3-PYRIMIDIN-4-YL-OXAZOLIDIN-2-ONES AS INHIBITORS OF MUTANT IDH

FIELD OF THE INVENTION

The present invention is directed to novel 3-pyrimidinyl-4-yl-oxazolidin-2-one compounds, compositions containing these compounds, the use of such compounds in the inhibition of mutant IDH proteins having a neomorphic activity and in the treatment of diseases or disorders associated with such mutant IDH proteins including, but not limited to, cell-proliferation disorders, such as cancer.

BACKGROUND OF THE INVENTION

Isocitrate dehydrogenase (IDH) is a key family of enzymes found in cellular metabolism. They are $NADP^+$ / NAD^+ and metal dependent oxidoreductases of the enzyme class EC 1.1.1.42. The wild type proteins catalyze the oxidative decarboxylation of isocitrate to alpha-ketoglutarate generating carbon dioxide and NADPH / NADH in the process. They are also known to convert oxalosuccinate into alpha-ketoglutarate. Mutations in IDH1 (cytosolic) and IDH2 (mitochondrial) have been identified in multiple cancer types including, but not limited to, glioma, glioblastoma multiforme, paraganglioma, supratentorial primordial neuroectodermal tumors, acute myeloid leukemia (AML), prostate cancer, thyroid cancer, colon cancer, chondrosarcoma, cholangiocarcinoma, peripheral T-cell lymphoma, and melanoma. (See L. Deng *et al.*, Trends Mol. Med., 2010, 16, 387; T. Shibata *et al.*, Am. J. Pathol., 2011, 178(3), 1395; Gaal *et al.*, J. Clin. Endocrinol. Metab. 2010; Hayden *et al.*, Cell Cycle, 2009; Balss *et al.*, Acta Neuropathol., 2008). The mutations have been found at or near key residues in the active site: G97D, R100, R132, H133Q, and A134D for IDH1, and R140 and R172 for IDH2. (See L. Deng *et al.*, Nature, 2009, 462, 739; L. Sellner *et al.*, Eur. J. Haematol., 2011, 85, 457).

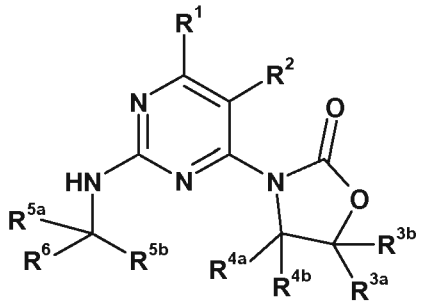
These mutant forms of IDH are shown to have a neomorphic activity (also known as a gain of function activity), reducing alpha-ketoglutarate to 2-hydroxyglutarate (2-HG). (See P.S. Ward *et al.*, Cancer Cell, 2010, 17, 225) In general, production of 2-HG is enantiospecific, resulting in generation of the D-enantiomer (also known as R enantiomer or R-2-HG). Normal cells have low native levels of 2-HG, whereas cells harboring these mutations in IDH1 or IDH2 show significantly elevated levels of 2-HG. High levels of 2-HG have been detected in tumors harboring the mutations. For example, high levels of 2-HG have been detected in the plasma of patients with mutant IDH containing AML. (See S. Gross *et al.*, J. Exp. Med., 2010, 207(2), 339). High levels of 2-HG are highly associated with tumorigenesis.

Mutant IDH2 is also associated with the rare neurometabolic disorder D-2-hydroxyglutaric aciduria type II (D-2-HGA type II). Germline mutations were found at R140 in IDH2 in 15 pateints having D-2-HGA type II. Patients having this disorder also have consistently increased levels of D-2-HG in their urine, plasma and cerebrospinal fluid. (See Kranendijk, M. *et al.*, Science, 2010, 330, 336). Finally, patients with Ollier Disease and Mafucci Syndrome (two rare disorders that predispose to cartilaginous tumors) have been shown to be somatically mosaic for IDH1 and 2 mutations and exhibit high levels of D-2-HG. (See Amary et al., Nature Genetics , 2011 and Pansuriya et al., Nature Genetics, 2011).

Thus, there is a need for small molecule inhibitors of mutant IDH proteins having a neomorphic activity for the treatment of diseases and disorders associated with these proteins.

SUMMARY OF THE INVENTION

In one aspect, this invention provides for a compound of formula (I)



(I)

or a pharmaceutically acceptable salt thereof, wherein R^1-R^6 are defined herein.

In a second aspect, this invention provides for a pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

In a third aspect, this invention provides for the use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, as an inhibitor of a mutant IDH protein having a neomorphic activity such as reducing alpha-ketoglutarate to 2-hydroxyglutarate (2-HG neomorphic activity). Suitably, this invention provides for the use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, as an inhibitor of mutant IDH1 having a neomorphic activity, such as 2-HG neomorphic activity, and/or mutant IDH2 having a neomorphic activity, such as 2-HG neomorphic activity. This invention further provides for the use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, as an inhibitor of IDH1 having a mutation at residue 97, 100 or 132, for example G97D, R100Q, R132H, R132C, R132S, R132G, R132L, and R132V;

and/or an inhibitor of IDH2 having a mutation at residue 140 or 172, for example R172K, R172M, R172S, R172G, and R172W.

In a fourth aspect, this invention provides for a method of treating a disease or disorder associated with a mutant IDH protein having a neomorphic activity comprising administration of an effective amount of a compound according to formula (I), or a pharmaceutically acceptable salt thereof, to a subject in need thereof. In one embodiment, the disease or disorder is a cell proliferation disorder, such as cancer. In another embodiment, the cancer is brain cancer, such as glioma, glioblastoma multiforme, paraganglioma, and supratentorial primordial neuroectodermal tumors (pNET); leukemia, such as acute myeloid leukemia (AML), myelodysplastic syndrome, and chronic myelogenous leukemia (CML); skin cancer, including melanoma; prostate cancer; thyroid cancer; colon cancer; lung cancer; sarcoma, including central chondrosarcoma, central and periosteal chondroma; and fibrosarcoma. In another embodiment the disease or disorder is D-2-hydroxyglutaric aciduria.

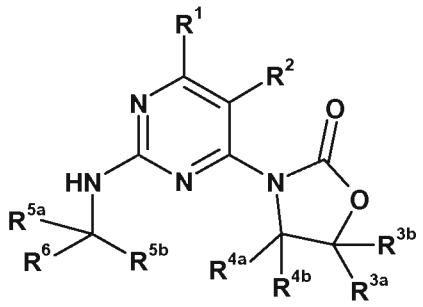
In a fifth aspect the invention provides for a compound of formula (I), or a pharmaceutically acceptable salt thereof, in combination with another therapeutic agent.

These and other aspects of the present invention are described further in the following detailed description of the invention.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to a compound of formula (I)

A compound of formula (I)



(I)

wherein:

R^1 and R^2 are each independently hydrogen, deuterium, halo, hydroxyl, NH_2, aryl, heteroaryl, or optionally substituted C_{1-4} alkyl,

wherein said C_{1-4} alkyl is optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, and NH_2;

R^{3a} is hydrogen, deuterium, C_{1-6} alkyl, phenyl, or benzyl and

R^{3b} is hydrogen, deuterium, or C_{1-6} alkyl; or

R^{3a} and R^{3b} are joined together forming an optionally substituted 3-7 membered cycloalkyl ring or an optionally substituted 4-7 membered heterocyclic ring,

wherein said cycloalkyl and heterocyclic rings are each optionally substituted with one or two substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl;

R^{4a} is hydrogen, C_{1-6} alkyl, optionally substituted phenyl, optionally substituted benzyl, optionally substituted heteroaryl, or methylene-dibenzene,

wherein said phenyl, benzyl, and heteroaryl rings are optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-4} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, phenyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, $-COOR^b$, $-SO_2R^b$, $-NHC(O)R^b$, and $-NR^bR^b$ and

R^{4b} is hydrogen, deuterium, or C_{1-3} alkyl; or

R^{4a} and R^{4b} are joined together forming an optionally substituted 3-7 membered cycloalkyl ring or an optionally substituted 4-7 membered heterocyclic ring,

wherein said cycloalkyl and heterocyclic rings are optionally substituted with one or two substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl,

provided that only one of R^{3a} and R^{3b} and R^{4a} and R^{4b} are joined together forming a ring;

R^{5a} is hydrogen or deuterium;

R^{5b} is hydrogen, deuterium, methyl, ethyl, CD_3, CF_3, CH_2F, or CHF_2 and

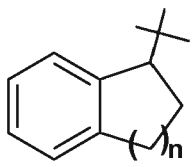
R^6 is optionally substituted C_{1-6} alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclic, or optionally substituted C_{3-10} cycloalkyl,

wherein said C_{1-6} alkyl is optionally substituted with one substituent selected from the group consisting of hydroxyl, C_{1-3} alkoxy and $-OR^a$,

wherein said aryl, heteroaryl, heterocyclic and C_{3-10} cycloalkyl are optionally substituted with one to three substituents each independently selected from the group

consisting of: halo; hydroxyl; cyano; nitro; C_{1-4} alkoxy; C_{1-3} haloalkyl; C_{1-3} haloalkoxy; C_{1-6} alkyl; C_{3-6} cycloalkyl optionally substituted with one to three substituents each independently selected from the group consisting of: hydroxyl, cyano, C_{1-3} alkyl, C_{1-3} alkoxy, and C_{1-3} haloalkyl; phenyl optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, $-COOR^b$, $-SO_2R^b$, $-NHC(O)R^b$, and $-NR^bR^b$; 5-6 membered heteroaryl optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, C_{1-3} alkyl, C_{1-3} alkoxy; 5-6 membered heterocyclic optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl; $-CH_2R^a$; $-OR^a$; $-C(O)R^a$; $-NR^aR^b$; $-COOR^a$; $-SO_2R^a$; $-SO_2R^b$; $NHC(O)R^a$; $-NHC(O)R^b$; $-C(O)NR^aR^b$; $-C(O)NHR^b$; and $-SO_2NR^bR^b$; or

R^{5b} and R^6 are joined together forming an optionally substituted C_{3-7} cycloalkyl group

or an optionally substituted group of formula (a):  (a),

wherein n is 1, 2, or 3 and

said C_{3-7} cycloalkyl and group of formula (a) are optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, benzyloxy, $-COOR^b$, $-SO_2R^b$, $-NHC(O)R^b$, and $-NR^bR^b$;

each R^a is independently optionally substituted phenyl, optionally substituted heteroaryl, optionally substituted heterocyclic, or optionally substituted C_{3-7} cycloalkyl,

wherein said phenyl and heteroaryl are optionally substituted with one to three substituents each independently selected from the group consisting of halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, and C_{1-3} alkyl,

wherein said heterocyclic is optionally substituted with one to three substituents each independently selected from the group consisting of halo, hydroxyl, oxo, C_{1-3}

alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-4} alkyl, C_{3-5} cycloalkyl, $-C(O)R^b$, and $-NR^bR^b$; and

wherein said C_{3-7} cycloalkyl is optionally substituted with one to three substituents each independently selected from the group consisting of halo, hydroxyl, oxo, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, and C_{1-3} alkyl; and

each R^b is independently hydrogen or C_{1-6} alkyl.

"Alkyl" refers to a monovalent saturated hydrocarbon chain having the specified number of carbon atoms. For example, C_{1-6} alkyl refers to an alkyl group having from 1 to 6 carbon atoms. Alkyl groups may be optionally substituted with one or more substituents as defined in formula (I). Alkyl groups may be straight or branched. Representative branched alkyl groups have one, two, or three branches. Examples of alkyl groups include, but are not limited to, methyl, ethyl, propyl (n-propyl and isopropyl), butyl (n-butyl, isobutyl, sec-butyl, and t-butyl), pentyl (n-pentyl, isopentyl, and neopentyl), and hexyl.

"Alkoxy" refers to any alkyl moiety attached through an oxygen bridge (i.e. a $-O-C_{1-3}$ alkyl group wherein C_{1-3} alkyl is as defined herein). Examples of such groups include, but are not limited to, methoxy, ethoxy, and propoxy.

"Aryl" refers to a hydrocarbon ring system having an aromatic ring. Aryl groups are monocyclic ring systems or bicyclic ring systems. Monocyclic aryl ring refers to phenyl. Bicyclic aryl rings refer to naphthyl and to rings wherein phenyl is fused to a C_{5-7} cycloalkyl or C_{5-7} cycloalkenyl ring as defined herein. Aryl groups may be optionally substituted with one or more substituents as defined in formula (I).

"Cycloalkyl" refers to a saturated hydrocarbon ring system having the specified number of carbon atoms. Cycloalkyl groups are monocyclic or bicyclic ring systems. For example, C_{5-10} cycloalkyl refers to a cycloalkyl group having from 5 to 10 carbon atoms. Cycloalkyl groups may be optionally substituted with one or more substituents as defined in formula (I). Examples of cycloalkyl groups include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and adamantanyl.

"Cycloalkenyl" refers to an unsaturated hydrocarbon ring system having the specified number of carbon atoms and having a carbon-carbon double bond within the ring. For example, C_{5-7} cycloalkenyl refers to a cycloalkenyl group having from 5 to 7 carbon atoms. In certain embodiments, cycloalkenyl groups have one carbon-carbon double bond within the ring. In other embodiments, cycloalkeneyl groups have more

than one carbon-carbon double bond within the ring. Cycloalkenyl rings are not aromatic. Cycloalkenyl groups may be optionally substituted with one or more substituents as defined in formula (I).

"Halo" refers to the halogen radicals fluoro, chloro, bromo, and iodo.

"Haloalkyl" refers to an alkyl group wherein at least one hydrogen atom attached to a carbon atom within the alkyl group is replaced with halo. The number of halo substituents includes, but is not limited to, 1, 2, 3, 4, 5, or 6 substituents. Haloalkyl includes, but is not limited to, monofluoromethyl, difluoroethyl, and trifluoromethyl.

"Haloalkoxy" refers to a haloalkyl moiety attached through an oxygen bridge (i.e. a $-O-C_{1-3}$ haloalkyl group wherein C_{1-3} haloalkyl is as defined herein). An example ofa haloalkoxy group is trifluoromethoxy.

"Heteroaryl" refers to an aromatic ring system containing from 1 to 5 heteroatoms. Heteroaryl groups containing more than one heteroatom may contain different heteroatoms. Heteroaryl groups may be optionally substituted with one or more substituents as defined in formula (I). Heteroaryl groups are monocyclic ring systems or are fused bicyclic ring systems. Monocyclic heteroaryl rings have from 5 to 6 ring atoms. Bicyclic heteroaryl rings have from 8 to 10 member atoms. Bicyclic heteroaryl rings include those ring systems wherein a heteroaryl ring is fused to a phenyl ring. Heteroaryl includes, but is not limited to, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, oxadiazolyl (including 1,3,4-oxadiazolyl and 1,2,4-oxadiazolyl), thiazolyl, isothiazolyl, thiadiazolyl, furanyl, furanzanyl, thienyl, triazolyl, pyridinyl (including 2-, 3-, and 4-pyridinyl), pyrimidinyl, pyridazinyl, pyrazinyl, trazinyl, tetrazinyl, tetrzolyl, indonyl, isoindolyl, indolizinyl, indazolyl, purinyl, quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, benzimidazolyl, benzopyranyl, benzopyranyl, benzoxazolyl, benzoisoxazolyl, benzofuranyl, benzothiazolyl, benzothienyl, naphthyridinyl, 1H-pyrrolo[2,3-b]pyridinyl, tetrazolo[1,5-a]pyridinyl, imidazo[2,1-b][1,3,4]thiadiazolyl and the like.

"Heteroatom" refers to a nitrogen, oxygen, or sulfur atom.

"Heterocyclic" refers to a 3 to 11 membered saturated or unsaturated monocyclic or bicyclic ring containing from 1 to 4 heteroatoms. Heterocyclic ring systems are not aromatic. Heterocyclic groups containing more than one heteroatom may contain different heteroatoms. Heterocyclic includes ring systems wherein a sulfur atom is oxidized to form SO or SO_2. Heterocyclic groups may be optionally substituted with one or more substituents as defined in formula (I). Heterocyclic groups are monocyclic, spiro, or fused or bridged bicyclic ring systems. Monocyclic heterocyclic rings have 3 to 7 ring atoms. Examples of monocyclic heterocyclic groups include oxtanyl, tetrahydrofuranyl, dihydrofuranyl, 1,4-dioxanyl, morpholinyl, 1,4-dithianyl, piperazinyl, piperidinyl, 1,3-

dioxolanyl, imidazolidinyl, imidazolinyl, pyrrolinyl, pyrrolidinyl, tetrahydropyranyl, dihydropyranyl, oxathiolanyl, dithiolanyl, 1,3-dioxanyl, 1,3-dithianyl, oxathianyl, thiomorpholinyl, tetrahydro-thiopyran1,1-dioxide, 1,4-diazepanyl, and the like. Fused heterocyclic ring systems have from 8 to 11 ring atoms and include groups wherein a heterocyclic ring is fused to a phenyl ring, a heteroaryl ring or another heterocyclic ring. Examples of fused heterocyclic rings include 2,3-dihydrobenzo[b][1,4]dioxinyl, octahydro-pyrrolo[1,2-a]pyrazinyl, octahydro-pyrido[1,2-a]pyrazinyl, octahydro-pyrrolo[3,4-c]pyrrolyl, 5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazinyl, 5,6,7,8-tetrahydro-imidazo[1,2-a]pyrazinyl and the like. Examples of bridged heterocyclic groups include 3,8-diaza-bicyclo[3.2.1]octanyl, 3,8-diaza-bicyclo[4.2.0]octanyl and the like. Examples of spiro heterocyclic groups include 4,7-diaza-spiro[2.5]octanyl and the like.

"4-7 membered heterocyclic" refers to a heterocyclic group as defined above, having from 4 to 7 ring atoms and containing from 1 to 4 heteroatoms.

"5-6 membered heterocylic" refers to a heterocyclic group as defined above, having 5 or 6 ring atoms and containing from 1 to 4 heteroatoms.

"Optionally substituted" indicates that a group, such as an alkyl, cycloalkyl, heteroaryl, heterocyclic, phenyl, and benzyl may be unsubstitued or the group may be substituted with one or more substituents as defined in formula (I).

"Oxo" refers to a C=O group.

"Pharmaceutically acceptable" means a compound which is suitable for pharmaceutical use. Salts and solvates (e.g. hydrates and hydrates of salts) of compounds of the invention which are suitable for use in medicine are those where in the counterion or associated solvent is pharmaceutically acceptable. However, salts and solvates having non-pharmaceutically acceptable counterions or associated solvents are within the scope of the present invention, for example, for use as intermediates in the preparation of other compounds of the invention and their pharmaceutically acceptable salts and solvates.

"Substituted" in reference to a group such as alkyl, phenyl, benzyl, heteroaryl, and heterocyclic, indicates that one or more hydrogen atoms attached to an atom within the group is replaced with a substituent selected from the group of defined substituents. It should be understood that the term "substituted" includes the implicit provision that such substitution be in accordance with permitted valence of the substituted atom and the substituent, and that the substitution results in a stable compound (i.e. one that does not spontaneously undergo transformation, for example, by hydrolysis, rearrangement, cyclization, or elimination and that is sufficiently robust to survive isolation from a reaction mixture). When it is stated that a group may contain one or more substituents, one or more (as appropriate) atoms within the group may be substituted. In addition, a

single atom within the group may be substituted with more than one substituent as long as such substitution is accordance with the permitted valence of the atom. Suitable substituents are defined for each substituted or optionally substituted group.

The skilled artisan will appreciate that salts, including pharmaceutically acceptable salts, of the compounds according to formula (I) may be prepared. These salts may be prepared *in situ* during the final isolation and purification of the compound, or by separately reacting the purified compound in its free acid or free base form with a suitable base or acid, respectively.

Pharmaceutically acceptable acid addition salts can be formed with inorganic acids and organic acids, e.g., acetate, aspartate, benzoate, besylate, bromide/hydrobromide, bicarbonate/carbonate, bisulfate/sulfate, camphorsulfonate, chloride/hydrochloride, chlortheophyllonate, citrate, ethandisulfonate, fumarate, gluceptate, gluconate, glucuronate, hippurate, hydroiodide/iodide, isethionate, lactate, lactobionate, laurylsulfate, malate, maleate, malonate, mandelate, mesylate, methylsulphate, naphthoate, napsylate, nicotinate, nitrate, octadecanoate, oleate, oxalate, palmitate, pamoate, phosphate/hydrogen phosphate/dihydrogen phosphate, polygalacturonate, propionate, stearate, succinate, sulfosalicylate, tartrate, tosylate and trifluoroacetate salts.

Inorganic acids from which salts can be derived include, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like.

Organic acids from which salts can be derived include, for example, acetic acid, propionic acid, glycolic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, toluenesulfonic acid, sulfosalicylic acid, and the like. Pharmaceutically acceptable base addition salts can be formed with inorganic and organic bases.

Inorganic bases from which salts can be derived include, for example, ammonium salts and metals from columns I to XII of the periodic table. In certain embodiments, the salts are derived from sodium, potassium, ammonium, calcium, magnesium, iron, silver, zinc, and copper; particularly suitable salts include ammonium, potassium, sodium, calcium and magnesium salts.

Organic bases from which salts can be derived include, for example, primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, basic ion exchange resins, and the like. Certain organic amines include isopropylamine, benzathine, cholinate, diethanolamine, diethylamine, lysine, meglumine, piperazine and tromethamine.

The pharmaceutically acceptable salts of the present invention can be synthesized from a basic or acidic moiety, by conventional chemical methods. Generally, such salts can be prepared by reacting free acid forms of these compounds with a stoichiometric amount of the appropriate base (such as Na, Ca, Mg, or K hydroxide, carbonate, bicarbonate or the like), or by reacting free base forms of these compounds with a stoichiometric amount of the appropriate acid. Such reactions are typically carried out in water or in an organic solvent, or in a mixture of the two. Generally, use of non-aqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile is desirable, where practicable. Lists of additional suitable salts can be found, e.g., in "Remington's Pharmaceutical Sciences", 20th ed., Mack Publishing Company, Easton, Pa., (1985); and in "Handbook of Pharmaceutical Salts: Properties, Selection, and Use" by Stahl and Wermuth (Wiley-VCH, Weinheim, Germany, 2002).

Solvates, including pharmaceutically acceptable solvates, of the compounds of formula (I) may also be prepared. "Solvate" refers to a complex of variable stoichiometry formed by a solute and solvent. Such solvents for the purpose of the invention may not interfere with the biological activity of the solute. Examples of suitable solvents include, but are not limited to, water, MeOH, EtOH, and AcOH. Solvates wherein water is the solvent molecule are typically referred to as hydrates. Hydrates include compositions containing stoichiometric amounts of water, as well as compositions containing variable amounts of water.

The compounds of formula (I), including salts and solvates thereof, may exist in crystalline forms, non-crystalline forms, or mixtures thereof. The compound or salt or solvate thereof may also exhibit polymorphism, i.e. the capacity of occurring in different crystalline forms. These different crystalline forms are typically known as "polymorphs". Polymorphs have the same chemical composition but differ in packing, geometrical arrangement, and other descriptive properties of crystalline solid state. Polymorphs, therefore, may have different physical properties such as shape, density, hardness, deformability, stability, and dissolution properties. Polymorphs typically exhibit different melting points, IR spectra, and X-ray powder diffraction patterns, all of which may be used for identification. One of ordinary skill in the art will appreciate that different polymorphs may be produced, for example, by changing or adjusting the conditions used in crystallizing/recrystallizing a compound of formula (I).

The invention also includes various isomers of the compounds of formula (I). "Isomer" refers to compounds that have the same composition and molecular weight but differ in physical and/or chemical properties. The structural difference may be in constitution (geometric isomers) or in the ability to rotate the plane of polarized light (stereosiomers). With regard to stereoisomers, the compounds of formula (I) may have

one or more asymmetric carbon atom and may occur as racemates, racemic mixtures and as individual enantiomers or diastereomers. All such isomeric forms are included within the present invention, including mixtures thereof. If the compound contains a double bond, the substituent may be in the E or Z configuration. If the compound contains a disubstituted cycloalkyl, the cycloalkyl substituent may have a cis- or trans-configuration. All tautomeric forms are also intended to be included.

Any asymmetric atom (e.g., carbon or the like) of a compound of formula (I) can be present in racemic or enantiomerically enriched, for example the (*R*)-, (*S*)- or (*R,S*)-configuration. In certain embodiments, each asymmetric atom has at least 50 % enantiomeric excess, at least 60 % enantiomeric excess, at least 70 % enantiomeric excess, at least 80 % enantiomeric excess, at least 90 % enantiomeric excess, at least 95 % enantiomeric excess, or at least 99 % enantiomeric excess in the (*R*)- or (*S*)-configuration. Substituents at atoms with unsaturated double bonds may, if possible, be present in *cis*- (*Z*)- or *trans*- (*E*)- form.

Accordingly, as used herein a compound of formula (I) can be in the form of one of the possible isomers, rotamers, atropisomers, tautomers or mixtures thereof, for example, as substantially pure geometric (*cis* or *trans*) isomers, diastereomers, optical isomers (antipodes), racemates or mixtures thereof.

Any resulting mixtures of isomers can be separated on the basis of the physicochemical differences of the constituents, into the pure or substantially pure geometric or optical isomers, diastereomers, racemates, for example, by chromatography and/or fractional crystallization.

Any resulting racemates of final products or intermediates can be resolved into the optical antipodes by known methods, *e.g.*, by separation of the diastereomeric salts thereof, obtained with an optically active acid or base, and liberating the optically active acidic or basic compound. In particular, a basic moiety may thus be employed to resolve the compounds of the present invention into their optical antipodes, *e.g.*, by fractional crystallization of a salt formed with an optically active acid, *e.g.*, tartaric acid, dibenzoyl tartaric acid, diacetyl tartaric acid, di-*O,O'*-*p*-toluoyl tartaric acid, mandelic acid, malic acid or camphor-10-sulfonic acid. Racemic products can also be resolved by chiral chromatography, *e.g.*, high pressure liquid chromatography (HPLC) using a chiral adsorbent.

The invention includes unlabeled forms as well as isotopically labeled forms of compounds of formula (I). Isotopically labeled compounds have structures depicted by the formulas given herein except that one or more atoms are replaced by an atom having a selected atomic mass or mass number. Examples of isotopes that can be incorporated into compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen,

phosphorous, fluorine, and chlorine, such as ^{2}H, ^{3}H, ^{11}C, ^{13}C, ^{14}C, ^{15}N, ^{18}F ^{31}P, ^{32}P, ^{35}S, ^{36}Cl, ^{125}I respectively. The invention includes various isotopically labeled compounds as defined herein, for example those into which radioactive isotopes, such as ^{3}H and ^{14}C, or those into which non-radioactive isotopes, such as ^{2}H and ^{13}C are present. Such isotopically labelled compounds are useful in metabolic studies (with ^{14}C), reaction kinetic studies (with, for example ^{2}H or ^{3}H), detection or imaging techniques, such as positron emission tomography (PET) or single-photon emission computed tomography (SPECT) including drug or substrate tissue distribution assays, or in radioactive treatment of patients. In particular, an ^{18}F or labeled compound may be particularly desirable for PET or SPECT studies. Isotopically-labeled compounds of formula (I) can generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described in the accompanying Examples and Preparations using an appropriate isotopically-labeled reagents in place of the non-labeled reagent previously employed.

Furthermore, substitution with heavier isotopes, particularly deuterium (i.e., ^{2}H or D) may afford certain therapeutic advantages resulting from greater metabolic stability, for example increased in vivo half-life or reduced dosage requirements or an improvement in therapeutic index. It is understood that deuterium in this context is regarded as a substituent of a compound of the formula (I). The concentration of such a heavier isotope, specifically deuterium, may be defined by the isotopic enrichment factor. The term "isotopic enrichment factor" as used herein means the ratio between the isotopic abundance and the natural abundance of a specified isotope. If a substituent in a compound of this invention is denoted deuterium, such compound has an isotopic enrichment factor for each designated deuterium atom of at least 3500 (52.5% deuterium incorporation at each designated deuterium atom), at least 4000 (60% deuterium incorporation), at least 4500 (67.5% deuterium incorporation), at least 5000 (75% deuterium incorporation), at least 5500 (82.5% deuterium incorporation), at least 6000 (90% deuterium incorporation), at least 6333.3 (95% deuterium incorporation), at least 6466.7 (97% deuterium incorporation), at least 6600 (99% deuterium incorporation), or at least 6633.3 (99.5% deuterium incorporation).

Representative Embodiments

Various embodiments of the invention are described herein. It will be recognized that features specified in each embodiment may be combined with other specified features to provide for further embodiments.

One embodiment of the present invention is a compound according to formula (I) wherein:

each R^1 and R^2 is independently hydrogen, deuterium, halo, hydroxyl, NH_2, aryl, heteroaryl, or optionally substituted C_{1-4} alkyl,

wherein said C_{1-4} alkyl is optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, and NH_2;

R^{3a} is hydrogen, deuterium, C_{1-6} alkyl, phenyl, or benzyl and

R^{3b} is hydrogen, deuterium, or C_{1-6} alkyl; or

R^{3a} and R^{3b} are joined together forming an optionally substituted 3-7 membered cycloalkyl ring or an optionally substituted 4-7 membered heterocyclic ring,

wherein said cycloalkyl and heterocyclic rings are optionally substituted with one or two substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl;

R^{4a} is hydrogen, C_{1-6} alkyl, optionally substituted phenyl, optionally substituted benzyl, optionally substituted heteroaryl, or methylene-dibenzene,

wherein said phenyl, benzyl, and heteroaryl rings are optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, $COOR^b$, SO_2R^b, $NHC(O)R^b$, and NR^bR^b and

R^{4b} is hydrogen, deuterium, or C_{1-3} alkyl; or

R^{4a} and R^{4b} are joined together forming an optionally substituted 3-7 membered cycloalkyl ring or an optionally substituted 4-7 membered heterocyclic ring,

wherein said cycloalkyl and heterocyclic rings are optionally substituted with one or two substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl,

provided that only one of R^{3a} and R^{3b} and R^{4a} and R^{4b} are joined together forming a ring;

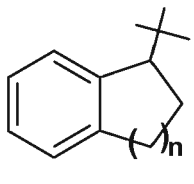
R^{5a} is hydrogen or deuterium;

R^{5b} is hydrogen, deuterium, methyl, ethyl, CD_3, CF_3, CH_2F, or CHF_2 and

R^6 is optionally substituted C_{1-6} alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclic, or optionally substituted C_{5-10} cycloalkyl,

wherein said C_{1-6} alkyl is optionally substituted with one substituent selected from the group consisting of hydroxyl, C_{1-3} alkoxy and $-OR^a$;

wherein said aryl, heteroaryl, heterocyclic and C_{5-10} cycloalkyl are optionally substituted with one to three substituents each independently selected from the group consisting of: halo; hydroxyl; cyano; nitro; C_{1-3} alkoxy; C_{1-3} haloalkyl; C_{1-3} haloalkoxy; C_{1-6} alkyl; C_{3-6} cycloalkyl; phenyl optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, $COOR^b$, SO_2R^b, $NHC(O)R^b$, and NR^bR^b; 5-6 membered heteroaryl; 5-6 membered heterocyclic optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl; $-CH_2R^a$; $-OR^a$; $-C(O)R^a$; $-NR^aR^b$; $-COOR^a$; $-SO_2R^a$; $NHC(O)R^a$; and $-SO_2NR^bR^b$; or

R^{5b} and R^6 are joined together forming an optionally substituted C_{3-7} cycloalkyl group or an optionally substituted group of formula (a):  (a),

wherein n is 1, 2, or 3 and

said C_{3-7} cycloalkyl and group of formula (a) are optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, benzyloxy, $COOR^b$, SO_2R^b, $NHC(O)R^b$, and NR^bR^b;

each R^a is independently optionally substituted phenyl, optionally substituted heteroaryl, or optionally substituted 4-7 membered heterocyclic,

wherein said phenyl and heteroaryl are optionally substituted with one to three substituents each independently selected from the group consisting of halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, and C_{1-3} alkyl,

wherein said 4-7 membered heterocyclic is optionally substituted with one to three substituents each independently selected from the group consisting of halo, hydroxyl, oxo, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, and C_{1-3} alkyl; and

each R^b is independently hydrogen or C_{1-6} alkyl.

In another embodiment of the present invention R^1 is hydrogen, halo, or optionally substituted C_{1-4} alkyl. Suitably R^1 is hydrogen, fluoro, chloro, or methyl. In another embodiment R^1 is hydrogen, fluoro or chloro. Suitably R^1 is hydrogen.

In another embodiment of the present invention R^2 is hydrogen, halo or optionally substituted C_{1-4} alkyl. Suitably R^2 is hydrogen, fluoro, chloro, or methyl. In another embodiment R^2 is hydrogen or fluoro. In another embodiment of the present invention R^2 is hydrogen.

In another embodiment of the present invention R^1 and R^2 are both hydrogen.

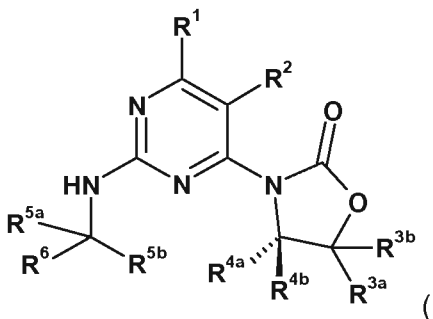
In another embodiment of the present invention R^{3a} is hydrogen, C_{1-6} alkyl, or phenyl. Suitably R^{3a} is hydrogen, methyl, or phenyl. Suitably R^{3a} is hydrogen or methyl. Suitably R^{3a} is hydrogen.

In another embodiment of the present invention R^{3b} is hydrogen or methyl. Suitably R^{3b} is hydrogen.

In another embodiment R^{3a} and R^{3b} are both hydrogen.

In another embodiment of the present invention R^{3a} and R^{3b} are joined together forming oxetanyl or tetrahydro-2H-pyranyl.

Another embodiment of the present invention is a compound according to formula (II).



(II)

In another embodiment of the present invention R^{4a} is hydrogen, C_{1-6} alkyl, optionally substituted phenyl, optionally substituted benzyl, optionally substituted heteroaryl, or methylene-dibenzene,

wherein said phenyl, benzyl, and heteroaryl rings are optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, $-COOR^b$, $-SO_2R^b$,- $NHC(O)R^b$, and- NR^bR^b .

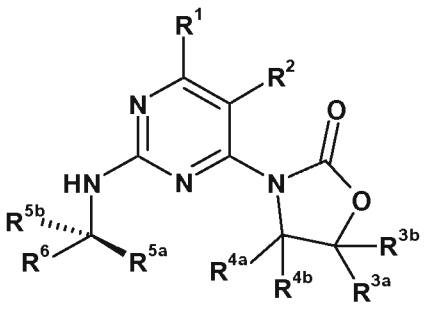
In another embodiment of the present invention R^{4a} is hydrogen, C_{1-4} alkyl, optionally substituted phenyl, optionally substituted benzyl, optionally substituted heteroaryl, or methylene-dibenzene. Suitably R^{4a} is hydrogen, C_{1-4} alkyl, optionally substituted phenyl, optionally substituted benzyl, optionally substituted pyridinyl, or methylene-dibenzene. More suitably R^{4a} is hydrogen, methyl, isopropyl, isobutyl, t-butyl, phenyl, 4-methoxyphenyl, 4-fluorophenyl, benzyl, or methylene-dibenzene. In another embodiment R^{4a} is hydrogen, methyl, ethyl, isopropyl, phenyl, 4-fluorophenyl, 4-methoxyphenyl, biphenyl, benzyl, or pyridinyl. Suitably R^{4a} is isopropyl.

In another embodiment of the present invention R^{4b} is hydrogen or methyl. Suitably R^{4b} is hydrogen.

In another embodiment R^{4a} is isopropyl and R^{4b} is methyl. In another embodiment R^{4a} is isopropyl and R^{4b} is hydrogen.

In another embodiment of the present invention R^{4a} and R^{4b} are joined together forming cyclopentyl.

Another embodiment of the present invention is a compound according to formula (III).



(III)

In another embodiment of the present invention R^{5a} is hydrogen. In another embodiment R^{5a} is deuterium.

In another embodiment of the present invention R^{5b} is hydrogen, methyl, ethyl, or CF_3. Suitably R^{5b} is methyl.

In another embodiment of the present invention R^6 is isopropyl, optionally substituted aryl, optionally substituted pyrazolyl, optionally substituted pyridinyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzo[b][1,4]dioxinyl, or optionally substituted C_{5-10} cycloalkyl. Suitably R^6 is isopropyl, optionally substituted phenyl, optionally substituted naphthyl, pyrazolyl, pyridinyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzo[b][1,4]dioxinyl, or C_{5-10} cycloalkyl, wherein said phenyl and naphthyl are each optionally substituted with one to three substituents each independently selected from the group consisting of: fluoro, chloro, bromo, hydroxy, cyano, methoxy, trifluoromethyl, methyl, t-butyl, phenyl, pyrrolyl, piperidinyl, 4-methylpiperazinyl, morpholinyl, phenoxy, and $-SO_2NH_2$.

In another embodiment of the present invention R^6 is optionally substituted heteroaryl, optionally substituted heterocyclic or optionally substituted C_{5-10} cycloalkyl.

In another embodiment of the present invention R^6 is methyl, C_{5-10} cycloalkyl, optionally substituted phenyl, optionally substituted pyridinyl, optionally substituted pyrimidinyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted triazolyl, optionally substituted pyrazolyl, optionally substituted thiazolyl, optionally substitued 1,3,4-oxadiazolyl, optionally substituted 1,2,4-oxadiazolyl, optionally substitued isoxazolyl, thienyl, oxazolyl, quinolinyl, optionally substituted benzimidazolyl, benzthiazolyl, benzoxazolyl, tetrazolo[1,5-a]pyridinyl, imidazo[2,1-b][1,3,4]thiadiazolyl, optionally substituted piperidinyl, optionally substituted piperazinyl, tetrahydrofuranyl, tetrahydropyranyl, optionally substituted tetrahydro-thiopyran1,1-dioxide, 1H-pyrrolo[2,3-b]pyridinyl, 2,3-dihydro-benzo[1,4]dioxinyl, 5,6,7,8-tetrahydro-[1,2,4]trazolo[4,3-a]pyrazinyl, 4,5,6,7-tetrahydro-benzothiazolyl, or indolizinyl, wherein said phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, triazolyl, pyrazolyl, thiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, isoxazolyl, benzimidazolyl, piperidinyl, piperazinyl, and tetrahydro-thiopyran1,1-dioxide are each optionally substituted with one or two substituents as defined in formula (I). Suitably R^6 is phenyl optionally substituted with one or two substituents. Suitably R^6 is optionally substituted 1,3,4-oxadiazolyl or 1,2,4-optionally substituted oxadiazolyl. Suitably R^6 is pyrimidinyl optionally substituted with one substituent.

In another embodiment R^6 is optionally substituted with one or two substituents each independently selected from the group consisting of: halo; hydroxy; nitro; C_{1-4} alkoxy; C_{1-3} haloalkyl; C_{1-3} haloalkoxy; C_{1-6} alkyl; C_{3-6} cycloalkyl optionally substituted

with one substituent selected from the group consisting of: cyano, C_{1-3} alkyl, and C_{1-3} alkoxy; phenyl optionally substituted with one or two substituents each independently selected from the group consisting of: fluoro, chloro, methyl, cyano, and methoxy; and 5-6 membered heteroaryl (for example, imidazolyl, pyrazolyl, trazolyl, and pyridinyl) optionally substituted with one or two methyl groups.

In another embodiment R^6 is substituted with one $-CH_2R^a$, $-C(O)R^a$, $-NHC(O)R^a$, $-NHC(O)R^b$, $-C(O)NHR^a$, $-C(O)NHR^b$, $-OR^a$, $-NR^aR^b$, $-SO_2NR^bR^b$, $-SO_2R^a$, or $-SO_2R^b$ group. Suitably R^6 is substituted with one $-CH_2R^a$, $-C(O)R^a$, or $-OR^a$ group.

In another embodiment R^6 is phenyl substituted with one fluoro or chloro group and one $-CH_2R^a$, $-C(O)R^a$, or $-C(O)NHR^a$ group wherein the $-CH_2R^a$, $-C(O)R^a$, or $-C(O)NHR^a$ group is in the para position of the phenyl ring. Suitably R^6 is phenyl substituted with one fluoro group and one $-CH_2R^a$, $-C(O)R^a$, or $-C(O)NHR^a$ group wherein the $-CH_2R^a$, $-C(O)R^a$, or $-C(O)NHR^a$ group is in the para position of the phenyl ring. In another embodiment R^6 is phenyl substituted with one $-CH_2R^a$, $-C(O)R^a$, or $-C(O)NHR^a$ group in the para position. In another embodiment R^6 is phenyl substituted by $-CH_2R^a$ in the para position.

In another embodiment R^a is phenyl optionally substituted with one or two substituents each independently selected from the group consisting of fluoro, chloro and bromo.

In another embodiment R^a is an optionally substituted 5-6 membered heteroaryl. Suitably R^a is optionally substituted pyridinyl or optionally substituted pyrimidinyl. Suitably R^a is pyridinyl or pyrimidinyl optionally substituted with one trifluoromethyl.

In another embodiment R^a is C_{5-7} cycloalkyl each of which is optionally substituted with one or two substituents each independently selected from the group consisting of fluoro, hydroxy, methyl, and C_{1-3} haloalkoxy.

In another embodiment R^a is optionally substituted heterocyclic. Suitably R^a is piperidinyl, piperazinyl, morpholinyl, tetrahydropyranyl, tetrahydro-thiopyran1,1-dioxide, 1,4-diazepanyl, 4,7-diaza-spiro[2.5]octanyl, 3,8-diaza-bicyclo[3.2.1]octanyl, 3,8-diaza-bicyclo[4.2.0]octanyl, octahydro-pyrrolo[1,2-a]pyrazinyl, octahydro-pyrido[1,2-a]pyrazinyl, octahydro-pyrrolo[3,4-c]pyrrolyl, and 5,6,7,8-tetrahydro-imidazo[1,2-a]pyrazinyl each of which is optionally substituted with one to three substituents each independently selected

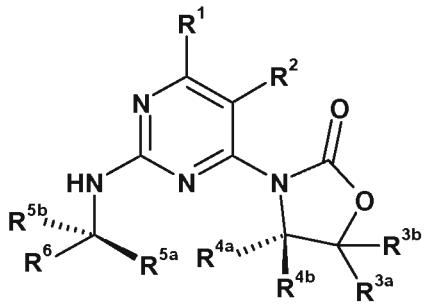
from the group consisting of: hydroxy, fluoro, amino, dimethylamino, C_{1-3} haloalkoxy, C_{1-3} alkyl, and C_{3-5} cycloalkyl. Suitably R^a is piperidinyl, piperazinyl, or morpholinyl each of which is optionally substituted with one to three substituents each independently selected from the group consisting of: hydroxy, fluoro, amino, dimethylamino, C_{1-3} haloalkoxy, C_{1-3} alkyl, and C_{3-5} cycloalkyl.

In another embodiment of the present invention R^{5b} and R^6 are joined together forming an optionally substituted C_{3-7} cycloalkyl group or an optionally substituted group of formula (a).

In another embodiment of the present invention each R^b is independently hydrogen or methyl.

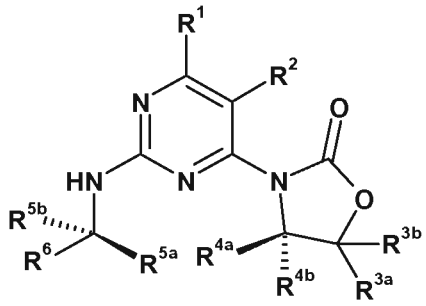
In another embodiment R^1 is hydrogen, R^2 is fluoro and R^{3a}, R^{3b}, R^{4a} and R^{4b} are each hydrogen.

Another embodiment of the present invention is a compound according to formula (IV).



(IV)

Another embodiment of the present invention is a compound according to formula (V):



(V), wherein R^{4a} is phenyl and R^{4b} is hydrogen.

Selected compounds of the present invention include:
(S)-4-isopropy-3-(2-(((S)-1-(4-(2-yl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one;
N-(4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)phenyl)cyclohexanecarboxamide;

(S)-3-(2-(((S)-1-(3-fluoro-4-((4-methylpiperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-4-isopropyl-3-(2-(((S)-1-(4-((3,3,4-trimethylpiperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one;
2-fluoro-N-(4-hydroxy-4-methylcyclohexyl)-4-((S)-1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)arnino)ethyl)benzarnide;
(S)-3-(2-((S)-1-(4-((4-amino-4-methylpiperidin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-((S)-1-(4-((4-(dimethylamino)piperidin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-4-isopropyl-3-(2-((S)-1-(4-((4-methylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;
(S)-4-isopropyl-4-methyl-3-(2-((S)-1-(4-((4-methylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;
(S)-4-isopropyl-3-(2-((S)-1-(6-phenylpyridin-3-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;
(S)-3-(2-((S)-1-(4-benzoylphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-4-isopropyl-3-(2-(((S)-1-(5-phenyl-1,3,4-thiadiazol-2-yl)ethyl) amino) pyrimidin-4-yl)oxazolidin-2-one;
(4S)-4-isopropyl-3-(2-(1-(5-phenylpyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;
3-(5-fluoro-2-((1-(5-(4-fluoro-3-methylphenyl)pyridin-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one;
(S)-4-isopropyl-3-(2-(((S)-1-(1-(3-methoxyphenyl)-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one;
(S)-3-(2-(((S)-1-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-(((S)-1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-4-isopropyl-3-(2-(((S)-1-(3-(m-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one;
(S)-3-(2-(((S)-1-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-((S)-1-(5-(4-fluoro-2-methylphenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-4-Isopropyl-3-{2-[(3-p-tolyl-[1,2,4]oxadiazol-5-ylmethyl)-amino]-pyrimidin-4-yl}-oxazolidin-2-one;

(S)-4-isopropyl-3-(2-((S)-1-(4-(1-methyl-1H-pyrazol-4-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;
(S)-3-(2-((S)-1-(2-fluoro-4-isopropylphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-((S)-1-(4-isobutoxy-3-methylphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-(((S)-1-(4-isobutoxyphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(5-fluoro-2-(((S)-1-(4-isobutoxyphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
2-fluoro-N-(*trans*-4-hydroxycyclohexyl)-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide;
(S)-3-(5-fluoro-2-((S)-1-(3-fluoro-4-(piperidine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
N-cyclohexyl-2-fluoro-4-((S)-1-(5-fluoro-4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide;
N-cyclohexyl-2-fluoro-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide; and
(S)-3-(5-fluoro-2-((S)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

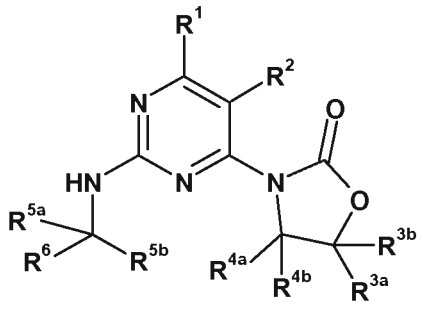
Selected compounds of the present invention include:
(S)-3-(2-(((S)-1-(3-fluoro-4-((3,3,4-trimethylpiperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-(((S)-1-(4-((4,4-difluoropiperidin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(5-fluoro-2-(1-(4-phenoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;
(S)-3-(2-((S)-1-(4-(4-fluorophenoxy)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-((S)-1-(4-(((2S,6R)-2,6-dimethylmorpholino)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-(((S)-1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-(((S)-1-(5-(4-chlorophenyl)-1,2,4-oxadiazol-3-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-((S)-1-(5-(4-fluoro-3-methylphenyl)pyridin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-((S)-1-(5-(4-fluorophenoxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-((S)-1-(5-(4-fluorophenoxy)pyrazin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-4-isopropyl-3-(2-((S)-1-(5-(3-(trifluoromethyl)phenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one; and
(S)-3-(2-((S)-1-(5-(4-fluoro-3-methylphenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

Selected compounds of the present invention include:
(S)-3-(2-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethylamino)-5-fluoropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one;
(S)-3-(6-chloro-2-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;
(S)-3-(2-((S)-1-(2-fluoro-4-(1-methylcyclopropyl) phenyl) ethylamino) pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-((S)-1-(2-fluoro -4-(trifluoromethyl) phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
2-chloro-N-cyclopentyl-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide;
(S)-3-(2-((S)-1-(4-((3,3-difluoropiperidin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-((S)-1-(4-(4,7-diazaspiro[2.5]octan-4-ylmethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-((S)-1-(4-((4-acetylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(2-(((S)-1-(4-isobutoxyphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;
(S)-3-(5-fluoro-2-(((S)-1-(4-isobutoxyphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one; and
2-fluoro-N-(trans-4-hydroxycyclohexyl)-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide.

Enumerated Embodiments

Embodiment 1. A compound of formula (I)



(I)

wherein:

each R^1 and R^2 is independently hydrogen, deuterium, halo, hydroxyl, NH_2, aryl, heteroaryl, or optionally substituted C_{1-4} alkyl,

wherein said C_{1-4} alkyl is optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, and NH_2;

R^{3a} is hydrogen, deuterium, C_{1-6} alkyl, phenyl, or benzyl and

R^{3b} is hydrogen, deuterium, or C_{1-6} alkyl; or

R^{3a} and R^{3b} are joined together forming an optionally substituted 3-7 membered cycloalkyl ring or an optionally substituted 4-7 membered heterocyclic ring,

wherein said cycloalkyl and heterocyclic rings are each optionally substituted with one or two substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl;

R^{4a} is hydrogen, C_{1-6} alkyl, optionally substituted phenyl, optionally substituted benzyl, optionally substituted heteroaryl, or methylene-dibenzene,

wherein said phenyl, benzyl, and heteroaryl rings are optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, $COOR^b$, SO_2R^b, $NHC(O)R^b$, and NR^bR^b and

R^{4b} is hydrogen, deuterium, or C_{1-3} alkyl; or

R^{4a} and R^{4b} are joined together forming an optionally substituted 3-7 membered cycloalkyl ring or an optionally substituted 4-7 membered heterocyclic ring,

wherein said cycloalkyl and heterocyclic rings are optionally substituted with one or two substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl,

provided that only one of R^{3a} and R^{3b} and R^{4a} and R^{4b} are joined together forming a ring;

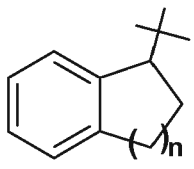
R^{5a} is hydrogen or deuterium;

R^{5b} is hydrogen, deuterium, methyl, ethyl, CD_3, CF_3, CH_2F, or CHF_2 and

R^6 is optionally substituted C_{1-6} alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclic, or optionally substituted C_{5-10} cycloalkyl,

wherein said C_{1-6} alkyl is optionally substituted with one substituent selected from the group consisting of hydroxyl, C_{1-3} alkoxy and $-OR^a$;

wherein said aryl, heteroaryl, heterocyclic and C_{5-10} cycloalkyl are optionally substituted with one to three substituents each independently selected from the group consisting of: halo; hydroxyl; cyano; nitro; C_{1-3} alkoxy; C_{1-3} haloalkyl; C_{1-3} haloalkoxy; C_{1-6} alkyl; C_{3-6} cycloalkyl; phenyl optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, $COOR^b$, SO_2R^b, $NHC(O)R^b$, and NR^bR^b; 5-6 membered heteroaryl; 5-6 membered heterocyclic optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl; $-CH_2R^a$; $-OR^a$; $-C(O)R^a$; $-NR^aR^b$; $-COOR^a$; $-SO_2R^a$; $NHC(O)R^a$; and $-SO_2NR^bR^b$; or

R^{5b} and R^6 are joined together forming an optionally substituted C_{3-7} cycloalkyl group or an optionally substituted group of formula (a):  (a),

wherein n is 1, 2, or 3 and

said C_{3-7} cycloalkyl and group of formula (a) are optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6}

cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, benzyloxy, $COOR^b$, SO_2R^b, $NHC(O)R^b$, and NR^bR^b;

each R^a is independently optionally substituted phenyl, optionally substituted heteroaryl, or optionally substituted 4-7 membered heterocyclic,

wherein said phenyl and heteroaryl are optionally substituted with one to three substituents each independently selected from the group consisting of halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, and C_{1-3} alkyl,

wherein said 4-7 membered heterocyclic is optionally substituted with one to three substituents each independently selected from the group consisting of halo, hydroxyl, oxo, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, and C_{1-3} alkyl; and

each R^b is independently hydrogen or C_{1-6} alkyl; or a pharmaceutically acceptabble salt thereof.

Embodiment 2. The compound according to embodiment 1 wherein R^2 is hydrogen; or a pharmaceutically acceptable salt thereof.

Embodiment 3. The compound according to embodiment 2 wherein R^1 is hydrogen, halo, or optionally substituted C_{1-4} alkyl; or a pharmaceutically acceptable salt thereof.

Embodiment 4. The compound according to embodiment 3 wherein R^1 is hydrogen, fluoro, chloro, or methyl; or a pharmaceutically acceptable salt thereof.

Embodiment 5. The compound according to embodiment 4 wherein R^{3a} is hydrogen, C_{1-6} alkyl, phenyl, or benzyl and R^{3b} is hydrogen or C_{1-6} alkyl; or a pharmaceutically acceptable salt thereof.

Embodiment 6. The compound according to embodiment 5 wherein R^{3b} is hydrogen or methyl; or a pharmaceutically acceptable salt thereof.

Embodiment 7. The compound according to embodiment 6 wherein R^{3a} is hydrogen, methyl, or phenyl; or a pharmaceutically acceptable salt thereof.

Embodiment 8. The compound according to embodiment 7 wherein R^{4a} is hydrogen, C_{1-6} alkyl, optionally substituted phenyl, optionally substituted benzyl, optionally substituted heteroaryl, or methylene-dibenzene,

wherein said phenyl, benzyl, and heteroaryl rings are optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, $COOR^b$, SO_2R^b, $NHC(O)R^b$, and NR^bR^b and

R^{4b} is hydrogen or C_{1-3} alkyl; or a pharmaceutically acceptable salt thereof.

Embodiment 9. The compound according to embodiment 8 wherein R^{4b} is hydrogen or methyl; or a pharmaceutically acceptable salt thereof.

Embodiment 10. The compound according to embodiment 9 wherein R^{4a} is hydrogen, C_{1-4} alkyl, optionally substituted phenyl, optionally substituted benzyl, optionally substituted heteroaryl, or methylene-dibenzene; or a pharmaceutically acceptable salt thereof.

Embodiment 11. The compound according to embodiment 10 wherein R^{4a} is hydrogen, methyl, isopropyl, isobutyl, t-butyl, phenyl, 4-methoxyphenyl, 4-fluorophenyl, benzyl, or methylene-dibenzene; or a pharmaceutically acceptable salt thereof.

Embodiment 12. The compound according to embodiment 11 wherein R^{5a} is H; or a pharmaceutically acceptable salt thereof.

Embodiment 13. The compound according to embodiment 12 wherein R^{5b} is hydrogen, methyl, ethyl, or CF_3.

Embodiment 14. The compound according to embodiment 13 wherein R^6 is isopropyl, optionally substituted aryl, optionally substituted pyrazolyl, optionally substituted pyridinyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzo[b][1,4]dioxinyl, or optionally substituted C_{5-10} cycloalkyl; or a pharmaceutically acceptable salt thereof.

Embodiment 15. A pharmaceutical composition comprising a compound according to embodiment 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

Embodiment 16. A method for the treatment of a disease or disorder associated with a mutant IDH protein having a neomorphic activity comprising administration of a therapeutically effective amount of a compound according to embodiment 1, or a pharmaceutically acceptable salt thereof, to subject in need of thereof.

Embodiment 17. A method for the treatment of a disease or disorder associated with a mutant IDH protein having a neomorphic activity comprising administration of a therapeutically effective amount of a compound according to embodiment 1, or a pharmaceutically acceptable salt thereof, and another therapeutic agent to subject in need of thereof.

General Synthetic Procedures

The compounds of the present invention may be made by a variety of methods, including standard chemistry. Suitable synthetic routes are depicted in the Schemes given below.

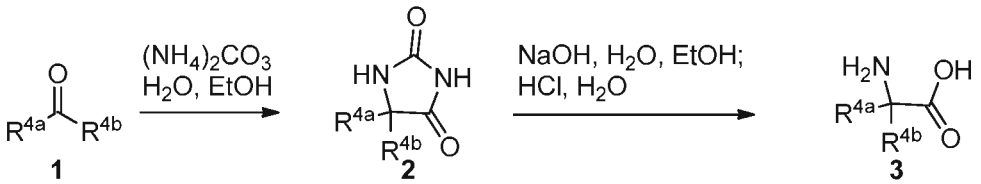
The compounds of formula (I) may be prepared by methods known in the art of organic synthesis as set forth in part by the following synthetic schemes. In the schemes described below, it is well understood that protecting groups for sensitive or reactive groups are employed where necessary in accordance with general principles or chemistry. Protecting groups are manipulated according to standard methods of organic synthesis (T. W. Greene and P. G. M. Wuts, "Protective Groups in Organic Synthesis", Third edition, Wiley, New York 1999). These groups are removed at a convenient stage of the compound synthesis using methods that are readily apparent to those skilled in the art. The selection processes, as well as the reaction conditions and order of their execution, shall be consistent with the preparation of compounds of formula (I).

Those skilled in the art will recognize if a stereocenter exists in the compounds of formula (I). Accordingly, the present invention includes both possible stereoisomers and includes not only racemic compounds but the individual enantiomers and/or diastereomers as well. When a compound is desired as a single enantiomer or diastereomer, it may be obtained by stereospecific synthesis or by resolution of the final product or any convenient intermediate. Resolution of the final product, an intermediate, or a starting material may be effected by any suitable method known in the art. See, for

example, “Stereochemistry of Organic Compounds” by E. L. Eliel, S. H. Wilen, and L. N. Mander (Wiley-Interscience, 1994).

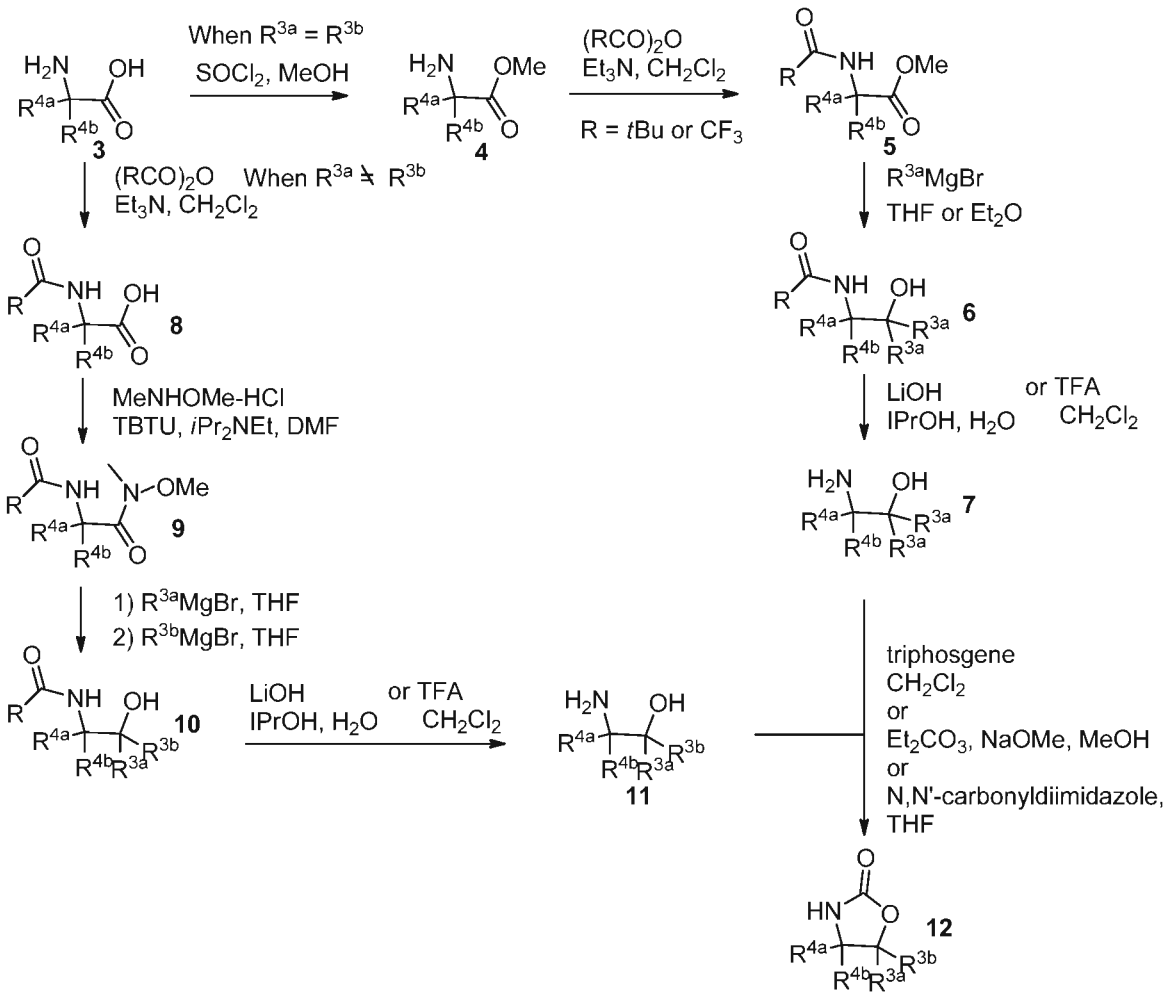
The compounds described herein may be made from commercially available starting materials or synthesized using known organic, inorganic, and/or enzymatic processes.

Scheme 1.



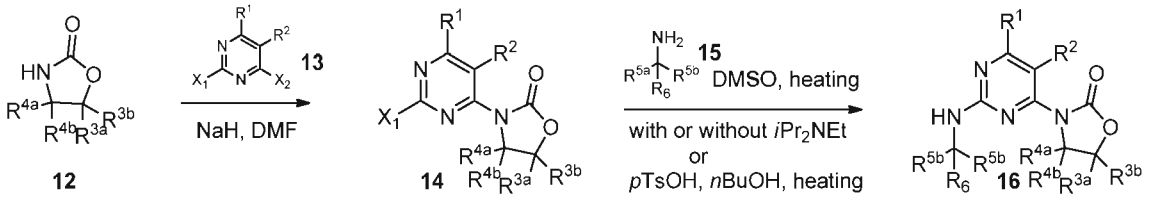
Non-commercial aminoacids can be prepared following the procedures of Scheme 1. Conversion of ketone **1** to the corresponding imidazolidine-2,4-dione **2** followed by hydrolysis provides aminoacid **3**.

Scheme 2.



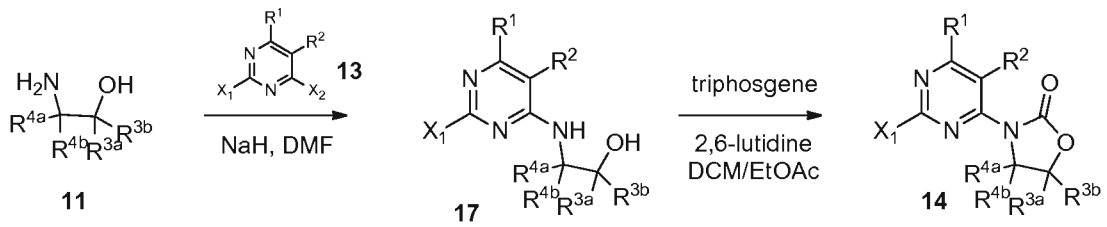
When aminoalcohol, precursor of oxazolidinone, is not commercially available, it can be prepared from aminoacid **3** following the procedures of Scheme 2. When $R^{3a} = R^{3b}$, protected aminoester **5** is treated with an appropriate Grignard reagent to give protected aminoalcohol **6** which goes through basic or acidic deprotection step. When $R^{3a} \neq R^{3b}$, protected aminoacid **8** is converted into Weinreb amide **9** which is treated with different Grignard reagents sequentially to provide protected aminoalcohol **10**. Either basic or acidic deprotection of **10** gives **11**. Insertion of CO unit into **7** or **11** to provide oxazolidinone **12** is accomplished with several reagents, including (but not limited to) triphosgene, Et_2CO_3 or N-N'-darbonyldiimidazole, as shown in Scheme 2.

Scheme 3.



Oxazolidinone **12** is coupled with dihalogen-pyrimidine **13** in the presence of NaH and the resulting **14** is treated with primary amine **15** under several different reaction conditions as shown in Scheme 3 to provide **16**.

Scheme 4.



Alternately intermediate **14** can be prepared by coupling the amino alcohol **11** and dihalogen-pyrimidine **13** in the presence of a base such as diisopropylethyl amine resulting in intermediate **17** which can be treated with triphosgene in the presence of a base such as 2,6-lutidine resulting in intermediate **14**.

Methods of Use

The compounds of the present invention are inhibitors of a mutant IDH protein having a neomorphic activity and are therefore useful in the treatment of diseases or disorders associated with such proteins including, but not limited to, cell proliferation disorders, such as cancer.

Examples of a mutant IDH protein having a neomorphic activity are mutant IDH1 and mutant IDH2. A neomorphic activity associated with mutant IDH1 and mutant IDH2 is the ability to produce 2-hydroxyglutarate (2-HG neomorphic activity), specifically R-2-HG (R-2-HG neomorphic activity). Mutations in IDH1 associated with 2-HG neomorphic activity, specifically R-2-HG neomorphic activity, include mutations at residues 97, 100, and 132, e.g. G97D, R100Q, R132H, R132C, R132S, R132G, R132L, and R132V. Mutations in IDH2 associated with 2-HG neoactivity, specifically R-2-HG neomorphic

activity, include mutations at residues 140 and 172, e.g. R140Q, R140G, R172K, R172M, R172S, R172G, and R172W.

Cell-proliferation disorders associated with a mutant IDH protein having a neomorphic activity include, but are not limited to, cancer. Examples of such cancers include Acute Lymphoblastic Leukemia, Adult; Acute Lymphoblastic Leukemia, Childhood; Acute Myeloid Leukemia, Adult; Adrenocortical Carcinoma; Adrenocortical Carcinoma, Childhood; AIDS-Related Lymphoma; AIDS-Related Malignancies; Anal Cancer; Astrocytoma, Childhood Cerebellar; Astrocytoma, Childhood Cerebral; Bile Duct Cancer, Extrahepatic; Bladder Cancer; Bladder Cancer, Childhood; Bone Cancer, Osteosarcoma/Malignant Fibrous Histiocytoma; Brain Stem Glioma, Childhood; Brain Tumor, Adult; Brain Tumor, Brain Stem Glioma, Childhood; Brain Tumor, Cerebellar Astrocytoma, Childhood; Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood; Brain Tumor, Ependymoma, Childhood; Brain Tumor, Medulloblastoma, Childhood; Brain Tumor, Supratentorial Primitive Neuroectodermal Tumors, Childhood; Brain Tumor, Visual Pathway and Hypothalamic Glioma, Childhood; Brain Tumor, Childhood (Other); Breast Cancer; Breast Cancer and Pregnancy; Breast Cancer, Childhood; Breast Cancer, Male; Bronchial Adenomas/Carcinoids, Childhood; Carcinoid Tumor, Childhood; Carcinoid Tumor, Gastrointestinal; Carcinoma, Adrenocortical; Carcinoma, Islet Cell; Carcinoma of Unknown Primaiy; Central Nervous System Lymphoma, Primary; Cerebellar Astrocytoma, Childhood; Cerebral Astrocytoma/Malignant Glioma, Childhood; Cervical Cancer; Childhood Cancers; Chronic Lymphocytic Leukemia; Chronic Myelogenous Leukemia; Chronic Myeloproliferative Disorders; Clear Cell Sarcoma of Tendon Sheaths; Colon Cancer; Colorectal Cancer, Childhood; Cutaneous T-Cell Lymphoma; Endometrial Cancer; Ependymoma, Childhood; Epithelial Cancer, Ovarian; Esophageal Cancer; Esophageal Cancer, Childhood; Ewing's Family of Tumors; Extracranial Germ Cell Tumor, Childhood; Extragonadal Germ Cell Tumor; Extrahepatic Bile Duct Cancer; Eye Cancer, Intraocular Melanoma; Eye Cancer, Retinoblastoma; Gallbladder Cancer; Gastric (Stomach) Cancer; Gastric (Stomach) Cancer, Childhood; Gastrointestinal Carcinoid Tumor; Germ Cell Tumor, Extracranial, Childhood; Germ Cell Tumor, Extragonadal; Germ Cell Tumor, Ovarian; Gestational Trophoblastic Tumor; Glioma, Childhood Brain Stem; Glioma, Childhood Visual Pathway and Hypothalamic; Hairy Cell Leukemia; Head and Neck Cancer; Hepatocellular (Liver) Cancer, Adult (Primary); Hepatocellular (Liver) Cancer, Childhood (Primary); Hodgkin's Lymphoma, Adult; Hodgkin's Lymphoma, Childhood; Hodgkin's Lymphoma During Pregnancy; Hypopharyngeal Cancer; Hypothalamic and Visual Pathway Glioma, Childhood; Intraocular Melanoma; Islet Cell Carcinoma (Endocrine Pancreas); Kaposi's Sarcoma; Kidney Cancer; Laryngeal Cancer; Laryngeal

Cancer, Childhood; Leukemia, Acute Lymphoblastic, Adult; Leukemia, Acute Lymphoblastic, Childhood; Leukemia, Acute Myeloid, Adult; Leukemia, Acute Myeloid, Childhood; Leukemia, Chronic Lymphocytic; Leukemia, Chronic Myelogenous; Leukemia, Hairy Cell; Lip and Oral Cavity Cancer; Liver Cancer, Adult (Primary); Liver Cancer, Childhood (Primary); Lung Cancer, Non-Small Cell; Lung Cancer, Small Cell; Lymphoblastic Leukemia, Adult Acute; Lymphoblastic Leukemia, Childhood Acute; Lymphocytic Leukemia, Chronic; Lymphoma, AIDS- Related; Lymphoma, Central Nervous System (Primary); Lymphoma, Cutaneous T-Cell; Lymphoma, Hodgkin's, Adult; Lymphoma, Hodgkin's, Childhood; Lymphoma, Hodgkin's During Pregnancy;Lymphoma, Non-Hodgkin' s, Adult; Lymphoma, Non- Hodgkin's, Childhood; Lymphoma, Non-Hodgkin's During Pregnancy; Lymphoma, Primary Central Nervous System; Macroglobulinemia, Waldenstrom's; Male Breast Cancer; Malignant Mesothelioma, Adult; Malignant Mesothelioma, Childhood; Malignant Thymoma; Medulloblastoma, Childhood; Melanoma; Melanoma, Intraocular; Merkel Cell Carcinoma; Mesothelioma, Malignant; Metastatic Squamous Neck Cancer with Occult Primary; Multiple Endocrine Neoplasia Syndrome, Childhood; Multiple Myeloma/Plasma Cell Neoplasm; Mycosis Fungoides; Myelodysplastic Syndromes; Myelogenous Leukemia, Chronic; Myeloid Leukemia, Childhood Acute; Myeloma, Multiple; Myeloproliferative Disorders, Chronic; Nasal Cavity and Paranasal Sinus Cancer; Nasopharyngeal Cancer; Nasopharyngeal Cancer, Childhood; Neuroblastoma; Non-Hodgkin's Lymphoma, Adult; Non-Hodgkin's Lymphoma, Childhood; Non- Hodgkin's Lymphoma During Pregnancy; Non-Small Cell Lung Cancer; Oral Cancer, Childhood; Oral Cavity and Lip Cancer; Oropharyngeal Cancer; steosarcoma/Malignant Fibrous Histiocytoma of Bone; Ovarian Cancer, Childhood; Ovarian Epithelial Cancer; Ovarian Germ Cell Tumor; Ovarian Low Malignant Potential Tumor; Pancreatic Cancer; Pancreatic Cancer, Childhood; Pancreatic Cancer, Islet Cell; Paranasal Sinus and Nasal Cavity Cancer; Parathyroid Cancer; Penile Cancer; Pheochromocytoma; Pineal and Supratentorial Primitive Neuroectodermal Tumors, Childhood; Pituitary Tumor; Plasma Cell Neoplasm/Multiple Myeloma; Pleuropulmonary Blastoma; Pregnancy and Breast Cancer; Pregnancy and Hodgkin's Lymphoma; Pregnancy and Non-Hodgkin's Lymphoma; Primary Central Nervous System Lymphoma; Primary Liver Cancer, Adult; Primary Liver Cancer, Childhood; Prostate Cancer; Rectal Cancer; Renal Cell (Kidney) Cancer; Renal Cell Cancer, Childhood; Renal Pelvis and Ureter, Transitional Cell Cancer; Retinoblastoma; Rhabdomyosarcoma, Childhood; Salivary Gland Cancer; Salivary Gland Cancer, Childhood; Sarcoma, Ewing's Family of Tumors; Sarcoma, Kaposi's; Sarcoma (Osteosarcoma)/Malignant Fibrous Histiocytoma of Bone; Sarcoma, Rhabdomyosarcoma, Childhood; Sarcoma, Soft Tissue, Adult; Sarcoma, Soft Tissue, Childhood; Sezary Syndrome; Skin Cancer; Skin Cancer,

Childhood; Skin Cancer (Melanoma); Skin Carcinoma, Merkel Cell; Small Cell Lung Cancer; Small Intestine Cancer; Soft Tissue Sarcoma, Adult; Soft Tissue Sarcoma, Childhood; Squamous Neck Cancer with Occult Primary, Metastatic; Stomach (Gastric) Cancer; Stomach (Gastric) Cancer, Childhood; Supratentorial Primitive Neuroectodermal Tumors, Childhood; T- Cell Lymphoma, Cutaneous; Testicular Cancer; Thymoma, Childhood; Thymoma, Malignant; Thyroid Cancer; Thyroid Cancer, Childhood; Transitional Cell Cancer of the Renal Pelvis and Ureter; Trophoblastic Tumor, Gestational; Unknown Primary Site, Cancer of, Childhood; Unusual Cancers of Childhood; Ureter and Renal Pelvis, Transitional Cell Cancer; Urethral Cancer; Uterine Sarcoma; Vaginal Cancer; Visual Pathway and Hypothalamic Glioma, Childhood; Vulvar Cancer; Waldenstrom's Macro globulinemia; and Wilms' Tumor.

In another embodiment the cancer associated with a mutant IDH protein having a neomorphic acitvity is brain cancer, such as astrocytic tumor (e.g., pilocytic astrocytoma, subependymal giant-cell astrocytoma, diffuse astrocytoma, pleomorphic xanthoastrocytoma, anaplastic astrocytoma, astrocytoma, giant cell glioblastoma, glioblastoma, secondary glioblastoma, primary adult glioblastoma, and primary pediatric glioblastoma); oligodendroglial tumor (e.g., oligodendroglioma, and anaplastic oligodendroglioma); oligoastrocytic tumor (e.g., oligoastrocytoma, and anaplastic oligoastrocytoma); ependymoma (e.g., myxopapillary ependymoma, and anaplastic ependymoma); medulloblastoma; primitive neuroectodermal tumor, schwannoma, meningioma, meatypical meningioma, anaplastic meningioma; and pituitary adenoma. In another embodiment, the brain cancer is glioma, glioblastoma multiforme, paraganglioma, or suprantentorial primordial neuroectodermal tumors (sPNET).

In another embodiment the cancer associated with a mutant IDH protein having a neomorphic acitvity is leukemia, such as acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), chronic myelogenous leukemia (CML), myeloproliferative neoplasm (MPN), MDS.MPN including chronic myelomonocytic leukemia, post MDS AML, post MPN AML, post MDS/MPN AML, del(5q)-associated high risk MDS or AML, blast-phase chronic myelogenous leukemia, angioimmunoblastic lymphoma and acute lymphoblastic leukemia.

In another embodiment the cancer associated with a mutant IDH protein having a neomorphic activity is skin cancer, including melanoma.

In another embodiment the cancer associated with a mutant IDH protein having a neomorphic activity is prostate cancer, thyroid cancer, colon cancer, or lung cancer.

In another embodiment the cancer associated with a mutant IDH protein having a neomorphic activity is sarcoma, including central chondrosarcoma, central and periosteal chondroma, and fibrosarcoma.

In another embodiment the cancer associated with a mutant IDH protein having a neomorphic activity is cholangiocarcinoma.

Another disease or disorder associated with a mutant IDH protein having R-2-HG neomorphic activity is D-2-hydroxyglutaric aciduria.

Another disease or disorder associated with a mutant IDH protein having R-2-HG neomorphic activity is Diller disease and Mafucci syndrome.

As used herein the term “neomorphic activity” refers to a gain of novel activity of a protein that the wild-type protein does not have or does not exhibit to a significant degree. For example, a neomorphic activity associated with a mutant form of IDH1 and IDH2 is the ability to reduce alpha-ketoglutarate to 2-hydroxyglutarate (i.e. 2-HG, specifically R-2-HG). The wild type form of IDH1 and IDH2 does not have the ability to reduce alpha-ketoglutarate to 2-hydroxyglutarate (i.e. 2-HG, specifically R-2-HG) or if it does have this ability, it does not produce significant (i.e. harmful or disease causing) amounts of 2-HG.

As used herein, the term “subject” refers to an animal. Typically the animal is a mammal. A subject also refers to for example, primates (*e.g.*, humans, male or female), cows, sheep, goats, horses, dogs, cats, rabbits, rats, mice, fish, birds and the like. In certain embodiments, the subject is a primate. In yet other embodiments, the subject is a human.

As used herein, the term “therapeutically effective amount” in reference to a compound of the invention means an amount of the compound sufficient to treat the subject’s disease or condition, but low enough to avoid serious sides effects (at a reasonable benefit/risk ratio) within the scope of sound medical judgment. A therapeutically effective amount of a compound will vary with the particular compound chosen (e.g. consider the potency, efficacy, and half-life of the compound); the route of administration chosen; the condition being treated; the severity of the condition being treated; the age, size, weight, and physical condition of the subject being treated; the medical history of the subject being treated; the duration of the treatment; the nature of the concurrent therapy; the desired therapeutic effect; and like factors and can be routinely determined by the skilled artisan.

As used herein, the term “treat”, “treating" or "treatment" of any disease or disorder refers in one embodiment, to ameliorating the disease or disorder (i.e., slowing or arresting or reducing the development of the disease or at least one of the clinical symptoms thereof). In another embodiment “treat”, "treating" or "treatment" refers to alleviating or ameliorating at least one physical parameter including those which may not be discernible by the patient. In yet another embodiment, “treat”, "treating" or "treatment" refers to modulating the disease or disorder, either physically, (*e.g.*, stabilization of a

discernible symptom), physiologically, (*e.g.*, stabilization of a physical parameter), or both. In yet another embodiment, “treat”, "treating" or "treatment" refers to preventing or delaying the onset or development or progression of the disease or disorder.

As used herein, a subject is “in need of” a treatment if such subject would benefit biologically, medically or in quality of life from such treatment.

The compounds of the present invention may be administered by any suitable route including oral and parenteral administration. Parenteral administration is typically by injection or infusion and includes intravenous, intramuscular, and subcontaneous injection or infusion.

The compounds of the invention may be administered once or according to a dosing regimen wherein a number of doses are administered at varying intervals of time for a given period of time. For example, doses may be administered one, two, three, or four times per day. Doses may be administered until the desired therapeutic effect is achieved or indefinitely to maintain the desired therapeutic effect. Suitable dosing regimens for a compound of the invention depend on the pharmacokinetic properties of that compound, such as absorption, distribution and half life which can be determined by the skilled artisan. In addition, suitable dosing regimens, including the duration such regimens are administered, for a compound of the invention depend on the disease or condition being treated, the severity of the disease or condition, the age and physical condition of the subject being treated, the medical history of the subject being treated, the nature of concurrent therapy, the desired therapeutic effect, and like factors within the knowledge and expertise of the skilled artisan. It will be further understood by such skilled artisans that suitable dosing regimens may require adjustment given an individual subject’s response to the dosing regimen or over time as the individual subject needs change. Typical daily dosages may vary depending upon the particular route of administration chosen. Typical daily dosages for oral administration, to a human weighing approximately 70kg would range from about 5mg to about 500mg of a compound of formula (I).

One embodiment of the present invention provides for a method of treating a disease or disorder associated with a mutant form of IDH having a neomorphic activity comprising administration of a therapeutically effective amount of a compound of formula (I) to a subject in need of treatment thereof. In one embodiment, the disease or disorder associated with a mutant form of IDH having a neomorphic activity is a cell proliferation disorder. In another embodiment, the cell proliferation disorder is cancer. In another embodiment, the cancer is a cancer associated with mutant IDH1 having 2-HG neomorphic activity or mutant IDH2 having 2-HG neomorphic activity. In another embodiment the neomorphic activity is R-2-HG neomorphic activity. In another

embodiment the cancer is associated with mutant IDH1 having 2-HG or R-2-HG neomorphic activity having a mutation at residues 97, 100, or 132, such as G97D, R100Q, R132H, R132C, R132S, R132G, R132L, and R132V. In another embodiment the cancer is associated with mutant IDH2 having 2-HG or R-2-HG neomorphic activity having a mutation at residues 140 or 172, e.g. R140Q, R140G, R172K, R172M, R172S, R172G, and R172W. In another embodiment the cancer is brain cancer, leukemia, skin cancer, prostate cancer, thyroid cancer, colon cancer, lung cancer or sarcoma. In another embodiment the cancer is glioma, glioblastoma multiforme, paraganglioma, suprantentorial primordial neuroectodermal tumors, acute myeloid leukemia, myelodysplastic syndrome, chronic myelogenous leukemia, melanoma, prostate, thyroid, colon, lung, central chondrosarcoma, central and periosteal chondroma tumors, fibrosarcoma, and cholangiocarcinoma.

Another embodiment of the present invention provides for a method of treating a disease or disorder associated with a mutant form of IDH having R-2-HG neomorphic activity comprising administration of a therapeutically effective amount of a compound according to formula (I) to a subject in need thereof wherein the disease or disorder is D-2-hydroxyglutaric aciduria, Ollier Disease, or Mafucci Syndrome.

Another embodiment of the present invention provides for the use of a compound of formula (I) in therapy. In a further embodiment the therapy is a disease or disorder associated with a mutant form of IDH having a neomorphic activity. In another embodiment the therapy is a cell proliferation disorder associated with a mutant form of IDH having a neomorphic activity. In another embodiment the therapy is cancer. In another embodiment the therapy is a cancer associated with a mutant IDH protein having a neomorphic activity, such as mutant IDH1 having 2-HG neomorphic activity or mutant IDH2 having 2-HG neomorphic activity. In another embodiment the neomorphic activity is R-2-HG neomorphic activity. In another embodiment the cancer is associated with mutant IDH1 having 2-HG or R-2-HG neomorphic activity having a mutation at residues 97, 100, or 132, such as G97D, R100Q, R132H, R132C, R132S, R132G, R132L, and R132V. In another embodiment the cancer is associated with mutant IDH2 having 2-HG or R-2-HG neomorphic activity having a mutation at residue at residues R140 or 172, e.g. R140Q, R140G, R172K, R172M, R172S, R172G, and R172W. In another embodiment the cancer is brain cancer, leukemia, skin cancer, prostate cancer, thyroid cancer, colon cancer, lung cancer or sarcoma. In another embodiment the cancer is glioma, glioblastoma multiforme, paraganglioma, suprantentorial primordial neuroectodermal tumors, acute myeloid leukemia, myelodysplastic syndrome, chronic myelogenous leukemia, melanoma, prostate, thyroid, colon, lung, central

chondrosarcoma, central and periosteal chondroma tumors, fibrosarcoma, and cholangiocarcinoma.

Another embodiment of the present invention provides for the use of a compound of formula (I) in therapy wherein the therapy is D-2-hydroxyglutaric aciduria, Ollier Disease, or Mafucci Syndrome.

