-yl)phenyl)acrylamide;
1014) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1015) N-(5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-isopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1016) N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
1017) N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
1018) N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1019) N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1020) N-(5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1021) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1022) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1023) N-(2-(4-(4-cyclobutylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-

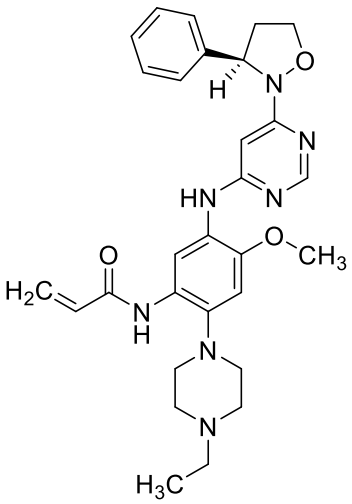
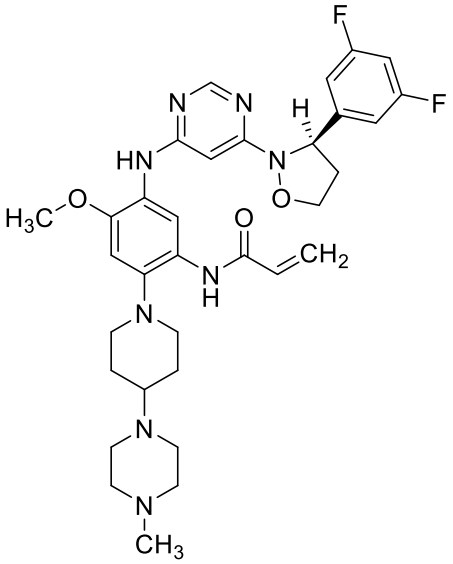
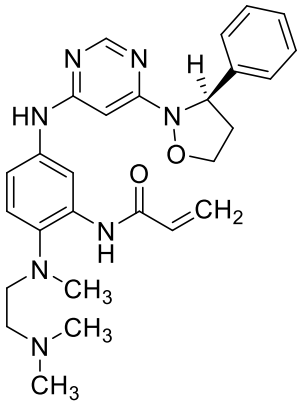
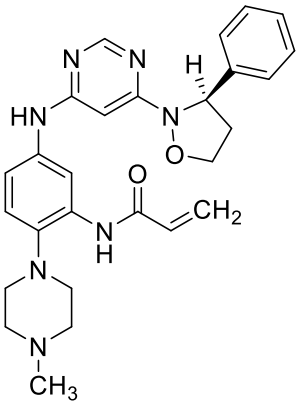
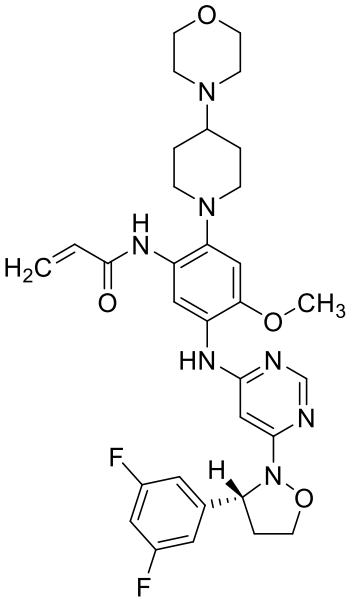
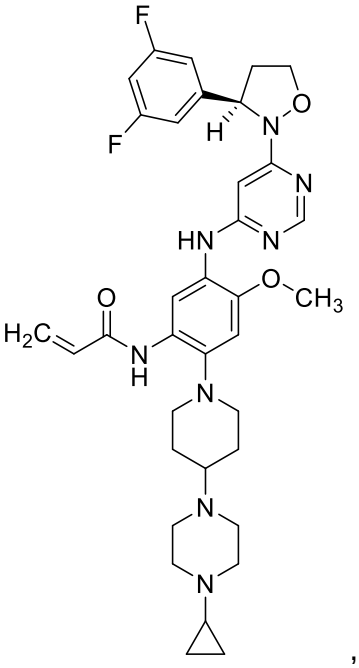
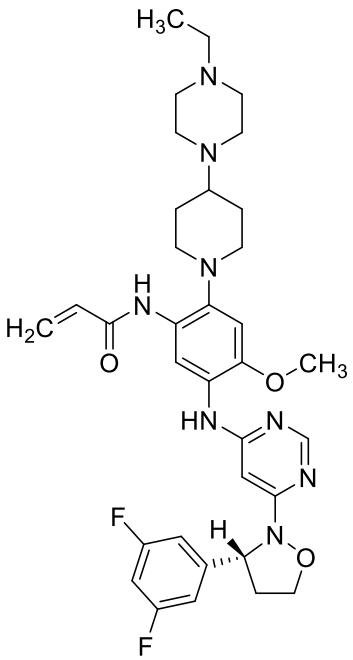
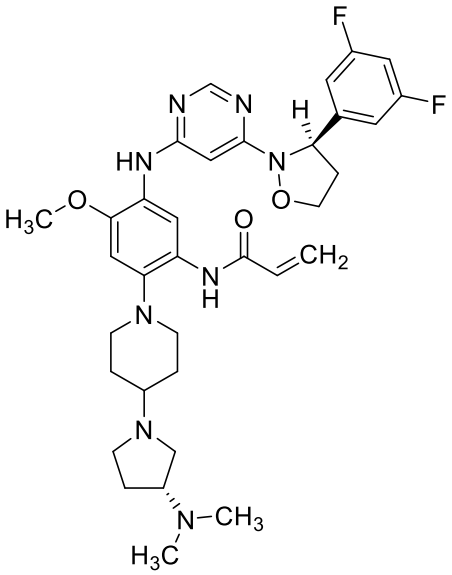
dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1024) N-(2-(4-(4-allylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(2,3-dichlorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1025) N-(5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1026) N-(5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
1027) N-(5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1028) N-(5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1029) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1030) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1031) N-(5-((6-((S)-3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-((2-(dimethylamino)ethyl)(methyl)amino)-4-methoxyphenyl)acrylamide;
1032) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-(S)-(3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1033) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1034) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1035) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3,5-difluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1036) N-(5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1037) N-(5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1038) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1039) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1040) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-fluoro-2-methylbenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;