Another embodiment of the present invention provides for the use of a compound according to formula (I) in the manufacture of a medicament for the treatment of disease or disorder associated with a mutant form of IDH having a neomorphic activity. In one embodiment the disease or disorder associated with a mutant form of IDH having a neomorphic activity is a cell proliferation disorder. In another embodiment, the cell proliferation disorder is cancer. In another embodiment the cancer is a cancer associated with a mutant IDH protein having a neomorphic activity, such as mutant IDH1 having 2-HG neomorphic activity or mutant IDH2 having 2-HG neomorphic activity. In another embodiment the neomorphic activity is R-2-HG neomorphic activity. In another embodiment the cancer is associated with mutant IDH1 having 2-HG or R-2-HG neomorphic activity having a mutation at residues 97, 100, or 132, such as G97D, R100Q, R132H, R132C, R132S, R132G, R132L, and R132V. In another embodiment the cancer is associated with mutant IDH2 having 2-HG or R-2-HG neomorphic activity having a mutation at residue at residues 140 or 172, e.g. R140Q, R140G, R172K, R172M, R172S, R172G, and R172W. In another embodiment the cancer is brain cancer, leukemia, skin cancer, prostate cancer, thyroid cancer, colon cancer, lung cancer or sarcoma. In another embodiment the cancer is glioma, glioblastoma multiforme, paraganglioma, suprantentorial primordial neuroectodermal tumors, acute myeloid leukemia, myelodysplastic syndrome, chronic myelogenous leukemia, melanoma, prostate, thyroid, colon, lung, central chondrosarcoma, central and periosteal chondroma tumors, fibrosarcoma, and cholangiocarcinoma.

Another embodiment of the present invention provides for the use of a compound according to formula (I) in the manufacture of a medicament for the treatment of disease or disorder associated with a mutant form of IDH having R-2-HG neomorphic activity wherein the disease or disorder is D-2-hydroxyglutaric aciduria, Ollier Disease, or Mafucci Syndrome.

Compositions

In another aspect, the present invention provides a pharmaceutical composition comprising a compound of formula (I) and a pharmaceutically acceptable carrier or excipient.

The pharmaceutical compositions of the invention may be prepared and packaged in bulk form wherein a therapeutically effective amount of a compound of the invention can be extracted and then given to a subject, such as with powders or syrups. Alternatively, the pharmaceutical compositions of the invention may be prepared and packaged in unit dosage form wherein each physically discrete unit contains a therapeutically effective amount of a compound of the invention. When prepared in unit dosage form, the pharmaceutical compositions of the invention typically contain from about 5mg to 500mg of a compound of formula (I).

As used herein the term "pharmaceutically acceptable carrier or excipient" means a pharmaceutically acceptable material, composition or vehicle that, for example, are involved in giving form or consistency to the pharmaceutical composition. Each excipient must be compatible with the other ingredients of the pharmaceutical composition when commingled such that interactions which would substantially reduce the efficacy of the compound of the invention when administered to a subject and interactions which would result in pharmaceutical compositions that are not pharmaceutically acceptable are avoided. In addition, each excipient must, of course, be of sufficiently high purity to render it pharmaceutically acceptable.

The compound of the invention and the pharmaceutically acceptable carrier or excipient(s) will typically be formulated into a dosage form adapted for administration to the subject by the desired route of administration. For example, dosage forms include those adapted for (1) oral administration such as tablets, capsules, caplets, pills, troches, powders, syrups, elixirs, suspensions, solutions, emulsions, sachets, and cachets; and (2) parenteral administration such as sterile solutions, suspensions, and powders for reconstitution. Suitable pharmaceutically acceptable excipients will vary depending upon the particular dosage form chosen. In addition, suitable pharmaceutically acceptable excipients may be chosen for a particular function that they may serve in the composition. For example, certain pharmaceutically acceptable excipients may be chosen for their ability to facilitate the production of uniform dosage forms. Certain pharmaceutically acceptable excipients may be chosen for their ability to facilitate the production of stable dosage forms. Certain pharmaceutically acceptable excipients may be chosen for their ability to facilitate the carrying or transporting of the compound or compounds of the invention, once administered to the subject, from one organ or portion of the body to another organ or another portion of the body. Certain pharmaceutically acceptable excipients may be chosen for their ability to enhance patient compliance.

Suitable pharmaceutically acceptable excipients include the following types of excipients: diluents, lubricants, binders, disintegrants, fillers, glidants, granulating agents, coating agents, wetting agents, solvents, co-solvents, suspending agents, emulsifiers,

sweeteners, flavoring agents, flavor masking agents, coloring agents, anti-caking agents, hemectants, chelating agents, plasticizers, viscosity increasing agents, antioxidants, preservatives, stabilizers, surfactants, and buffering agents.

Skilled artisans possess the knowledge and skill in the art to enable them to select suitable pharmaceutically acceptable carriers and excipients in appropriate amounts for the use in the invention. In addition, there are a number of resources available to the skilled artisan, which describe pharmaceutically acceptable carriers and excipients and may be useful in selecting suitable pharmaceutically acceptable carriers and excipients. Examples include Remington's Pharmaceutical Sciences (Mack Publishing Company), The Handbook of Pharmaceutical Additives (Gower Publishing Limited), and The Handbook of Pharmaceutical Excipients (the American Pharmaceutical Association and the Pharmaceutical Press).

The pharmaceutical compositions of the invention are prepared using techniques and methods known to those skilled in the art. Some methods commonly used in the art are described in Remington's Pharmaceutical Sciences (Mack Publishing Company).

In one aspect, the invention is directed to a solid oral dosage form such as a tablet or capsule comprising a therapeutically effective amount of a compound of the invention and a diluent or filler. Suitable diluents and fillers include lactose, sucrose, dextrose, mannitol, sorbitol, starch (e.g. corn starch, potato starch, and pre-gelatinized starch), cellulose and its derivatives, (e.g. microcrystalline cellulose), calcium sulfate, and dibasic calcium phosphate. The oral solid dosage form may further comprise a binder. Suitable binders include starch (e.g. corn starch, potato starch, and pre-gelatinized starch) gelatin, acacia, sodium alginate, alginic acid, tragacanth, guar gum, povidone, and cellulose and its derivatives (e.g. rnicrocrystalline cellulose). The oral solid dosage form may further comprise a disintegrant. Suitable disintegrants include crospovidone, sodium starch glycolate, croscarmelose, alginic acid, and sodium carboxymethyl cellulose. The oral solid dosage form may further comprise a lubricant. Suitable lubricants include stearic acid, magnesium stearate, calcium stearate, and talc.

Where appropriate, dosage unit formulations for oral administration can be microencapsulated. The composition can also be prepared to prolong or sustain the release as, for example, by coating or embedding particulate material in polymers, wax, or the like.

The compounds of the invention may also be coupled with soluble polymers as targetable drug carriers. Such polymers can include polyvinylpyrrolidone, pyrancopolymer, polyhydroxypropylmethacrylamidephenol, polyhydroxyethylaspartamidephenol, or polyethyleneoxidepolylysine substituted with palmitoyl residues. Furthermore, the compounds of the invention may be coupled to a

class of biodegradable polymers useful in achieving controlled release of a drug, for example polylactic acid, polepsilon caprolactone, polyhydroxy butyric acid, polyorthoesters, polyacetals, polydihydropyrans, polycyanacrylates and cross-linked or amphipathic block copolymers of hydrogels.

In another aspect, the invention is directed to a liquid oral dosage form. Oral liquids such as solution, syrups and elixirs can be prepared in dosage unit form so that a given quantity contains a predetermined amount of a compound of the invention. Syrups can be prepared by dissolving the compound of the invention in a suitably flavored aqueous solution; while elixirs are prepared through the use of a non-toxic alcoholic vehicle. Suspensions can be formulated by dispersing the compound of the invention in a non-toxic vehicle. Solubilizers and emulsifiers such as ethoxylated isostearyl alcohols and polyoxy ethylene sorbitol ethers, preservatives, flavor additives such as peppermint oil or other natural sweeteners or saccharin or other artificial sweeteners and the like can also be added.

In another aspect, the invention is directed to parenteral administration. Pharmaceutical compositions adapted for parenteral administration include aqueous and non-aqueous sterile injection solutions which may contain anti-oxidants, buffers, bacteriostats and solutes which render the formulation isotonic with the blood of the intended recipient; and aqueous and non-aqueous sterile suspensions which may include suspending agents and thickening agents. The compositions may be presented in unit-dose or multi-dose containers, for example sealed ampoules and vials, and may be stored in a freeze dried (lyophilized) condition requiring only the addition of the sterile liquid carrier, for example water for injections, immediately prior to use. Extemporaneous injection solutions and suspensions may be prepared from sterile powders, granules and tablets.

Combinations

The compound of the present invention may be administered either simultaneously with, or before or after, one or more other therapeutic agent(s). The compound of the present invention may be administered separately, by the same or different route of administration, or together in the same pharmaceutical composition as the other agent(s).

In one embodiment, the invention provides a product comprising a compound of formula (I) and at least one other therapeutic agent as a combined preparation for simultaneous, separate or sequential use in therapy. In one embodiment, the therapy is the treatment of a disease or disorder associated with a mutant form of IDH. Products provided as a combined preparation include a composition comprising the compound of

formula (I) and the other therapeutic agent(s) together in the same pharmaceutical composition, or the compound of formula (I) and the other therapeutic agent(s) in separate form, *e.g.* in the form of a kit.

In one embodiment, the invention provides a pharmaceutical composition comprising a compound of formula (I) and another therapeutic agent(s). Optionally, the pharmaceutical composition may comprise a pharmaceutically acceptable excipient, as described above.

In one embodiment, the invention provides a kit comprising two or more separate pharmaceutical compositions, at least one of which contains a compound of formula (I). In one embodiment, the kit comprises means for separately retaining said compositions, such as a container, divided bottle, or divided foil packet. An example of such a kit is a blister pack, as typically used for the packaging of tablets, capsules and the like.

The kit of the invention may be used for administering different dosage forms, for example, oral and parenteral, for administering the separate compositions at different dosage intervals, or for titrating the separate compositions against one another. To assist compliance, the kit of the invention typically comprises directions for administration.

In the combination therapies of the invention, the compound of the invention and the other therapeutic agent may be manufactured and/or formulated by the same or different manufacturers. Moreover, the compound of the invention and the other therapeutic agent may be brought together into a combination therapy: (i) prior to release of the combination product to physicians (*e.g.* in the case of a kit comprising the compound of the invention and the other therapeutic agent); (ii) by the physician themselves (or under the guidance of the physician) shortly before administration; (iii) in the patient themselves, *e.g.* during sequential administration of the compound of the invention and the other therapeutic agent.

Accordingly, the invention provides the use of a compound of formula (I) for treating a disease or disorder associated with a mutant form of IDH, wherein the medicament is prepared for administration with another therapeutic agent. The invention also provides the use of another therapeutic agent for treating a disease or disorder associated with a mutant form of IDH, wherein the medicament is administered with a compound of formula (I).

The invention also provides a compound of formula (I) for use in a method of treating a disease or disorder associated with a mutant form of IDH, wherein the compound of formula (I) is prepared for administration with another therapeutic agent. The invention also provides another therapeutic agent for use in a method of treating a disease or disorder associated with a mutant form of IDH, wherein the other therapeutic agent is prepared for administration with a compound of formula (I). The invention also

provides a compound of formula (I) for use in a method of treating a disease or disorder associated with a mutant form of IDH, wherein the compound of formula (I) is administered with another therapeutic agent. The invention also provides another therapeutic agent for use in a method of treating a disease or disorder associated with a mutant form of IDH, wherein the other therapeutic agent is administered with a compound of formula (I).

The invention also provides the use of a compound of formula (I) for treating a disease or disorder associated with a mutant form of IDH, wherein the patient has previously (*e.g.* within 24 hours) been treated with another therapeutic agent. The invention also provides the use of another therapeutic agent for treating a disease or disorder associated with a mutant form of IDH, wherein the patient has previously (*e.g.* within 24 hours) been treated with a compound of formula (I).

In one embodiment, the other therapeutic agent is selected from: vascular endothelial growth factor (VEGF) receptor inhibitors, topoisomerase II inhibitors, smoothen inhibitors, alkylating agents, anti-tumor antibiotics, anti-metabolites, retinoids, and other cytotoxic agents.

Examples of vascular endothelial growth factor (VEGF) receptor inhibitors include, but are not limited to, bevacizumab (sold under the trademark Avastin® by Genentech/Roche), axitinib, (*N*-methyl-2-[[3-[(*E*)-2-pyridin-2-ylethenyl]-1*H*-indazol-6-yl]sulfanyl]benzamide, also known as AG013736, and described in PCT Publication No. WO 01/002369), Brivanib Alaninate ((*S*)-((*R*)-1-(4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-*f*][1,2,4]triazin-6-yloxy)propan-2-yl)2-aminopropanoate, also known as BMS-582664), motesanib (N-(2,3-dihydro-3,3-dimethyl-1H-indol-6-yl)-2-[(4-pyridinylmethyl)amino]-3-pyridinecarboxamide, and described in PCT Publication No. WO 02/066470), pasireotide (also known as SOM230, and described in PCT Publication No. WO 02/010192), and sorafenib (sold under the tradename Nexavar®).

Examples of topoisomerase II inhibitors, include but are not limited to, etoposide (also known as VP-16 and Etoposide phosphate, sold under the tradenames Toposar®, VePesid® and Etopophos®), and teniposide (also known as VM-26, sold under the tradename Vumon®).

Examples of alkylating agents, include but are not limited to, temozolomide (sold under the tradenames Temodar® and Temodal® by Schering-Plough/Merck), dactinomycin (also known as actinomycin-D and sold under the tradename Cosmegen®), melphalan (also known as L-PAM, L-sarcolysin, and phenylalanine mustard, sold under the tradename Alkeran®), altretamine (also known as hexamethylmelamine (HMM), sold under the tradename Hexalen®), carmustine (sold under the tradename BiCNU®), bendamustine (sold under the tradename Treanda®),

busulfan (sold under the tradenames Busulfex® and Myleran®), carboplatin (sold under the tradename Paraplatin®), lomustine (also known as CCNU, sold under the tradename CeeNU®), cisplatin (also known as CDDP, sold under the tradenames Platinol® and Platinol®-AQ), chlorambucil (sold under the tradename Leukeran®), cyclophosphamide (sold under the tradenames Cytoxan® and Neosar®), dacarbazine (also known as DTIC, DIC and imidazole carboxarnide, sold under the tradename DTIC-Dome®), altretamine (also known as hexamethylmelarnine (HMM) sold under the tradename Hexalen®), ifosfamide (sold under the tradename Ifex®), procarbazine (sold under the tradename Matulane®), mechlorethamine (also known as nitrogen mustard, mustine and mechloroethamine hydrochloride, sold under the tradename Mustargen®), streptozocin (sold under the tradename Zanosar®), thiotepa (also known as thiophosphoamide, TESPA and TSPA, and sold under the tradename Thioplex®.

Examples of anti-tumor antibiotics include, but are not limited to, doxorubicin (sold under the tradenames Adriamycin® and Rubex®), bleomycin (sold under the tradename lenoxane®), daunorubicin (also known as dauorubicin hydrochloride, daunomycin, and rubidomycin hydrochloride, sold under the tradename Cerubidine®), daunorubicin liposomal (daunorubicin citrate liposome, sold under the tradename DaunoXome®), mitoxantrone (also known as DHAD, sold under the tradename Novantrone®), epirubicin (sold under the tradename Ellence™), idarubicin (sold under the tradenames Idamycin®, Idamycin PFS®), and mitomycin C (sold under the tradename Mutamycin®).

Examples of anti-metabolites include, but are not limited to, claribine (2-chlorodeoxyadenosine, sold under the tradename leustatin®), 5-fluorouracil (sold under the tradename Adrucil®), 6-thioguanine (sold under the tradename Purinethol®), pemetrexed (sold under the tradename Alimta®), cytarabine (also known as arabinosylcytosine (Ara-C), sold under the tradename Cytosar-U®), cytarabine liposomal (also known as Liposomal Ara-C, sold under the tradename DepoCyt™), decitabine (sold under the tradename Dacogen®), hydroxyurea (sold under the tradenames Hydrea®, Droxia™ and Mylocel™), fludarabine (sold under the tradename Fludara®), floxuridine (sold under the tradename FUDR®), cladribine (also known as 2-chlorodeoxyadenosine (2-CdA) sold under the tradename Leustatin™), methotrexate (also known as amethopterin, methotrexate sodim (MTX), sold under the tradenames Rheumatrex® and Trexall™), and pentostatin (sold under the tradename Nipent®).

Examples of retinoids include, but are not limited to, alitretinoin (sold under the tradename Panretin®), tretinoin (all-*trans* retinoic acid, also known as ATRA, sold under the tradename Vesanoid®), Isotretinoin (13-*cis*-retinoic acid, sold under the tradenames Accutane®, Amnesteem®, Claravis®, Clarus®, Decutan®, Isotane®, Izotech®,

Oratane®, Isotret®, and Sotret®), and bexarotene (sold under the tradename Targretin®).

Examples of other cytotoxic agents include, but are not limited to, arsenic trioxide (sold under the tradename Trisenox®), asparaginase (also known as L-asparaginase, and Erwinia L-asparaginase, sold under the tradenames Elspar® and Kidrolase®).

Intermediates and Examples

The following examples are intended to be illustrative only and not limiting in any way. Unless otherwise noted, the following Intermediates and Examples were purified vial silica gel column chromatograph using RediSep® Rf columns from Teledyne Isco, Inc. Abbreviations used are those conventional in the art or the following:

ACN acetonitrial
BSA bovine serum albumin
C Celsius
CDI 1,1'-carbonyldiimidazole
d doublet
dd doublet of doublets
DAST diethylaminosulfur trifluoride
DEAD diethyl azodicarboxylate
DIPEA NN-diisopropylethylamine
DMF N,N-dimethylformamide
DMSO dimethylsulfoxide
DTT dithiothreitol
EtOAc ethyl acetate
EtOH ethanol
g gram
h hour(s)HATU 2-(1H-7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate
HEPES 4-(2-hydroxyethyl)-1-piperazineethylanesulfonic acid
HPLC high pressure liquid chromatography
Hunig's Base NN-diisopropylethylamine
kg kilogram
L liter
LC liquid chromatographyLCMS liquid chromatography and mass spectrometry
MeOH methanol
MS mass spectrometry
m multiplet

min minutes
mL milliliter(s)
µM micromolar
m/z mass to charge ratio
nm nanometer
nM nanomolar
N normal
NADPH nicotinamide adenine dinucleotide phosphate
NMP N-methylpyrrolidone
NMR nuclear magnetic resonance
$PdCl_2(dppf).CH_2Cl_2$ 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex
pTsOH p-toluenesulfonic acid
rac racemic
Rt retention time
s singlet
sat. saturated
t triplet
TBTU O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate
TCEP tris(2-carboxyethyl)phosphine
TEA triethylamine
TFA trifluoroacetic acid
THF tetrahydrofuran
TLC thin layer chromatography
TMS-CN trimethylsilyl cyanide

Instrumentation

LCMS:

LCMS data (also reported herein as simply MS) were recorded using a Waters System (Acuity UPLC and a Micromass ZQ mass spectrometer; Column: Acuity HSS C18 1.8-micron, 2.1 x 50 mm; gradient: 5-95 % acetonitrile in water with 0.05 % TFA over a 1.8 min period; flow rate 1.2 mL/min; molecular weight range 200-1500; cone Voltage 20 V; column temperature 50 °C). All masses reported are those of the protonated parent ions unless recorded otherwise.

High Resolution Mass Spectrometry (HRMS):

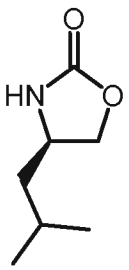
HRMS Method A: ESI-MS data were recorded using a Synapt G2 HDMS (TOF mass spectrometer, Waters) with electrospray ionization source. The resolution of the MS system was approximately 15000. Leucine Enkephalin was used as lock mass (internal standards) infused from lockspary probe. The compound was infused into the mass spectrometer by UPLC (Acquity, Waters) from sample probe. The separation was performed on Acquity UPLC BEH C18 1x50 mm column at 0.2 mL/min flow rate with the gradient from 5% to 95% in 3 min. Solvent A was Water with 0.1% Formic Acid and solvent B was Acetonitrile with 0.1% Formic Acid. The mass accuracy of the system has been found to be <5 ppm with lock mass.

HRMS Method B: LC-MS/ESI-MS data were recorded on an Acquity G2 Xevo QTof - Rs(FWHM) > 20000 Accuracy < 5 ppm. The separation was performed on Acquity CSH 1.7µm 2.1x50mm - 50°C column Eluent A: Water + 3.75 mM ammonium acetate. Eluent B: Acetonitrile. Gradient: from 2 to 98% B in 4.4 min - flow 1.0 mL/min.

HRMS methods A and B are referred to throughout as HRMS(A) or HRMS(B), respectively.

Intermediates

Intermediate A: (*R*)-4-isobutyloxazolidin-2-one

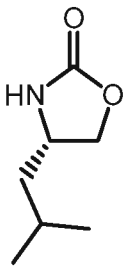
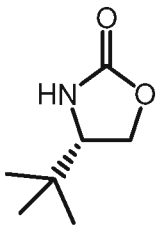
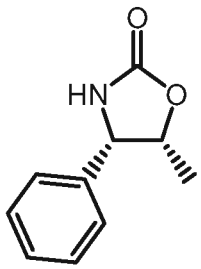
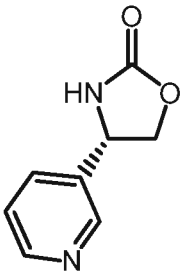
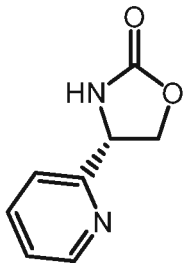
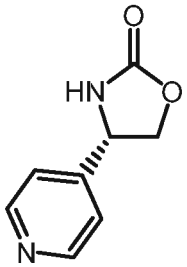


To a cooled (4 °C) solution of (*R*)-2-amino-4-methylpentan-1-ol (2.98 g, 25.4 mmol) and triethylamine (7.6 mL, 54 mmol, 2.1 equiv) in CH_2Cl_2 (80 mL) was added dropwise a solution of triphosgene (2.52g, 8.49 mmol, 0.334 equiv) in 10 ml of CH_2Cl_2 over 30 min. The reaction mixture was stirred at 4 °C for 15 min, warmed up to room temperature and stirred for an additional 1 h. The mixture was treated with saturated NH_4Cl (25 mL), followed by CH_2Cl_2 (50 mL) and the resulting mixture was stirred for 20 min. The layers were separated and the organic layer was washed with water. The combined aqueous layers were extracted with CH_2Cl_2 (50 mL). The combined organic layers were dried

over Na_2SO_4, filtered and concentrated to give (*R*)-4-isobutyloxazolidin-2-one (3.22 g) in 88% yield. The crude product was used for the next reaction without purification. ^{1}H NMR (400 MHz, CD_3OD) δ 4.53 – 4.47 (m, 1 H), 4.00 – 3.92 (m, 2 H), 1.67 (ddq, J = 13, 8.0, 6.5 Hz, 1 H), 1.56 – 1.48 (m, 1 H), 1.40 – 1.32 (m, 1 H), 0.95 (d, J = 6.1 Hz, 3 H), 0.93 (d, J = 6.1 Hz, 3 H).

The Intermediates in Table 1 were prepared by a method similar to the one described for the preparation of Intermediate A.

Table 1.

Intermediate B	Intermediate C	Intermediate D
		
Intermediate E	Intermediate F	Intermediate G
		
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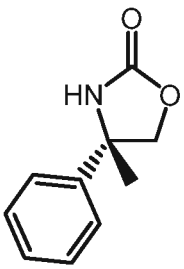
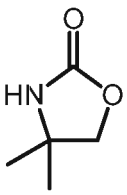
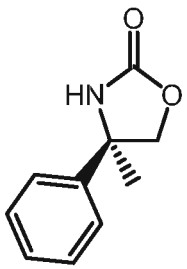
		
Intermediate K	Intermediate L	

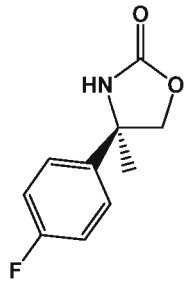
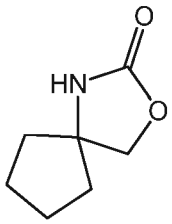
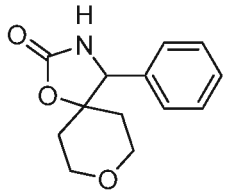
		

Table 2. Chemical name, NMR chemical shifts and LCMS signal for each intermediate listed in Table 1.

Intermediate: Name	^{1}H NMR **(400 MHz)** δ **ppm**	**LCMS**
B: (*S*)-4-isobutyloxazolidin-2-one	($CDCl_3$) 6.59 (br s, 1 H), 4.53 – 4.48 (m, 1 H), 4.01 – 3.92 (m, 2 H), 1.71 – 1.54 (m, 2 H), 1.42 – 1.35 (m, 1 H), 0.94 (d, J = 6.5 Hz, 3 H), 0.93 (d, J = 6.5 Hz, 3 H).	no UV signal
C: (*S*)-4-tert-butyloxazolidin-2-one	(CD_3OD) 4.37 (t, J = 9.1 Hz, 1 H), 4.23 (dd, J = 9.1, 5.6 Hz, 1 H), 3.61 (dd, J = 9.1, 5.6 Hz, 1 H), 0.90 (s, 9 H)	no UV signal
D: (4S,5R)-5-methyl-4-phenyloxazolidin-2-one	(CD_3OD) δ 7.42 – 7.32 (m, 3 H), 7.27 – 7.24 (m, 2 H), 5.05 (dq, J = 8.0, 6.4 Hz, 1 H), 4.98 (d, J = 8.0 Hz, 1 H), 0.89 (d, J = 6.5 Hz, 3 H)	no UV signal
E: (*S*)-4-(pyridin-3-yl)oxazolidin-2-one		MS *m/z* 165.1 $(M + H)^+$
F: (*S*)-4-(pyridin-2-yl)oxazolidin-2-one	($CDCl_3$) 8.62 (dt, J = 5.4, 1.1 Hz, 1 H), 7.80 (td, J = 7.8, 1.5 Hz, 1 H), 7.45 (d, J = 7.5 Hz, 1 H), 7.33 – 7.28 (m, 1 H), 6.40 (br s, 1 H), 5.12 (dd, J = 8.8, 5.8 Hz, 1 H), 4.86 (t, J = 9.0 Hz, 1 H), 4.43 (dd, J = 8.5, 5.5 Hz, 1 H)	HRMS(B) *m/z* 165.0663 $(M + H)^+$
G: (S)-4-(pyridin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.67 – 8.66 (m, 2 H), 7.36 – 7.34 (m, 2 H), 6.50 (br s, 1 H), 5.04 – 5.00 (m, 1 H), 4.80 (t, J = 8.8 Hz, 1 H), 4.16 (dd, J = 8.5, 6.5 Hz, 1 H)	HRMS(B) *m/z* 165.0664 $(M + H)^+$
H: (*S*)-4-methyl-4-phenyloxazolidin-2-one	($CDCl_3$) 7.45 – 7.33 (m, 5 H), 6.10 (br s, 1 H), 4.39 (q, J = 8.4 Hz, 2 H), 1.79 (s, 3 H)	HRMS(B) *m/z* 178.0871 $(M + H)^+$
I: 4,4-dimethyloxazolidin-2-one	($CDCl_3$) 4.96 (br s, 1 H), 4.12 (s, 2 H), 1.40 (s, 6 H)	no UV signal
J: (*S*)-4-methyl-4-phenyloxazolidin-2-one	($CDCl_3$) 7.33 – 7.19 (m, 5 H), 6.86 (br s, 1 H), 4.32 – 4.27 (m, 2 H), 1.67 (s, 3 H)	MS *m/z* 177.9 $(M + H)^+$
K: (R)-4-(4-fluorophenyl)-4-methyloxazolidin-2-one	($CDCl_3$) δ 7.41 – 7.36 (m, 2 H), 7.14 – 7.08 (m, 2 H), 6.06 (br s, 1 H), 4.39 (d, J = 8.3 Hz, 1 H), 4.33 (d, J = 8.3 Hz, 1 H), 1.78 (s, 3 H)	MS m/z 195.9 (M + H)+

L: 3-oxa-1-azaspiro[4.4]nonan-2-one	($CDCl_3$) δ 5.62 (br s, 1 H), 4.25 (s, 2 H), 1.90 – 1.65 (m, 8 H)	no UV signal

Intermediate M: 4-phenyl-1,8-dioxa-3-azaspiro[4.5]decan-2-one



Step 1: Preparation of 4-(amino(phenyl)methyl)tetrahydro-2H-pyran-4-ol

To dihydro-2H-pyran-4(3H)-one (1001 mg, 10 mmol) and triethylarnine (0.279 mL, 2.00 mmol) was slowly added TMS-CN (1190 mg, 12.00 mmol) [Caution: exothermic reaction]. After stirring for 1hour, the mixture was concentrated under reduced pressure. The residue, dissolved in diethyl ether (10 mL), was added dropwise to phenylmagnesium bromide (3M solution in diethyl ether, 4.33 mL, 13.00 mmol). Additional ~5 mL of diethyl ether was added and the suspension was stirred for ~4 hour. To the reaction mixture was added very slowly MeOH (3.0 mL), followed by the careful and slow additions of $NaBH_4$ (454 mg, 12.00 mmol) and MeOH (12 mL) in portions (gas development observed). The reaction mixture was stirred overnight and water (~6 mL) was added carefully, followed by 10% aqueous HCl solution (~20 mL). The mixture was vigrously stirred for 4 hour and diethyl ether was added. The separated organic layer was extracted with 10% aqueous HCl solution (1x ~20 mL). The combined aqueous layers were washed with diethylether (2x). The acidic layers were made basic by the addition of 6N aqueous NaOH solution. The milky white mixture was extracted with DCM (1x), ethyl acetate/THF (1:1; 1x) and ethyl acetate (2x). The organic layers (DCM and ethyl acetate solutions independently) were washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4, filtered off and concentrated under reduced pressure providing crude 4-(amino(phenyl)methyl)tetrahydro-2H-pyran-4-ol, which was directly used in the next reaction without further purification.

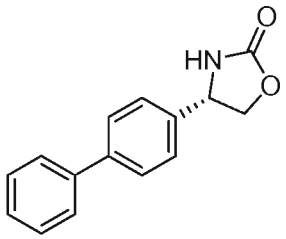
Yellowish liquid. Yield: 451 mg. LCMS *m/z* 208.2 $(M + H)^+$, Rt 0.29 min.

Step 2: Preparation of 4-phenyl-1,8-dioxa-3-azaspiro[4.5]decan-2-one

To a mixture of CDI (388 mg, 2.394 mmol) in THF (1.5 mL) was added slowly a solution of 4-(amino(phenyl)methyl)tetrahydro-2H-pyran-4-ol (451 mg, 2.176 mmol) in THF (3 mL). The mixture was stirred under argon for ~5 hours. The mixture was diluted with saturated aqueous $NaHCO_3$ solution and DCM. The separated aqueous layer was extracted with DCM (2x) and the combined organic layers were washed with 0.5N

aqueous HCl solution and brine, dried over sodium sulfate, filtered off and concentrated under reduced pressure. The residue was purified by column chromatography [SiO_2, 12 g, 0 - 100% heptane/ethyl acetate] providing 4-phenyl-1,8-dioxa-3-azaspiro[4.5]decan-2-one as a white solid. Yield: 330 mg. LCMS *m/z* 234.1 $(M + H)^+$; Rt 0.52 min.

Intermediate N: (S)-4-(biphenyl-4-yl)oxazolidin-2-one



Step 1: Preparation of vinylbiphenyl

To a suspension of methyltriphenylphosphonium bromide (5.10 g, 14.27 mmol) in THF (26 mL) was slowly added potassium tert-butoxide (1M solution in THF, 14.27 mL) over ~20 min at 0 °C. The reaction mixture was allowed to warm up to room temperature and stirred for 10 min. The mixture was cooled to 0°C and a solution of 4-biphenylcarbaldehyde (2.0 g, 10.98 mmol) in THF (9 mL) was added over 20 min. The reaction mixture was allowed to warm up to room temperature and stirred for ~19 hour. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was dissolved/suspended in DCM and filtered through a silica pad and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography [SiO_2, 80 g, EtOAc/heptane] to provide vinylbiphenyl (1.845 g) as a white solid. LCMS Rt 0.79 min.

Step 2: Preparation of (S)-tert-butyl 1-(biphenyl-4-yl)-2-hydroxyethylcarbamate

To a solution of tert-butyl carbamate (2.82 g, 24.08 mmol) in 1-propanol (30 mL) was added aqueous NaOH solution (0.38M, 61.5 mL, 23.36 mmol). The mixture was stirred for 5 min and 1,3-dichloro-5,5-dimethylimidazolidine-2,4-dione (2.351 g, 11.93 mmol) was added. The mixture was stirred stirred for 10 min and $(DHQ)_2PHAL$ (0.303 g, 0.388 mmol), dissolved in 1-propanol (30 mL), was added followed by a solution of vinylbiphenyl (1.4 g, 7.77 mmol) in 1-propanol (60 mL). A suspension of potassium osmate dihydrate (0.114 g, 0.311 mmol) in aqueous NaOH solution, (0.38M, 0.613 mL, 0.233 mmol) was added and the mixture was stirred for ~ 16 hours. The reaction mixture was diluted with water (200 mL) and extracted with EtOAc (3 x 200 mL). The combined organic layers were washed with brine (2x 400 mL), dried over sodium sulfate, filtered off and concentrated under reduced pressure. The residue was purified by column

chromatography [SiO_2, 80 g, EtOAc/heptane] to provide (S)-tert-butyl 1-(biphenyl-4-yl)-2-hydroxyethylcarbamate (609 mg). LCMS *m/z* 258.2 (M + H; loss of *t*-Bu)$^+$, Rt 0.97 min. ^{1}H NMR (400 MHz, CD_3OD) δ ppm 7.62 - 7.56 (m, 4 H), 7.45 - 7.37 (m, 4 H), 7.34 - 7.2(m, 1 H), 4.69 (t, *J* = 5.8 Hz, 1 H), 3.76 - 3.63 (m, 2H), 1.44 (br. s., 9 H)

Step 3: Preparation of (S)-2-amino-2-(biphenyl-4-yl)ethanol

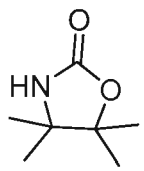
To a solution of (S)-tert-butyl 1-(biphenyl-4-yl)-2-hydroxyethylcarbamate (608 mg, 1.940 mmol) in MeOH (3 mL) was added HCl (4M in dioxane, 8 mL) at room temperature. The mixture was stirred for 1 hour and concentrated under reduced pressure. The residue was dissolved in DCM (10 mL)/water (1.0 mL) and stirred with $NaHCO_3$ for 1 hour. The mixture was filtered off and rinsed with DCM. The filtrate was dried over sodium sulfate, filtered off and concentrated under reduced pressure providing (S)-2-amino-2-(biphenyl-4-yl)ethanol (171 mg) as a white solid. LCMS *m/z* 214.2 (M + H)$^+$, Rt 0.58 min.

Step 4: Preparation of (S)-4-(biphenyl-4-yl)oxazolidin-2-one

To a solution of (S)-2-amino-2-(biphenyl-4-yl)ethanol (171 mg, 0.802 mmol) in THF (12 mL) under argon atmosphere was added CDI (132 mg, 0.814 mmol). The solution was stirred at room temperature for 2 hours. The mixture was diluted with saturated aqueous $NaHCO_3$ solution (40 mL) and extracted with EtOAc (2x 30 mL). The combined organic layers were washed with 0.5M aqueous HCl solution (30 mL), brine (40 mL), dried over sodium sulfate, filtered off and concentrated under reduced pressure. The residue was dissolved in DCM and concentrated under rduced pressure to provide crude (S)-4-(biphenyl-4-yl)oxazolidin-2-one (156 mg) as a beige solid, which was used without further purification. LCMS *m/z* 240.1 (M + H)$^+$, Rt 0.80 min.

^{1}H NMR (400 MHz, CD_3OD) δ ppm 4.19 (dd, *J*=8.61, 6.50 Hz, 1 H) 4.80 (t, *J*=8.73 Hz, 1 H) 5.05 (dd, *J*=8.78, 6.48 Hz, 1 H) 7.31 - 7.38 (m, 1 H) 7.39 - 7.54 (m, 4 H) 7.55 - 7.71 (m, 4 H).

Intermediate P: 4,4,5,5-tetramethyloxazolidin-2-one



Step 1: Preparation of Methyl 2-(tert-butoxycarbonylamino)-2-methylpropanoate

To a solution of 2-(tert-butoxycarbonylamino)-2-methylpropanoic acid (10.03 g, 49.4 mmol) in MeOH/DCM (60mL/140mL) at room temperature was added drop wise (trimethylsilyl)diazomethane (37.0 mL, 74.0 mmol). The reaction mixture was stirred for 30 minutes. Acetic acid was added drop wise to quench (trimethylsilyl)diazomethane. The reaction mixture was concentrated under reduced pressure to afford the desired product as a white solid (10.56 g). LCMS *m/z* 240.2 $(M + Na)^+$, Rt 0.71 min.

Step 2: Preparation of tert-butyl 3-hydroxy-2,3-dimethylbutan-2-ylcarbamate

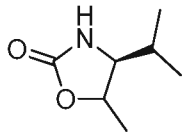
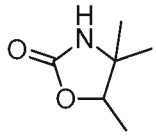
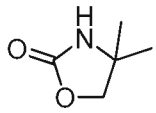
To a solution of methyl 2-(tert-butoxycarbonylamino)-2-methylpropanoate (10.56 g, 48.6 mmol) in THF (300mL) at 0 °C was added drop wise methylmagnesium bromide (64.8 mL, 194 mmol). Cold bath was removed after 1 hour. The reaction was stirred at 20 °C for 4 hours. The reaction was cooled back 0 °C and quenched with saturated NH_4Cl solution (10mL). The reaction mixture was then allowed to warm to room temperature, and diluted with EtOAc (100mL) and water (50mL). The phases were separated and the aqueous layer was extracted with EtOAc (2x100mL). The combined organics were then dried (Na_2SO_4) and concentrated. The residue was purified via silica gel flash chromatography (0-20% EtOAc-Hexanes) to afford the desired product as a white solid (9.02 g). LCMS *m/z* 240.1 $(M + Na)^+$, Rt 0.78 min.

Step 3: Preparation of 4,4,5,5-tetramethyloxazolidin-2-one

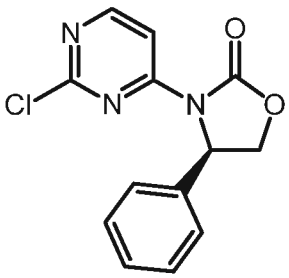
To tert-butyl 3-hydroxy-2,3-dimethylbutan-2-ylcarbamate (10.02 g, 46.1 mmol) in THF (300 ml) was added portion wise potassium 2-methylpropan-2-olate (7.24 g, 64.6 mmol). The reaction was stirred for five hours and quenched with HCl (1M, 66mL) to pH=2. The reaction mixture was then concentrated under vacuum to about one third of the volume, and diluted with water (50mL). The aqueous layer was then extracted with DCM (3x100mL). The combined organic was washed with brine (50mL), dried (Na_2SO_4) and concentrated to give crude product as a light tan oil (6.25 g). LCMS *m/z* 144.1 $(M + H)^+$, Rt 0.42 min.

The Intermediates in Table 2b were prepared by a method similar to the one described for the preparation of Intermediate P.

Table 2b.

Intermediate: Name	Structure	LCMS
Q: (4S)-4-isopropyl-5-methyloxazolidin-2-one		MS *m/z* (M + H)$^+$ 144.4, Rt 0.47 min
R: 4,4,5-trimethyloxazolidin-2-one		MS *m/z* (M + H)$^+$ 130.4, Rt 0.36 min
S: 4,4-dimethyloxazolidin-2-one		MS m/z (M + H)+ 116.0, Rt 0.28 min

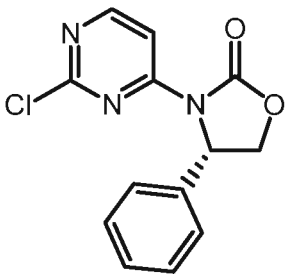
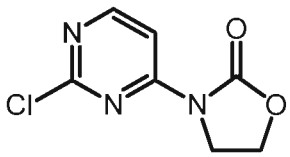
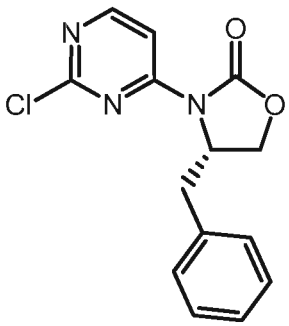
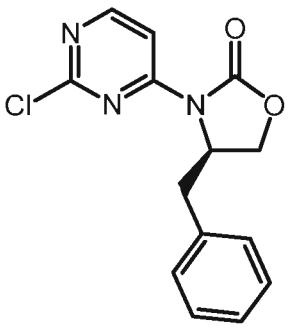
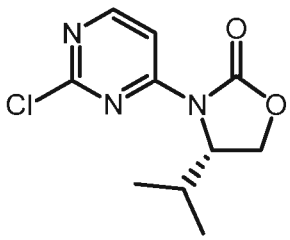
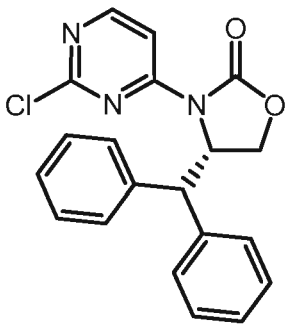
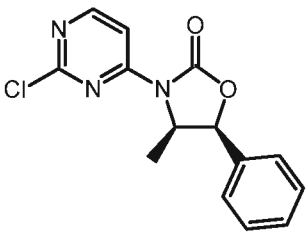
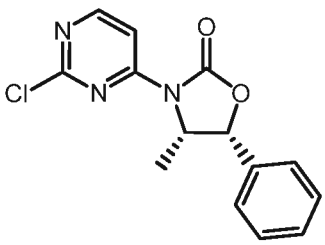
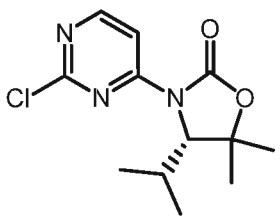
Intermediate 1: (*R*)-3-(2-chloropyrimidin-4-yl)-4-phenyloxazolidin-2-one



A solution of (*R*)-4-phenyloxazolidin-2-one (2.9484 g, 18.07 mmol) and 2,4-dichloropyrimidine (3.1872 g, 21.39 mmol, 1.184 equiv) in DMF (30 mL) was treated with NaH (95 %, 0.4773 g, 18.89 mmol, 1.046 equiv), then the resulting mixture (yellow to red cloudy) was stirred at room temperature for 3 h. The reaction mixture was diluted with EtOAc (200 mL), washed with sat. NH_4Cl (75 mL) and 4% aqueous NaCl (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 0 to 40%) provided (*R*)-3-(2-chloropyrimidin-4-yl)-4-phenyloxazolidin-2-one (2.7020 g, white sticky solid) in 46.9% yield. ^{1}H NMR (400 MHz, CD_3OD) δ 8.47 (d, J = 5.6 Hz, 1 H), 8.18 (d, J = 6.1 Hz, 1 H), 7.38 – 7.30 (m, 5 H), 5.81 (dd, J = 8.6, 3.5 Hz, 1 H), 4.88 (t, J = 8.6 Hz, 1 H), 4.37 (dd, J = 8.6, 3.5 Hz, 1 H) ; MS *m/z* 276.4 (M + H)$^+$.

The Intermediates in Table 3 were prepared by a method similar to the one described for the preparation of Intermediate 1.

Table 3.

Intermediate 2	Intermediate 3	Intermediate 4
		
Intermediate 5	Intermediate 6	Intermediate 7
		
Intermediate 8	Intermediate 9	Intermediate 10
		
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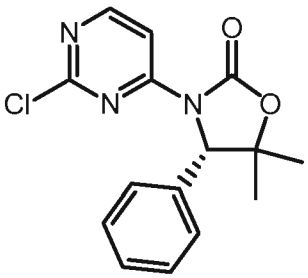	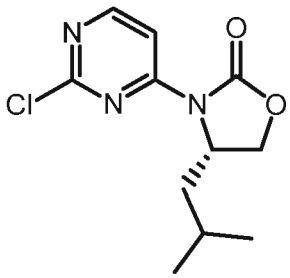	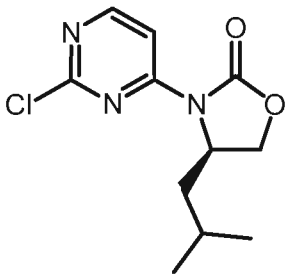
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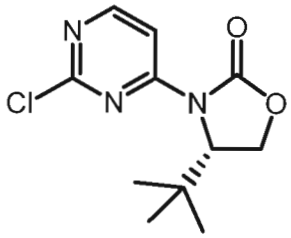	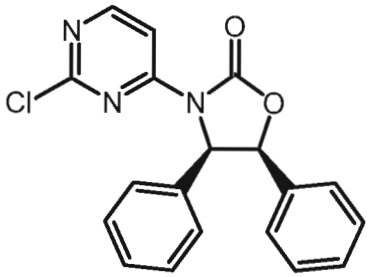	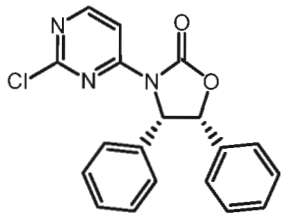
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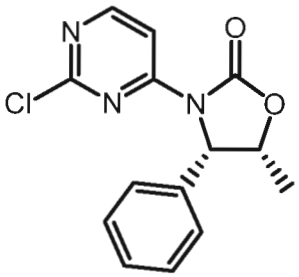	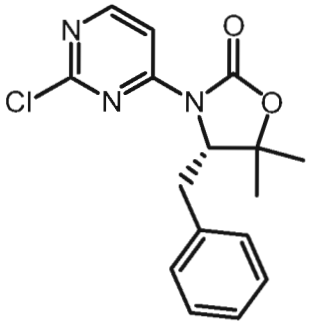	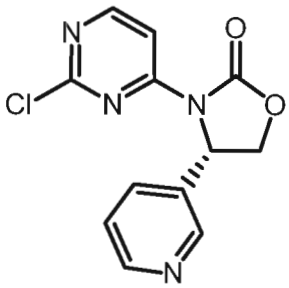
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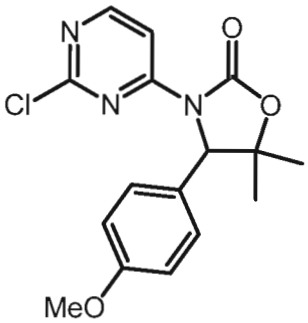	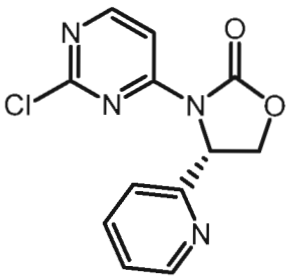	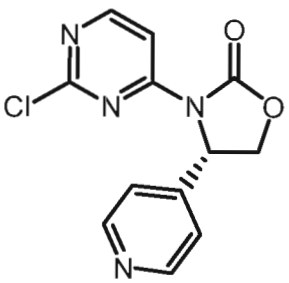
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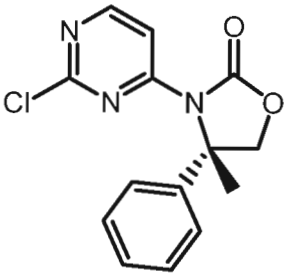
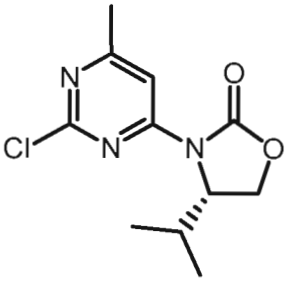
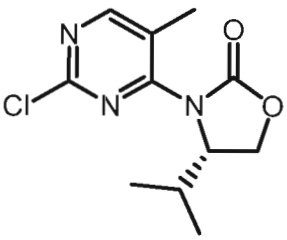
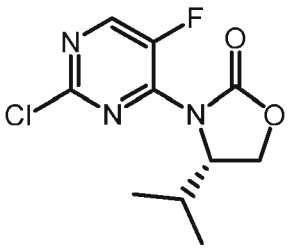
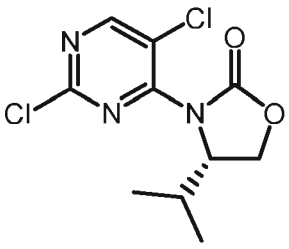
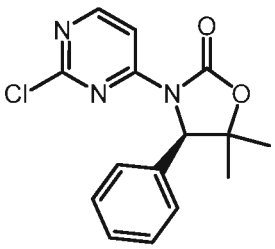
		
Intermediate 26	Intermediate 27	Intermediate 28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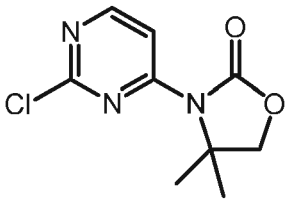
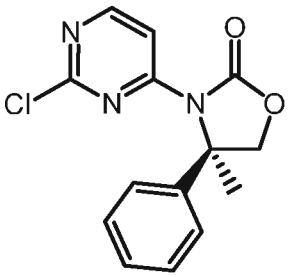
		

Table 4. Chemical name, NMR chemical shifts and LCMS signal for each intermediate listed in Table 3.

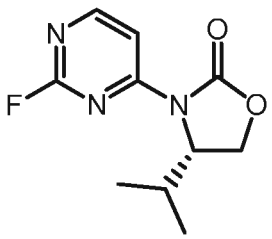
Intermediate: Name	**^{1}H NMR (400 MHz) δ ppm**	**LCMS**
2: (*S*)-3-(2-chloropyrimidin-4-yl)-4-phenyloxazolidin-2-one	($CDCl_3$) 8.47 (d, J = 6.1 Hz, 1 H), 8.18 (d, J = 5.7 Hz, 1 H), 7.39 – 7.29 (m, 5 H), 5.81 (dd, J = 8.6, 3.5 Hz, 1 H), 4.88 (t, J = 8.8 Hz, 1 H), 4.37 (dd, J = 8.8, 3.8 Hz, 1 H)	MS *m/z* 276.5 $(M + H)^+$
3: 3-(2-chloropyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 8.48 (d, J = 6.1 Hz, 1 H), 8.16 (d, J = 6.1 Hz, 1 H), 4.54 (t, J = 7.8 Hz, 2 H), 4.22 (t, J = 8.1 Hz, 2 H)	MS *m/z* 200.4 $(M + H)^+$
4: (*S*)-4-benzyl-3-(2-chloropyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 8.52 (d, J = 6.1 Hz, 1 H), 8.15 (d, J = 6.1 Hz, 1 H), 7.32 – 7.22 (m, 5 H), 5.07 – 5.02 (m, 1 H), 4.46 – 4.37 (m, 2 H), 3.30 – 3.27 (m, 1 H), 3.06 (dd, J = 13, 8.1 Hz, 1 H)	MS *m/z* 290.3 $(M + H)^+$
5: (*R*)-4-benzyl-3-(2-chloropyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 8.51 (d, J = 5.6 Hz, 1 H), 8.13 (d, J = 5.6 Hz, 1 H), 7.31 – 7.21 (m, 5 H), 5.06 – 4.98 (m, 1 H), 4.45 – 4.34 (m, 2 H), 3.30 – 3.25 (m, 1 H), 3.04 (dd, J = 14, 8.1 Hz, 1 H)	MS *m/z* 290.3 $(M + H)^+$
6: (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 8.50 (d, J = 5.9 Hz, 1 H), 8.17 (d, J = 5.8 Hz, 1 H), 4.83 – 4.76 (m, 1 H), 4.48 – 4.43 (m, 2 H), 2.56 (dtd, J = 14, 7.0, 3.8 Hz, 1 H), 0.99 (d, J = 7.1 Hz, 3 H), 0.87 (d, J = 7.1 Hz, 3 H)	MS *m/z* 242.6 $(M + H)^+$
7: (*S*)-4-benzhydryl-3-(2-chloropyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 8.41 (d, J = 5.8 Hz, 1 H), 8.01 (d, J = 5.8 Hz, 1 H), 7.35 – 7.26 (m, 3 H), 7.24 – 7.12 (m, 7 H), 5.86 – 5.70 (m, 1 H), 4.74 (d, J = 7.1 Hz, 1 H),	MS *m/z* 366.1 $(M + H)^+$

	4.64 (t, J = 8.5 Hz, 1 H), 4.45 (dd, J = 9.1, 2.0 Hz, 1 H)	
8: (*4R,5S*)-3-(2-chloropyrimidin-4-yl)-4-methyl-5-phenyloxazolidin-2-one	(CD_3OD) 8.52 (d, J = 6.1 Hz, 1 H), 8.20 (d, J = 6.1 Hz, 1 H), 7.48 – 7.38 (m, 5 H), 5.92 (d, J = 7.6 Hz, 1 H), 5.15 (quin, J = 6.8 Hz, 1 H), 0.98 (d, J =6.6 Hz, 3 H)	MS *m/z* 290.3 $(M + H)^+$
9: (*4S,5R*)-3-(2-chloropyrimidin-4-yl)-4-methyl-5-phenyloxazolidin-2-one	(CD_3OD) 8.52 (d, J = 6.1 Hz, 1 H), 8.20 (d, J = 6.1 Hz, 1 H), 7.48 – 7.38 (m, 5 H), 5.92 (d, J = 7.6 Hz, 1 H), 5.15 (quin, J = 6.7 Hz, 1 H), 0.98 (d, J =6.6 Hz, 3 H)	MS *m/z* 290.3 $(M + H)^+$
10: (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyl-5,5-dimethyloxazolidin-2-one	(CD_3OD) 8.48 (d, J = 5.8 Hz, 1 H), 8.20 (d, J = 5.8 Hz, 1 H), 4.63 (d, J = 3.1 Hz, 1 H), 2.29 (dtd, J = 14, 7.0, 3.1, 1 H), 1.60 (s, 3 H), 1.47 (s, 3 H), 1.05 (d, J = 7.1 Hz, 3 H), 0.99 (d, J = 7.1 Hz, 3 H)	MS *m/z* 270.1 $(M + H)^+$
11: (*S*)-3-(2-chloropyrimidin-4-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one	(CD_3OD) 8.48 (d, J = 5.8 Hz, 1 H), 8.25 (d, J = 5.8 Hz, 1 H), 7.39 – 7.30 (m, 3 H), 7.22 (br s, 2 H), 1.67 (s, 3 H), 1.04 (s, 3 H)	MS *m/z* 304.3 $(M + H)^+$
12: (*S*)-3-(2-chloropyrimidin-4-yl)-4-isobutyloxazolidin-2-one	(CD_3OD) 8.49 (d, J = 5.9 Hz, 1 H), 8.13 (d, J = 5.9 Hz, 1 H),4.83 (ddt, J = 10, 7.6, 2.9 Hz, 1 H), 4.58 – 4.54 (m, 1 H), 4.31 (dd, J = 8.8, 2.8 Hz, 1 H), 1.87 – 1.81 (m, 1 H), 1.75 – 1.65 (m, 1 H), 1.62 – 1.55 (m, 1 H), 1.05 (d, J = 6.5 Hz, 3 H), 0.99 (d, J = 6.5 Hz, 3 H)	MS *m/z* 256.3 $(M + H)^+$
13: (*R*)-3-(2-chloropyrimidin-4-yl)-4-isobutyloxazolidin-2-one	(CD_3OD) 8.48 (d, J = 5.8 Hz, 1 H), 8.12 (d, J = 6.0 Hz, 1 H),4.87 – 4.79 (m, 1 H), 4.57 (t, J = 8.6 Hz, 1 H), 4.31 (dd, J = 8.6, 2.5 Hz, 1 H), 1.87 – 1.81 (m, 1 H), 1.75 – 1.65 (m, 1 H), 1.62 – 1.56 (m, 1 H), 1.05 (d, J = 6.6 Hz, 3 H), 0.99 (d, J = 6.6 Hz, 3 H)	MS *m/z* 256.3 $(M + H)^+$
14: (*S*)-4-tert-butyl-3-(2-chloropyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 8.50 (d, J = 5.9 Hz, 1 H), 8.12 (d, J = 5.9 Hz, 1 H), 4.94 (dd, J = 7.6, 1.5 Hz, 1 H), 4.54 (dd, J = 9.1, 1.5 Hz, 1 H), 4.46 – 4.42 (m, 1 H), 0.95 (s, 9 H)	MS *m/z* 256.4 $(M + H)^+$
15: (*4R,5S*)-3-(2-chloropyrimidin-4-yl)-4,5-diphenyloxazolidin-2-one	(CD_3OD) 8.52 (d, J = 5.9 Hz, 1 H), 8.33 (d, J = 5.9 Hz, 1 H), 7.14 – 7.05 (m, 8 H), 6.93 – 6.91 (m, 2 H), 6.18 – 6.11 (m, 2 H)	MS *m/z* 352.4 $(M + H)^+$
16: (*4S,5R*)-3-(2-chloropyrimidin-4-yl)-4,5-diphenyloxazolidin-2-one	(CD_3OD) 8.52 (d, J = 5.9 Hz, 1 H), 8.33 (d, J = 5.9 Hz, 1 H), 7.14 – 7.05 (m, 8 H), 6.93 – 6.91 (m, 2 H), 6.18 – 6.11 (m, 2 H)	MS *m/z* 352.3 $(M + H)^+$
17: (*4S,5R*)-3-(2-chloropyrimidin-4-yl)-5-methyl-4-phenyloxazolidin-2-one	(CD_3OD) 8.47 (d, J = 5.9 Hz, 1 H), 8.25 (d, J = 5.9 Hz, 1 H), 7.40 – 7.31 (m, 3 H), 7.21 (d, J = 7.0 Hz, 2 H), 5.80 (d, J = 7.5 Hz, 1 H), 5.18 – 5.12 (m, 1 H), 1.02 (d, J = 6.5 Hz, 3 H);	MS *m/z* 290.4 $(M + H)^+$
18: (*S*)-4-benzyl-3-(2-	($CDCl_3$) 8.45 (d, J = 5.8 Hz, 1 H), 8.16	MS *m/z*

chloropyrimidin-4-yl)-5,5-dimethyloxazolidin-2-one	(d, J = 5.8 Hz, 1 H), 7.37 – 7.28 (m, 4 H), 7.25 – 7.21 (m, 1 H), 4.87 (dd, J = 9.0, 4.5 Hz, 1 H), 3.24 (dd, J = 15, 4.5 Hz, 1 H), 2.97 (dd, J = 14, 9.0 Hz, 1 H), 1.51 (s, 3 H), 1.45 (s, 3 H)	318.1 (M + H)$^+$
19: (*S*)-3-(2-chloropyrimidin-4-yl)-4-(pyridin-3-yl)oxazolidin-2-one	($CDCl_3$) 8.76 – 8.75 (m, 1 H), 8.62 (d, J = 3.5 Hz, 1 H), 8.47 (d, J = 5.8 Hz, 1 H), 8.16 (d, J = 5.8 Hz, 1 H), 7.74 (dt, J = 8.0, 2.0 Hz, 1 H), 7.35 (dd, J = 7.8, 4.8 Hz, 1 H), 5.83 (dd, J = 8.8, 3.8 Hz, 1 H), 4.90 (t, J = 9.0 Hz, 1 H), 4.50 (dd, J = 9.0, 3.5 Hz, 1 H)	MS *m/z* 277.4 (M + H)$^+$
20: 3-(2-chloropyrimidin-4-yl)-4-(4-methoxyphenyl)-5,5-dimethyloxazolidin-2-one	($CDCl_3$) 8.44 (d, J = 5.8 Hz, 1 H), 8.25 (d, J = 5.8 Hz, 1 H), 7.13 (br d, J = 7.0 Hz, 2 H), 6.89 (d, J = 9.0 Hz, 2 H), 5.39 (s, 1 H), 3.82 (s, 3 H), 1.67 (s, 3 H), 1.11 (s, 3 H)	HRMS(B) *m/z* 334.0954 (M + H)$^+$
21: (*S*)-3-(2-chloropyrimidin-4-yl)-4-(pyridin-2-yl)oxazolidin-2-one	($CDCl_3$) 8.62 – 8.60 (m, 1 H), 8.45 (d, J = 5.8 Hz, 1 H), 8.22 (d, J = 5.8 Hz, 1 H), 7.73 (td, J = 7.7, 1.8 Hz, 1 H), 7.43 (d, J = 7.5 Hz, 1 H), 7.29 – 7.26 (m, 1 H), 5.85 (dd, J = 8.5, 3.5 Hz, 1 H), 4.82 (t, J = 8.8 Hz, 1 H), 4.64 (dd, J = 8.8, 3.8 Hz, 1 H)	MS *m/z* 277.0 (M + H)$^+$
22: (*S*)-3-(2-chloropyrimidin-4-yl)-4-(pyridin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.72 – 8.70 (m, 1 H), 8.52 (d, J = 5.8 Hz, 1 H), 8.20 (d, J = 5.8 Hz, 1 H), 7.43 – 7.42 (m, 1 H), 5.81 (dd, J = 8.8, 3.8 Hz, 1 H), 4.91 (t, J = 9.0 Hz, 1 H), 4.44 (dd, J = 9.3, 3.8 Hz, 1 H)	MS *m/z* 276.9 (M + H)$^+$
23: (*S*)-3-(2-chloropyrimidin-4-yl)-4-methyl-4-phenyloxazolidin-2-one	($CDCl_3$) 8.44 (d, J = 5.8 Hz, 1 H), 8.13 (d, J = 5.8 Hz, 1 H), 7.41 – 7.28 (m, 5 H), 4.46 (d, J = 8.5 Hz, 1 H), 4.38 (d, J = 8.5 Hz, 1 H), 2.23 (s, 3 H)	MS *m/z* 289.9 (M + H)$^+$
24: (*S*)-3-(2-chloro-6-methylpyrimidin-4-yl)-4-isopropyloxazolidin-2-one	($CDCl_3$) 8.06 (s, 1 H), 4.83 – 4.77 (m, 1 H), 4.44 – 4.34 (m, 2 H), 2.65 – 2.55 (m, 1 H), 2.53 (s, 3 H), 1.00 (d, J = 8 Hz, 3 H), 0.88 (d, J = 8 Hz, 3 H)	MS *m/z* 255.8 (M + H)$^+$
25: (*S*)-3-(2-chloro-5-methylpyrimidin-4-yl)-4-isopropyloxazolidin-2-one	($CDCl_3$) 8.50 (s, 1 H), 5.01 – 4.96 (m, 1 H), 4.53 (t, J = 9.0 Hz, 1 H), 4.28 (t, J = 8.8 Hz, 1 H), 2.35 (s, 3 H), 2.16 (td, J = 7.0 Hz, J = 4.5 Hz, 1 H), 0.93 (d, J = 7.0 Hz, 3 H), 0.84 (d, J = 6.5 Hz, 3 H)	MS *m/z* 255.9 (M + H)$^+$
26: (*S*)-3-(2-chloro-5-fluoropyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO-d_6) 8.95 (d, J = 3.0 Hz, 1 H), 4.79 – 4.73 (m, 1 H), 4.58 (t, J = 9.0 Hz, 1 H), 4.41 (dd, J = 8.5 Hz, J = 6.5 Hz, 1 H), 2.24 – 2.16 (m, 1 H), 0.86 (d, J = 7.0 Hz, 3 H), 0.78 (d, J = 6.5 Hz, 3 H)	MS *m/z* 259.9 (M + H)$^+$
27: (*S*)-3-(2,5-dichloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO-d_6) 9.01 (s, 1 H), 4.81 (ddd, J = 9.1 Hz, J = 7.8 Hz, J = 4.3 Hz, 1 H), 4.59 (t, J = 8.8 Hz, 1 H), 4.38 – 4.33 (m, 1H), 2.06 (td, J = 7.0 Hz, J = 4.3 Hz, 1 H), 0.84 (d, J = 6.8 Hz, 3 H), 0.78 (d, J = 6.8 Hz, 3 H)	MS *m/z* 274.2 (M - H)$^-$
28: (*R*)-3-(2-chloropyrimidin-4-	($CDCl_3$) 8.20 (d, J = 5.8 Hz, 1 H), 8.01	MS *m/z*

yl)-5,5-dimethyl-4-phenyloxazolidin-2-one	(d, J = 5.8 Hz, 1 H), 7.16 – 7.07 (m, 3 H), 6.98 – 6.96 (m, 2 H), 5.19 (s, 1 H), 1.46 (s, 3 H), 0.87 (s, 3 H)	303.9 (M + H)$^+$
29: 3-(2-chloropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	($CDCl_3$) 8.47 (d, J = 5. 8 Hz, 1 H), 8.06 (d, J = 5.8 Hz, 1 H), 4.17 (s, 2 H), 1.77 (s, 6 H)	MS *m/z* 228.3 (M + H)$^+$
30: (*R*)-3-(2-chloropyrimidin-4-yl)-4-methyl-4-phenyloxazolidin-2-one	($CDCl_3$) 8.43 (d, J = 5.8 Hz, 1 H), 8.13 (d, J = 5.8 Hz, 1 H), 7.40 – 7.36 (m, 4 H), 7.35 – 7.28 (m, 1 H), 4.45 (d, J = 8.6 Hz, 1 H), 4.38 (d, J = 8.6 Hz, 1 H), 2.22 (s, 3 H)	MS *m/z* 289.9 (M + H)$^+$

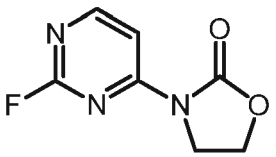
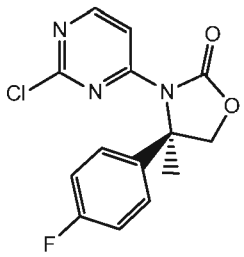
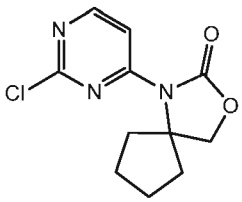
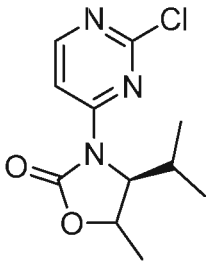
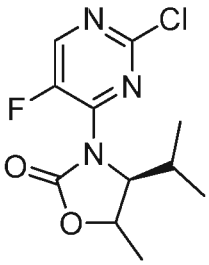
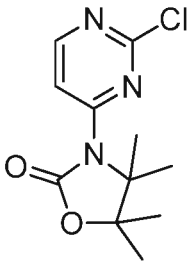
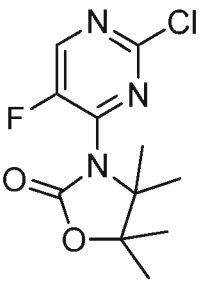
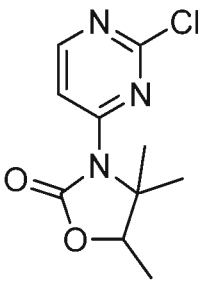
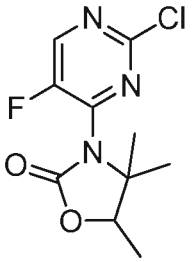
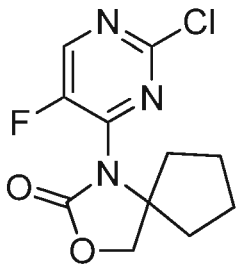
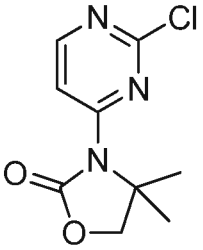
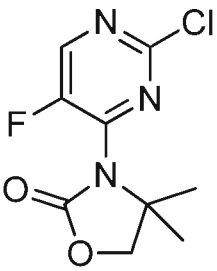
Intermediate 31: (S)-3-(2-fluoropyrimidin-4-yl)-4-isopropyloxazolidin-2-one



A solution of 2,4-difluoropyrimidine (3.5 mL, 41 mmol) and (S)-4-isopropyloxazolidin-2-one (5.3 g 41 mmol) in 30 mL DMF was cooled to 0 °C under N_2 atmosphere. NaH (2.1 g of 60% suspension, 53 mmol) was slowly added. Bubbling exotherm observed. Internal temp was kept below 5 °C. After 5 minutes, cold bath was removed. Reaction mixture (a sandy suspension) was allowed to warm to room temp and stir 18 h. The reaction mixture was diluted with water (100 mL) and extracted with (3 x 75 mL) EtOAc. Organic layer was washed with 50 mL each water, and brine. Dried over Na_2SO_4, and concentrated on silica gel in vacuo. Column chromatography (EtOAc/heptane 10 to 100% gradient) gave 3.1 g (S)-3-(2-fluoropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (IV) as a crystalline white solid (33%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (dd, J = 5.8, 2.2 Hz, 1H), 8.19 (dd, J = 5.8, 3.8 Hz, 1H), 4.79 (dt, J = 8.1, 3.5 Hz, 1H), 4.48 – 4.34 (m, 2H), 2.64 (heptd, J = 7.0, 3.6 Hz, 1H), 1.01 (d, J = 7.0 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H). MS m/z 471.8 and 471.8 (M + H)+.

The Intermediates in Table 4b were prepared by a method similar to the one described for the preparation of Intermediate 1 and 31.

Table 4b.

Intermediate 32	Intermediate 33	Intermediate 34
		
Intermediate 35	Intermediate 36	Intermediate 37
		
Intermediate 38	Intermediate 39	Intermediate 40
		
Intermediate 41	Intermediate 42	Intermediate 43
		
Intermediate 44		

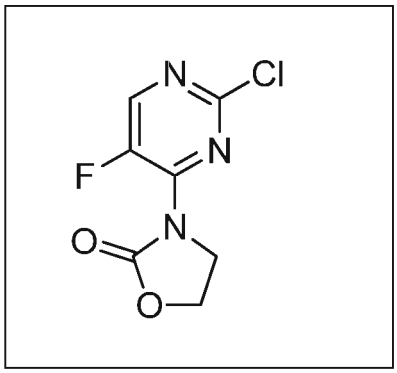
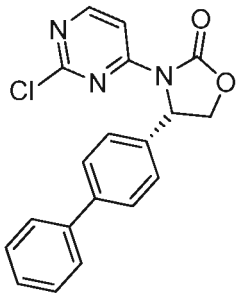


Table 4c. Chemical name, NMR chemical shifts and LCMS signal for each intermediate listed in Table 4b.

Intermediate: Name	**^{1}H NMR (400 MHz) δ ppm**	**LCMS**
32: 3-(2-fluoropyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.51 (dd, J = 5.8, 2.0 Hz, 1 H), 8.17 (dd, J = 5.8, 2.0 Hz, 1 H), 4.61 - 4.57 (m, 2 H), 4.31 - 4.27 (m, 2 H)	MS *m/z* 184.0 (M + H)
33: (R)-3-(2-chloropyrimidin-4-yl)-4-(4-fluorophenyl)-4-methyloxazolidin-2-one	($CDCl_3$) 8.45 (d, J = 5.8 Hz, 1 H), 8.12 (d, J = 5.8 Hz, 1 H), 7.40 – 7.35 (m, 2 H), 7.10 – 7.04 (m, 2 H), 4.40 – 4.37 (m, 2 H), 2.22 (s, 3 H)	MS m/z 308.0 (M + H)+
34: 1-(2-chloropyrimidin-4-yl)-3-oxa-1-azaspiro[4.4]nonan-2-one	($CDCl_3$) 8.48 (d, J = 5.8 Hz, 1 H), 8.12 (d, J = 5.8 Hz, 1 H), 4.22 (s, 2 H), 2.66 – 2.59 (m, 2 H), 2.22 – 2.14 (m, 2 H), 1.75 – 1.62 (m, 4 H)	MS m/z 254.1 (M + H)+
35: (4S)-3-(2-chloropyrimidin-4-yl)-4-isopropyl-5-methyloxazolidin-2-one		MS m/z (M + H)+ 256.2, Rt 0.87 min
36: (4S)-3-(2-chloro-5-fluoropyrimidin-4-yl)-4-isopropyl-5-methyloxazolidin-2-one		MS m/z (M + H)+ 274.1, Rt 0.82 min
37: 3-(2-chloropyrimidin-4-yl)-4,4,5,5-tetramethyloxazolidin-2-one		MS m/z (M + H)+ 256.1, Rt 0.85 min
38: 3-(2-chloro-5-fluoropyrimidin-4-yl)-4,4,5,5-tetramethyloxazolidin-2-one		MS m/z (M + H)+ 274.1, Rt 0.83 min
39: 3-(2-chloropyrimidin-4-yl)-4,4,5-trimethyloxazolidin-2-one		MS m/z (M + H)+ 242.1, Rt 0.81 min
40: 3-(2-chloro-5-fluoropyrimidin-4-yl)-4,4,5-trimethyloxazolidin-2-one		MS m/z (M + H)+ 260.1, Rt 0.77 min
41: 1-(2-chloro-5-fluoropyrimidin-4-yl)-3-oxa-1-azaspiro[4.4]nonan-2-one	($CDCl_3$) 8.47 (d, J = 2 Hz, 1 H), 4.28 (s, 2 H), 2.54 – 2.44 (m, 2 H), 2.11 – 1.99 (m, 2 H), 1.90 – 1.82 (m, 2 H), 1.72 – 1.61 (m, 42 H)	MS m/z (M + H)+ 272.4
42: 3-(2-chloropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one		MS m/z (M + H)+ 228.0, Rt 0.73 min

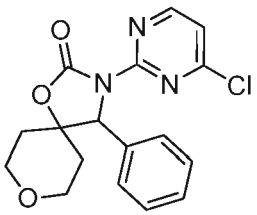
43: 3-(2-chloro-5-fluoropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one		MS m/z (M + H)+ 246.0, Rt 0.70 min
44: 3-(2-chloro-5-fluoropyrimidin-4-yl)oxazolidin-2-one		MS m/z (M + H)+ 218.0, Rt 0.47 min

Intermediate 46: (S)-4-(biphenyl-4-yl)-3-(2-chloropyrimidin-4-yl)oxazolidin-2-one



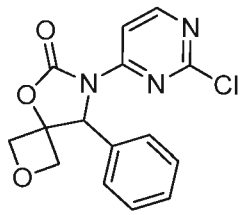
To a solution of 2,4-dichloropyrimidine (46.5 mg, 0.312 mmol) and (S)-4-(biphenyl-4-yl)oxazolidin-2-one (74.7 mg, 0.312 mmol) in DMF (700 µL) was added NaH (60%wt., 10.49 mg, 0.437 mmol) in two portions within ~5 min [Caution: exotherm; gas development] at room temperature (water bath). The reaction mixture was stirred for 1.5 hour. The mixture was diluted with EtOAc (25 mL), stirred for 5 min and then diluted slowly with diluted brine (10 mL; 1:1 brine/water). The mixture was poured into diluted brine (40 mL) and EtOAc (25 mL). The separated organic phase was washed with diluted brine (3x 40 ml), dried over Na_2SO_4, filtered off and concentrated under reduced pressure. The residue was purified by column chromatography [SiO_2, 40 g, EtOAc/heptane] to provide (S)-4-(biphenyl-4-yl)-3-(2-chloropyrimidin-4-yl)oxazolidin-2-one (49.5 mg). LCMS *m/z* 352.2 $(M + H)^+$, Rt 1.06 min.

Intermediate 47 : 3-(2-chloropyrimidin-4-yl)-4-phenyl-1,8-dioxa-3-azaspiro[4.5]decan-2-one



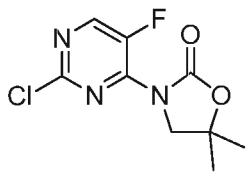
To a mixture of 4-phenyl-1,8-dioxa-3-azaspiro[4.5]decan-2-one (300 mg, 1.286 mmol) and 2,4-dichloropyrimidine (192 mg, 1.286 mmol) in DMF (7 mL) under argon was added NaH (60%wt., 67.9 mg, 2.83 mmol) in two portions. The mixture was stirred for ~1 hour. The reaction mixture was carefully poured into ice-colled 0.25N aqueous HCl solution. DCM and aqueous $NaHCO_3$ solution were added. The separated aqueous layer was extracted with DCM (3x) and ethyl acetate (1x). The organic layers (DCM and ethyl acetate containing layers independently) were washed with brine, dried over Na_2SO_4 and filtered off. The organic layers were combined and concentrated under reduced pressure providing crude 3-(2-chloropyrimidin-4-yl)-4-phenyl-1,8-dioxa-3-azaspiro[4.5]decan-2-one (330 mg) as a yellowish liquid, which was directly used in the next reaction without further purification. LCMS *m/z* 346.1 $(M + H)^+$, Rt 0.83 min.

Intermediate 48 : 7-(2-chloropyrimidin-4-yl)-8-phenyl-2,5-dioxa-7-azaspiro[3.4]octan-6-one



Prepared using similar methods as described above for 3-(2-chloropyrimidin-4-yl)-4-phenyl-1,8-dioxa-3-azaspiro[4.5]decan-2-one, but starting with oxetan-3-one.
LCMS *m/z* 318.1 $(M + H)^+$, Rt 0.78 min.

Intermediate 50: 3-(2-chloro-5-fluoropyrimidin-4-yl)-5,5-dimethyloxazolidin-2-one



Step 1
A solution of 2,4-dichloro-5-fluoropyrimidine (2 g, 11.98 mmol) in acetonitrile (10 mL) was cooled to -40 °C, avoiding freezing. To this solution was added diisopropylamine (3.82 mL, 21.88 mmol) followed by 1-amino-2-methylpropan-2-ol (1.5 g, 16.83 mmol). The reaction mixture was removed from the cooling bath, warmed to room temperature and allowed to stir overnight (~18 hours). Solvents were removed in vacuo and the residue was taken up in a minimum of dichloromethane (~1.5-2 mL) and diluted with heptane

until slightly cloudy.This mixture was loaded onto a 40 gram BioRad silica gel cartridge. Purification by flash chromatorgraphy (Analogix System, 20 min gradient, 0-25% methanol/dichloromethane, 40 mL/min.) provided 1-(2-chloro-5-fluoropyrimidin-4-ylamino)-2-methylpropan-2-ol as a white solid. LCMS *m/z* 220.1, 221.8 $(M + H)^+$, Rt 0.49 min.

Step 2

To a suspension of 1-(2-chloro-5-fluoropyrimidin-4-ylamino)-2-methylpropan-2-ol (400 mg, 1.82) in DCM/ethylacetate (5 mL) was added 2,6-lutidine (1 mL, 8.59 mmol). The reaction was cooled to -78°C and triphosgene (292 mg, 0.983 mmol) was added in a single portion. The reaction was removed from the cooling bath and allowed to warm to room temperature. The reaction had a pinkish coloration at this time. LCMS indicated consumption of starting material and conversion the intermediate acyl chloroformate adduct of 1-(2-chloro-5-fluoropyrimidin-4-ylamino)-2-methylpropan-2-ol. The reaction was sealed and stirred overnight. The reaction was stirred at room temperature overnight to provide only partial closure of the intermediate acyl formate to the cyclic carbamate. The reaction (sealed) was then heated at 60°C for ~4 hours until intermediate acyl chloroformate was consumed. Reaction was cooled to room temperature, diluted with DCM (~50 mL) and washed with water (1x50 mL) and sat. $NaHCO_3$ (1x50 mL). Aqueous layers were back extracted with DCM (~50 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated in vacuo. The solid was dissolved in DCM (~15 mL) and celite (~4 gram) was added. The mixture was concentrated and dried in vacuo to provide a solid pre-load for subsequent purification. Purification by flash chromatography(Analogix System, 80 gram silica gel column, 25 min. gradient, 0-25% methanol/dichloromethane, 40 mL/min) provided 3-(2-chloro-5-fluoropyrimidin-4-yl)-5,5-dimethyloxazolidin-2-one as a white solid. ^1H NMR (400 MHz, METHANOL-*d*4) δ ppm 1.58 (s, 8 H) 4.02 (s, 2 H) 8.59 (d, *J*=3.13 Hz, 1 H): LCMS *m/z* $(M + H)^+$ 246.1, 247.8.0, Rt 0.61 min

The Intermediates in Table 4d were prepared by methods similar to the one described for the preparation of Intermediate 50.

Table 4d.

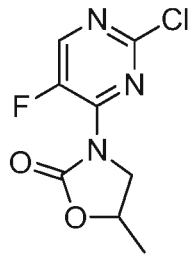
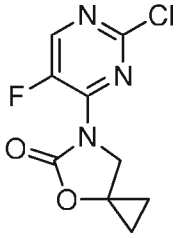
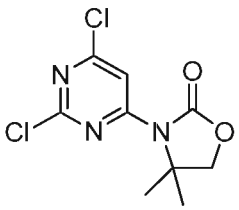
Intermediate 51	Intermediate 52
	

Table 4e. Chemical name, NMR chemical shifts and LCMS signal for each intermediate listed in Table 4d.

Intermediate: Name	^{1}H NMR (400 MHz, METHANOL-d4) δ ppm	LCMS
51: 3-(2-chloro-5-fluoropyrimidin-4-yl)-5-methyloxazolidin-2-one	1.52 (d, *J*=6.26 Hz, 3 H) 3.89 (dd, *J*=9.78, 7.43 Hz, 1 H) 4.26 (dd, *J*=9.78, 7.43 Hz, 1 H) 4.90 - 4.98 (m, 1 H) 8.58 (d, *J*=2.74 Hz, 1 H)	MS *m/z* (M + H)$^+$ 232.0, 233.9, Rt 0.52 min
52: 6-(2-chloro-5-fluoropyrimidin-4-yl)-4-oxa-6-azaspiro[2.4]heptan-5-one	0.90 - 1.08 (m, 2 H) 1.18 - 1.37 (m, 2 H) 4.31 (s, 2 H) 8.61 (d, *J*=3.13 Hz, 1 H)	MS *m/z* (M + H)$^+$ 244.0, 245.8, Rt 0.61 min

Intermediate 53: 3-(2,6-dichloropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one



A solution of 4,4-dimethyloxazolidin-2-one (0.103 g, 0.895 mmol) and 2,4,6-trichloropyrimidine (0.181 g, 0.984 mmol, 1.10 equiv) in DMF (3 mL) was treated with NaH (60 %, 0.0429 g, 1.07 mmol, 1.2 equiv), then the resulting mixture (yellow) was stirred at room temperature for 1 h. The reaction mixture was diluted with EtOAc (20 mL), washed with saturated aqueous NaCl (2 x 20 mL), dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 0 to 40%) provided3-(2,6-dichloropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one (0.146 g, white solid) in 62.3% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (s,1 H), 4.16 (s, 2 H), 1.74 (s, 9H); LCMS *m/z* 261.9 (M + H)$^+$, Rt 0.91 min.

The Intermediates in Table 4f were prepared by a method similar to the one described for the preparation of Intermediate 53.

Table 4f.

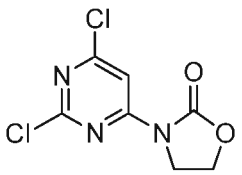
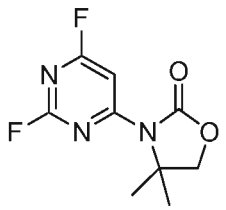
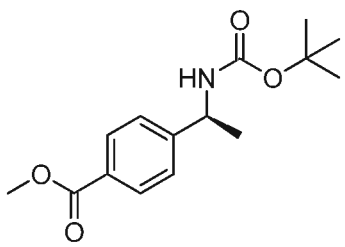
Intermediate 54	Intermediate 55
	

Table 4g. Chemical name, NMR chemical shifts and LCMS signal for each intermediate listed in Table 4f.

Intermediate: Name	**^{1}H NMR (400 MHz) δ ppm**	**LCMS**
54: 3-(2,6-dichloropyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.20 (s, 1 H), 4.59 (t, J = 8.0 Hz, 2 H), 4.29 (t J = 8.0 Hz, 2 H)	MS *m/z* 234.0 (M + H)$^+$, Rt 0.67 min
55: 3-(2,6-difluoropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	($CDCl_3$) 7.68 (d, J = 2.0 Hz, 1 H), 4.16 (s, 2 H), 1.74 (s, 6 H)	MS *m/z* 230.1 (M + H)$^+$, Rt 0.79 min

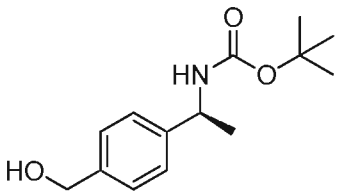
Intermediate 56 : (S)-methyl 4-(1-(tert-butoxycarbonylamino)ethyl)benzoate



To a solution of (S)-methyl 4-(1-aminoethyl)benzoate (4.9 g, 22.7 mmol) in DCM (114 mL) was added di-tert-butyl dicarbonate (5.95 g, 27.3 mmol) and triethylamine (6.97 mL, 50 mmol). The solution was stirred for 16 h at room temperature then washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/heptane 0 to 80%) provided (S)-methyl 4-(1-(tert-butoxycarbonylamino)ethyl)benzoate as a white solid (6.35 g, 100% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 7.96 (m, 2H), 7.40 – 7.33 (m, 2H), 4.83 (s, 1H), 3.91 (s, 3H), 1.43 – 1.23 (m, 12H); MS m/z 224.0 (M - 56 + H).

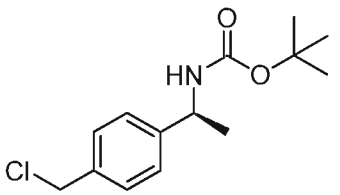
Intermediate 57 : (S)-tert-butyl 1-(4-(hydroxymethyl)phenyl)ethylcarbamate



To a cooled (0 °C) solution of (S)-methyl 4-(1-(tert-butoxycarbonylamino)ethyl)benzoate (6.35 g, 22.7 mmol) in THF (114 mL) was added a solution of LAH in THF (2.0 M, 13.64 mL, 27.3 mmol) and the resulting mixture was stirred at room temperature for 40 min. The reaction mixture was quenched by addition of a 1N NaOH solution until gas evolution ceased. The reaction mixture was filtered, washed with EtOAc. After separation, the aqueous phase was washed with EtOAc (2 x 150 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/heptane 0 to 100%) provided (S)-tert-butyl 1-(4-(hydroxymethyl)phenyl)ethylcarbamate as a white solid (5.01 g, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.23 (m, 4H), 4.80 – 4.71 (m, 1H), 4.67 (s,2H), 2.04 (bs, 1H), 1.47 – 1.37 (m, 12H); MS m/z 196.0 (M - 56 + H).

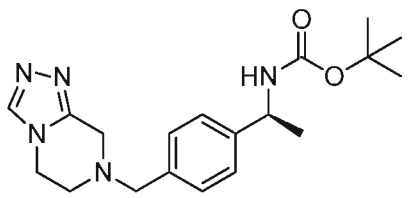
Intermediate 58: (S)-tert-butyl 1-(4-(chloromethyl)phenyl)ethylcarbamate



To a solution of (S)-tert-butyl 1-(4-(hydroxymethyl)phenyl)ethylcarbamate (503 mg, 2 mmol) in DCM (10 mL) was added methanesulfonyl chloride (275 mg, 2.4 mmol) and triethylamine (0.56 mL, 4 mmol). The solution was stirred for 16 h at room temperature then washed with water and brine. After separation, the organic phase was dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/heptane 0 to 80%) provided (S)-tert-butyl 1-(4-(chloromethyl)phenyl)ethylcarbamate as a white solid (254 g, 47.1% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.24 (m, 4H), 4.79 (s, 1H), 4.58 (s, 2H), 1.50 – 1.30 (br m, 12H); MS m/z 214.0 (M - 56 + H).

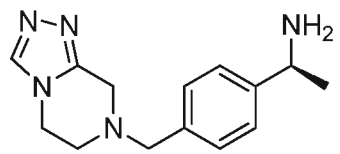
Intermediate 59: (S)-tert-butyl 1-(4-((5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methyl)phenyl)ethylcarbamate



A solution of (S)-tert-butyl 1-(4-(chloromethyl)phenyl)ethylcarbamate (127 mg, 0.47 mmol), 5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine (91 mg, 0.56 mmol) and DIPEA (183 mg, 1.41 mmol) in DMSO (2.3 mL) was heated at 80 °C for 16 h. The reaction mixture was diluted with EtOAc (20 mL) and washed with water (20 mL). After separation, the aqueous phase was washed with EtOAc (2 x 15 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. The crude product was used to next step without further purification.

MS m/z 358.3 (M + H)

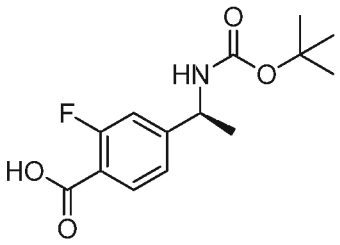
Intermediate 60: (S)-1-(4-((5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methyl)phenyl)ethanamine



To a solution of (S)-tert-butyl 1-(4-((5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methyl)phenyl)ethylcarbamate (168 mg, 0.47 mmol) in DCM (2 mL) was added TFA (2 mL, 26 mmol) slowly at -78 °C. The reaction was stirred at room temperature for 1 h then concentrated and diluted with DCM (10 mL). The solution was stirred with 3 eq. of MP-carbonate resin (3.28 mmol/g, Biotage) for 1 hour at room temperature. The resin was removed by filtration and washed (2 x 5 mL) with DCM. The filtrate was concentrated and the crude residue was used to next step without further purification.

MS m/z 258.2 (M + H).

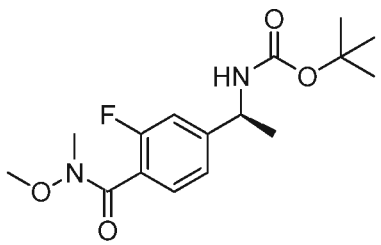
Intermediate 61: (S)-4-(1-(tert-butoxycarbonylamino)ethyl)-2-fluorobenzoic acid



To a solution of (S)-4-(1-aminoethyl)-2-fluorobenzoic acid (5 g, 22.76 mmol) in water (66 mL) and THF (66 mL) was added di-tert-butyl dicarbonate (6.95 g, 31.9 mmol) and sodium carbonate (5.74 g, 68.3 mmol). The solution was stirred for 16 h at room temperature then THF was removed under reduced pressure. The aqueous solution was acidified with 1N HCl to pH 3-4 and extracted with EtOAc (3 x 60 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated to give a white solid (1.94 g, 30.1% yield). The crude product was used to next step without further purification.

^{1}H NMR (400 MHz, MeOD) δ 7.89 (t, J = 7.8 Hz, 1H), 7.20 (dd, J = 8.2, 1.7 Hz, 1H), 7.13 (dd, J = 12.0, 1.6 Hz, 1H), 4.70 (d, J = 7.1 Hz, 1H), 1.47 – 1.35 (m, 12H); MS m/z 282.0 (M - H).

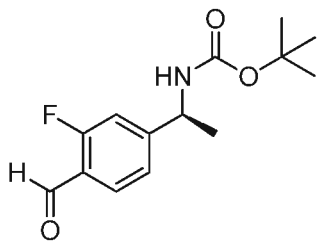
Intermediate 62: (S)-tert-butyl 1-(3-fluoro-4-(methoxy(methyl)carbamoyl)phenyl) ethylcarbamate



A solution of (S)-4-(1-(tert-butoxycarbonylamino)ethyl)-2-fluorobenzoic acid (1.416 g, 5mmol), N,O-dimethylhydroxylamine hydrochloride (732 mg, 7.5 mmol), HATU (2.85 g, 7.5 mmol) and DIPEA (3.49 mL, 20 mmol) in DMF (25 mL) was stirred at room temperature for 16 h. The reaction mixture was diluted with EtOAc and washed with water. After separation, the aqueous phase was washed with EtOAc (2 x 75 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/heptane 12 to 100%) provided (S)-tert-butyl 1-(3-fluoro-4-(methoxy(methyl)carbamoyl)phenyl)ethylcarbamate as a white solid (1.5 g, 92 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (t, J = 7.4 Hz, 1H), 7.13 (dd, J = 7.8, 1.6 Hz, 1H), 7.04 (dd, J = 10.7, 1.6 Hz, 1H), 4.80 (br s, 1H), 3.56 (s, 3H), 3.34 (s, 3H), 1.50 – 1.29 (m, 12H); MS m/z 327.1 (M + H).

Intermediate 63 : (S)-tert-butyl 1-(3-fluoro-4-formylphenyl)ethylcarbamate

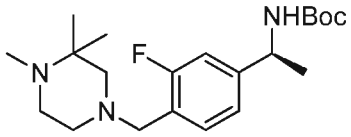


Procedure 1: To a cooled (0 °C) solution of (S)-tert-butyl 1-(3-fluoro-4-(methoxy(methyl)carbamoyl)phenyl)ethylcarbamate (1.175 g, 3.6 mmol) in THF (36 mL) was added a solution of LAH in THF (1.0 M, 18 mL, 18 mmol) and the resulting mixture was stirred at 0 °C for 20 min. The reaction mixture was quenched by addition of a saturated Na_2SO_4 solution until gas evolution ceased. The reaction mixture was extracted with EtOAc (2 x 100 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/heptane 12 to 100%) provided (S)-tert-butyl 1-(3-fluoro-4-formylphenyl)ethylcarbamate as a white solid (760 mg, 79% yield).

Procedure 2: A solution of (S)-tert-butyl 1-(4-bromo-3-fluorophenyl)ethylcarbamate (318 mg, 1 mmol) in dry THF (5 mL) was cooled to -78 °C. BuLi (2.5 M, 840 µL, 2.1 mmol) was added dropwise and the resulting solution was stirred at -78 °C for 1 h. Then DMF (232 µL, 3.00 mmol) was added in one portion. The reaction was stirred for another 30 min at -78 °C then quenched with sat. NH4Cl solution. The reaction was stirred at room temperature for another 30 min then diluted with EtOAc, washed with water and brine. The separated organic was dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/heptane 0 to 80%) provided (S)-tert-butyl 1-(3-fluoro-4-formylphenyl)ethylcarbamate as a white solid (70 mg, 26.2% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.31 (s, 1H), 7.87 – 7.80 (m, 1H), 7.20 (dd, J = 8.2, 1.3 Hz, 1H), 7.11 (dd, J = 11.5, 1.4 Hz, 1H), 4.80 (br s, 1H), 1.45 (br s, 12H); MS m/z 212.1 (M - 56 + H).

Intermediate 64: (S)-tert-butyl 1-(3-fluoro-4-((3,3,4-trimethylpiperazin-1-yl)methyl)phenyl)ethylcarbamate

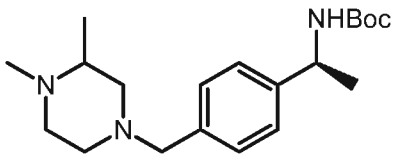


(General procedure A for reductive amination)

A solution of (S)-tert-butyl 1-(3-fluoro-4-formylphenyl)ethylcarbamate (267 mg, 1 mmol) and 1,2,2-trimethylpiperazine dihydrochloride (402 mg, 2 mmol) in THF (5 mL) was stirred at room temperature for 1 h and treated with sodium triacetoxyborohydride (848 mg, 4 mmol). The resulting mixture was stirred at room temperature for 16 h. The reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ (15 mL) and extracted with EtOAc (3 x 25 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography ($MeOH/CH_2Cl_2$ 0 to 10%) provided (S)-tert-butyl 1-(3-fluoro-4-((3,3,4-trimethylpiperazin-1-yl)methyl)phenyl)ethylcarbamate as a white solid (186 mg, 49% yield).

^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (t, J = 7.7 Hz, 1H), 7.03 (dd, J = 7.9, 1.9 Hz, 1H), 6.95 (dd, J = 11.1, 1.8 Hz, 1H), 4.77 (s, 1H), 3.49 (s, 2H), 2.56 (br s, 4H), 2.24 (br s, 5H), 1.42 (br s, 12H), 1.04 (s, 6H); MS m/z 380.4 (M + H).

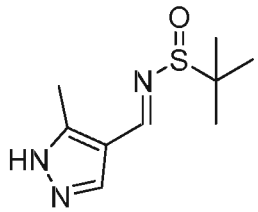
Intermediate 65: tert-butyl (1S)-1-(4-((3,4-dimethylpiperazin-1-yl)methyl)phenyl)ethylcarbamate



A solution of (S)-tert-butyl 1-(4-formylphenyl)ethylcarbamate (84.1 mg, 0.337 mmol) [obtained from (S)-1-(4-bromophenyl)ethanamine following the procedure of Hashihayata, Takashi PCT Int. Appl., 2008081910, 10 Jul 2008] and 1,2-dimethylpiperazine (86.3 mg, 0.756 mmol, 2.24 equiv) in THF (1.5 mL) was stirred at room temperature for 65 min and treated with sodium triacetoxyborohydride (277.2 mg, 1.308 mmol, 3.88 equiv). The resulting mixture was stirred at room temperature for 16 hours. The reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ (15 mL) and extracted with EtOAc (5 x 15 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography ($MeOH/CH_2Cl_2$ 0 to 20%) provided tert-butyl (1S)-1-(4-((3,4-dimethylpiperazin-1-yl)methyl)phenyl)ethyl carbamate (90.7 mg) in 34.5% yield.

^{1}H NMR (400 MHz, CD_3OD) δ 7.29 (s, 4 H), 4.68 (br s, 1 H), 3.54 - 3.47 (m, 2 H), 3.37 (s, 1 H), 2.84 - 2.74 (m, 3 H), 2.38 (td, J = 12, 2.5 Hz, 1 H), 2.31 (s, 3 H), 2.28 - 2.22 (m, 2 H), 1.94 - 1.89 (m, 1 H), 1.40 (br s, 9 H), 1.38 (d, J = 6.9 Hz, 3 H), 1.06 (d, J = 6.3 Hz, 3 H); MS m/z 348.2 (M + H)

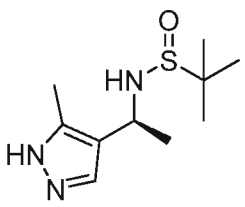
Intermediate 66: (R,E)-2-methyl-N-((3-methyl-1H-pyrazol-4-yl)methylene)propane-2-sulfinamide



3-methyl-1H-pyrazole-4-carbaldehyde (2.03g, 18.44mmol) was dissolved in THF (30ml) and (R)-2-methylpropane-2-sulfinamide (2.35, 19.39mmol) was added followed by Ti(OEt)4 (8.41mmol, 36.90mmol). The resulting reaction mixture was stirred at 80°C for 18h. LCMS shows mostly product. The reaction mixture was diluted with EtOAc (300 mL), washed with 4% aqueous NaCl (2 x 150, 2X50 mL). The combined aq. layers were back extracted with EtOAc (100ml). The combined organic layers were washed with brine (100ml), dried over Na_2SO_4, filtered and concentrated. Purified by column chromatography (REDI 80g, EtOAc/heptane 20-100% over 33 min 100% for 7min.) to give title compound (2.25g, 10.55mmol).

^{1}H NMR (400 MHz, MeOD) δ 8.55 (s, 1H), 2.53 (s, 3H), 1.25 (s, 9H). MS 214.2 m/z (M+H)

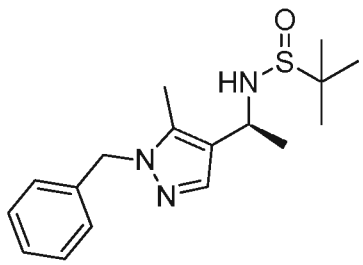
Intermediate 67: (R)-2-methyl-N-((S)-1-(3-methyl-1H-pyrazol-4-yl)ethyl)propane-2-sulfinamide



(R,E)-2-methyl-N-((3-methyl-1H-pyrazol-4-yl)methylene)propane-2-sulfinamide (2.25g, 10.55mmol) was dissolved in THF and cooled to 0C. Methylmagnesium bromide (3M, 12.5ml, 37.5mmol) was added dropwise and the resulting solution was stirred for 1h. Ice

bath was removed and the reaction was stirred for another 15h. Another 2.5eq. of methylmagnesium bromide MeMgBr was added (at 0°C
). Not a lot of change by LCMS.
The reaction mixture was quenched with sat NH4Cl and the aq. layer was washed with THF (2X). Combined organic layers washed with brine, dried over Na_2SO_4, filtered and concentrated to give title compound (1.79g, 7.80mmol)
^{1}H NMR (400 MHz, MeOD) δ 7.48 (s, 1H), 4.49 (qd, J = 6.7, 4.7 Hz, 1H), 2.26 (s, 3H), 1.57 (dd, J = 6.5, 1.3 Hz, 3H), 1.23 (s, 9H). MS 230.2 m/z (M+H)

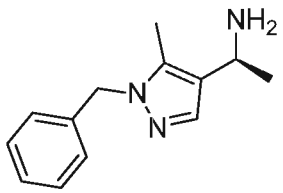
Intermediate 68: (R)-N-((S)-1-(1-benzyl-3-methyl-1H-pyrazol-4-yl)ethyl)-2-methylpropane-2-sulfinamide



(R)-2-methyl-N-((S)-1-(3-methyl-1H-pyrazol-4-yl)ethyl)propane-2-sulfinamide (290mg, 1.26mmol) was dissolved in DMF (5ml) and added dropwise to a solution of Cs2CO3 (458mg, 1.41mmol) in DMF (4ml). The resulting reaction mixture was stirred at room temperature for 15min. benzylbromide (216mg, 1.26mmol) was added and the reaction was stirred at room temperature for 2h. LCMS shows mostly product with some starting pyrazole. Added another 0.1ml of BnBr and 135mg of Cs_2CO_3. Stirred another 24H at 50ºC.The reaction mixture was diluted with EtOAc (300 mL), washed with 4% aqueous NaCl (2 x 150, 2X50 mL). The combined aq. layers were back extracted with EtOAc (100ml). The combined organic layers were washed with brine (100ml), dried over Na_2SO_4, filtered and concentrated. Silica gel chromatography, EtOAc/heptane 20-80% to give title compound (mix of regioisomers, 150mg, 0.470mmol).
^{1}H NMR (400 MHz, MeOD) δ 7.54 (s, 0.6H), 7.46 (s, 0.4H), 7.36 – 6.99 (m, 5H), 5.31 (s, 0.8H), 5.21 (s, 1.2H), 4.44 (t, J = 6.9 Hz, 1H), 2.21 (2s, 3H), 1.54 (2dt, 3H), 1.17 (s, 9H). MS 320.2 m/z (M+H)

Intermediate 69:

(S)-1-(1-benzyl-3-methyl-1H-pyrazol-4-yl)ethanamine hydrochloride



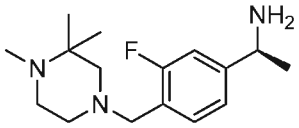
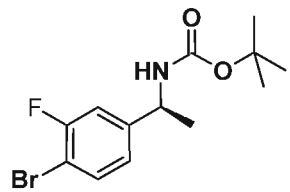
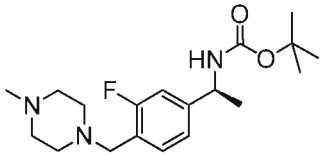
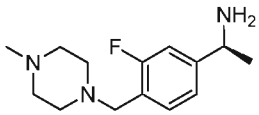
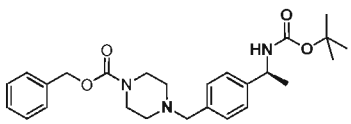
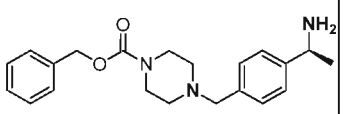
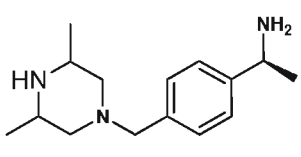
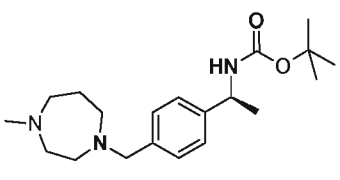
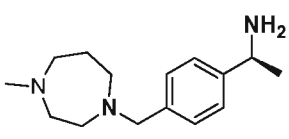
(R)-N-((S)-1-(1-benzyl-3-methyl-1H-pyrazol-4-yl)ethyl)-2-methylpropane-2-sulfinamide was dissolved in dioxane (5ml) and 4N HCl in dioxane (1.2ml, 10eq.) was added. Stirred 1H at room termperature. The solvents were removed and co-vapped twice with CH_2Cl_2. Some t-butyl observed by NMR. Resubmitted to reaction conditions and work-up to give title compound.

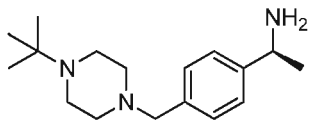
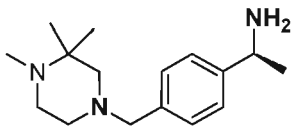
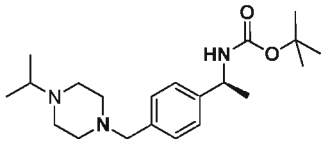
^{1}H NMR mixture of regioisomers (400 MHz, MeOD) δ 8.00 (s, 0.7H), 7.80 (s, 0.3H), 7.52 – 6.96 (m, 5H), 5.40 (s, 0.6H), 5.36 (s, 1.4H), 4.47 (q, J = 6.9 Hz, 1H), 2.34 (s, 2.1H), 2.32 (s, 0.9H), 1.62 (2d, J = 6.9 Hz, 3H).

MS 216.3 m/z (M+H)

The Intermediates in Table 4h were prepared by methods substantially similar to those described for the preparation of Intermediates 56 through 69.

Table 4h.

Intermediate 70	Intermediate 71	Intermediate 72
		
Intermediate 73	Intermediate 74	Intermediate 75
		
Intermediate 76	Intermediate 77	Intermediate 78
		

Intermediate 79	Intermediate 80	Intermediate 81
		
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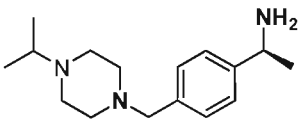	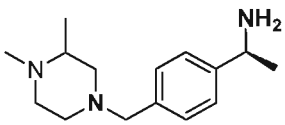	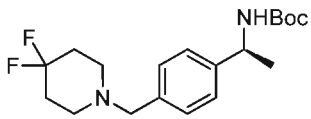
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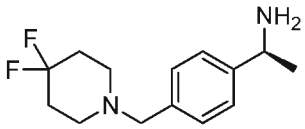	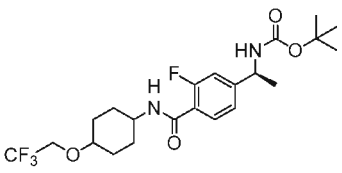	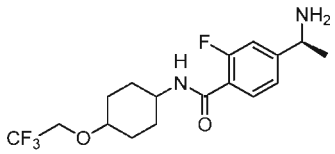
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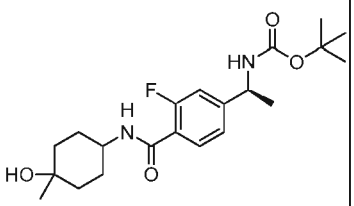	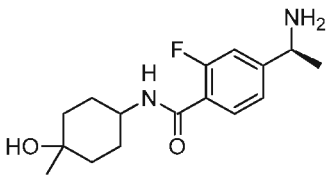	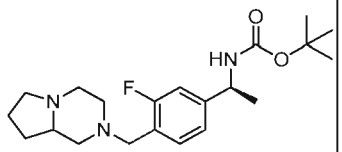
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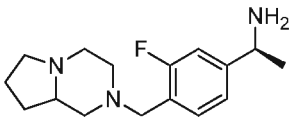	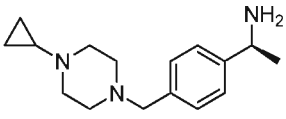	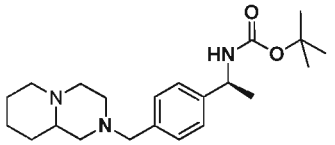
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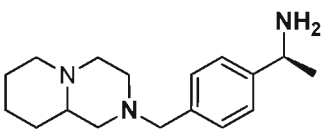	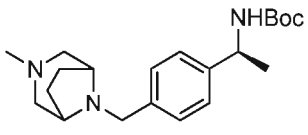	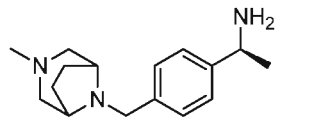
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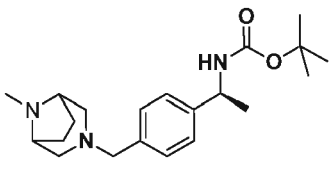	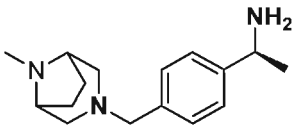	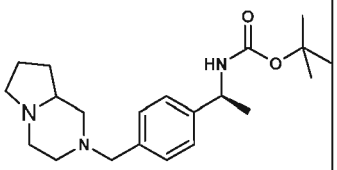
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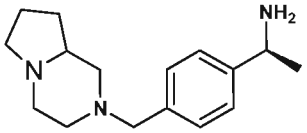	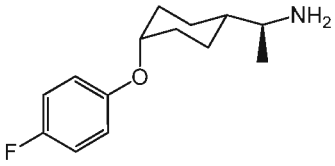	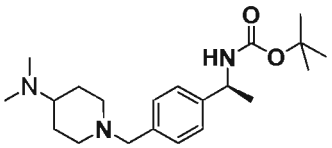
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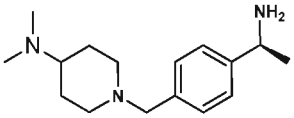	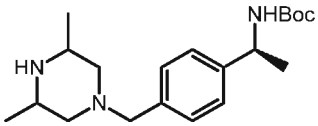	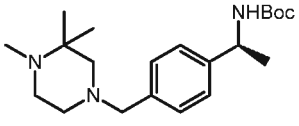
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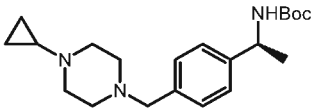	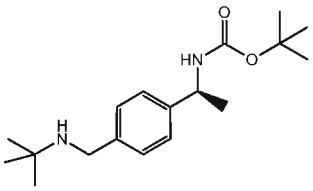	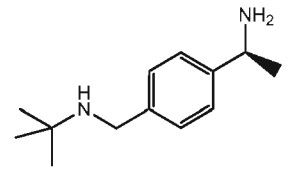
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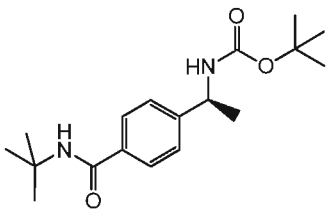	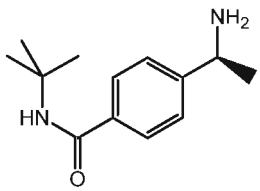	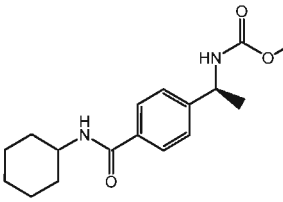
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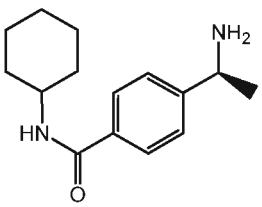	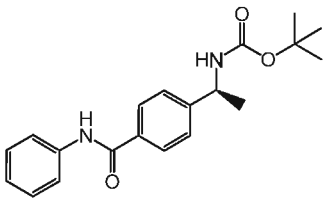	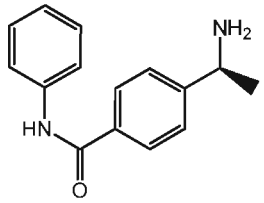
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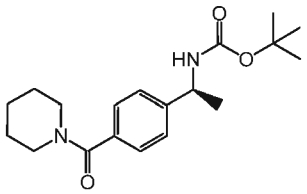	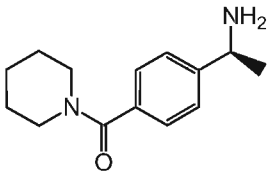	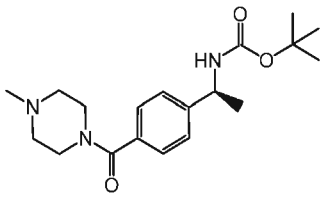
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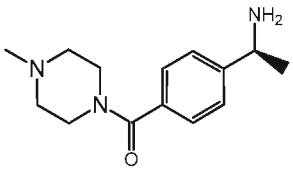	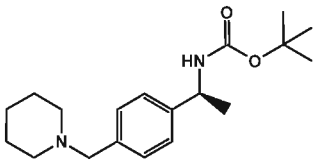	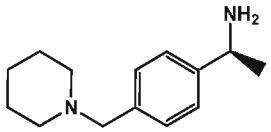
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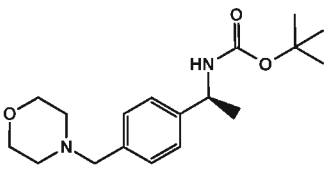	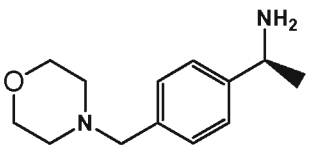	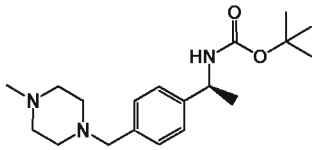
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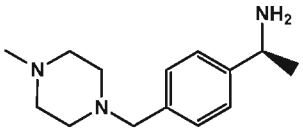
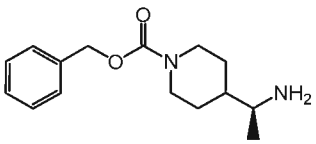
		

Table 4i. Chemical name, NMR chemical shifts and LCMS signal for each intermediate listed in Table 4h.

Intermediate: Name	^{1}H NMR **(400 MHz)** δ **ppm**	**LCMS**
70: (S)-1-(3-fluoro-4-((3,3,4-trimethylpiperazin-1-yl)methyl)phenyl)ethanamine		MS m/z 280.2 (M + H).
71: (S)-tert-butyl 1-(4-bromo-3-fluorophenyl)ethylcarbamate	($CDCl_3$) 7.51 – 7.45 (m, 1H), 7.07 (dd, J = 9.8, 2.0 Hz, 1H), 6.98 (dd, J = 8.4, 2.1 Hz, 1H), 4.67 (br s, 1H),, 1.41(br s, 12H)	MS m/z 317.9 (M + H).
72: (S)-tert-butyl 1-(3-fluoro-4-((4-methylpiperazin-1-yl)methyl)phenyl)ethylcarbamate	($CDCl_3$) 7.28 (t, J = 7.7 Hz, 1H), 7.01 (dd, J = 7.7, 1.8 Hz, 1H), 6.94 (dd, J = 10.8, 1.9 Hz, 1H), 4.86 (br s, 1H), 4.74 (br s, 1H), 3.54 (s, 2H), 2.67 – 2.29 (m, 8H), 2.25 (s, 3H), 1.51 – 1.26 (m, 12H)	MS m/z 353.2 (M + H)
73: (S)-1-(3-fluoro-4-((4-		MS m/z

methylpiperazin-1-yl)methyl)phenyl)ethanamine		252.1 (M + H)
74: (S)-benzyl 4-(4-(1-(tert-butoxycarbonylamino) ethyl)benzyl)piperazine-1-carboxylate	($CDCl_3$) 7.43 – 7.19 (m, 9H), 5.12 (s, 2H), 4.78 (br s, 2H), 3.95 – 3.20 (m, 6H), 2.43 (br s, 4H), 1.43 (br s, 12H)	MS m/z 454.3 (M + H)
75: (S)-benzyl 4-(4-(1-aminoethyl)benzyl)piperazine-1-carboxylate		MS m/z 354.3 (M + H)
76: (1S)-1-(4-((3,5-dimethylpiperazin-1-yl)methyl)phenyl)ethanamine		MS m/z 248.2 (M + H)
77: (S)-tert-butyl 1-(4-((4-methyl-1,4-diazepan-1-yl)methyl)phenyl)ethylcarbamate	($CDCl_3$) 7.31 – 7.20 (m, 4H), 4.78 (s, 1H), 3.61 (s, 2H), 2.81-2.69 (m, 8H), 2.44 (s, 3H), 1.94 – 1.85 (m, 2H), 1.43 (br s, 12H)	MS m/z 349.4 (M + H)
78: (S)-1-(4-((4-methyl-1,4-diazepan-1-yl)methyl)phenyl)ethanamine		MS m/z 248.1 (M + H)
79: (S)-1-(4-((4-tert-butylpiperazin-1-yl)methyl)phenyl)ethanamine		MS m/z 276.2 (M + H)
80: (S)-1-(4-((3,3,4-trimethylpiperazin-1-yl)methyl)phenyl)ethanamine		MS m/z 262.2 (M + H)
81: (S)-tert-butyl 1-(4-((4-isopropylpiperazin-1-yl)methyl)phenyl)ethylcarbamate	($CDCl_3$) 7.28-7.22 (m, 4H), 4.78 (s, 1H), 3.49 (s, 2H), 2.88 – 2.22 (m, 9H), 1.42 (br s, 12H), 1.05 (d, J = 6.5 Hz, 6H)	MS m/z 363.4 (M + H)
82: (S)-1-(4-((4-isopropylpiperazin-1-yl)methyl)phenyl)ethanamine		MS m/z 262.2 (M + H)
83: (1S)-1-(4-((3,4-dimethylpiperazin-1-yl)methyl)phenyl)ethanamine		MS m/z 248.2 (M + H)
84: (S)-tert-butyl 1-(4-((4,4-difluoropiperidin-1-yl)methyl)phenyl)ethylcarbamate		MS m/z 356.2 (M + H)
85: (S)-1-(4-((4,4-difluoropiperidin-1-yl)methyl)phenyl)ethanamine		MS m/z 255.2 (M + H)
86: (S)-tert-butyl 1-(3-fluoro-4-(4-(2,2,2-trifluoroethoxy) cyclohexylcarbamoyl) phenyl)ethylcarbamate	($CDCl_3$) 8.01 (t, J = 8.1 Hz, 1H), 7.16 (d, J = 7.9, 1H), 7.04 (d, J = 13.2, 1H), 6.67 -6.63(m, 1H), 4.96 (br s, 1H), 4.76 (br s, 1H), 4.06 (br s, 1H), 3.85-3.77 (m, 2H), 3.64 (br s, 1H), 1.92 – 1.74 (m, 4H), 1.73 – 1.59 (m, 4H), 1.40 (br s, 12H)	MS m/z 463.3 (M + H)
87: (S)-4-(1-aminoethyl)-2-fluoro-N-(4-(2,2,2-trifluoroethoxy)cyclohexyl)benzamide		MS m/z 363.2 (M + H)
88: (S)-tert-butyl 1-(3-fluoro-4-(4-hydroxy-4-methylcyclohexylcarbamoyl) phenyl)ethylcarbamate	($CDCl_3$) 8.04 (t, J = 8.1 Hz, 1H), 7.19 (d, J = 8.3, 1H), 7.05 (dd, J = 13.2, 1.7 Hz, 1H), 6.65 (br dd, J = 12.1, 6.6 Hz, 2H), 4.84 (br s, 1H), 4.77 (br s, 1H), 4.17 – 4.06 (m, 1H), 2.09 – 2.00 (m,	MS m/z 395.1 (M + H)

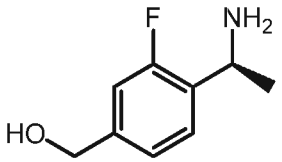
	2H), 1.61-1.59 (m, 4H), 1.55-1.47 (m, 2H), 1.42 (br s, 12H), 1.30 (s, 3H)	
89: (S)-4-(1-aminoethyl)-2-fluoro-N-(4-hydroxy-4-methylcyclohexyl)benzamide		MS m/z 295.2 (M + H)
90: tert-butyl (1S)-1-(3-fluoro-4-((hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)methyl)phenyl)ethylcarbamate		MS m/z 376.1 (M - H)
91: (1S)-1-(3-fluoro-4-((hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)methyl)phenyl)ethanamine		MS m/z 278.1 (M + H)
92: (S)-1-(4-((4-cyclopropylpiperazin-1-yl)methyl)phenyl)ethanamine		MS m/z 260.2 (M + H)
93: tert-butyl (1S)-1-(4-((dihydro-1H-pyrido[1,2-a]pyrazin-2(6H,7H,8H,9H,9aH)-yl)methyl)phenyl)ethylcarbamate	($CDCl_3$) 7.30 – 7.20 (m, 4H), 4.78 (s, 2H), 3.46 (s, 2H), 2.89 – 2.61 (m, 4H), 2.39 – 2.21 (m, 2H), 2.10 – 1.93 (m, 2H), 1.86 (t, J = 10.7 Hz, 1H), 1.79 – 1.68 (m, 1H), 1.62 (br s, 2H), 1.43 (br s, 13H), 1.32-1.19 (m, 2H)	MS m/z 372.4 (M - H)
94: (1S)-1-(4-((dihydro-1H-pyrido[1,2-a]pyrazin-2(6H,7H,8H,9H,9aH)-yl)methyl)phenyl)ethanamine		MS m/z 274.2 (M + H)
95: tert-butyl (1S)-1-(4-((3-methyl-3,8-diazabicyclo[3.2.1]octan-8-yl)methyl)phenyl)ethylcarbamate		MS m/z 361.3 (M + H)
96: (1S)-1-(4-((3-methyl-3,8-diazabicyclo[3.2.1]octan-8-yl)methyl)phenyl)ethanamine		MS m/z 260.2 (M + H)
97: tert-butyl (1S)-1-(4-((8-methyl-3,8-diazabicyclo[3.2.1]octan-3-yl)methyl)phenyl)ethylcarbamate	($CDCl_3$) 7.28 – 7.19 (m, 4H), 4.77 (br s, 2H), 3.44 (s,2H), 3.03 (br s, 2H), 2.55 (dd, J = 10.8, 2.9 Hz, 2H), 2.29 (d, J = 10.3 Hz, 2H), 2.25 (s, 3H), 1.93 – 1.78 (m, 4H), 1.64 (br s, 1H), 1.43 (br s, 12H)	MS m/z 360.6 (M + H)
98: (1S)-1-(4-((8-methyl-3,8-diazabicyclo[3.2.1]octan-3-yl)methyl)phenyl)ethanamine		MS m/z 260.2 (M + H).
99: tert-butyl (1S)-1-(4-((hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)methyl)phenyl)ethylcarbamate	($CDCl_3$) 7.30 – 7.21 (m, 4H), 4.78 (br s, 1H), 3.61 – 3.44 (m, 2H), 3.05 (td, J = 8.6, 1.9 Hz, 1H), 3.00 – 2.93 (m, 2H), 2.86 – 2.76 (m, 1H), 2.33 – 2.19 (m, 2H), 2.17 – 2.00 (m, 2H), 1.87 – 1.65 (m, 4H), 1.43 (br s, 12H)	MS m/z 361.3 (M + H)
100: (1S)-1-(4-((hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)methyl)phenyl)ethanamine		MS m/z 260.2 (M + H)
101: (S)-1-[4-(4-Fluoro-phenoxy)-cyclohexyl]-ethylamine		LC-MS m/z 237.4 (M +

		H)+; RT.: 1.08 min.
102: (S)-tert-butyl 1-(4-((4-(dimethylamino)piperidin-1-yl)methyl)phenyl)ethylcarbamate	($CDCl_3$) 7.28 – 7.20 (m, 4H), 4.79 (br s, 2H), 3.46 (s, 2H), 2.91 (br d, J = 12.1 Hz, 2H), 2.26 (s, 6H), 2.17–2.09 (m, 1H), 1.94 (td, J = 11.8, 2.4 Hz, 2H), 1.85 (br s, 1H), 1.81 – 1.71 (m, 2H), 1.53 (td, J = 12.1, 3.7 Hz, 2H), 1.44–1.42 (m, 12H)	MS m/z 361.8 (M + H)
103: (S)-1-(4-(1-aminoethyl)benzyl)-N,N-dimethylpiperidin-4-amine		MS m/z 262.1 (M + H)
104: tert-butyl (1S)-1-(4-((3,5-dimethylpiperazin-1-yl)methyl)phenyl)ethylcarbamate	(CD_3OD) 7.29 (s, 4 H), 4.68 (br s, 1 H), 3.52 (s, 2 H), 2.96 - 2.88 (m, 2 H), 2.82 - 2.79 (m, 2 H), 1.69 (t, J = 11 Hz, 2 H), 1.44 (br s, 9 H), 1.40 (d, J = 7.1 Hz, 3 H), 1.06 (d, J = 6.5 Hz, 6 H);	MS *m/z* 348.3 (M + H)
105: (S)-tert-butyl 1-(4-((3,3,4-trimethylpiperazin-1-yl)methyl)phenyl)ethylcarbamate	(CD_3OD) δ 7.35 - 7.25 (m, 4 H), 4.67 (br s, 1 H), 4.59 (s, 1 H), 3.45 (s, 2 H), 3.31 (s, 1 H), 2.62 (br s, 2 H), 2.51 (br s, 1 H), 2.24 (s, 3 H), 2.18 (br s, 1 H), 1.43 (br s, 9 H), 1.40 (d, J = 7.1 Hz, 3 H), 1.07 (s, 6 H);	MS *m/z* 362.3 (M + H)
106: ((S)-tert-butyl 1-(4-((4-cyclopropylpiperazin-1-yl)methyl)phenyl)ethylcarbamate	($CDCl_3$) δ 7.21 - 7.16 (m, 4 H), 5.23 (s, 1 H), 4.72 (br s, 1 H), 3.42 (s, 2 H), 2.58 (br s, 4 H), 2.38 (br s, 4 H), 1.57 - 1.51 (m, 1 H), 1.41 - 1.30 (br m, 12 H), 0.39 - 0.33 (m, 4 H);	MS *m/z* 359.8 (M + H)
107: (S)-tert-butyl 1-(4-((tert-butylamino)methyl)phenyl) ethylcarbamate	($CDCl_3$) 7.32 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 8.2 Hz, 1H), 4.77 (s, 1H), 3.72 (s, 1H), 1.43 (d, J = 5.4 Hz, 6H), 1.18 (s, 4H)	MS m/z 308.2 (M + H)+
108: (S)-N-(4-(1-aminoethyl)benzyl)-2-methylpropan-2-amine		MS m/z 207.2 (M + H) +
109: (S)-tert-butyl 1-(4-(tert-butylcarbamoyl)phenyl)ethyl carbamate	($CDCl_3$) 7.71 – 7.62 (m, 2H), 7.33 (d, J = 8.1 Hz, 2H), 5.90 (s, 1H), 4.80 (br s, 2H), 1.46-1.41 (m, 21H)	MS m/z 321.2 (M + H)+
110: (S)-4-(1-aminoethyl)-N-tert-butylbenzamide hydrochloride		MS m/z 221.3 (M + H) +
111: (S)-tert-butyl 1-(4-(cyclohexylcarbamoyl)phenyl)ethyl carbamate	($CDCl_3$) 7.71 (dd, J = 8.3, 1.8 Hz, 2H), 7.35 (d, J = 7.8 Hz, 2H), 5.91 (d, J = 8.3 Hz, 1H), 4.94 – 4.59 (m, 2H), 3.97 (ddt, J = 10.8, 6.5, 2.9 Hz, 1H), 2.02 (dt, J = 12.6, 3.7 Hz, 2H), 1.75 (dp, J = 11.8, 3.9 Hz, 2H), 1.66 – 1.56 (m, 3H), 1.49 – 1.30 (m, 12H), 1.23 (m, 3H)	MS m/z 347.2 (M + H)+
112: (S)-4-(1-aminoethyl)-N-		MS m/z 247.3

cyclohexylbenzamide hydrochloride		(M + H) +
113: (S)-tert-butyl 1-(4-(phenylcarbamoyl)phenyl)ethyl carbamate	($CDCl_3$) 7.90 – 7.83 (m, 2H), 7.81 – 7.62 (m, 3H), 7.49 – 7.36 (m, 4H), 7.18 (td, J = 7.4, 1.2 Hz, 1H), 4.87 (br s, 2H), 1.58 (s, 3H), 1.46 (m, 9H)	MS m/z 340.6 (M + H) +
114: (S)-4-(1-aminoethyl)-N-phenylbenzamide hydrochloride		MS m/z 241.2 (M + H) +
115: (S)-tert-butyl 1-(4-(piperidine-1-carbonyl)phenyl)ethylcarbamate	($CDCl_3$) 7.33 (q, J = 8.3 Hz, 4H), 4.80 (br s, 2H), 3.70 (br s, 2H), 3.47 – 3.22 (m, 2H), 1.70-1.63 (m, 4H), 1.53 – 1.26 (m, 14H)	MS m/z 333.2 (M + H) +
116: (S)-(4-(1-aminoethyl)phenyl) (piperidin-1-yl)methanone hydrochloride		MS m/z 233.2 (M + H) +
117: (S)-tert-butyl 1-(4-(4-methylpiperazine-1-carbonyl)phenyl)ethylcarbamate	($CDCl_3$) 7.35 (q, J = 8.2 Hz, 4H), 4.81 (br s, 1H), 3.79 (brs, 2H), 3.45 (br s, 2H), 2.50 - 2.32 (m, 7H), 1.61 (s, 1H), 1.51 – 1.29 (m, 12H)	MS m/z 348.2 (M + H) +
118: (S)-(4-(1-aminoethyl)phenyl)(4-methylpiperazin-1-yl)methanone hydrochloride		MS m/z 248.2 (M + H) +
119: (S)-tert-butyl 1-(4-(piperidin-1-ylmethyl)phenyl)ethylcarbamate	($CDCl_3$) 7.27 (q, J = 7.9 Hz, 4H), 4.80 (br s, 2H), 3.49 (s, 2H), 2.60 – 2.28 (m, 4H), 1.60 (p, J = 5.5 Hz, 4H), 1.52 – 1.31 (m, 15H)	MS m/z 319.0 (M + H) +
120: (S)-1-(4-(piperidin-1-ylmethyl)phenyl)ethanamine		MS m/z 219.1 (M + H) +
121: (S)-tert-butyl 1-(4-(morpholinomethyl)phenyl)ethyl carbamate	($CDCl_3$) 7.48 – 7.10 (m, 4H), 4.82 (d, J = 25.7 Hz, 2H), 3.80 – 3.62 (m, 3H), 3.48 (s, 2H), 2.61 – 2.24 (m, 3H), 1.44 (m, 13H)	MS m/z 321.2 (M + H) +
122: (S)-1-(4-(morpholinomethyl) phenyl)ethanamine		MS m/z 220.9 M + H) +
123: (S)-tert-butyl 1-(4-((4-methylpiperazin-1-yl)methyl)phenyl)ethylcarbamate	($CDCl_3$) 7.39 – 7.15 (m, 7H), 4.79 (br s, 2H), 3.51 (s, 2H), 2.41 (m, 9H), 1.46 (m, 11H)	MS m/z 321.2 (M + H) +
124: (S)-1-(4-((4-methylpiperazin-1-yl)methyl)phenyl)ethanamine		MS m/z 234.2 (M + H) +
125: 4-((S)-1-Amino-ethyl)-piperidine-1-carboxylic acid benzyl ester		LC-MS (M+H) = 263.1 RT.: 0.91 min.

5

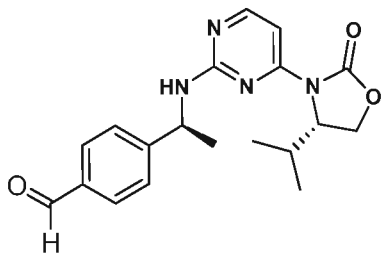
Intermediate 126: (S)-(4-(1-aminoethyl)-3-fluorophenyl)methanol



To a cooled (0 °C) suspension of (S)-methyl 4-(1-aminoethyl)-3-fluorobenzoate hydrochloride (0.109 g, 0.468 mmol) in THF (15 mL) was added a solution of LAH in THF (2.0 M, 1.05 mL, 2.10 mmol, 4.49 equiv) and the resulting mixture was stirred at 0 °C for 2 h 20 min and at room temperature for 2 1/2 h. The reaction mixture was quenched by addition of a mixture of Na_2SO_4 decahydrate and Celite (1:1 by weight) until gas evolution ceased. The reaction mixture was filtered, washed with EtOAc. The filtrate was concentrated and used for the next reaction without purification.

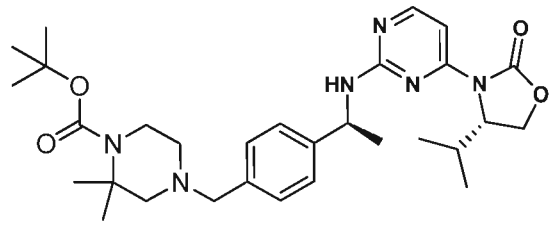
^{1}H NMR (400 MHz, CD_3OD) δ 7.43 (t, J = 7.7 Hz, 1 H), 7.15 (d, J = 8.1 Hz, 1 H), 7.08 (d, J = 12 Hz, 1 H), 4.60 (s, 2 H), 4.32 (q, J = 6.6 Hz, 1 H), 1.42 - 1.40 (m, 3 H).

Intermediate 127: 4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzaldehyde



A solution of (S)-3-(2-((S)-1-(4-(hydroxymethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (285 mg, 0.8 mmol) and manganese dioxide (2.78 g, 32 mmol, 40 equiv) in DCM (16 mL) was stirred at room temperature for 30 min. The solution was filtered through a pad of celite and washed with DCM. The filtrated was concentrated and used to next step without further purification.

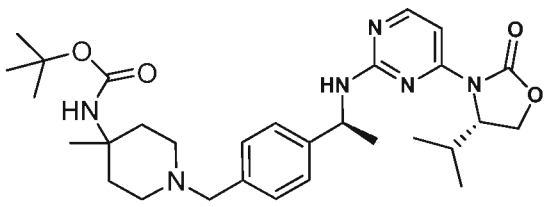
Intermediate 128: tert-butyl 4-(4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzyl)-2,2-dimethylpiperazine-1-carboxylate



A solution of 4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzaldehyde (71 mg, 0.2 mmol) and tert-butyl 2,2-dimethylpiperazine-1-carboxylate (47.1 mg, 0.22 mmol) in MeOH (4 mL) was added acetic acid (14.4 mg, 0.24 mmol) and 5-Ethyl-2-methylpyridine borane complex (27 mg, 0.2 mmol, sigma aldrich). The solution was stirred at 50 °C for 4 h then 5 drops of water was added. The solution was stirred at room temperature for another 2 h then diluted with EtOAc (10 mL) and washed with water (10 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 10 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. The crude material was purified through Silica gel column chromatography (MeOH/EtOAc 0 to 10%) to give tert-butyl 4-(4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzyl)-2,2-dimethylpiperazine-1-carboxylate as a white solid (80 mg, 72.4% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (br s, 1H), 7.44 (d, J = 5.7 Hz, 1H), 7.24-7.29 (m, 4H), 5.46 (br s, 1H), 5.03 (br s, 1H), 4.59-4.63 (m, 1H), 4.29 (t, J = 8.7 Hz, 1H), 4.22 (dd, J = 9.1, 3.1 Hz, 1H), 3.44 (br s, 4H), 2.40 (s, 2H), 2.16 (s, 2H), 1.54 (d, J = 6.9 Hz, 3H), 1.45 (s, 9H), 1.36 (s, 6H), 0.80 – 0.57 (m, 6H); MS m/z 252.1 (M + H).

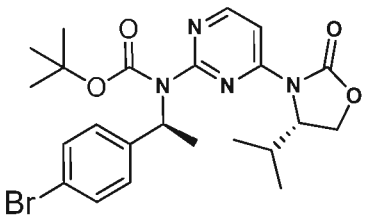
Intermediate 129: tert-butyl 1-(4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzyl)-4-methylpiperidin-4-ylcarbamate



Prepared by a method similar to that described for the preparation of Intermediate 128.

^{1}H NMR (400 MHz, $CDCl_3$) 8.17 (d, J = 5.7 Hz, 1H), 7.43 (d, J = 5.7 Hz, 1H), 7.26 (br s, 4H), 5.40 (br s, 1H), 5.02 (br s, 1H), 4.60 (dt, J = 8.2, 3.1 Hz, 1H), 4.34 – 4.19 (m, 3H), 3.47 (br s, 2H), 2.54 (br s, 2H), 2.26 (br s, 2H), 1.95 (br s, 3H), 1.60 (br s, 2H), 1.53 (d, J = 6.9 Hz, 3H), 1.43 (s, 9H), 1.33 (s, 3H), 0.69 (br s, 3H), 0.63 (br s, 3H). MS m/z 553.6 (M + H).

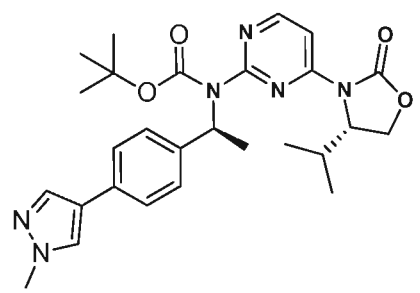
Intermediate 130: tert-butyl (S)-1-(4-bromophenyl)ethyl(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)carbamate



To a solution of (S)-3-(2-((S)-1-(4-bromophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (1.62 g, 4 mmol) in THF (20 mL) was added di-tert-butyl dicarbonate (1.31 g, 6 mmol), DMAP (49 mg, 0.4 mmol) and DIPEA (1.40 mL, 8 mmol). The solution was stirred at 50 °C for 7 days then concentrated under reduced pressure. The residue was diluted with EtOAc (40 mL) and washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/heptane 0 to 80%) provided tert-butyl (S)-1-(4-bromophenyl)ethyl(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)carbamate as a white solid (1.03 g, 50.9% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 5.8 Hz, 1H), 7.99 (d, J = 5.8 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.33 – 7.28 (m, 2H), 5.63 (q, J = 7.2 Hz, 1H), 4.63 (dt, J = 8.0, 3.3 Hz, 1H), 4.39 – 4.26 (m, 2H), 2.47-2.39 (m, 1H), 1.66 (d, J = 7.1 Hz, 3H), 1.30 (s, 9H), 0.84 (d, J = 7.0, 3H),0.83 (d, J = 7.0, 3H); MS m/z 507.0 (M + H).

Intermediate 131: tert-butyl 4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl((S)-1-(4-(1-methyl-1H-pyrazol-4-yl)phenyl)ethyl)carbamate

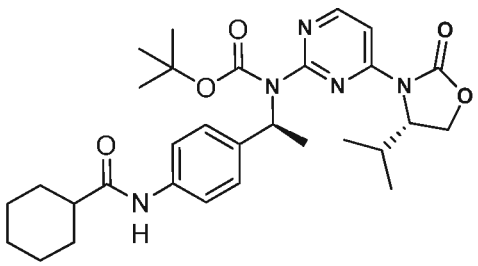


In a 5 mL microwave vial a solution of tert-butyl (S)-1-(4-bromophenyl)ethyl(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)carbamate (101 mg, 0.2 mmol), 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (50 mg, 0.24 mmol), Sodium bicarbonate (0.2 mL, 0.4 mmol, 2 M aqueous solution) in Dioxane (2 mL) was bubbled

N2 for 3 min then $Cl_2Pd(dppf)CH_2Cl_2$ (16 mg, 0.02 mmol) was added. The capped tube was heated to 100°C for 16 h. After cooling the reaction mixture was diluted with EtOAc (10 mL) and washed with water (10 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 10 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. The crude material was purified through silica gel column chromatography (EtOAc in Heptane 12 to 100%) to give a white solid (50 mg, 49.3% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 5.7 Hz, 1H), 7.97 (d, J = 5.8 Hz, 1H), 7.74 (s, 1H), 7.59 (s, 1H), 7.39 (s, 4H), 5.71 (q, J = 7.0 Hz, 1H), 4.65 (dt, J = 8.1, 3.2 Hz, 1H), 4.36 – 4.24 (m, 2H), 3.94 (s, 3H), 2.50-2.42 (m, 1H), 1.71 (d, J = 7.0 Hz, 3H), 1.29 (s, 9H), 0.82 (d, J = 7.0 Hz, 3H), 0.80 (d, J = 7.0 Hz, 3H); MS m/z 507.1 (M + H).

Intermediate 132: tert-butyl (S)-1-(4-(cyclohexanecarboxamido)phenyl)ethyl(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)carbamate

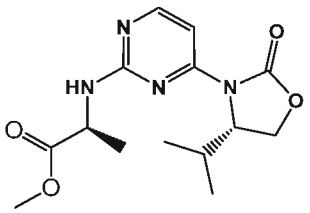


In a 5 ml microwave reaction vial was added tert-butyl (S)-1-(4-bromophenyl)ethyl(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)carbamate (101 mg, 0.2 mmol), cyclohexanecarboxamide (30 mg, 0.24 mol), cesium carbonate (91 mg, 0.28 mmol), XANTPHOS (7 mg, 0.012 mmol, strem chemicals), and $Pd_2(dba)_3$ (4 mg, 0.02 mmol). The vial was sealed, evacuated and purged with dry nitrogen three times before adding dioxane (1.6 mL). The reaction mixture was heated to 100°C for 16 hours in an oil bath. After cooling the reaction was diluted with EtOAc (10 mL) and washed with water (10 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 10 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. The crude material was purified through silica gel column chromatography (EtOAc in Heptane 12 to 100%) to give a white solid (65 mg, 58.9% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 5.8 Hz, 1H), 7.95 (d, J = 5.8 Hz, 1H), 7.48 – 7.43 (m, 2H), 7.38 – 7.32 (m, 2H), 7.13 (br s, 1H), 5.66 (q, J = 7.1 Hz, 1H), 4.64 (dt, J = 8.2, 3.2 Hz, 1H), 4.38 – 4.26 (m, 2H), 2.51 – 2.43 (m, 1H), 2.20 (tt, J = 11.8, 3.5 Hz, 1H), 1.95 (d, J = 13.2, 2H), 1.87 – 1.81 (m, 2H), 1.71– 1.68 (m, 4H), 1.60 – 1.47 (m, 2H),

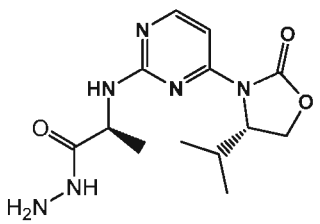
1.33-1.25(m, 12H), 0.85 (d, J = 6.9 Hz, 3H), 0.82 (d, J = 6.9 Hz, 3H); MS m/z 552.1 (M + H).

Intermediate 133: (S)-methyl 2-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)propanoate



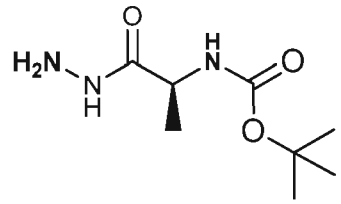
To a solution of (S)-methyl 2-aminopropanoate (270 mg, 2.0 mmol, 1.2 equv.in 10 ml of DMSO) and (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (430 mg, 1.8 mmol, 1.0 equv.) was added DIPEA (805 mg, 6.23 mmol, 3.5 equiv), and the reaction mixture was heated at 110 °C for 120 min. The reaction mixture was poured into water (40ml) and extracted with EtOAc (2x30 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (ethyl acetate in heptane 10 to 80%) to provide (S)-methyl 2-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)propanoate (260 mg, white solid) in 47.4% yield. LCMS *m/z* 309.1 $(M + H)^+$ RT=1.53 min.

Intermediate 134: (S)-2-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)propanehydrazide



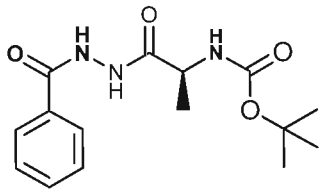
To a solution of (S)-methyl 2-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)propanoate (120 mg, 0.39 mmol in 5 ml of MeOH) was added 99% hydrazine hydrate, the reaction solution was stirred at room temperature overnight (24 hours), the solvent was removed to yield the desired product (99 mg) in 78% yield, and was used for next step without purification. LCMS *m/z* 309.1 $(M + H)^+$ RT=1.25 min.

Intermediate 135: (S)-tert-butyl (1-hydrazinyl-1-oxopropan-2-yl)carbamate



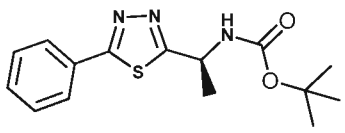
A solution of hydrazine (234 mg, 7.31 mmol, 1.5 equv. in 8 ml of THF) was added to (S)-methyl 2-(tert-butoxycarbonylamino)propanoate (1000 mg, 4.88 mmol, 1.0 equv.), it was stirred in a sealed tube and refluxed (72°C) overnight (18 hours), the solvent was removed to yield the desired product (880 mg, white solid) in 84% yield.

Intermediate 136: (S)-tert-butyl (1-(2-benzoylhydrazinyl)-1-oxopropan-2-yl)carbamate



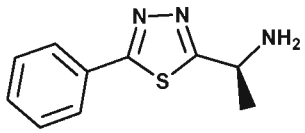
To a solution of (S)-tert-butyl (1-hydrazinyl-1-oxopropan-2-yl)carbamate (293 mg, 1.44 mmol, 1.0 equv. in 3 ml of DCM) was added benzoyl fluoride (179 mg, 1.44 mmol in 2 ml of DCM), the reaction solution was stirred at room temperature for 50 min., the solvent was removed to yield the desired product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.78 (m, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 5.32 (b, 1H), 4.45 (b, 1H), 1.46 (s, 9H).

Intermediate 137: (S)-tert-butyl (1-(5-phenyl-1,3,4-thiadiazol-2-yl)ethyl)carbamate



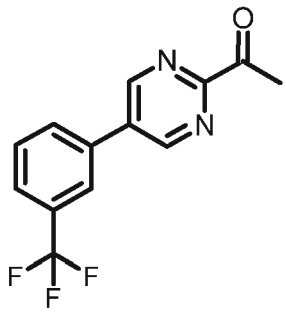
To a solution of (S)-tert-butyl (1-(2-benzoylhydrazinyl)-1-oxopropan-2-yl)carbamate (155 mg, 0.5 mmol, 1.0 equv. in 5 ml of THF) was added Lawesson's reagent (36.4 mg, 0.5 mmol, 1.0 equv.) the reaction mixture was stirred at reflux for 3 hours, the reaction mixture was filtered and the solvent was removed to yield the crude product. Silica gel column chromatography (ethyl acetate in heptane 10 to 50%) to provide (S)-tert-butyl (1-(5-phenyl-1,3,4-thiadiazol-2-yl)ethyl)carbamate (114.6 mg, white solid) in 70.7% yield. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.94 – 7.72 (m, 2H), 7.52 – 7.26 (m, 3H), 5.59 (b, 1H), 5.11 (b, 1H), 1.57 (d, *J* = 7.0 Hz, 3H), 1.34 (s, 9H).

Intermediate 138: (S)-1-(5-phenyl-1,3,4-thiadiazol-2-yl)ethanamine



To a solution of (S)-tert-butyl (1-(5-phenyl-1,3,4-thiadiazol-2-yl)ethyl)carbamate (110 mg, 0.4 mmol, in 5 ml of DCM) was added 1 ml of TFA, the reaction mixture was stirred at room temperature for 3 hours, the solvent was removed to yield the desired product (52 mg) in 66.8% yield. LCMS *m/z* 206.0 $(M + H)^+$ RT=0.97min.

Intermediate 139: 1-(5-(3-(trifluoromethyl)phenyl)pyrimidin-2-yl)ethanone

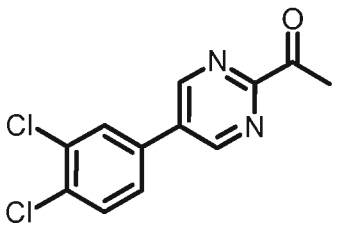


A cloudy solution of 1-(5-bromopyrimidin-2-yl)ethanone (300 mg, 1.49 mmol), 3-(trifluoromethyl)phenylboronic acid (567 mg, 2.98 mmol), K_3PO_4 (950 mg, 4.48 mmol), DavePhos ligand [2-dicyclohexylphosphino-2′-(N,N-dimethylamino)biphenyl] (59 mg, 0.15 mmol), and $Pd(OAc)_2$ (17 mg, 0.075 mmol) in 6 mL toluene was heated at 100°C for 1 h. The mixture was cooled to room temperature, and filtered through Celite. Filter cake was rinsed with 30 mL EtOAc. The filtrate was poured into 20 mL water. Layers were separated, and the aqueous was further extracted with EtOAc (20 mL). Combined organics were washed with water (20mL) and brine (20mL), dried over Na_2SO_4, filtered and concentrated directly onto silica gel. Column chromatography (10 - 100% EtOAc/heptane) gave 0.26 g 1-(5-(3-(trifluoromethyl)phenyl)pyrimidin-2-yl)ethanone (V) as tan solid. MS m/z 267.1 (M + H)+. ^1H NMR (400 MHz, $CDCl_3$) δ 9.16 (s, 2H), 7.93 – 7.69 (m, 4H), 2.87 (s, 3H).

The Following intermediates were prepared using a method similar to that described for the preparation of **Intermediate 139**. Using Anal. RP-HPLC Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50°C. Eluents =A: Water (5 mM

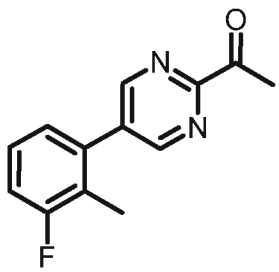
Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.)

Intermediate 140: 1-(5-(3,4-dichlorophenyl)pyrimidin-2-yl)ethanone.



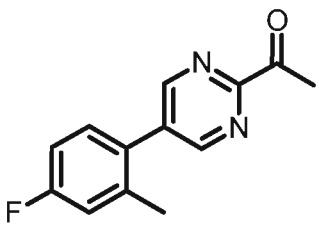
Anal. RP-HPLC tR = 1.17 min. MS m/z 266.9 (M + H)+.

Intermediate 141: 1-(5-(3-fluoro-2-methylphenyl)pyrimidin-2-yl)ethanone.



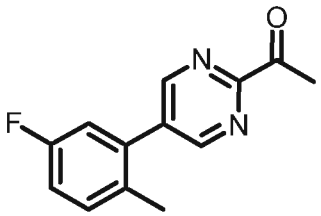
Anal. RP-HPLC tR = 1.07 min. MS m/z 231.1 (M + H)+.

Intermediate 142: 1-(5-(4-fluoro-2-methylphenyl)pyrimidin-2-yl)ethanone.



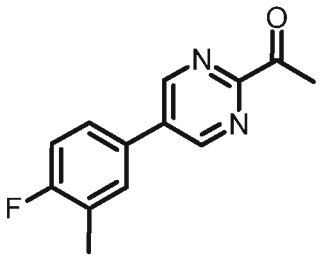
Anal. RP-HPLC tR = 1.18 min.MS m/z 231.1 (M + H)+.

Intermediate 143: 1-(5-(5-fluoro-2-methylphenyl)pyrimidin-2-yl)ethanone



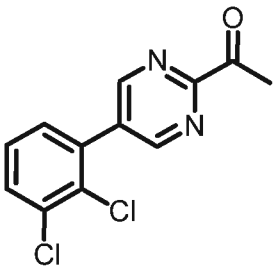
Anal. RP-HPLC tR = 1.16 min. MS m/z 231.2 (M + H)+.

Intermediate 144: 1-(5-(4-fluoro-3-methylphenyl)pyrimidin-2-yl)ethanone



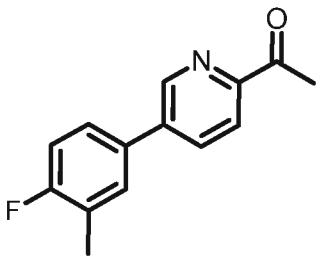
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 2H), 7.52 – 7.41 (m, 2H), 7.24 – 7.16 (m, 1H), 2.85 (s, 3H), 2.41 (d, J = 2.0 Hz, 3H). Anal. RP-HPLC tR = 1.20 min.MS m/z 231.0 (M + H)+.

Intermediate 145: 1-(5-(2,3-dichlorophenyl)pyrimidin-2-yl)ethanone



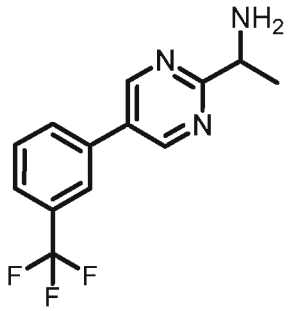
Anal. RP-HPLC tR = 1.15 min. MS m/z 267.9 (M + H)+.

Intermediate 146: 1-(5-(4-fluoro-3-methylphenyl)pyridin-2-yl)ethanone.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (dd, J = 2.3, 0.8 Hz, 1H), 8.13 (dd, J = 8.1, 0.8 Hz, 1H), 7.98 (dd, J = 8.1, 2.3 Hz, 1H), 7.50 – 7.39 (m, 2H), 7.21 – 7.12 (m, 1H), 2.78 (s, 3H), 2.42 – 2.36 (m, 3H). Anal. RP-HPLC tR = 1.40 min. MS m/z 230.8 (M + H)+.

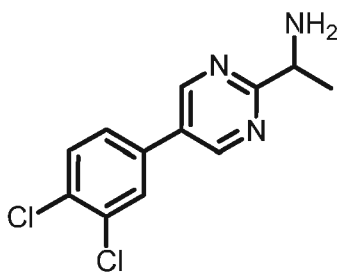
Intermediate 147: 1-(5-(3-(trifluoromethyl)phenyl)pyrimidin-2-yl)ethanamine



1-(5-(3-(Trifluoromethyl)phenyl)pyrimidin-2-yl)ethanone (260 mg, 0.977 mmol), NH4OAc (1.13 g, 14.6 mmol), and NaBH3CN (245 mg, 3.91 mmol) were taken up in 8 mL 200 proof EtOH, and heated at 120ºC for 5 minutes in a microwave apparatus. The mixture was concentrated to remove the EtOH. Crude was taken up in 30 ml water + 25 mL EtOAc. 6N NaOH was added until aqueous pH was ~10. Separated layers, and extracted aqueous with EtOAc (25 ml). The combined organic layer was washed with 25 mL brine and dried with Na_2SO_4. Filtered and concentrated with reduced pressure to give 262 mg crude yellow oil, which was carried forward without further purification. Anal. RP-HPLC tR = 0.90 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 268.1 (M + H)+.

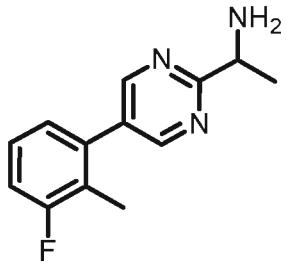
The Following intermediates were prepared using a method similar to that described for the preparation of **Intermediate 147**.

Intermediate 148: 1-(5-(3,4-dichlorophenyl)pyrimidin-2-yl)ethanamine.



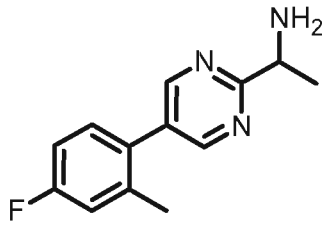
Anal. RP-HPLC tR = 1.09 min (Gradient: 2 to 98% B in 1.7 min - flow 1 mL/min. Eluent A: Water + 3.75 mM NH4Ac + 2% ACN. Column: Acquity CSH 1.7µm 2.1x50mm - 50°C.) MS m/z 268.4 (M + H)+.

Intermediate 149: 1-(5-(3-fluoro-2-methylphenyl)pyrimidin-2-yl)ethanamine.



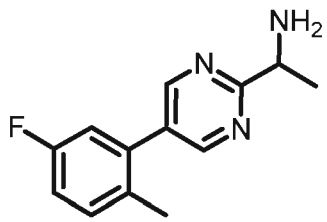
Anal. RP-HPLC tR = 0.99 min. (Gradient: 2 to 98% B in 1.7 min - flow 1 mL/min. Eluent A: Water + 3.75 mM NH4Ac + 2% ACN. Column: Acquity CSH 1.7µm 2.1x50mm - 50°C.) MS m/z 232.4 (M + H)+.

Intermediate 150: 1-(5-(4-fluoro-2-methylphenyl)pyrimidin-2-yl)ethanamine.



Anal. RP-HPLC tR = 0.87 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 231.0 (M)-.

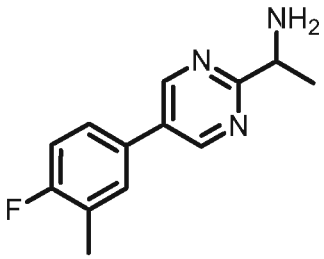
Intermediate 151: 1-(5-(5-fluoro-2-methylphenyl)pyrimidin-2-yl)ethanarnine



Anal. RP-HPLC tR = 0.79 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN);

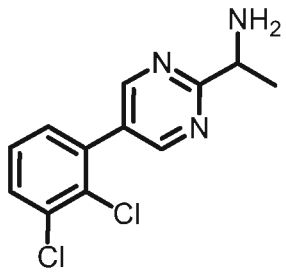
B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 232.0 (M + H)+.

Intermediate 152: 1-(5-(4-fluoro-3-methylphenyl)pyrimidin-2-yl)ethanamine



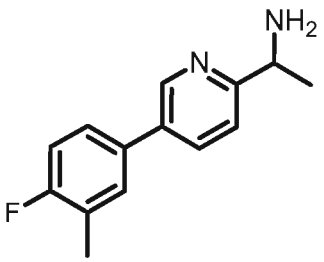
Anal. RP-HPLC tR = 0.81 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 231.9 (M + H)+.

Intermediate 153: 1-(5-(2,3-dichlorophenyl)pyrimidin-2-yl)ethanamine



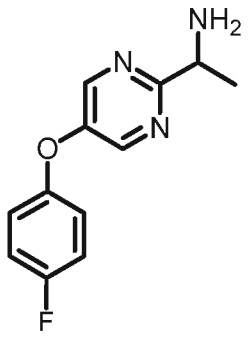
Anal. RP-HPLC tR = 1.01 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 269.0 (M + H)+.

Intermediate 154: 1-(5-(4-fluoro-3-methylphenyl)pyridin-2-yl)ethanamine



Anal. RP-HPLC tR = 0.92 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 230.9 (M + H)+.

Intermediate 155: 1-(5-(4-fluorophenoxy)pyrirnidin-2-yl)ethanamine

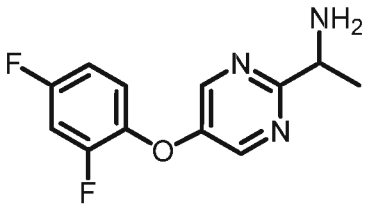


Step 1: A solution of 1-(5-fluoropyrimidin-2-yl)ethanone (700 mg, 5.0 mmol) and 4-fluorophenol (616 mg, 5.50 mmol) in 6 mL DMF was treated with potassium carbonate (829 mg 6.0 mmol) and heated to 50ºC for 3.5 h. The reaction mixture was poured into 20 mL water, and extracted with EtOAc (2 x 20 mL). Organics were washed with 20 mL each water, brine, and dried over Na_2SO_4. Mixture was filtered and concentrated on silica gel. Column chromatography (10 - 100% EtOAc/hept) gave 295 mg (25%) 1-(5-(4-fluorophenoxy)pyrimidin-2-yl)ethanone as a white solid used directly in the following step. MS m/z 233.2 (M + H)+. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 2H), 7.23 – 7.07 (m, 4H), 2.78 (s, 3H).

Step 2: 1-(5-(4-fluorophenoxy)pyrimidin-2-yl)ethanone (290 mg, 1.25 mmol), NH4OAc (1.9 g, 24.6 mmol), and $NaBH_3CN$ (314 mg, 5.00 mmol) were taken up in 20 mL 200 proof EtOH, and heated at 130 C for 3 minutes in a microwave apparatus. The mixture was concentrated to remove the EtOH. Crude was taken up in 30 ml water + 25 mL EtOAc. 6N NaOH was added until aqueous pH was ~10. Separated layers, and extracted aqueous with EtOAc (25 ml). The combined organic layer was washed with 25 mL brine and dried with Na_2SO_4. Filtered and concentrated with reduced pressure to give 275 mg crude tan oil, which was carried forward without further purification. Major product Anal. RP-HPLC tR = 1.26 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 234.1 (M + H)+.

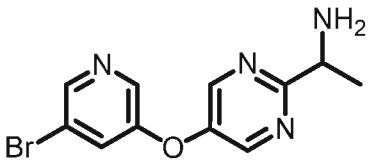
The Following intermediates were prepared using methods similar to those described for the preparation of **Intermediate 155**.

Intermediate 156: 1-(5-(2,4-difluorophenoxy)pyrimidin-2-yl)ethanamine



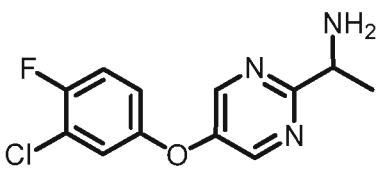
Anal. RP-HPLC tR = 0.81 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 252.1 (M + H)+.

Intermediate 157: 1-(5-(5-bromopyridin-3-yloxy)pyrimidin-2-yl)ethanamine



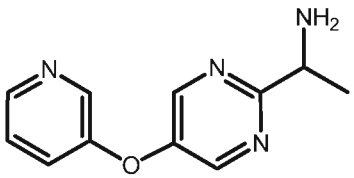
Anal. RP-HPLC tR = 1.29 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 297.3 (M + H)+.

Intermediate 158: 1-(5-(3-chloro-4-fluorophenoxy)pyrimidin-2-yl)ethanamine



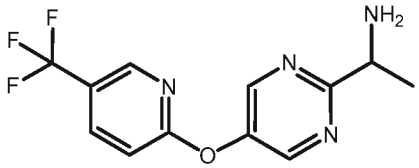
Anal. RP-HPLC tR = 1.40 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 268.0 (M + H)+.

Intermediate 159: 1-(5-(pyridin-3-yloxy)pyrimidin-2-yl)ethanamine



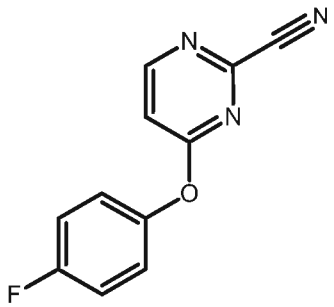
Anal. RP-HPLC tR = 1.21 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 218.4 (M + H)+.

Intermediate 160: 1-(5-(5-(trifluoromethyl)pyridin-2-yloxy)pyrimidin-2-yl)ethanamine



Anal. RP-HPLC tR = 1.16 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 285.4 (M + H)+.

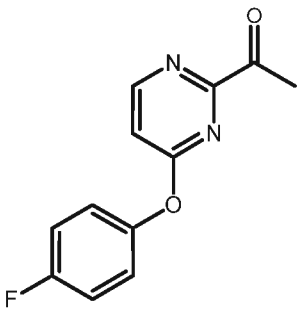
Intermediate 161: 4-(4-fluorophenoxy)pyrimidine-2-carbonitrile



A solution of 4-chloropyrimidine-2-carbonitrile (0.63 g, 4.51 mmol) and 4-fluorophenol (0.51 g, 4.51 mmol) in 5 mL DMF was cooled to 0ºC under N2 atmosphere. NaH (0.217 g of 60% suspension, 5.42 mmol) was slowly added. Bubbling exotherm observed. Internal temp was kept below 5ºC. After 15 minutes, cold bath was removed. The reaction mixture was allowed to warm to room temp and stir 1 h. The reaction mixture was diluted with water (40 mL) and extracted with (3 x 25 mL) EtOAc. The organic layer

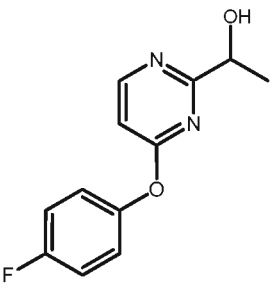
was washed with 40 mL each water, and brine. Dried over Na_2SO_4, and concentrated on silica gel in vacuo. Column chromatography (EtOAc/heptane 10 to 100% gradient) gave 0.72 g (74%) of (4-fluorophenoxy)pyrimidine-2-carbonitrile as a crystalline white solid. Anal. RP-HPLC tR = 1.38 min, Gradient: 2 to 98% B in 1.7 min - flow 1 mL/min. Eluent A: Water + 3.75 mM NH4Ac + 2% ACN. Column: Acquity CSH 1.7µm 2.1x50mm - 50°C. MS m/z 216.1 (M + H)+.

Intermediate 162: 1-(4-(4-fluorophenoxy)pyrimidin-2-yl)ethanone



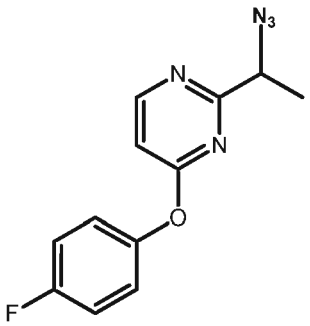
4-(4-fluorophenoxy)pyrimidine-2-carbonitrile (450 mg, 2.09 mmol) was suspended in 12 mL anhydrous ether under N2 atmosphere. Vessel was cooled to 0° C. MeMgBr (3.1 mL of 1.0 M solution in butyl ether, 3.10 mmol) was added over 5 min. The yellow-green suspension was stirred 30 minutes, then quenched with 50 mL sat'd NH4Cl solution. Adjusted pH to ~6 with conc. HCl. The mixture was extracted with (2 x 40 mL) EtOAc. Washed organics with 30 mL brine, and dried over Na_2SO_4. Filtered and concentrated on silica gel. Column chromatography (10 - 100% EtOAc in hept) gave 157 mg (32%) 1-(4-(4-fluorophenoxy)pyrimidin-2-yl)ethanone as a yellow oil. Anal. RP-HPLC tR = 1.44 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 233.2 (M + H)+.

Intermediate 163: 1-(4-(4-fluorophenoxy)pyrimidin-2-yl)ethanol



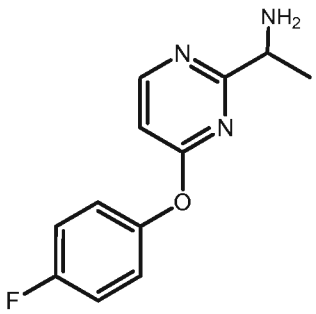
1-(4-(4-fluorophenoxy)pyrimidin-2-yl)ethanone (0.150 g 0.646 mmol) was taken up in 2.5 mL 4:1 MeOH:DCM, and cooled to 0ºC. $NaBH_4$ (49 mg 1.30 mmol) was added. Fizzing was observed. After 10 min, cold bath was removed, and the reaction was stirred 1 h. Solvent was removed in vacuo. White residue was taken up in 10 mL water, and extracted with (2 x 10 mL) EtOAc. Washed organics with 10 mL brine. Dried over Na_2SO_4. Filtered and concentrated to give 143 mg (95%) 1-(4-(4-fluorophenoxy)pyrimidin-2-yl)ethanol as a colorless oil. Anal. RP-HPLC tR = 1.38 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 235.1 (M + H)+.

Intermediate 164: 2-(1-azidoethyl)-4-(4-fluorophenoxy)pyrimidine



Under N_2 atmosphere, 1-(4-(4-fluorophenoxy)pyrimidin-2-yl)ethanol (140 mg, 0.598 mmol) was dissolved in 3 mL anhydrous DCM. Triethylamine (0.175 mL, 1.26 mmol) was added, and the mixture was cooled to 0° C. MsCl (0.070 mL, 0.897 mmol) was added, and the mixture was stirred 15 minutes. Maintaining 0°C, DCM solvent was removed under N_2 stream. Residue was taken up in 2 mL dry DMF. NaN_3 (78 mg, 1.19 mmol) added, and the reaction was stirred at rt for 24 h. Mixture was poured into 20 mL water, and extracted with 20 mL EtOAc. Organic layer was washed with 20 mL brine and dried over Na_2SO_4. Filtered and concentrated to give 120 mg (77%) 2-(1-azidoethyl)-4-(4-fluorophenoxy)pyrimidine as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 5.7 Hz, 1H), 7.16 – 6.90 (m, 4H), 6.70 (d, J = 5.7 Hz, 1H), 4.34 (q, J = 6.9 Hz, 1H), 1.55 – 1.46 (m, 3H).