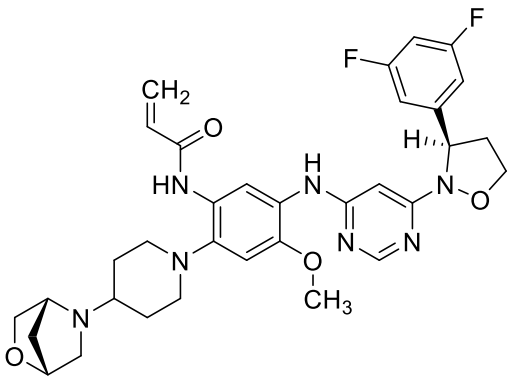
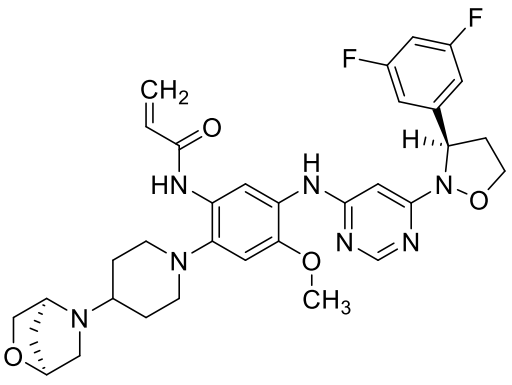
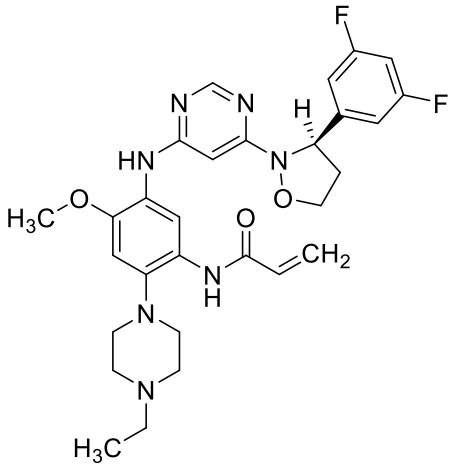
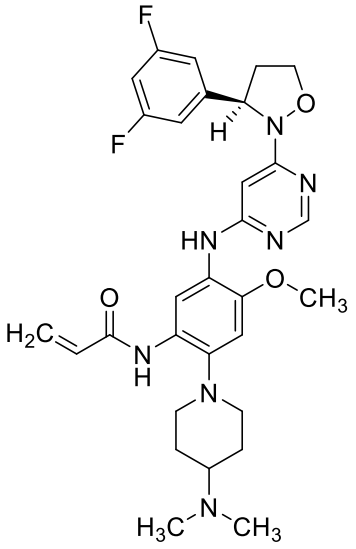
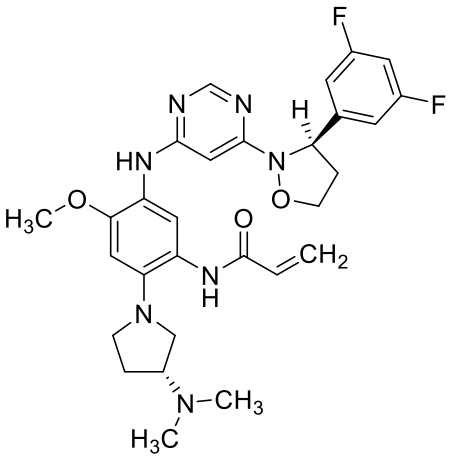
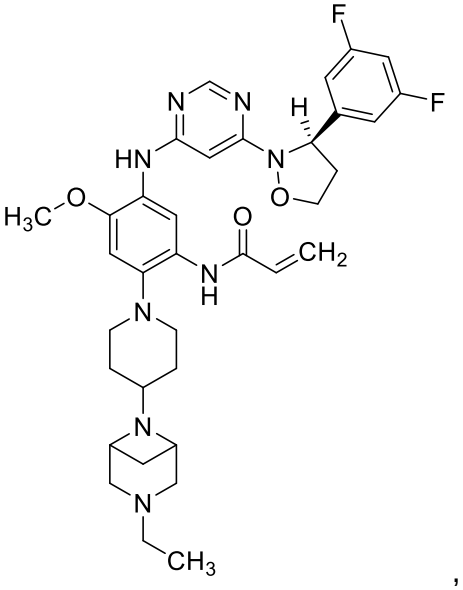
1041) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1042) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(2-chloro-3-fluorobenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1043) N-(2-(4-cyclopropylpiperazine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1044) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1045) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1046) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1047) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1048) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-(dimethylamino)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1049) N-(2-(4-cyclopropylpiperazine-1-yl)-4-methoxy-5-((6-((S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1050) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1051) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1052) N-(2-(4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(4-(trifluoromethyl)benzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1053) N-(5-((6-((S)-3-(3-chloro-2-methoxybenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-cyclopropylpiperazine-1-yl)-4-methoxyphenyl)acrylamide;
1054) N-(5-((6-((S)-3-(3-chloro-2-methoxybenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxyphenyl)acrylamide;
1055) N-(2-(4-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-yl)piperidine-1-yl)-5-((6-((S)-3-(3-chloro-2-methoxybenzyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)-4-methoxyphenyl)acrylamide;
1056) N-(2-(4-((R)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1057) N-(2-(4-((S)-4-cyclopropyl-3-methylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-3-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide;
1058) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((R)-3-(pyridine-2-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-

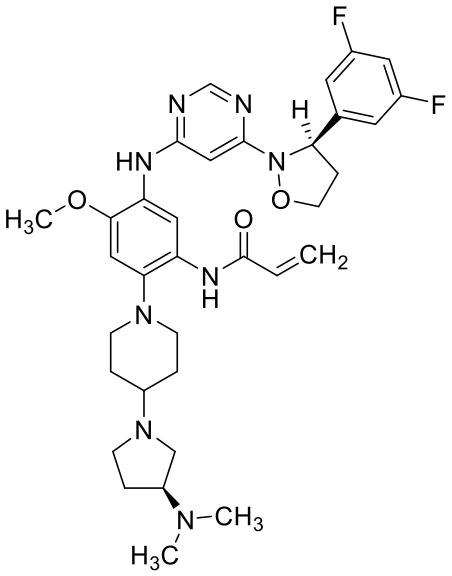
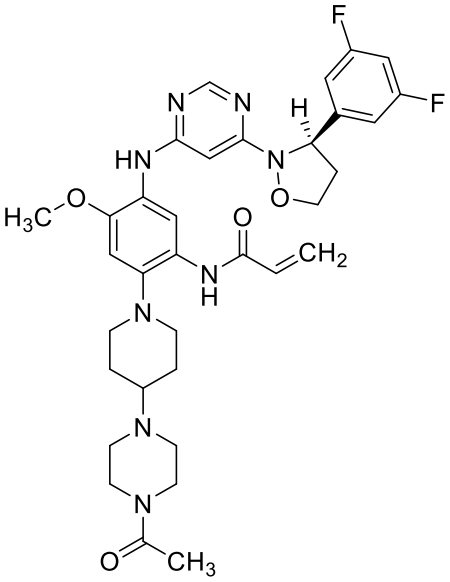
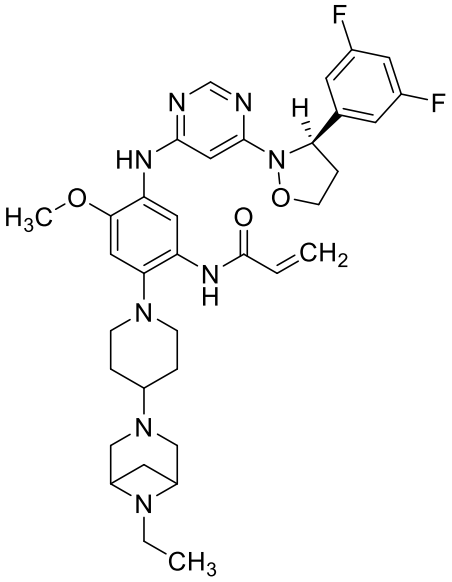
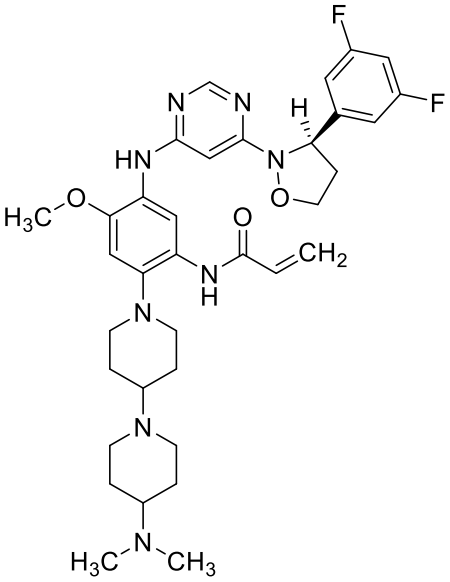
yl)amino)phenyl)acrylamide;
1059) N-(2-(4-(4-cyclopropylpiperazine-1-yl)piperidine-1-yl)-4-methoxy-5-((6-((S)-3-(pyridine-2-ylmethyl)isoxazolidine-2-yl)pyrimidine-4-yl)amino)phenyl)acrylamide.