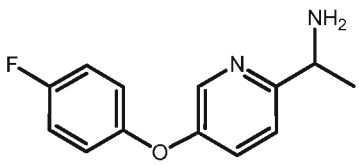
Intermediate 165: 1-(4-(4-fluorophenoxy)pyrimidin-2-yl)ethanamine



2-(1-azidoethyl)-4-(4-fluorophenoxy)pyrimidine (120 mg, 0.463 mmol) was dissolved in 2 mL neat EtOH. 24.6 mg (0.023 mmol) of 10% Palladium on carbon catalyst was added. With vigorous stirring, the reaction vial was evacuated and purged 3 times with H_2. The reaction vessel was fitted with an H_2 balloon and stirred for 2 h. The mixture was filtered through Celite and concentrated in vacuo to give 75 mg (69%) 1-(4-(4-fluorophenoxy)pyrimidin-2-yl)ethanamine as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, J = 5.7 Hz, 1H), 7.13 – 6.92 (m, 4H), 6.59 (d, J = 5.7 Hz, 1H), 4.00 (q, J = 6.8 Hz, 1H), 1.34 – 1.30 (m, 3H). Anal. RP-HPLC tR = 1.18 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 234.2 (M + H)+.

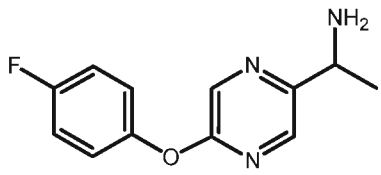
The Following intermediates were prepared using methods similar to those described for the preparation of **Intermediates 161 to 165**.

Intermediate 166: 1-(5-(4-fluorophenoxy)pyridin-2-yl)ethanamine



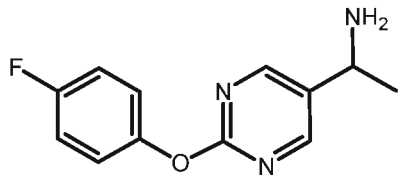
Anal. RP-HPLC tR = 0.91 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 233.1 (M + H)+.

Intermediate 167: 1-(5-(4-fluorophenoxy)pyrazin-2-yl)ethanamine



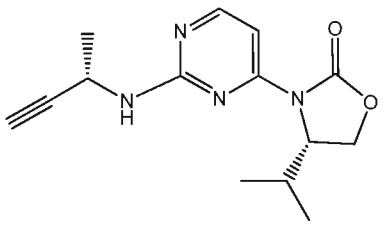
Anal. RP-HPLC tR = 1.39 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 217.1 (Major fragment + H)+.

Intermediate 168: 1-(2-(4-fluorophenoxy)pyrimidin-5-yl)ethanamine



Anal. RP-HPLC tR = 1.20 min. (Column = Inertsil C8 Column, 3.0 µm, 3.0 x 30 mm. Column Temperature =50ºC. Eluents =A: Water (5 mM Ammonium formate, 2% ACN); B: ACN. Flow Rate =2 mL/min. Gradient =0 min 5% B; 5% to 95% B in 1.70 min; 0.3 min 95% B; 2.1 min 1%B.) MS m/z 233.9 (M + H)+.

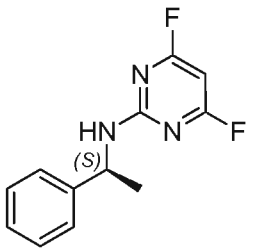
Intermediate 169: (S)-4-Isopropyl-3-[2-((S)-1-methyl-prop-2-ynylamino)-pyrimidin-4-yl]-oxazolidin-2-one



To a solution of compound (S)-3-(2-Chloro-pyrimidin-4-yl)-4-isopropyl-oxazolidin-2-one (1.03 g , 4.3 mmol) in DMSO (12 mL) was added methyl-prop-2-ynylamine HCl salt (450 mg, 4.3 mmol) and diisopropylethylamine (2.2 mL, 12.6 mmol). The reaction was heated to 110C for 18 hours. The reaction mixture was diluted with EtOAc (50 mL) and washed with water (25 mL) and brine (25 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified on silica gel column chromatography (EtOAc/Heptane 0 to 75%) provided (S)-4-Isopropyl-3-[2-((S)-1-methyl-prop-2-ynylamino)-pyrimidin-4-yl]-oxazolidin-2-one (360 mg) in 31% yield.

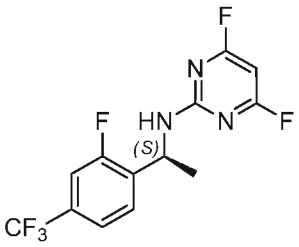
LC-MS m/z : 275.1 (M - Boc)+; RT.: 1.33 min.

Intermediate 170: (S)-4,6-difluoro-N-(1-phenylethyl)pyrimidin-2-amine



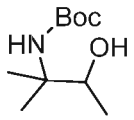
A solution of 2,4,6-trifluoropyrimidine (128.4 mg, 0.96 mmol) and isopropylethylamine (0.50 mL, 2.9 mmol, 3 equiv) in dioxane (5 mL) was cooled to 0 °C with an ice bath. After 30 min, the ice bath was removed, and the reaction was allowed to warm to room temperature. After stirriing overnight, the reaction was concentrated to a light brown oil and purified by silica gel column chromatography (EtOAc/Heptane 0 to 100%) to provide (S)-4,6-difluoro-N-(1-phenylethyl)pyrimidin-2-amine (151.2 mg, white solid) in 45% yield. ^{1}H NMR (400 MHz, CD_3OD) δ 7.35 - 7.40 (m, 2H), 7.29 - 7.34 (m, 2H), 7.20 - 7.26 (m, 1H), 5.84 (s, 1H), 5.08 (q, *J* = 6.91 Hz, 1H), 1.52 (d, *J* = 7.04 Hz, 3H); LCMS *m/z* 236.1 $(M + H)^+$, R_t 0.95 min.

Intermediate 171: (S)-4,6-difluoro-N-(1-(2-fluoro-4-(trifluoromethyl)phenyl)ethyl) pyrimidin-2-amine



Intermediate 171 was prepared by a method similar to the one described for the preparation of Intermediate 170. ^{1}H NMR (400 MHz, CD_3OD) 7.58 (t, J = 7.63 Hz, 1H), 7.34 - 7.48 (m, 2H), 5.84 (br. s., 1H), 5.35 (q, J = 6.91 Hz, 1H), 1.54 (d, J = 7.04 Hz, 3H). MS m/z 321.9 (M + H)+, Rt 1.11 min.

Intermediate 172: tert-butyl 3-hydroxy-2-methylbutan-2-ylcarbamate



Step 1: Preparation of tert-butyl 1-(methoxy(methyl)amino)-2-methyl-1-oxopropan-2-ylcarbamate

2-(tert-butoxycarbonylamino)-2-methylpropanoic acid (6.62 g, 32.6 mmol), O,N-dimethylhydroxylamine hydrochloride (3.50 g, 35.8 mmol), and HATU (14.86 g, 39.1 mmol) were combined in DMF (100 mL). To this solution was added Hunig'sBase (17.07 mL, 98 mmol). The reaction was stirred for overnight (17 hours). The reaction was then concentrated under vacuum and the residue was diluted with EtOAc (300mL) and washed with water (2x80mL). The organic layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified via silica gel flash chromatography (10-50 percent EtOAc-Hexanes) to afford the desired product as a white solid (6.36 g). LCMS *m/z* 247.2 $(M + H)^+$, Rt 0.61 min.

Step 2: Preparation of tert-butyl 2-methyl-3-oxobutan-2-ylcarbamate

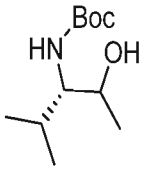
To a solution of tert-butyl 1-(methoxy(methyl)amino)-2-methyl-1-oxopropan-2-ylcarbamate (4.26 g, 17.30 mmol) in THF (100 mL) at -70 °C was added drop wise methyl lithium (32.4 mL, 51.9 mmol). Cold bath was replaced with -40 °C bath and the reaction was stirred for 4 hours. Saturated NH_4Cl solution (10mL) was then added cautiously to quench the reaction. The reaction mixture was then allowed to warm to room temperature, and diluted with EtOAc (100mL) and water (50mL). The phases were separated and the aqueous layer was extracted with EtOAc (2x100mL). The combined organics were then dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified via silica gel flash chromatography (10-50% EtOAc-Hexanes) to afford the desired product as a white solid (2.36 g). LCMS *m/z* 224.2 $(M + Na)^+$, Rt 0.7 min.

Step 3: Preparation of tert-butyl 3-hydroxy-2-methylbutan-2-ylcarbamate

To a solution of tert-butyl 2-methyl-3-oxobutan-2-ylcarbamate (2.36g, 11.73 mmol) in MeOH (30mL) at 0 °C was added portion wise $NaBH_4$ (0.887 g, 23.45 mmol). Cold bath was removed and the reaction was stirred for 1 hour. HCl solution (1 M, 0.2mL) was then added cautiously to quench the reaction. The reaction mixture was then concentrated and diluted with EtOAc (50mL) and water (10mL). The phases were separated and the aqueous layer was extracted with EtOAc (2x20mL). The combined organics were then dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified via silica gel flash chromatography (10-50% EtOAc-Hexanes) to

afford the desired product as a white solid (2.12 g). LCMS *m/z* 204.1 $(M + H)^+$, Rt 0.69 min.

Intermediate 173: tert-butyl ((3S)-2-hydroxy-4-methylpentan-3-yl)carbamate



Step 1: Preparation of tert-butyl 1-(methoxy(methyl)amino)-2-methyl-1-oxopropan-2-ylcarbamate

To a solution of (S)-2-(tert-butoxycarbonylamino)-3-methylbutanoic acid (5.86 g, 27.0 mmol) in DCM (100mL) at 0 °C was added portion wise di(1H-imidazol-1-yl)methanone (4.81 g, 29.7 mmol). Cold bath was removed and the reaction was stirred at 20 °C for 30 minutes. O,N-dimethylhydroxylamine hydrochloride (3.16 g, 32.4 mmol) was then added and followed by slow addition of triethylamine (3.28 g, 32.4 mmol). The reaction mixture was stirred at 20 °C for overnight (18 hr), and diluted with DCM (200mL) and washed with HCl (1 M, 2x50mL) and saturated $NaHCO_3$ solution (2x50mL), H2O (50mL) and brine (50mL). The organic was then dried (Na_2SO_4) and concentrated under reduced pressure to give crude product (6.61 g). LCMS *m/z* 261.2 $(M + H)^+$, Rt 0.77 min.

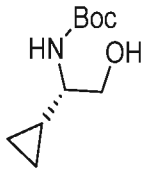
Step 2: Preparation of (S)-tert-butyl 2-methyl-4-oxopentan-3-ylcarbamate

To a solution of (S)-tert-butyl 1-(methoxy(methyl)amino)-3-methyl-1-oxobutan-2-ylcarbamate (4.23 g, 16.25 mmol) in THF (100 mL) at -70 °C was added drop wise methyl lithium (1.071 g, 48.7 mmol). Cold bath was replaced with -40 °C bath (MeCN in dry ice) removed and the reaction was stirred for 4 hours. Saturated NH_4Cl solution (10mL) was then added cautiously to quench the reaction. The reaction mixture was then allowed to warm to room temperature, and diluted with EtOAc (100mL) and water (50mL). The phases were separated and the aqueous layer was extracted with EtOAc (2x100mL). The combined organics were then dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified via silica gel flash chromatography (10-50% EtOAc-Hexanes) to afford the desired product as a white solid (3.01 g). LCMS *m/z* 238.2 $(M + Na)^+$, Rt 0.78 min.

Step 3: Preparation of tert-butyl 3-hydroxy-2-methylbutan-2-ylcarbamate

To a solution of (S)-tert-butyl 2-methyl-4-oxopentan-3-ylcarbamate (2.65 g, 12.31 mmol) in MeOH (30mL) at 0 °C was added portion wise $NaBH_4$ (0.931 g, 24.62 mmol). Cold bath was removed and the reaction was stirred for 1 hour. HCl solution (1 M, 0.3 mL) was then added cautiously to quench the reaction. The reaction mixture was then concentrated and diluted with EtOAc (50mL) and water (10mL). The phases were separated and the aqueous layer was extracted with EtOAc (2x20mL). The combined organics were then dried (Na_2SO_4) and concentrated. The residue was purified via silica gel flash chromatography (10-50% EtOAc-Hexanes) to afford the desired product as a white solid (2.05 g). LCMS *m/z* 240.2 $(M + Na)^+$, Rt 0.69 min.

Intermediate 174: (S)-tert-butyl (1-cyclopropyl-2-hydroxyethyl)carbamate



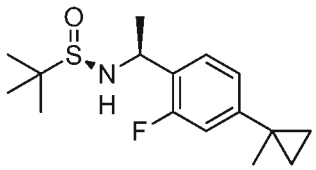
Step 1: Preparation of tert-butyl 1-(methoxy(methyl)amino)-2-methyl-1-oxopropan-2-ylcarbamate

To (S)-2-(tert-butoxycarbonylamino)-2-cyclopropylacetic acid (5.01 g, 23.28 mmol) in MeOH (50mL) was added drop wise trimethylsilyldiazomethane (18.62 ml, 37.2 mmol) until no bubbles. The reaction was stirred for 30 minutes and quenched with drops of HOAc (0.1 mL). The reaction mixture was then concentrated under reduced pressure to give crude product as a light tan oil (5.35 g). LCMS *m/z* 252.1 $(M + Na)^+$, Rt 0.77 min.

Step 2: Preparation of (S)-tert-butyl (1-cyclopropyl-2-hydroxyethyl)carbamate

To a solution of (S)-methyl 2-(tert-butoxycarbonylamino)-2-cyclopropylacetate (5.35 g, 23.33 mmol) in Et_2O (100 ml) was added $LiBH_4$ (0.762 g, 35.0 mmol), followed by drop wise addition of methanol (1.420 ml, 35.0 mmol). The reaction was refluxed at 40 °C for one hour. The reaction mixture was then cooled to 0 °C, and quenched with HCl (1M) until pH=2 for aqueous layer. The phases were separated and the aqueous layer was extracted with DCM (3x100mL). The organic was then dried (Na_2SO_4) and concentrated under reduced pressure to give final crude product (4.16 g). LCMS *m/z* 224.1 $(M + Na)^+$, Rt 0.62 min.

Intermediate 175: (R)-N-((S)-1-(2-fluoro-4-(1-methylcyclopropyl)phenyl)ethyl)-2-methylpropane-2-sulfinamide



Step 1

To an oven dried round bottom flask with stir bar was added 4-bromo-2-fluorobenzaldehyde (5 g, 24.6 mmol), (R)-2-methylpropane-2-sulfinamide (3.28 g, 27.1 mmol) and DCE (49 mL). To this mixture was then added copper (II) sulfate (5.90 g, 36.9 mmol). Reaction mixture was heated in a preheated oil bath to 55 °C for 18 hours. Reaction mixture was filtered through a pad celite, washing the solids with CH_2Cl_2. The filtrate was concentrated to afford a viscous yellow oil of (R,E)-N-(4-bromo-2-fluorobenzylidene)-2-methylpropane-2-sulfinamide (7.73 g, 25.2 mmol, 103 % yield). ^{1}H NMR (400 MHz, $CDCL_3$) δ 1.27 (s, 9 H) 7.31 - 7.42 (m, 2 H) 7.87 (t, *J*=7.87 Hz, 1 H) 8.83 (s, 1 H). LCMS *m/z* 307.9 $(M + H)^+$, Rt 1.01 min.

Step 2

To a solution of (R,E)-N-(4-bromo-2-fluorobenzylidene)-2-methylpropane-2-sulfinamide (7.73 g, 25.2 mmol) in CH_2Cl_2 (252 mL), cooled to 0°C (water/ice bath) under nitrogen, was added 3M methyl magnesium bromide (33.7 mL, 101 mmol) in Et_2O. Reaction mixture allowed to stir for 30 min at 0°C, then gradually allowed to warm to room temperature and stirred for 1 hour at room temperature. Reaction mixture was cooled to 0°C then quenched with the slow addition of a saturated solution of NH_4Cl. Aqueous mixture extracted with EtOAc. Organic phases combined, washed with water, brine, dried (Na_2SO_4), filtered and concentrated onto silica gel. Silica gel column chromatography (EtOAc/Heptane 40 to 100%) provided (R)-N-((S)-1-(4-bromo-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (4.93 g, 15.3 mmol, 60% yield) as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCL_3$) δ 1.20 (s, 9 H) 1.56 (d, *J*=6.70 Hz, 3 H) 3.34 (br. s., 1 H) 4.77 - 4.87 (m, 1 H) 7.19 - 7.31 (m, 3 H). LCMS *m/z* 324.0 $(M + H)^+$, Rt 0.90 min.

Step 3

To a microwave vial with stir bar was added (R)-N-((S)-1-(4-bromo-2-fluorophenyl)ethyl)-2-methylpropane-2- (1 g, 3.10 mmol), isopropenyl boronic acid pinacol ester (1.51 ml, 8.07 mmol), DME (8 ml), sodium carbonate (7.76 ml, 15.5 mmol) (2.0 M aq) and $PdCl_2$(dppf). CH_2Cl_2 adduct (0.127 g, 0.155 mmol). Vessel was capped and heated by microwave irradiation for 20 min at 100 °C. Reaction mixture was diluted with a saturated solution of NH_4Cl. The aqueous mixture was extracted with EtOAc. Organic phases combined, washed with water, brine, dried (Na_2SO_4), filtered and concentrated onto silica gel. Silica gel column chromatography (EtOAc/Heptane 50 to 100%) provided (R)-N-((S)-1-(2-fluoro-4-(prop-1-en-2-yl)phenyl)ethyl)-2-methylpropane-2-sulfinamide (830 mg, 2.93 mmol, 94 % yield) as a pale brown crystalline. ^{1}H NMR (400 MHz, DMSO) δ 1.08 - 1.11 (m, 9 H) 1.47 (d, *J*=6.80 Hz, 3 H) 2.09 (d, *J*=0.54 Hz, 3 H) 4.61 - 4.71 (m, 1 H) 5.14 (t, *J*=1.32 Hz, 1 H) 5.43 (d, *J*=5.58 Hz, 1 H) 5.49 (s, 1 H) 7.24 - 7.30 (m, 1 H) 7.31 - 7.36 (m, 1 H) 7.41 - 7.47 (m, 1 H). LCMS *m/z* 284.0 $(M + H)^+$, Rt 0.93 min.

Step 4

To a round bottom flask containing (R)-N-((S)-1-(2-fluoro-4-(prop-1-en-2-yl)phenyl)ethyl)-2-methylpropane-2- (0.37 g, 1.31 mmol) in DCE (13 mL) at 0 °C was added under argon diethylzinc (1.0M in hexanes) (13.1 mL, 13.1 mmol) followed by the dropwise addition of chloroiodomethane (0.95 mL, 13.1 mmol). Reaction mixture allowed to warm to room temperature and stirred for 1 hour. Reaction mixture was cooled to 0 °C whereupon a second addition of diethylzinc (1.0M in hexanes) (13.1 mL, 13.1 mmol) took place followed by the addition of chloroiodomethane (0.95 mL, 13.1 mmol). Reaction mixture allowed to warm to room temperature and stirred 18 hours under argon. Reaction mixture was cooled to 0 °C in a ice bath and to the cold reaction mixture was slowly added a saturated solution of NH_4Cl. The aqueous mixture was extracted with EtOAc. Organic phases combined, washed with water, brine, dried (Na_2SO_4), filtered and concentrated onto silica gel. Silica gel column chromatography (EtOAc/Heptane 20 to 100%) provided a white crystalline of (R)-N-((S)-1-(2-fluoro-4-(1-methylcyclopropyl)phenyl)ethyl)-2-methylpropane-2-sulfinamide (89 mg, 0.299 mmol, 22.92 % yield). ^{1}H NMR (400 MHz, $CDCL_3$) δ 0.75 - 0.79 (m, 2 H) 0.85 - 0.90 (m, 2 H) 1.20 (s, 9 H) 1.55 (s, 3 H) 1.57 (d, *J*=6.80 Hz, 1 H) 3.34 (d, *J*=5.23 Hz, 1 H) 4.75 - 4.85 (m, 1 H) 6.90 (dd, *J*=12.30, 1.74 Hz, 1 H) 6.97 (dd, *J*=8.05, 1.78 Hz, 1 H) 7.22 (t, *J*=7.97 Hz, 1 H). LCMS *m/z* 298.1 $(M + H)^+$, Rt 1.01 min.

The Intermediates in Table 4k were prepared by a method similar to the one described for the preparation of Intermediate 175.

Table 4k

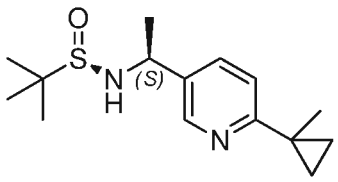
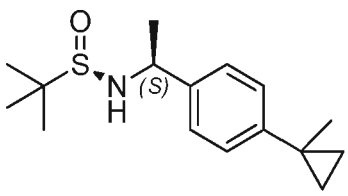
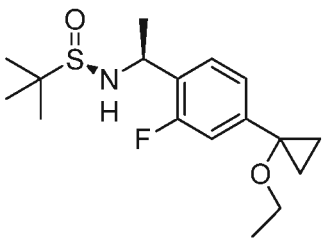
Intermediate 176	Intermediate 177
	

Table 4m. Chemical name, NMR chemical shifts and LCMS signal for each intermediate listed in Table 4k.

Intermediate: Name	^{1}H NMR (400 MHz) δ ppm	LCMS
176: (R)-2-methyl-N-((S)-1-(6-(1-methylcyclopropyl)pyridin-3-yl)ethyl) propane-2-sulfinamide		MS *m/z* 282.1 (M + H)$^+$, Rt 0.48 min.
177: (R)-2-methyl-N-((S)-1-(4-(1-methylcyclopropyl) phenyl)ethyl) propane-2-sulfinamide	($CDCl_3$) 0.71 - 0.76 (m, 2 H) 0.85 - 0.89 (m, 2 H) 1.20 - 1.22 (m, 9 H) 1.41 (s, 3 H) 1.53 (d, *J*=6.65 Hz, 3 H) 3.29 (d, *J*=3.57 Hz, 1 H) 4.50 - 4.57 (m, 1 H) 7.21 (s, 2 H) 7.23 (s, 2 H)	MS *m/z* 280.1 (M + H)$^+$, Rt 0.98 min.

Intermediate 178: (R)-N-((S)-1-(4-(1-ethoxycyclopropyl)-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide



Step 1

To a microwave vial with stir bar was added (R)-N-((S)-1-(4-bromo-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (500 mg, 1.55 mmol) followed by the addition of tributyl(1-ethoxyvinyl)stannane (1.12 g, 3.10 mmol), triethylamine (0.65 ml, 4.65 mmol) and $PdCl_2$(dppf). CH_2Cl_2 adduct (63 mg, 0.078 mmol). To the solids was added toluene (10 ml). Vial capped and heated in a preheated sand bath at 100 °C for 1 hour. Reaction mixture was loaded onto silica gel column. Silica gel column chromatography

(MeOH/ CH_2Cl_2 0 to 10% with 1% NH_4OH buffer) provided (R)-N-((S)-1-(4-(1-ethoxyvinyl)-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (498 mg, 1.59 mmol, 102 % yield) as a brown viscous oil which crystallizes upon standing. ^{1}H NMR (400 MHz, $CDCL_3$) δ 1.20 (s, 9 H) 1.43 (t, *J*=6.97 Hz, 3 H) 1.58 (d, *J*=6.75 Hz, 3 H) 3.35 (d, *J*=4.74 Hz, 1 H) 3.92 (q, *J*=6.96 Hz, 2H) 4.23 (d, *J*=2.79 Hz, 1 H) 4.65 (d, *J*=2.79 Hz, 1 H) 4.79 - 4.89 (m, 1 H) 7.16 - 7.20 (m, 1 H) 7.29 - 7.34 (m, 1 H) 7.39 (dd, *J*=8.07, 1.66 Hz, 1 H).

Step 2

To a round bottom flask containing (R)-N-((S)-1-(4-(1-ethoxyvinyl)-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (0.49 g, 1.56 mmol) and chloroiodomethane (1.14 mL, 15.6 mmol) in toluene (15 mL) at 0 °C under argon was added diethylzinc (1.0M in hexanes) (15.6 mL, 15.6 mmol). Reaction mixture allowed to warm to room temperature and stirred for 1 hour. Reaction mixture was cooled to 0 °C in an ice bath and to the cold reaction mixture was slowly added a saturated solution of NH_4Cl. The aqueous mixture was extracted with EtOAc. Organic phases combined, washed with water, brine, dried (Na_2SO_4), filtered and concentrated onto silica gel. Silica gel column chromatography (MeOH/CH_2Cl_2 0 to 10%) provided (R)-N-((S)-1-(4-(1-ethoxycyclopropyl)-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (145 mg, 0.44 mmol, 28 % yield) as a viscous brown oil. ^{1}H NMR (300 MHz, $CDCL_3$) δ 0.93 - 0.99 (m, 2 H) 1.14 - 1.20 (m, 3 H) 1.21 (s, 9 H) 1.22 - 1.27 (m, 2 H) 1.57 - 1.61 (m, 4 H) 3.35 (d, *J*=4.98 Hz, 1 H) 3.45 (q, *J*=7.07 Hz, 2 H) 4.77 - 4.87 (m, 1 H) 6.98 (dd, *J*=7.58, 1.43 Hz, 3 H) 7.00 - 7.03 (m, 4 H) 7.28 - 7.32 (m, 1 H). LCMS *m/z* 328.1 $(M + H)^+$, Rt 0.95 min.

The Intermediate in Table 4n were prepared by a method similar to the one described for the preparation of Intermediate 178.

Table 4n.

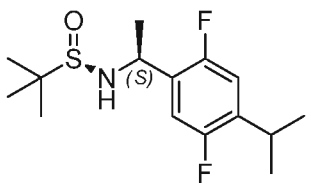
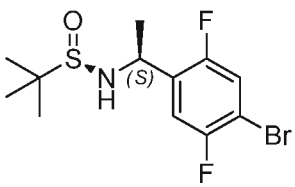
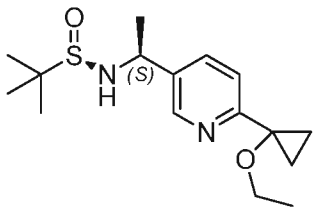
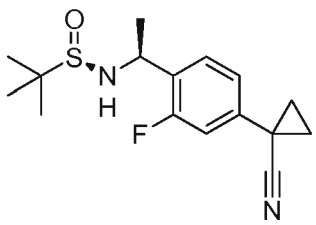
Intermediate 179	Intermediate 180	Intermediate 181
		

Table 4p. Chemical name, NMR chemical shifts and LCMS signal for each intermediate listed in Table 4n.

Intermediate: Name	^{1}H NMR (400 MHz) δ ppm	LCMS
179: (R)-N-((S)-1-(2,5-difluoro-4-isopropylphenyl)ethyl)-2-methylpropane-2-sulfinamid		MS *m/z* 304.2 $(M + H)^+$, Rt 1.04 min.
180: (R)-N-((S)-1-(4-bromo-2,5-difluorophenyl)ethyl)-2-methylpropane-2-sulfinamide		MS *m/z* 340.1, 342.1 $(M + H)^+$, Rt 0.96 min.
181: (R)-N-((S)-1-(6-(1-ethoxycyclopropyl)pyridin-3-yl)ethyl)-2-methylpropane-2-sulfinamide		MS *m/z* 311.1 $(M + H)^+$, Rt 0.52 min.

Intermediate 182: (R)-N-((S)-1-(4-(1-cyanocyclopropyl)-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide



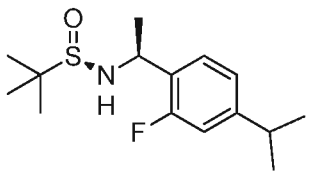
Step 1

To a microwave vial with a stir bar was added (R)-N-((S)-1-(4-bromo-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (300 mg, 0.93 mmol), 4-isoxazoleboronic acid pinacol ester (218 mg, 1.12 mmol), $PdCl_2(dppf).CH_2Cl_2$ adduct (76 mg, 0.09 mmol), potassium fluoride (2.7 mL, 1.0 M in water, 2.79 mmol) and finally DMSO (9 mL). The reaction mixture was degassed with bubbling nitrogen (3 min) and the vial capped and heated in a preheated oil bath at 130 °C for 18 hours. The reaction mixture was diluted with a saturated solution of NH_4Cl and extracted with EtOAc. Organic phases combined, washed with water, brine, dried (Na_2SO_4), filtered and concentrated onto silica gel. Silica gel column chromatography (EtOAc/Heptanes 40 to 100%) provided (R)-N-((S)-1-(4-(cyanomethyl)-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (136 mg, 0.48 mmol, 52 % yield) as a viscous brown oil. ^{1}H NMR (400 MHz, $CDCL_3$) δ 1.19 (s, 9 H) 1.57 (d, *J*=6.80 Hz, 3 H) 3.39 (d, *J*=4.35 Hz, 1 H) 3.74 (s, 2 H) 4.81 - 4.88 (m, 1 H) 7.04 (d, *J*=10.66 Hz, 1 H) 7.11 (d, *J*=7.97 Hz, 1 H) 7.38 (t, *J*=7.73 Hz, 1 H). LCMS *m/z* 283.0 $(M + H)^+$, Rt 0.72 min.

Step 2

To a scintillation vial containing (R)-N-((S)-1-(4-(cyanomethyl)-2-fluorophenyl)ethyl)-2-methylpropane-2- (86 mg, 0.31 mmol) and a stir bar was added toluene (2 mL). To this mixture was then added tetrabutylammonium bromide (19 mg, 0.06 mmol) followed by the addition of NaOH (1.52 ml, 1.0 M (aq), 1.52 mmol) and 1,2-dibromoethane (0.11 ml, 1.22 mmol). Vial capped and reaction mixture was stirred vigorously at room temperature for 18 hours. Whereupon, 1,2-dibromoethane (0.11 ml, 1.22 mmol) and tetrabutylammonium bromide (19 mg, 0.06 mmol) were added and reaction mixture allowed to stir an additional 18 hours. A third addition of 1,2-dibromoethane (0.11 ml, 1.22 mmol) was added and the reaction mixture heated to 50 °C for an additional 18 hours in a preheated aluminum tray. The reaction mixture was quenched with a saturated solution of NH_4Cl and the aqueous mixture extracted with EtOAc. Organics combined and washed twice with water, brine, dried (Na_2SO_4), filtered and concentrated. Crude material was passed through a small plug of silica gel using 10%MeOH:90%DCM to elute product. The solution was concentrated to afford a viscous orange oil of (R)-N-((S)-1-(4-(1-cyanocyclopropyl)-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (23 mg, 0.08 mmol, 24 % yield). ^{1}H NMR (400 MHz, $CDCL_3$) δ 1.20 (s, 9 H) 1.38 - 1.44 (m, 2 H) 1.56 (d, *J*=6.75 Hz, 3 H) 1.73 - 1.79 (m, 2 H) 3.37 (d, *J*=4.45 Hz, 1 H) 4.78 - 4.88 (m, 1 H) 6.94 (dd, *J*=11.35, 1.91 Hz, 1 H) 7.09 (dd, *J*=8.07, 1.91 Hz, 1 H) 7.34 (t, *J*=7.90 Hz, 1 H). LCMS *m/z* 309.2 $(M + H)^+$, Rt 0.83 min.

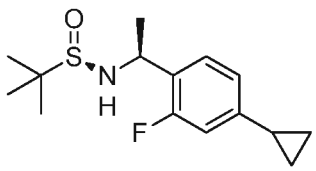
Intermediate 183: (R)-N-((S)-1-(2-fluoro-4-isopropylphenyl)ethyl)-2-methylpropane-2-sulfinamide



To a round bottom flask containing (R)-N-((S)-1-(2-fluoro-4-(prop-1-en-2-yl)phenyl)ethyl)-2-methylpropane-2-sulfinamide (204 mg, 0.72 mmol) and a stir bar was added MeOH (7.2 mL). To this solution was added palladium on carbon (77 mg, 10%, 0.07 mmol) in MeOH (1 mL). A hydrogen atmosphere was inserted and the resulting reaction mixture stirred at room temperature for 18 hours, at which time more palladium on carbon was added (300 mg) in MeOH (5 mL). A hydrogen atmosphere was inserted again and the reaction mixture allowed to stir an additional 18 hours at room temperature. The reaction mixture was filtered through a syringe filter and concentrated to afford a light brown

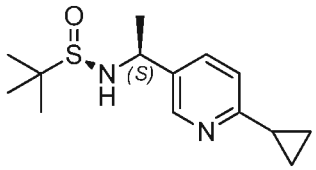
viscous oil of (R)-N-((S)-1-(2-fluoro-4-isopropylphenyl)ethyl)-2-methylpropane-2-sulfinamide (149 mg, 0.52 mmol, 73 % yield) which crystallizes upon standing. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 9 H) 1.24 (d, *J*=5.87 Hz, 6 H) 1.58 (d, *J*=6.70 Hz, 3 H) 2.89 (dt, *J*=13.79, 6.90 Hz, 1 H) 3.35 (d, *J*=5.04 Hz, 1 H) 4.76 - 4.85 (m, 1 H) 6.90 (dd, *J*=12.03, 1.52 Hz, 1 H) 6.98 (dd, *J*=7.90, 1.54 Hz, 1 H) 7.24 (t, *J*=7.97 Hz, 1 H). LCMS *m/z* 286.3 $(M + H)^+$, Rt 1.01 min.

Intermediate 184: (R)-N-((S)-1-(4-cyclopropyl-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide



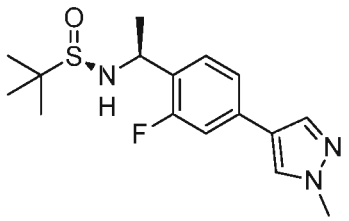
To a microwave vial containing a stir bar was added (R)-N-((S)-1-(4-bromo-2-fluorophenyl) ethyl)-2-methylpropane-2-sulfinamide (100 mg, 0.31 mmol) followed by the addition of potassium cyclopropyltrifluoroborate (459 mg, 3.10 mmol), cesium carbonate (506 mg, 1.55 mmol) and $Pd(OAc)_2$ (7 mg, 0.03 mmol) and di(1-adamantyl)-n-butylphosphine (22 mg, 0.06 mmol), toluene (2.6 mL) and finally water (0.5 mL). The vial capped and heated by microwave irraditation for 20 min at 100 °C, followed by thermal heating at 100°C in a preheated aluminum tray for 18 hours. The reaction mixture was diluted with a saturated solution of NH_4Cl. The aqueous mixture extracted with EtOAc. Organic phases combined, washed with water, brine, dried (Na_2SO_4), filtered and concentrated to afford a yellow crystalline of (R)-N-((S)-1-(4-cyclopropyl-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (116 mg, 0.33 mmol, 106 % yield). LCMS *m/z* 284.0 $(M + H)^+$, Rt 0.90 min.

Intermediate 185: (R)-N-((S)-1-(6-cyclopropylpyridin-3-yl)ethyl)-2-methylpropane-2-sulfinamide



(R)-N-((S)-1-(6-cyclopropylpyridin-3-yl)ethyl)-2-methylpropane-2-sulfinamide is prepared with a method similar to that used to access Intermediate 184. MS m/z 267.1 (M + H)+, Rt 0.44 min.

Intermediate 186: (R)-N-((S)-1-(2-fluoro-4-(1-methyl-1H-pyrazol-4-yl)phenyl)ethyl)-2-methylpropane-2-sulfinamide



To a two microwave vials with stir bars were added (R)-N-((S)-1-(4-bromo-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (1.5 g, 4.65 mmol), 1-methyl-4-1H-pyrazoleboronic acid pinacol ester (2.91 g, 13.9 mmol), DME (20 mL), sodium carbonate (11.6 mL, 23.3 mmol, 2.0 M aq) and $PdCl_2(dppf).CH_2Cl_2$ adduct (190 mg, 0.23 mmol) divided between the two vials. The vials were capped and heated by microwave irradiation for 20 min at 100 °C respectively. The reaction mixtures combined, diluted with a saturated solution of NH_4Cl and EtOAc. The phases were partitioned and the aqueous phase extracted with EtOAc. Organic phases combined, washed with water, brine, dried (Na_2SO_4), filtered and concentrated onto silica gel. Silica gel column chromatography (EtOAc/Heptane 40 to 100%) provided a orange crystalline of (R)-N-((S)-1-(2-fluoro-4-(1-methyl-1H-pyrazol-4-yl)phenyl)ethyl)-2-methylpropane-2-sulfinamide (1.07 g, 3.31 mmol, 71 % yield. ^{1}H NMR (400 MHz, $CDCL_3$) δ ppm 1.21 (s, 9 H) 1.60 (d, *J*=6.80 Hz, 3 H) 3.36 (d, *J*=4.25 Hz, 1 H) 3.96 (s, 3 H) 4.79 - 4.91 (m, 1 H) 7.13 (dd, *J*=11.69, 1.61 Hz, 1 H) 7.23 (dd, *J*=8.00, 1.64 Hz, 1 H) 7.30 - 7.37 (m, 1 H) 7.60 (s, 1 H) 7.74 (s, 1 H). LCMS *m/z* 324.0 $(M + H)^+$, Rt 0.74 min.

The Intermediates in Table 4q were prepared by a method similar to the one described for the preparation of Intermediate 186.

Table 4q.

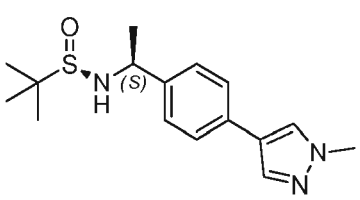
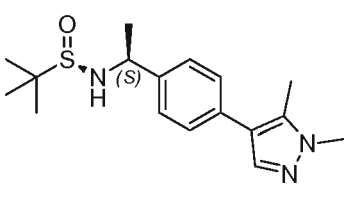
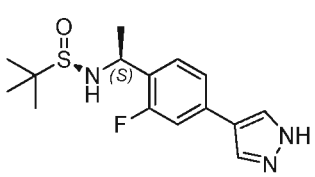
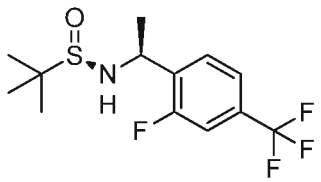
Intermediate 187	Intermediate 188	Intermediate 189
		

Table 4r. Chemical name, NMR chemical shifts and LCMS signal for each intermediate listed in Table 4q.

Intermediate: Name	^{1}H NMR (400 MHz) δ ppm	LCMS
187: (R)-2-methyl-N-((S)-1-(4-(1-methyl-1H-pyrazol-4-yl)phenyl)ethyl)propane-2-sulfinamide		MS *m/z* 306.0 (M + H)$^+$, Rt 0.71 min.
188: (R)-N-((S)-1-(4-(1,5-dimethyl-1H-pyrazol-4-yl)phenyl)ethyl)-2-methylpropane-2-sulfinamide		MS *m/z* 320.0 (M + H)$^+$, Rt 0.72 min.
189: (R)-N-((S)-1-(2-fluoro-4-(1H-pyrazol-4-yl)phenyl)ethyl)-2-methylpropane-2-sulfinamide	(DMSO) 1.10 (s, 9 H) 1.47 (d, *J*=6.75 Hz, 3 H) 4.60 - 4.70 (m, 1 H) 5.41 (d, *J*=5.48 Hz, 1 H) 7.38 - 7.44 (m, 3 H) 7.96 (br. s., 1 H) 8.23 (br. s., 1 H) 12.97 (br. s., 1 H)	MS *m/z* 310.0 (M + H)$^+$, Rt 0.67 min.

Intermediate 190: (R)-N-((S)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethyl)-2-methylpropane-2-sulfinamide



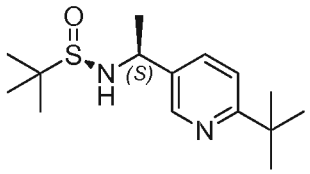
Step 1

To a oven dried round bottom flask with stir bar was added 2-fluoro-4-(trifluoromethyl) benzaldehyde (5 g, 26.0 mmol), (R)-2-methylpropane-2-sulfinamide (3.47 g, 28.6 mmol) and DCE (52 mL). To this mixture was then added copper (II) sulfate (6.23 g, 39.0 mmol). The reaction mixture was heated in a preheated oil bath at 55 °C for 18 hours. The reaction mixture was filtered through a pad celite, washing the solids with DCE. The filtrate was concentrated to afford a viscous green oil of (R,E)-N-(2-fluoro-4-(trifluoromethyl)benzylidene)-2-methyl propane-2-sulfinamide (7.3 g, 24.7 mmol, 95 % yield). Material was taken onto next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 1.29 (s, 9 H) 7.44 (d, *J*=10.08 Hz, 1 H) 7.51 (d, *J*=8.27 Hz, 1 H) 8.13 (t, *J*=7.46 Hz, 1 H) 8.92 (s, 1 H). LCMS *m/z* 296.0 (M + H)$^+$, Rt 1.02 min.

Step 2

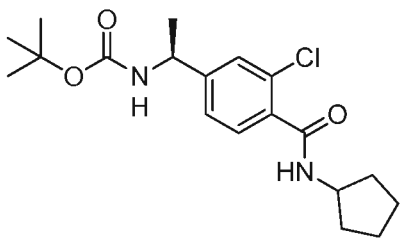
To a solution of (R,E)-N-(2-fluoro-4-(trifluoromethyl)benzylidene)-2-methylpropane-2-sulfinamide (7.3 g, 24.7 mmol) in CH_2Cl_2 (247 mL) cooled to 0°C (water/ice bath) under nitrogen, was added 3M methyl magnesium bromide (33 mL, 99 mmol) in Et_2O. Reaction mixture allowed to stir for 30 min at 0°C, then gradually allowed to warm to room temperature and stirred for 1 hour at room temperature. Reaction mixture was cooled to 0°C then quenched with the slow addition of a saturated solution of NH_4Cl. Aqueous mixture extracted with EtOAc. Organic phases combined, washed with water, brine, dried (Na_2SO_4), filtered and concentrated onto silica gel. Silica gel column chromatography (EtOAc/Heptane 40 to 100%) provided (R)-N-((S)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethyl)-2-methylpropane-2-sulfinamide (4.68 g, 15.0 mmol, 61% yield) as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCL_3$) δ 1.22 (s, 9 H) 1.60 (d, *J*=6.80 Hz, 3 H) 3.38 (d, *J*=4.01 Hz, 1 H) 4.87 - 4.97 (m, 1 H) 7.33 (d, *J*=10.32 Hz, 1 H) 7.39 - 7.45 (m, 1 H) 7.49 - 7.55 (m, 1 H). LCMS *m/z* 312.0 $(M + H)^+$, Rt 0.92 min.

Intermediate 191: (R)-N-((S)-1-(6-tert-butylpyridin-3-yl)ethyl)-2-methylpropane-2-sulfinamide



(R)-N-((S)-1-(6-tert-butylpyridin-3-yl)ethyl)-2-methylpropane-2-sulfinamide is prepared with methods similar to those used to prepare Intermediate 190. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 9 H) 1.37 (s, 9 H) 1.57 (d, *J*=6.75 Hz, 3 H) 3.31 (d, *J*=3.37 Hz, 1 H) 4.56 - 4.65 (m, 1 H) 7.32 (d, *J*=8.22 Hz, 1 H) 7.57 (dd, *J*=8.24, 2.23 Hz, 1 H) 8.54 (d, *J*=2.05 Hz, 1 H). MS m/z 283.1 (M + H)+, Rt 0.51 min.

Intermediate 192: (S)-tert-butyl 1-(3-chloro-4-(cyclopentylcarbamoyl)phenyl)ethyl carbamate



Step 1

To a round bottom flask with stir bar was added 4-((S)-1aminoethyl-2-chlorobenzoic acid HCl salt (1.05 g, 4.45 mmol) followed by the addition of THF (40 mL). To this solution was added DIEA (1.86 ml, 10.7 mmol). The reaction mixture becomes cloudy white followed by the addition of di-tert-butyl dicarbonate (1.07 g, 4.89 mmol). Resulting reaction mixture allowed to stir for 18 hours at room temperature. At which time the reaction mixture was then heated to 60 °C for 2 hours in a oil bath. Di-tert-butyl dicarbonate (1.07 g, 4.89 mmol) and NMP (20 ml) were then added and the resulting reaction mixture allowed to stir for 2 hours at 60 °C. Volatiles were removed. The resulting oil was diluted with a saturated solution of NH_4Cl and the aqueous mixture extracted with EtOAc. The organic phases combined, washed twice with water, brine, dried (Na_2SO_4), filtered and concentrated to a viscous yellow oil of (S)-4-(1-(tert-butoxycarbonylamino)ethyl)-2-chlorobenzoic acid (2.32 g, 6.19 mmol, 139 % yield) which contains some excess di-tert-butyl dicarbonate and NMP. LCMS *m/z* 284.9 $(M + H)^+$(carboxylic acid fragment + CH_3CN adduct), Rt 0.75 min.

Step 2

To a round bottom flask with stir bar was added (S)-4-(1-(tert-butoxycarbonylamino)ethyl)-2-chlorobenzoic acid (450 mg, 1.20 mmol), cyclopentylamine (355 µL, 3.60 mmol), EDC HCl (460 mg, 2.40 mmol), 1-hydroxy-7-aza-benzotriazole (229 mg, 1.68 mmol) and DMF (6 mL). To this mixture was then added DIEA (629 µL, 3.60 mmol). Reaction mixture was allowed to stir at room temperature for 18 hours. The reaction mixture was diluted with water and extracted with EtOAc. The organic phases were combined, washed with twice with water, brine, dried (Na_2SO_4), filtered and concentrated to a brown crystalline of (S)-tert-butyl 1-(3-chloro-4-(cyclopentylcarbamoyl) phenyl)ethylcarbamate (476 mg, 1.17 mmol, 97 % yield). LCMS *m/z* 367.0 $(M + H)^+$, Rt 0.90 min.

The Intermediates in Table 4s were prepared by a method similar to the one described for the preparation of Intermediate 192.

Table 4s.

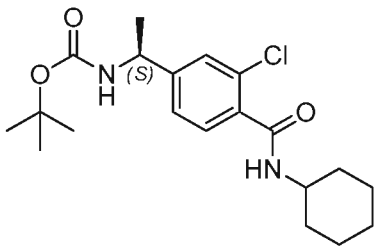
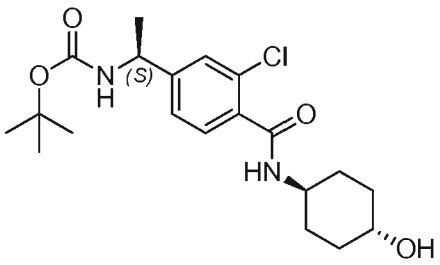
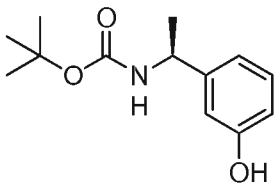
Intermediate 193	Intermediate 194
	

Table 4t. Chemical name and LCMS signal for each intermediate listed in Table 4s.

Intermediate: Name	LCMS
193: (S)-tert-butyl 1-(3-chloro-4-(cyclohexyl carbamoyl) phenyl) ethylcarbamate	MS *m/z* 381.1 $(M + H)^+$, Rt 0.96 min.
194: tert-butyl (S)-1-(3-chloro-4-((1r,4S)-4-hydroxycyclohexyl carbamoyl)phenyl)ethylcarbamate	MS *m/z* 391.1 $(M + H)^+$, Rt 0.71 min.

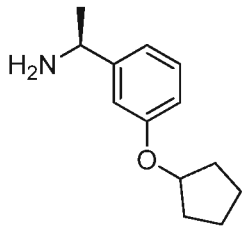
Intermediate 195: (S)-tert-butyl 1-(3-hydroxyphenyl)ethylcarbamate



A slurry of (S)-3-(1-aminoethyl)phenol (1.188 g, 6.84 mmol) and Boc_2O (1.747 mL, 7.53 mmol) in DCM (17.10 mL) was stirred at room temperature under N_2 while slowly adding DIEA (1.434 mL, 8.21 mmol). The initially insoluble starting materials slowly dissolve. The solution was stirred at room temperature for 16 hours and then concentrated. The oily residue was re-dissolved in EtOAc and washed with Na_2CO_3 saturated, followed by brine. The original aqueous layer was re-extracted with EtOAc, which was then washed with brine and combined with the previous EtOAc batch. The combined organics were dried over Na_2SO_4, filtered and concentrated to 2.4g crude clear yellowish oil which was purified by silica gel column chromatography (EtOAc/Heptane 0 to 30%), yielding (S)-tert-butyl 1-(3-hydroxyphenyl)ethylcarbamate as a clear colourless oil, which solidifies upon sitting (1.79 g, 7.55 mmol, 110 % yield). ^1H NMR (400 MHz, $CDCL_3$) δ 1.44 (br. s.,

12 H) 4.08 - 4.18 (m, 1 H) 4.76 (br. s., 1 H) 6.72 (dd, *J*=7.46, 1.83 Hz, 1 H) 6.78 (br. s., 1 H) 6.88 (br. s., 1 H) 7.16 - 7.24 (m, 1 H). LCMS *m/z* 223.0/182.0 (the parent not observed, just the Boc fragments) $(M + H)^+$, Rt 0.71 min.

Intermediate 196: (S)-1-(3-(cyclopentyloxy)phenyl)ethanamine hydrochloride



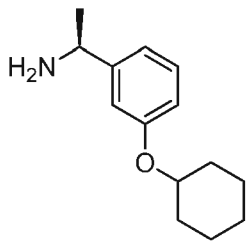
Step 1: Mitsunobu A

To a solution of (S)-tert-butyl 1-(3-hydroxyphenyl)ethylcarbamate (107.5 mg, 0.453 mmol), PPh_3 (238 mg, 0.906 mmol) and cyclopentanol (0.164 ml, 1.812 mmol) in THF (2 ml) at room temperature was added DEAD (0.143 ml, 0.906 mmol) dropwise under N_2. The resulting yellow solution was stirred for 4 hours and then concentrated. The viscous yellow oil was re-dissolved in DMSO and purified by reverse phase HPLC. The combined product fractions were desalted by addition of equal amount of EtOAc and about 250mg Na_2CO_3 in a separatory funnel. The phases were separated and the organic washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield (S)-tert-butyl 1-(3-(cyclopentyloxy)phenyl)ethylcarbamate (75.1 mg, 0.246 mmol, 54.3 % yield) as a white solid film. LCMS *m/z* 291.1/250.0 (the parent not observed, just the Boc fragments) $(M + H)^+$, Rt 1.07 min.

Step 2

(S)-tert-butyl 1-(3-(cyclopentyloxy)phenyl)ethylcarbamate (75.1 mg, 0.246 mmol) was dissolved in 4M HCl in dioxane (1 ml, 4.00 mmol) and the resulting mixture was allowed to sit for 1hour, then concentrated to yield (S)-1-(3-(cyclopentyloxy)phenyl)ethanamine as an HCl salt (yield assumed quantitative). LCMS *m/z* 206.1 $(M + H)^+$, Rt 0.61 min.

Intermediate 197: (S)-1-(3-(cyclohexyloxy)phenyl)ethanamine hydrochloride



Step 1: Mitsunobu B

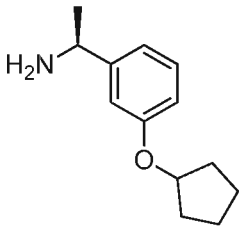
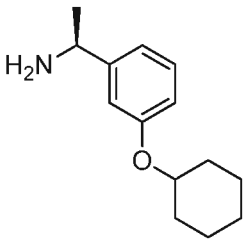
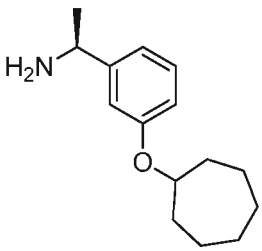
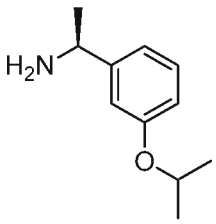
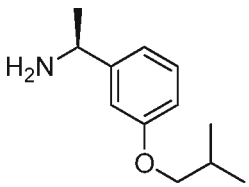
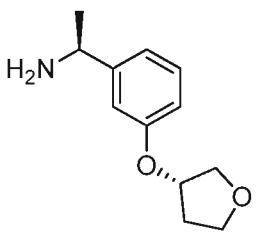
To a solution of (S)-tert-butyl 1-(3-hydroxyphenyl)ethylcarbamate (100 mg, 0.421 mmol), cyclohexanol (0.180 ml, 1.686 mmol) and PPh_3 (221 mg, 0.843 mmol) in THF (2 ml), was added DEAD (0.133 ml, 0.843 mmol) dropwise, under N_2, at room temperature. The resulting yellow solution was stirred for 3 hours, at which point another batch of cyclohexanol (0.180 ml, 1.686 mmol), PPh_3 (221 mg, 0.843 mmol), and 10rnin later DEAD (0.133 ml, 0.843 mmol), was added at room temperature. The reaction mixture was stirred for 16 hours and then concentrated. The crude clear oil was re-dissolved in DMSO and purified by reverse phase HPLC. The combined product fractions were desalted by addition of equal amount of EtOAc and about 250mg Na_2CO_3 in a separatory funnel. The phases were separated and the organic washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield (S)-tert-butyl 1-(3-(cyclohexyloxy)phenyl)ethylcarbamate (74.1 mg, 0.232 mmol, 55.0 % yield) as a clear colourless film. LCMS *m/z* 305.0/264.0 (the parent not observed, just the Boc fragments) $(M + H)^+$, Rt 1.12 min.

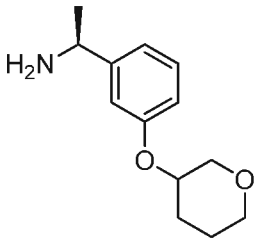
Step 2

(S)-tert-butyl 1-(3-(cyclohexyloxy)phenyl)ethylcarbamate (74.1 mg, 0.232 mmol) was dissolved in 4M HCl in dioxane (1 ml, 4.00 mmol) and the resulting mixture was allowed to sit for 1 hour, then concentrated to yield (S)-1-(3-(cyclohexyloxy)phenyl)ethanamine as an HCl salt (yield assumed quantitative). LCMS *m/z* 220.1 $(M + H)^+$, Rt 0.66 min.

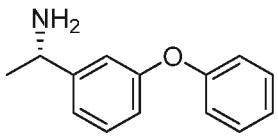
The Intermediates in Table 4v were prepared using either the method described for the preparation of Intermediate 196 or Intermediate 197.

Table 4v.

Intermediate: Name	Structure	LCMS
198: (S)-1-(3-(cyclopentyloxy)phenyl)ethanamine		MS m/z 206.1 (M + H)$^+$, Rt 0.61 min.
199: (S)-1-(3-(cyclohexyloxy)phenyl)ethanamine		MS m/z 220.1 (M + H)$^+$, Rt 0.66 min.
200: (S)-1-(3-(cycloheptyloxy)phenyl)ethanamine		MS m/z 234.1 (M + H)$^+$, Rt 0.73 min.
201: (S)-1-(3-isopropoxyphenyl)ethanamine		MS m/z 180.1 (M + H)$^+$, Rt 0.50 min.
202: (S)-1-(3-isobutoxyphenyl)ethanamine		MS m/z 194.1 (M + H)$^+$, Rt 0.61 min.
203: (S)-1-(3-((S)-tetrahydrofuran-3-yloxy)phenyl)ethanamine		MS m/z 208.1 (M + H)$^+$, Rt 0.41 min.

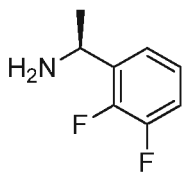
204: (1S)-1-(3-(tetrahydro-2H-pyran-3-yloxy)phenyl)ethanamine		MS m/z 222.1 (M + H)$^+$, Rt 0.46 min.

Intermediate 205: (S)-1-(3-phenoxyphenyl)ethanamine



Into a 20ml microwave vial was weighted 1-(pyridin-2-yl)propan-2-one ligand (90 mg, 0.665 mmol), phenol (407 mg, 4.32 mmol), CuBr (47.7 mg, 0.332 mmol) and Cs_2CO_3 (2166 mg, 6.65 mmol). To the mixture was added DMSO (5 ml) and (S)-1-(3-bromophenyl)ethanamine (0.5 ml, 3.32 mmol). The tube was flushed with N_2, capped, and the black mixture heated in the oil bath at 90°C for 18 hours. The heterogenous mixture was diluted with EtOAc and filtered through a glass-fritted funnel, eluting with EtOAc and another 5mls of DMSO. The volatiles were then removed *in vacuo* and the crude brown liquid was filtered through 1μm PTFE filter and purified by reverse phase HPLC. The combined product fractions were desalted by addition of equal amount of EtOAc and about 250mg Na_2CO_3 in a separatory funnel. The phases were separated and the organic washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield (S)-1-(3-phenoxyphenyl)ethanamine (361.5 mg, 1.678 mmol, 50.5 % yield) as an amber oil. LCMS *m/z* 214.1 (M + H)$^+$, Rt 0.61 min.

Intermediate 206: (S)-1-(2,3-difluorophenyl)ethanamine



Step 1

To a oven dried round bottom flask with stir bar was added 2,3-difluorobenzaldehyde (0.5 g, 3.52 mmol), (R)-2-methylpropane-2-sulfinamide (0.469 g, 3.87 mmol) and DCE

(7.04 mL). To this mixture was then added Copper (II) Sulfate (0.842 g, 5.28 mmol). Reaction mixture heated in a preheated oil bath to 55 °C for 24 hours. The reaction mixture was filtered through a celite pad washing solids with DCE. Combined filtrate was concentrated to afford a viscous yellow oil of (R,E)-N-(2,3-difluorobenzylidene)-2-methylpropane-2-sulfinamide (0.8007 g, 3.26 mmol, 93 % yield). LCMS *m/z* 246.1 (M + H)+, Rt 0.91 min.

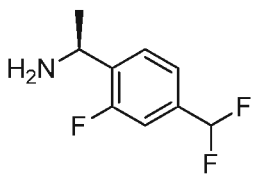
Step 2

To a solution of (R,E)-N-(2,3-difluorobenzylidene)-2-methylpropane-2-sulfinamide (0.800 g, 3.26 mmol) in DCM (32.6 mL), cooled to 0°C (water/icebath) under N2, was added 3M MeMgBr (4.35 mL, 13.05 mmol) in diethyl ether. Reaction mixture allowed to stir for 30 min at 0 °C. Then gradually allowed to warm to room temperature and stirred for 30min at room temperature. Reaction mixture was cooled to 0 °C then quenched with the slow addition of a saturated solution of NH4Cl and diluted with EtOAc. Phases partitioned aqueous phase extracted with EtOAc and the organic layers combined washed with water, brine, dried with MgSO4, filtered and concentrated to afford (R)-N-((S)-1-(2,3-difluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (0.7868 g, 3.01 mmol, 92 % yield) as yellow solid. LCMS *m/z* 262.0 (M + H)+, Rt 0.70 min.

Step 3

To a round bottom flask containing (R)-N-((S)-1-(2,3-difluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (786.8 mg, 3.01 mmol) was added Dioxane (10.000 mL). To this solution was added HCl in dioxane 4.0M (1.505 mL, 6.02 mmol) and the solution was allowed to stir 15 min at room temperature. The reaction mixture was concentrated, dissolved in Et2O 10 ml, and concentrated again. Et2O was again added and resulting mixture sonnicated and a solid material was filtered and dried to afford (S)-1-(2,3-difluorophenyl)ethanamine (0.4213 g, 2.176 mmol, 72.3 % yield) as a white crystalline HCl salt. ^{1}H NMR (400 MHz, D2O) d ppm 1.55 (d, J=6.99 Hz, 3 H) 4.71 (q, J=6.96 Hz, 1 H) 7.10 - 7.26 (m, 3 H); LCMS *m/z* 158.0 (M + H)+, Rt 0.37 min.

Intermediate 207: (S)-1-(4-(difluoromethyl)-2-fluorophenyl)ethanamine



Step 1: Preparation of 1-bromo-4-(difluoromethyl)-2-fluorobenzene

A mixture of 4-bromo-3-fluorobenzaldehyde (2.03 g, 10 mmol) and (diethylamino)sulfur trifluoride (DAST; 1.32 mL, 10 mmol) is heated carefully until exothermic reaction occurs, then heated at 60 °C for 15 min, and allowed to cool to room temperature. The mixture was diluted with DCM (20 mL) and poured into ice/water (30 mL). The mixture was neutralized with $NaHCO_3$ to ~pH 8. The separated aqueous layer was extracted with DCM (20 mL). The combined organic layers were dried over Na_2SO_4, filtered off, and concentrated under reduced pressure. The residue was purified by column chromatography [SiO_2, 40 g, heptane/ethyl acetate], providing 1-bromo-4-(difluoromethyl)-2-fluorobenzene (0.845 g) as a clear colorless oil.

Step 2: Preparation of 4-(difluoromethyl)-2-fluorobenzaldehyde

To a solution of 1-bromo-4-(difluoromethyl)-2-fluorobenzene (311 mg, 1.382 mmol) in THF (2.99 mL) was added butyllithium (1.6M solution in hexanes; 0.881 mL, 1.410 mmol) over ~5 min at -78 °C. The reaction mixture was stirred for 30 min at -78 °C then DMF (0.161 mL, 2.073 mmol) was added dropwise over ~1 min. Stirring was continued for 20 min. The reaction mixture was quenched with aqueous 1M HCl solution/MeOH (2:1, 3 mL) and allowed to warm to room temperature. The mixture was diluted with 5 mL of water. The separated aqueous layer was with ether (5 mL). The combined organic layers were washed with 1M aqueous NaOH solution (10 mL) and saturated brine (10 mL), dried over $MgSO_4$, filtered off and concentrated under reduced pressure. Repeated reaction with 420 mg of 1-bromo-4-(difluoromethyl)-2-fluorobenzene and combined crude materials for purification. The crude material was purified by column chromatography [SiO_2, 24 g, heptane/ethyl acetate], providing 4-(difluoromethyl)-2-fluorobenzaldehyde (162.8 mg) as a yellow oil.

Step 3: Preparation of (R,E)-N-(4-(difluoromethyl)-2-fluorobenzylidene)-2-methylpropane-2-sulfinamide

To a mixture of 4-(difluoromethyl)-2-fluorobenzaldehyde (162 mg, 0.930 mmol) and (R)-2-methylpropane-2-sulfinamide (124 mg, 1.023 mmol) in DCE (3 mL) was added copper sulfate (223 mg, 1.396 mmol). Reaction mixture was heated in a preheated oil bath to 55 °C for 38 hours. The mixture was allowed to cool to room temperature, filtered through a pad of celites and washed with DCE. Combined filtrates were concentrated under reduced pressure to afford (R,E)-N-(4-(difluoromethyl)-2-fluorobenzylidene)-2-methylpropane-2-sulfinamide (266 mg) as a yellow oil, which was used without further purification. LCMS *m/z* 278.1 $(M + H)^+$, Rt 0.98 min.

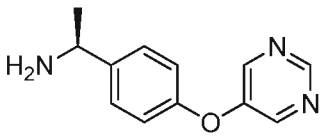
Step 4: Preparation of (R)-N-((S)-1-(4-(difluoromethyl)-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide

To a solution of (R,E)-N-(4-(difluoromethyl)-2-fluorobenzylidene)-2-methylpropane-2-sulfinamide (266 mg, 0.959 mmol) in DCM (9.6 mL) was added methylmagnesium bromide (3M in diethylether; 1.20 mL) at 0 °C. The reaction mixture was allowed to stir for 30 min at 0 °C, gradually allowed to warm to room temperature and stirred for 1 hour at room temperature. The mixture was cooled to 0 °C, and carefully quenched with saturated aqueous NH_4Cl solution (3 mL). The separated aqueous phase was extracted with DCM. The combined organic layers were washed with brine, dried over sodium sulfate, filtered off and concentrated under reduced pressure. The crude material was purified by column chromatography [SiO_2, 40 g, heptane/ethyl acetate], providing (R)-N-((S)-1-(4-(difluoromethyl)-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (160.5 mg) as a white solid. LCMS *m/z* 294.5 $(M + H)^+$, Rt 0.85 min.

Step 5: Preparation of (S)-1-(4-(difluoromethyl)-2-fluorophenyl)ethanamine

To (R)-N-((S)-1-(4-(difluoromethyl)-2-fluorophenyl)ethyl)-2-methylpropane-2-sulfinamide (160 mg, 0.545 mmol) was added 4M HCl in dioxane (409 µL) to give a yellow solution. The resulting mixture was stirred at room temperature for ~1hour. To the mixture was added slowly diethylether (~20 mL). The solids were filtered off, suspended in diethylether, filtered off and rinsed with diethylether, dried under reduced pressure providing (S)-1-(4-(difluoromethyl)-2-fluorophenyl)ethanamine (103 mg) as an off-white solid, which was used without further purification. LCMS *m/z* 190.1 $(M + H)^+$, Rt 0.42 min.

Intermediate 208: (S)-1-(4-(pyrimidin-5-yloxy)phenyl)ethanamine



Step 1: Preparation of 4-(pyrimidin-5-yloxy)benzaldehyde

To a solution of pyrimidin-5-ol (500 mg, 5.20 mmol) in DMF (5.20 mL) under argon was added 4-fluorobenzaldehyde (0.558 mL, 5.20 mmol), sodium methanesulfinate (133 mg, 1.30 mmol), and potassium carbonate (1.079 g, 7.81 mmol). The reaction mixture was heated at 120 °C for 3 hour. The mixture was allowed to cool to room temperature and was diluted with water (25 mL). The mixture was extracted with EtOAc (2x 25 mL). The combined organic layers were washed with brine (2x 50 mL), dried over sodium sulfate, filtered off and concentrated under reduced pressure. The residue was purified by

column chromatography [SiO_2, 24 g, heptane/ethyl acetate], providing 4-(pyrimidin-5-yloxy)benzaldehyde (666 mg) as a yellow solid. LCMS *m/z* 201.0 $(M + H)^+$, Rt 0.52 min.

Step 2: Preparation of (R,E)-2-methyl-N-(4-(pyrimidin-5-yloxy)benzylidene)propane-2-sulfinamide

A mixture of 4-(pyrimidin-5-yloxy)benzaldehyde (666 mg, 3.33 mmol), (R)-(+)-tert-butanesulfinamide (450 mg, 3.71 mmol) and copper sulfate (796 mg, 4.99 mmol) in anhydrous in dichloroethane (7.648 mL) and under argon was heated at 55 °C for ~21 hours. The reaction mixture was allowed to cool to room temperature. The slurry was filtered through a celite pad, eluted with DCM (5x 10 mL). The combined filtrates were concentrated under reduced pressure and the resulting yellowish oil was purified by column chromatography [SiO_2, 24 g, heptane/ethyl acetate] providing (R,E)-2-methyl-N-(4-(pyrimidin-5-yloxy)benzylidene)propane-2-sulfinamide (836 mg) as a pale viscous oil. LCMS *m/z* 304.0 $(M + H)^+$, Rt 0.79 min.

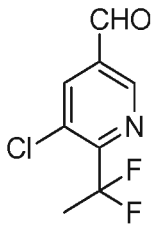
Step 3: Preparation of 2-methyl-N-((S)-1-(4-(pyrimidin-5-yloxy)phenyl)ethyl)propane-2-sulfinamide

A solution of (R,E)-2-methyl-N-(4-(pyrimidin-5-yloxy)benzylidene)propane-2-sulfinamide (830 mg, 2.74 mmol) in DCM (6.72 mL) was cooled to -40 °C. To the solution was added methylmagnesium bromide (3M in diethylether; 1.81 mL) dropwise over 10 min. Additional DCM (5 mL) were added to retain stirring. The yellow suspension was stirred at -40 °C for ~30 min while warming to -20 °C. The mixture was cooled to -40 °C and additional methylmagnesium bromide (3M in diethylether; 1.8 mL) was added. The suspension was stirred for ~3 hour while slowly warming to -20 °C. The mixture was cooled to ~-40 °C, and additional methylmagnesium bromide (3M in diethylether; 0.4mL) was added. The suspension was stirred for 30 min and allowed to warm to -10 °C. The mixture was quenched slowly over 10 min with saturated aqueous NH_4Cl solution (10 mL). The mixture was diluted with saturated aqueous NH_4Cl solution (30 mL) and water (15 mL). The separated aqueous phase was extract with DCM (2x 75 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered off and concentrated under reduced pressure. The residue was purified by column chouromatography [SiO_2, 40 g, heptane/ethyl acetate followed by 5% MeOH in EtOAc] providing 2-methyl-N-((S)-1-(4-(pyrimidin-5-yloxy)phenyl)ethyl)propane-2-sulfinamide (55 mg; purity ~87%) as an off-white solid. LCMS *m/z* 320.0 $(M + H)^+$, Rt 0.69 min.

Step 4: Preparation of (S)-1-(4-(pyrimidin-5-yloxy)phenyl)ethanamine

To 2-methyl-N-((S)-1-(4-(pyrimidin-5-yloxy)phenyl)ethyl)propane-2-sulfinamide (55 mg, 0.172 mmol) was added 4M HCl in dioxane (800 µL, 3.20 mmol) to give a white suspension. This resulting mixture was stirred at room temperature for ~35 min and concentrated under reduced pressure to provide crude (S)-1-(4-(pyrimidin-5-yloxy)phenyl)ethanamine (44 mg) as its HCl salt, which was used without further purification. LCMS *m/z* 217.1 $(M + H)^+$, Rt 0.37 min.

Intermediate 209: 5-chloro-6-(1,1-difluoroethyl)nicotinaldehyde



Step 1: Preparation of ethyl 5,6-dichloronicotinate

To a solution of 5,6-dichloronicotinic acid (20.01 g, 104 mmol) in EtOH (500 mL) at 20 °C was added chlorotrimethylsilane (132 mL, 1042 mmol). The reaction was stirred for 72 hours. The reaction mixture was then concentrated and diluted with EtOAc (500mL), and washed with saturated $NaHCO_3$ (2x100mL) and brine (100mL). The organic was then dried (Na_2SO_4) and concentrated under reduced pressure to give final crude product (21.25 g). LCMS *m/z* 220.1 $(M + H)^+$, Rt 0.94 min.

Step 2: Preparation of ethyl 6-acetyl-5-chloronicotinate

To a suspension of ethyl 5,6-dichloronicotinate (5.26 g, 23.90 mmol) and tetraethylammonium-chloride (11.88 g, 71.7 mmol) in MeCN (50 mL) was added tributyl(1-ethoxyvinyl)stannane (9.50 g, 26.3 mmol) and $PdCl_2(PPh_3)_2$ (0.671 g, 0.956 mmol). The reaction was sealed, heated at 80 °C for 5 hours. A dark color clear solution resulted. The reaction mixture was then cooled to 20 °C, concentrated and diluted with EtOAc (200mL), and washed with water (50mL) and brine (50mL). The organic was then dried (Na_2SO_4) and concentrated to give crude ethyl 5-chloro-6-(1-ethoxyvinyl)nicotinate. The residue was then dissolved in THF (100mL) and HCl (20mL, 3M in H_2O) was added. The reaction mixture was stirred at 20 °C for 5 hours, and saturated $NaHCO_3$ solution was added until pH=8. The mixture was then diluted with EtOAc (200mL) and water (50mL). The phases were separated and the aqueous layer was extracted with EtOAc (2x50mL). The combined organics was washed with brine

(20mL), dried (Na_2SO_4) and concentrated to afford the desired product (3.56 g). LCMS *m/z* 228.5 $(M + H)^+$, Rt 0.83 min.

Step 3: Preparation of ethyl 5-chloro-6-(1,1-difluoroethyl)nicotinate

To a solution of ethyl 6-acetyl-5-chloronicotinate (3.01 g, 13.22 mmol) in CHCl3 (7 mL) was added DAST (5.20 mL, 39.7 mmol) and ethanol (0.061 g, 1.32 mmol). The reaction was sealed, heated at 60 °C for 24 hours. A dark color clear solution resulted. The reaction mixture was then cooled to 20 °C, and added cautiously with cold concentrated $NaHCO_3$ aqueous solution (50mL). The aqueous layer was extracted with DCM (2x100mL). The combined organic was then dried (Na_2SO_4) and concentrated. The residue was purified via silica gel flash chromatography (0-20percent EtOAc-Hexanes) to afford the desired product as yellow oil (2.88 g). LCMS *m/z* 250.1 $(M + H)^+$, Rt 0.99 min.

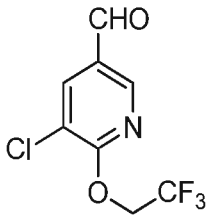
Step 4: Preparation of (5-chloro-6-(1,1-difluoroethyl)pyridin-3-yl)methanol

To a solution of ethyl 5-chloro-6-(1,1-difluoroethyl)nicotinate (2.68 g, 10.74 mmol) in Et_2O (40mL) was added $LiBH_4$ (0.351 g, 16.10 mmol), followed by dropwise addition of methanol (0.653 mL, 16.10 mmol). The reaction was refluxed at 40 °C for one hour. The reaction mixture was then cooled to 0 °C, and quenched with HCl (1M) until pH=2 for aqueous layer. The phases were separated and the aqueous layer was extracted with DCM (3x50mL). The organic was then dried (Na_2SO_4) and concentrated under reduced pressure to give final crude product (2.12 g). LCMS *m/z* 208.0 $(M + H)^+$, Rt 0.63 min.

Step 5: Preparation of 5-chloro-6-(1,1-difluoroethyl)nicotinaldehyde

To a solution of (5-chloro-6-(1,1-difluoroethyl)pyridin-3-yl)methanol (2.12 g, 10.21 mmol) in DCM (100 ml) was added PCC (3.30 g, 15.32 mmol). The reaction was stirred at 20 °C for 3 hours. A dark color suspension resulted. LCMS showed clean conversion to the product. The reaction mixture was then filtered through a pad of celite, and washed with DCM (200mL). The filtrate was then concentrated to give crude product (1.78 g). LCMS *m/z* 224.0 $(M + H2O + H)^+$, Rt 0.72 min.

Intermediate 210: 5-chloro-6-(2,2,2-trifluoroethoxy)nicotinaldehyde



Step 1: Preparation of ethyl 5-chloro-6-(2,2,2-trifluoroethoxy)nicotinate

To a solution of ethyl 5,6-dichloronicotinate (6.28 g, 28.5 mmol) and 2,2,2-trifluoroethanol (2.71 ml, 37.1 mmol) in THF (90 ml) at -73oC was added NaHMDS (37.1 ml, 37.1 mmol). The reaction was stirred at -73 °C for 30 minutes, then at 0 °C for 5 hours. The reaction was quenched with 30 mL saturated NH_4Cl solution. The reaction mixture was then poured into 50 mL brine and phases were separated. The aqueous layer was extracted with DCM (2x100mL). The combined organics were dried (Na_2SO_4) and concentrated. Silica gel chromatography with 100% heptane to 30% EtOAc in heptane provided final product (7.51 g). LCMS *m/z* 284.1 $(M + H)^+$, Rt 1.07 min.

Step 2: Preparation of (5-chloro-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)methanol

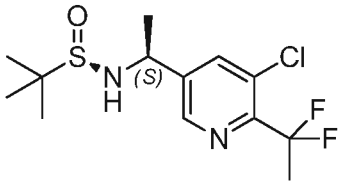
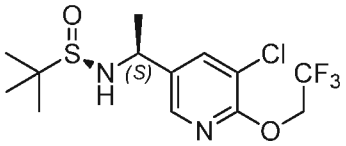
To a solution of ethyl 5-chloro-6-(2,2,2-trifluoroethoxy)nicotinate (7.51 g, 26.5 mmol) in Et2O (200mL) was added $LiBH_4$ (0.865 g, 39.7 mmol), followed by drop wise addition of methanol (1.611 ml, 39.7 mmol). The reaction was refluxed at 40 °C for one hour. The reaction mixture was then cooled to 0 °C, and quenched with HCl (1M) until pH=2 for aqueous layer. The phases were separated and the aqueous layer was extracted with DCM (3x200mL). The organic was then dried (Na_2SO_4) and concentrated under reduced pressure to give final crude product (6.31 g). LCMS *m/z* 242.1 $(M + H)^+$, Rt 0.77 min.

Step 3: Preparation of 5-chloro-6-(2,2,2-trifluoroethoxy)nicotinaldehyde

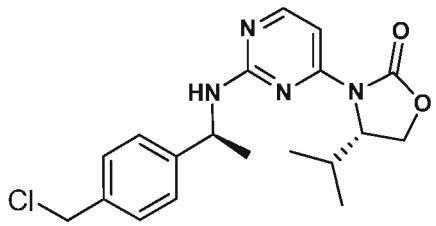
To a solution of (5-chloro-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)methanol (4.00 g, 16.56 mmol) in EtOAc (15 mL) was added manganese(IV) oxide (16.93 g, 166 mmol). The reaction was heated with microwave at 120 °C for 30 minutes. The mixture was then filtered through a pad of celite, and rinsed with EtOAc. The filtrated was concentrated to give crude product (3.38 g).

The intermediates in Table 4w were prepared with procedures similar to those used to prepare Intermediate 210 and 192.

Table 4w.

Intermediate: Name	Structure	LCMS
211: (R)-N-((S)-1-(5-chloro-6-(1,1-difluoroethyl)pyridin-3-yl)ethyl)-2-methylpropane-2-sulfinamide		MS *m/z* 325.2 $(M + H)^+$, Rt 0.85 min.
212: (R)-N-((S)-1-(5-chloro-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)ethyl)-2-methylpropane-2-sulfinamide		MS *m/z* 359.1 $(M + H)^+$, Rt 0.95 min.

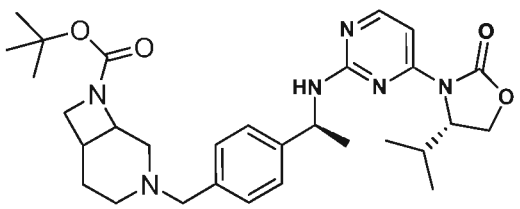
Intermediate 213 : (S)-3-(2-((S)-1-(4-(chloromethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one



To a solution of (S)-3-(2-((S)-1-(4-(hydroxymethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (71 mg, 0.2 mmol) in DCM (2 mL) was added methanesulfonyl chloride (27 mg, 0.24 mmol) and DIPEA (0.070 mL, 0.4 mmol). The solution was stirred for 16 h at room temperature then washed with water and brine. After separation, the organic phase was dried over Na_2SO_4, filtered and concentrated. The crude product was used to next step without further purification.

MS m/z 373.4 (M - H).

Intermediate 214: tert-butyl 3-(4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzyl)-3,8-diazabicyclo[4.2.0]octane-8-carboxylate

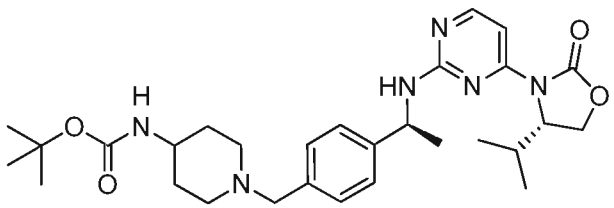


Title compound was prepared as a white solid (64 mg, 58.1% yield), with procedures similar to those used to prepare Intermediate 128, but utilizing 4-((S)-1-(4-((S)-4-

isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzaldehyde and tert-butyl 3,8-diazabicyclo[4.2.0]octane-8-carboxylate.

^{1}H NMR (400 MHz, CDCl3) δ 8.17 (dd, J = 5.9, 0.9 Hz, 1H), 7.42 (d, J = 5.7 Hz, 1H), 7.28 - 7.23 (m, 4H), 5.39 (br s, 1H), 5.02 (br s, 1H), 4.62-4.59 (m, 1H), 4.28 (t, J = 8.7 Hz, 1H), 4.21 (dd, J = 9.0, 3.2 Hz, 2H), 3.89 (td, J = 7.7, 1.9 Hz, 1H), 3.54 - 3.50 (m, 2H), 3.03 (d, J = 12.2 Hz, 1H), 2.65 - 2.60 (m, 1H), 2.54 – 2.40 (m, 2H), 2.10 (br s, 1H), 1.99 - 1.88 (m, 1H), 1.79 - 1.72 (m, 1H), 1.65 (br s, 1H), 1.52 (dd, J = 6.8, 1.9 Hz, 3H), 1.38 (t, J = 7.7 Hz, 9H), 0.71 (br s, 3H), 0.66 (br s, 3H). MS m/z 569.1 (M + H).

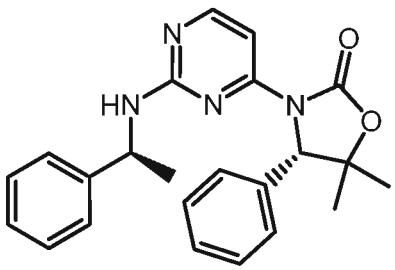
Intermediate 215: tert-butyl 1-(4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzyl)piperidin-4-ylcarbamate



Title compound was prepared as a white solid (32 mg, 59% yield), with procedures similar to those used to prepare Intermediate 128, but utilizing 4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzaldehyde and tert-butyl piperidin-4-ylcarbamate. MS m/z 539.4 (M + H).

Examples

Example 1: (*S*)-5,5-dimethyl-4-phenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one

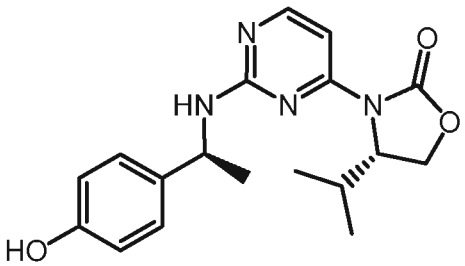


A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one (33.9 mg, 0.112 mmol) and (*S*)-(-)-1-phenylethanamine (0.15 mL, 1.2 mmol, 10 equiv) in DMSO (1 mL) was heated at 110 °C for 140 min. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was

extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 10 to 50%) provided (*S*)-5,5-dimethyl-4-phenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl) oxazolidin-2-one (37.0 mg, white solid) in 85% yield. ^{1}H NMR (400 MHz, CD_3OD) δ 8.06 (d, J = 5.8 Hz, 1 H), 7.43 (d, J = 5.8 Hz, 1 H), 7.31 – 7.24 (m, 3 H), 7.19 – 7.11 (m, 5 H), 7.01 (br s 2 H), 5.48 (s, 1 H), 4.86 – 4.80 (m, 1 H), 1.65 (s, 3 H), 1.43 (d, J = 7.0 Hz, 3 H), 0.98 (s, 3 H); HRMS(B) *m/z* 389.1987 $(M + H)^+$.

Alternative Procedure

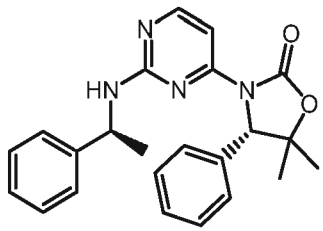
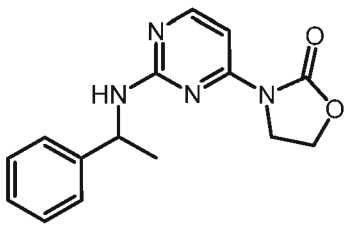
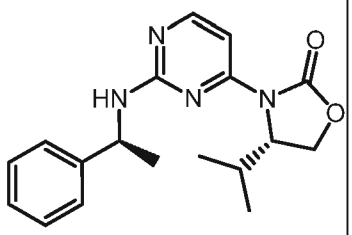
Example 113: (*S*)-3-(2-((*S*)-1-(4-hydroxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one



A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (42 mg, 0.17 mmol), (*S*)-4-(1-aminoethyl)phenol hydrochloride (107 mg, 0.616 mmol, 3.5 equiv) and *i*Pr_2Net (0.121 mL, 0.695 mmol, 4.0 equiv) in DMSO (1 mL) was heated at 110 °C for 3 h and at 130 °C for additional 2 h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 10 to 80%) provided (*S*)-3-(2-((*S*)-1-(4-hydroxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (3 mg) in 5 % yield. ^{1}H NMR (400 MHz, CD_3OD) δ 8.11 (d, J = 5.8 Hz, 1 H), 7.33 (d, J = 5.8 Hz, 1 H), 7.12 (d, J 8.1 Hz, 2 H), 6.72 – 6.68 (m, 2 H), 4.95 (q, J = 6.9 Hz, 1 H), 4.69 – 4.65 (m, 1 H), 4.35 – 4.28 (m, 2 H), 1.47 (d, J = 7.1 Hz, 3 H), 0.75 (br s, 3 H), 0.62 (br s, 3 H); HRMS(B) *m/z* 343.1776 $(M + H)^+$.

The compounds in Table 5 were prepared using methods similar to those described for the preparation of Examples 1 and 113.

Table 5.

1	2	3
		
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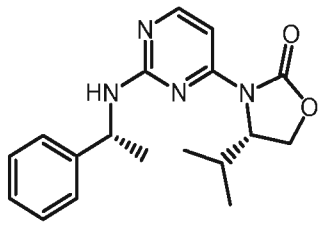	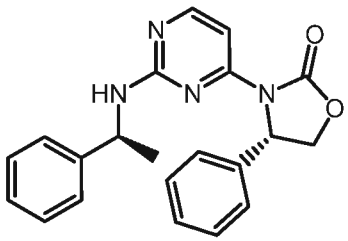	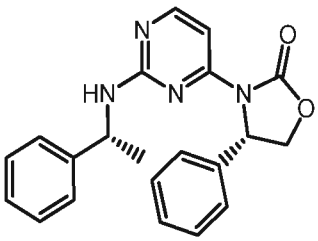
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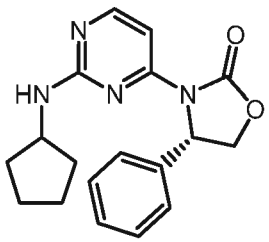	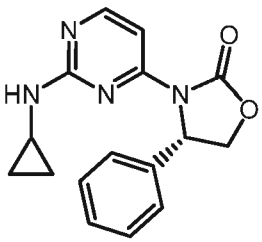	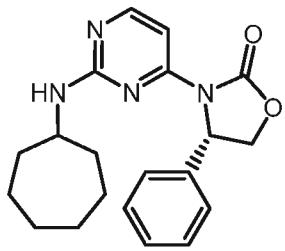
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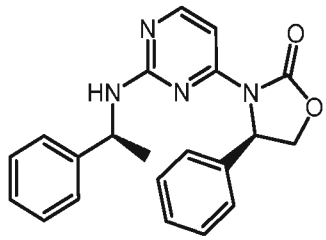	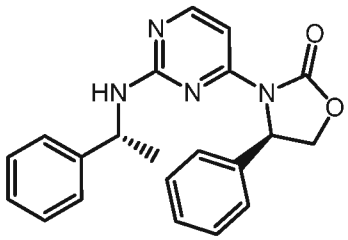	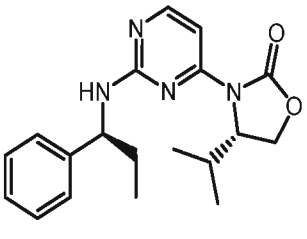
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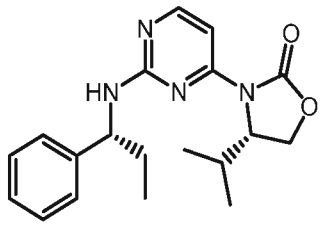	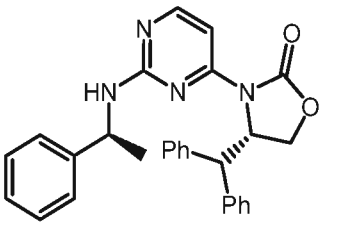	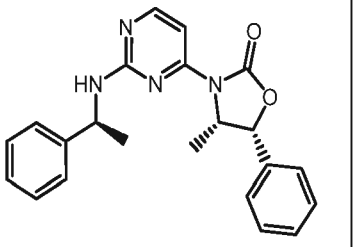
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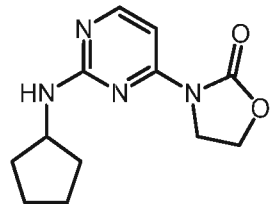	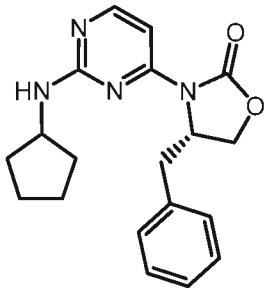	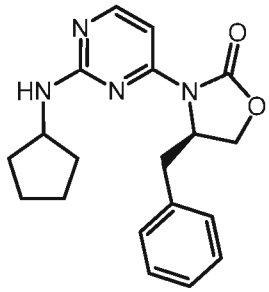
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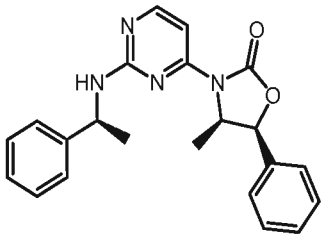	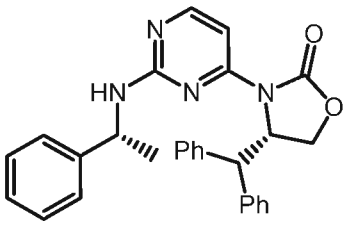	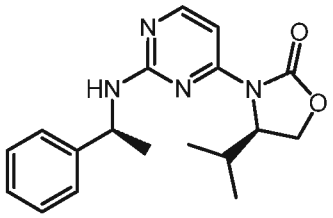
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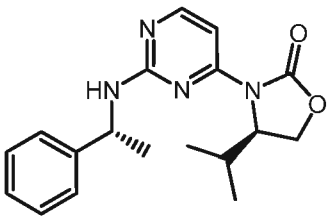	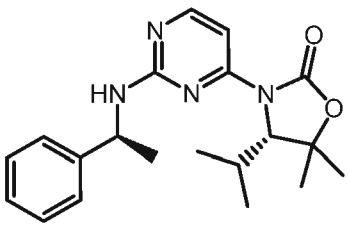	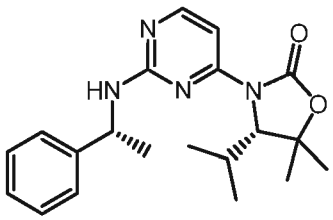
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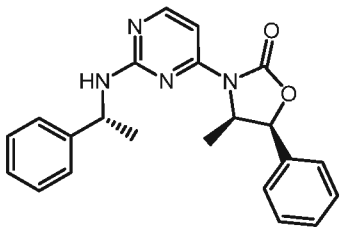	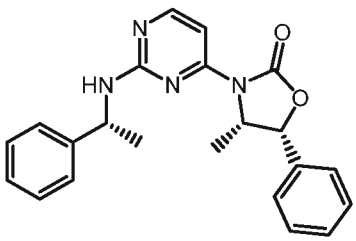	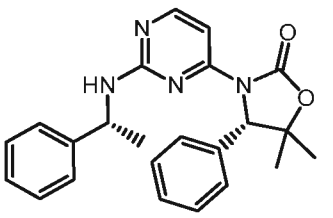
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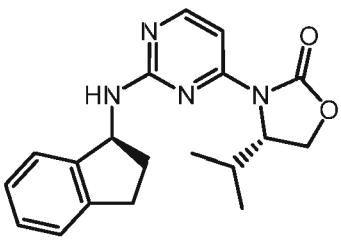	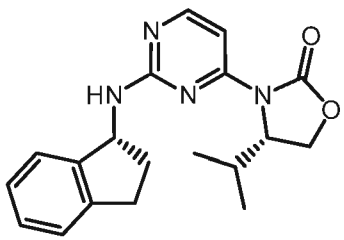	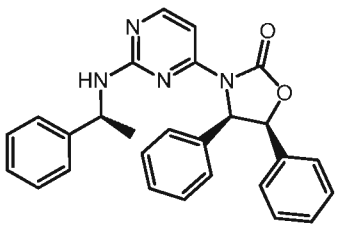
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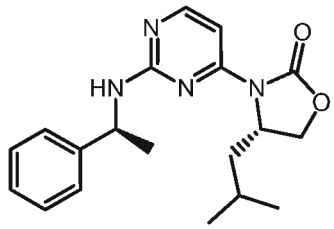	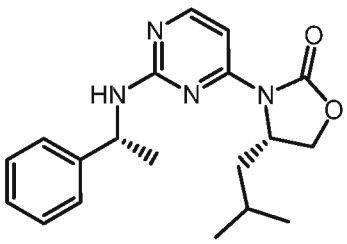	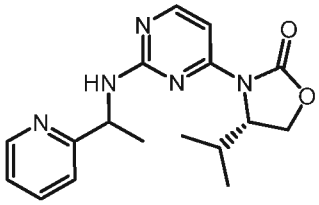
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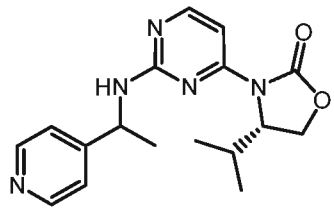	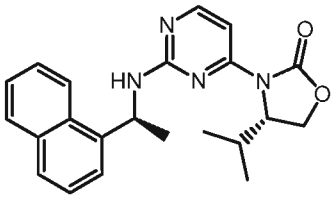	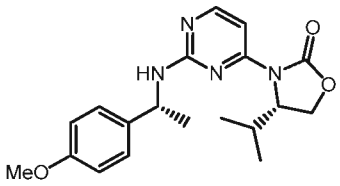
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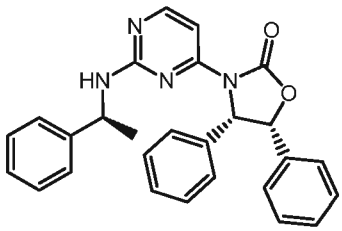	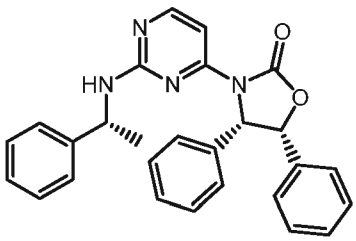	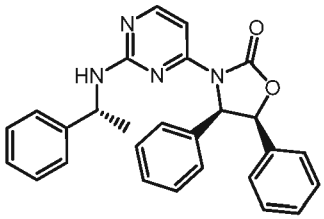
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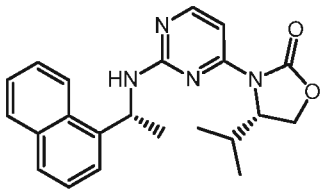	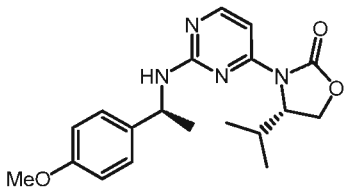	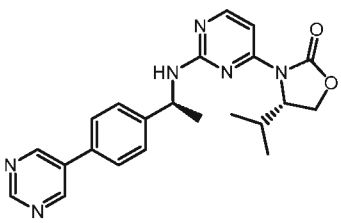
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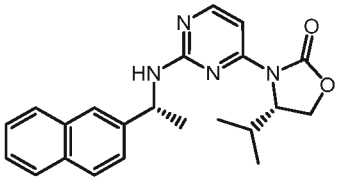	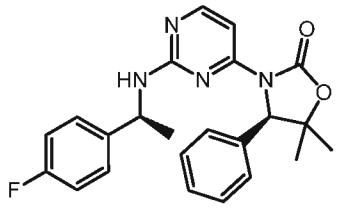	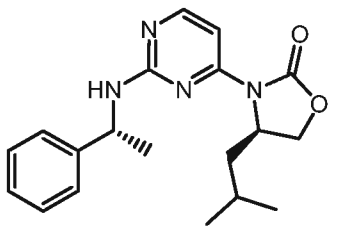
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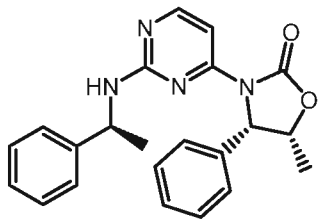	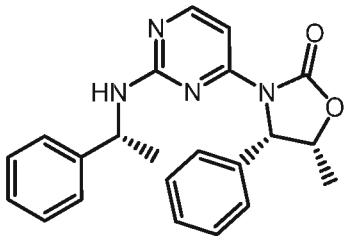	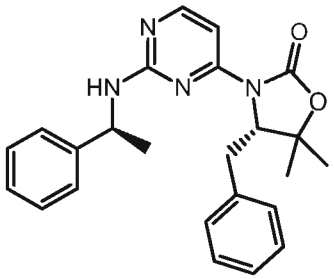
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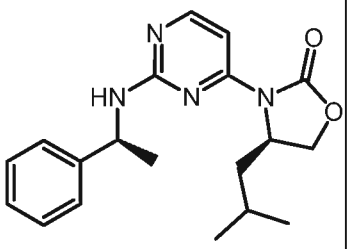	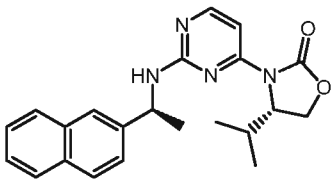	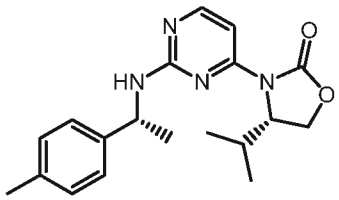
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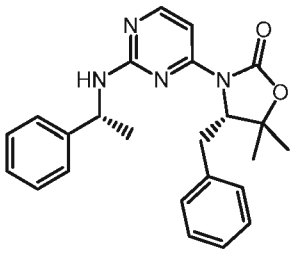	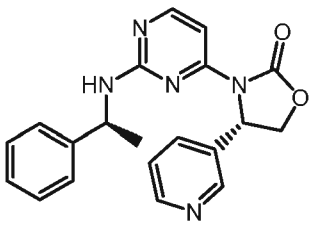	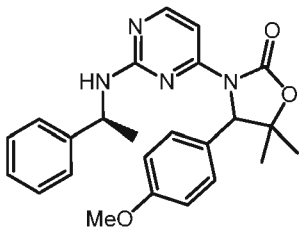
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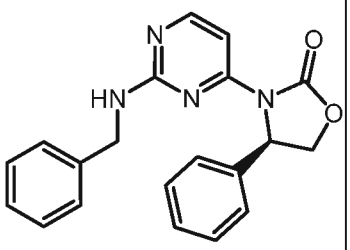	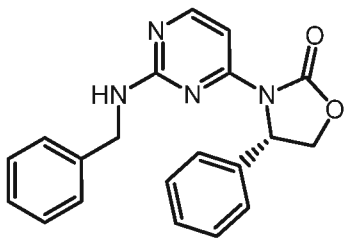	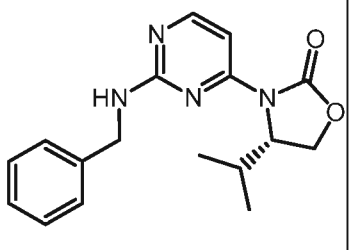
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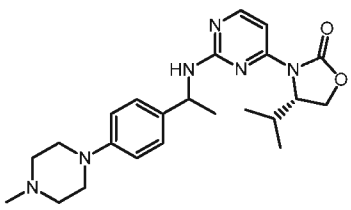	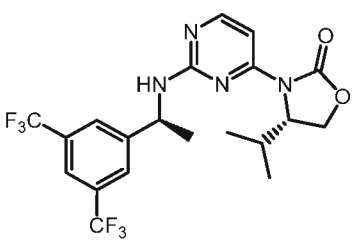	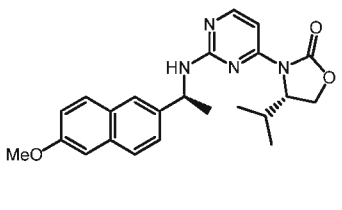
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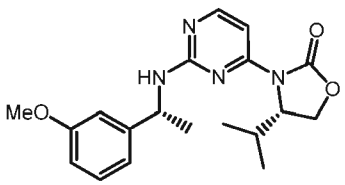	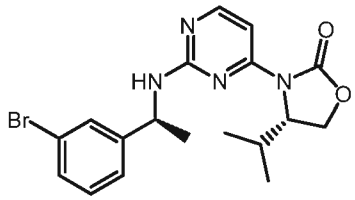	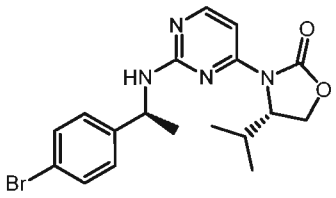
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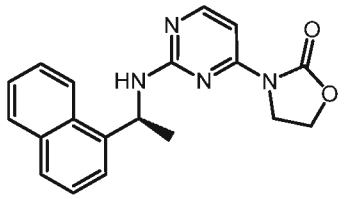	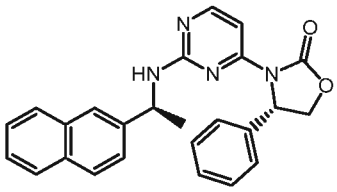	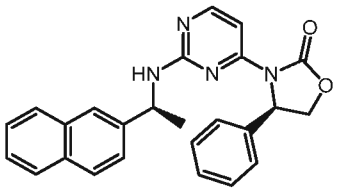
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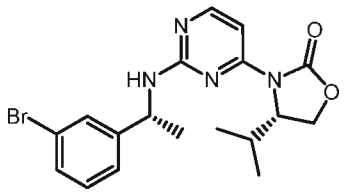	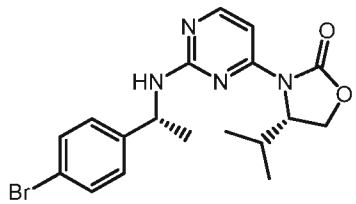	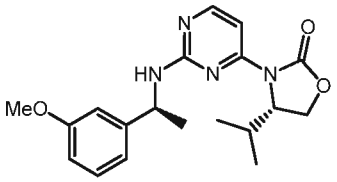
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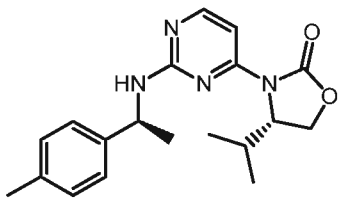	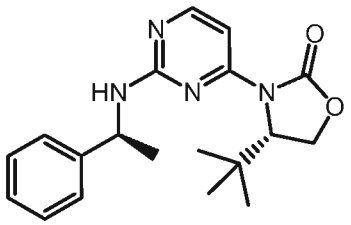	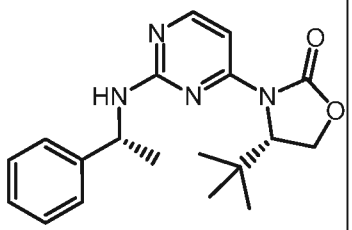
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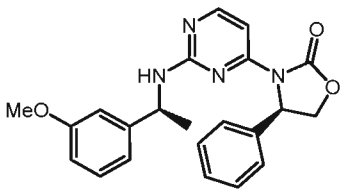	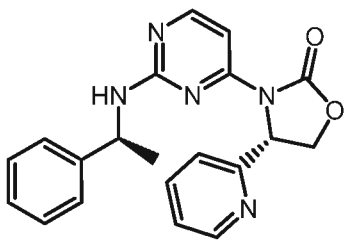	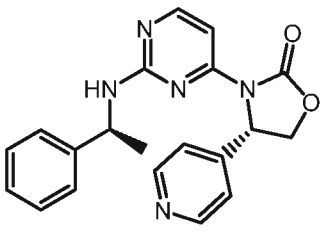
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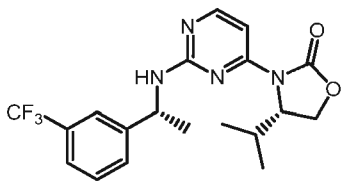	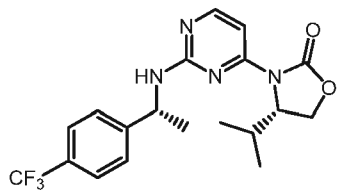	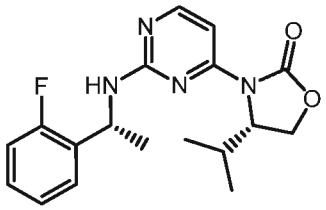
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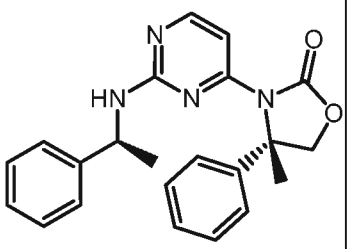	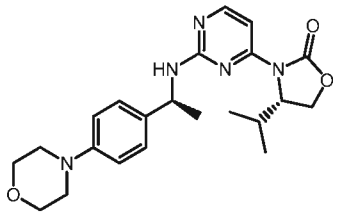	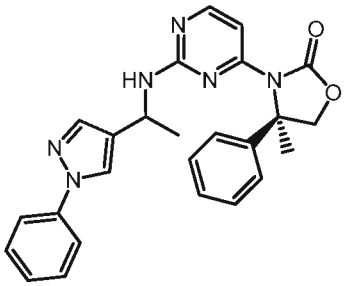
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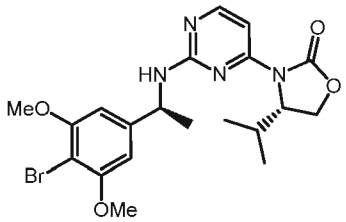	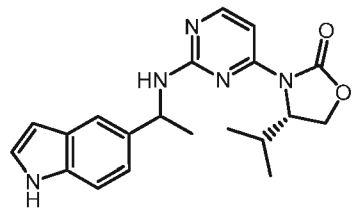	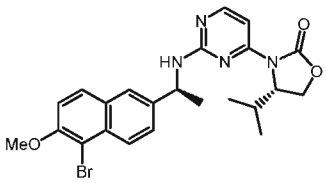
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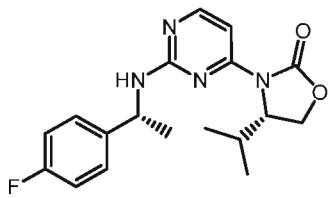	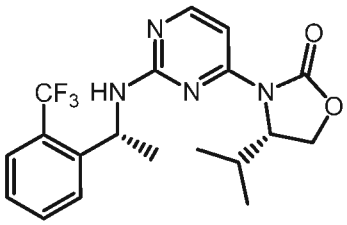	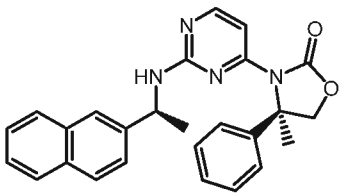
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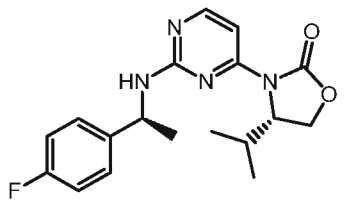	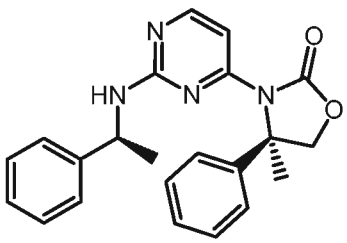	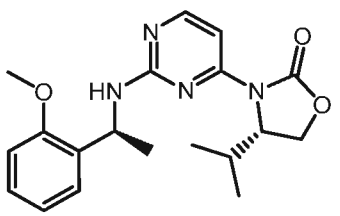
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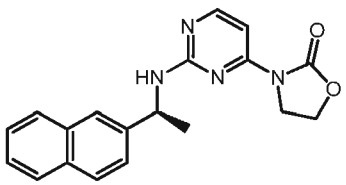	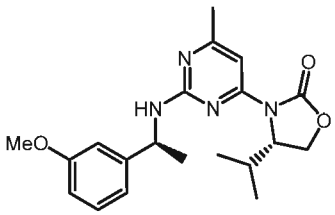	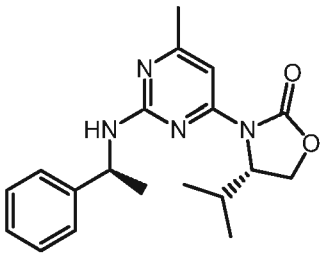
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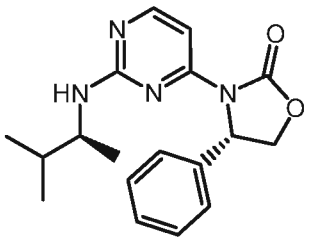	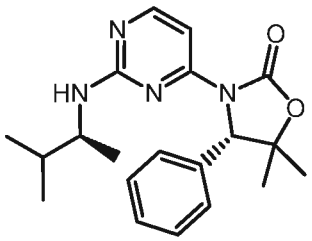	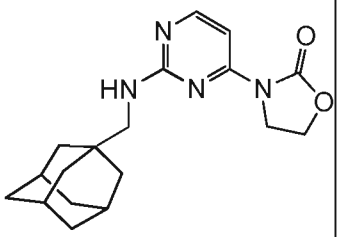
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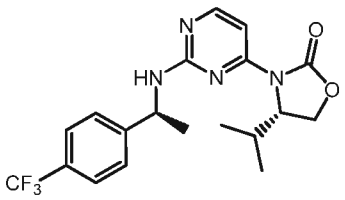	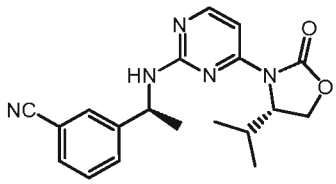	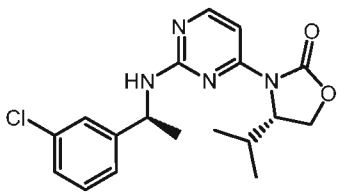
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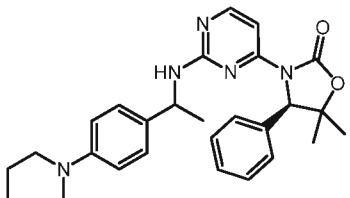	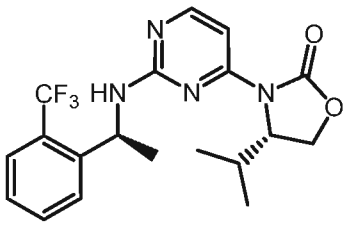	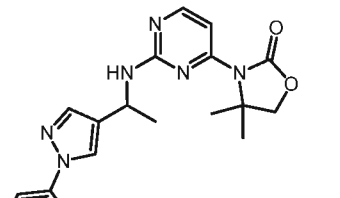
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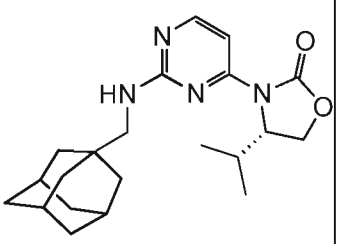	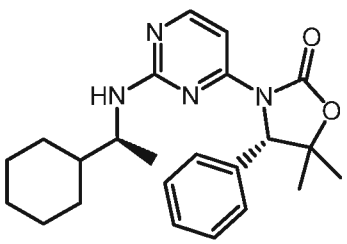	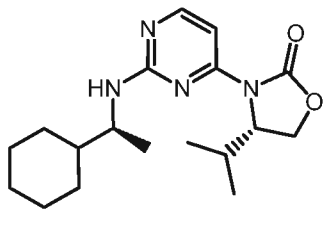
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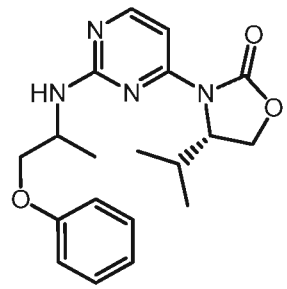	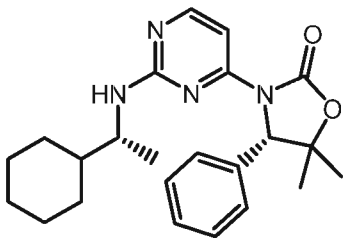	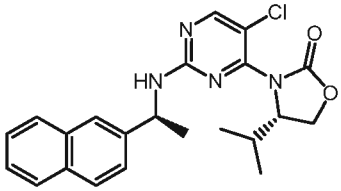
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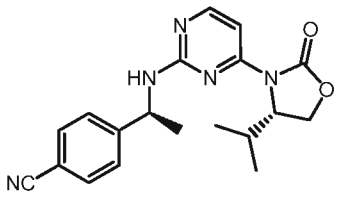	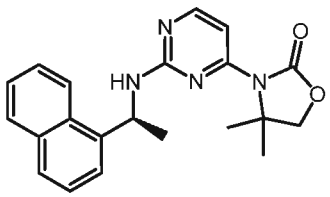	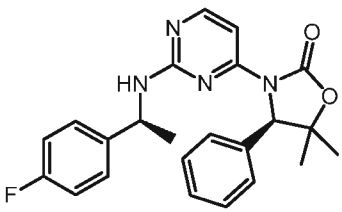
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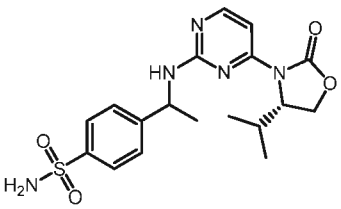	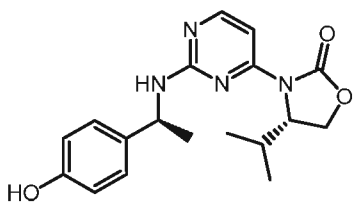	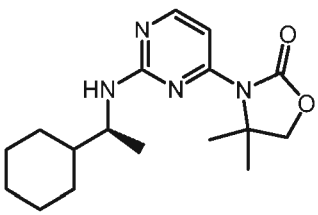
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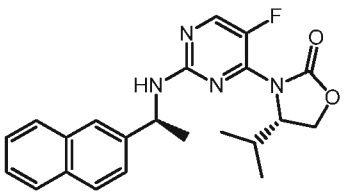	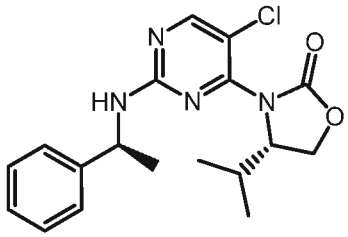	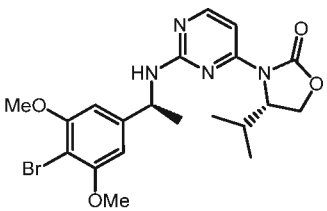
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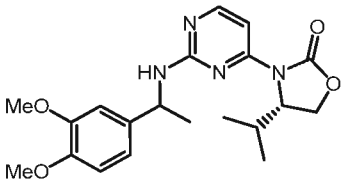	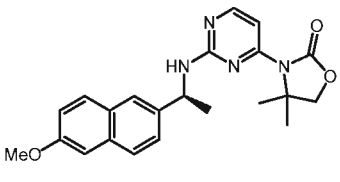	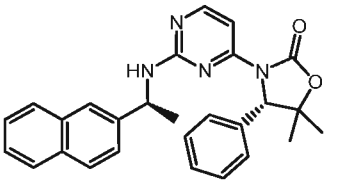
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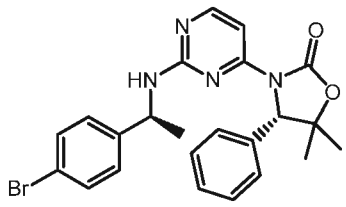	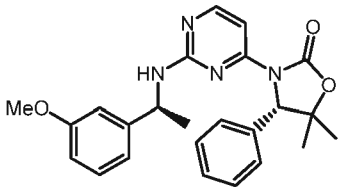	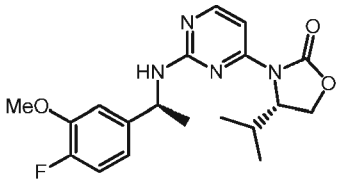
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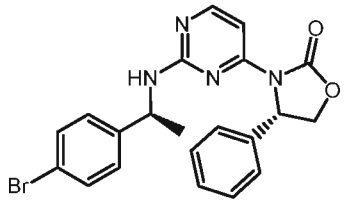	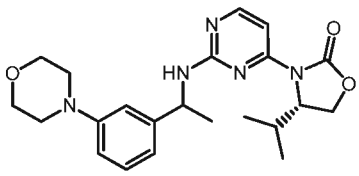	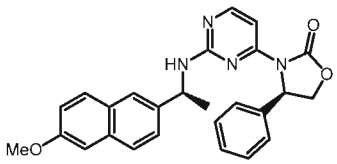
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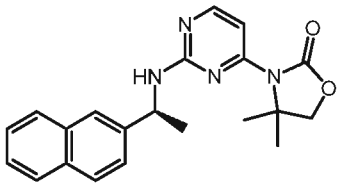	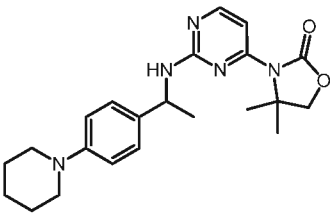	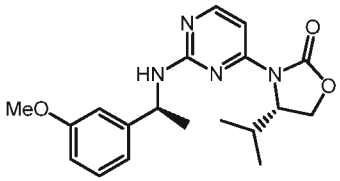
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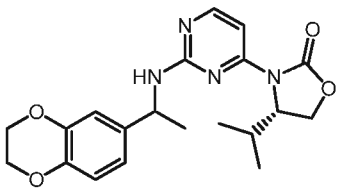	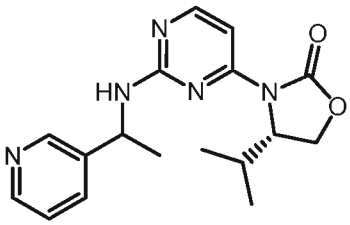	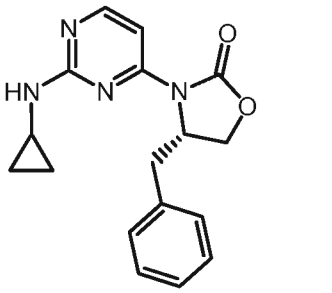
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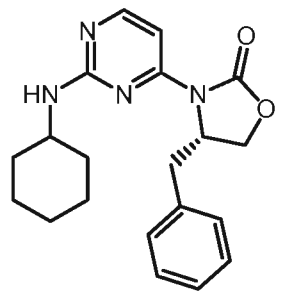	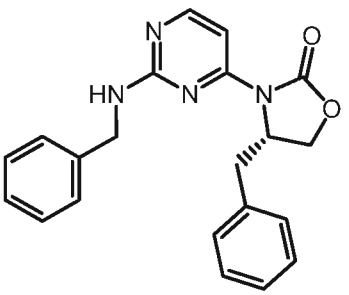	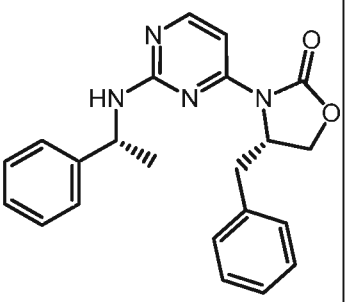
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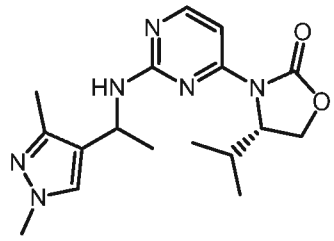	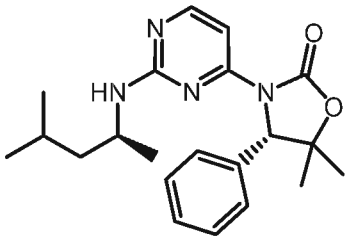	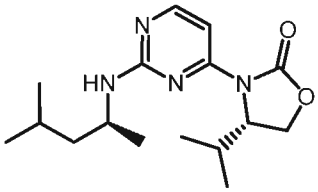
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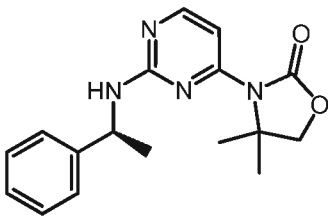	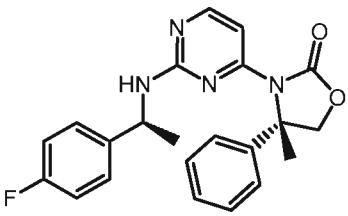	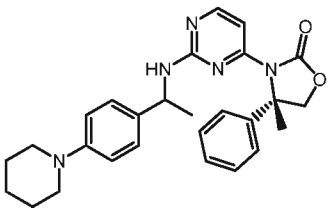
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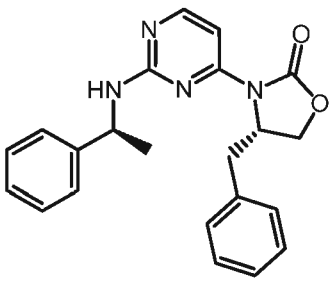	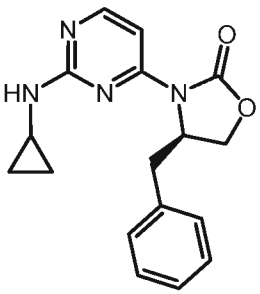	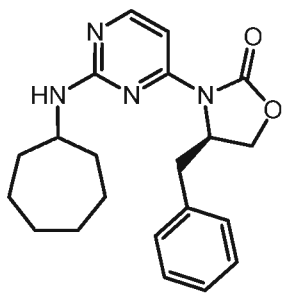
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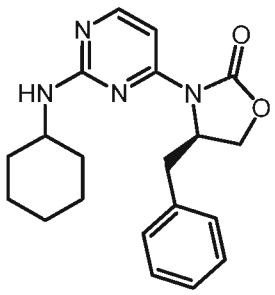	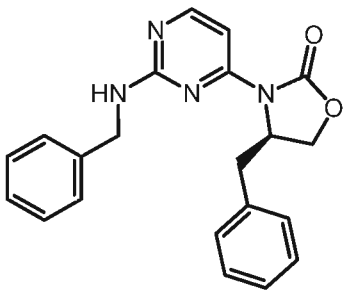	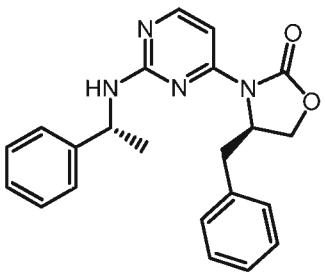
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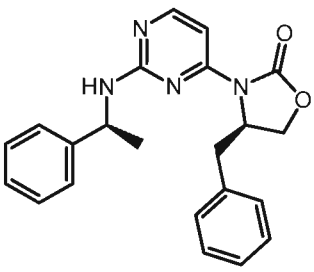	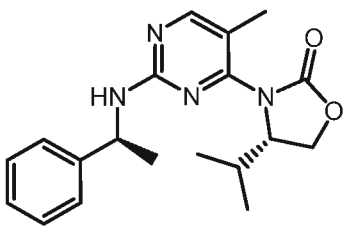	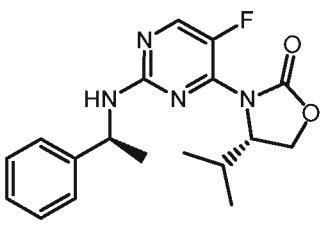

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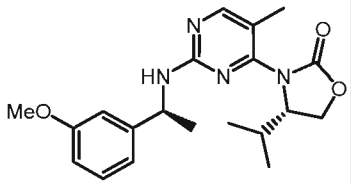	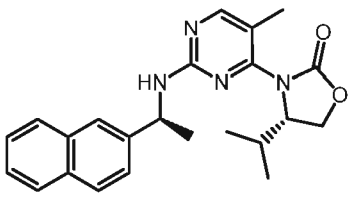	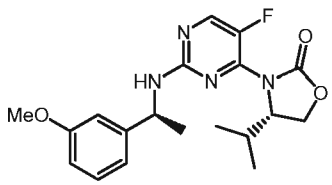
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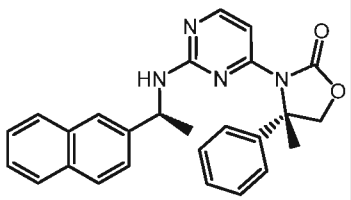	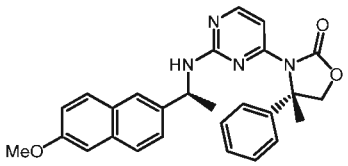	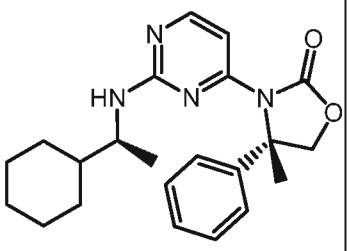
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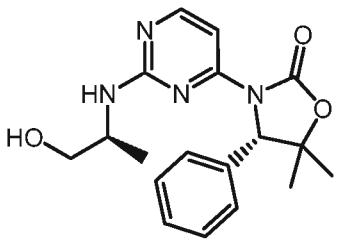	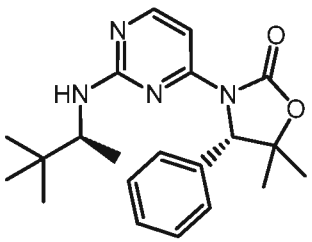	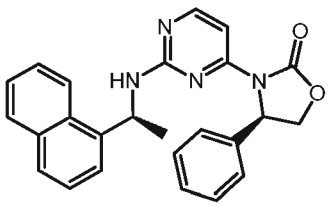
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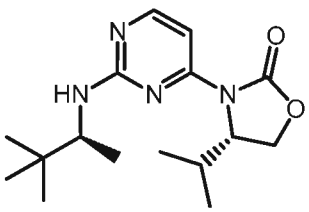	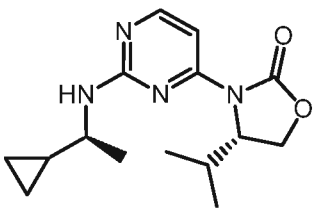	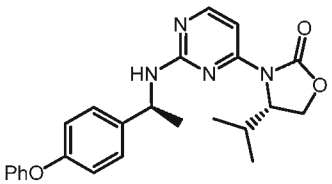
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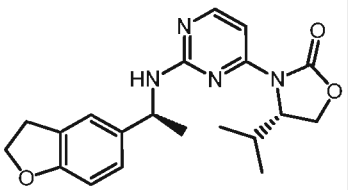	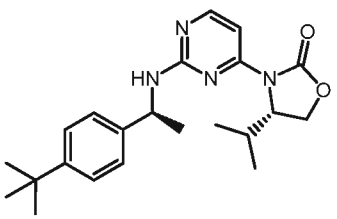	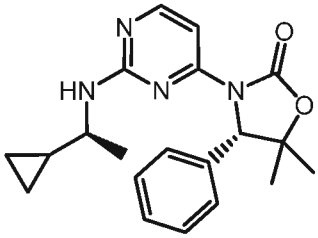
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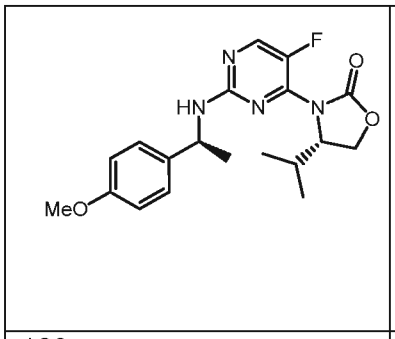

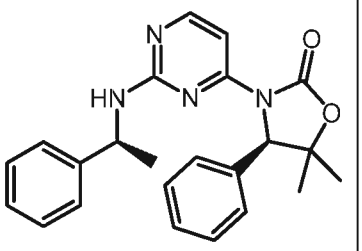

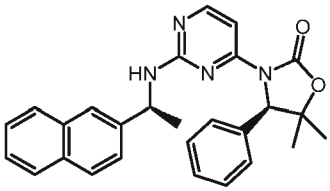

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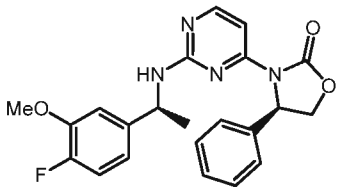


Table 6. Chemical name, NMR chemical shifts and LCMS signal for each compound listed in Table 5.

Example: Name	^{1}H NMR **(400 MHz,** CD_3OD**) δ ppm (other solvents described)**	**LCMS**
1: (*S*)-5,5-dimethyl-4-phenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.06 (d, J = 5.8 Hz, 1 H), 7.43 (d, J = 5.8 Hz, 1 H), 7.31 – 7.24 (m, 3 H), 7.19 – 7.11 (m, 5 H), 7.01 (br s 2 H), 5.48 (s, 1 H), 4.86 – 4.80 (m, 1 H), 1.65 (s, 3 H), 1.43 (d, J = 7.0 Hz, 3 H), 0.98 (s, 3 H)	HRMS(B) *m/z* 389.1987 $(M + H)^+$
2: 3-(2-(1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.06 (d, J = 6.1 Hz, 1 H), 7.37 – 7.26 (m, 5 H), 7.22 – 7.15 (m, 1 H), 5.04 (q, J = 6.9 Hz, 1 H), 4.43 (sxt, J = 8.2 Hz, 2 H), 4.17 (td, J = 9.8, 7.1 Hz, 1 H), 3.92 (br s, 1 H), 1.50 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 284.1275 M^+
3: (*S*)-4-isopropyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.12 (d, J = 5.6 Hz, 1 H), 7.34 – 7.26 (m, 5 H), 7.22 – 7.13 (m, 1 H), 5.04 (q, J = 7.1 Hz, 1 H), 4.64 (br s, 1 H), 4.34 – 4.26 (m, 2 H), 1.85 (br s, 1 H), 1.50 (d, J = 7.1 Hz, 3 H), 0.70 (br s, 3 H), 0.57 (br s, 3 H)	HRMS(B) *m/z* 326.1745 M^+
4: (*S*)-4-isopropyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.10 (d, J = 5.8 Hz, 1 H), 7.35 – 7.27 (m, 5 H), 7.23 – 7.15 (m, 1 H), 4.96 (q, J = 6.9 Hz, 1 H), 4.44 (br s, 1 H), 4.34 – 4.23 (m, 2 H), 2.72 – 2.58 (m, 1 H), 1.51 (d, J = 6.6 Hz, 3 H), 0.99 (d, J = 7.1 Hz, 3 H), 0.85 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 326.1746 M^+
5: (*S*)-4-phenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.07 (d, J = 5.6 Hz, 1 H), 7.38 (d, J = 5.6 Hz, 1 H), 7.28 – 7.05 (m, 10 H), 5.84 (dd, J = 8.6, 3.5 Hz, 2 H), 4.88 (q, J = 6.8 Hz, 1 H), 4.83 – 4.79 (m, 1 H), 4.24 (dd, J = 8.6, 3.5 Hz, 1 H), 1.44 (d, J = 6.8 Hz, 3 H)	HRMS(B) *m/z* 361.1666 $(M + H)^+$
6: (*S*)-4-phenyl-3-(2-((*R*)-1-	8.08 (d, J = 5.8 Hz, 1 H), 7.43 – 7.18 (m, 11 H), 5.55 (br s, 1H), 4.74 (t, J = 8.6 Hz, 1	HRMS(B) *m/z*

phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	H), 4.63 (br s, 1 H), 4.18 (dd, J = 8.3, 3.8 Hz, 1 H), 1.19 (d, J = 6.7 Hz, 3 H)	360.1591 M^+
7: (*S*)-3-(2-(cyclopentylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.06 (d, J = 6.1 Hz, 1 H), 7.39 – 7.28 (m, 6 H), 5.80 (dd, J = 8.8, 3.8 Hz, 1 H), 4.83 – 4.80 (m, 1 H), 4.20 (dd, J = 8.6, 4.0 Hz, 1 H), 3.79 (br m, 1 H), 1.90 – 1.99 (m, 1 H), 1.72 – 1.53 (m, 4 H), 1.49 – 1.35 (m, 3 H)	HRMS(B) *m/z* 325.1671 $(M + H)^+$
8: (*S*)-3-(2-(cyclopropylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.10 (d, J = 5.6 Hz, 1 H), 7.44 (d, J = 5.6 Hz, 1 H), 7.36 – 7.26 (m, 5 H), 5.86 (dd, J = 8.6, 3.5 Hz, 1 H), 4.83 – 4.80 (m, 1 H), 4.26 (dd, J = 8.6, 3.5 Hz, 1 H), 2.40 (br s, 1 H), 0.64 – 0.71 (m, 1 H), 0.54 (br s, 1 H), 0.44 – 0.37 (m, 1 H), 0.25 (br s, 1 H)	HRMS(B) *m/z* 297.1356 $(M + H)^+$
9: (*S*)-3-(2-(cycloheptylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.06 (d, J = 6.1 Hz, 1 H), 7.38 – 7.27 (m, 6 H), 5.82 (dd, J = 8.6, 3.5 Hz, 1 H), 4.83 – 4.80 (m, 1 H), 4.21 (dd, J = 8.6, 3.5 Hz, 1 H), 3.57 (br s, 1 H), 1.90 (br s, 1 H), 1.69 – 1.42 (m, 8 H), 1.32 – 1.18 (m, 3 H)	HRMS(B) *m/z* 353.1961 $(M + H)^+$
10: (*R*)-4-phenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.08 (d, J = 5.8 Hz, 1 H), 7.43 – 7.18 (m, 11 H), 5.54 (br s, 1 H), 4.74 (t, J = 8.6 Hz, 1 H), 4.62 (br s, 1 H), 4.18 (dd, J = 8.8, 3.8 Hz, 1 H), 1.19 (d, J = 6.6 Hz, 3 H)	HRMS(B) *m/z* 361.1712 $(M + H)^+$
11: (*R*)-4-phenyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.07 (d, J = 5.8 Hz, 1 H), 7.38 (d, J = 5.8 Hz, 1 H), 7.28 – 7.05 (m, 10 H), 5.84 (dd, J = 8.3, 3.3 Hz, 1 H), 4.88 (q, J = 6.9 Hz, 1 H), 4.82 – 4.78 (m, 1 H), 4.24 (dd, J = 8.6, 3.5 Hz, 1 H), 1.44 (d, J = 6.9 Hz, 3 H)	HRMS(B) *m/z* 361.1661 $(M + H)^+$
12: (*S*)-4-isopropyl-3-(2-((*S*)-1-phenylpropylamino)pyrimidin-4-yl)oxazolidin-2-one	8.11 (d, J = 5.6 Hz, 1 H), 7.33 – 7.26 (m, 5 H), 7.22 – 7.15 (m, 1 H), 4.83 – 4.79 (m, 1 H), 4.68 (br s, 1 H), 4.36 – 4.28 (m, 2 H), 1.84 (quin, J = 7.3 Hz, 2 H), 0.99 (t, J = 7.3 Hz, 3 H), 0.76 (br s, 3 H), 0.59 (br s, 3 H)	HRMS(B) *m/z* 341.1974 $(M + H)^+$
13: (*S*)-4-isopropyl-3-(2-((*R*)-1-phenylpropylamino)pyrimidin-4-yl)oxazolidin-2-one	8.09 (d, J = 5.8 Hz, 1 H), 7.34 – 7.27 (m, 5 H), 7.24 – 7.16 (m, 1 H), 4.74 (t, J = 6.8 Hz, 1 H), 4.52 (br s, 1 H), 4.36 – 4.26 (m, 2 H), 2.66 (td, J = 6.9, 3.8 Hz, 1 H), 1.95 – 1.75 (m, 2 H), 1.02 (d, J = 7.1 Hz, 3 H), 0.96 (t, J = 7.3 Hz, 3 H), 0.86 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 341.1976 $(M + H)^+$
14: provided (*S*)-4-benzhydryl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.09 (d, J = 5.8 Hz, 1 H), 7.32 – 7.23 (m, 3 H), 7.20 – 7.16 (br m, 6 H), 7.00 (br s, 5 H), 6.72 (br s, 2 H), 5.76 – 5.68 (m, 1 H), 5.04 (q, J = 7.1 Hz, 1 H), 4.59 (t, J = 8.8 Hz, 1 H), 4.50 (br s, 1H), 4.47 (dd, J = 9.1, 2.5 1H), 1.44 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 451.2126 $(M + H)^+$
15: (*4S,5R*)-4-methyl-5-phenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.12 (d, J = 5.8 Hz, 1 H), 7.45 – 7.30 (m, 8 H), 7.20 (t, J = 7.6 Hz, 2 H), 7.10 – 7.07 (m, 1 H), 5.80 (d, J = 7.1 Hz, 1 H), 5.10 – 4.92 (m, 2 H), 1.49 (d, J = 7.0 Hz, 3 H), 0.37 (br s, 3 H)	HRMS(B) *m/z* 375.1823 $(M + H)^+$
16: 3-(2-(cyclopentylamino)pyrimidin-4-yl)oxazolidin-2-one	8.07 (d, J = 5.7 Hz, 1 H), 7.32 (d, J = 5.8 Hz, 1 H),4.48 (t, J = 8.1 Hz, 2 H), 4.22 – 4.16 (m, 3 H), 2.02 (dq, J = 12, 6.1 Hz, 2 H), 1.70 – 1.80 (m, 2 H), 1.67 – 1.47 (m, 4 H)	HRMS(B) *m/z* 248.1275 M^+

17: (*S*)-4-benzyl-3-(2-(cyclopentylamino)pyrimidin-4-yl)oxazolidin-2-one	8.13 (d, J = 5.8 Hz, 1 H), 7.35 – 7.21 (m, 6 H), 5.14 – 5.04 (m, 1 H), 4.36 (t, J = 8.4 Hz, 1 H), 4.33 – 4.24 (m, 2 H), 3.37 – 3.33 (m, 1 H), 3.06 (dd, J = 13, 8.3 Hz, 1 H), 2.11 – 1.98 (m, 2 H), 1.86 – 1.71 (m, 2 H), 1.70 – 1.53 (m, 4 H)	HRMS(B) *m/z* 338.1749 M^+
18: (*R*)-4-benzyl-3-(2-(cyclopentylamino)pyrimidin-4-yl)oxazolidin-2-one	8.13 (d, J = 5.6 Hz, 1 H), 7.35 – 7.21 (m, 6 H), 5.14 – 5.05 (m, 1 H), 4.36 (t, J = 8.5 Hz, 1 H), 4.32 – 4.26 (m, 2 H), 3.37 – 3.33 (m, 1 H), 3.06 (dd, J = 13, 8.3 Hz, 1 H), 2.13 – 1.99 (m, 2 H), 1.85 – 1.71 (m, 2 H), 1.70 – 1.51 (m, 4 H)	HRMS(B) *m/z* 338.1748 M^+
19: (*4R,5S*)-4-methyl-5-phenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.11 (d, J = 5.8 Hz, 1 H), 7.48 – 7.28 (m, 10 H), 7.24 – 7.21 (m, 1 H), 5.70 (d, J = 6.8 Hz, 1 H), 4.96 – 4.90 (m, 1 H), 4.65 (br s, 1 H)1.49 (d, J = 7.1 Hz, 3 H), 0.97 (d, J = 6.6 Hz, 3 H)	HRMS(B) *m/z* 375.1824 $(M + H)^+$
20: (*S*)-4-benzhydryl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.13 (d, J = 5.8 Hz, 1 H), 7.47 – 7.40 (m, 2 H), 7.35 – 7.22 (m, 5 H), 7.19 – 7.10 (m, 5 H), 7.01 – 6.99 (m, 2 H), 6.89 (br s, 2 H), 5.26 (br s, 1 H), 5.09 (br s, 1 H), 4.76 (br s, 1 H), 4.54 – 4.44 (m, 2 H), 1.37 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 451.2134 $(M + H)^+$
21: (*R*)-4-isopropyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.10 (d, J = 5.8 Hz, 1 H), 7.35 – 7.27 (m, 5 H), 7.20 – 7.17 (m, 1 H), 4.96 (q, J = 6.7 Hz, 1 H), 4.44 (br s, 1 H), 4.32 (dd, J = 9.1, 2.5 Hz, 1 H), 4.25 (t, J = 8.6 Hz, 1 H), 2.65 (dtd, J = 14, 7.0, 3.5 Hz, 1 H), 1.51 (d, J = 7.1 Hz, 3 H), 0.99 (d, J = 7.1 Hz, 3 H), 0.85 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 327.1824 $(M + H)^+$
22: (*R*)-4-isopropyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.12 (d, J = 5.8 Hz, 1 H), 7.37 – 7.25 (m, 5 H), 7.19 – 7.16 (m, 1H), 5.04 (q, J = 6.9 Hz, 1 H), 4.64 (br s, 1 H), 4.35 – 4.26 (m, 2 H), 1.88 (br s, 1 H), 1.50 (d, J = 6.6 Hz, 3 H), 0.70 (br s, 3 H), 0.57 (br s, 3 H)	HRMS(B) *m/z* 327.1821 $(M + H)^+$
23: (*S*)-4-isopropyl-5,5-dimethyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.13 (d, J = 5.8 Hz, 1 H), 7.35 – 7.26 (m, 5 H), 7.19 – 7.16 (m, 1H), 5.08 – 5.03 (m, 1 H), 4.45 (br s, 1 H), 1.99 (br s, 1 H), 1.52 (s, 3 H), 1.50 (d, J = 7.1 Hz, 3 H), 1.41 (s, 3 H), 0.73 (br s, 3 H), 0.58 (br s, 3 H)	HRMS(B) *m/z* 355.2132 $(M + H)^+$
24: (*S*)-4-isopropyl-5,5-dimethyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.10 (d, J = 5.8 Hz, 1 H), 7.34 – 7.25 (m, 5 H), 7.18 – 7.15 (m, 1 H), 4.93 (br s, 1 H), 4.32 (br s, 1 H), 2.25 (td, J = 6.8, 3.5 Hz, 1 H), 1.50 (d, J = 7.1 Hz, 3 H), 1.49 (s, 3 H), 1.09 (br s, 3 H), 1.03 (d, J = 7.1 Hz, 3 H), 0.95 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 355.2128 $(M + H)^+$
25: (*4R,5S*)-4-methyl-5-phenyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.12 (d, J = 5.8 Hz, 1 H), 7.45 – 7.30 (m, 8 H), 7.20 (t, J = 7.3 Hz, 2 H), 7.10 – 7.06 (m, 1 H), 5.80 (d, J = 7.0 Hz, 1 H), 5.01 – 4.94 (m, 2 H), 1.49 (d, J 7.0 Hz, 3 H), 0.30 (br s, 3 H)	HRMS(B) *m/z* 375.1823 $(M + H)^+$
26: (*4S,5R*)-4-methyl-5-phenyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.10 (d, J = 5.8 Hz, 1 H), 7.48 – 7.28 (m, 10 H), 7.24 – 7.20 (m, 1 H), 5.69 (br s, 1 H), 5.01 – 4.93 (m, 1 H), 4.59 (br s, 1 H)1.49 (d, J = 7.1 Hz, 3 H), 0.96 (d, J = 6.5	HRMS(B) *m/z* 375.1819 $(M + H)^+$

	Hz, 3 H)	
27: (*S*)-5,5-dimethyl-4-phenyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	δ 8.08 (d, J = 5.9 Hz, 1 H), 7.44 – 7.39 (m, 3 H), 7.36 – 7.29 (m, 5 H), 7.22 – 7.17 (m, 3 H), 5.16 (br s, 1 H), 4.55 (br s, 1 H), 1.49 (s, 3 H), 1.18 (d, J = 6.8 Hz, 3 H), 0.96 (s, 3 H)	HRMS(B) *m/z* 389.1974 $(M + H)^+$
28: (*S*)-3-(2-((*S*)-2,3-dihydro-1H-inden-1-ylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.16 (d, J = 5.8 Hz, 1 H), 7.41 (d, J = 5.9 Hz, 1 H), 7.25 – 7.13 (m, 4 H), 5.48 (t, J = 7.8 Hz, 1 H), 4.79 – 4.68 (m, 1 H), 4.36 (d, J = 6.1 Hz, 2 H), 3.01 (ddd, J = 16, 8.6, 3.0 Hz, 1 H), 2.94 – 2.81 (m, 1 H), 2.66 – 2.54 (m, 2 H), 2.01 – 1.92 (m, 1 H), 0.86 (d, J = 6.9 Hz, 3 H), 0.85 (d, J = 6.9 Hz, 3 H)	HRMS(B) *m/z* 339.1825 $(M + H)^+$
29: (*S*)-3-(2-((*R*)-2,3-dihydro-1H-inden-1-ylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.15 (d, J = 5.8 Hz, 1 H), 7.41 (d, J = 5.8 Hz, 1 H), 7.29 – 7.15 (m, 4 H), 5.48 (t, J = 7.6 Hz, 1 H), 4.83 – 4.79 (m, 1 H), 4.41 – 4.36 (m, 2 H), 3.03 (ddd, J = 16, 8.8, 3.3 Hz, 1 H), 2.86 (dt, J = 16, 8.0 Hz, 1 H), 2.64 – 2.50 (m, 2 H), 2.00 – 1.91 (m, 1 H), 0.93 (d, J = 7.1 Hz, 3 H), 0.87 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 339.1830 $(M + H)^+$
30: (*4R,5S*)-4,5-diphenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.12 (d, J = 5.8 Hz, 1 H), 7.48 (d, J = 5.8 Hz, 1 H), 7.33 – 7.20 (m, 5 H), 7.13 – 7.08 (m, 6 H), 7.03 – 7.00 (m, 2 H), 6.88 – 6.86 (m, 2 H), 5.99 (d, J = 8.0 Hz, 1 H), 5.76 (br s, 1 H), 4.53 (br s, 1 H), 1.11 (br s, 3 H)	HRMS(B) *m/z* 437.1982 $(M + H)^+$
31: (*S*)-4-isobutyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.11 (d, J = 5.8 Hz, 1 H), 7.36 – 7.28 (m, 5 H), 7.21 – 7.18 (m, 1 H), 5.18 (q, J = 6.9 Hz, 1 H), 4.83 – 4.79 (m, 1 H), 4.46 (t, J = 8.5 Hz, 1 H), 4.23 (dd, J = 9.0, 3.0 Hz, 1 H), 1.57 (br s, 2 H), 1.53 (d, J = 7.0 Hz, 3 H), 1.33 (br s, 1 H), 0.82 (br s, 3 H), 0.73 (br s, 3 H)	HRMS(B) *m/z* 341.1974 $(M + H)^+$
32: (*S*)-4-isobutyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.09 (d, J = 5.8 Hz, 1 H), 7.36 – 7.27 (m, 5 H), 7.21 – 7.18 (m, 1 H), 5.16 (q, J = 7.0 Hz, 1 H), 4.69 (br s, 1 H), 4.42 (t, J = 8.3 Hz, 1 H), 4.24 (dd, J = 8.8, 2.8 Hz, 1 H), 1.92 – 1.86 (m, 1 H), 1.80 – 1.70 (m, 1 H), 1.58 (ddd, J = 13, 10, 4.8 Hz, 1 H), 1.52 (d, J = 7.0 Hz, 3 H), 1.07 (d, J = 6.5 Hz, 3 H), 0.98 (d, J = 6.5 Hz, 3 H)	HRMS(B) *m/z* 341.1972 $(M + H)^+$
33: (4*S*)-4-isopropyl-3-(2-(1-(pyridin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.49 – 8.48 (m, 1 H), 8.13 (dd, J = 10, 5.8 Hz, 1 H), 7.75 (td, J = 7.7, 1.8 Hz, 1 H), 7.43 – 7.36 (m, 2 H), 7.29 – 7.23 (m, 1 H), 5.08 – 4.99 (m, 1 H), 4.60 (br s, 0.5 H), 4.34 – 4.22 (m, 2.5 H), 2.63 – 2.56 (m, 0.5 H), 1.55 (d, J = 7.0 Hz, 1.5 H), 1.54 (d, J = 7.0 Hz, 1.5 H), 1.53 (br s, 0.5 H), 0.97 (d, J = 7.1 Hz, 1.5 H), 0.83 (d, J = 7.1 Hz, 1.5 H), 0.65 (br s, 1.5 H), 0.55 (br s, 1.5 H)	HRMS(B) *m/z* 328.1762 $(M + H)^+$
34: (4*S*)-4-isopropyl-3-(2-(1-(pyridin-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.45 – 8.43 (m, 2 H), 8.14 (dd, J = 12, 5.6 Hz, 1 H), 7.43 – 7.37 (m, 2 H), 5.05 (q, J = 7.1 Hz, 0.5 H), 4.99 – 4.95 (br m, 0.5 H), 4.59 (br s, 0.5 H), 4.33 – 4.26 (m, 2.5 H), 2.64 – 2.59 (m, 0.5 H), 1.53 (d, J = 7.1 Hz,	HRMS(B) *m/z* 328.1772 $(M + H)^+$

	3.5 H), 0.97 (d, J = 7.1 Hz, 1.5 H), 0.84 (d, J = 7.1 Hz, 1.5 H), 0.62 (br s, 1.5 H), 0.57 (br s, 1.5 H)	
35: (*S*)-4-isopropyl-3-(2-((*S*)-1-(naphthalen-1-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.19 – 8.16 (m, 2 H), 7.88 (d, J = 8.1 Hz, 1 H), 7.72 (d, J = 8.1 Hz, 1 H), 7.56 – 7.45 (m, 3 H), 7.40 – 7.32 (m, 2 H), 5.80 (q, J = 6.6 Hz, 1 H), 4.32 (br s, 1 H), 4.17 – 4.13 (m, 1 H), 4.05 (br s, 1 H), 1.64 (d, J = 7.1 Hz, 3 H), 1.15 (br s, 1 H), 0.23 (br s, 3 H), -0.31 (br s, 3 H)	HRMS(B) *m/z* 377.1969 $(M + H)^+$
36: (*S*)-4-isopropyl-3-(2-((*R*)-1-(4-methoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.09 (d, J = 5.6 Hz, 1 H), 7.33 (d, J = 6.1 Hz, 1 H), 7.28 – 7.24 (m, 2 H), 6.87 – 6.83 (m, 2 H), 4.93 (q, J = 6.9 Hz, 1 H), 4.52 (br s, 1 H), 4.35 – 4.26 (m, 2 H), 3.75 (s, 3 H), 2.65 (ddt, J = 10, 6.9, 3.5, 1 H), 1.48 (d, J = 7.1 Hz, 3 H), 0.99 (d, J = 7.1 Hz, 3 H), 0.83 (d, J = 6.8 Hz, 3 H)	HRMS(B) *m/z* 357.1928 $(M + H)^+$
37: (*4S,5R*)-4,5-diphenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.10 (d, J = 5.8 Hz, 1 H), 7.50 (d, J = 5.8 Hz, 1 H), 7.12 – 7.09 (m, 6 H), 7.06 – 7.03 (m, 2 H), 7.01 – 6.97 (m, 5 H), 6.83 – 6.81 (m, 2 H), 6.10 (s, 2 H), 4.86 – 4.81 (br m, 1 H), 1.42 (d, J = 6.5 Hz, 3 H)	HRMS(B) *m/z* 437.1984 $(M + H)^+$
38: (*4S,5R*)-4,5-diphenyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.11 – 8.09 (m, 1 H), 7.47 (d, J = 5.8 Hz, 1 H), 7.32 – 7.20 (m, 5 H), 7.12 – 7.07 (m, 6 H), 7.02 – 6.99 (m, 2 H), 6.86 (d, J = 6.5 Hz, 2 H), 5.98 – 5.93 (br m, 1 H), 5.75 (br s, 1 H), 4.53 (br s, 1 H), 1.11 (br s, 3 H)	HRMS(B) *m/z* 437.1970 $(M + H)^+$
39: (*4R,5S*)-4,5-diphenyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.09 (d, J = 5.9 Hz, 1 H), 7.50 (d, J = 5.8 Hz, 1 H), 7.11 – 7.09 (m, 6 H), 7.05 – 7.03 (m, 2 H), 7.00 – 6.95 (m, 5 H), 6.82 – 6.80 (m, 2 H), 6.09 (s, 2 H), 4.87 – 4.81 (br m, 1 H), 1.41 (d, J = 7.0 Hz, 3 H)	HRMS(B) *m/z* 437.1975 $(M + H)^+$
40: (*S*)-4-isopropyl-3-(2-((*R*)-1-(naphthalen-1-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.16 (d, J = 8.4 Hz, 1 H), 8.12 (d, J = 5.8 Hz, 1 H), 7.73 (d, J = 8.2 Hz, 1 H), 7.56 – 7.45 (m, 3 H), 7.42 – 7.38 (m, 1 H), 7.33 (d, J = 5.8 Hz, 1 H), 5.81 (q, J = 6.6 Hz, 1 H), 4.15 (br s, 1 H), 4.03 (br s, 1 H), 2.56 (td, J = 7.1, 3.5 Hz, 1 H), 1.65 (d, J = 7.1 Hz, 3 H), 0.78 (d, J = 6.6 Hz, 3 H), 0.74 (br s, 3 H)	HRMS(B) *m/z* 377.1981 $(M + H)^+$
41: (*S*)-4-isopropyl-3-(2-((*S*)-1-(4-methoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.11 (d, J = 5.8 Hz, 1 H), 7.33 (d, J = 5.9 Hz, 1 H), 7.22 (d, J = 8.6 Hz, 2 H), 6.85 – 6.82 (m, 2 H), 4.98 (q, J = 6.9 Hz, 1 H), 4.67 – 4.63 (m, 1 H), 4.34 – 4.27 (m, 2 H), 3.75 (s, 3 H), 1.94 (br s, 1 H), 1.48 (d, J = 7.1 Hz, 3 H), 0.73 (br s, 3 H), 0.61 (br s, 3 H)	HRMS(B) *m/z* 357.1922 $(M + H)^+$
42: (*S*)-4-isopropyl-3-(2-((*S*)-1-(4-(pyrimidin-5-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	9.11 (s, 1 H), 9.03 (s, 2 H), 8.14 (d, J = 5.8 Hz, 1 H), 7.69 – 7.66 (m, 2 H), 7.52 (d, J = 8.1 Hz, 2 H), 7.35 (d, J = 5.8 Hz, 1 H), 5.11 (q, J = 6.9 Hz, 1 H), 4.65 (br s, 1 H), 4.35 – 4.26 (m, 2 H), 1.80 (br s, 1 H), 1.55 (d, J = 7.1 Hz, 3 H), 0.66 (br s, 3 H), 0.55 (br s, 3 H)	HRMS(B) *m/z* 405.2035 $(M + H)^+$
43: (*S*)-4-isopropyl-3-(2-	8.10 (d, J = 5.9 Hz, 1 H), 7.80 – 7.75 (m, 4	HRMS(B)

((*R*)-1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	H), 7.51 – 7.48 (m, 1 H), 7.43 – 7.36 (m, 2 H), 7.32 (d, J = 5.8 Hz, 1 H), 5.15 – 5.07 (m, 1 H), 4.36 (br s, 1 H), 4.24 (dd, J = 9.1, 2.5 Hz, 1 H), 4.14 – 4.06 (br m, 1 H), 2.67 (dtd, J = 14, 6.9, 3.5 Hz, 1 H), 1.60 (d, J = 7.1 Hz, 3 H), 0.99 (d, J = 7.1 Hz, 3 H), 0.83 (d, J = 7.1 Hz, 3 H)	*m/z* 377.1984 $(M + H)^+$
44: (*R*)-3-(2-((*S*)-1-(4-fluorophenyl)ethylamino)pyrimidin-4-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one	8.09 – 8.07 (m, 1 H), 7.41 – 7.18 (m, 8 H), 7.12 – 7.07 (m, 2 H), 5.21 (s, 1 H), 4.99 – 4.93 (m, 1 H), 1.50 (s, 3 H), 1.24 (d, J = 7.1 Hz, 3 H), 0.98 (s, 3 H)	HRMS(B) *m/z* 407.188 $(M + H)^+$
45: (*R*)-4-isobutyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.10 (d, J = 5.8 Hz, 1 H), 7.36 – 7.27 (m, 5 H), 7.22 – 7.17 (m, 1 H), 5.18 (q, J = 6.9 Hz, 1 H), 4.82 – 4.78 (m, 1 H), 4.46 (t, J = 8.6 Hz, 1 H), 4.22 (dd, J = 8.6, 3.0 Hz, 1 H), 1.62 – 1.54 (m, 2 H), 1.53 (d, J = 7.0 Hz, 3 H), 1.36 – 1.30 (m, 1 H), 0.82 (br s, 3 H), 0.73 (br s, 3 H)	HRMS(B) *m/z* 341.1967 $(M + H)^+$
46: (*4S,5R*)-5-methyl-4-phenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.05 (d, J = 5.8 Hz, 1 H), 7.42 (d, J = 5.8 Hz, 1 H), 7.31 – 7.26 (m, 3 H), 7.19 – 7.11 (m, 5 H), 7.02 (br s, 2 H), 5.80 (d, J = 7.5 Hz, 1 H), 5.11 – 5.04 (m, 1 H), 4.85 (q, J = 6.7 Hz, 1 H), 1.44 (d, J = 7.0 Hz, 3 H), 0.97 (d, J = 6.5 Hz, 3 H)	HRMS(B) *m/z* 375.1828 $(M + H)^+$
47: (*4S,5R*)-5-methyl-4-phenyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.06 (d, J = 5.8 Hz, 1 H), 7.43 – 7.40 (m, 3 H), 7.37 – 7.30 (m, 5 H), 7.23 – 7.17 (m, 3 H), 5.51 (br d, J = 7.1 Hz, 1 H), 4.99 (quin, J = 6.8 Hz, 1 H), 4.63 (br s, 1 H), 1.16 (br d, J = 6.3 Hz, 3 H), 0.95 (d, J = 6.5 Hz, 3 H)	HRMS(B) *m/z* 375.1819 $(M + H)^+$
48: (*S*)-4-benzyl-5,5-dimethyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.18 (d, J = 5.7 Hz, 1 H), 7.43 (d, J = 5.7 Hz, 1 H), 7.31 – 7.17 (m, 10 H), 5.34 (br s, 1 H), 5.14 (quin, J = 7.0 Hz, 1 H), 4.85 (dd, J = 10, 3.5 Hz, 1 H), 3.22 (br d, J = 14 Hz, 1 H), 2.72 (br s, 1 H), 1.57 (d, J = 6.5 Hz, 3 H), 1.42 (s, 3 H), 1.33 (s, 3 H)	HRMS(B) *m/z* 403.2133 $(M + H)^+$
49: (*R*)-4-isobutyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.09 (d, J = 6.1 Hz, 1 H), 7.36 – 7.27 (m, 5 H), 7.21 – 7.17 (m, 1 H), 5.16 (q, J = 7.1 Hz, 1 H), 4.69 (t, J = 8.6 Hz, 1 H), 4.41 (t, J = 8.3 Hz, 1 H), 4.23 (dd, J = 8.6, 3.0 Hz, 1 H), 1.92 – 1.86 (m, 1 H), 1.79 – 1.69 (m, 1 H), 1.57 (ddd, J = 13, 10, 4.8 Hz, 1 H), 1.52 (d, J = 7.1 Hz, 3 H), 1.07 (d, J = 6.6 Hz, 3 H), 0.98 (d, J = 6.6 Hz, 3 H)	HRMS(B) *m/z* 341.1973 $(M + H)^+$
50: (*S*)-4-isopropyl-3-(2-((*S*)-1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.15 (d, J = 5.7 Hz, 1 H), 7.81 – 7.73 (m, 4 H), 7.49 – 7.38 (m, 3 H), 7.33 (d, J = 5.8 Hz, 1 H), 5.18 (q, J = 7.1 Hz, 1 H), 4.57 (br s, 1 H), 4.30 – 4.25 (m, 1 H), 4.20 (br s, 1 H), 1.60 (d, J = 7.1 Hz, 3 H), 1.59 (br s, 1 H), 0.34 (br s, 6 H)	HRMS(B) *m/z* 377.1979 $(M + H)^+$
51: (*S*)-4-isopropyl-3-(2-((*R*)-1-p-tolylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.08 (d, J = 5.6 Hz, 1 H), 7.32 (d, J = 5.6 Hz, 1 H), 7.22 (d, J = 8.1 Hz, 2 H), 7.10 (d, J = 8.1 Hz, 2 H), 4.95 – 4.90 (m, 1 H), 4.48 (br s, 1 H), 4.32 (dd, J 9.1, 3.0 Hz, 1 H),	HRMS(B) *m/z* 341.1972 $(M + H)^+$

	4.25 (t, J = 8.8 Hz, 1 H), 2.65 (dtd, J = 14, 7.1, 3.5 Hz, 1 H), 2.28 (s, 3 H), 1.48 (d, J = 7.1 Hz, 3 H), 0.99 (d, J = 7.1 Hz, 3 H), 0.84 (d, J = 7.1 Hz, 3 H)	
52: (*S*)-4-benzyl-5,5-dimethyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.17 (d, J = 5.7 Hz, 1 H), 7.44 (d, J = 5.7 Hz, 1 H), 7.38 – 7.21 (m, 10 H), 5.32 (br s, 1 H), 5.02 (br s, 1 H), 4.69 – 4.68 (br m, 1 H), 3.34 (dd, J = 15, 4.0 Hz, 1 H), 2.93 (dd, J = 15, 9.5 Hz, 1 H), 1.51 (d, J = 6.9 Hz, 3 H), 1.35 (s, 3 H), 1.29 (s, 3 H)	HRMS(B) *m/z* 403.2133 $(M + H)^+$
53: (*S*)-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)-4-(pyridin-3-yl)oxazolidin-2-one	($CDCl_3$) 8.56 – 8.53 (br m, 2 H), 8.18 (d, J = 5.7 Hz, 1 H), 7.48 (d, J = 5.7 Hz, 1 H), 7.45 – 7.34 (m, 1 H), 7.30 – 7.16 (m, 6 H), 5.77 (dd, J = 8.8, 3.8 Hz, 1 H), 5.26 (br s, 1 H), 4.83 (br s, 1 H), 4.81 (t, J = 8.8 Hz, 1 H), 4.31 (dd, J = 8.8, 3.8 Hz, 1 H), 1.51 (d, J = 6.8 Hz, 3 H)	HRMS(B) *m/z* 362.1620 $(M + H)^+$
54: 4-(4-methoxyphenyl)-5,5-dimethyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.06 (d, J = 5.7 Hz, 1 H), 7.55 – 7.52 (m, 1 H), 7.37 – 7.20 (m, 4 H), 7.13 – 6.99 (m, 3 H), 6.91 (d, J = 8.0 Hz, 1 H), 6.78 (d, J = 8.0 Hz, 1 H), 5.87 (br s, 0.5 H), 5.67 (br s, 0.5 H), 5.01 (br s, 0.5 H), 4.82 (br s, 0.5 H), 4.64 (br s, 0.5 H), 3.83 (s, 1.5 H), 3.78 (s, 1.5 H), 3.36 (br s, 0.5 H), 1.66 (s, 1.5 H), 1.51 (d, J = 6.9 Hz, 1.5 H), 1.49 (s, 1.5 H), 1.29 – 1.27 (m, 1.5 H), 1.04 (s, 1.5 H), 1.00 (s, 1. 5 H)	HRMS(B) *m/z* 419.2093 $(M + H)^+$
55: (*R*)-3-(2-(benzylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.08 (d, J = 5.8 Hz, 1 H), 7.41 (d, J = 5.8 Hz, 1 H), 7.30 – 7.17 (m, 8 H), 7.09 (br d, J = 7.1 Hz, 2 H), 5.69 (br dd, J =8.1, 3.0 Hz, 1 H), 4.76 (t, J = 8.8 Hz, 1 H), 4.28 (dd, J = 44, 15 Hz, 2 H), 4.19 (dd, J = 8.8, 3.8 Hz, 1 H)	HRMS(B) *m/z* 347.1512 $(M + H)^+$
56: (*S*)-3-(2-(benzylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.10 (d, J = 5.7 Hz, 1 H), 7.42 (d, J = 5.9 Hz, 1 H), 7.31 – 7.16 (m, 8 H), 7.09 (br d, J = 7.1 Hz, 2 H), 5.71 (br m, 1 H), 4.78 (t, J = 8.8 Hz, 1 H), 4.28 (dd, J = 45, 15 Hz, 2 H), 4.21 (dd, J = 8.6, 3.5 Hz, 1 H)	HRMS(B) *m/z* 347.1499 $(M + H)^+$
57: (*S*)-3-(2-(benzylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.13 (d, J = 5.8 Hz, 1 H), 7.37 (d, J = 5.8 Hz, 1 H), 7.28 (d, J = 4.6 Hz, 4 H), 7.20 (dq, J = 8.5, 4.2 Hz, 1 H), 4.64 (br s, 1 H), 4.56 (dd, J = 51, 16 Hz, 2 H), 4.35 – 4.29 (m, 2 H), 2.31 (br s, 1 H), 0.77 (br s, 3 H), 0.72 (br d, J = 6.6 Hz, 3 H)	HRMS(B) *m/z* 312.1584 M^+
58: (4*S*)-4-isopropyl-3-(2-(1-(4-(4-methylpiperazin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.23 (d, J = 5.8 Hz, 1 H), 7.40 (d, J = 5.8 Hz, 1 H), 7.28 – 7.24 (m, 2 H), 7.01 – 6.98 (m, 2 H), 4.85 – 4.82 (m, 1 H), 4.44 – 4.39 (m, 2 H), 4.03 – 3.98 (m, 1 H), 3.93 – 3.90 (m, 4 H), 3.30 (s, 3 H), 3.21 – 3.18 (m, 4 H), 2.60 (dtt, J = 10, 6.9, 3.5 Hz, 1 H), 1.37 (d, J = 7.1 Hz, 3 H), 1.00 (d, J = 7.1 Hz, 3 H), 0.87 (d, J = 6.9 Hz, 3 H)	HRMS(B) *m/z* 425.2651 $(M + H)^+$
59: (*S*)-3-(2-((*S*)-1-(3,5-bis(trifluoromethyl)phenyl)ethylamino)pyrimidin-4-yl)-	8.17 (br d, J = 5.0 Hz, 1 H), 7.93 (s, 2 H), 7.82 (s, 1 H), 7.40 (d, J = 5.9 Hz, 1 H), 5.21 (q, J = 7.1 Hz, 1 H), 4.59 (br s, 1 H),	HRMS(B) *m/z* 463.1564