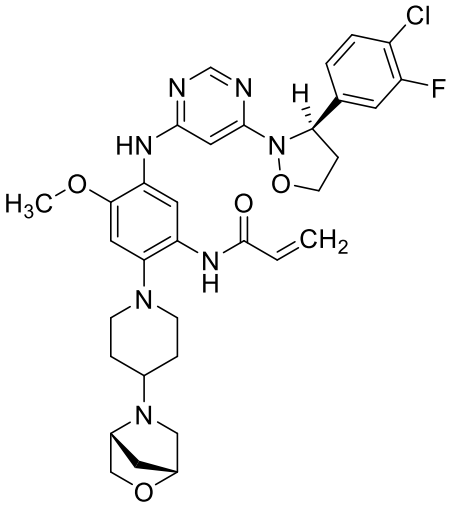
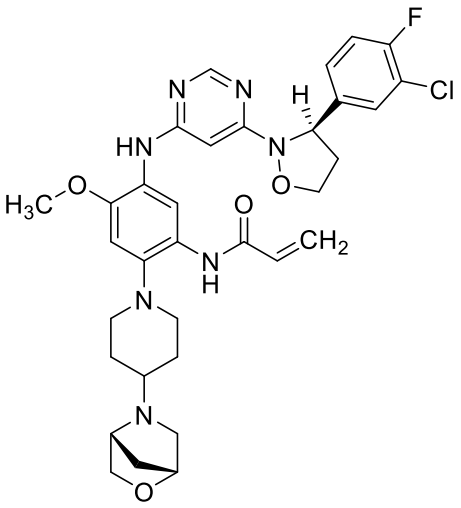
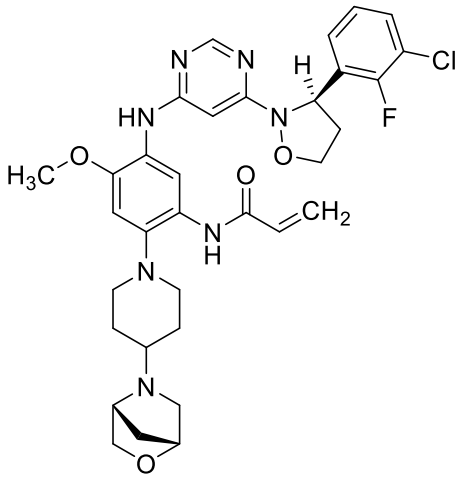
[Claim 2] A compound of claim 1 selected from the group consisting of:


,

,

,

,

,

,

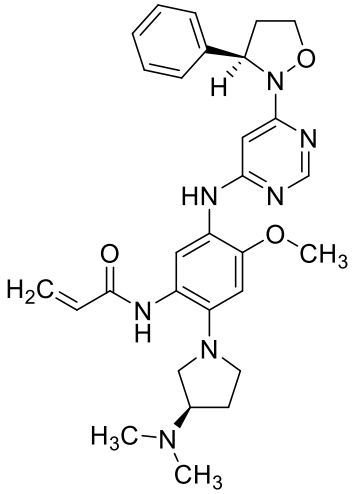
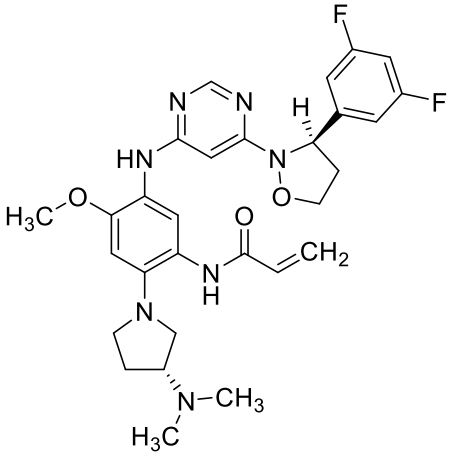

,

,

,

,

,

,

,

,


,

,

,

,

,

,

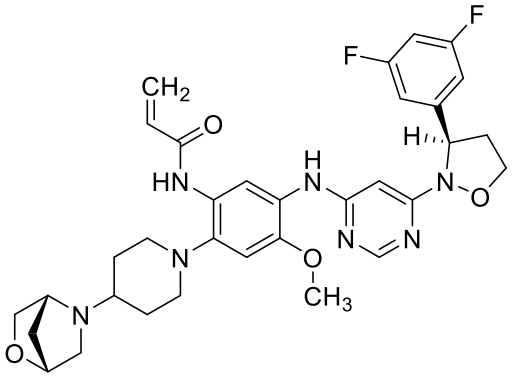
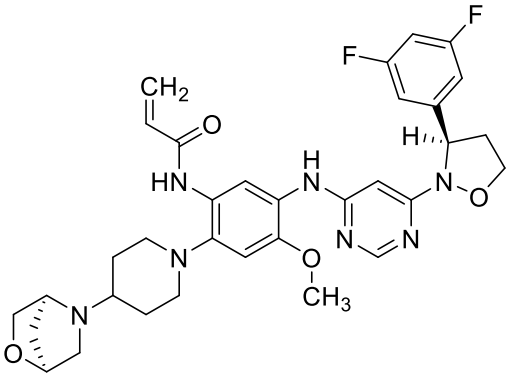
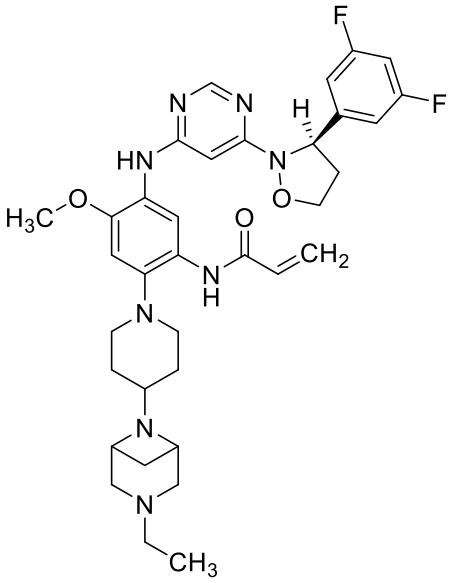
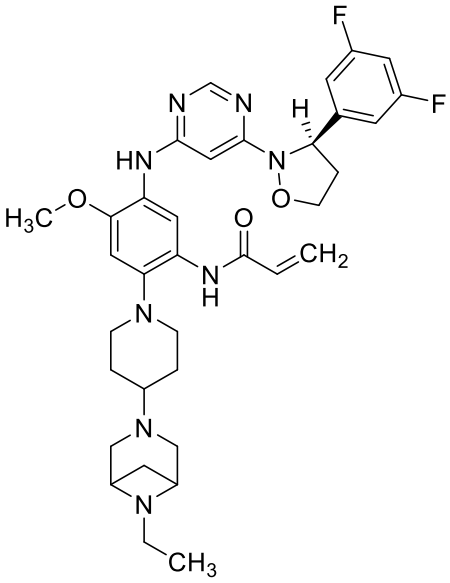

,

,

,

,



, and

,
or a pharmaceutically acceptable salt thereof.

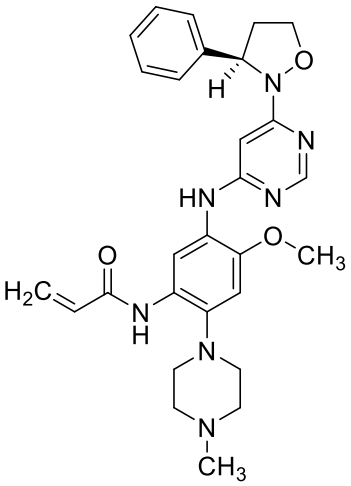
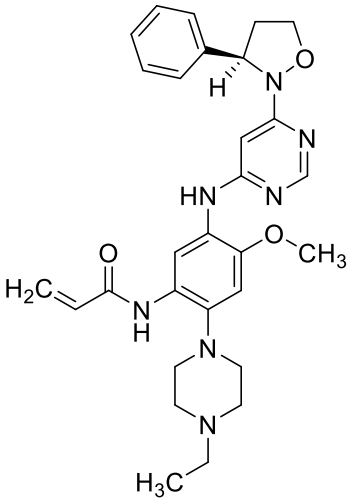
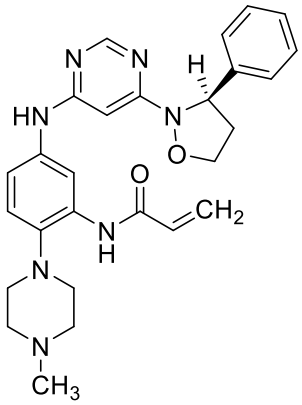
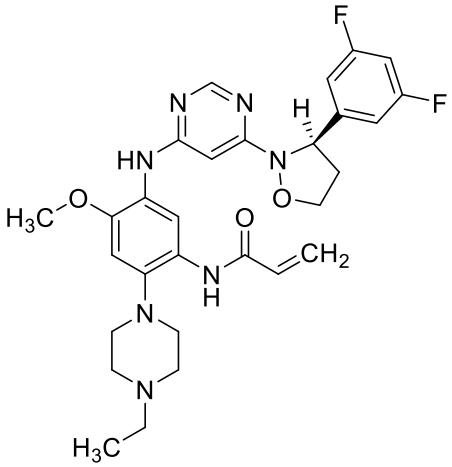
[Claim 3] A compound of Claim 2 which is selected from the group consisting of:

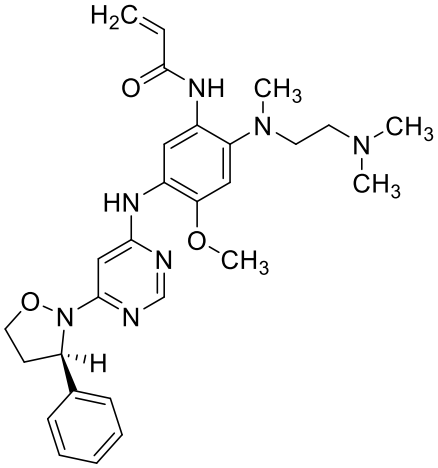
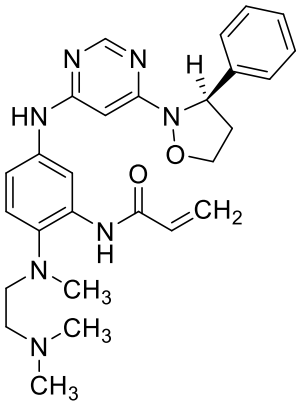

and

,
or a pharmaceutically acceptable salt thereof.

[Claim 4] A compound of Claim 2 which is selected from the group consisting of:

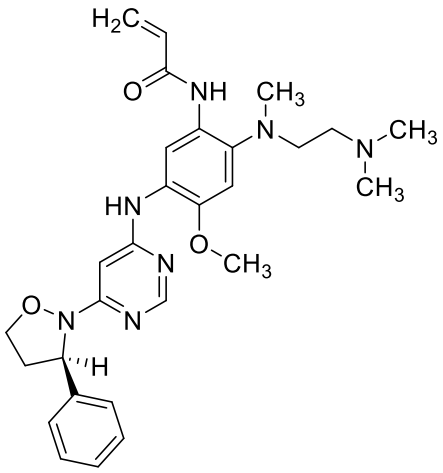

,

,

, and

,
or a pharmaceutically acceptable salt thereof.

[Claim 5] A compound of Claim 2 which is selected from the group consisting of:


,

,

, and

,
or a pharmaceutically acceptable salt thereof.

[Claim 6] A compound of Claim 2 which is selected from the group consisting of:

and

,
or a pharmaceutically acceptable salt thereof.