4-isopropyloxazolidin-2-one	4.33 – 4.25 (m, 2 H), 1.69 (br s, 1 H), 1.57 (d, J = 7.1 Hz, 3 H), 0.57 (br s, 6 H)	$(M + H)^+$
60: (*S*)-4-isopropyl-3-(2-((*S*)-1-(6-methoxynaphthalen-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.14 (d, J = 5.8 Hz, 1 H), 7.71 (d, J = 8.6 Hz, 1 H), 7.67 – 7.64 (m, 2 H), 7.42 (dd, J = 8.3, 1.8 Hz, 1 H), 7.33 (d, J = 5.8 Hz, 1 H), 7.19 (d, J = 2.5 Hz, 1 H), 7.08 (dd, J = 9.1, 2.5 Hz, 1 H), 5.15 (q, J = 7.1 Hz, 1 H), 4.59 (br s, 1 H), 4.29 (t, J = 8.8 Hz, 1 H), 4.24 – 4.19 (br m, 1 H), 3.88 (s, 3 H), 1.74 (br s, 1 H), 1.58 (d, J = 7.1 Hz, 3 H), 0.39 (br s, 6 H)	HRMS(B) *m/z* 407.2084 $(M + H)^+$
61: (*S*)-4-isopropyl-3-(2-((*R*)-1-(3-methoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.09 (d, J = 5.8 Hz, 1 H), 7.33 (d, J = 5.9 Hz, 1 H), 7.20 (t, J = 7.8 Hz, 1 H), 6.92 – 6.90 (m, 2 H), 6.75 (ddd, J = 8.1, 2.5, 1.0 Hz, 1 H), 4.94 – 4.89 (m, 1 H), 4.46 (br s, 1 H), 4.34 – 4.23 (m, 2 H), 3.75 (s, 3 H), 2.65 (dtd, J = 14, 6.9, 3.5 Hz, 1 H), 1.49 (d, J = 7.1 Hz, 3 H), 0.99 (d, J = 7.1 Hz, 3 H), 0.85 (d, J = 6.9 Hz, 3 H)	HRMS(B) *m/z* 357.1927 $(M + H)^+$
62: (*S*)-3-(2-((*S*)-1-(3-bromophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.14 (d, J 5.8 Hz, 1 H), 7.48 (s, 1 H), 7.37 – 7.28 (m, 3 H), 7.20 (t, J = 7.1 Hz, 1 H), 5.01 (q, J = 7.1 Hz, 1 H), 4.62 (br s, 1 H), 4.34 – 4.26 (m, 2 H), 1.83 (br s, 1 H), 1.50 (d, J = 7.1 Hz, 3 H), 0.71 (br s, 3 H), 0.59 (br s, 3 H)	HRMS(B) *m/z* 405.0937 $(M + H)^+$
63: (*S*)-3-(2-((*S*)-1-(4-bromophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.13 (d, J 5.8 Hz, 1 H), 7.44 – 7.41 (m, 2 H), 7.35 (d, J = 5.8 Hz, 1 H), 7.26 – 7.22 (m, 2 H), 4.98 (q, J = 7.1 Hz, 1 H), 4.60 (br s, 1 H), 4.33 – 4.26 (m, 2 H), 1.73 (br s, 1 H), 1.49 (d, J = 7.1 Hz, 3 H), 0.68 (br s, 3 H), 0.58 (br s, 3 H)	HRMS(B) *m/z* 405.0912 $(M + H)^+$
64: (*S*)-3-(2-(1-(naphthalen-1-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.23 (d, J = 8.1 Hz, 1 H), 8.07 (d, J = 5.8 Hz, 1 H), 7.88 – 7.86 (m, 1 H), 7.73 (d, J = 8.1 Hz, 1 H), 7.58 (d, J = 7.1 Hz, 1 H), 7.54 – 7.45 (m, 2 H), 7.42 – 7.39 (m, 1 H), 7.29 (d, J = 5.8 Hz, 1 H), 5.90 (q, J = 6.7 Hz, 1 H), 4.32 (br s, 1 H), 4.22 (br s, 1 H), 3.98 (br s, 1 H), 3.37 (br s, 1 H), 1.65 (d, J = 6.9 Hz, 3 H)	HRMS(B) *m/z* 335.1500 $(M + H)^+$
65: (*S*)-3-(2-((*S*)-1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.11 (d, J = 5.8 Hz, 1 H), 7.80 – 7.77 (m, 1 H), 7.73 – 7.68 (m, 2 H), 7.56 (s, 1 H), 7.45 – 7.40 (m, 2 H), 7.37 (d, J = 5.8 Hz, 1 H), 7.23 (dd, J = 8.6, 1.5 Hz, 1 H), 7.08 – 7.00 (m, 5 H), 5.80 (dd, J = 8.8, 3.8 Hz, 1 H), 5.07 (q, J = 6.9 Hz, 1 H), 4.79 (t, J = 8.7 Hz, 1 H), 4.20 (dd, J = 8.6, 3.5 Hz, 1 H), 1.55 (d, J = 6.9 Hz, 3 H)	HRMS(B) *m/z* 411.1820 $(M + H)^+$
66: (*R*)-3-(2-((*S*)-1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.10 (d, J = 5.8 Hz, 1 H), 7.82 – 7.78 (m, 3 H), 7.69 (s, 1 H), 7.47 – 7.40 (m, 5 H), 7.38 – 7.29 (m, 4 H), 5.53 (dd, J = 8.8, 3.8 Hz, 1 H), 4.82 (q, J = 6.9 Hz, 1 H), 4.68 (t, J = 8.6 Hz, 1 H), 4.15 (dd, J = 8.6, 4.0 Hz, 1 H), 1.31 (d, J = 6.9 Hz, 3 H)	HRMS(B) *m/z* 411.1821 $(M + H)^+$
67: (*S*)-3-(2-((*R*)-1-(3-bromophenyl)ethylamino)	8.10 (d, J 5.8 Hz, 1 H), 7.53 – 7.50 (m, 1 H), 7.36 – 7.31 (m, 3 H), 7.21 (t, J = 7.8	HRMS(B)

pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Hz, 1 H), 4.94 – 4.86 (m, 1 H), 4.42 (br s, 1 H), 4.33 (dd, J = 9.1, 2.5, 1 H), 4.26 (t, J = 8.8 Hz, 1 H), 2.65 (dtd, J = 14, 7.0, 3.8 Hz, 1 H), 1.50 (d, J = 7.1 Hz, 3 H), 1.00 (d, J = 7.1 Hz, 3 H), 0.85 (d, J = 7.1 Hz, 3 H)	*m/z* 405.0930 $(M + H)^+$
68: (*S*)-3-(2-((*R*)-1-(4-bromophenyl)ethylamino) pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.10 (d, J 5.8 Hz, 1 H), 7.45 – 7.42 (m, 2 H), 7.35 (d, J = 5.9 Hz, 1 H), 7.29 – 7.25 (m, 2 H), 4.95 – 4.90 (m, 1 H), 4.44 (br s, 1 H), 4.34 – 4.25 (m, 2 H), 2.63 (dtd, J = 14, 6.9, 3.5 Hz, 1 H), 1.49 (d, J = 7.1 Hz, 3 H), 0.98 (d, J = 7.1 Hz, 3 H), 0.84 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 405.0934 $(M + H)^+$
69: (*S*)-4-isopropyl-3-(2-((*S*)-1-(3-methoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.12 (d, J = 5.8 Hz, 1 H), 7.34 (d, J = 6.0 Hz, 1 H), 7.20 – 7.16 (m, 1 H), 6.89 – 6.87 (m, 2 H), 6.75 – 6.73 (m, 1 H), 4.99 (q, J = 6.7 Hz, 1 H), 4.63 (br s, 1 H), 4.34 – 4.25 (m, 2 H), 3.74 (s, 3 H), 1.84 (br s, 1 H), 1.49 (d, J = 7.1 Hz, 3 H), 0.68 (br s, 3 H), 0.57 (br s, 3 H)	HRMS(B) *m/z* 357.1918 $(M + H)^+$
70: (*S*)-4-isopropyl-3-(2-((*S*)-1-p-tolylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.11 (d, J = 5.8 Hz, 1 H), 7.33 (d, J = 5.9 Hz, 1 H), 7.18 (d, J = 8.1 Hz, 2 H), 7.08 (d, J = 8.1 Hz, 2 H), 4.99 (q, J = 7.1 Hz, 1 H), 4.63 (br s, 1 H), 4.34 – 4.26 (m, 2 H), 2.28 (s, 3 H), 1.86 (br s, 1 H), 1.48 (d, J = 7.1 Hz, 3 H), 0.69 (br s, 3 H), 0.58 (br s, 3 H)	HRMS(B) *m/z* 341.1977 $(M + H)^+$
71: (*S*)-4-tert-butyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.14 (d, J = 5.7 Hz, 1 H), 7.37 – 7.34 (m, 2 H), 7.30 – 7.26 (m, 2 H), 7.19 – 7.15 (m, 2 H), 5.00 (q, J = 6.9 Hz, 1 H), 4.76 (br s, 1 H), 4.41 – 4.33 (m, 2 H), 1.48 (d, J = 7.1 Hz. 3 H), 0.55 (br s, 9 H)	HRMS(B) *m/z* 341.1979 $(M + H)^+$
72: (*S*)-4-tert-butyl-3-(2-((*R*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.09 (d, J = 5.7 Hz, 1 H), 7.35 – 7.32 (m, 2 H), 7.29 – 7.24 (m, 3 H), 7.19 – 7.15 (m, 1 H), 5.01 – 4.96 (m, 1 H), 4.68 (br s, 1 H), 4.39 (d, H = 9.2 Hz, 1 H), 4.15 (br s, 1 H), 1.50 (d, J = 7.0 Hz. 3 H), 0.94 (s, 9 H)	HRMS(B) *m/z* 341.1974 $(M + H)^+$
73: (*R*)-3-(2-((*S*)-1-(3-methoxyphenyl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.09 (d, J = 5.8 Hz, 1 H), 7.42 – 7.37 (m, 3 H), 7.34 – 7.28 (m, 3 H), 7.21 (t, J = 7.8 Hz, 1 H), 6.86 – 6.83 (m, 2 H), 6.78 – 6.76 (m, 1 H), 5.58 (dd, J = 8.6, 4.0 Hz, 1 H), 4.74 (t, J = 8.7 Hz, 1 H), 4.66 – 4.61 (m, 1 H), 4.18 (dd, J = 8.6, 4.0 Hz, 1 H), 3.77 (s, 3 H), 1.20 (d, J = 6.9 Hz, 3 H)	HRMS(B) *m/z* 391.1768 $(M + H)^+$
74: (*S*)-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)-4-(pyridin-2-yl)oxazolidin-2-one	8.55 (d, J = 4.5 Hz, 1 H), 8.10 (d, J = 6.0 Hz, 1 H), 7.64 (d, J = 6.0 Hz, 1 H), 7.43 (br s, 1 H), 7.26 – 7.15 (m, 4 H), 7.06 (br s, 2 H), 6.92 (br s, 1 H), 5.84 (dd, J = 8.7, 3.2 Hz, 1 H), 4.94 (br s, 1 H), 4.88 – 4.78 (m, 2 H), 4.48 (dd, J = 8.7, 3.2 Hz, 1 H), 1.51 (d, J = 6.9 Hz, 3 H)	HRMS(B) *m/z* 362.1624 $(M + H)^+$
75: (*S*)-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)-4-(pyridin-4-yl)oxazolidin-2-one	8.43 (br s, 2 H), 8.16 (br d, J = 5.0 Hz, 1 H), 7.65 (br s, 1 H), 7.36 – 7.09 (br m, 6 H), 6.90 (br s, 1 H), 5.88 (br s, 1 H), 4.83 (t, J = 8.8 Hz, 1 H), 4.78 (br s, 1 H), 4.23 (br s, 1 H), 1.34 (d, J = 7.0 Hz, 3 H)	HRMS(B) *m/z* 362.1623 $(M + H)^+$
76: (*S*)-4-isopropyl-3-(2-	8.11 (d, J = 5.8 Hz, 1 H), 7.66 (s, 1 H),	HRMS(B)

((*R*)-1-(3-(trifluoromethyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	7.64 – 7.61 (m, 1 H), 7.53 – 7.49 (m, 2 H), 7.36 (d, J = 5.9 Hz, 1 H), 5.05 – 4.99 (m, 1 H), 4.42 (br s, 1 H), 4.33 (dd, J = 9.1, 3.0 Hz, 1 H), 4.24 (t, J = 8.6 Hz, 1 H), 2.68 – 2.60 (m, 1 H), 1.54 (d, J = 7.1 Hz, 3 H), 0.99 (d, J = 7.1 Hz, 3 H), 0.85 (d, J = 7.0 Hz, 3 H)	*m/z* 395.1686 $(M + H)^+$
77: (*S*)-4-isopropyl-3-(2-((*R*)-1-(4-(trifluoromethyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.11 (d, J = 5.8 Hz, 1 H), 7.60 (d, J = 8.3 Hz, 2 H), 7.54 (d, J = 8.3 Hz, 2 H), 7.36 (d, J = 5.8 Hz, 1 H), 5.07 – 5.00 (m, 1 H), 4.39 (br s, 1 H), 4.33 – 4.30 (m, 1 H), 4.27 – 4.23 (m, 1 H), 2.63 (dtd, J = 14, 7.1, 3.5 Hz, 1 H), 1.54 (d, J = 7.0 Hz, 3 H), 0.98 (d, J = 7.1 Hz, 3 H), 0.84 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 395.1698 $(M + H)^+$
78: (*S*)-3-(2-((*R*)-1-(2-fluorophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.10 (d, J = 5.8 Hz, 1 H), 7.40 – 7.34 (m, 2 H), 7.24 – 7.18 (m, 1 H), 7.10 – 7.02 (m, 2 H), 5.28 (q, J = 7.1 Hz, 1 H), 4.42 (br s, 1 H), 4.32 (dd, J = 9.1, 2.5 Hz, 1 H), 4.24 (t, J = 8.8 Hz, 1 H), 2.64 (dtd, J = 14, 7.0, 3.8 Hz, 1 H), 1.50 (d, J = 7.1 Hz, 3 H), 0.98 (d, J = 7.1 Hz, 3 H), 0.84 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 345.1727 $(M + H)^+$
79: (*S*)-4-methyl-4-phenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.15 (d, J = 5.8 Hz, 1 H), 7.44 – 7.38 (m, 3 H), 7.36 – 7.21 (m, 6 H), 7.15 – 7.13 (m, 2 H), 5.40 (br s, 1 H), 4.22 – 4.17 (m, 2 H), 4.15 (br s, 1 H), 1.63 (br s, 3 H), 1.15 (d, J 6.6 Hz, 3 H)	HRMS(B) *m/z* 375.1809 $(M + H)^+$
80: (*S*)-4-isopropyl-3-(2-((*S*)-1-(4-morpholinophenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.11 (d, J = 5.8 Hz, 1 H), 7.33 (d, J = 5.8 Hz, 1 H), 7.22 – 7.19 (m, 2 H), 6.92 – 6.89 (m, 2 H), 5.00 – 4.95 (m, 1 H), 4.66 (br s, 1 H), 4.58 (br s, 1 H), 4.35 – 4.27 (m, 2 H), 3.82 – 3.80 (m, 4 H), 3.09 – 3.07 (m, 4 H), 1.48 (d, J = 7.1 Hz, 3 H), 0.73 (br s, 3 H), 0.60 (br s, 3 H)	HRMS(B) *m/z* 412.2359 $(M + H)^+$
81: (4*R*)-4-methyl-4-phenyl-3-(2-((1-(1-phenyl-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one		HRMS(B) *m/z* 441.2049 $(M + H)^+$
82: (*S*)-3-(2-((*S*)-1-(4-bromo-3,5-dimethoxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.16 (d, J = 5.8 Hz, 1 H), 7.36 (d, J = 5.8 Hz, 1 H), 6.64 (s, 2 H), 5.00 – 4.95 (m, 1 H), 4.58 (br s, 1 H), 4.33 – 4.23 (m, 2 H), 3.79 (s, 6 H), 1.54 (d, J = 7.0 Hz, 3 H), 0.55 (br s, 6 H)	HRMS(B) *m/z* 465.1134 $(M + H)^+$
83: (4*S*)-3-(2-(1-(1*H*-indol-5-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.11 (d, J = 5.8 Hz, 0.5 H), 8.09 (d, J = 5.8 Hz, 0.5 H), 7.52 (s, 0.5 H), 7.46 (s, 0.5 H), 7.32 – 7.29 (m, 2 H), 7.19 – 7.18 (m, 1 H), 7.10 (ddd, J = 14, 8.6, 1.5 Hz, 1 H), 6.36 (dt, J = 4.0, 3.0 Hz, 1 H), 5.11 (q, J = 6.9 Hz, 0.5 H), 5.05 (q, J = 6.8 Hz, 0.5 H), 4.64 (br s, 0.5 H), 4.50 (br s, 0.5 H), 4.33 – 4.19 (m, 2 H), 2.74 – 2.64 (m, 0.5 H), 1.86 (br s, 0.5 H), 1.55 (d, J = 7.1 Hz, 3 H), 1.02 (d, J = 7.1 Hz, 1.5 H), 0.86 (d, J = 7.1 Hz, 1.5 H), 0.57 (br s, 1.5 H), 0.46 (br s, 1.5 H)	HRMS(B) *m/z* 366.1928 $(M + H)^+$
84: (*S*)-3-(2-((*S*)-1-(5-	δ 8.16 – 8.12 (m, 2 H), 7.80 (d, J = 9.1 Hz,	HRMS(B)

bromo-6-methoxynaphthalen-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	1 H), 7.72 (s, 1 H), 7.56 (dd, J = 8.8, 1.8 Hz, 1 H), 7.37 (d, J = 9.1 Hz, 1 H), 7.32 (d, J = 5.7 Hz, 1 H), 5.18 (q, J = 6.7 Hz, 1 H), 4.60 – 4.54 (m, 1 H), 4.28 (t, J = 8.8 Hz, 1 H), 4.19 (dd, J = 9.1, 3.0 Hz, 1 H), 3.99 (s, 3 H), 1.72 (br s, 1 H), 1.61 (d, J = 7.1 Hz, 3 H), 0.39 (br d, J = 6.6 Hz, 3 H), 0.43 (br d, J = 6.1 Hz, 3 H)	*m/z* 485.1184 $(M + H)^+$
85: (*S*)-3-(2-((*R*)-1-(4-fluorophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.09 (d, J = 5.9 Hz, 1 H), 7.38 – 7.33 (m, 3 H), 7.04 – 6.98 (m, 2 H), 4.96 (q, J = 6.7 Hz, 1 H), 4.48 (br s, 1 H), 4.35 – 4.25 (m, 2 H), 2.64 (dtd, J = 14, 7.1, 3.5 Hz, 1 H), 1.50 (d, J = 6.6 Hz, 3 H), 0.98 (d, J = 7.1 Hz, 3 H), 0.85 (d, J = 7.0 Hz, 3 H)	HRMS(B) *m/z* 345.1725 $(M + H)^+$
86: (S)-4-isopropyl-3-(2-((R)-1-(2-(trifluoromethyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.12 (d, J = 5.8 Hz, 1 H), 7.77 (d, J = 8.1 Hz, 1 H), 7.66 (d, J = 8.1 Hz, 1 H), 7.60 (t, J = 7.6 Hz, 1 H), 7.42 – 7.36 (m, 2 H), 5.58 (q, J = 6.7 Hz, 1 H), 4.70 (dt, J = 7.8, 3.7 Hz, 1 H), 4.38 – 4.31 (m, 2 H), 2.58 (dtd, J = 14, 7.0, 3.8 Hz, 1 H), 1.50 (d, J = 6.9 Hz, 3 H), 0.98 (d, J = 7.0 Hz, 3 H), 0.85 (d, J = 6.9 Hz, 3 H)	HRMS(B) *m/z* 395.1706 $(M + H)^+$
87: (*R*)-4-methyl-3-(2-((*S*)-1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one		HRMS(B) *m/z* 425.1967 $(M + H)^+$
88: (*S*)-3-(2-((*S*)-1-(4-fluorophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.12 (d, J = 5.8 Hz, 1 H), 7.35 – 7.31 (m, 3 H), 7.03 – 6.97 (m, 2 H), 5.03 (q, J = 7.1 Hz, 1 H), 4.66 – 4.63 (br m, 1 H), 4.35 – 4.27 (m, 2 H), 1.85 (br s, 1 H), 1.49 (d, J = 7.0 Hz, 3 H), 0.71 (br s, 3 H), 0.60 (br s, 3 H)	HRMS(B) *m/z* 345.1724 $(M + H)^+$
89: (*R*)-4-methyl-4-phenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.12 (d, J = 5.8 Hz, 1 H), 7.43 (d, J = 5.8 Hz, 1 H) 7.32 – 7.20 (m, 8 H), 6.99 (br s, 2 H), 5.20 (br s, 1 H), 4.33 (br s, 1 H), 4.32 – 4. 27 (m, 2 H), 2.20 (s, 3 H), 1.41 (d, J = 6.8 Hz, 3 H)	HRMS(B) *m/z* 375.1822 $(M + H)^+$
90: (*S*)-4-isopropyl-3-(2-((*S*)-1-(2-methoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.11 (d, J = 5.8 Hz, 1 H), 7.33 (d, J = 5.8 Hz, 3 H), 7.20 – 7.16 (m, 2 H), 6.95 (d, J = 8.1 Hz, 1 H), 6.86 – 6.82 (m, 1 H), 5.28 (q, J = 7.1 Hz, 1 H), 4.63 (br s, 1 H), 4.35 – 4.26 (m, 2 H), 3.87 (s, 3 H), 1.86 (br s, 1 H), 1.46 (d, J = 6.9 Hz, 3 H), 0.69 (br s, 3 H), 0.56 (br s, 3 H)	HRMS(B) *m/z* 357.1924 $(M + H)^+$
91: (*S*)-3-(2-(1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.08 (d, J = 5.8 Hz, 1 H), 7.82 – 7.78 (m, 4 H), 7.52 (dd, J = 8.6, 1.5 Hz, 1 H), 7.45 – 7.38 (m, 2 H), 7.29 (d, J = 5.8 Hz, 1 H), 5.23 (q, J = 6.9 Hz, 1 H), 4.46 – 4.33 (m, 2 H), 4.21 – 4.15 (m, 1 H), 3.93 – 3.86 (m, 1 H), 1.61 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 335.1509 $(M + H)^+$
92: (*S*)-4-isopropyl-3-(2-((*S*)-1-(3-methoxyphenyl)ethylamin	($CDCl_3$) 15.12 (br s, 1 H), 9.23 (br s, 1 H), 7.67 – 7.56 (m, 1 H), 7.24 (dd, J = 8, 8 Hz, 1 H), 6.92 – 6.72 (m, 3 H), 5.04 – 4.86 (m,	HRMS(B) *m/z* 371.2082

o)-6-methylpyrimidin-4-yl)oxazolidin-2-one hydrochloride	1 H), 4.72 – 4.51 (m, 1 H), 4.42 – 4.25 (m, 2 H), 3.81 (s, 3 H), 2.56 (s, 3 H), 1.90 – 1.76 (m, 1 H), 1.64 (br s, 3 H), 0.73 (d, J = 8 Hz, 3 H), 0.64 (d, J = 8 Hz, 3 H)	$(M + H)^+$
93: (*S*)-4-isopropyl-3-(6-methyl-2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 7.57 – 7.19 (m, 6 H), 5.05 – 4.86 (m, 1 H), 4.63 – 4.09 (m, 3 H), 2.561 / 2.49 (2 x s, 3 H), 1.91 – 1.70 (m, 1 H), 1.62 / 1.54 (2 x d, 3 H), 0.75 – 0.45 (m, 6 H)	HRMS(B) *m/z* 341.1982 $(M + H)^+$
94: (*S*)-3-(2-(((*S*)-3-methylbutan-2-yl)amino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	(DMSO-d_6) 8.11 (d, *J* = 5.5 Hz, 1 H), 7.39 – 7.32 (m, 2 H), 7.31 – 7.19 (m, 4 H), 6.95 – 6.82 (m, 1 H), 5.83 – 5.73 (m, 1 H), 4.82 (t, *J* = 8.5 Hz, 1 H), 4.15 (br s., 1 H), 1.37 – 1.21 (m, 1 H), 0.97 (d, *J* = 7.0 Hz, 3 H), 0.58 (br s., 3 H), 0.47 (br s., 3 H)	HRMS(B) *m/z* 327.1822 $(M + H)^+$
95: (*S*)-5,5-dimethyl-3-(2-(((*S*)-3-methylbutan-2-yl)amino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	(DMSO-d_6) 8.10 (d, *J* = 5.5 Hz, 1 H), 7.39 – 7.32 (m, 2 H), 7.31 – 7.23 (m, 2 H), 7.18 (br. s, 1 H), 6.93 – 6.79 (m, 1 H), 5.43 (s, 1 H), 1.62 (s, 3 H), 1.30 – 1.14 (m, 1 H), 0.96 (d, *J* = 6.5 Hz, 3 H), 0.90 (s, 3 H), 0.54 (d, *J* = 5.0 Hz, 3 H), 0.43 (d, *J* = 5.0 Hz, 3 H)	HRMS(B) *m/z* 355.2123 $(M + H)^+$
96: 3-(2-(((3r,5r,7r)-adamantan-1-ylmethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	(DMSO-d_6) 8.11 (br s, 1 H), 7.15 (br s, 1 H), 4.52 – 4.36 (m, 2 H), 4.09 (br s, 2 H), 3.03 (br s, 2 H), 1.92 (br s, 3 H), 1.74 – 1.31 (m, 12 H)	HRMS(B) *m/z* 329.1971 $(M + H)^+$
97: (*S*)-4-isopropyl-3-(2-((*S*)-1-(4-(trifluoromethyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.14 (d, J = 5.8 Hz, 1 H), 7.59 (d, J = 8.1 Hz, 2 H), 7.51 (d, J = 8.1 Hz, 2 H), 7.36 (d, J = 5.8 Hz, 1 H), 5.08 (q, J = 6.9 Hz, 1 H), 4.59 (br s, 1 H), 4.33 – 4.25 (m, 2 H), 1.57 (br s, 1 H), 1.54 (d, J = 7.1 Hz, 3 H), 0.60 (br s, 3 H), 0.53 (br s, 3 H)	HRMS(B) *m/z* 395.1686 $(M + H)^+$
98: 3-((*S*)-1-(4-((*S*)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzonitrile	8.14 (d, J = 5.8 Hz, 1 H), 7.69 – 7.65 (m, 2 H), 7.58 – 7.56 (m, 1 H), 7.48 (t, J = 7.7 Hz, 1 H), 7.37 (d, J = 5.8 Hz, 1 H), 5.09 (q, J = 7.1 Hz, 1 H), 4.64 (br s, 1 H), 4.35 – 4.27 (m, 2 H), 1.74 (br s, 1 H), 1.52 (d, J = 7.1 Hz, 3 H), 0.71 (br s, 3 H), 0.60 (br s, 3 H)	HRMS(B) *m/z* 352.1764 $(M + H)^+$
99: (*S*)-3-(2-((*S*)-1-(3-chlorophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.14 (d, J = 5.8 Hz, 1 H), 7.36 (d, J = 5.8 Hz, 1 H), 7.32 (br s, 1 H), 7.29 – 7.23 (m, 2 H), 7.20 – 7.17 (m, 1 H), 5.02 (q, J = 6.9 Hz, 1 H), 4,63 (br s, 1 H), 4.34 – 4.27 (m, 2 H), 1.82 (br s, 1 H), 1.50 (d, J = 7.1 Hz, 3 H), 0.70 (br s, 3 H), 0.59 (br s, 3 H)	HRMS(B) *m/z* 361.1424 $(M + H)^+$
100: (4*R*)-5,5-dimethyl-4-phenyl-3-(2-(1-(4-(piperidin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.07 (d, J = 5.8 Hz, 0.5 H), 8.06 (d, J = 5.8 Hz, 0.5 H), 7.41 – 7.37 (m, 2 H), 7.34 – 7.26 (m, 2 H), 7.19 – 7.14 (m, 3 H), 6.95 – 6.89 (m, 2 H), 6.81 – 6.78 (m, 1 H), 5.46 (s, 0.5 H), 5.25 (s, 0.5 H), 4.73 – 4.68 (m, 0.5 H), 4.60 – 4.55 (m, 0.5 H), 3.12 – 3.07 (m, 4 H), 1.73 – 1.68 (m, 4 H), 1.65 (s, 1.5 H), 1.61 – 1.57 (m, 2 H), 1.54 (s, 1.5 H), 1.41 (d, J = 6.9 Hz, 1.5 H), 1.14 (d, J = 6.9 Hz, 1.5 H), 0.99 (d, J = 4.7 Hz, 3 H)	HRMS(B) *m/z* 472.2715 $(M + H)^+$
101: (*S*)-4-isopropyl-3-(2-((*S*)-1-(2-	8.15 (d, J = 5.8 Hz, 1 H), 7.74 (d, J = 8.1 Hz, 1 H), 7.69 (d, J = 8.1 Hz, 1 H), 7.58 (t,	HRMS(B) *m/z*

(trifluoromethyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	J = 7.6 Hz, 1 H), 7.42 – 7.35 (m, 2 H), 5.35 (q, J = 6.6 Hz, 1 H), 4.65 (dt, J = 8.0, 3.8 Hz, 1 H), 4.35 – 4.26 (m, 2 H), 1.76 (br s, 1 H), 1.52 (d, J = 6.6 Hz, 3 H), 0.64 (br d, J = 5.5 Hz, 3 H), 0.58 (br d, J = 6.3 Hz, 3 H)	395.1682 $(M + H)^+$
102: 4,4-dimethyl-3-(2-(1-(1-phenyl-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.22 (d, J = 5.8 Hz, 1 H), 7.87 (s, 1 H), 7.69 – 7.65 (m, 3 H), 7.48 – 7.43 (m, 2 H), 7.35 – 7.28 (m, 2 H), 5.34 (br s, 1 H), 5.24 – 5.17 (m, 1 H), 4.09 – 4.05 (m, 2 H), 1.74 (s, 3 H), 1.64 (d, J = 7.1 Hz, 3 H), 1.58 (s, 3 H)	HRMS(B) *m/z* 379.1890 $(M + H)^+$
103: (*S*)-3-(2-(((3*S*,5*S*,7*S*)-adamantan-1-ylmethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO-d_6) 8.13 (d, *J* = 5.5 Hz, 1 H), 7.20 (br s., 1 H), 7.17 (d, *J* = 5.5 Hz, 1 H), 4.69 – 4.63 (m, 1 H), 4.44 – 4.33 (m, 2 H), 3.11 – 2.85 (m, 2 H), 2.54 (br s, 1 H), 1.92 (br s., 3 H), 1.70 – 1.53 (m, 6 H), 1.47 (br s., 6 H), 0.93 (d, *J* = 7.0 Hz, 3 H), 0.78 (d, *J* = 6.5 Hz, 3 H);	HRMS(B) *m/z* 371.2448 $(M + H)^+$
104: (*S*)-3-(2-(((*S*)-1-cyclohexylethyl)amino)pyrimidin-4-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one	(DMSO-d_6) 8.09 (d, *J* = 5.5 Hz, 1 H), 7.40 – 7.32 (m, 2 H), 7.32 – 7.23 (m, 3 H), 6.83 (d, *J* = 9.0 Hz, 1 H), 5.42 (s, 1 H), 3.36 (br s, 1 H), 1.72 – 1.23 (m, 9 H), 1.02 – 0.82 (m, 10 H), 0.62 (s, 1 H), 0.20 – 0.04 (m, 1 H)	HRMS(B) *m/z* 395.2446 $(M + H)^+$
105: (*S*)-3-(2-(((*S*)-1-cyclohexylethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO-d_6) 8.13 (d, *J* = 5.8 Hz, 1 H), 7.19 – 7.09 (m, 2 H), 4.68 (br s, 1 H), 4.41 – 4.33 (m, 2 H), 3.77 (br s, 1 H), 2.47 (br s, 1 H), 1.76 – 1.58 (m, 5 H), 1.43 – 1.35 (m, 1 H), 1.15 – 1.04 (m, 6 H), 0.97 – 0.88 (m, 5 H), 0.77 (d, *J* = 6.8 Hz, 3 H);	HRMS(B) *m/z* 333.2288 $(M + H)^+$
106: (4*S*)-4-isopropyl-3-(2-((1-phenoxypropan-2-yl)amino)pyrimidin-4-yl)oxazolidin-2-one	(DMSO-d_6) 8.19 (d, *J* = 5.6 Hz, 1 H), 7.30 – 7.24 (m, 3 H), 7.18 (br s, 1 H), 6.96 – 6.85 (m, 3 H), 4.70 – 4.52 (m, 1 H), 4.39 – 4.19 (m, 3 H), 4.12 – 4.00 (m, 1 H), 3.92 – 3.78 (m, 1 H), 2.46 (br s, 1 H), 1.29 – 1.21 (m, 3 H), 0.93 – 0.58 (m, 6 H)	HRMS(B) *m/z* 357.1921 $(M + H)^+$
107: (S)-3-(2-(((R)-1-cyclohexylethyl)amino)pyrimidin-4-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one	(DMSO-d_6) 8.09 (d, *J* = 5.6 Hz, 1 H), 7.38 – 7.12 (m, 6 H), 6.71 (br s, 1 H), 5.36 (s, 1 H), 1.77 – 1.56 (m, 9 H), 1.31 – 1.05 (m, 4 H), 0.92 (s, 6 H), 0.48 (br s., 2 H)	HRMS(B) *m/z* 395.2440 $(M + H)^+$
108: (*S*)-3-(5-chloro-2-((*S*)-1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	($CDCl_3$) 8.29 (s, 1 H), 7.84 – 7.74 (m, 4 H), 7.49 – 7.43 (m, 3 H), 5.76 (br s, 1 H), 5.17 – 5.10 (m, 1 H), 4.39 – 4.30 (m, 1 H), 4.31 (t, J = 8.1 Hz, 1 H), 4.09 – 4.05 (m, 1 H), 1.66 (d, J = 7.0 Hz, 3 H), 1.40 – 1.30 (m, 1 H), 0.52 (d, J = 6.1 Hz, 3 H), 0.27 (br s, 3 H)	HRMS(B) *m/z* 411.1588 $(M + H)^+$
109: 4-((*S*)-1-(4-((*S*)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzonitrile	8.14 (d, J = 5.8 Hz, 1 H), 7.68 – 7.66 (m, 2 H), 7.52 (d, J = 8.1 Hz, 3 H), 7.36 (d, J = 5.9 Hz, 1 H), 5.08 (q, J = 7.1 Hz, 1 H), 4.61 (br s, 1 H), 4.34 – 4.26 (m, 2 H), 1.60 (br s, 1 H), 1.52 (d, J = 7.1 Hz, 3 H), 0.65 (br s, 3 H), 0.58 (br s, 3 H)	HRMS(B) *m/z* 352.1775 $(M + H)^+$
110: (*S*)-4,4-dimethyl-3-(2-(1-(naphthalen-1-	($CDCl_3$) 8.10 (d, J = 5.8 Hz, 1 H), 8.01 (d, J = 8.6 Hz, 1 H), 7.81 – 7.78 (m, 1 H), 7.66	HRMS(B) *m/z*

yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	(d, J = 8.1 Hz, 1 H), 7.52 (d, J = 6.6 Hz, 1 H), 7.48 – 7.39 (m, 2 H), 7.36 – 7.32 (m, 1 H), 7.19 – 7.18 (m, 1 H), 5.66 (br s, 2 H), 3.78 – 3.69 (m, 2 H), 1.65 (s, 3 H), 1.64 (s, 3 H), 1.35 (br s, 3 H)	363.1822 $(M + H)^+$
111: (*R*)-3-(2-((*S*)-1-(4-fluorophenyl)ethylamino)pyrimidin-4-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one	8.09 (d, J = 5.7 Hz, 1 H), 7.41 – 7.07 (m, 10 H), 5.21 (s, 3 H), 4.96 (q, J = 7.1 Hz, 1 H), 1.50 (s, 3 H), 1.24 (d, J = 7.1 Hz, 3 H), 0.98 (s, 3 H)	HRMS(B) *m/z* 407.188 $(M + H)^+$
112: 4-(1-(4-((*S*)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzenesulfonamide	8.13 (d, J = 5.8 Hz, 0.5 H), 8.11 (d, J = 5.8 Hz, 0.5 H), 7.85 – 7.80 (m, 2 H), 7.51 (d, J = 8.6 Hz, 1 H), 7.49 (d, J = 8.6 Hz, 1 H), 7.36 (d, J = 5.7 Hz, 0.5 H), 7.35 (d, J = 5.7 Hz, 0.5 H), 5.09 (q, J = 6.9 Hz, 0.5 H), 5.03 – 4.97 (br m, 0.5 H), 4.61 (br s, 0.5 H), 4.33 – 4.24 (m, 2.5 H), 2.66 – 2.58 (m, 0.5 H), 1.62 (br s, 0.5 H), 1.532 (d, J = 7.1 Hz, 1.5 H), 1.527 (d, J = 7.1 Hz, 1.5 H), 0.98 (d, J = 7.0 Hz, 1.5 H), 0.84 (d, J = 7.0 Hz, 1.5 H), 0.67 (br s, 1.5 H), 0.56 (br s, 1.5 H)	HRMS(B) *m/z* 406.1553 $(M + H)^+$
113: (*S*)-3-(2-((*S*)-1-(4-hydroxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.11 (d, J = 5.8 Hz, 1 H), 7.33 (d, J = 5.8 Hz, 1 H), 7.12 (d, J 8.1 Hz, 2 H), 6.72 – 6.68 (m, 2 H), 4.95 (q, J = 6.9 Hz, 1 H), 4.69 – 4.65 (m, 1 H), 4.35 – 4.28 (m, 2 H), 1.47 (d, J = 7.1 Hz, 3 H), 0.75 (br s, 3 H), 0.62 (br s, 3 H)	HRMS(B) *m/z* 343.1776 $(M + H)^+$
114: (*S*)-3-(2-(1-cyclohexylethylamino)pyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	($CDCl_3$) 8.14 (d, J = 5.8 Hz, 1 H), 7.24 (d, J = 5.8 Hz, 1 H), 5.08 (br s, 1 H), 4.10 (s, 2 H), 3.87 (q, J = 7.0 Hz, 1 H), 1.83 – 1.68 (m, 6 H), 1.75 (s, 3 H), 1.74 (s, 3 H), 1.48 (dddd, J = 12, 8.7, 5.7, 2.8 Hz, 1 H), 1.28 – 1.03 (m, 4 H), 1.17 (d, J = 6.8 Hz, 3 H)	HRMS(B) *m/z* 319.2132 $(M + H)^+$
115: (*S*)-3-(5-fluoro-2-((*S*)-1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	($CDCl_3$) 8.15 (d, J = 3.5 Hz, 1 H), 7.83 – 7.72 (m, 4 H), 7.49 – 7.42 (m, 3 H), 5.06 – 5.03 (m, 1 H), 4.35 – 4.28 (m, 2 H), 4.10 – 4.08 (m, 1 H), 1.65 (d, J = 7.0 Hz, 3 H), 1.33 – 1.26 (m, 1 H), 0.38 (br s, 3 H), 0.14 (br s, 3 H)	HRMS(B) *m/z* 395.1884 $(M + H)^+$
116: (*S*)-3-(5-chloro-2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO-d_6) 8.39 – 8.31 (m, 2 H), 7.35 – 7.32 (m, 2 H), 7.28 (t, J = 7.8 Hz, 2 H), 7.17 (t, J = 7.8 Hz, 1 H), 4.89 -4.82 (m, 1 H), 4.49 – 4.45 (m, 2 H), 4.16 (br s, 1 H), 1.42 (d, J = 7.0 Hz, 3 H), 1.24 (br s, 1 H), 0.86 – 0.78 (m, 3 H), 0.48 (br s, 3 H)	HRMS(B) *m/z* 361.1431 $(M + H)^+$
117: (*S*)-3-(2-((*S*)-1-(4-bromo-3,5-dimethoxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.16 (d, J = 5.8 Hz, 1 H), 7.36 (d, J = 5.8 Hz, 1 H), 6.64 (s, 2 H), 5.00 – 4.95 (m, 1 H), 4.58 (br s, 1 H), 4.33 – 4.23 (m, 2 H), 3.79 (s, 6 H), 1.54 (d, J = 7.0 Hz, 3 H), 0.55 (br s, 6 H)	HRMS(B) *m/z* 465.1134 $(M + H)^+$
118: (4*S*)-3-(2-(1-(3,4-dimethoxyphenyl)ethylami	8.12 (d, J = 5.8 Hz, 0.5 H), 8.10 (d, J = 5.8 Hz, 0.5 H), 7.35 – 7.32 (m, 1 H), 6.97 –	HRMS(B) *m/z*

no)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	6.85 (m, 3 H), 5.00 – 4.91 (m, 1 H), 4.65 (br s, 0.5 H), 4.55 (br s, 0.5 H), 4.36 – 4.27 (m, 2 H), 3.80 – 3.79 (m, 6 H), 2.69 – 2.61 (m, 0.5 H), 1.87 (br s, 0.5 H), 1.50 (d, J = 7.1 Hz, 3 H), 1.00 (d, J = 7.1 Hz, 1.5 H), 0.86 (d, J = 7.0 Hz, 1.5 H), 0.69 (br s, 1.5 H), 0.60 (br s, 1.5 H)	387.2035 $(M + H)^+$
119: (*S*)-3-(2-(1-(6-methoxynaphthalen-2-yl)ethylamino)pyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	($CDCl_3$) 8.09 (d, J = 5.8 Hz, 1 H), 7.64 – 7.59 (m, 3 H), 7.36 (dd, J = 8.3, 1.8 Hz, 1 H), 7.20 – 7.18 (m, 1 H), 7.07 – 7.03 (m, 2 H), 5.56 (br s, 1 H), 5.07 – 5.03 (br m, 1 H), 3.91 – 3.82 (m, 5 H), 1.61 (s, 3 H), 1.56 (d, J = 6.8 Hz, 3 H), 0.97 (br s, 3 H)	HRMS(B) *m/z* 393.1925 $(M + H)^+$
120: (*S*)-5,5-dimethyl-3-(2-((*S*)-1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.09 (d, J = 5.8 Hz, 1 H), 7.81 – 7.79 (m, 1 H), 7.74 – 7.68 (m, 2 H), 7.52 (br s, 1 H), 7.46 – 7.41 (m, 3 H), 7.18 (br s, 1 H), 7.02 (br s, 2 H), 6.99 (s, 3 H), 5.43 (s, 1 H), 5.02 (q, 6.6 Hz, 1 H), 1.62 (s, 3 H), 1.53 (d, J = 6.6 Hz, 3 H), 0.93 (s, 3 H)	HRMS(B) *m/z* 439.2131 $(M + H)^+$
121: (*S*)-3-(2-((*S*)-1-(4-bromophenyl)ethylamino)pyrimidin-4-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one	8.08 (d, J = 5.8 Hz, 1 H), 7.44 (d, J = 5.8 Hz, 1 H), 7.29 – 7.24 (m, 5 H), 7.06 (br s, 2 H), 6.92 (br s, 2 H), 5.44 (s, 1 H), 4.88 – 4.84 (m, 1 H), 1.63 (s, 3 H), 1.42 (d, J = 7.1 Hz, 3 H), 0.95 (s, 3 H)	HRMS(B) *m/z* 467.1088 $(M + H)^+$
122: (*S*)-3-(2-((*S*)-1-(3-methoxyphenyl)ethylamino)pyrimidin-4-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one	8.07 (d, J = 5.8 Hz, 1 H), 7.42 (d, J = 5.8 Hz, 1 H), 7.28 – 7.21 (m, 3 H), 7.11 – 7.08 (m, 3 H), 6.72 (dd, J = 8.3, 1.8 Hz, 1 H), 6.66 (br s, 1 H), 6.62 (br s, 1 H), 5.46 (s, 1 H), 4.80 – 4.74 (m, 1 H), 3.73 (s, 3 H), 1.64 (s, 3 H), 1.42 (d, J = 7.1 Hz, 3 H), 0.98 (s, 3 H)	HRMS(B) *m/z* 419.2067 $(M + H)^+$
123: (*S*)-3-(2-((*S*)-1-(4-fluoro-3-methoxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.14 (d, J = 6.6 Hz, 1 H), 7.57 (d, J = 6.6 Hz, 1 H), 7.08 – 6.99 (m, 2 H), 6.88 (ddd, J = 8.5, 4.2, 2.0 Hz, 1 H), 5.07 (q, J = 7.1 Hz, 1 H), 4.68 (dt, J = 7.8, 3.7 Hz, 1 H), 4.40 – 4.32 (m, 2 H), 3.86 (s, 3 H), 1.99 (br s, 1 H), 1.57 (d, J = 7.1 Hz, 3 H), 0.75 (d, J = 7.1 Hz, 3 H), 0.66 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 375.1824 $(M + H)^+$
124: (*S*)-3-(2-((*S*)-1-(4-bromophenyl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.10 (d, J = 5.8 Hz, 1 H), 7.39 (d, J = 5.8 Hz, 1 H), 7.29 – 7.26 (m, 2 H), 7.25 – 7.21 (m, 3 H), 7.12 (dd, J = 6.3, 2.8 Hz, 2 H), 6.96 (d, J = 8.6 Hz, 2 H), 5.80 (dd, J = 8.6, 3.5 Hz, 1 H), 4.87 (q, J = 7.1 Hz, 1 H), 4.79 (t, J = 8.6 Hz, 1 H), 4.20 (dd, J = 8.6, 3.5 Hz, 1 H), 1.43 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 439.0763 $(M + H)^+$
125: (4*S*)-4-isopropyl-3-(2-((1-(3-morpholinophenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	8.215 (d, J = 6.1 Hz, 0.5 H), 8.212 (d, J = 6.1 Hz, 0.5 H), 7.52 (t, J = 7.1 Hz, 2 H), 7.46 (dd, J = 5.8, 3.8 Hz, 1 H), 7.43 – 7.34 (m, 3 H), 5.86 (qd, J = 8.2, 4.0 Hz, 1 H), 4.83 – 4.75 (m, 1 H), 4.42 – 4.33 (m, 2 H), 2.62 (dtd, J = 14, 7.0, 3.8 Hz, 0.5 H), 2.28 (br s, 0.5 H), 1.02 (d, J = 7.1 Hz, 1.5 H), 0.91 (d, J = 7.1 Hz, 1.5 H), 0.88 (d, J = 7.11 Hz, 1.5 H), 0.73 (d, J = 7.1 Hz, 1.5 H)	HRMS(B) *m/z* 412.2342 $(M + H)^+$
126: (*R*)-3-(2-((*S*)-1-(6-	8.10 (d, J = 5.6 Hz, 1 H), 7.69 (d, J = 9.1	HRMS(B)

methoxynaphthalen-2-yl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	Hz, 1 H), 7.72 (d, J = 8.6 Hz, 1 H), 7.62 (s, 1 H), 7.44 – 7.29 (m, 7 H), 7.20 (d, J = 2.5 Hz, 1 H), 7.11 (dd, J = 9.1, 2.5 Hz, 1 H), 5.55 (dd, J = 8.8, 3.8 Hz, 1 H), 4.80 (q, J = 7.1 Hz, 1 H), 4.69 (t, J = 8.6 Hz, 1 H), 4.16 (dd, J = 8.6, 4.0 Hz, 1 H), 3.90 (s, 3 H), 1.28 (d, J = 7.1 Hz, 3 H)	*m/z* 441.1929 $(M + H)^+$
127: (*S*)-4,4-dimethyl-3-(2-(1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.20 (d, J = 5.8 Hz, 1 H), 7.84 – 7.79 (m, 4 H), 7.51 – 7.43 (m, 3 H), 7.29 (d, J = 5.8 Hz, 1 H), 5.65 (br s, 1 H), 5.19 – 5.16 (br m, 1 H), 3.98 (d, J = 8.1 Hz, 1 H), 3.91 (d, J = 8.1 Hz, 1 H), 1.70 (s, 3 H), 1.66 (d, J = 6.9 Hz, 3 H), 1.02 (br s, 3 H)	HRMS(B) *m/z* 363.1819 $(M + H)^+$
128: 4,4-dimethyl-3-(2-(1-(4-(piperidin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.17 (d, J = 5.8 Hz, 1 H), 7.26 – 7.22 (m, 3 H), 6.91 (d, J = 8.6 Hz, 2 H), 5.39 (br s, 1 H), 5.01 – 4.94 (m, 1 H), 4.04 – 3.99 (m, 2 H), 3.14 – 3.12 (m, 4 H), 1.75 – 1.69 (m, 8 H), 1.61 – 1.57 (m, 2 H), 1.55 (d, J = 7.1 Hz, 3 H), 1.34 – 1.29 (br m, 2 H)	HRMS(B) *m/z* 396.2396 $(M + H)^+$
129: (*S*)-3-(2-((*S*)-1-(3-methoxyphenyl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.09 (d, J = 5.8 Hz, 1 H), 7.36 (d, J = 5.8 Hz, 1 H), 7.26 – 7.16 (m, 5 H), 7.11 (t, J = 7.8 Hz, 3 H), 6.74 – 6.66 (m, 3 H), 5.81 (dd, J = 8.6, 3.5 Hz, 1 H), 4.86 – 4.79 (m, 2 H), 4.23 (dd, J = 8.8, 3.8 Hz, 1 H), 3.73 (s, 3 H), 1.44 (d, J 7.1 Hz, 3 H)	HRMS(B) *m/z* 391.1771 $(M + H)^+$
130: (4*S*)-3-(2-(1-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.11 (d, J = 5.8 Hz, 0.5 H), 8.09 (d, J = 5.8 Hz, 0.5 H), 7.34 – 7.33 (m, 1 H), 6.81 – 6.71 (m, 3 H), 4.93 – 4.88 (m, 1 H), 4.65 (br s, 0.5 H), 4.52 (br s, 0.5 H), 4.36 – 4.27 (m, 2 H), 4.20 – 4.17 (m, 4 H), 2.66 (dtd, J = 14, 6.9, 3.5 Hz, 0.5 H), 1.99 (br s, 0.5 H), 1.456 (d, J = 7.1 Hz, 1.5 H), 1.454 (d, J = 7.1 Hz, 1.5 H), 1.00 (d, J = 7.1 Hz, 1.5 H), 0.85 (d, J = 7.1 Hz, 1.5 H), 0.75 (br s, 1.5 H), 0.63 (br s, 1.5 H)	HRMS(B) *m/z* 385.1854 $(M + H)^+$
131: (4*S*)-4-isopropyl-3-(2-(1-(pyridin-3-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.545 (d, J = 6.1 Hz, 0.5 H), 8.540 (d, J = 6.1 Hz, 0.5 H), 8.39 (dt, J = 4.9, 1.6 Hz, 1 H), 8.13 (dd, J = 11, 5.7 Hz, 1 H), 7.86 – 7.80 (m, 1 H), 7.40 – 7.36 (m, 2 H), 5.12 (q, J = 7.1 Hz, 0.5 H), 5.02 (m, 0.5 H), 4.65 (br s, 0.5 H), 4.42 (br s, 0.5 H), 4.35 – 4.25 (m, 2 H), 2.67 – 2.62 (m, 0.5 H), 1.76 (br s, 0.5 H), 1.56 (d, J = 7.1 Hz, 1.5 H), 1.55 (d, J = 7.1 Hz, 1.5 H), 0.99 (d, J = 7.1 Hz, 1.5 H), 0.85 (d, J = 7.1 Hz, 1.5 H), 0.70 (br s, 1.5 H), 0.60 (br s, 1.5 H)	HRMS(B) *m/z* 328.1771 $(M + H)^+$
132: (*S*)-4-benzyl-3-(2-(cyclopropylamino)pyrimidin-4-yl)oxazolidin-2-one	8.17 (d, *J* = 5.5 Hz, 1 H), 7.46 (d, *J* = 6.0 Hz, 1 H), 7.32 – 7.18 (m, 4 H), 7.15 (d, *J* = 7.0 Hz, 2 H), 5.04 – 4.91 (m, 1 H) 5.39 (br s, 1 H), 4.25 – 4.11 (m, 2 H), 3.51 (d, *J* = 13.0 Hz, 1 H), 2.80 (dd, *J* = 13.3, 9.79 Hz, 1 H), 2.76 – 2.69 (m, 1 H), 0.84 – 0.71 (m, 2 H), 0.60 – 0.47 (m, 2 H)	HRMS(B) *m/z* 311.1515 $(M + H)^+$
133: (*S*)-4-benzyl-3-(2-(cyclohexylamino)pyrimidi	($CDCl_3$) 8.18 (d, *J* = 5.5 Hz, 1 H), 7.48 (d, *J* = 6.0 Hz, 1 H), 7.42 – 7.31 (m, 3 H), 7.26	HRMS(B)

n-4-yl)oxazolidin-2-one	(d, *J* = 7.0 Hz, 2 H), 5.56 (br s, 1 H), 5.02 (ddd, *J* = 9.9, 3.6, 3.5 Hz, 1 H), 4.33 – 4.22 (m, 2 H), 3.96 – 3.83 (m, 1 H), 3.53 (d, *J* = 12.6 Hz, 1 H), 2.85 (dd, *J* = 13.3, 9.8 Hz, 1 H), 1.89 – 1.75 (m, 2 H), 2.16 – 2.05 (m, 2 H), 1.73 – 1.63 (m, 1 H), 1.52 – 1.26 (m, 7 H)	*m/z* 353.1979 $(M + H)^+$
134: (*S*)-4-benzyl-3-(2-(benzylamino)pyrimidin-4-yl)oxazolidin-2-one	8.17 (d, *J* = 5.8 Hz, 1 H), 7.38 (d, *J* = 5.8 Hz, 1 H), 7.36 – 7.30 (m, 2 H), 7.30 – 7.11 (m, 6 H), 7.02 (br s, 2 H), 4.95 (br s, 1 H), 4.76 – 4.65 (m, 1 H), 4.65 – 4.55 (m, 1 H), 4.30 (t, *J* = 8.4 Hz, 1 H), 4.26 – 4.18 (m, 1 H), 3.05 (br s, 1 H), 2.84 (br s, 1 H)	HRMS(B) *m/z* 361.1669 $(M + H)^+$
135: (*S*)-4-benzyl-3-(2-(((*R*)-1-phenylethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.22 (d, *J* = 5.5 Hz, 1 H), 7.48 (d, *J* = 5.5 Hz, 1 H), 7.42 – 7.29 (m, 8 H), 7.19 (d, *J* = 7.0 Hz, 2 H), 5.62 (br s, 1 H), 5.15 (t, *J* = 6.8 Hz, 1 H), 4.77 (br s, 1 H), 4.25 – 4.16 (m, 2 H), 3.45 (dd, *J* = 13.8, 3.3 Hz, 1 H), 2.94 (dd, *J* = 13.6, 9.0 Hz, 1 H), 1.61 (d, *J* = 7.0 Hz, 3 H)	HRMS(B) *m/z* 375.1817 $(M + H)^+$
136: (4*S*)-3-(2-(1-(1,3-dimethyl-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.14 (d, J = 5.8 Hz, 0.5 H), 8.13 (d, J = 5.8 Hz, 0.5 H), 7.42 (s, 0.5 H), 7.35 (s, 0.5 H), 7.35 (d, J = 5.7 Hz, 0.5 H), 7.34 (d, J = 5.8 Hz, 0.5 H), 5.10 – 5.00 (m, 1 H), 4.75 (dq, J = 7.8, 4.0 Hz, 1 H), 4.41 – 4.32 (m, 2 H), 3.76 (s, 1.5 H), 3.74 (s, 1.5 H), 2.64 – 2.57 (m, 0.5 H), 2.41 – 2.32 (m, 0.5 H), 2.18 (s, 3 H), 1.493 (d, J = 7.1 Hz, 1.5 H), 1.488 (d, J = 7.1 Hz, 1.5 H), 0.97 (d, J = 7.1 Hz, 1.5 H), 0.88 (d, J = 7.1 Hz, 3 H), 0.78 (d, J = 7.1 Hz, 1.5 H)	HRMS(B) *m/z* 345.2038 $(M + H)^+$
137: (*S*)-3-[2-((*S*)-1,3-dimethyl-butylamino)-pyrimidin-4-yl]-5,5-dimethyl-4-phenyl-oxazolidin-2-one	(DMSO-d_6) 8.10 (m, 1 H), 7.34 (m, 2 H), 7.26 (m, 3 H), 7.17 (br s, 1 H), 6.83 (s, 1 H), 5.39 (s, 1 H), 1.61 (s, 3 H), 1.39 (s, 1 H), 1.26 (s, 1 H), 1.02 (m, 4 H), 0.90 (s, 3 H), 0.81 (s, 1 H), 0.71 (s, 3 H), 0.41 (s, 3 H)	HRMS(B) *m/z* 369.2297 $(M + H)^+$
138: (*S*)-3-[2-((*S*)-2-hydroxy-1-methyl-ethylamino)-pyrimidin-4-yl]-5,5-dimethyl-4-phenyl-oxazolidin-2-one	(DMSO-d_6) 8.14 (d, *J* = 5.8 Hz, 1 H), 7.17 (d, *J* = 5.8 Hz, 1 H), 7.03 (br s, 1 H), 4.67 (br s, 1 H), 4.42 – 4.34 (m, 2 H), 3.96 (br s, 1 H), 2.46 (m, 1 H), 1.63 (m, 1 H), 1.47 (m, 1 H), 1.21 (m, 1 H), 1.09 (d, *J* = 6.3 Hz, 3 H), 0.89 (d, *J* = 7.3 Hz, 3 H), 0.87 (d, *J* = 6.5 Hz, 3 H), 0.84 (d, *J* = 6.5 Hz, 3 H), 0.77 (d, *J* = 6.8 Hz, 3 H)	HRMS(B) *m/z* 307.2141 $(M + H)^+$
139: (*S*)-4,4-dimethyl-3-(2-(1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.08 (d, J = 5.8 Hz, 1 H), 7.27 – 7.20 (m, 4 H), 7.17 (d, J = 5.6 Hz, 1 H), 7.15 – 7.11 (m, 1 H), 5.42 (br s, 1 H), 4.94 – 4.87 (m, 1 H), 3.92 – 3.86 (m, 2 H), 1.58 (s, 3 H), 1.47 (d, J = 6.9 Hz, 3 H), 1.06 (br s, 3 H)	HRMS(B) *m/z* 313.1668 $(M + H)^+$
140: (*S*)-3-(2-((*S*)-1-(4-fluorophenyl)ethylamino)p	($CDCl_3$) 8.17 (d, J = 5.8 Hz, 1 H), 7.45 – 7.31 (m, 4 H), 7.28 – 7.24 (m, 2 H), 7.09 –	HRMS(B) *m/z*

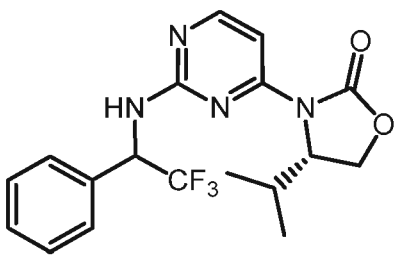
yrimidin-4-yl)-4-methyl-4-phenyloxazolidin-2-one	7.06 (m, 2 H), 7.01 – 6.95 (m, 2 H), 5.21 (br s, 1 H), 4.20 (s, 2 H), 4.13 (br s, 1 H), 1.65 (br s, 3 H), 1.13 (d, J = 6.8 Hz, 3 H)	393.1729 $(M + H)^+$
141: (4*S*)-4-methyl-4-phenyl-3-(2-(1-(4-(piperidin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.14 (d, J = 5.8 Hz, 0.35 H), 8.12 (d, J = 5.8 Hz, 0.65 H), 7.42 – 7.27 (m, 6 H), 7.04 (d, J = 8.6 Hz, 0.65 H), 6.91 – 6.82 (m, 3.35 H), 5.16 (br s, 0.35 H), 5.02 (br s, 0.65 H), 4.30 (s, 1.3 H), 4.22 (s, 0.7 H), 4.19 (br s, 1 H), 3.16 – 3.13 (m, 4 H), 2.20 (s, 1.95 H), 1.79 – 1.70 (br m, 5.05 H), 1.62 – 1.56 (m, 2 H), 1.37 (d, J = 6.8 Hz, 1.95 H), 1.06 (d, J = 6.3 Hz, 1.05 H)	HRMS(B) *m/z* 458.2551 $(M + H)^+$
142: (*S*)-4-benzyl-3-(2-(((*S*)-1-phenylethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	8.15 (d, *J* = 5.77 Hz, 1 H), 7.40 – 7.30 (m, 3 H), 7.25 – 7.13 (m, 5 H), 7.07 (t, *J* = 7.0 Hz, 1 H), 6.91 (br s, 2 H), 5.13 (q, *J* = 7.0 Hz, 1 H), 5.01 (t, *J* = 7.4 Hz, 1 H), 4.34 (t, *J* = 8.5 Hz, 1 H), 4.20 (dd, *J* = 8.9, 2.4 Hz, 1 H), 2.64 (br s, 1 H), 2.47 (br s, 1 H), 1.54 (d, *J* = 7.3 Hz, 3 H)	HRMS(B) *m/z* 375.1817 $(M + H)^+$
143: (*R*)-4-benzyl-3-(2-(cyclopropylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.19 (d, *J* = 5.0 Hz, 1 H), 7.62 (d, *J* = 6.0 Hz, 1 H), 7.41 – 7.29 (m, 4 H), 7.26 – 7.19 (m, 2 H), 6.42 (br s, 1 H), 5.07 (t, *J* = 8.3 Hz, 1 H), 4.30 – 4.24 (m, 2 H), 3.60 (d, *J* = 12.6 Hz, 1 H), 2.97 – 2.79 (m, 2 H), 0.95 – 0.81 (m, 2 H), 0.75 – 0.62 (m, 2 H)	HRMS(B) *m/z* 311.1516 $(M + H)^+$
144: (*R*)-4-benzyl-3-(2-(cycloheptylamino)pyrimidin-4-yl)oxazolidin-2-one	8.12 (d, *J* = 6.0 Hz, 1 H), 7.36 – 7.28 (m, 3 H), 7.28 – 7.19 (m, 3 H), 5.15 – 5.05 (m, 1 H), 4.37 (t, *J* = 8.5 Hz, 1 H), 4.30 – 4.24 (m, 1 H), 4.04 (br s., 1 H), 3.09 (dd, *J* = 13.6, 8.0 Hz, 1 H), 2.11 – 1.94 (m, 2 H), 1.78 – 1.48 (m, 11 H)	HRMS(B) *m/z* 367.2134 $(M + H)^+$
145: (*R*)-4-benzyl-3-(2-(cyclohexylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.18 (d, *J* = 5.0 Hz, 1 H), 7.48 (d, *J* = 6.0 Hz, 1 H), 7.42 – 7.29 (m, 3 H), 7.26 (d, *J* = 7.0 Hz, 2 H), 5.55 (br s, 1 H), 5.10 – 4.94 (m, 1 H), 4.33 – 4.22 (m, 2 H), 3.96 – 3.82 (m, 1 H), 3.53 (d, *J* = 12.1 Hz, 1 H), 2.85 (dd, *J* = 13.3, 9.8 Hz, 1 H), 2.22 – 2.01 (m, 2 H), 1.81 (td, *J* = 13.6, 4.0 Hz, 2 H), 1.68 (dd, *J* = 9.0, 3.5 Hz, 1 H), 1.51 – 1.22 (m, 6 H)	HRMS(B) *m/z* 353.1981 $(M + H)^+$
146: (*R*)-4-benzyl-3-(2-(benzylamino)pyrimidin-4-yl)oxazolidin-2-one	8.17 (d, *J* = 5.8 Hz, 1 H), 7.38 (d, *J* = 6.0 Hz, 1 H), 7.35 – 7.30 (m, 2 H), 7.29 – 7.18 (m, 5 H), 7.15 (t, *J* = 7.3 Hz, 1 H), 7.02 (br s, 2 H), 4.95 (br s, 1 H), 4.75 – 4.65 (m, 1 H), 4.65 – 4.56 (m, 1 H), 4.30 (t, *J* = 8.5 Hz, 1 H), 4.27 – 4.20 (m, 1 H), 3.05 (br s, 1 H), 2.82 (br s, 1 H)	HRMS(B) *m/z* 361.1659 $(M + H)^+$
147: (*R*)-4-benzyl-3-(2-(((*R*)-1-phenylethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.21 (d, *J* = 5.5 Hz, 1 H), 7.50 (d, *J* = 6.0 Hz, 1 H), 7.43 – 7.29 (m, 5 H), 7.28 – 7.12 (m, 4 H), 7.00 (br s., 2 H), 5.97 (br s, 1 H), 5.17 (t, *J* = 6.8 Hz, 1 H), 5.03 – 4.89 (m, 1 H), 4.28 (t, *J* = 8.5 Hz, 1 H), 4.19 (dd, *J* = 9.0, 3.0 Hz, 1 H), 2.97 (br s, 1 H), 2.53 (br s, 1 H), 1.63 (d, *J* = 7.0 Hz, 3 H)	HRMS(B) *m/z* 375.1822 $(M + H)^+$
148: (*R*)-4-benzyl-3-(2-	($CDCl_3$) 8.21 (d, *J* = 6.0 Hz, 1 H), 7.49 (d, *J*	HRMS(B)

(((*S*)-1-phenylethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	= 5.5 Hz, 1 H), 7.44 – 7.29 (m, 8 H), 7.19 (d, *J* = 6.5 Hz, 2 H), 5.69 (br s, 1 H),, 5.15 (t, *J* = 7.0 Hz, 1 H), 4.76 (br s, 1 H), 4.24 – 4.16 (m, 2 H), 3.45 (dd, *J* = 13.8, 3.3 Hz, 1 H), 2.94 (dd, *J* = 13.6, 9.5 Hz, 1 H), 1.61 (d, *J* = 7.0 Hz, 3 H)	*m/z* 375.1816 $(M + H)^+$
149: (*S*)-4-isopropyl-3-(5-methyl-2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.13 (s, 1 H), 7.35 – 7.28 (m, 4 H), 7.24 – 7.20 (m, 1 H), 5.73 (br s, 1 H), 5.00 – 4.92 (m, 1 H), 4.59 – 4.51 (m, 1 H), 4.38 (t, J = 8.8 Hz, 1 H), 4.12 (t, J = 8.8 Hz, 1 H), 2.14 (s, 3 H), 1.55 (d, J = 6.5 Hz, 3 H), 1.44 (br s, 1 H), 0.59 (d, J = 6.5 Hz, 3 H), 0.53 (d, J = 5.0 Hz, 3 H)	HRMS(B) *m/z* 341.1974 $(M + H)^+$
150: (*S*)-3-(5-fluoro-2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	($CDCl_3$) 8.18 (d, J = 3.0 Hz, 1 H), 7.32 – 7.28 (m, 4 H), 7.25 – 7.20 (m, 1 H), 5.64 (br s, 1 H), 4.92 – 4.87 (m, 1 H), 4.47 – 4.40 (m, 1 H), 4.39 (t, J = 8.5 Hz, 1 H), 4.17 (t, J = 8.6 Hz, 1 H), 1.86 (br s, 1 H), 1.54 (d, J = 7.0 Hz, 3 H), 0.68 – 0.56 (m, 6 H)	HRMS(B) *m/z* 345.1724 $(M + H)^+$
151: (*S*)-4-isopropyl-3-(2-((*S*)-1-(3-methoxyphenyl)ethylamino)-5-methylpyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.11 (s, 1 H), 7.24 – 7.20 (m, 1 H), 6.94 – 6.89 (m, 2H), 6.76 (dd, J = 7.6 Hz, J = 2.5 Hz, 1 H), 5.99 (br s, 1 H), 4.97 (quin, J = 6.8 Hz, 1 H), 4.58 (td, J = 8.8 Hz, J = 5.1 Hz, 1 H), 4.39 (t, J = 8.8 Hz, 1 H), 4.13 (t, J = 8.6 Hz, 1 H), 3.80 (s, 3 H), 2.16 (s, 3 H), 1.62 – 1.56 (m, 1 H), 1.57 (d, J = 6.5 Hz, 3 H), 0.64 (d, J = 7.1 Hz, 3 H), 0.59 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 371.2083 $(M + H)^+$
152: (*S*)-4-isopropyl-3-(5-methyl-2-((*S*)-1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.13 (s, 1 H), 7.81 – 7.74 (m, 4 H), 7.48 – 7.40 (m, 3 H), 5.87 (br s, 1 H), 5.17 – 5.10 (m, 1 H), 4.42 (td, J = 8.7 Hz, J = 4.8 Hz, 1 H), 4.29 (t, J = 8.8 Hz, 1 H), 4.02 (t, J = 8.6 Hz, 1 H), 2.13 (s, 3 H), 1.64 (d, J = 7.0 Hz, 3 H), 1.35 – 1.28 (m, 1 H), 0.42 (d, J = 7.1 Hz, 3 H), 0.17 (d, J = 7.0 Hz, 3 H)	HRMS(B) *m/z* 391.2135 $(M + H)^+$
153: (*S*)-3-(5-fluoro-2-((*S*)-1-(3-methoxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	($CDCl_3$) 8.16 (d, J = 2.5 Hz, 1 H), 7.23 (t, J = 7.8 Hz, 1 H), 6.91 – 6.83 (m, 2 H), 6.78 – 6.74 (m, 1 H), 6.05 (br s, 1 H), 4.86 (br s, 1 H), 4.49 – 4.38 (m, 2 H), 4.19 (t, J = 7.8 Hz, 1 H), 3.79 (s, 3 H), 1.54 (d, J = 8.0 Hz, 3 H), 1.32 – 1.25 (m, 1 H), 0.66 – 0.58 (m, 6 H)	HR-MS *m/z* (M + H)$^+$
154: (*S*)-4-methyl-3-(2-((*S*)-1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	($CDCl_3$) 8.17 (d, J = 5.8 Hz, 1 H), 7.84 – 7.78 (m, 3 H), 7.55 (s, 1 H), 7.51 – 7.43 (m, 5 H), 7.39 – 7.36 (m, 1 H), 7.29 – 7.25 (m, 3 H), 5.54 (br s, 1 H), 4.31 (br s, 1 H), 4.19 – 4.12 (m, 2 H), 1.84 (br s, 3 H), 1.24 (d, J = 6.8 Hz, 3 H)	HRMS(B) *m/z* 425.1972 $(M + H)^+$
155: (*S*)-3-(2-((*S*)-1-(6-methoxynaphthalen-2-yl)ethylamino)pyrimidin-4-yl)-4-methyl-4-phenyloxazolidin-2-one	($CDCl_3$) 8.18 (d, J = 5.8 Hz, 1 H), 7.69 (t, J = 7.8 Hz, 2 H), 7.47 – 7.41 (m, 4 H), 7.38 – 7.34 (m, 1 H), 7.28 – 7.23 (m, 3 H), 7.17 – 7.13 (m, 2 H), 5.31 (br s, 1 H), 4.31 (br s, 1 H), 4.19 – 4.13 (m, 2 H), 3.94 (s, 3 H), 1.56	HRMS(B) *m/z* 455.2081

	(br s, 3 H), 1.20 (d, J = 6.6 Hz, 3 H)	$(M + H)^+$
156: (*S*)-3-(2-((*S*)-1-cyclohexylethylamino)pyrimidin-4-yl)-4-methyl-4-phenyloxazolidin-2-one	($CDCl_3$) 8.11 (d, J = 5.8 Hz, 1 H), 7.38 – 7.32 (m, 5 H), 7.29 – 7.25 (m, 1 H), 4.81 (br s, 1 H), 4.31 – 4.26 (m, 2 H), 3.16 (br s, 1 H), 2.17 (s, 3 H), 1.77 – 1.57 (m, 6 H), 1.28 – 1.09 (m, 4 H), 0.99 – 0.85 (m, 2 H), 0.55 (br s, 2 H)	HRMS(B) *m/z* 381.2280 $(M + H)^+$
157: (*S*)-3-[2-((*S*)-2-hydroxy-1-methyl-ethylamino)-pyrimidin-4-yl]-5,5-dimethyl-4-phenyl-oxazolidin-2-one	(DMSO-d_6) 8.13 (m, 1 H), 7.36 (m, 2 H), 7.29 (m, 3 H), 7.19 (br s, 1 H), 6.65 (s, 1 H), 5.44 (s, 1 H), 4.30 (br s, 1 H), 2.95 (br s, 1 H), 2.77 (br s, 3 H), 1.61 (s, 3 H), 1.25 (s, 1 H), 1.04 (m, 3 H), 0.92 (s, 3 H)	HRMS(B) *m/z* 343.1778 $(M + H)^+$
158: (*S*)-5,5-dimethyl-4-phenyl-3-[2-((*S*)-1,2,2-trimethyl-propylamino)-pyrimidin-4-yl]-oxazolidin-2-one	(DMSO-d_6) 8.10 (d, *J* = 5.5 Hz, 1 H), 7.37 – 7.33 (m, 2 H), 7.29 – 7.25 (m, 3 H), 7.20 (br s, 1 H), 6.75 (d, *J* = 10 Hz, 1 H), 5.42 (s, 1 H), 3.47 (m, 1 H), 1.62 (s, 3 H), 0.96 (d, *J* = 6.8 Hz, 3 H), 0.88 (s, 3 H), 0.46 (s, 9 H)	HRMS(B) *m/z* 369.2277 $(M + H)^+$
159: (*R*)-3-(2-((*S*)-1-(naphthalen-1-yl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.11 (d, J = 6.1 Hz, 1 H), 8.04 (d, J = 8.6 Hz, 1 H), 7.89 (d, J = 8.1 Hz, 1 H), 7.74 (d, J = 8.1 Hz, 1 H), 7.60 – 7.56 (m, 1 H), 7.53 – 7.49 (m, 1 H), 7.46 – 7.44 (m, 1 H), 7.42 – 7.31 (m, 5 H), 7.21 – 7.18 (m, 2 H), 5.52 (q, J = 6.9 Hz, 1 H), 5.44 (dd, J = 8.8, 3.8 Hz, 1 H), 4.63 (t, J = 8.7 Hz, 1 H), 4.10 (dd, J = 8.6, 4.0 Hz, 1 H), 1.33 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 411.1823 $(M + H)^+$
160: (*S*)-4-isopropyl-3-[2-((*S*)-1,2,2-trimethyl-propylamino)-pyrimidin-4-yl]-oxazolidin-2-one	(DMSO-d_6) 8.14 (d, *J* = 5.5 Hz, 1 H), 7.16 (d, *J* = 5.5 Hz, 1 H), 7.00 (br. s, 1 H), 4.73 – 4.66 (m, 1 H), 4.41 – 4.34 (m, 2 H), 3.92 (br s, 1 H), 2.46 (br s, 1 H), 1.05 (d, *J* = 6.8 Hz, 3 H), 0.91 (d, *J* = 7.3 Hz, 3 H), 0.87 (s, 9 H), 0.77 (d, *J* = 6.8 Hz, 3 H)	HRMS(B) *m/z* 307.2130 $(M + H)^+$
161: (*S*)-3-[2-((*S*)-1-cyclopropyl-ethylamino)-pyrimidin-4-yl]-4-isopropyl-oxazolidin-2-one	(DMSO-d_6) 8.13 (d, *J* = 5.5 Hz, 1 H), 7.17 (d, *J* = 5.5 Hz, 1 H), 7.09 (br s, 1 H), 4.67 – 4.63 (m, 1 H), 4.37 (m, 2 H), 3.52 – 3.43 (m, 1 H), 2.46 (br s, 1 H), 1.19 (d, *J* = 6.8 Hz, 3 H), 1.01 – 0.93 (m, 1 H), 0.89 (d, *J* = 7.0 Hz, 3 H), 0.77 (d, *J* = 6.8 Hz, 3 H), 0.41 (m, 1 H), 0.33 (m, 1 H), 0.22 (br s, 1 H), 0.10 (br s, 1 H)	HRMS(B) *m/z* 291.1812 $(M + H)^+$
162: (*S*)-4-isopropyl-3-(2-((*S*)-1-(4-phenoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.13 (d, J = 5.8 Hz, 1 H), 7.34 – 7.28 (m, 5 H), 7.09 – 7.05 (m, 1 H), 6.96 – 6.90 (m, 4 H), 5.06 (q, J = 7.1 Hz, 1 H), 4.71 – 4.67 (m, 1 H), 4.37 – 4.28 (m, 2 H), 2.08 (br s, 1 H), 1.52 (d, J = 7.1 Hz, 3 H), 0.76 (d, J = 7.1 Hz, 3 H), 0.67 (d, J = 7.1 Hz, 3 H)	HRMS(B) *m/z* 419.2081 $(M + H)^+$
163: (*S*)-3-(2-((*S*)-1-(2,3-dihydrobenzofuran-5-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.12 (d, J = 5.6 Hz, 1 H), 7.32 (d, J = 5.6 Hz, 1 H), 7.17 (s, 1 H), 7.04 – 7.02 (m, 1 H), 6.63 (d, J = 8.1 Hz, 1 H), 4.98 (q, J = 7.1 Hz, 1 H), 4.69 – 4.65 (m, 1 H), 4.51 – 4.47 (m, 2 H), 4.36 – 4.27 (m, 2 H), 3.16 – 3.12 (m, 2 H), 2.09 (br s, 1 H), 1.48 (d, J = 7.0 Hz, 3 H), 0.75 (d, J = 7.0 Hz, 3 H), 0.65	HRMS(B) *m/z* 369.1915 $(M + H)^+$

	(d, J = 7.1 Hz, 3 H)	
164: (*S*)-3-(2-((*S*)-1-(4-tert-butylphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.12 (d, J = 5.8 Hz, 1 H), 7.34 – 7.31 (m, 3 H), 7.24 – 7.21 (m, 2 H), 5.02 (q, J = 7.1 Hz, 1 H), 4.66 – 4.63 (m, 1 H), 4.35 – 4.25 (m, 2 H), 1.95 (br s, 1 H), 1.50 (d, J = 7.0 Hz, 3 H), 1.29 (s, 9 H), 0.69 (d, J = 7.0 Hz, 3 H), 0.58 (d, J = 6.9 Hz, 3 H)	HRMS(B) *m/z* 383.2449 $(M + H)^+$
165: (*S*)-3-[2-((*S*)-1-cyclopropyl-ethylamino)-pyrimidin-4-yl]-5,5-dimethyl-4-phenyl-oxazolidin-2-one	(DMSO-d_6) 8.10 (d, *J* = 5.5 Hz, 1 H), 7.37 – 7.33 (m, 2 H), 7.30 – 7.24 (m, 3 H), 7.15 (br s, 1 H), 7.00 (br s, 1 H), 5.37 (s, 1 H), 2.82 (br s, 1 H), 1.61 (s, 3 H), 1.07 (d, *J* = 6.5 Hz, 3 H), 0.89 (s, 3 H), 0.65 (br s, 1 H), 0.17 (br s, 1 H), 0.00 (br s, 1 H), -0.23 (br s, 1 H), -0.65 (br s, 1 H)	HRMS(B) *m/z* 353.1974 $(M + H)^+$
166: (*S*)-3-(5-fluoro-2-((*S*)-1-(4-methoxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO-d_6) 8.36 (br s, 1 H), 7.95 (br s, 1 H), 7.24 (d, J = 8.5 Hz, 2 H), 6.82 (d, J = 9.0 Hz, 2 H), 6.05 (br s, 1 H), 4.77 (br s, 1 H), 4.54 – 4.45 (m, 2 H), 4.24 (br s, 1 H), 3.70 (s, 3 H), 1.38 (d, J = 7.0 Hz, 3 H), 1.26 – 1.22 (m, 1 H), 0.66 – 0.47 (m, 6 H)	HRMS(B) *m/z* 375.1815 $(M + H)^+$
167: (*R*)-5,5-dimethyl-4-phenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.08 (d, J = 5.8 Hz, 1 H), 7.42 – 7.38 (m, 3 H), 7.35 – 7.27 (m, 5 H), 7.22 – 7.17 (m, 3 H), 5.18 (s, 1 H), 4.62 – 4.57 (m,1 H), 1.51 (s, 3 H), 1.19 (d, J = 7.0 Hz, 3 H), 0.98 (s, 3 H)	HRMS(B) *m/z* 389.1975 $(M + H)^+$
168: (*R*)-5,5-dimethyl-3-(2-((*S*)-1-(naphthalen-2-yl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.10 (d, J = 5.8 Hz, 1 H), 7.82 (d, J = 8.1 Hz, 3 H), 7.73 (s, 1 H), 7.48 – 7.33 (m, 7 H), 7.19 (d, J = 7.1 Hz, 2 H), 5.07 (s, 1 H), 4.74 (q, J = 6.6 Hz, 1 H), 1.32 (d, J = 6.9 Hz, 3 H), 1.29 (s, 3 H), 0.92 (s, 3 H)	HRMS(B) *m/z* 439.2132 $(M + H)^+$
169: (*R*)-3-(2-((*S*)-1-(4-fluoro-3-methoxyphenyl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	δ 8.10 (d, J = 5.8 Hz, 1 H), 7.41 – 7.28 (m, 6 H), 7.02 – 6.97 (m, 2 H), 6.82 (ddd, J = 8.2, 4.4, 2.0 Hz, 1 H), 5.61 (dd, J = 8.6, 4.0 Hz, 1 H), 4.77 (t, J = 8.6 Hz, 1 H), 4.65 (q, J = 7.1 Hz, 1 H), 4.19 (dd, J = 9.1, 4.0 Hz, 1 H), 3.83 (s, 3 H), 1.20 (d, J = 7.9 Hz, 3 H)	HRMS(B) *m/z* 409.1677 $(M + H)^+$

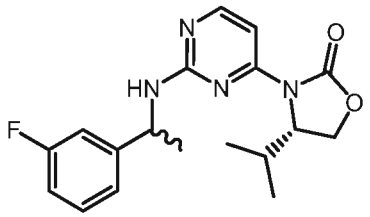
Example 170: (4*S*)-4-isopropyl-3-(2-(2,2,2-trifluoro-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one



A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (163 mg, 0.674 mmol), 2,2,2-trifluoro-1-phenylethanamine (624 mg, 3.56 mmol, 5.3 equiv) and *p*-

toluenesulfonic acid monohydrate (321 mg, 1.69 mmol, 2.5 equiv) in n-BuOH (3 mL) was heated at 110 °C for 2 h and treated with additional *p*-toluenesulfonic acid monohydrate (321 mg, 1.69 mmol, 2.5 equiv), then heated at 110 °C for 1 ½ h. After cooling, the solid reaction mixture was treated with MeCN, sonicated and filtered. The filtrated was concentrated and purified by silica gel column chromatography (EtOAc/Heptane 0 to 30%) to give (4*S*)-4-isopropyl-3-(2-(2,2,2-trifluoro-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one (65 mg) in 25% yield. ^{1}H NMR (400 MHz, CD_3OD) δ 8.215 (d, J = 6.1 Hz, 0.5 H), 8.212 (d, J = 6.1 Hz, 0.5 H), 7.52 (t, J = 7.1 Hz, 2 H), 7.46 (dd, J = 5.8, 3.8 Hz, 1 H), 7.43 – 7.34 (m, 3 H), 5.86 (qd, J = 8.2, 4.0 Hz, 1 H), 4.83 – 4.75 (m, 1 H), 4.42 – 4.33 (m, 2 H), 2.62 (dtd, J = 14, 7.0, 3.8 Hz, 0.5 H), 2.28 (br s, 0.5 H), 1.02 (d, J = 7.1 Hz, 1.5 H), 0.91 (d, J = 7.1 Hz, 1.5 H), 0.88 (d, J = 7.11 Hz, 1.5 H), 0.73 (d, J = 7.1 Hz, 1.5 H); HRMS(B) *m/z* 381.1545 $(M + H)^+$.

Examples 171 and 172



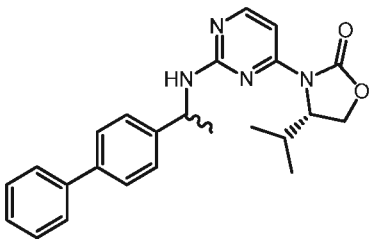
A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (106 mg, 0.439 mmol) and 1-(3-fluorophenyl)ethanamine (196 mg, 1.41 mmol, 3.21 equiv) in DMSO (1 mL) was heated at 110 °C for 1 ½ h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 10 to 50%) provided (*S*)-3-(2-((*R*)-1-(3-fluorophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (*S*)-3-(2-((*S*)-1-(3-fluorophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

Example 171 first eluted product (28 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.11 (d, J = 5.8 Hz, 1 H), 7.36 – 7.27 (m, 2 H), 7.16 (d, J = 7.6 Hz, 1 H), 7.07 (dt, J = 10, 2.0 Hz, 1 H), 6.92 – 6.88 (m, 1 H), 4.98 – 4.93 (m, 1 H), 4.42 (br s, 1 H), 4.32 (dd, J = 9.1, 2.8 Hz, 1 H), 4.26 (t, J = 8.7 Hz, 1 H), 2.64 (dtd, J = 14, 7.1, 3.5 Hz, 1 H), 1.50 (d, J = 7.0 Hz, 3 H), 0.98 (d, J = 7.1 Hz, 3 H), 0.85 (d, J = 7.0 Hz, 3 H); HRMS(B) *m/z* 345.1729 $(M + H)^+$.

Example 172 second eluted product (22 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.13 (d, J = 5.7 Hz, 1 H), 7.36 (d, J = 5.8 Hz, 1 H), 7.29 (td, J = 8.1, 6.1 Hz, 1 H), 7.13 (d, J = 7.6 Hz,

1 H), 7.06 – 7.04 (m, 1 H), 6.94 – 6.87 (m, 1 H), 5.03 (q, J = 7.1 Hz, 1 H), 4.64 (br s, 1 H), 4.34 – 4.26 (m, 2 H), 1.79 (br s, 1 H), 1.50 (d, J = 7.1 Hz, 3 H), 0.70 (br s, 3 H), 0.58 (br s, 3 H); HRMS(B) *m/z* 345.1727 $(M + H)^+$.