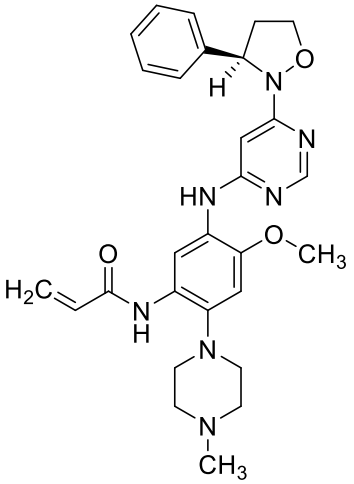
[Claim 7] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

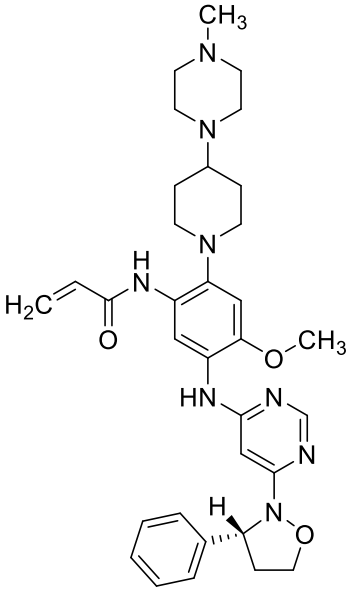
[Claim 8] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

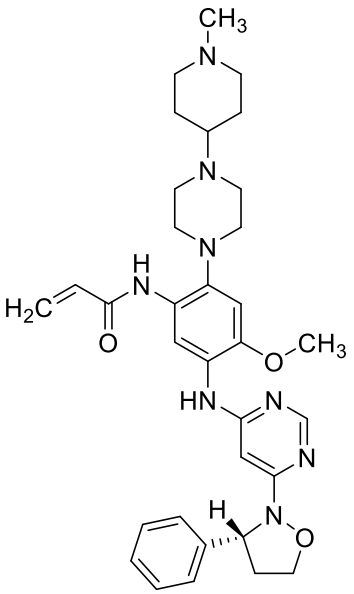
[Claim 9] A compound of Claim 2 which is



,

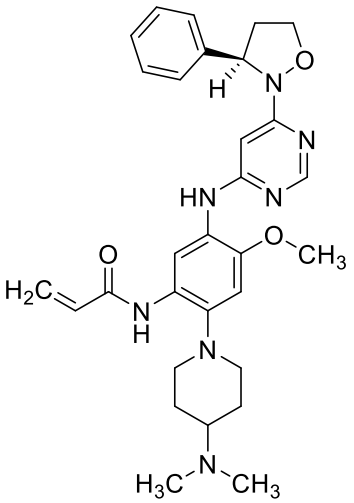
or a pharmaceutically acceptable salt thereof.

[Claim 10] A compound of Claim 2 which is



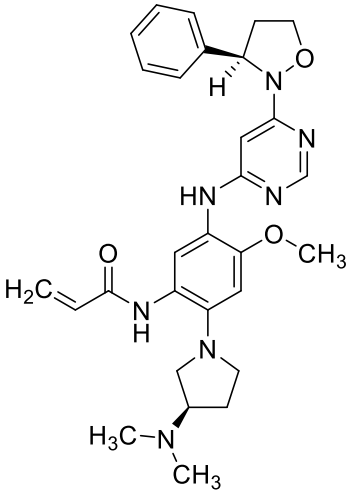
or a pharmaceutically acceptable salt thereof.

[Claim 11] A compound of Claim 2 which is



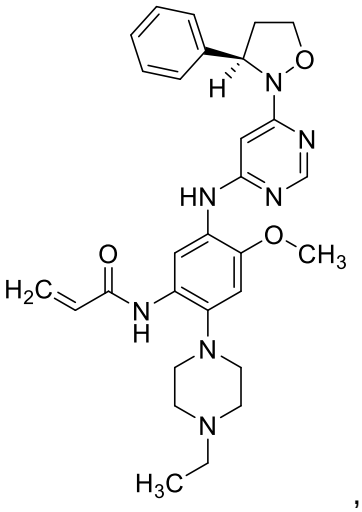
or a pharmaceutically acceptable salt thereof.

[Claim 12] A compound of Claim 2 which is



or a pharmaceutically acceptable salt thereof.

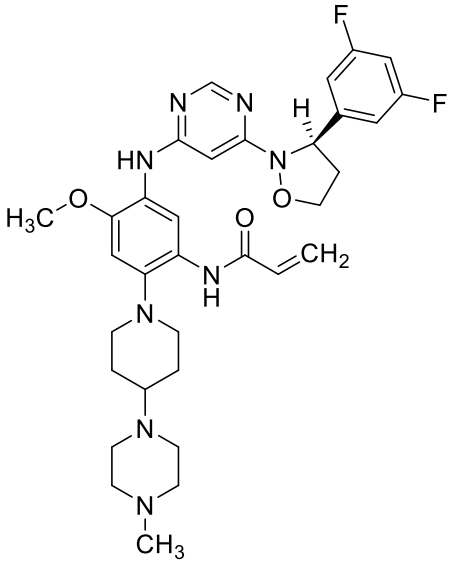
[Claim 13] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

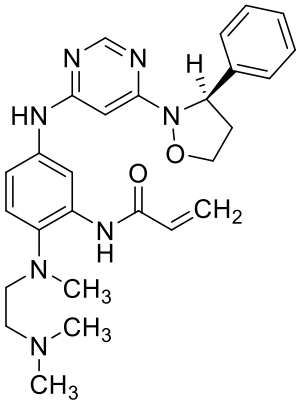
[Claim 14] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

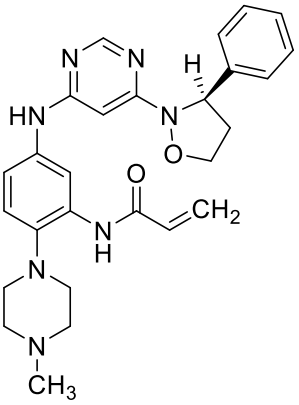
[Claim 15] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

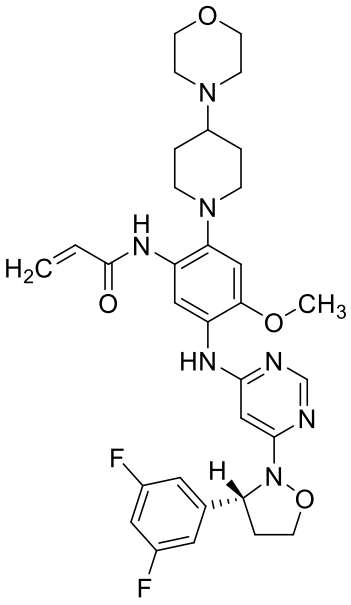
[Claim 16] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

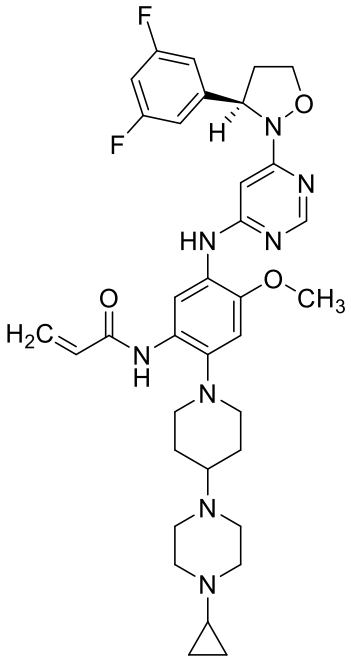
[Claim 17] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

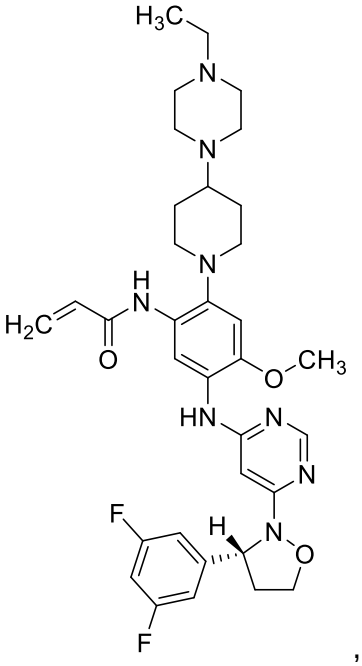
[Claim 18] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

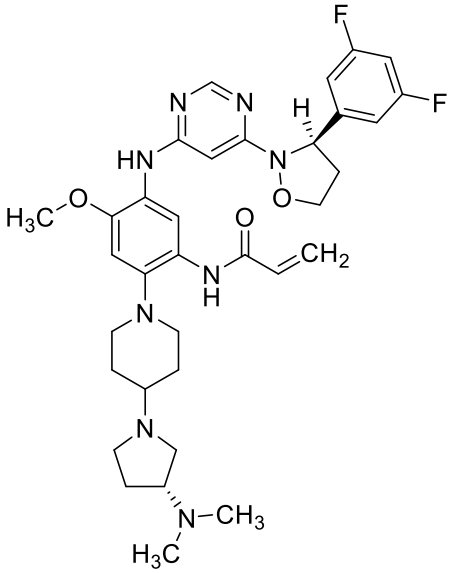
[Claim 19] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

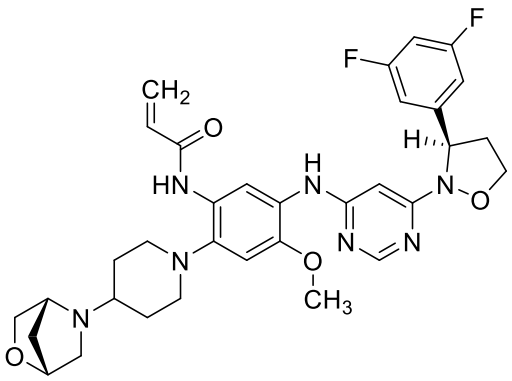
[Claim 20] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

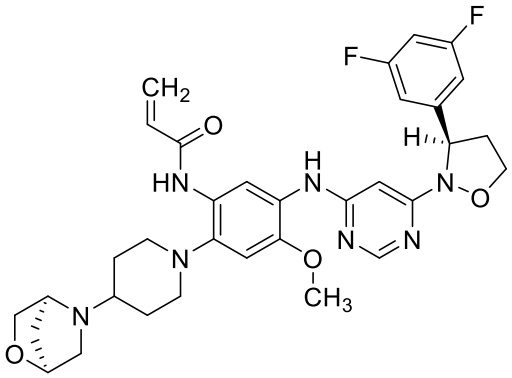
[Claim 21] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

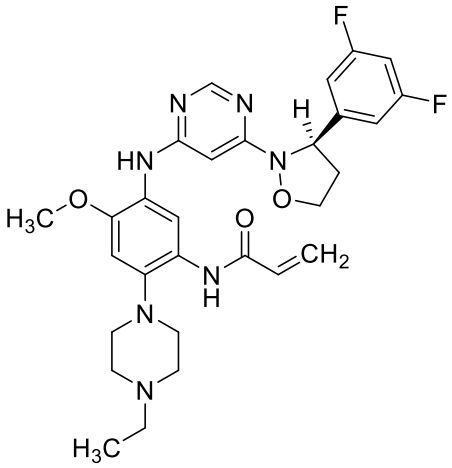
[Claim 22] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

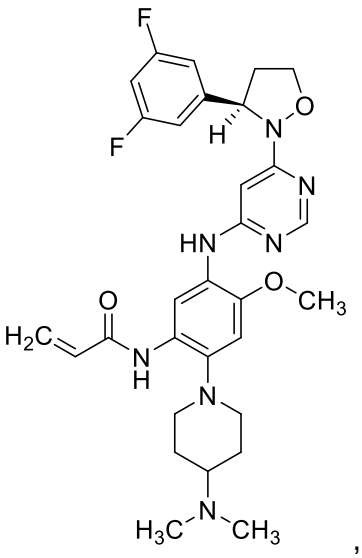
[Claim 23] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

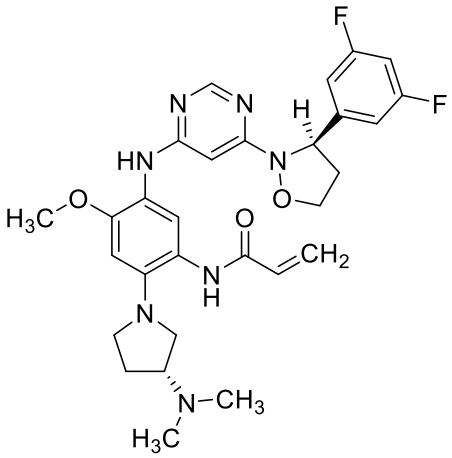
[Claim 24] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

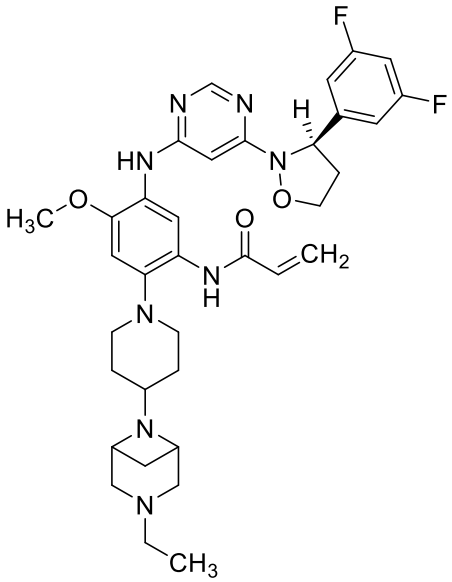
[Claim 25] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