Examples 173 and 174

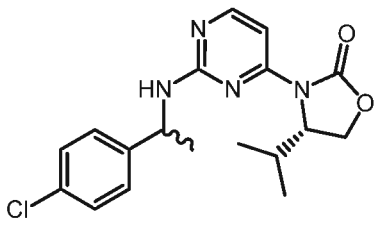


A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (90 mg, 0.37 mmol), *i*Pr_2NEt (0.455 mL, 2.61 mmol, 7.0 equiv) and 1-(biphenyl-4-yl)ethanamine hydrochloride (87 mg, 0.37 mmol) in DMSO (1 mL) was heated at 110 °C for 2 h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 10 to 50%) provided (*S*)-3-(2-((*R*)-1-(biphenyl-4-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (*S*)-3-(2-((*S*)-1-(biphenyl-4-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

Example 173 first eluted product (17 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.11 (d, J = 5.8 Hz, 1 H), 7.59 – 7.54 (m, 4 H), 7.43 – 7.28 (m, 6 H), 5.01 (q, J = 6.8 Hz, 1 H), 4.49 (br s, 1 H), 4.32 (dd, J = 9.1, 3.0 Hz, 1 H), 4.26 (t, J = 8.6 Hz, 1 H), 2.67 (dtd, J = 14, 7.0, 3.5 Hz, 1 H), 1.55 (d, J = 7.1 Hz, 3 H), 1.01 (d, J = 7.1 Hz, 3 H), 0.86 (d, J = 7.0 Hz, 3 H); HRMS(B) *m/z* 403.2141 $(M + H)^+$.

Example 174 second eluted product (21 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.14 (d, J = 5.8 Hz, 1 H), 7.58 – 7.52 (m, 4 H), 7.42 – 7.28 (m, 6 H), 5.06 (q, J = 7.1 Hz, 1 H), 4.63 (br s, 1 H), 4.34 – 4.25 (m, 2 H), 1.79 (br s, 1 H), 1.55 (d, J = 7.1 Hz, 3 H), 0.65 (br s, 3 H), 0.53 (br s, 3 H); HRMS(B) *m/z* 403.2139 $(M + H)^+$.

Examples 175 and 176

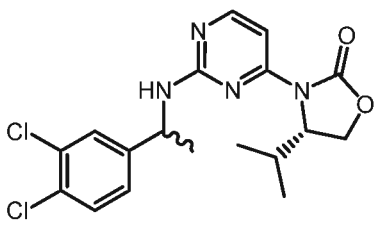


A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (96 mg, 0.40 mmol) and 1-(4-chlorophenyl)ethanamine (204 mg, 1.31 mmol, 3.3 equiv) in DMSO (1 mL) was heated at 110 °C for 3 h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 10 to 50%) provided (*S*)-3-(2-((*R*)-1-(4-chlorophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (*S*)-3-(2-((*S*)-1-(4-chlorophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

Example 175 first eluted product (32 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.10 (d, J = 5.8 Hz, 1 H), 7.36 – 7.28 (m, 5 H), 4.95 (q, J = 6.7 Hz, 1 H), 4.45 (br s, 1 H), 4.35 – 4.26 (m, 2 H), 2.64 (dtt, J = 11, 7.0, 3.4 Hz, 1 H), 1.50 (d, J = 7.1 Hz, 3 H), 0.98 (d, J = 7.1 Hz, 3 H), 0.85 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 361.1430 $(M + H)^+$.

Example 176 second eluted product (40 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.13 (d, J = 5.7 Hz, 1 H), 7.36 – 7.26 (m, 5 H), 5.00 (q, J = 7.1 Hz, 1 H), 4,62 (br s, 1 H), 4.34 – 4.26 (m, 2 H), 1.77 (br s, 1 H), 1.50 (d, J = 7.1 Hz, 3 H), 0.68 (br s, 3 H), 0.59 (br s, 3 H); HRMS(B) *m/z* 361.1431 $(M + H)^+$.

Examples 177 and 178



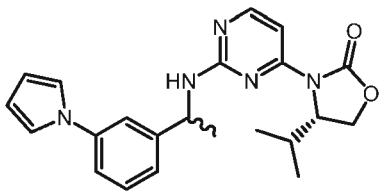
A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (93 mg, 0.38 mmol) and 1-(3,4-dichlorophenyl)ethanamine (73.1 mg, 0.385 mmol, 1.0 equiv) in DMSO (1 mL) was heated at 110 °C for 1 ½ h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted

with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 10 to 50%) provided (*S*)-3-(2-((*R*)-1-(3,4-dichlorophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (*S*)-3-(2-((*S*)-1-(3,4-dichlorophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

Example 177 first eluted product (21 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.12 (d, J = 5.8 Hz, 1 H), 7.50 (d, J = 2.0 Hz, 1 H), 7.44 (d, J = 8.2 Hz, 1 H), 7.37 (d, J = 5.8 Hz, 1 H), 7.28 (dd, J = 8.6, 2.0 Hz, 1 H), 4.94 – 4.88 (m, 1 H), 4.43 (br s, 1 H), 4.35 – 4.26 (m, 2 H), 2.68 – 2.60 (m, 1 H), 1.50 (d, J = 7.1 Hz, 3 H), 0.99 (d, J = 7.1 Hz, 3 H), 0.85 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 395.1035 $(M + H)^+$.

Example 178 second eluted product (28 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.15 (d, J = 5.8 Hz, 1 H), 7.47 – 7.42 (m, 2 H), 7.37 (d, J = 5.8 Hz, 1 H), 7.25 (dd, J = 8.1, 2.0 Hz, 1 H), 5.01 – 4.96 (m, 1 H), 4.61 (br s, 1 H), 4.34 – 4.26 (m, 2 H), 1.72 (br s, 1 H), 1.50 (d, J = 7.1 Hz, 3 H), 0.67 (br s, 3 H), 0.60 (br s, 3 H); HRMS(B) *m/z* 395.1044 $(M + H)^+$.

Examples 179 and 180



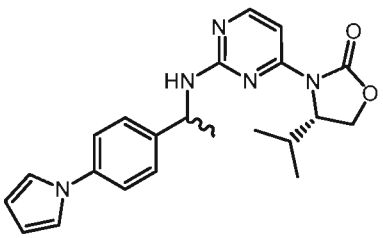
A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (86 mg, 0.36 mmol) and 1-(3-(1*H*-pyrrol-1-yl)phenyl)ethanamine (100 mg, 0.537 mmol, 1.5 equiv) in DMSO (1 mL) was heated at 110 °C for 1 ½ h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 10 to 50%) provided (*S*)-3-(2-((*R*)-1-(3-(1H-pyrrol-1-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (*S*)-3-(2-((*S*)-1-(3-(1H-pyrrol-1-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

Example 179 first eluted product (14 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8. 11 (d, J = 5.8 Hz, 1 H), 7.45 (t, J = 1.8 Hz, 1 H), 7.39 – 7.29 (m, 3 H), 7.23 (d, J = 7.6 Hz, 1 H), 7.13 (t, J = 2.0 Hz, 2 H), 6.25 (t, J = 2.1 Hz, 2 H), 5.03 – 4.97 (m, 1 H), 4.46 (br s, 1 H), 4.31 –

4.20 (m, 2 H), 2.64 (dtd, J = 14, 7.0, 3.8 Hz, 1 H), 1.56 (d, J = 7.1 Hz, 3 H), 0.95 (d, J = 7.1 Hz, 3 H), 0.84 (d, J = 7.0 Hz, 3 H); HRMS(B) *m/z* 392.2092 $(M + H)^+$.

Example 180 second eluted product (10 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.14 (d, J = 5.7 Hz, 1 H), 7.42 (br s, 1 H), 7.38 – 7.28 (m, 3 H), 7.20 (d, J = 7.6 Hz, 1 H), 7.12 (t, J = 2.3 Hz, 2 H), 6.25 (t, J = 2.0 Hz, 2 H), 5.09 (q, J = 6.9 Hz, 1 H), 4.64 (br s, 1 H), 4.32 – 4.23 (m, 2 H), 1.84 (br s, 1 H), 1.55 (d, J = 7.1 Hz, 3 H), 0.54 (br s, 6 H); HRMS(B) *m/z* 392.2090 $(M + H)^+$.

Examples 181 and 182

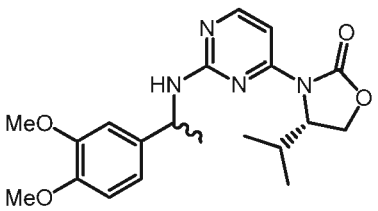


A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (44 mg, 0.18 mmol) and 1-(4-(1*H*-pyrrol-1-yl)phenyl)ethanamine (33.9 mg, 0.182 mmol, 1 equiv) in DMSO (1 mL) was heated at 110 °C for 2 h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 10 to 50%) provided (*S*)-3-(2-((*R*)-1-(4-(1H-pyrrol-1-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (*S*)-3-(2-((*S*)-1-(4-(1H-pyrrol-1-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

Example 181 first eluted product (18 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.11 (d, J = 5.8 Hz, 1 H), 7.44 – 7.39 (m, 4 H), 7.35 (d, J = 5.9 Hz, 1 H), 7.13 (t, J = 2.2 Hz, 2 H), 6.24 (t, J = 2.0 Hz, 2 H), 5.02 – 4.96 (m, 1 H), 4.49 (br s, 1 H), 4.34 – 4.25 (m, 2 H), 2.66 (dtd, J = 14, 7.0, 3.3 Hz, 1 H), 1.53 (d, J = 7.1 Hz, 3 H), 1.00 (d, J = 7.1 Hz, 3 H), 0.86 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 392.2089 $(M + H)^+$.

Example 182 second eluted product (9 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.14 (d, J = 5.8 Hz, 1 H), 7.39 (s, 4 H), 7.35 (d, J = 5.9 Hz, 1 H), 7.12 (t, J = 2.2 Hz, 2 H), 6.25 (t, J = 2.0 Hz, 2 H), 5.05 (q, J = 7.1 Hz, 1 H), 4.64 (br s, 1 H), 4.34 – 4.26 (m, 2 H), 1.87 (br s, 1 H), 1.53 (d, J = 7.1 Hz, 3 H), 0.68 (br s, 3 H), 0.57 (br s, 3 H); HRMS(B) *m/z* 392.2082 $(M + H)^+$.

Examples 183 and 184

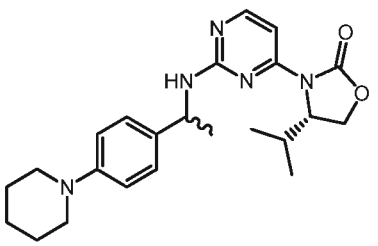


A mixture of (4*S*)-3-(2-((1-(3,4-dimethoxyphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (example 118) was resolved on a column (AS-H 4.6 x 100 mm) using 30% *i*PrOH in CO_2 to give (*S*)-3-(2-((*R*)-1-(3,4-dimethoxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (*S*)-3-(2-((*S*)-1-(3,4-dimethoxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

Example 183 first eluted product (13 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.11 (d, J = 5.8 Hz, 1 H), 7.33 (d, J = 5.8 Hz, 1 H), 6.97 (br d, J = 1.5 Hz, 1 H), 6.92 – 6.88 (m, 2 H), 4.96 (q, J = 6.7 Hz, 1 H), 4.61 – 4.55 (m, 1 H), 4.35 – 4.28 (m, 2 H), 3.803 (s, 3 H), 3.800 (s, 3 H), 2.63 (dtd, J = 14, 7.0, 3.5 Hz, 1 H), 1.51 (d, J = 7.1 Hz, 3 H), 0.99 (d, J = 7.1 Hz, 3 H), 0.86 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 387.2031 $(M + H)^+$.

Example 184 second eluted product (10 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.13 (d, J = 5.8 Hz, 1 H), 7.32 (d, J = 5.7 Hz, 1 H), 6.94 (br d, J = 1.1 Hz, 1 H), 6.89 – 6.84 (m, 2 H), 4.99 (q, J = 7.1 Hz, 1 H), 4.67 – 4.63 (m, 1 H), 4.36 – 4.26 (m, 2 H), 3.79 (s, 6 H), 2.01 (br s, 1 H), 1.51(d, J = 7.1 Hz, 3 H), 0.71 (d, J = 7.1 Hz, 3 H), 0.63 (d, J = 7.0 Hz, 3 H); HRMS(B) *m/z* 387.2029 $(M + H)^+$.

Examples 185 and 186

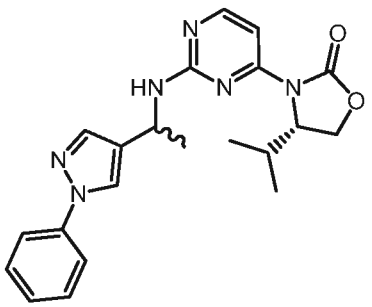


A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (93 mg, 0.38 mmol) and 1-(4-(piperidin-1-yl)phenyl)ethanamine (410 mg, 2.01 mmol, 5.2 equiv) in DMSO (1 mL) was heated at 110 °C for 2 h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 10 to 100%)

provided (4*S*)-4-isopropyl-3-(2-((1-(4-(piperidin-1-yl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one (57 mg) in 36% yield. A mixture of (4*S*)-4-isopropyl-3-(2-(1-(4-(piperidin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one was resolved on a column (AD-H 4.6 x 100 mm) using 5 to 55% MeOH with 0.2% Et_2NH in CO_2 to give (*S*)-4-isopropyl-3-(2-((*R*)-1-(4-(piperidin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one and (*S*)-4-isopropyl-3-(2-((*S*)-1-(4-(piperidin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one.

Example 185 first eluted product (16 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.10 (d, J = 5.8 Hz, 1 H), 7.31 (d, J = 5.8 Hz, 1 H), 7.24 – 7.20 (m, 2 H), 6.94 – 6.91 (m, 2 H), 4.93 (q, J = 7.1 Hz, 1 H), 4.58 – 4.54 (m, 1 H), 4.34 – 4.27 (m, 2 H), 3.11 – 3.08 (m, 4 H), 2.63 (dtd, J = 14, 7.1, 3.5 Hz, 1 H), 1.73 – 1.67 (m, 4 H), 1.60 – 1.54 (m, 2 H), 1.49 (d, J = 7.1 Hz, 3 H), 0.98 (d, J = 7.1 Hz, 3 H), 0.86 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 410.2555 $(M + H)^+$.
Example 186 second eluted product (16 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.11 (d, J = 5.8 Hz, 1 H), 7.31 (d, J = 5.8 Hz, 1 H), 7.20 – 7.16 (m, 2 H), 6.93 – 6.89 (m, 2 H), 4.98 (q, J = 6.9 Hz, 1 H), 4.69 – 4.65 (m, 1 H), 4.36 – 4.26 (m, 2 H), 3.10 – 3.07 (m, 4 H), 2.07 (br s, 1 H), 1.73 – 1.67 (m, J = 4 H), 1.60 – 1.54 (m, 2 H), 1.48 (d, J = 7.1 Hz, 3 H), 0.75 (d, J = 7.0 Hz, 3 H), 0.63 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 410.2556 $(M + H)^+$.

Examples 187 and 188

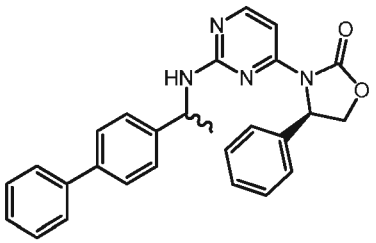


A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (96 mg, 0.40 mmol) and 1-(1-phenyl-1*H*-pyrazol-4-yl)ethanamine (387 mg, 2.97 mmol, 5.2 equiv) in DMSO (1.5 mL) was heated at 110 °C for 1 ½ h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 rnL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 20 to 80%) provided (*S*)-4-isopropyl-3-(2-((*R*)-1-(1-phenyl-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one and (*S*)-4-isopropyl-3-(2-((*S*)-1-(1-phenyl-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one.

Example 187 first eluted product (13 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.16 (d, J = 5.8 Hz, 1 H), 8.10 (s, 1 H), 7.70 – 7.66 (m, 3 H), 7.48 – 7.43 (m, 2 H), 7.37 (d, J = 5.7 Hz, 1 H), 7.32 – 7.28 (m, 1 H), 5.20 (q, J = 6.6 Hz, 1 H), 4.75 (dt, J = 7.7, 4.0 Hz, 1 H), 4.40 – 4.33 (m, 2 H), 2.61 (dtt, J = 11, 7.0, 3.6 Hz, 1 H), 1.60 (d, J = 6.9 Hz, 3 H), 0.96 (d, J = 7.1 Hz, 3 H), 0.87 (d, J = 6.9 Hz, 3 H); HRMS(B) *m/z* 393.2029 $(M + H)^+$.

Example 188 second eluted product (11 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.17 (d, J = 5.8 Hz, 1 H), 8.03 (s, 1 H), 7.68 – 7.62 (m, 3 H), 7.48 – 7.43 (m, 2 H), 7.37 (d, J = 5.8 Hz, 1 H), 7.32 – 7.27 (m, 1 H), 5.19 (q, J = 7.1 Hz, 1 H), 4.74 (dt, J = 8.5, 3.6 Hz, 1 H), 4.38 – 4.29 (m, 2 H), 2.37 – 2.33 (m, 1 H), 1.60 (d, J = 7.1 Hz, 3 H), 0.79 (d, J = 7.1 Hz, 3 H), 0.73 (s, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 393.2039 $(M + H)^+$.

Examples 189 and 190



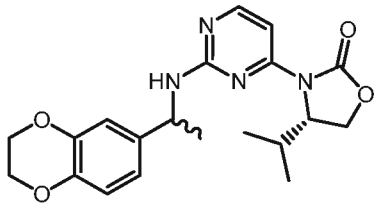
A solution of (*R*)-3-(2-chloropyrimidin-4-yl)-4-phenyloxazolidin-2-one (97 mg, 0.35 mmol), 1-(biphenyl-4-yl)ethanamine hydrochloride (304 mg, 1.30 mmol, 3.7 equiv) and *i*Pr_2NEt (0.307 mL, 1.76 mmol, 5.0 equiv) in DMSO (1 mL) was heated at 110 °C for 1 ½ h and at 130 °C for 20 h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 10 to 50%) provided (*R*)-3-(2-((*R*)-1-(biphenyl-4-yl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one and (*R*)-3-(2-((*S*)-1-(biphenyl-4-yl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one.

Example 189 first eluted product (12 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.10 (d, J = 5.8 Hz, 1 H), 7.58 – 7.55 (m, 2 H), 7.44 – 7.37 (m, 6 H), 7.33 – 7.28 (m, 1 H), 7.24 – 7.14 (m, 6 H), 5.84 (dd, J = 8.6, 3.5 Hz, 1 H), 4.94 (q, J = 6.7 Hz, 1 H), 4.81 (t, J = 8.6 Hz, 1 H), 4.22 (dd, J = 8.8, 3.8 Hz, 1 H), 1.49 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 437.1981 $(M + H)^+$.

Example 190 second eluted product (11 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.10 (d, J = 5.8 Hz, 1 H), 7.60 – 7.54 (m, 4 H), 7.44 – 7.28 (m, 11 H), 5.60 (dd, J = 8.6, 4.0 Hz, 1 H),

4.77 – 4.69 (m, 2 H), 4.19 (dd, J = 8.6, 4.0 Hz, 1 H), 1.25 (d, J = 7.0 Hz, 3 H); HRMS(B) *m/z* 437.1971 $(M + H)^+$.

Examples 191 and 192

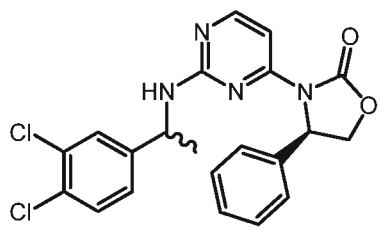


(4*S*)-3-(2-(1-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (example 130, 52 mg) was resolved on a column (IA 4.6 x 100 mm) using 40% *i*PrOH in CO_2 to give (*S*)-3-(2-((*R*)-1-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (*S*)-3-(2-((*S*)-1-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

Example 191 first eluted product (7 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.10 (d, J = 5.6 Hz, 1 H), 7.33 – 7.31 (m, 1 H), 6.82 – 6.74 (m, 3 H), 4.88 (q, J = 7.1 Hz, 1 H), 4.58 – 4.53 (m, 1 H), 4.34 – 4.28 (m, 2 H), 4.21 – 4.18 (m, 4 H), 2.63 (td, J = 7.1, 3.5 Hz, 1 H), 1.47 (d, J = 7.1 Hz, 3 H), 0.99 (d, J = 7.1 Hz, 3 H), 0.86 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 385.1875 $(M + H)^+$.

Example 192 second eluted product (19 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.12 (d, J = 5.8 Hz, 1 H), 7.33 – 7.31 (m, 1 H), 6.78 – 6.72 (m, 3 H), 4.93 (q, J = 6.7 Hz, 1 H), 4.68 – 4.64 (m, 1 H), 4.36 – 4.27 (m, 2 H), 2.08 (br s, 1 H), 1.47 (d, J = 7.1 Hz, 3 H), 0.76 (d, J = 7.1 Hz, 3 H), 0.65 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 385.1873 $(M + H)^+$.

Examples 193 and 194



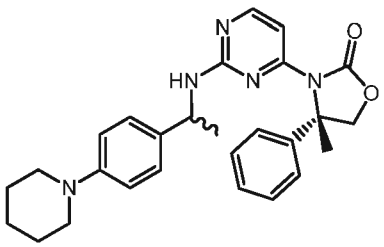
A solution of (*R*)-3-(2-chloropyrimidin-4-yl)-4-phenyloxazolidin-2-one (83 mg, 0.30 mmol) and 1-(3,4-dichlorophenyl)ethanamine (260 mg, 1.37 mmol, 4.5 equiv) in DMSO (1.5 mL) was heated at 110 °C for 1 ½ h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and

concentrated. Silica gel column chromatography (EtOAc/Heptane 0 to 40%) provided (*R*)-3-(2-((*R*)-1-(3,4-dichlorophenyl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one and (*R*)-3-(2-((*S*)-1-(3,4-dichlorophenyl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one.

Example 193 first eluted product (13 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.11 (d, J = 5.6 Hz, 1 H), 7.44 – 7.38 (m, 5 H), 7.35 – 7.31 (m, 1 H), 7.27 – 7.25 (m, 2 H), 7.18 (dd, J = 8.3, 2.3 Hz, 1 H), 5.53 (dd, J = 8.8, 3.8 Hz, 1 H), 4.76 (t, J = 8.8 Hz, 1 H), 4.59 – 4.53 (m, 1 H), 4.18 (dd, J = 8.8, 4.3 Hz, 1 H), 1.22 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 429.0899 (M + H)$^+$.

Example 194 second eluted product (26 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.13 (d, J = 5.6 Hz, 1 H), 7.41 (d, J = 6.1 Hz, 1 H), 7.25 – 7.18 (m, 5 H), 7.09 – 7.06 (m, 2 H), 6.95 – 6.93 (m, 1 H), 5.78 (dd, J = 8.6, 3.5 Hz, 1 H), 4.89 (q, J = 6.7 Hz, 1 H), 4.79 (t, J = 8.6 Hz, 1 H), 4.18 (dd, J = 8.8, 3.8 Hz, 1 H), 1.42 (d. J = 7.1 Hz, 3 H); HRMS(B) *m/z* 429.0887 (M + H)$^+$.

Examples 195 and 196

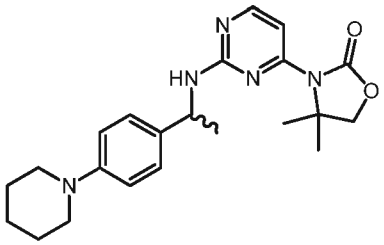


(4*S*)-4-methyl-4-phenyl-3-(2-(1-(4-(piperidin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one (example 141, 51 mg) was resolved on a column (IA 4.6 x 100 mm) using 45% MeOH in CO_2 to give (*S*)-4-methyl-4-phenyl-3-(2-((*S*)-1-(4-(piperidin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one and (*S*)-4-methyl-4-phenyl-3-(2-((*R*)-1-(4-(piperidin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one.

Example 195 first eluted product (21.6 mg) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 5.8 Hz, 1 H), 7.41 (d, J = 5.8 Hz, 1 H), 7.36 – 7.33 (m, 4 H), 7.32 – 7.26 (m, 1 H), 6.88 – 6.82 (br m, 4 H), 5.01 (br s, 1 H), 4.30 (s, 2 H), 3.16 – 3.13 (m, 4 H), 2.20 (s, 3 H), 1.76 – 1.57 (br m, 6 H), 1.37 (d, J = 6.7 Hz, 3 H); HRMS(B) *m/z* 458.2558 (M + H)$^+$.

Example 196 second eluted product (20.6 mg) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 5.8 Hz, 1 H), 7.50 – 7.27 (m, 6 H), 7.05 (d, J = 8.6 Hz, 2 H), 6.96 – 6.92 (br m, 2 H), 5.27 (br s, 1 H), 4.22 (s, 2 H), 3.21 – 3.13 (m, 4 H), 1.78 – 1.76 (br m, 7 H), 1.63 – 1.57 (br m, 2 H), 1.07 (d, J = 6.1 Hz, 3 H); HRMS(B) *m/z* 458.2559 (M + H)$^+$.

Examples 197 and 198

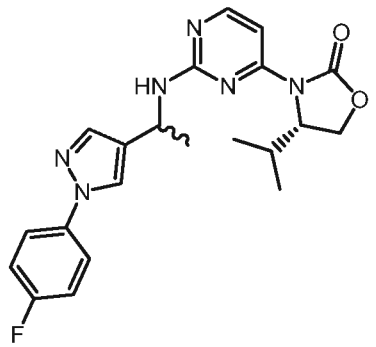


4,4-dimethyl-3-(2-(1-(4-(piperidin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one (example 183, 70 mg) was resolved on a column (IA 4.6 x 100 mm) using 40% MeOH in CO_2 to give (*S*)-4,4-dimethyl-3-(2-(1-(4-(piperidin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one and (*R*)-4,4-dimethyl-3-(2-(1-(4-(piperidin-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one.

Example 197 first eluted product (23.8 mg) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (br d, J = 5.8 Hz, 1 H), 7.28 – 7.23 (m, 3 H), 6.93 (br d, J = 7.7 Hz, 2 H), 5.44 (br s, 1 H), 4.97 (br s, 1 H), 4.05 – 3.99 (m, 2 H), 3.15 – 3.12 (m, 4 H), 1.77 – 1.70 (m, 8 H), 1.61 – 1.54 (m, 5 H), 1.32 (br s, 2 H); HRMS(B) *m/z* 396.2413 $(M + H)^+$.

Example 198 second eluted product (22.3 mg) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (br d, J = 5.5 Hz, 1 H), 7.28 – 7.23 (m, 3 H), 6.94 (br d, J = 7.5 Hz, 2 H), 5.48 (br s, 1 H), 4.97 (br s, 1 H), 4.05 – 3.99 (m, 2 H), 3.15 – 3.12 (m, 4 H), 1.77 – 1.70 (m, 8 H), 1.61 – 1.54 (m, 5 H), 1.31 (br s, 2 H); HRMS(B) *m/z* 396.2410 $(M + H)^+$.

Examples 199 and 200



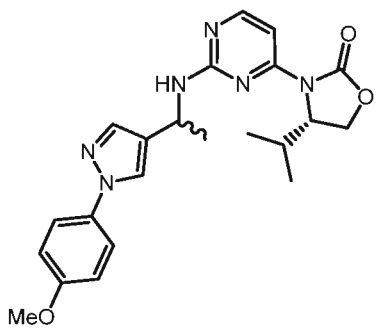
A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (98 mg, 0.41 mmol), 1-(1-(4-fluorophenyl)-1H-pyrazol-4-yl)ethanamine hydrochloride (502 mg, 2.08 mmol, 5.1 equiv) and *i*Pr_2NEt (0.637 mL, 3.65 mmol, 9.0 equiv) in DMSO (1.5 mL) was heated at 110 °C for 16 h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with

EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 20 to 80%) provided (*S*)-3-(2-((*R*)-1-(1-(4-fluorophenyl)-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (*S*)-3-(2-((*S*)-1-(1-(4-fluorophenyl)-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

Example 199 first eluted product (49 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.16 (d, J = 5.8 Hz, 1 H), 8.06 (s, 1 H), 7.71 – 7.67 (m, 3 H), 7.37 (d, J = 5.9 Hz, 1 H), 7.22 – 7.16 (m, 2 H), 5.20 (q, J = 6.6 Hz, 1 H), 4.74 (dt, J = 7.6, 3.8 Hz, 1 H), 4.40 – 4.34 (m, 2 H), 2.60 (dtd, J = 14, 7.0, 3.5 Hz, 1 H), 1.59 (d, J = 6.9 Hz, 3 H), 0.96 (d, J = 7.1 Hz, 3 H), 0.87 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 411.1943 $(M + H)^+$.

Example 200 second eluted product (27 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.17 (d, J = 5.8 Hz, 1 H), 8.00 (s, 1 H), 7.69 – 7.66 (m, 2 H), 7.61 (s, 1 H), 7.37 (d, J = 5.9 Hz, 1 H), 7.22 – 7.16 (m, 2 H), 5.19 (q, J = 6.7 Hz, 1 H), 4.73 (dt, J = 8.1, 3.5 Hz, 1 H), 4.39 – 4.30 (m, 2 H), 2.38 – 2.31 (m, 1 H), 1.59 (d, J = 6.8 Hz, 3 H), 0.79 (d, J = 7.1 Hz, 3 H), 0.73 (d, J = 7.0 Hz, 3 H); HRMS(B) *m/z* 411.1937 $(M + H)^+$.

Examples 201 and 202

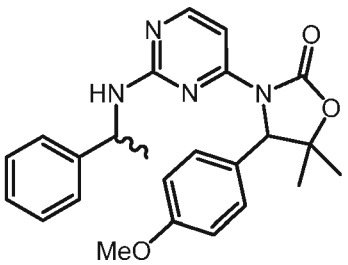


A solution of (*S*)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (93 mg, 0.38 mmol), 1-(1-(4-methoxyphenyl)-1H-pyrazol-4-yl)ethanamine hydrochloride (514 mg, 2.03 mmol, 5.3 equiv) and *i*Pr_2NEt (0.605 mL, 3.46 mmol, 9.0 equiv) in DMSO (1.5 mL) was heated at 110 °C for 16 h. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/Heptane 10 to 70%) provided (*S*)-4-isopropyl-3-(2-((*R*)-1-(1-(4-methoxyphenyl)-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one and (*S*)-4-isopropyl-3-(2-((*S*)-1-(1-(4-methoxyphenyl)-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one.

Example 201 first eluted product (17 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.15 (d, J = 5.8 Hz, 1 H), 7.98 (s, 1 H), 7.63 (s, 1 H), 7.58 – 7.54 (m, 2 H), 7.37 (d, J = 5.8 Hz, 1 H), 7.03 – 6.99 (m, 2 H), 5.19 (q, J = 7.1 Hz, 1 H), 4.75 (dt, J = 7.7, 4.0 Hz, 1 H), 4.40 – 4.33 (m, 2 H), 3.83 (s, 3 H), 2.61 (dtd, J = 14, 7.1, 3.5 Hz, 1 H), 1.59 (d, J = 7.1 Hz, 3 H), 0.96 (d, J = 7.1 Hz, 3 H), 0.87 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 423.2138 $(M + H)^+$.

Example 202 second eluted product (18 mg) ^{1}H NMR (400 MHz, CD_3OD) δ 8.16 (d, J = 5.8 Hz, 1 H), 7.91 (s, 1 H), 7.58 – 7.53 (m, 3 H), 7.37 (d, J = 5.9 Hz, 1 H), 7.03 – 6.99 (m, 2 H), 5.18 (q, J = 6.7 Hz, 1 H), 4.76 – 4.72 (m, 1 H), 4.39 – 4.30 (m, 2 H), 3.83 (s, 3 H), 2.31 (br s, 1 H), 1.59 (d, J = 7.1 Hz, 3 H), 0.80 (d, J = 7.1 Hz, 3 H), 0.73 (d, J = 7.1 Hz, 3 H); HRMS(B) *m/z* 423.214 $(M + H)^+$.

Examples 203 and 204

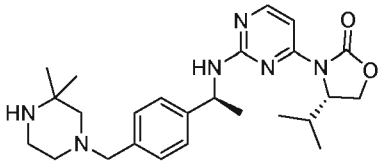


4-(4-methoxyphenyl)-5,5-dimethyl-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one (example 54, 62 mg) was resolved in on a column (AD-H 4.6 x 100 mm) with 30% MeOH modified with 0.2% Et_2NH in CO_2 to give (*S*)-4-(4-methoxyphenyl)-5,5-dimethyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one and (*R*)-4-(4-methoxyphenyl)-5,5-dimethyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one.

Example 203 first eluted product (22 mg) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (br d, J = 5.6 Hz, 1 H), 7.53 (d, J = 5.7 Hz, 1 H), 7.37 – 7.24 (m, 5 H), 7.08 – 7.05 (m, 2 H), 6.92 – 6.89 (m, 2 H), 5.47 (br s, 1 H), 5.02 (br s, 1 H), 4.66 (br s, 1 H), 3.83 (s, 3 H), 1.50 (s, 3 H), 1.28 (br d, J = 6.6 Hz, 3 H), 1.01 (s, 3 H); HRMS(B) *m/z* 419.208 $(M + H)^+$.

Example 204 second eluted product (22.2 mg) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (br d, J = 6.1 Hz, 1 H), 7.55 (d, J = 5.8 Hz, 1 H), 7.28 – 7.22 (m, 3 H), 7.08 (br s, 2 H), 7.01 (d, J = 8.6 Hz, 2 H), 6.79 (d, J = 8.6 Hz, 2 H), 5.40 (br s, 1 H), 5.30 (s, 1 H), 4.83 (br s, 1 H), 3.78 (s, 3 H), 1.66 (s, 3 H), 1.51 (d, J = 6.8 Hz, 3 H), 1.04 (s, 2 H); HRMS(B) *m/z* 419.2083 $(M + H)^+$.

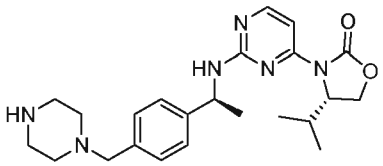
Example 205



To a solution of tert-butyl 4-(4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzyl)-2,2-dimethylpiperazine-1-carboxylate (78 mg, 0.14 mmol) in DCM (1 mL) was added TFA (1 mL, 12 mmol) slowly at -78 °C. The reaction was stirred at room temperature for 1 h then was concentrated and diluted with DCM (10 mL). The solution was stirred with 3 eq. of MP-carbonate resin (3.28 mmol/g, Biotage) for 1 h at room temperature. The resin was removed by filtration and washed (2 x 5 mL) with DCM. The filtrate was concentrated and purified through HPLC to give (S)-3-(2-(((S)-1-(4-((3,3-dimethylpiperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one as a white solid (23 mg, 36% yield).

^{1}H NMR (400 MHz, MeOD) δ 8.07 (d, J = 5.8 Hz, 1H), 7.30 (d, J = 5.8 Hz, 1H), 7.26 – 7.18 (m, 4H), 5.00 (q, J = 6.9 Hz, 1H), 4.62 (br s, 1H), 4.36 – 4.16 (m, 2H), 3.36 (s, 2H), 2.81 (br t, J = 5.1 Hz, 2H), 2.30 (br s, 2H), 2.10 (br s, 2H), 1.82 (br s, 1H), 1.45 (d, J = 7.0 Hz, 3H), 1.08 (s, 6H), 0.67 (br s, 3H), 0.52 (br s, 3H); HRMS(B) m/z 453.2969 (M + H)+.

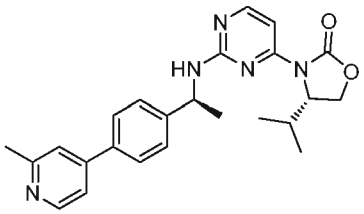
Example 206



A mixture of benzyl 4-(4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzyl)piperazine-1-carboxylate (190 mg, 0.34 mmol) and 10% Pd-C (40 mg, 0.038 mmol) in ethanol (3.4 ml) is stirred under 1 atmosphere pressure of hydrogen for 3 h. The mixture is filtered and concentrated to give (S)-4-isopropyl-3-(2-(((S)-1-(4-(piperazin-1-ylmethyl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one as a white solid (97 mg, 67.2% yield).

^{1}H NMR (400 MHz, MeOD) δ 8.08 (d, J = 5.8 Hz, 1H), 7.30 (d, J = 5.8 Hz, 1H), 7.28 – 7.19 (m, 4H), 5.01 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.37 – 4.14 (m, 2H), 3.44 (s, 2H), 2.78 (t, J = 5.0 Hz, 4H), 2.39 (br s, 4H), 1.89 (br s, 1H), 1.45 (d, J = 7.0 Hz, 3H), 0.68 (br s, 3H), 0.52 (br s, 3H); HRMS(B) m/z 425.2662 (M + H)+.

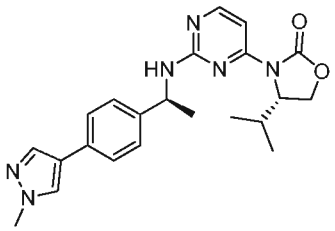
Example 207



In a 5 mL microwave vial a solution of (S)-3-(2-((S)-1-(4-bromophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (86 mg, 0.21 mmol), pyridin-4-ylboronic acid (26 mg, 0.21 mmol), Sodium bicarbonate (0.21 mL, 0.42 mmol, 2 M solution) in Dioxane (1 mL) was bubbled N2 for 3 min then Cl2Pd(dppf).CH_2Cl_2 (17 mg, 0.021 mmol) was added. The capped tube was heated to 100°C for 16 h. After cooling the reaction mixture was diluted with EtOAc (10 mL) and washed with water (10 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 10 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. The crude material was purified through silica gel column chromatography (EtOAc in Heptane 12 to 100%) to yield (S)-4-isopropy-3-(2-(((S)-1-(4-(2-yl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one as a white solid (27 mg, 30.5% yield).

^{1}H NMR (400 MHz, MeOD) δ 8.35 (d, J = 5.4 Hz, 1H), 8.08 (d, J = 5.9 Hz, 1H), 7.64 – 7.60 (m, 2H), 7.49 (br d, J = 1.8 Hz, 1H), 7.43 – 7.39 (m, 3H), 7.30 (d, J = 5.8 Hz, 1H), 5.02 (q, J = 6.8 Hz, 1H), 4.55 (br s, 1H), 4.27 – 4.18 (m, 2H), 2.52 (s, 3H), 1.65 (br s, 1H), 1.49 (d, J = 7.1 Hz, 3H), 0.55 (br s, 3H), 0.43 (br s, 3H); HRMS(B) m/z 418.2227 (M + H)+.

Example 208

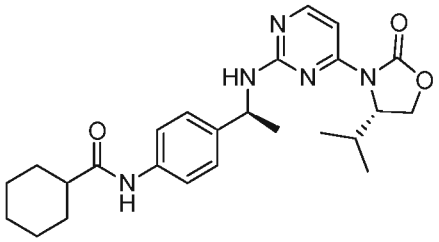


To a solution of tert-butyl 4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl((S)-1-(4-(1-methyl-1H-pyrazol-4-yl)phenyl)ethyl)carbamate (45 mg, 0.09 mmol) in DCM (1 mL) was added TFA (1 mL, 12 mmol) slowly at -78 °C. The reaction was stirred at room temperature for 1 h then was concentrated and diluted with DCM (10 mL). The solution was washed with saturated $NaHCO_3$ solution and brine. After separation, the aqueous phase was extracted with DCM (3 x 10 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated to give (S)-4-isopropyl-3-(2-(((S)-1-(4-(1-methyl-1H-

pyrazol-4-yl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one as a white solid (35 mg, 97% yield).

^{1}H NMR (400 MHz, MeOD) δ 8.09 (d, J = 5.9 Hz, 1H), 7.86 (s, 1H), 7.72 (d, J = 0.8 Hz, 1H), 7.45 – 7.41 (m, 2H), 7.30 (d, J = 5.8 Hz, 1H), 7.25 (d, J = 7.9 Hz, 2H), 4.97 (q, J = 7.0 Hz, 1H), 4.58 (br s, 1H), 4.30 – 4.21 (m, 2H), 3.86 (s, 3H), 1.66 (br s, 1H), 1.48 (d, J = 7.0 Hz, 3H), 0.60 (br s, 3H), 0.48 (br s, 3H); HRMS(B) m/z 407.2179 (M + H)+.

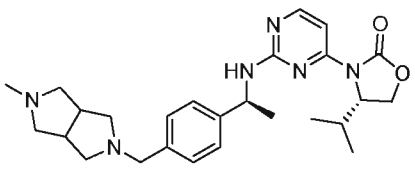
Example 209



Following the above procedure for Example 208, N-(4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)phenyl)cyclohexanecarboxamide was prepared as a white solid (45 mg, 92 % yield) from tert-butyl (S)-1-(4-(cyclohexanecarboxamido)phenyl)ethyl(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)carbamate.

^{1}H NMR (400 MHz, MeOD) δ 8.08 (d, J = 5.9 Hz, 1H), 7.47 – 7.41 (m, 2H), 7.30 (d, J = 5.8 Hz, 1H), 7.23 – 7.16 (m, 2H), 4.95 (q, J = 7.0 Hz, 1H), 4.60 (br s, 1H), 4.32 – 4.19 (m, 2H), 2.30 (tt, J = 11.8, 3.3 Hz, 1H), 1.89 – 1.72 (m, 4H), 1.72 – 1.63 (m, 1H), 1.54 – 1.39 (m, 5H), 1.39 – 1.14 (m, 4H), 0.67 (br s, 3H), 0.54 (br s, 3H); HRMS(B) m/z 452.2636 (M + H)+.

Example 210

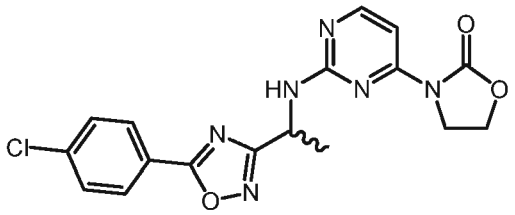


A solution of 4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzaldehyde (35 mg, 0.1 mmol) and 2-methyloctahydropyrrolo[3,4-c]pyrrole (14 mg, 0.11 mmol) in MeOH (2 mL) was added acetic acid (7.2 mg, 0.12 mmol) and 5-Ethyl-2-methylpyridine borane complex (14 mg, 0.1 mmol, sigmaaldrich). The solution was stirred at 50 °C for 4 h then 5 drops of water was added. The solution was stirred at room temperature for another 2 h then diluted with EtOAc (10 mL) and

washed with water (10 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 10 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. The crude material was purified through HPLC to give (4S)-4-isopropyl-3-(2-(((1S)-1-(4-((5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one as a white solid (10 mg, 21.7% yield).

^{1}H NMR (400 MHz, MeOD) δ 8.07 (d, J = 5.8 Hz, 1H), 7.29 (d, J = 5.8 Hz, 1H), 7.25 – 7.20 (m, 4H), 5.00 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.31 – 4.23 (m, 2H), 3.55 – 3.48 (m, 2H), 2.68 (dh, J = 13.6, 4.3, 3.7 Hz, 2H), 2.64 – 2.48 (m, 4H), 2.36 – 2.29 (m, 4H), 2.28 (s, 4H), 1.84 (br s, 1H), 1.45 (d, J = 7.0 Hz, 3H), 0.68 (br s, 3H), 0.52 (br s, 3H); HRMS(B) m/z 465.2975 (M + H)+.

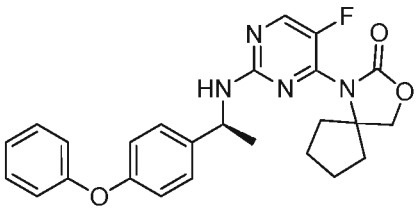
Example 211



A solution of 3-(2-fluoropyrimidin-4-yl)oxazolidin-2-one (89.1 mg, 0.487 mmol), 1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethanamine (115.9 mg, 0.518 mmol, 1.06 equiv), and DIPEA (0.20 mL, 1.1 mmol, 2.4 equiv) in DMSO (1.5 mL) was heated at 110 °C for 100 min. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (MeOH in CH_2Cl_2 0 to 5%) provided 3-(2-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one (18.2 mg, white solid) in 10.3% yield.

^{1}H NMR (400 MHz, DMSO-d_6) 8.21 (br s, 1 H), 8.00 – 7.97 (m, 2 H), 7.65 – 7.61 (m, 2 H), 7.30 (br s, 1 H), 5,28 (br s, 1 H), 4.44 – 4.38 (br m, 2 H), 4.14 – 4.08 (m, 1 H), 3.99 (br s, 0.5 H), 3.75 (br s, 0.5 H), 1.64 (d, J = 7.0 Hz, 3 H); HRMS(B) *m/z* 387.0962 $(M + H)^+$

Example 212

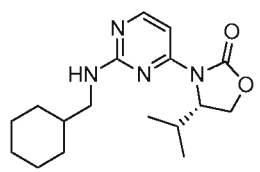
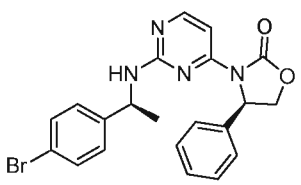
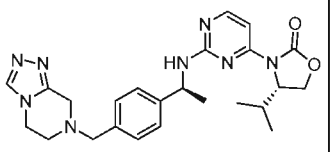


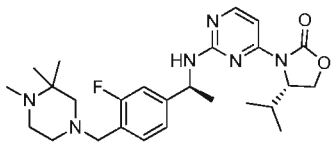
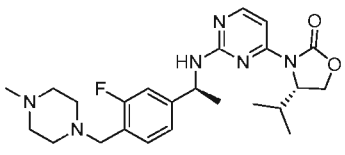
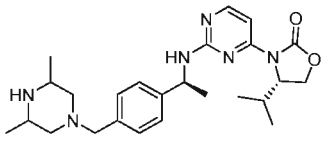
A solution of (S)-1-(4-phenoxyphenyl)ethanamine hydrochloride (281mg, 1.125mmol), 3-(2-chloro-5-fluoropyrimidin-4-yl)oxazolidin-2-one (103mg, 0.379mmol) and DIPEA (0.331ml, 1.896mmol) in DMSO was heated to 110ºC for 1h. LCMS showed little product. Heated for an additional 16h. LCMS still showed starting material. Added an additional 5 equivalents of DIPEA and 1 equivalent of KF. Heated to 110ºC for 2h. LCMS shows product. The reaction mixture was diluted with EtOAc (8 mL) and washed with water (30 mL). After separation, the aqueous phase was extracted with EtOAc (3 x 8 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Purified by column chromatography (10% to 50% EtOAc/Heptane) to give (S)-1-(5-fluoro-2-(1-(4-phenoxyphenyl)ethylamino) pyrimidin-4-yl)-3-oxa-1-azaspiro[4.4]nonan-2-one (62mg, 0.138mmol).

^{1}H NMR (400 MHz, MeOD) δ 8.25 (d, J = 2.8 Hz, 1H), 7.34 (ddd, J = 8.7, 4.9, 2.3 Hz, 4H), 7.16 – 7.04 (m, 1H), 7.02 – 6.90 (m, 4H), 4.96 (q, J = 7.0 Hz, 1H), 4.30 – 4.25 (m, 2H), 2.38 (dt, J = 13.1, 8.4 Hz, 1H), 2.02 (br s, 1H), 1.80 (ddd, J = 12.7, 7.3, 4.2 Hz, 1H), 1.71 – 1.63 (br m, 2H), 1.61 – 1.49 (m, 3H), 1.53 (d, J = 7.0 Hz, 3 H). HRMS(B) (M+H) 449.1984 Calc'd (M+H) 449.1989

The compounds in Table 7 were prepared using methods substantially similar to those described for the preparation of Examples 1, 113, 211 and 212.

Table 7.

213	214:	215
		
216	217	218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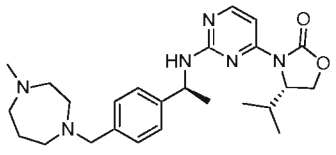	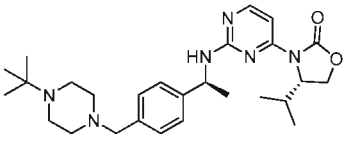	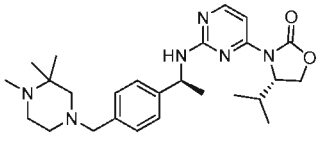
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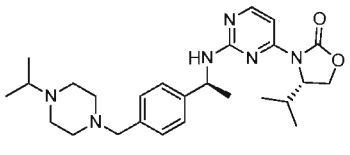	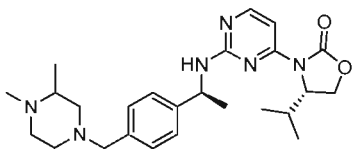	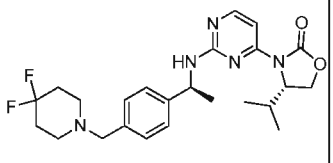
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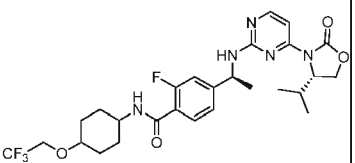
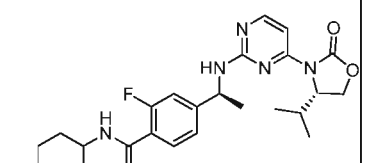
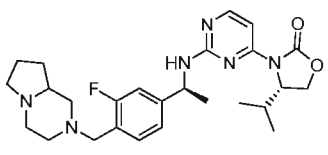
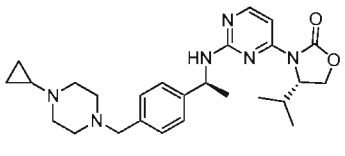
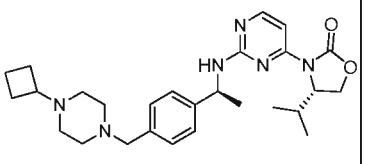
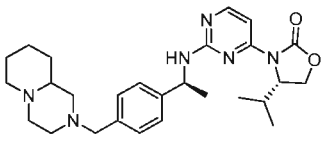
		
228	229	230
		
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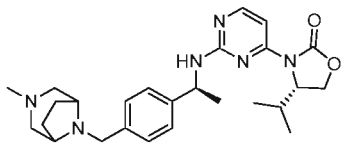	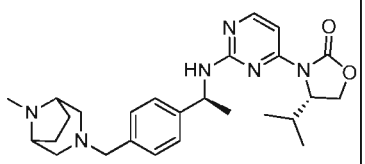	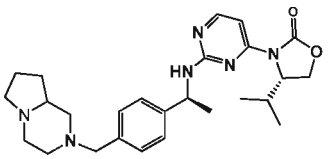
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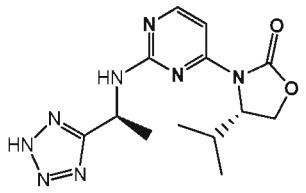	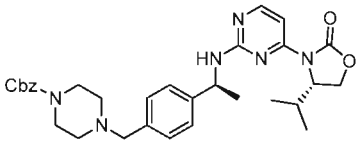	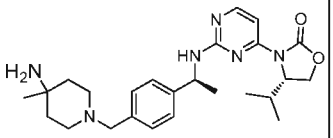
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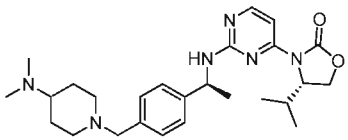	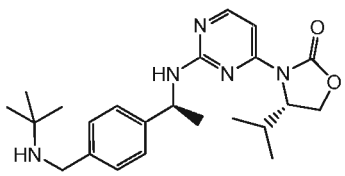	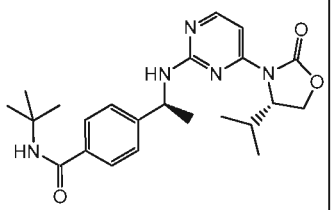
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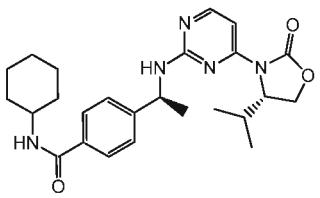	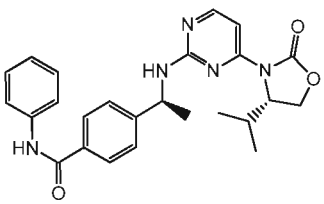	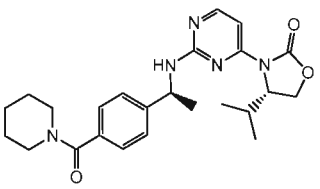
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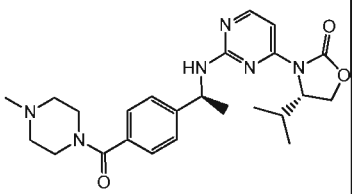	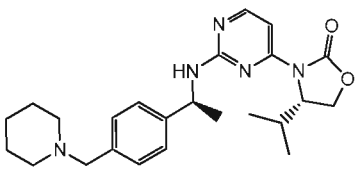	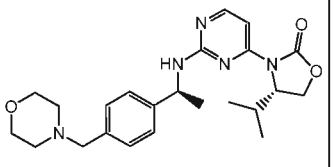
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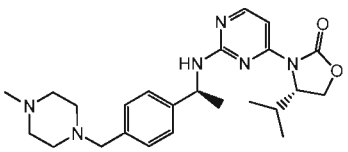	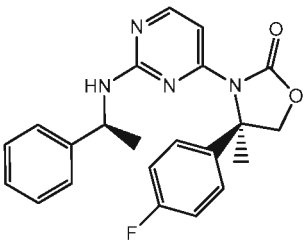	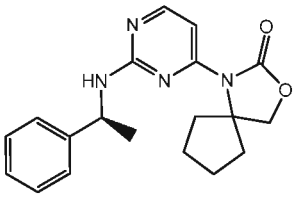
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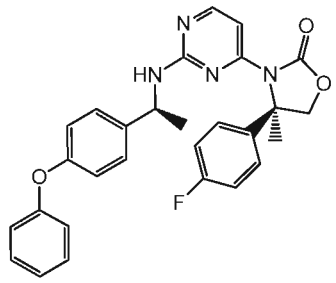	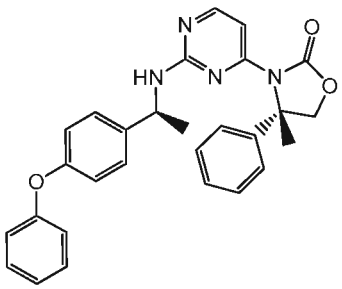	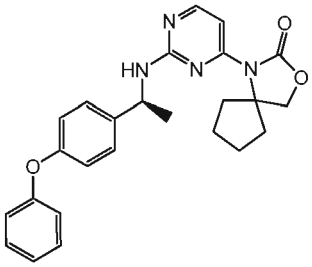
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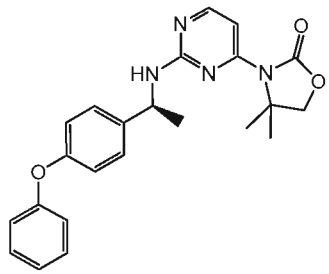	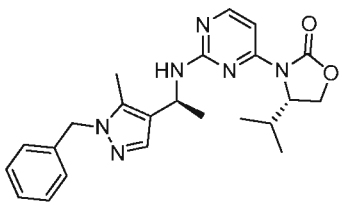	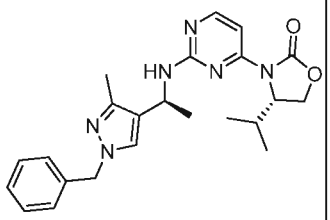
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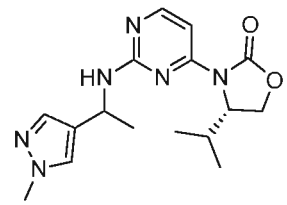	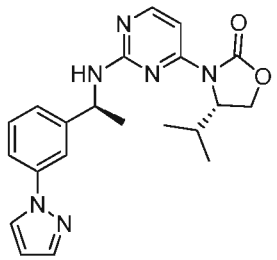	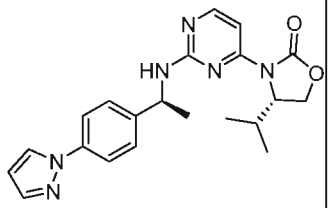
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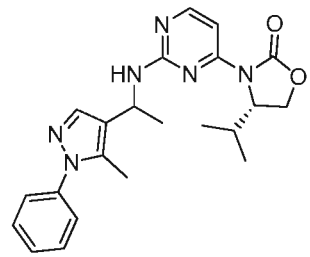	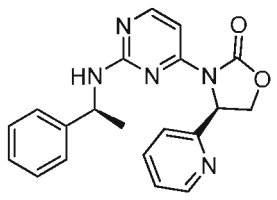	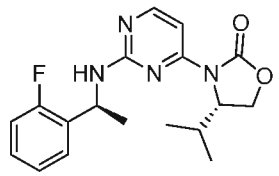
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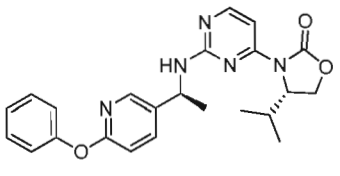	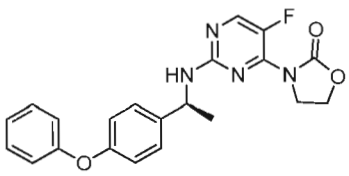	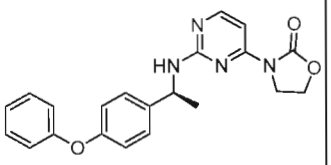
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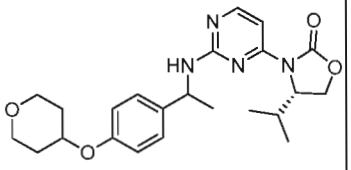	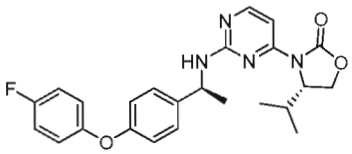	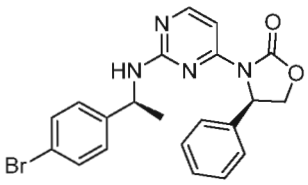
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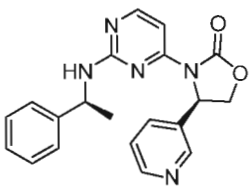	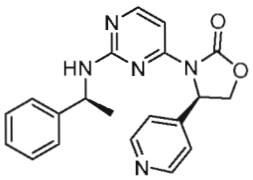	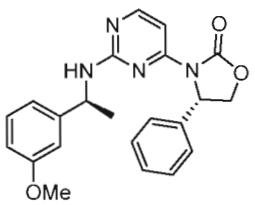
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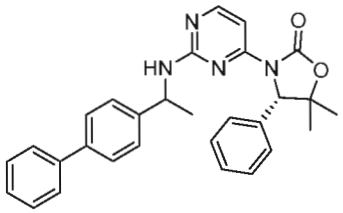	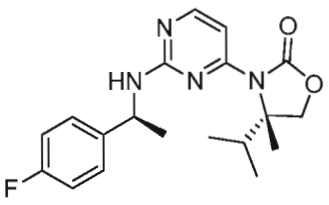	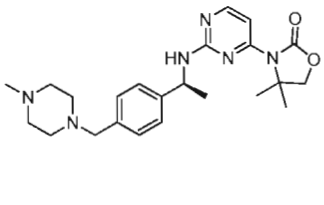
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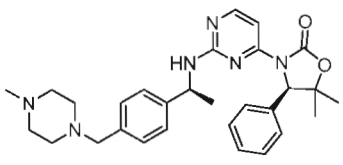	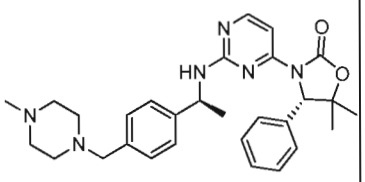	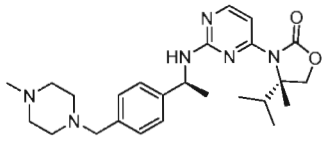
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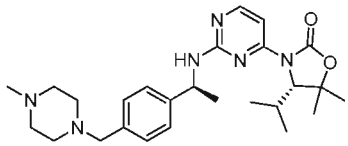	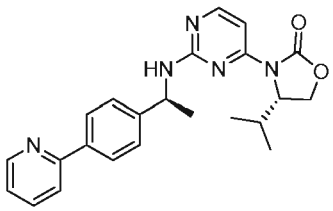	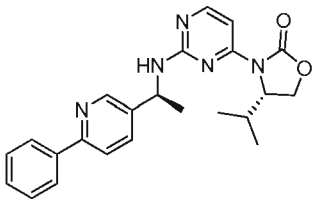
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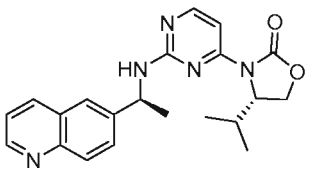	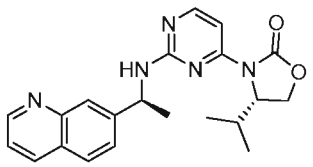	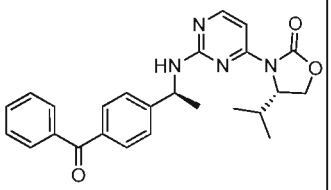
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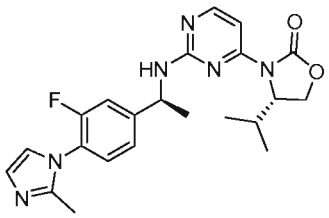	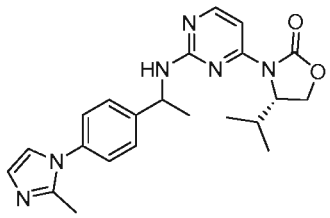	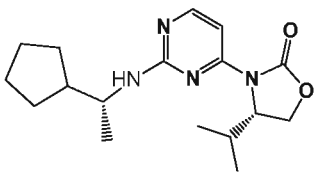
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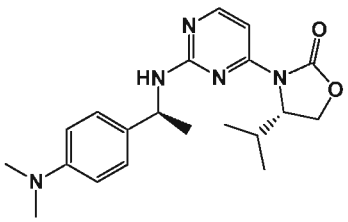	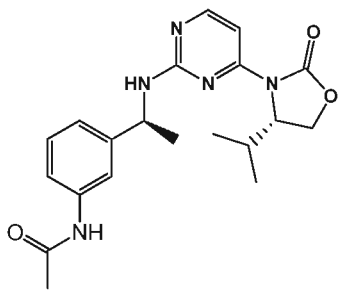	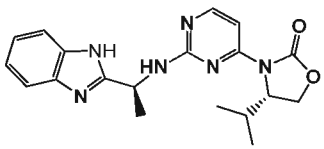
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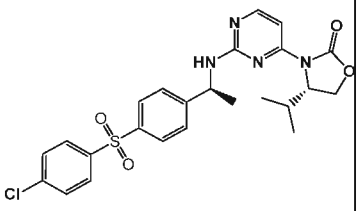	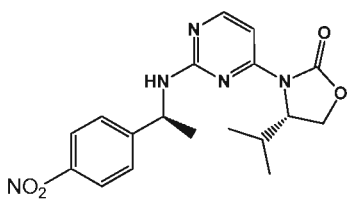	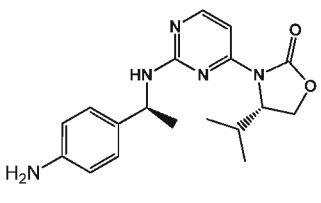
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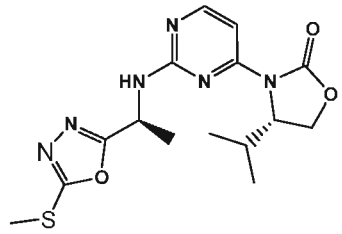	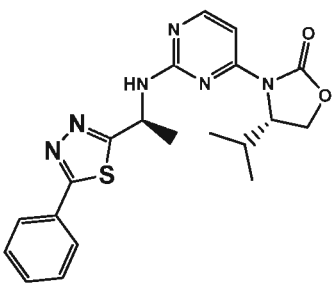	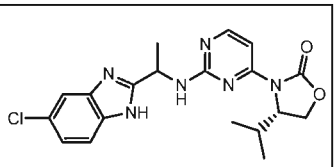
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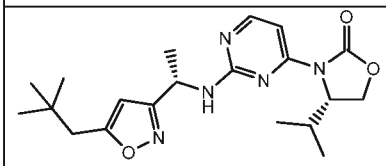	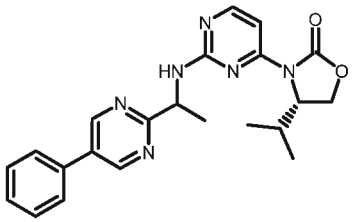	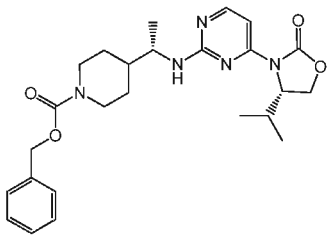
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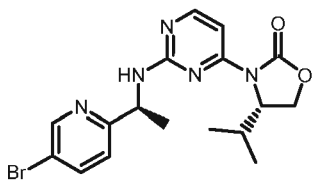	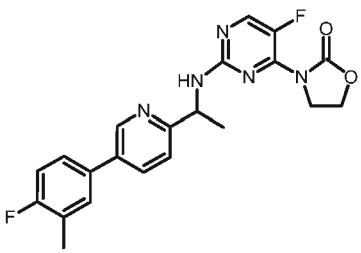	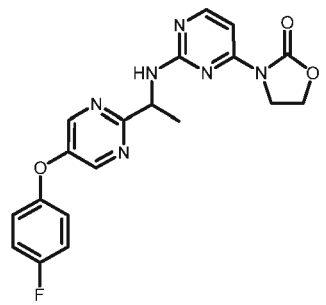
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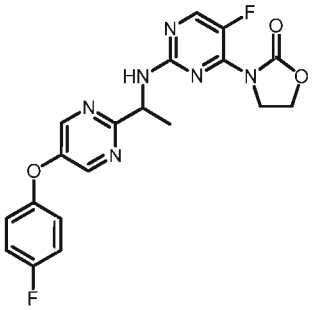	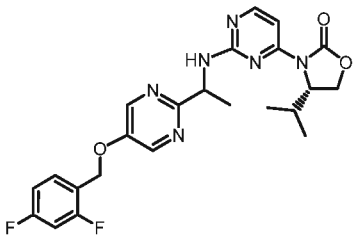	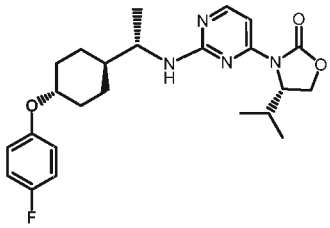
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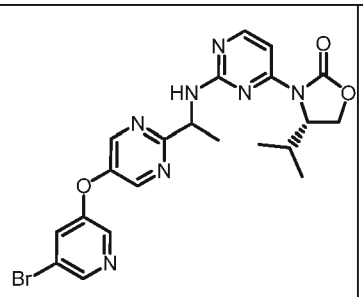	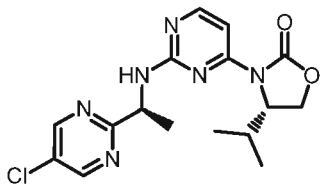	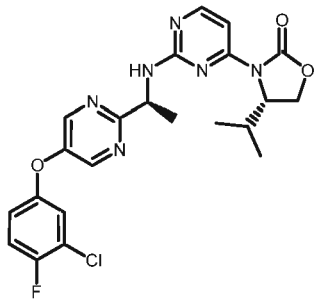
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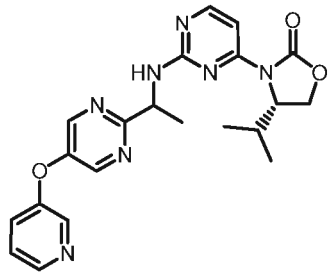	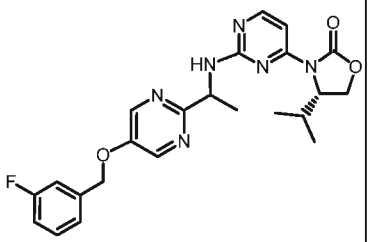	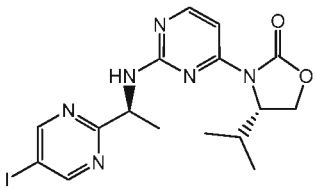
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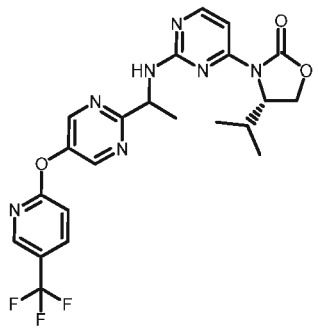	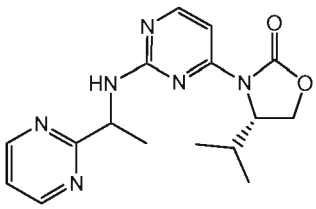	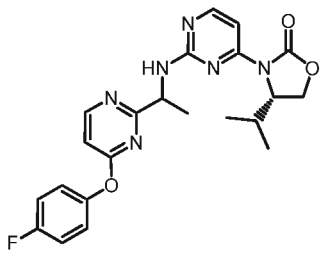
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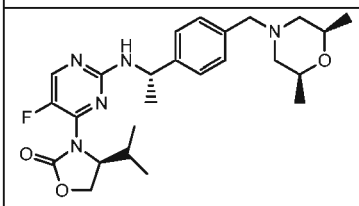		

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Table 8. Chemical name, NMR chemical shifts and LCMS signal for each compound listed in Table 7.

Example: Name	^{1}H NMR **(400 MHz,** CD_3OD**) δ ppm (other solvents described)**	**LCMS**
213: (S)-3-(2-((cyclohexylmethyl)amino) pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.08 (d, J = 5.8 Hz, 1 H), 7.33 (d, J = 5.8 Hz, 1 H), 4.80 - 4.76 (m, 1 H), 4.42 - 4.37 (m, 2 H), 3.24 (dd, J = 13, 6.3 Hz, 1 H), 3.10 (dt, J = 13, 6.8 Hz, 1 H), 2.68 - 2.60 (m, 1 H), 1.82 - 1.56 (m, 7 H), 1.31 - 1.18 (m, 4 H), 0.98 (d, J = 7.1 Hz, 3 H), 0.87 (d, J = 7.0 Hz, 3 H);	HRMS(B) m/z 319.2132 (M + H)+
214: (R)-3-(2-(((S)-1-(4-bromophenyl)ethyl)amino) pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.46 (d, *J* = 5.8 Hz, 1H), 7.85 – 7.73 (m, 5H), 7.73 – 7.67 (m, 1H), 7.64 (dd, *J* = 7.1, 1.8 Hz, 2H), 7.58 – 7.52 (m, 2H), 5.92 (dd, *J* = 8.6, 4.0 Hz, 1H), 5.13 (t, *J* = 8.7 Hz, 1H), 4.98 (d, *J* = 7.0 Hz, 1H), 4.55 (dd, *J* = 8.7, 4.0 Hz, 1H), 1.58 (d, *J* = 7.0 Hz, 3H);	HRMS(B) *m/z* 439.0762 M^+
215: (S)-3-(2-(((S)-1-(4-((5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.38 (s, 1H), 8.07 (d, J = 5.9 Hz, 1H), 7.30 (d, J = 6.0 Hz, 1H), 7.28 (s, 4H), 5.03 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.31 – 4.23 (m, 2H), 4.08 (t, J = 5.5 Hz, 2H), 3.78 – 3.69 (m, 4H), 2.89 (td, J = 5.4, 2.1 Hz, 2H), 1.80 (br s, 1H), 1.46 (d, J = 7.0 Hz, 3H), 0.68 (br s, 3H), 0.53 (br s, 3H)	HRMS(B) m/z 463.2567 (M + H)+
216: (S)-3-(2-(((S)-1-(3-fluoro-4-((3,3,4-trimethylpiperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.04 (d, J = 5.9 Hz, 1H), 7.36 – 7.15 (m, 2H), 7.02 (dd, J = 7.9, 1.8 Hz, 1H), 6.94 (dd, J = 11.0, 1.8 Hz, 1H), 4.95 (q, J = 7.0 Hz, 1H), 4.58 (br s, 1H), 4.32 – 4.11 (m, 2H), 3.38 (br s, 2H), 2.46 (br t, J = 4.9 Hz, 2H), 2.32 (br s, 2H), 2.14 (br s, 2 H), 2.10 (s, 3H), 1.73 (br s, 1H), 1.40 (d, J = 7.1 Hz, 3H), 0.95 (s, 3H), 0.95 (s, 3H), 0.63 (br s, 3H), 0.49 (br s, 3H)	HRMS(B) m/z 485.3107 (M + H)+
217: (S)-3-(2-(((S)-1-(3-fluoro-4-((4-methylpiperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.09 (d, J = 6.0 Hz, 1H), 7.41 – 7.20 (m, 2H), 7.11 (dd, J = 7.8, 1.7 Hz, 1H), 7.04 (dd, J = 11.0, 1.8 Hz, 1H), 5.01 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.36 – 4.16 (m, 2H), 3.57 (s, 2H), 2.82 (br s, 4H), 2.60 (br s, 4H), 2.51 (s, 3H), 1.83 (br s, 1H), 1.45 (d, J = 7.1 Hz, 3H), 0.69 (s, 3H), 0.54 (s, 3H)	HRMS(B) m/z 457.2699 (M + H)+.
218: (4S)-3-(2-(((1S)-1-(4-((3,5-dimethylpiperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.07 (d, J = 5.8 Hz, 1H), 7.30 (d, J = 5.8 Hz, 1H), 7.28 – 7.19 (m, 4H), 5.01 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.34 – 4.18 (m, 2H), 3.46 – 3.39 (m, 2H), 2.89 – 2.76 (m, 2H), 2.76 – 2.67 (m, 2H), 1.82 (br s, 1H), 1.59 (t, J = 10.9 Hz, 2H), 1.45 (d, J = 7.0 Hz, 3H), 0.98 (s, 3H), 0.96 (s, 3H), 0.68 (br s, 3H), 0.52 (br s, 3H)	HRMS(B) m/z 453.2971 (M + H)+
219: (S)-4-isopropyl-3-(2-(((S)-1-(4-((4-methyl-1,4-diazepan-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-	8.07 (d, J = 5.8 Hz, 1H), 7.30 (d, J = 5.9 Hz, 1H), 7.28 – 7.24 (m, 4H), 5.02 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.35 – 4.22 (m, 2H), 3.67 – 3.59 (m, 2H), 3.09 – 3.07 (m, 2H), 2.99 (dd, J = 6.2, 3.5 Hz, 2H),	HRMS(B) m/z 453.2968 (M + H)+

yl)oxazolidin-2-one	2.79 – 2.77 (m, 2H), 2.72 (t, J = 6.0 Hz, 2H), 2.63 (s, 3H), 1.93 – 1.87 (m, 3H), 1.80 (br s, 1H), 1.45 (d, J = 7.0 Hz, 3H), 0.69 (br s, 3H), 0.54 (br s, 3H)	
220: (S)-3-(2-(((S)-1-(4-((4-(tert-butyl)piperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.07 (d, J = 5.9 Hz, 1H), 7.30 (d, J = 5.8 Hz, 1H), 7.24 (q, J = 8.2 Hz, 4H), 5.01 (q, J = 6.9 Hz, 1H), 4.63 (br s, 1H), 4.31 – 4.24 (m, 2H), 3.49 – 3.42 (m, 2H), 2.60 (br s, 4H), 2.46 (br s, 4H), 1.76 (br s, 1H), 1.45 (d, J = 7.0 Hz, 3H), 1.03 (s, 9H), 0.69 (s, 3H), 0.53 (s, 3H)	HRMS(B) m/z 481.3283 (M + H)+
221: (S)-4-isopropyl-3-(2-(((S)-1-(4-((3,3,4-trimethylpiperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	8.08 (d, J = 5.8 Hz, 1H), 7.30 (d, J = 5.8 Hz, 1H), 7.26 – 7.18 (m, 4H), 5.01 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.31 – 4.24 (m, 2H), 3.37 (s, 2H), 2.54 (br t, J = 5.0 Hz, 2H), 2.38 (br s, 2H), 2.17 (s, 3H),2.14 (br s, 2H), 1.85 (br s, 1H), 1.45 (d, J = 7.0 Hz, 3H), 1.01 (s, 6H), 0.68 (br s, 3H), 0.53 (br s, 3H)	HRMS(B) m/z 467.3127 (M + H)+
222: (S)-4-isopropyl-3-(2-(((S)-1-(4-((4-isopropylpiperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	8.07 (d, J = 5.8 Hz, 1H), 7.30 (d, J = 5.8 Hz, 1H), 7.24 (q, J = 8.3 Hz, 4H), 5.01 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.31 – 4.24 (m, 2H), 3.46 (s, 2H), 2.63 – 2.44 (m, 9H), 1.84 (br s, 1H), 1.45 (d, J = 7.1 Hz, 3H), 1.02 (d, J = 6.5 Hz, 6H), 0.68 (br s, 3H), 0.53 (br s, 3H)	HRMS(B) m/z 467.3120 (M + H)+
223: (4S)-3-(2-(((1S)-1-(4-((3,4-dimethylpiperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.07 (d, J = 5.9 Hz, 1H), 7.30 (d, J = 5.8 Hz, 1H), 7.23 (q, J = 8.1 Hz, 4H), 5.01 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.35 – 4.20 (m, 2H), 3.51 – 3.35 (m, 2H), 2.82 – 2.61 (m, 3H), 2.36 – 2.24 (m, 1H), 2.23 (s, 3H), 2.20 – 2.08 (m, 2H), 1.89 – 1.80 (m, 2H), 1.45 (d, J = 7.0 Hz, 3H), 0.99 (d, J = 6.3 Hz, 3H), 0.68 (br s, 3H), 0.52 (br s, 3H)	HRMS(B) m/z 453.2960 (M + H)+
224: (S)-3-(2-(((S)-1-(4-((4,4-difluoropiperidin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.08 (d, J = 5.8 Hz, 1H), 7.31 (d, J = 5.8 Hz, 1H), 7.25 (q, J = 8.2 Hz, 4H), 5.02 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.32 – 4.24 (m, 2H), 3.51 (s, 2H), 2.52 (br t, J = 5.8 Hz, 4H), 1.98 – 1.87 (m, 4H), 1.81 (br s, 1H), 1.46 (d, J = 7.0 Hz, 3H), 0.68 (br s, 3H), 0.52 (br s, 3H)	HRMS(B) m/z 460.2514 (M + H)+
225: 2-fluoro-4-((S)-1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)ethyl)-N-(4-(2,2,2-trifluoroethoxy)cyclohexyl) benzamide	8.09 (d, J = 5.7 Hz, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.33 (d, J = 5.8 Hz, 1H), 7.20 (dd, J = 7.9, 1.6 Hz, 1H), 7.13 (dd, J = 12.1, 1.7 Hz, 1H), 5.03 (q, J = 7.0 Hz, 1H), 4.61 (br s, 1H), 4.31 – 4.24 (m, 2H), 3.97 – 3.80 (m, 3H), 3.65 (dt, J = 4.7, 2.3 Hz, 1H), 1.90 (dt, J = 12.5, 4.0 Hz, 2H), 1.72 – 1.58 (m, 6H), 1.47 (d, J = 7.0 Hz, 3H), 0.68 (br s, 3H), 0.56 (br s, 3H)	HRMS(B) m/z 568.2549 (M + H)+
226: 2-fluoro-N-(4-hydroxy-4-methylcyclohexyl)-4-((S)-1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-	8.09 (d, J = 6.0 Hz, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.33 (d, J = 5.8 Hz, 1H), 7.20 (dd, J = 8.0, 1.6 Hz, 1H), 7.13 (dd, J = 12.0, 1.7 Hz, 1H), 5.03 (q, J = 7.0 Hz, 1H), 4.61 (br s, 1H), 4.31 – 4.25 (m, 2H), 3.89 (dt, J = 9.4,	HRMS(B) m/z 500.2589 (M + H)+

yl)pyrimidin-2-yl)amino)ethyl)benzamide	4.7 Hz, 1H), 1.95 – 1.82 (m, 2H), 1.75 – 1.49 (m, 7H), 1.47 (d, J = 7.0 Hz, 3H), 1.21 (s, 3H), 0.68 (br s, 3H), 0.56 (br s, 3H)	
227: (4S)-3-(2-(((1S)-1-(3-fluoro-4-((hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.09 (d, J = 5.8 Hz, 1H), 7.32 (d, J = 5.8 Hz, 1H), 7.29 (t, J = 7.7 Hz, 1H), 7.10 (dd, J = 7.9, 1.8 Hz, 1H), 7.03 (dd, J = 11.0, 1.8 Hz, 1H), 5.00 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.31 – 4.24 (m, 2H), 3.62 – 3.53 (m, 2H), 2.98 – 2.91 (m, 3H), 2.80 – 2.75 (m, 1H), 2.34 – 2.18 (m, 2H), 2.18 – 2.01 (m, 2H), 1.90 (t, J = 10.4 Hz, 1H), 1.83 – 1.65 (m, 4H), 1.45 (d, J = 7.0 Hz, 3H), 1.36 – 1.27 (m, 1H), 0.68 (br s, 3H), 0.54 (br s, 3H)	HRMS(B) m/z 483.2878 (M + H)+
228: (S)-3-(2-((S)-1-(4-((4-cyclopropylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.07 (d, J = 5.9 Hz, 1H), 7.30 (d, J = 5.8 Hz, 1H), 7.23 (q, J = 8.0 Hz, 4H), 5.01 (q, J = 7.0 Hz, 1H), 4.62 (br s, 1H), 4.35 – 4.19 (m, 2H), 3.45 (s, 2H), 2.62 (br s, 4H), 2.41 (br s, 4H), 1.79 (br s, 1H), 1.65 – 1.56 (m, 1H), 1.45 (d, J = 7.0 Hz, 3H), 0.67 (br s, 3H), 0.52 (br s, 3H), 0.45 – 0.38 (m, 2H), 0.38 – 0.29 (m, 2H)	HRMS(B) m/z 465.2975 (M + H)+
229: (S)-3-(2-((S)-1-(4-((4-cyclobutylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.08 (d, J = 7.2 Hz, 1H), 7.70 (d, J = 7.2 Hz, 1H), 7.47 – 7.24 (m, 4H), 5.28 – 5.06 (m, 1H), 4.66 (q, J = 4.8, 4.4 Hz, 1H), 4.34 (d, J = 5.7 Hz, 2H), 3.91 (s, 2H), 3.61 (p, J = 8.3 Hz, 1H), 3.20 (br s, 4H), 3.02 (br s, 4H), 2.32 – 2.04 (m, 4H), 1.90 – 1.66 (m, 3H), 1.52 (d, J = 7.0 Hz, 3H), 0.71 (d, J = 7.0 Hz, 3H), 0.54 (d, J = 6.7 Hz, 3H)	HRMS(B) m/z 479.3165 (M + H)+
230: (4S)-3-(2-((1S)-1-(4-((dihydro-1H-pyrido[1,2-a]pyrazin-2(6H,7H,8H,9H,9aH)-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.07 (d, J = 5.8 Hz, 1H), 7.34 – 7.19 (m, 5H), 5.01 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.33 – 4.22 (m, 2H), 3.49 – 3.39 (m, 2H), 2.83 – 2.71 (m, 2H), 2.66 (dq, J = 11.0, 2.2 Hz, 2H), 2.32 – 2.14 (m, 2H), 2.09 – 1.94 (m, 2H), 1.82 (t, J = 10.8 Hz, 1H), 1.70 (dt, J = 12.4, 3.5 Hz, 1H), 1.64 – 1.50 (m, 2H), 1.48 – 1.39 (m, 5H), 1.35 – 1.21 (m, 1H), 1.14 (tdd, J = 13.0, 10.8, 3.6 Hz, 1H), 0.68 (br s, 3H), 0.52 (br s, 3H)	HRMS(B) m/z 479.3131 (M + H)+
231: (4S)-4-isopropyl-3-(2-((1S)-1-(4-((3-methyl-3,8-diazabicyclo[3.2.1]octan-8-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.07 (d, J = 5.9 Hz, 1H), 7.36 – 7.21 (m, 5H), 5.01 (q, J = 7.0 Hz, 1H), 4.62 (br s, 1H), 4.33 – 4.21 (m, 2H), 3.45 (s, 2H), 3.07 (qd, J = 4.6, 4.2, 1.9 Hz, 2H), 2.63 – 2.50 (m, 2H), 2.25 (ddd, J = 10.7, 4.4, 1.8 Hz, 2H), 2.15 (s, 3H), 2.04 – 1.93 (m, 2H), 1.83 – 1.72 (m, 3H), 1.45 (d, J = 7.0 Hz, 3H), 0.67 (br s, 3H), 0.51 (br s, 3H)	HRMS(B) m/z 465.2964 (M + H)+
232: (4S)-4-isopropyl-3-(2-((1S)-1-(4-((8-methyl-3,8-diazabicyclo[3.2.1]octan-3-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.17 (d, J = 5.7 Hz, 1H), 7.42 (d, J = 5.7 Hz, 1H), 7.23 (s, 4H), 5.46 (br s, 1H), 5.01 (br s, 1H), 4.60 (dt, J = 6.9, 3.3 Hz, 1H), 4.28 (t, J = 8.7 Hz, 1H), 4.21 (dd, J = 9.1, 3.1 Hz, 1H), 3.42 (d, J = 1.7 Hz, 2H), 3.10 – 2.96 (m, 2H), 2.58 – 2.48 (m, 2H), 2.33 – 2.18 (m, 5H), 2.06 – 1.84 (m, 3H),	HRMS(B) m/z 465.2963 (M + H)+