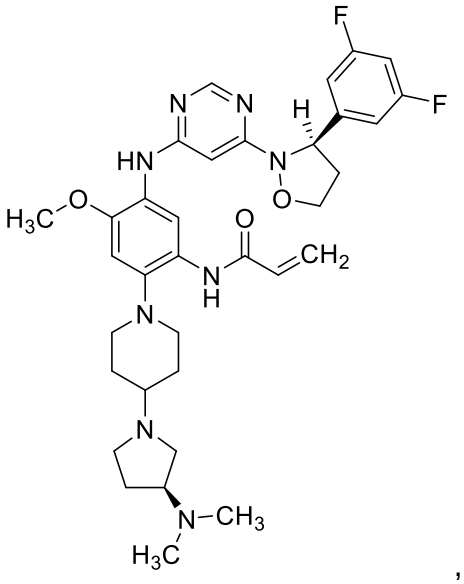
[Claim 26] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

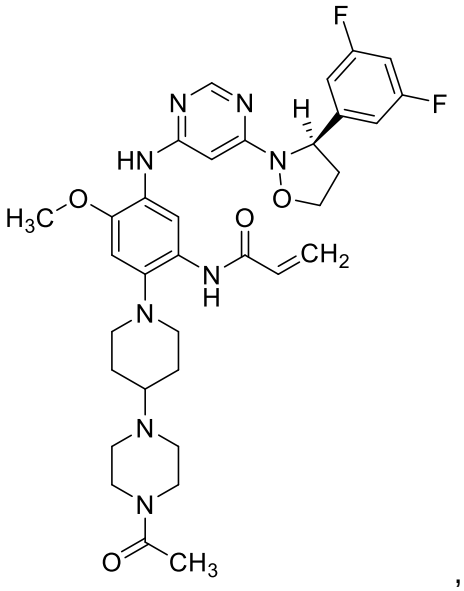
[Claim 27] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

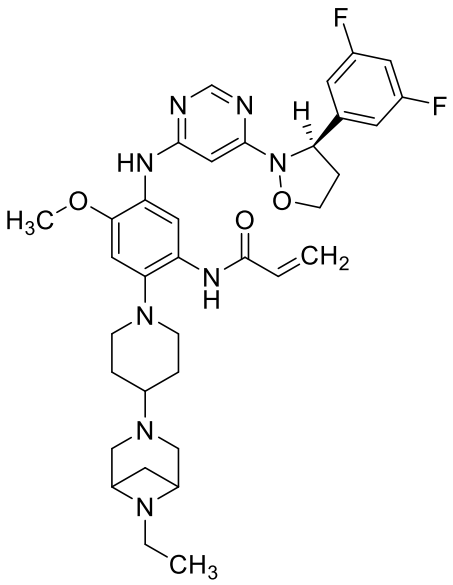
[Claim 28] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

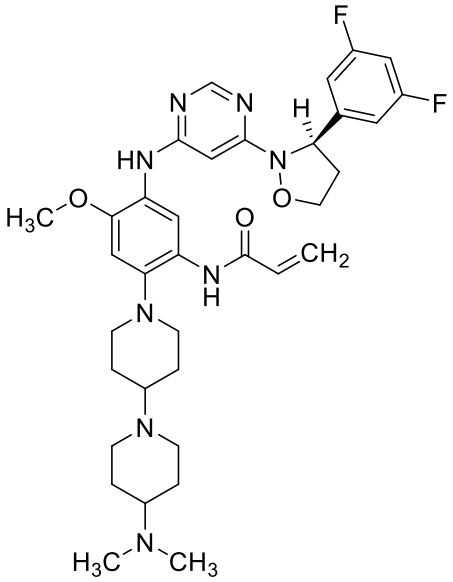
[Claim 29] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

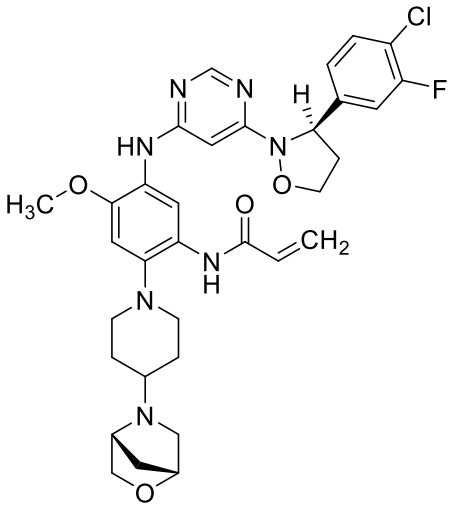
[Claim 30] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

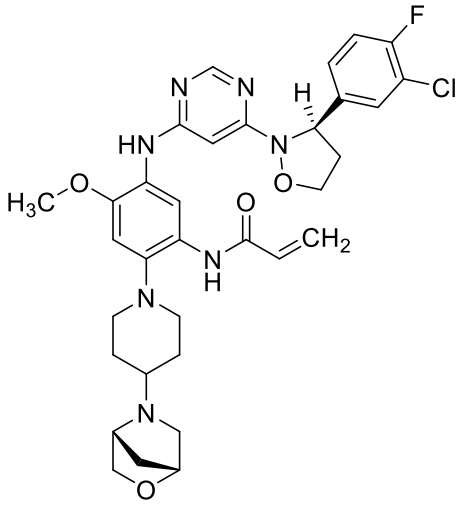
[Claim 31] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

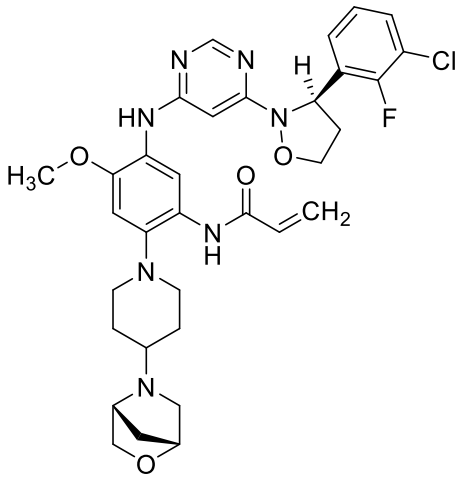
[Claim 32] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

[Claim 33] A compound of Claim 2 which is



,

or a pharmaceutically acceptable salt thereof.

[Claim 34] A compound of any of Claims 1 to 33, or a pharmaceutically acceptable salt thereof, for use in treating cancer.

[Claim 35] The compound for use of Claim 34, wherein the cancer comprises an epidermal growth factor receptor (EGFR) mutation or one or more wild-type or mutant kinases selected from the group consisting of: ERBB2 and ERBB4.

[Claim 36] The compound for use of Claim 34, wherein the cancer comprises one or more mutations selected from the group consisting of: EGFR Del19/T790M, EGFR L858R/T790M, EGFR L858R, EGFR Exon20 ins NPH, EGFR Exon20 ins SVD, EGFR Exon20 ins FQEA, EGFR Exon20 ins H, EGFR Exon20 ins ASV, and a mutation of ERBB2, and wherein the mutation of ERBB2 is Her2 Exon20 ins YVMA.

[Claim 37] The compound for use of Claim 34, wherein the cancer is selected from the group consisting of: pseudomyxoma, intrahepatic cholangiocarcinoma, hepatoblastoma, liver cancer, thyroid cancer, colorectal cancer, testicular cancer, myelodysplastic syndrome, glioblastoma, oral cancer, lip cancer, mycosis fungoides,

acute myeloid leukemia, acute lymphocytic leukemia, basal cell carcinoma, ovarian epithelial cancer, ovarian germ cell cancer, male breast cancer, brain cancer, pituitary adenomas, multiple myeloma, gallbladder cancer, biliary tract cancer, colorectal cancer, chronic myelogenous leukemia, chronic lymphocytic leukemia, retinoblastoma, choroidal melanoma, ampulla of vater cancer, bladder cancer, peritoneal cancer, parathyroid cancer, adrenal cancer, nasal and paranasal sinus cancer, non-small cell lung cancer, tongue cancer, astrocytoma, small cell lung cancer, childhood brain cancer, pediatric lymphoma, pediatric leukemia, small intestine cancer, meningioma, esophageal cancer, glioma, renal carcinoma, kidney cancer, heart cancer, duodenal cancer, malignant soft tissue cancer, malignant bone cancer, malignant lymphoma, malignant mesothelioma, malignant melanoma, eye cancer, vulvar cancer, ureter cancer, urethral cancer, cancer of unknown primary site, gastric lymphoma, gastric cancer, gastric carcinoid tumors, gastrointestinal stromal tumors, Wilms cancer, breast cancer, sarcoma, penile cancer, pharyngeal cancer, gestational choriocarcinoma, cervical cancer, endometrial cancer, uterine sarcoma, prostate cancer, metastatic bone cancer, metastatic brain cancer, mediastinal cancer, rectal cancer, rectal carcinoid tumors, vaginal cancer, spinal carcinoma, pancreatic cancer, salivary gland cancer, Kaposi's sarcoma, Paget's disease, tonsillar cancer, squamous cell carcinoma, lung adenocarcinoma, lung cancer, lung squamous cell carcinoma, skin cancer, anal cancer, rhabdomyosarcoma, laryngeal cancer, pleural cancer, blood cancer, and thymic carcinoma.

[Claim 38] The compound for use of Claim 37, wherein the cancer is selected from the group consisting of: metastatic brain cancer, breast cancer, and non-small cell lung cancer.

[Claim 39] The compound for use of Claim 38, wherein the cancer is metastatic brain cancer.

[Claim 40] The compound for use of Claim 38, wherein the cancer is breast cancer.

[Claim 41] The compound for use of Claim 38, wherein the cancer is non-small cell lung cancer.

[Claim 42] Use of a compound of any one of Claims 1 to 33, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for the treatment of cancer.

[Claim 43] The use of Claim 42, wherein the cancer comprises an epidermal growth factor receptor (EGFR) mutation or one or more wild-type or mutant kinases selected from the group consisting of: ERBB2 and ERBB4.

[Claim 44] The use of Claim 42, wherein the cancer comprises one or more mutations selected from the group consisting of: EGFR Del19/T790M, EGFR L858R/T790M, EGFR L858R, EGFR Exon20 ins NPH, EGFR Exon20 ins SVD, EGFR Exon20 ins FQEA, EGFR Exon20 ins H, EGFR Exon20 ins ASV and a mutation of ERBB2, and wherein the mutation of ERBB2 is Her2 Exon20 ins YVMA.

[Claim 45] The use of Claim 42, wherein the cancer is selected from the group consisting of: pseudomyxoma, intrahepatic cholangiocarcinoma, hepatoblastoma, liver cancer, thyroid cancer, colorectal cancer, testicular cancer, myelodysplastic syndrome, glioblastoma, oral cancer, lip cancer, mycosis fungoides, acute myeloid leukemia, acute lymphocytic leukemia, basal cell carcinoma, ovarian epithelial cancer, ovarian germ cell cancer, male breast cancer, brain cancer, pituitary adenomas, multiple myeloma,

gallbladder cancer, biliary tract cancer, colorectal cancer, chronic myelogenous leukemia, chronic lymphocytic leukemia, retinoblastoma, choroidal melanoma, ampulla of vater cancer, bladder cancer, peritoneal cancer, parathyroid cancer, adrenal cancer, nasal and paranasal sinus cancer, non-small cell lung cancer, tongue cancer, astrocytoma, small cell lung cancer, childhood brain cancer, pediatric lymphoma, pediatric leukemia, small intestine cancer, meningioma, esophageal cancer, glioma, renal carcinoma, kidney cancer, heart cancer, duodenal cancer, malignant soft tissue cancer, malignant bone cancer, malignant lymphoma, malignant mesothelioma, malignant melanoma, eye cancer, vulvar cancer, ureter cancer, urethral cancer, cancer of unknown primary site, gastric lymphoma, gastric cancer, gastric carcinoid tumors, gastrointestinal stromal tumors, Wilms cancer, breast cancer, sarcoma, penile cancer, pharyngeal cancer, gestational choriocarcinoma, cervical cancer, endometrial cancer, uterine sarcoma, prostate cancer, metastatic bone cancer, metastatic brain cancer, mediastinal cancer, rectal cancer, rectal carcinoid tumors, vaginal cancer, spinal carcinoma, pancreatic cancer, salivary gland cancer, Kaposi's sarcoma, Paget's disease, tonsillar cancer, squamous cell carcinoma, lung adenocarcinoma, lung cancer, lung squamous cell carcinoma, skin cancer, anal cancer, rhabdomyosarcoma, laryngeal cancer, pleural cancer, blood cancer, and thymic carcinoma.

[Claim 46] The use of Claim 45, wherein the cancer is selected from the group consisting of metastatic brain cancer, breast cancer, and non-small cell lung cancer.

[Claim 47] The use of Claim 46, wherein the cancer is metastatic brain cancer.

[Claim 48] The use of Claim 46, wherein the cancer is breast cancer.

[Claim 49] The use of Claim 46, wherein the cancer is non-small cell lung cancer.

[Claim 50] A pharmaceutical composition comprising a compound of any one of Claims 1 to 33, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

HETEROARYL DERIVATIVE, METHOD FOR PRODUCING SAME, AND PHARMACEUTICAL COMPOSITION COMPRISING SAME AS EFFECTIVE COMPONENT

Abstract

The present invention relates to a 6-(isooxazolidin-2-yl)-N-phenylpyrimidin-4-amine derivative, and a pharmaceutical composition for preventing or treating cancer comprising the compound as an effective component. The compound exhibits high inhibitory activity against an epidermal growth factor receptor (EGFR) variant, or wild-type or variants of one or more of ERBB2 and ERBB4, and thus may be usefully used in the treatment of cancers in which same are expressed. In particular, the compound exhibits excellent inhibitory activity on proliferation of lung cancer cell lines, and thus can be usefully used in the treatment of lung cancer.

[Figure 1]