	1.81 (dd, J = 7.8, 4.4 Hz, 2H), 1.52 (d, J = 6.8 Hz, 3H), 0.71 (br s, 3H), 0.64 (br s, 3H)	
233: (4S)-3-(2-((1S)-1-(4-((hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.12 (d, J = 5.8 Hz, 1H), 7.34 (d, J = 5.8 Hz, 1H), 7.33 – 7.24 (m, 4H), 5.05 (q, J = 7.0 Hz, 1H), 4.67 (br s, 1H), 4.38 – 4.26 (m, 2H), 3.64 – 3.49 (m, 2H), 3.11 – 3.00 (m, 2H), 2.96 (br d, J = 11.0 Hz, 1H), 2.83 (br d, J = 11.2 Hz, 1H), 2.45 – 2.34 (m, 1H), 2.32– 2.25 (m, 3H), 1.94 (t, J = 10.5 Hz, 1H), 1.88 – 1.77 (m, 4H), 1.49 (d, J = 7.0 Hz, 3H), 1.47 – 1.35 (m, 1H), 0.72 br (s, 3H), 0.56 (br s, 3H)	HRMS(B) m/z 465.2972 (M + H)+
234: (S)-3-(2-(((S)-1-(2H-tetrazol-5-yl) ethyl) amino) pyrimidin-4-yl)-4-isopropyloxazolidin-2-one		HRMS(B) m/z 319.1624 (M+H)+, RT=1.33 min.
235: benzyl 4-(4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzyl)piperazine-1-carboxylate	8.07 (d, J = 5.8 Hz, 1H), 7.34 – 7.18 (m, 10H), 5.05 (s, 2H), 5.01 (q, J = 6.9 Hz, 1H), 4.62 (br s, 1H), 4.32 – 4.18 (m, 2H), 3.49 – 3.34 (m, 4H), 3.46 (s, 2H), 2.36 (t, J = 5.1 Hz, 4H), 1.75 (br s, 1H), 1.45 (d, J = 7.0 Hz, 3H), 0.66 (br s, 3H), 0.50 (br s, 3H)	HRMS(B) m/z 559.3026 (M + H)+
236: (S)-3-(2-((S)-1-(4-((4-amino-4-methylpiperidin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.07 (d, J = 5.8 Hz, 1H), 7.30 (d, J = 5.8 Hz, 1H), 7.27 – 7.21 (m, 4H), 5.01 (q, J = 7.0 Hz, 1H), 4.63 (br s, 1H), 4.34 – 4.18 (m, 2H), 3.53 – 3.40 (m, 2H), 2.59 – 2.21 (br m, 4H), 1.78 (br s, 1H), 1.52 (ddt, J = 11.8, 8.7, 5.2 Hz, 4H), 1.45 (d, J = 7.0 Hz, 3H), 1.07 (s, 3H), 0.67 (br s, 3H), 0.51 (br s, 3H)	HRMS(B) m/z 453.2972 (M + H)+
237: (S)-3-(2-((S)-1-(4-((4-(dimethylamino)piperidin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	($CDCl_3$) 8.17 (d, J = 5.7 Hz, 1H), 7.42 (d, J = 5.7 Hz, 1H), 7.25 (d, J = 8.2 Hz, 4H), 5.43 (br s, 1H), 5.01 (br s, 1H), 4.60 (dt, J = 8.6, 3.3 Hz, 1H), 4.28 (t, J = 8.7 Hz, 1H), 4.21 (dd, J = 9.1, 3.2 Hz, 1H), 3.44 (s, 2H), 2.89 (dp, J = 11.5, 2.8 Hz, 2H), 2.26 (s, 6H), 2.11 (tt, J = 11.3, 3.6 Hz, 1H), 1.93 (td, J = 11.9, 2.4 Hz, 2H), 1.90 (br s, 1H), 1.75 (dq, J = 12.0, 2.8 Hz, 2H), 1.60 – 1.43 (m, 2H), 1.53 (d, J = 6.8 Hz, 3H), 0.70 (br s, 3H), 0.63 (br s, 3H)	HRMS(B) m/z 467.3121 (M + H)+
238: (S)-3-(2-((S)-1-(4-((tert-butylamino)methyl)phenyl) ethylamino)pyrirmidin-4-yl)-4-isopropyloxazolidin-2-one	($CDCl_3$) δ 8.18 (dd, J = 5.8, 1.3 Hz, 1H), 7.44 (dd, J = 5.7, 1.2 Hz, 1H), 7.37 – 7.22 (m, 5H), 5.52 (br s, 1H), 5.15 – 4.95 (m, 1H), 4.70 – 4.55 (m, 1H), 4.30 (td, J = 8.8, 2.1 Hz, 1H), 4.23 (dd, J = 9.1, 3.0 Hz, 1H), 3.71 (d, J = 2.0 Hz, 2H), 2.06 (s, 1H), 1.54 (dd, J = 7.1, 1.9 Hz, 3H), 1.18 (sm, 9H), 0.85 – 0.59 (m, 6H);	HRMS(B) m/z 412.2701 (M + H)+
239: N-tert-butyl-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-	($CDCl_3$) δ 8.16 (dd, J = 5.8, 1.2 Hz, 1H), 7.66 (d, J = 8.3 Hz, 2H), 7.43 (dd, J = 5.8, 0.9 Hz, 1H), 7.35 (d, J = 7.9 Hz, 2H), 5.88 (s, 1H), 5.57 (br s, 1H), 5.04 (br s, 1H),	HRMS(B) m/z 426.2488 (M + H)+

ylamino)ethyl)benzamide	4.55 (br s, 1H), 4.26 (t, J = 8.7 Hz, 1H), 4.19 (dd, J = 9.2, 3.2 Hz, 1H), 1.53 (d, J = 6.9 Hz, 3H), 1.45 (s, 9H), 0.64 (m, 6H)	
240: N-cyclohexyl-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide	($CDCl_3$) δ 8.17 (d, J = 5.7 Hz, 1H), 7.69 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 5.8 Hz, 1H), 7.36 (d, J = 7.9 Hz, 2H), 5.91 (d, J = 8.3 Hz, 1H), 5.51 (br s, 1H), 5.04 (br s, 1H), 4.53 (br s, 1H), 4.26 (t, J = 8.7 Hz, 1H), 4.19 (dd, J = 9.1, 3.2 Hz, 1H), 4.04 – 3.89 (m, 1H), 2.07 – 1.95 (m, 2H), 1.74 (dp, J = 11.5, 3.8 Hz, 2H), 1.64 (tt, J = 7.4, 3.7 Hz, 2H), 1.54 (d, J = 6.9 Hz, 3H), 1.42 (qt, J = 12.4, 3.5 Hz, 2H), 1.30 – 1.17 (m, 3H), 0.64 (br s, 6H)	HRMS(B) m/z 452.2640 (M + H)+
241: 4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)-N-phenylbenzamide	($CDCl_3$) δ 8.19 (d, J = 5.8 Hz, 1H), 7.83 (d, J = 8.2 Hz, 2H), 7.77 (s, 1H), 7.68 – 7.59 (m, 2H), 7.48 – 7.41 (m, 3H), 7.37 (dd, J = 8.5, 7.3 Hz, 2H), 7.22 – 7.11 (m, 1H), 5.48 (br s, 1H), 5.08 (br s, 1H), 4.56 (br s, 1H), 4.27 (t, J = 8.7 Hz, 1H), 4.20 (dd, J = 9.2, 3.2 Hz, 1H), 1.57 (t, J = 5.6 Hz, 3H), 0.65 (br s, 6H);	HRMS(B) m/z 446.2170 (M + H)+
242: (S)-4-isopropyl-3-(2-((S)-1-(4-(piperidine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) δ 8.18 (d, J = 5.7 Hz, 1H), 7.45 (d, J = 5.7 Hz, 1H), 7.33 (s, 4H), 5.45 (br s, 1H), 5.05 (br s, 1H), 4.59 (dt, J = 7.3, 2.9 Hz, 1H), 4.27 (t, J = 8.7 Hz, 1H), 4.21 (dd, J = 9.1, 3.2 Hz, 1H), 3.51 (d, J = 141.8 Hz, 4H), 1.60 (dd, J = 52.4, 5.9 Hz, 10H), 0.68 (d, J = 25.5 Hz, 6H);	HRMS(B) m/z 438.2492 (M + H)+
243: (S)-4-isopropyl-3-(2-((S)-1-(4-(4-methylpiperazine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) δ 8.18 (d, J = 5.7 Hz, 1H), 7.45 (d, J = 5.7 Hz, 1H), 7.35 (s, 4H), 5.42 (br s, 1H), 5.05 (br s, 1H), 4.58 (br s, 1H), 4.28 (t, J = 8.8 Hz, 1H), 4.21 (dd, J = 9.2, 3.1 Hz, 1H), 3.78 (br s, 2H), 3.44 (br s, 2H), 2.53 – 2.39 (m, 2H), 2.32 (s, 4H), 1.65 (m, 2H), 1.53 (d, J = 6.9 Hz, 3H), 0.82 – 0.50 (m, 6H)	HRMS(B) m/z 453.2611 (M + H)+
244: (S)-4-isopropyl-3-(2-((S)-1-(4-(piperidin-1-ylmethyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) δ 8.16 (d, J = 5.7 Hz, 1H), 7.42 (d, J = 5.7 Hz, 1H), 7.24 (s, 4H), 5.58 (br s, 1H), 5.15 – 4.85 (m, 1H), 4.60 (dt, J = 8.4, 3.4 Hz, 1H), 4.27 (t, J = 8.7 Hz, 1H), 4.20 (dd, J = 9.1, 3.2 Hz, 1H), 3.43 (s, 2H), 2.54 – 2.22 (m, 4H), 1.99 (br s, 1H), 1.61 – 1.48 (m, 7H), 1.42 (q, J = 6.6, 6.0 Hz, 2H), 0.86 – 0.41 (m, 6H);	HRMS(B) m/z 424.2704 (M + H) +
245: (S)-4-isopropyl-3-(2-((S)-1-(4-(morpholinomethyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) δ 8.18 (d, J = 5.7 Hz, 1H), 7.45 (d, J = 5.7 Hz, 1H), 7.28 (s, 4H), 5.56 (br s, 1H), 5.16 – 4.94 (m, 1H), 4.63 (dt, J = 7.6, 3.5 Hz, 1H), 4.30 (t, J = 8.8 Hz, 1H), 4.23 (dd, J = 9.0, 3.1 Hz, 1H), 3.72 (t, J = 4.6 Hz, 4H), 3.49 (s, 2H), 2.45 (t, J = 4.6 Hz, 4H), 2.19 – 1.82 (m, 1H), 1.55 (d, J = 6.9 Hz, 3H), 0.90 – 0.46 (m, 6H);	HRMS(B) m/z 426.2487 (M + H) +
246: (S)-4-isopropyl-3-(2-((S)-1-(4-((4-	($CDCl_3$) δ 8.17 (d, J = 5.8 Hz, 1H), 7.43 (d, J = 5.8 Hz, 1H), 7.27 (d, J = 6.2 Hz, 4H),	HRMS(B) m/z

methylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	5.52 (br s, 1H), 5.03 (br s, 0H), 4.62 (dt, J = 8.5, 3.4 Hz, 1H), 4.29 (t, J = 8.7 Hz, 1H), 4.22 (dd, J = 9.1, 3.2 Hz, 1H), 3.48 (s, 2H), 2.46 (br s, 9H), 2.30 (s, 3H), 1.54 (d, J = 6.9 Hz, 3H), 0.97 – 0.57 (m, 6H);	439.2801 (M + H) +
247: (R)-4-(4-fluorophenyl)-4-methyl-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) δ 8.18 (d, J = 5.8 Hz, 1 H), 7.41 (d, J = 5.8 Hz, 1 H), 7.33 – 7.29 (m, 2 H), 7.25 – 7.20 (m, 3 H), 7.15 – 7.06 (m, 4 H), 5.17 (br s, 1 H), 4.21 (br s, 1 H), 4.20 – 4.15 (m, 2 H), 1.61 (s, 3 H), 1.21 (d, J = 7.1 Hz, 3 H)	HRMS(B) m/z 393.1726 (M + H)+.
248: (S)-1-(2-(1-phenylethylamino)pyrimidin-4-yl)-3-oxa-1-azaspiro[4.4]nonan-2-one	($CDCl_3$) δ 8.19 (d, J = 5.8 Hz, 1 H), 7.37 – 7.33 (m, 4 H), 7.29 – 7.24 (m, 2 H), 5.39 (br s, 1 H), 5.12 – 5.05 (m, 1 H), 4.09 – 4.05 (m, 2 H), 2.83 – 2.75 (m, 1 H), 2.35 (br s, 1 H), 1.95 – 1.86 (m, 1 H), 1.71 (br s, 1 H), 1.67 – 1.61 (m, 2 H), 1.58 (d, J = 7.0 Hz, 3 H), 1.45 (br s, 2 H)	HRMS(B) m/z 339.1805 (M + H)+
249: (R)-4-(4-fluorophenyl)-4-methyl-3-(2-((S)-1-(4-phenoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) δ 8.18 (d, J = 5.8 Hz, 1 H), 7.42 (d, J = 5.8 Hz, 1 H), 7.38 – 7.33 (m, 2 H), 7.26 – 7.22 (m, 2 H), 7.14 – 7.06 (m, 5 H), 7.00 – 6.94 (m, 4 H), 5.21 (br s, 1 H), 4.23 – 4.17 (m, 3 H), 1.71 (br s, 3 H), 1.20 (d, J = 6.8 Hz, 3 H)	HRMS(B) m/z 485.1979 (M + H)+
250: (S)-4-methyl-3-(2-((S)-1-(4-phenoxyphenyl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	($CDCl_3$) δ 8.17 (dd, J = 5.9, 1.1 Hz, 1H), 7.47 – 7.23 (m, 8H), 7.16 – 7.05 (m, 3H), 7.02 – 6.91 (m, 4H), 5.10 (br s, 1H), 4.22 (s, 2H), 1.73 (s, 3H), 1.67 – 1.53 (m, 1H), 1.14 (d, J = 7.0 Hz, 3H);	HRMS(B) m/z 467.2065 (M + H) +
251: (S)-1-(2-(1-(4-phenoxyphenyl)ethylamino)pyrimidin-4-yl)-3-oxa-1-azaspiro[4.4]nonan-2-one	($CDCl_3$) δ 8.19 (d, J = 5.8 Hz, 1 H), 7.37 – 7.28 (m, 5 H), 7.13 – 7.09 (m, 1 H), 7.01 – 6.96 (m, 4 H), 5.47 (br s, 1 H), 5.12 – 5.05 (m, 1 H), 4.11 – 4.07 (m, 2 H), 2.84 – 2.76 (m, 1 H), 2.42 (br s, 1 H), 1.97 – 1.88 (m, 1 H), 1.77 (br s, 1 H), 1.68 – 1.61 (m, 2 H), 1.58 (d, J = 6.9 Hz, 3 H), 1.54 – 1.46 (m, 2 H)	HRMS(B) m/z 431.2073 (M + H)+
252: (S)-4,4-dimethyl-3-(2-(1-(4-phenoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) δ 8.19 (d, J = 5.8 Hz, 1H), 7.38 – 7.26 (m, 5H), 7.11 (tt, J = 7.4, 1.1 Hz, 1H), 7.01 – 6.94 (m, 4H), 5.37 (br s, 1H), 5.01 (d, J = 9.1 Hz, 1H), 4.09 – 3.93 (m, 2H), 1.71 (s, 3H), 1.57 (d, J = 6.9 Hz, 3H), 1.28 (m, 3H);	MS m/z 405.1 (M + H) +
253: (S)-3-(2-(((S)-1-(1-benzyl-5-methyl-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.49 (d, J = 5.7 Hz, 1H), 7.84 – 7.38 (m, 7H), 5.65 (s, 1.2H), 5.55 (s, 0.8H), 5.43 (dq, J = 8.9, 6.9 Hz, 1H), 5.11 (tt, J = 6.1, 3.6 Hz, 1H), 4.79 – 4.60 (m, 2H), 2.76 (dtt, J = 22.3, 7.2, 3.5 Hz, 1H), 2.56 (2s, 3H), 1.87 (2d, J =6.9 Hz, 3H), 1.22 (2d, J = 7.1 Hz, 3H), 1.13 (dd, J = 6.9 Hz, 3H)	HRMS(B) (M+H) 421.2338
254: (S)-3-(2-(((S)-1-(1-benzyl-3-methyl-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-	8.14 (d, J = 5.8 Hz, 1H), 7.50 (s, 1H), 7.38 (d, J = 5.8 Hz, 1H), 7.36 – 7.25 (m, 3H), 7.24 – 7.17 (m, 2H), 5.21 (s, 2H), 5.06 (q, J = 6.9 Hz, 1H), 4.76 (dt, J = 7.5, 3.9 Hz, 1H), 4.42 – 4.32 (m, 2H), 2.38 (br s, 1H),	HRMS(B) (M+H) 421.2340

2-one	2.22 (s, 3H), 1.51 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 7.0 Hz, 3H), 0.75 (d, J = 6.9 Hz, 3H).	
255: (4S)-4-isopropyl-3-(2-(1-(1-methyl-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	^{1}H NMR (400 MHz, MeOD) δ 8.16 (d, J = 5.8 Hz, 0.5H), 8.14 (d, J = 5.8 Hz, 0.5H), 7.54 (s, 0.5H), 7.48 (s, 0.5H), 7.44 (s, 0.5H), 7.40 (d, J = 2.0 Hz, 0.5H), 7.38 (d, J = 2.0 Hz, 0.5H), 7.38 (s, 0.5H), 5.11 (q, J = 6.9 Hz, 1H), 4.75 (dq, J = 9.4, 3.7 Hz, 1H), 4.46 – 4.29 (m, 2H), 3.85 (d, J = 5.5 Hz, 3H), 2.62 (ddq, J = 10.4, 7.0, 3.5 Hz, 0.5H), 2.40 (br s, 0.5H), 1.53 (d, J = 6.9 Hz, 3H), 0.98 (d, J = 7.1 Hz, 1.5H), 0.88 (d, J = 7.1 Hz, 1.5H), 0.86 (d, J = 7.0 Hz, 1.5H), 0.78 (d, J = 7.0 Hz, 1.5H). HRMS(B) (M+H) 421.2340 Calc'd (M+H) 421.2352	HRMS(B) (M+H) 421.2340
256: (S)-3-(2-((S)-1-(3-(1H-pyrazol-1-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.20 (d, J = 2.5 Hz, 1H), 8.16 (d, J = 5.8 Hz, 1H), 7.75 (t, J = 2.0 Hz, 1H), 7.72 (d, J = 1.8 Hz, 1H), 7.58 (ddd, J = 8.0, 2.2, 1.0 Hz, 1H), 7.43 (t, J = 7.8 Hz, 1H), 7.37 (d, J = 5.8 Hz, 1H), 7.32 (d, J = 7.6 Hz, 1H), 6.56 – 6.49 (m, 1H), 5.13 (q, J = 7.0 Hz, 1H), 4.66 (br s, 1H), 4.39 – 4.19 (m, 2H), 1.82 (br s, 1H), 1.58 (d, J = 7.0 Hz, 3H), 0.56 (br s, 6H).	HRMS(B) (M+H) 393.2036
257: (S)-3-(2-((S)-1-(4-(1H-pyrazol-1-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.18 (d, J = 2.5 Hz, 1H), 8.16 (d, J = 5.8 Hz, 1H), 7.72 (d, J = 1.8 Hz, 1H), 7.69 (d, J = 1.9 Hz, 1H), 7.67 (d, J = 2.0 Hz, 1H), 7.52 – 7.44 (m, 2H), 7.37 (d, J = 5.8 Hz, 1H), 6.56 – 6.49 (m, 1H), 5.11 (q, J = 7.1 Hz, 1H), 4.68 (s, 1H), 4.40 – 4.24 (m, 2H), 1.86 (s, 1H), 1.57 (d, J = 7.1 Hz, 3H), 0.71 (s, 3H), 0.59 (s, 3H).	HRMS(B) (M+H) 393.2050
258: (4S)-4-isopropyl-3-(2-(1-(5-methyl-1-phenyl-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.17 (dd, J = 5.8, 4.6 Hz, 1H), 7.67 (s, 0.5H), 7.61 (s, 0.5H), 7.55 (dd, J = 8.5, 6.7 Hz, 2H), 7.52 – 7.47 (m, 1H), 7.44 (ddd, J = 8.1, 3.3, 1.4 Hz, 2H), 7.40 (d, J = 5.8 Hz, 1H), 5.17 (dq, J = 10.4, 6.9 Hz, 1H), 4.83 – 4.77 (m, 1H), 4.45 – 4.34 (m, 2H), 2.66 (td, J = 7.0, 3.5 Hz, 0.5H), 2.45 (br s, 0.5H), 2.32 (s, 1.5H), 2.31 (s, 1.5H), 1.59 (dd, J = 6.8, 1.7 Hz, 3H), 1.01 (d, J = 7.0 Hz, 1.5H), 0.94 – 0.85 (m, 3H), 0.81 (d, J = 6.9 Hz, 1.5H).	HRMS(B) (M+H) 407.2202
259: (R)-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)-4-(pyridin-2-yl)oxazolidin-2-one	8.60 (ddd, J = 4.8, 1.7, 0.9 Hz, 1H), 8.10 (d, J = 5.7 Hz, 1H), 7.89 (td, J = 7.7, 1.8 Hz, 1H), 7.46 – 7.36 (m, 3H), 7.33 – 7.28 (m, 4H), 7.21 (ddd, J = 8.6, 5.5, 2.2 Hz, 1H), 5.66 (br s, 1H), 4.79 (t, J = 8.9 Hz, 1H), 4.60 (br s, 1H), 4.31 (dd, J = 8.9, 3.8 Hz, 1H), 1.22 (d, J = 6.6 Hz, 3H).	HRMS(B) (M+H) 362.1617
260: (S)-3-(2-((S)-1-(2-fluorophenyl)ethylamino)pyrimidin-4-yl)-4-	8.51 (d, J = 5.7 Hz, 1H), 7.76 – 7.51 (m, 3H), 7.48 – 7.37 (m, 2H), 5.71 (q, J = 7.0 Hz, 1H), 5.06 – 5.02 (m, 1H), 4.75 – 4.61	HRMS(B) (M+H) 393.2026

isopropyloxazolidin-2-one	(m, 2H), 2.30 (br s, 1H), 1.89 (d, J = 7.0, 3H), 1.10 (d, J = 7.1 Hz, 3H), 0.95 (d, J = 7.0 Hz, 3H).	
261: (S)-4-isopropyl-3-(2-((S)-1-(6-phenoxypyridin-3-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.25 – 8.05 (m, 2H), 7.83 (dd, J = 8.6, 2.5 Hz, 1H), 7.50 – 7.34 (m, 3H), 7.27 – 7.16 (m, 1H), 7.15 – 7.02 (m, 2H), 6.89 (d, J = 8.5 Hz, 1H), 5.10 (q, J = 7.1 Hz, 1H), 4.75 – 4.61 (m, 1H), 4.41 – 4.29 (m, 2H), 1.94 (br s, 1H), 1.56 (d, J = 7.1 Hz, 3H), 0.78 (br s, 3H), 0.70 (br s, 3H).	HRMS(B) (M+H) 420.2019
262: (S)-3-(5-fluoro-2-(1-(4-phenoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.16 (d, J = 3.5 Hz, 1H), 7.45 – 7.28 (m, 4H), 7.09 (tt, J = 7.3, 1.1 Hz, 1H), 7.02 – 6.89 (m, 4H), 4.99 (q, J = 6.9 Hz, 1H), 4.58 – 4.48 (m, 2H), 4.18 (ddd, J = 9.7, 8.5, 7.2 Hz, 1H), 3.99 (br s, 1H), 1.52 (d, J = 6.9 Hz, 3H).	HRMS(B) (M+H) 395.1507
263: (S)-3-(2-(1-(4-phenoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.09 (d, J = 5.8 Hz, 1H), 7.43 – 7.29 (m, 5H), 7.09 (tt, J = 7.3, 1.1 Hz, 1H), 7.00 – 6.90 (m, 4H), 5.07 (q, J = 7.0 Hz, 1H), 4.53 – 4.41 (m, 2H), 4.21 (ddd, J = 10.5, 9.2, 7.0 Hz, 1H), 4.01 (br s, 1H), 1.53 (d, J = 7.0 Hz, 3H).	HRMS(B) (M+H) 377.1600
264: (4S)-4-isopropyl-3-(2-((1-(4-((tetrahydro-2H-pyran-4-yl)oxy)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	8.12 (dd, J = 8.5, 5.8 Hz, 1H), 7.35 (dd, J = 5.8, 1.0 Hz, 1H), 7.32 – 7.19 (m, 2H), 6.95 – 6.86 (m, 2H), 4.98 (dq, J = 25.6, 7.2 Hz, 1H), 4.68 (br s, 0.5H), 4.59 – 4.48 (m, 1.5H), 4.39 – 4.25 (m, 2H), 4.01 – 3.90 (m, 2H), 3.65 – 3.53 (m, 2H), 2.74 – 2.61 (m, 0.5H), 2.08 – 1.96 (m, 2H), 1.95 (br s, 0.5H), 1.78 – 1.64 (m, 2H), 1.50 (dd, J = 6.9, 1.6 Hz, 3H), 1.01 (d, J = 7.0 Hz, 1.5H), 0.88 (d, J = 6.9 Hz, 1.5H), 0.75 (br s, 1.5H), 0.62 (br s, 1.5H).	
265: (S)-3-(2-((S)-1-(4-(4-fluorophenoxy)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.14 (d, J = 5.8 Hz, 1H), 7.37 (d, J = 5.8 Hz, 1H), 7.36 – 7.31 (m, 2H), 7.12 – 7.05 (m, 2H), 7.01 – 6.94 (m, 2H), 6.94 – 6.89 (m, 2H), 5.06 (q, J = 7.0 Hz, 1H), 4.71 (br s, 1H), 4.41 – 4.29 (m, 2H), 1.99 (br s, 1H), 1.52 (d, J = 7.0 Hz, 3H), 0.77 (br s, 3H), 0.67 (br s, 3H).	HRMS(B) (M+H) 437.1981
266: (R)-3-(2-((S)-1-(4-bromophenyl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.46 (d, J = 5.8 Hz, 1H), 7.84 – 7.73 (m, 5H), 7.72 – 7.67 (m, 1H), 7.64 (dd, J = 7.1, 1.8 Hz, 2H), 7.59 – 7.53 (m, 2H), 5.92 (dd, J = 8.6, 4.0 Hz, 1H), 5.13 (t, J = 8.7 Hz, 1H), 4.98 (q, J = 8.4, 7.5 Hz, 1H), 4.55 (dd, J = 8.7, 4.0 Hz, 1H), 1.58 (d, J = 7.0 Hz, 3H).	HRMS(B) (M+H) 439.0762
267: (R)-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)-4-(pyridin-3-yl)oxazolidin-2-one	8.60 (d, J = 2.5 Hz, 1H), 8.55 (dd, J = 4.8, 1.5 Hz, 1H), 8.12 (d, J = 5.8 Hz, 1H), 7.81 (dt, J = 7.8, 2.0 Hz, 1H), 7.54 – 7.47 (m, 1H), 7.41 (d, J = 5.8 Hz, 1H), 7.36 – 7.25 (m, 4H), 7.25 – 7.17 (m, 1H), 5.60 (br s, 1H), 4.80 (t, J = 8.9 Hz, 1H), 4.61 (br s, 1H), 4.27 (dd, J = 9.0, 4.1 Hz, 1H), 1.25 (br d, J = 7.5 Hz, 3H).	HRMS(B) (M+H) 362.1615

268: (R)-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)-4-(pyridin-4-yl)oxazolidin-2-one	8.61 – 8.60 (m, 2H), 8.14 (d, J = 5.8 Hz, 1H), 7.43 (d, J = 5.8 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.32 (t, J = 7.5 Hz, 2H), 7.28 – 7.17 (m, 3H), 5.57 (br s, 1H), 4.80 (t, J = 9.0 Hz, 1H), 4.55 (br s, 1H), 4.22 (dd, J = 9.0, 4.1 Hz, 1H), 1.20 (br s, 3H).	HRMS(B) (M+H) 362.1610
269: (S)-3-(2-((S)-1-(3-methoxyphenyl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.46 (d, J = 5.7 Hz, 1H), 7.73 (d, J = 5.8 Hz, 1H), 7.64 – 7.52 (m, 5H), 7.48 (t, J = 7.8 Hz, 1H), 7.11 – 7.03 (m, 3H), 6.18 (dd, J = 8.7, 3.7 Hz, 1H), 5.25 – 5.13 (m, 2H), 4.60 (dd, J = 8.7, 3.7 Hz, 1H), 4.10 (s, 3H), 1.81 (d, J = 7.0 Hz, 3H).	HRMS(B) (M+H) 391.1771
270: (4S)-3-(2-(1-(biphenyl-4-yl)ethylamino)pyrimidin-4-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one	8.50 – 8.45 (m, 1H), 7.95 (ddt, J = 7.6, 5.3, 2.3 Hz, 3H), 7.83 – 7.64 (m, 8H), 7.63 – 7.54 (m, 2H), 7.49 (dd, J = 4.9, 3.0 Hz, 2H), 5.83 (s, 0.5H), 5.57 (s, 0.5H), 5.29 – 5.24 (m, 0.5H), 5.04 – 4.99 (m, 0.5H), 2.02 (s, 1.5H), 1.85 – 1.84 (m, 3H), 1.62 (d, J = 7.0 Hz, 1.5H), 1.35 (d, J = 3.3 Hz, 3H).	HRMS(B) (M+H) 465.2284
271: (S)-3-(2-((S)-1-(4-fluorophenyl)ethylamino)pyrirnidin-4-yl)-4-isopropyl-4-methyloxazolidin-2-one	8.15 (d, J = 5.8 Hz, 1H), 7.41 – 7.29 (m, 2H), 7.25 (d, J = 5.8 Hz, 1H), 7.09 – 6.98 (m, 2H), 4.96 (q, J = 7.1 Hz, 1H), 4.29 (d, J = 9.0 Hz, 1H), 3.88 (d, J = 8.9 Hz, 1H), 2.17 (br s, 1H), 1.70 (s, 3H), 1.53 (d, J = 7.0 Hz, 3H), 0.70 (br s, 3H), 0.44 (br s, 3H).	HRMS(B) (M+H) 359.1889
272: (S)-4,4-dimethyl-3-(2-(1-(4-((4-methylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.12 (d, J = 5.8 Hz, 1H), 7.35 – 7.26i (m, 4H), 7.17 (d, J = 5.9 Hz, 1H), 5.02 (q, J = 6.9 Hz, 1H), 4.06 (q, J = 8.4 Hz, 2H), 3.51 (s, 2H), 2.49 (br s, 8H), 2.28 (s, 3H), 1.70 (s, 3H), 1.53 (d, J = 7.0 Hz, 3H), 1.15 (br s, 3H).	HRMS(B) (M+H) 425.2661
273: (R)-5,5-dimethyl-3-(2-((S)-1-(4-((4-methylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.09 (d, J = 5.8 Hz, 1H), 7.50 – 7.39 (m, 3H), 7.36 (tt, J = 7.1, 1.4 Hz, 1H), 7.30 (s, 4H), 7.21 (br s, 2H), 5.22 (br s, 1H), 4.58 (br s, 1H), 3.53 (s, 2H), 2.50 (br s, 8H), 2.28 (s, 3H), 1.52 (s, 3H), 1.19 (d, J = 6.8 Hz, 3H), 0.99 (s, 3H).	HRMS(B) (M+H) 501.2971
274: (S)-5,5-dimethyl-3-(2-((S)-1-(4-((4-methylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	8.08 (d, J = 5.8 Hz, 1H), 7.45 (d, J = 5.8 Hz, 1H), 7.38 – 7.23 (m, 3H), 7.16 (t, J = 7.5 Hz, 4H), 7.00 (br s, 2H), 5.51 (s, 1H), 4.89 – 4.83 (m, 1H), 3.49 (d, J = 2.3 Hz, 2H), 2.50 (br s, 8H), 2.29 (s, 3H), 1.67 (s, 3H), 1.44 (d, J = 6.9 Hz, 3H), 1.00 (s, 3H).	HRMS(B) (M+H) 501.2981
275: (S)-4-isopropyl-4-methyl-3-(2-((S)-1-(4-((4-methylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.14 (d, J = 5.9 Hz, 1H), 7.29 (s, 4H), 7.24 (d, J = 5.9 Hz, 1H), 4.97 (p, J = 7.0 Hz, 1H), 4.60 (br s, 1H), 4.29 (d, J = 8.8 Hz, 1H), 3.88 (d, J = 9.0 Hz, 1H), 3.51 (s, 2H), 2.59 (br s, 8H), 2.28 (s, 3H), 1.71 (s, 3H), 1.52 (d, J = 6.9 Hz, 3H), 0.70 (br s, 3H), 0.39 (br s, 3H).	
276: (S)-4-isopropyl-5,5-dimethyl-3-(2-(((S)-1-(4-((4-methylpiperazin-1-yl)methyl)phenyl)ethyl)ami	8.14 (d, J = 5.8 Hz, 1H), 7.39 – 7.20 (m, 5H), 5.09 (q, J = 7.0 Hz, 1H), 4.49 (br s, 1H), 3.52 (s, 2H), 2.57 (br s, 8H), 2.32 (s, 3H), 2.03 (br s, 1H), 1.54 (s, 3H), 1.51 (d, J	HRMS(B) (M+H) 453.2975

no)pyrimidin-4-yl)oxazolidin-2-one	= 7.0 Hz, 3H), 1.42 (s, 3H), 0.75 (br s, 3H), 0.62 (br s, 3H).	
277: (S)-4-isopropyl-3-(2-((S)-1-(4-(pyridin-2-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.60 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H), 8.16 (d, J = 5.8 Hz, 1H), 7.94 – 7.86 (m, 3H), 7.84 (dt, J = 7.9, 1.2 Hz, 1H), 7.51 – 7.43 (m, 2H), 7.41 – 7.32 (m, 2H), 5.12 (q, J = 7.0 Hz, 1H), 4.67 (br s, 1H), 4.40 – 4.18 (m, 2H), 1.83 (br s, 1H), 1.58 (d, J = 7.1 Hz, 3H), 0.68 (br s, 3H), 0.56 (br s, 3H).	HRMS(B) (M+H) 404.2089
278: (S)-4-isopropyl-3-(2-((S)-1-(6-phenylpyridin-3-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.60 (d, J = 2.2 Hz, 1H), 8.18 (d, J = 5.8 Hz, 1H), 7.95 – 7.89 (m, 2H), 7.87 (dd, J = 8.2, 2.3 Hz, 1H), 7.81 (dd, J = 8.3, 0.8 Hz, 1H), 7.55 – 7.42 (m, 3H), 7.40 (d, J = 5.8 Hz, 1H), 5.16 (q, J = 7.1 Hz, 1H), 4.66 (br s, 1H), 4.40 – 4.22 (m, 2H), 1.74 (br s, 1H), 1.62 (d, J = 7.0 Hz, 3H), 0.67 (br s, 3H), 0.57 (br s, 3H).	HRMS(B) (M+H) 404.2079
279: (S)-4-isopropyl-3-(2-((S)-1-(quinolin-6-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.81 (dd, J = 4.3, 1.6 Hz, 1H), 8.32 (dt, J = 8.2, 1.1 Hz, 1H), 8.18 (d, J = 5.8 Hz, 1H), 8.01 (d, J = 8.7 Hz, 1H), 7.89 – 7.76 (m, 2H), 7.53 (dd, J = 8.3, 4.4 Hz, 1H), 7.37 (d, J = 5.8 Hz, 1H), 5.24 (q, J = 7.1 Hz, 1H), 4.59 (br s, 1H), 4.30 (t, J = 8.7 Hz, 1H), 4.22 (br s, 1H), 1.64 (d, J = 7.1 Hz, 3H), 1.49 (br s, 1H), 0.35 (br s, 6H).	HRMS(B) (M+H) 378.1930
280: (S)-4-isopropyl-3-(2-((S)-1-(quinolin-7-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.81 (dd, J = 4.3, 1.7 Hz, 1H), 8.34 (dt, J = 8.4, 1.2 Hz, 1H), 8.13 (d, J = 5.9 Hz, 1H), 8.00 (d, J = 1.6 Hz, 1H), 7.93 (d, J = 8.5 Hz, 1H), 7.68 (dd, J = 8.6, 1.8 Hz, 1H), 7.50 (dd, J = 8.3, 4.4 Hz, 1H), 7.36 (d, J = 5.8 Hz, 1H), 5.23 – 5.17 (m, 1H), 4.50 (br d, J = 84.2 Hz, 1H), 4.35 – 4.25 (m, 1H), 4.19 (br s, 1H), 2.68 (pd, J = 7.0, 3.5 Hz, 1H), 1.65 (d, J = 7.0 Hz, 3H), 1.01 (d, J = 7.0 Hz, 3H), 0.86 (d, J = 6.9 Hz, 3H).	HRMS(B) (M+H) 378.1941
281: (S)-3-(2-((S)-1-(4-benzoylphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.17 (d, J = 5.8 Hz, 1H), 7.81 – 7.71 (m, 4H), 7.69 – 7.61 (m, 1H), 7.59 – 7.49 (m, 4H), 7.39 (d, J = 5.8 Hz, 1H), 5.15 (q, J = 7.1 Hz, 1H), 4.67 (br s, 1H), 4.41 – 4.23 (m, 2H), 1.75 (br s, 1H), 1.58 (d, J = 7.1 Hz, 3H), 0.69 (br s, 3H), 0.61 (br s, 3H).	HRMS(B) (M+H) 431.2072
282 : (S)-3-(2-((S)-1-(3-fluoro-4-(2-methyl-1H-imidazol-1-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	8.18 (d, J = 7.1 Hz, 1H), 7.75 (d, J = 7.3 Hz, 1H), 7.71 – 7.62 (m, 3H), 7.58 (dd, J = 10.9, 1.9 Hz, 1H), 7.51 (dd, J = 8.2, 1.8 Hz, 1H), 5.33 (br s, 1H), 4.81 – 4.73 (m, 1H), 4.46 – 4.36 (m, 2H), 2.54 (s, 3H), 2.03 (br s, 1H), 1.64 (d, J = 7.0 Hz, 3H), 0.84 (br d, J = 7.2 Hz, 3H), 0.70 (br d, J = 7.2 Hz, 3H).	HRMS(B) (M+H) 425.2093
283: (4S)-4-isopropyl-3-(2-(1-(4-(2-methyl-1H-imidazol-1-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	8.15 (dd, J = 8.9, 5.8 Hz, 1H), 7.60 – 7.50 (m, 2H), 7.42 – 7.32 (m, 3H), 7.14 (dd, J = 13.3, 1.5 Hz, 1H), 6.96 (dd, J = 3.5, 1.5 Hz, 1H), 5.17 (q, J = 7.1 Hz, 0.5H), 5.07 (d, J = 7.4 Hz, 0.5H), 4.71 (br s, 0.5H), 4.50 (br s, 0.5H), 4.40 – 4.24 (m, 2H), 2.67 (ddq, J = 10.6, 7.0, 3.6 Hz, 0.5H), 2.323 (s, 1.5H),	HRMS(B) (M+) 406.2217

	2.321 (s, 1.5H), 1.95 (br s, 0.5H), 1.58 (dd, J = 7.0, 2.3 Hz, 3H), 1.02 (d, J = 7.0 Hz, 1.5H), 0.88 (d, J = 6.9 Hz, 1.5H), 0.76 (br s, 1.5H), 0.64 (br s, 1.5H).	
284: (S)-3-(2-(((R)-1-cyclopentylethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one		HRMS(B) m/z 319.2133 (M+H)+, RT=2.68 min.
285: (S)-3-(2-(((S)-1-(4-(dimethylamino)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one		HRMS(B) m/z 370.2227 (M+H)+, RT=2.47 min.
286: N-(3-((S)-1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino) Ethylphenyl)acetamide		HRMS(B) m/z 384.2032 (M+H)+, RT=1.97 min
287: (S)-3-(2-(((S)-1-(1H-benzo[d]imidazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one		HRMS(B) m/z 367.1887 (M+H)+ RT=2.39 min.
288: (S)-3-(2-(((S)-1-(4-((4-chlorophenyl)sulfonyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one		HRMS(B) m/z 501.1343, (M+H)+ RT=2.68 min.
289: (S)-4-isopropyl-3-(2-(((S)-1-(4-nitrophenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one		HRMS(B) m/z 372.1672, (M+H)+, RT=2.59 min.
290: (S)-3-(2-(((S)-1-(4-aminophenyl)ethyl)amino) pyrimidin-4-yl)-4-isopropyloxazolidin-2-one		HRMS(B) m/z 342.1931, (M+H)+, RT=2.17 min
291: (S)-4-isopropyl-3-(2-(((S)-1-(5-(methylthio)-1,3,4-oxadiazol-2-yl)ethyl)amino) pyrimidin-4-yl)oxazolidin-2-one		HRMS(B) m/z 365.1367, (M+H)+, RT=1.88 min.
292: (S)-4-isopropyl-3-(2-(((S)-1-(5-phenyl-1,3,4-thiadiazol-2-yl)ethyl)	($CDCl_3$) δ 8.15 (d, J = 5.9 Hz, 1H), 7.87 – 7.74 (m, 2H), 7.51 (d, J = 5.9 Hz, 1H), 7.46 – 7.28 (m, 3H), 6.39 (b, 1H), 5.43 (s, 1H),	HRMS(B) m/z 411.1596(

amino) pyrimidin-4-yl)oxazolidin-2-one	4.58 (dt, J = 8.3, 3.3 Hz, 1H), 4.29 – 4.12 (m, 2H), 1.94 – 1.80 (b, 1H), 1.74 (d, J = 7.0 Hz, 3H), 0.69 (d, J = 6.8 Hz, 3H), 0.60 (d, J = 7.2 Hz, 3H)	M +H)+, RT=2.54min.
293: (S)-3-{2-[1-(5-Chloro-1H-benzoimidazol-2-yl)-ethylamino]-pyrimidin-4-yl}-4-isopropyl-oxazolidin-2-one		HRMS(B) m/z 400.1414, RT=2.04 min.
294: (S)-3-(2-{(S)-1-[5-(2,2-Dimethyl-propyl)-isoxazol-3-yl]-ethylamino}-pyrimidin-4-yl)-4-isopropyl-oxazolidin-2-one	($CDCl_3$) δ 8.22 (d, J = 5.7 Hz, 1.0 H), 7.52 (d, J = 5.8 Hz, 0.95 H), 5.92 (s, 0.96 H), 5.50 (d, J = 7.5 Hz, 0.97 H), 5.22 (s, 0.83H), 4.72 (d, J = 8.3 Hz, 1.0 H), 4.42 – 4.20 (m, 2.06 H), 3.51 (s, 0.27 H), 2.61 (s, 2.05 H), 1.62 (d, J = 7.0 Hz, 4.13 H), 0.97 (s, 8.95 H), 0.90 (d, J = 7.0 Hz, 2.56 H), 0.80 (d, J = 7.0 Hz, 2.93 H).	HRMS(B) m/z 387.2271
295: (4S)-4-isopropyl-3-(2-(1-(5-phenylpyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) δ 8.93 (d, J = 5.9 Hz, 4H), 8.26 – 8.17 (m, 2H), 7.64 – 7.44 (m, 12H), 6.41 (br s, 1H), 5.31 (br s, 1H), 4.79 – 4.65 (m, 2H), 4.41 – 4.24 (m, 4H), 2.65 (dddd, J = 27.4, 14.1, 7.1, 3.5 Hz, 1H), 2.20 (br s, 1H), 1.75-1.64 (m, 4H), 1.07 – 0.85 (m, 9H), 0.78 (s, 3H).	HRMS(B) m/z 405.2024 and 405.2025 (M + H)+.
296: 4-{(S)-1-[4-((S)-4-Isopropyl-2-oxo-oxazolidin-3-yl)-pyrimidin-2-ylamino]-ethyl}-piperidine-1-carboxylic acid benzyl ester		HRMS(B) (M+) = 467.2533 RT.: 2.83 min.
297: (S)-3-(2-((S)-1-(5-bromopyridin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.		HRMS(B) m/z 406.0870 (M + H)+. RT.: 2.50 min.
298: 3-(5-fluoro-2-((1-(5-(4-fluoro-3-methylphenyl)pyridin-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one		HRMS(B) m/z 412.1578 (M + H)+. RT.: 2.35 min.
299: 3-(2-(1-(5-(4-fluorophenoxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one.		HRMS(B) m/z 411.1572 (M + H)+. RT.: 2.25 min.
300: 3-(5-fluoro-2-(1-(5-(4-fluorophenoxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one.		HRMS(B) m/z 415.1320 (M + H)+. RT.: 2.26 min.
301: (4S)-3-(2-(1-(5-(2,4-	($CDCl_3$) δ 8.45 (d, J = 4.6 Hz, 4H), 8.21 (d,	MS m/z

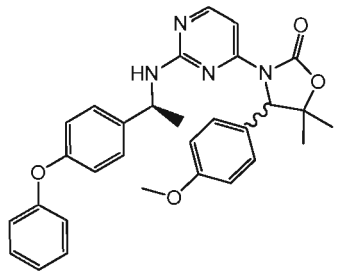
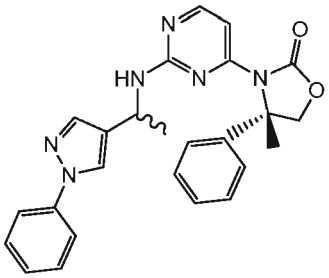
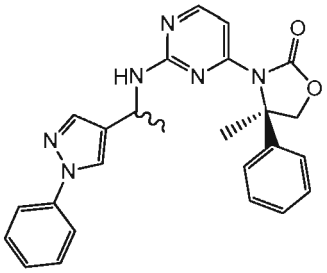
difluorobenzyloxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	J = 5.8 Hz, 2H), 7.53 – 7.41 (m, 4H), 6.93 (ddddd, J = 19.9, 9.8, 8.7, 2.6, 1.2 Hz, 4H), 6.21 (s, 1H), 6.11 (s, 1H), 5.21 (br s, 2H), 5.18 (s, 2H), 5.16 (s, 2H), 4.74 (dt, J = 7.7, 3.3 Hz, 1H), 4.66 (d, J = 7.4 Hz, 1H), 4.38 – 4.24 (m, 4H), 2.65 (ddq, J = 10.5, 7.1, 3.5 Hz, 1H), 2.30 (br s, 1H), 1.65-1.59 (m, 6H), 1.01 (d, J = 7.0 Hz, 3H), 0.89 (dq, J = 7.6, 4.9, 4.4 Hz, 6H), 0.79 (d, J = 6.5 Hz, 3H).	471.8 (M + H)+.
302: (S)-3-(2-{(S)-1-[4-(4-Fluoro-phenoxy)-cyclohexyl]-ethylamino}-pyrimidin-4-yl)-4-isopropyl-oxazolidin-2-one		LC-MS m/z 442.53 (M + H)+; RT.: 1.77 min.
303: (4S)-3-(2-(1-(5-(5-bromopyridin-3-yloxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	($CDCl_3$) δ 8.62 – 8.49 (m, 6H), 8.44 – 8.36 (m, 2H), 8.22 (dd, J = 5.7, 0.6 Hz, 2H), 7.57 – 7.46 (m, 4H), 6.14 (br s, 2H), 5.33 (br s, 2H), 4.76 (dt, J = 8.2, 3.4 Hz, 1H), 4.67 (s, 1H), 4.40 – 4.26 (m, 4H), 2.67 (pd, J = 7.0, 3.4 Hz, 1H), 2.32 (br s, 1H), 1.69 – 1.61 (m, 6H), 1.02 (d, J = 7.0 Hz, 3H), 0.99 – 0.80 (m, 9H).	HRMS(B) m/z 500.1038 and 500.1034 (M + H)+.
304: (S)-3-(2-((S)-1-(5-chloropyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.	($CDCl_3$) δ 8.58 (s, 2H), 8.12 (d, J = 5.8 Hz, 1H), 7.40 (d, J = 5.8 Hz, 1H), 5.97 (br s, 1H), 5.17 (br s, 1H), 4.63 (dt, J = 8.0, 3.2 Hz, 1H), 4.29 – 4.15 (m, 2H), 2.10 (br s, 1H), 1.50 – 1.46 (m, 3H), 0.88 – 0.66 (m, 6H).	LC-MS m/z 363.1 (M + H)+; RT.: 1.39 min.
305: (S)-3-(2-((S)-1-(5-(3-chloro-4-fluorophenoxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.	($CDCl_3$) δ 8.36 (s, 2H), 8.13 (s, 1H), 7.41 (d, J = 5.4 Hz, 1H), 7.15 – 7.00 (m, 2H), 6.85 (ddd, J = 9.0, 3.7, 3.0 Hz, 1H), 6.08 (s, 1H), 5.21 (br s, 1H), 4.66 (dt, J = 8.3, 3.4 Hz, 1H), 4.30 – 4.16 (m, 2H), 2.25 (br s, 1H), 1.56-1.51 (m, 3H), 0.85-0.78 (m, 3H), 0.77 – 0.70 (m, 3H).	HRMS(B) m/z 473.1484 (M + H)+.
306: (4S)-4-isopropyl-3-(2-(1-(5-(pyridin-3-yloxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one		HRMS(B) m/z 422.1938, RT 1.91min and 422.1944, RT 2.01min (M + H)+.
307: (4S)-3-(2-(1-(5-(3-fluorobenzyloxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	($CDCl_3$) δ 8.43 (d, J = 4.9 Hz, 4H), 8.21 (d, J = 5.7 Hz, 2H), 7.49 – 7.34 (m, 4H), 7.26 – 7.02 (m, 6H), 6.20 (br s, 1H), 6.11 (br s, 1H), 5.22 (br s, 2H), 5.16 (s, 2H), 4.74 (dt, J = 7.7, 3.3 Hz, 1H), 4.66 (br s, 1H), 4.38 – 4.23 (m, 4H), 2.66 (heptd, J = 7.0, 3.5 Hz, 1H), 2.26 (br s, 1H), 1.64-1.58 (m, 6H), 1.00 (d, J = 7.0 Hz, 3H), 0.94 – 0.85 (m,	HRMS(B) m/z 453.2048 and 453.2047 (M + H)+.

	6H), 0.78 (br s, 3H).	
308: (S)-3-(2-((S)-1-(5-iodopyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.		HRMS(B) m/z 454.0614 (M +). RT 2.35min
309: (4S)-4-isopropyl-3-(2-(1-(5-(5-(trifluoromethyl)pyridin-2-yloxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one		HRMS(B) m/z 490.1800, RT 2.17min and 490.1795, RT 2.23min (M + H)+.
310: (4S)-4-isopropyl-3-(2-(1-(pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one		HRMS(B) m/z 329.1728, RT 1.81min and 329.1726, RT 1.93min (M + H)+.
311: (4S)-3-(2-(1-(4-(4-fluorophenoxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	($CDCl_3$) δ 8.56 (dd, J = 5.7, 2.3 Hz, 2H), 8.20 (dd, J = 5.7, 4.0 Hz, 2H), 7.46 (dd, J = 5.7, 4.4 Hz, 2H), 7.20 – 7.00 (m, 8H), 6.71 (dd, J = 5.7, 2.0 Hz, 2H), 6.03 (br s, 1H), 5.87 (br s, 1H), 5.11 (br s, 2H), 4.72 – 4.61 (m, 2H), 4.40 – 4.23 (m, 4H), 2.59 (ddp, J = 10.5, 7.1, 3.5 Hz, 1H), 2.21 (br s, 1H), 1.59-1.55 (m, 6H), 1.00 – 0.85 (m, 9H), 0.80 (d, J = 6.3 Hz, 3H).	HRMS(B) m/z 439.1887 and 439.1887 (M + H)+.
312: (S)-3-(2-((S)-1-(4-(((2S,6R)-2,6-dimethylmorpholino)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	^{1}H NMR (400 MHz, CD_3OD) δ ppm 0.63 (br. s., 3 H) 0.79 (br. s., 3 H) 1.20 (dd, J=6.26, 2.74 Hz, 6 H) 1.58 (d, J=7.04 Hz, 3 H) 2.54 - 2.82 (m, 2H) 3.73 - 3.90 (m, 2 H) 4.32 (d, J=3.52 Hz, 2 H) 4.39 (d, J=5.87 Hz, 2 H) 4.68 - 4.78 (m, 1 H) 5.15 - 5.31 (m, 1 H) 7.51 (s, 4 H) 7.62 - 7.76 (m, 1 H) 8.08 - 8.22 (m, 1 H)	LCMS m/z 454.3 (M + H)+, Rt 0.57 min

The compounds in Table 9 were prepared using methods substantially similar to those described for the preparation of Examples 1, 113, and 171 through 212, including chiral separation to isolate the two diastereomers.

5

Table 9.

313 & 314	315 & 316	317 & 318
		
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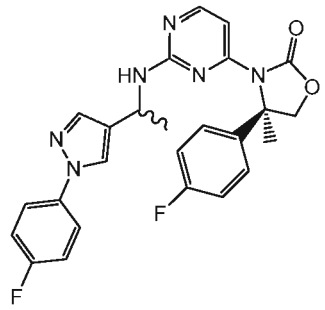	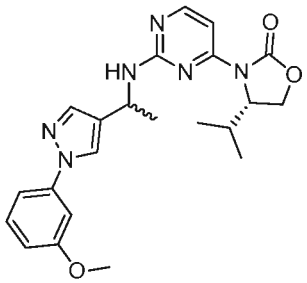	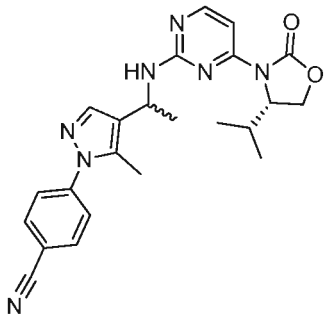
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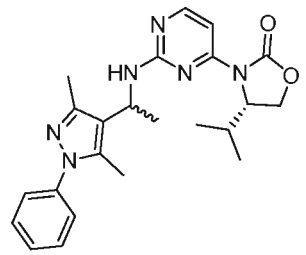	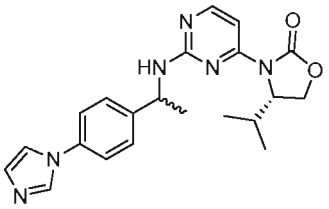	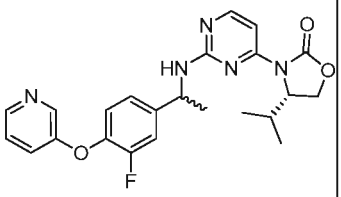
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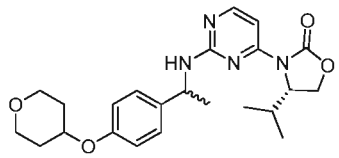	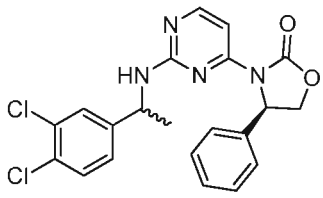	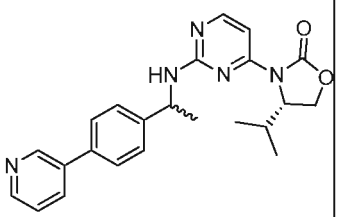
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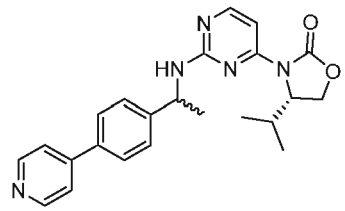	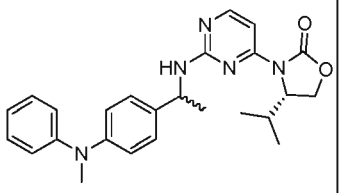	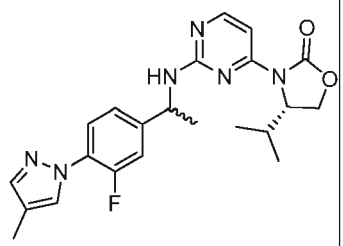
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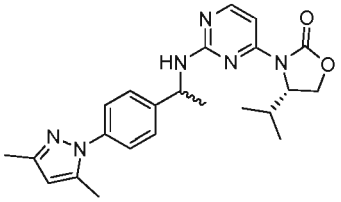	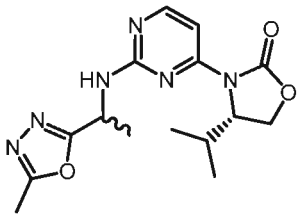	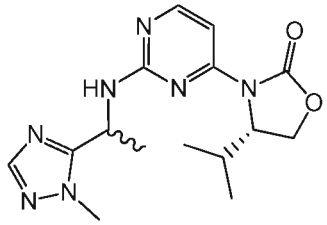
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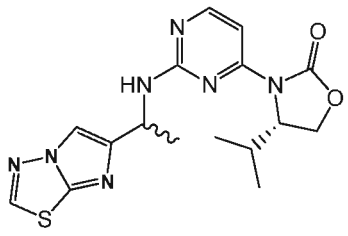	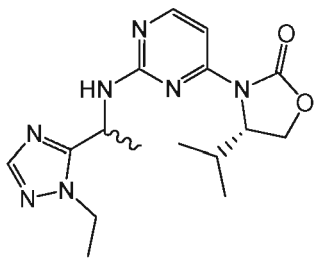	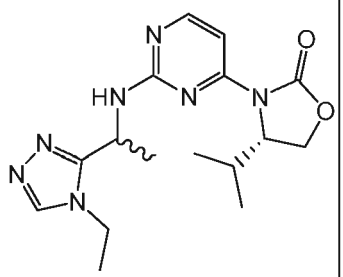
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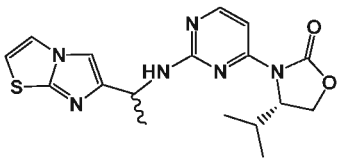	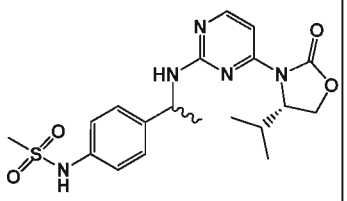	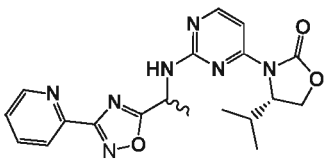
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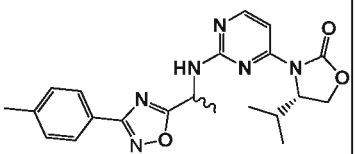	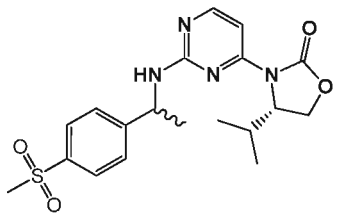	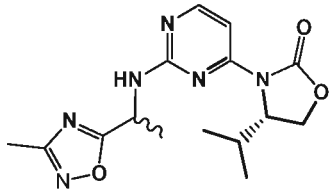
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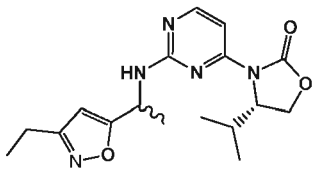	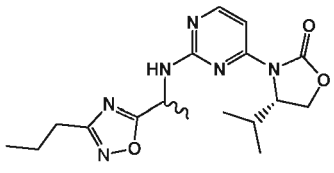	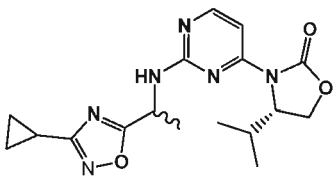
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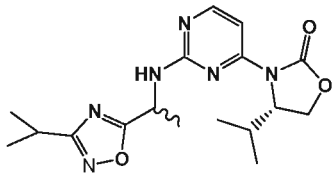	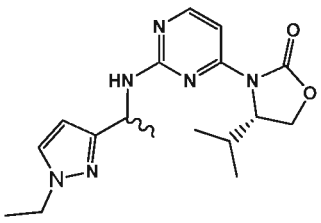	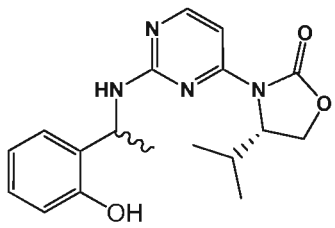
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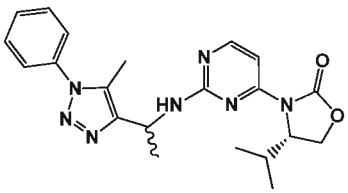	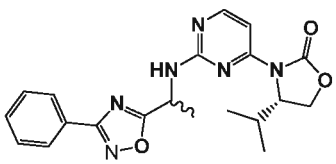	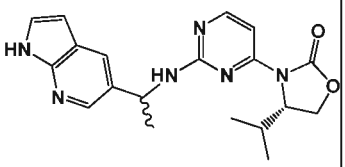
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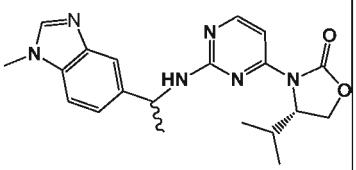	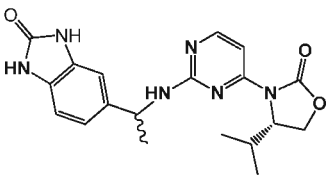	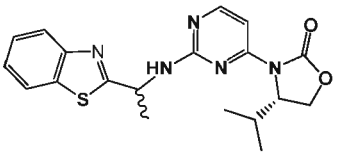
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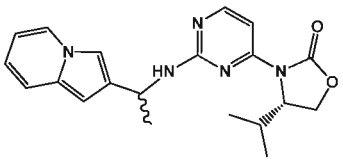	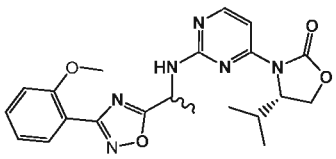	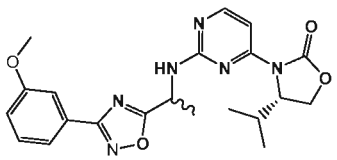
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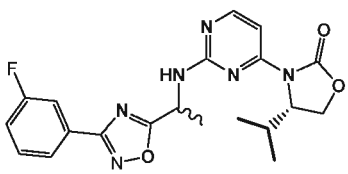	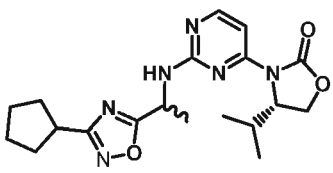	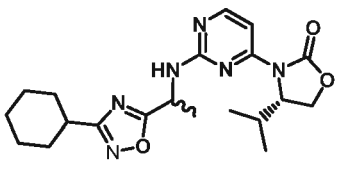
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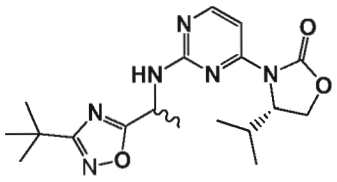	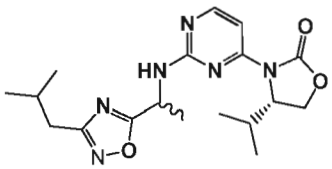	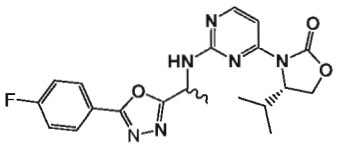
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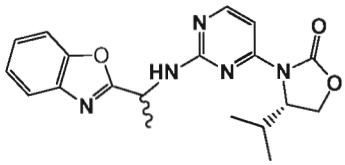	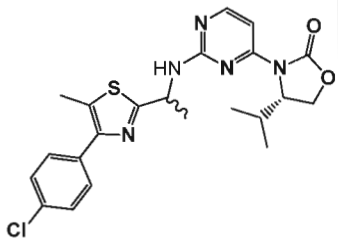	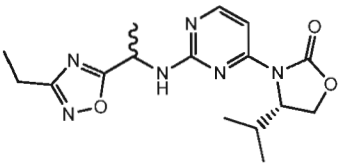
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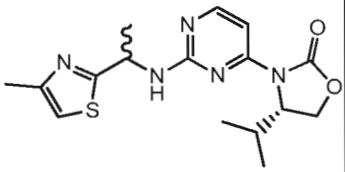	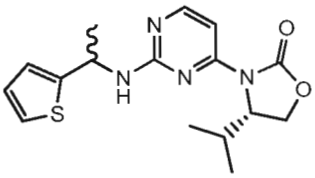	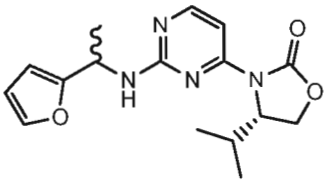
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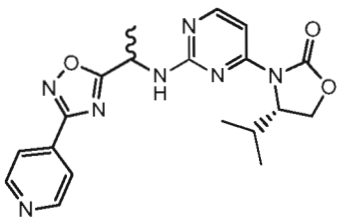	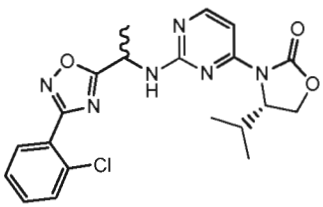	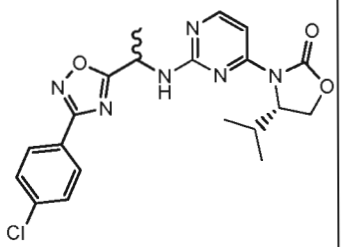
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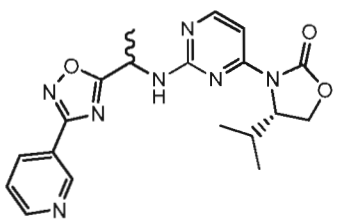	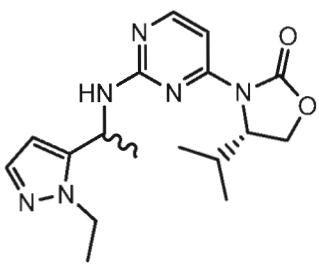	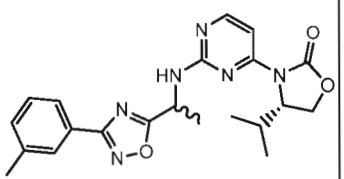
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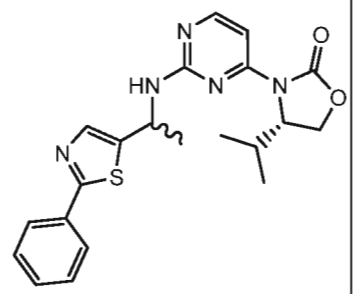	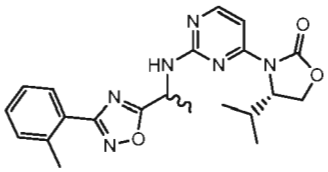	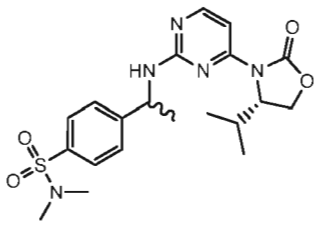
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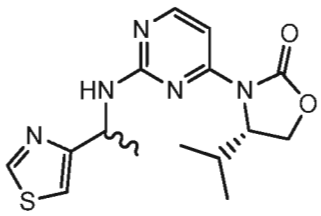	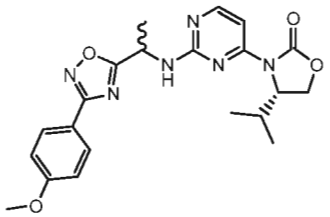	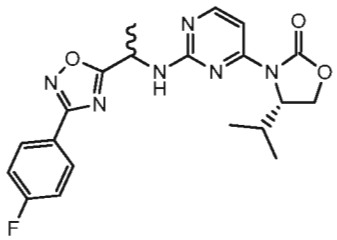
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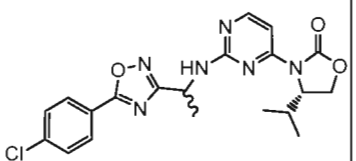	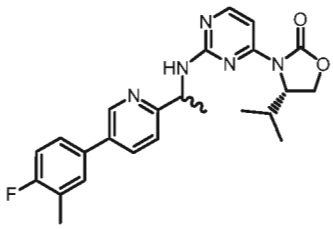	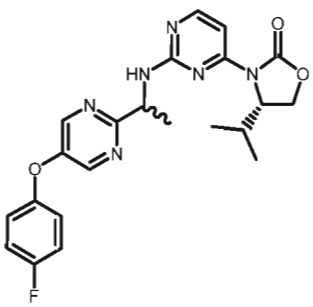
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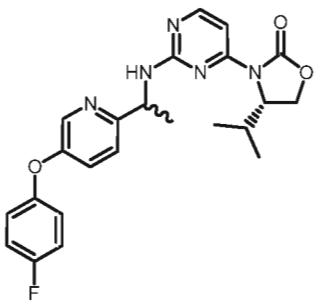	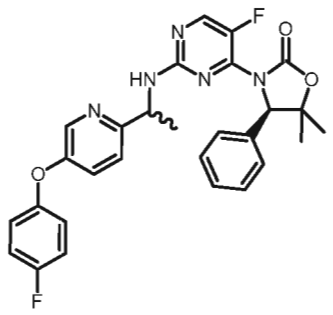	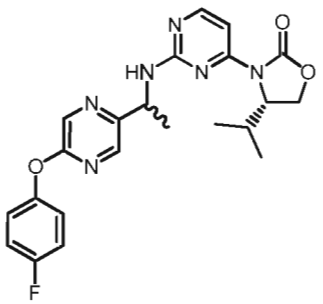
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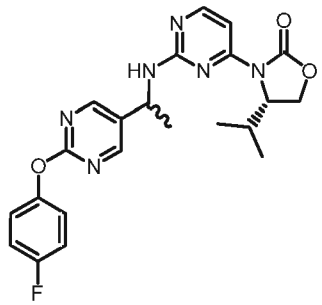	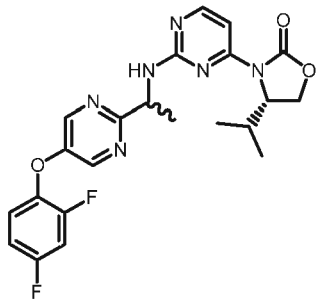	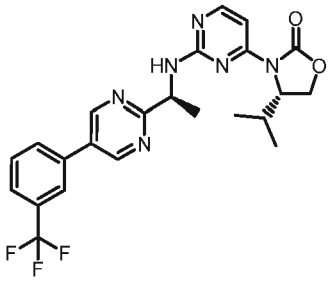
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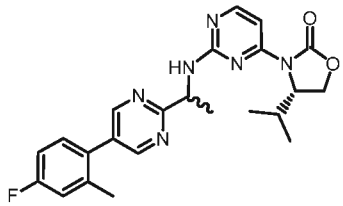
		

Table 10. Chemical name, NMR chemical shifts, chiral separation conditions and LCMS signal for each compound listed in Table 9.

Example: Name	**Chiral separation conditions, peak identification and analytical data**
331 & 314: 4-(4-methoxyphenyl)-5,5-dimethyl-3-(2-((S)-1-(4-phenoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	The chiral separation was carried out with SFC (IA-H, 5µM, 20 x 50 mm) using 28% MeOH in CO2 to give (R)-4-(4-methoxyphenyl)-5,5-dimethyl-3-(2-(((S)-1-(4-phenoxyphenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-(4-methoxyphenyl)-5,5-dimethyl-3-(2-(((S)-1-(4-phenoxyphenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one. 1st Peak 313: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, J = 5.9, 1.6 Hz, 1H), 7.43 (d, J = 5.7 Hz, 1H), 7.30 – 7.22 (m, 2H), 7.20 – 7.14 (m, 2H), 7.06 – 7.00 (m, 1H), 6.98 (d, J = 8.2 Hz, 2H), 6.94 – 6.86 (m, 4H), 6.83 – 6.76 (m, 2H), 5.24 (br s, 1H), 5.01 (s, 1H), 4.57 (br s, 1H), 3.72 (s, 3H), 1.46 (s, 3H), 1.24 – 1.09 (m, 3H), 0.92 (s, 3H); HRMS(B) m/z 511.2326 (M + H) +. 2nd Peak 314 : ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 5.7 Hz, 1H), 7.51 (d, J = 5.7 Hz, 1H), 7.38 – 7.29 (m, 2H), 7.10 (tt, J = 7.3, 1.2 Hz, 1H), 7.06 – 6.90 (m, 6H), 6.89 – 6.82 (m, 2H), 6.82 – 6.75 (m, 2H), 5.29 (s, 1H), 5.09 (br s, 1H), 4.80 (br s, 1H), 3.72 (s, 3H), 1.63 (s, 3H), 1.48 (d, J = 6.8 Hz, 3H), 1.01 (s, 3H); HRMS(B) m/z 511.2323 (M + H) +.

315 & 316: (S)-4-methyl-4-phenyl-3-(2-(1-(1-phenyl-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	The chiral separation was carried out with SFC (IA, 5µm, 20 x 250 mm) using 45% iPrOH with 0.2% Et2NH in CO2 to give (S)-4-methyl-4-phenyl-3-(2-(((R)-1-(1-phenyl-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-methyl-4-phenyl-3-(2-(((S)-1-(1-phenyl-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one. 1st Peak 315: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 5.8 Hz, 1 H), 7.63 – 7.60 (m, 2 H), 7.49 – 7.44 (m, 4 H), 7.37 – 7.28 (m, 4 H), 7.26 – 7.22 (m, 2 H), 7.12 – 7.08 (m, 1 H), 4.94 (br s, 1 H), 4.45 (br s, 1 H), 4.31 – 4.27 (m, 2 H), 2.19 (s, 3 H), 1.44 (d, J = 6.8 Hz, 3 H); HRMS(B) m/z 441.2036 (M + H)+. 2nd Peak 316: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 5.8 Hz, 1 H), 7.67 – 7.63 (m, 3 H), 7.53 (s, 1 H), 7.49 – 7.44 (m, 3 H), 7.40 – 7.37 (m, 2 H), 7.33 – 7.30 (m, 4 H), 4.99 (br s, 1 H), 4.38 (br s, 1 H), 4.26 (s, 2 H), 2.00 (s, 3 H), 1.07 (br s, 3 H); HRMS(B) m/z 441.2039 (M + H)+.
317 & 318: (R)-4-methyl-4-phenyl-3-(2-(1-(1-phenyl-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	The chiral separation was carried out with SFC (IA, 5µm, 20 x 250 mm) with 45% iPrOH modified with 0.2% Et2NH in CO2 to give (R)-4-methyl-4-phenyl-3-(2-(((S)-1-(1-phenyl-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-methyl-4-phenyl-3-(2-(((S)-1-(1-phenyl-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one. 1st peak 317: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 5.8 Hz, 1 H), 7.68 – 7.63 (m, 3 H), 7.53 (s, 1 H), 7.49 – 7.44 (m, 3 H), 7.41 – 7.37 (m, 2 H), 7.33 – 7.30 (m, 4 H), 4.98 (br s, 1 H), 4.39 (br s, 1 H), 4.26 (s, 2 H), 2.00 (s, 3 H), 1.07 (br s, 3 H); HRMS(B) m/z 441.2037 (M + H)+. 2nd peak 318: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 5.8 Hz, 1 H), 7.63 – 7.60 (m, 2 H), 7.49 – 7.44 (m, 4 H), 7.36 – 7.29 (m, 4 H), 7.26 – 7.22 (m, 2 H), 7.12 – 7.08 (m, 1 H), 5.02 (br s, 1 H), 4.45 (br s, 1 H), 4.31 – 4.26 (m, 2 H), 2.19 (s, 3 H), 1.44 (d, J = 6.8 Hz, 3 H); HRMS(B) m/z 441.2039 (M + H)+.
319 & 320: (R)-4-(4-fluorophenyl)-3-(2-(1-(1-(4-fluorophenyl)-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)-4-methyloxazolidin-2-one	Separation was achieved on a normal phase silica gel column with 10 to 50% ethylacetate / heptane to give (R)-4-(4-fluorophenyl)-3-(2-(((R)-1-(1-(4-fluorophenyl)-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)-4-methyloxazolidin-2-one and (R)-4-(4-fluorophenyl)-3-(2-(((S)-1-(1-(4-fluorophenyl)-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)-4-methyloxazolidin-2-one. 1st peak 319: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 5.8 Hz, 1 H), 7.53 – 7.48 (m, 3 H), 7.44 (s, 1 H), 7.36 (d, J = 5.8 Hz, 1 H), 7.22 – 7.17 (m, 2 H), 7.09 – 7.03 (m, 2 H), 7.01 – 6.95 (m, 2 H), 4.98 (br s, 1 H), 4.33 (br s, 1 H), 4.15 (q, J = 8.6 Hz, 2 H), 1.90 (s, 3 H), 1.04 (br s, 3 H); HRMS(B) m/z 477.1827 (M + H)+. 2nd peak 320: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 5.8 Hz, 1 H), 7.62 – 7.56 (m, 2 H), 7.45 – 7.39 (m, 3 H), 7.31 – 7.26 (m, 2 H), 7.18 – 7.12 (m, 2 H), 6.93 (t, J = 8.6 Hz, 2 H), 5.01 (br s, 1 H), 4.50 (br s, 1 H), 4.30 –

	4.23 (m, 2 H), 2.17 (s, 3 H), 1.45 (d, J = 6.8 Hz, 3 H); HRMS(B) m/z 477.1829 (M + H)+.
321 & 322: (S)-4-isopropyl-3-(2-(1-(1-(3-methoxyphenyl)-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	Separation was achieved on a normal phase silica gel column with 10 to 50% ethylacetate / heptane to give (S)-4-isopropyl-3-(2-(((R)-1-(1-(3-methoxyphenyl)-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(1-(3-methoxyphenyl)-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one. 1st peak 321: ^{1}H NMR (400 MHz, MeOD) δ 8.18 (dd, J = 3.3, 2.5 Hz, 2H), 7.70 (s, 1H), 7.42 (d, J = 5.8 Hz, 1H), 7.38 (t, J = 8.1 Hz, 1H), 7.31 (t, J = 2.3 Hz, 1H), 7.27 (ddd, J = 8.0, 2.1, 0.9 Hz, 1H), 6.89 (ddd, J = 8.1, 2.5, 0.9 Hz, 1H), 5.21 (q, J = 6.8 Hz, 1H), 4.81 – 4.73 (m, 1H), 4.44 – 4.34 (m, 2H), 3.87 (s, 3H), 2.64 (pd, J = 7.0, 3.5 Hz, 1H), 1.61 (d, J = 6.9 Hz, 3H), 0.99 (d, J = 7.1 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H).HRMS(B) (M+H) 423.2141 Calc'd (M+H) 423.2145 2nd peak 322: ^{1}H NMR (400 MHz, MeOD) δ 8.18 (d, J = 5.8 Hz, 1H), 8.10 (s, 1H), 7.63 (s, 1H), 7.41 (d, J = 5.8 Hz, 1H), 7.37 (t, J = 8.2 Hz, 1H), 7.28 (t, J = 2.3 Hz, 1H), 7.24 (ddd, J = 8.1, 2.1, 0.9 Hz, 1H), 6.88 (ddd, J = 8.3, 2.5, 0.9 Hz, 1H), 5.19 (q, J = 6.9 Hz, 1H), 4.74 (dt, J = 7.6, 3.5 Hz, 1H), 4.42 – 4.28 (m, 2H), 3.86 (s, 3H), 2.31 (br s, 1H), 1.61 (d, J = 6.9 Hz, 3H), 0.79 (br s, 3H), 0.75 – 0.64 (br m, 3H). HRMS(B) (M+H) 423.2139 Calc'd (M+H) 423.2145
323 & 324: 4-(4-(1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)-5-methyl-1H-pyrazol-1-yl)benzonitrile	Chiral separation was achieved by SFC. (Column: Chiralpak-ID (Semi-Prep 20mm x 250mm) Isocratic:65%CO2:35%MeOH (5mM NH4OH additive) to give (S)-4-isopropyl-3-(2-(((R)-1-(1-(3-methoxyphenyl)-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(1-(3-methoxyphenyl)-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one. 1st peak 323: ^{1}H NMR (400 MHz, MeOD) δ 8.16 (d, J = 5.8 Hz, 1H), 7.95 – 7.88 (m, 2H), 7.75 (s, 1H), 7.73 – 7.67 (m, 2H), 7.40 (d, J = 5.8 Hz, 1H), 5.19 (q, J = 6.9 Hz, 1H), 4.79 (td, J = 5.7, 3.5 Hz, 1H), 4.40 (d, J = 5.7 Hz, 2H), 2.65 (pd, J = 7.0, 3.6 Hz, 1H), 2.41 (s, 3H), 1.59 (d, J = 6.8 Hz, 3H), 1.00 (d, J = 7.0 Hz, 3H), 0.89 (d, J = 6.9 Hz, 3H). HRMS(B) (M+H) 432.2138 Calc'd (M+H) 432.2148 2nd peak 324: ^{1}H NMR (400 MHz, MeOD) δ 8.17 (d, J = 5.8 Hz, 1H), 7.97 – 7.84 (m, 2H), 7.77 – 7.63 (m, 3H), 7.40 (d, J = 5.8 Hz, 1H), 5.16 (q, J = 6.8 Hz, 1H), 4.79 (dt, J = 7.5, 3.8 Hz, 1H), 4.43 – 4.33 (m, 2H), 2.41 (s, 4H), 1.59 (d, J = 6.9 Hz, 3H), 0.87 (br d, J = 7.1 Hz, 3H), 0.80 (br d, J = 6.9 Hz, 3H). HRMS(B) (M+H) 432.2137 Calc'd (M+H) 432.2148
325 & 326: (S)-3-(2-(1-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-	Chiral separation was achieved by chiral SFC column chromatography (Column AD-H 5mM 20x250mm column 15% MeOH+DEA) to give (S)-3-(2-(((R)-1-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-

2-one	one and (S)-3-(2-(((S)-1-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one. 1st peak 325: ^{1}H NMR (400 MHz, MeOD) δ 8.16 (d, J = 5.8 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.48 – 7.42 (m, 1H), 7.42 – 7.38 (m, 3H), 5.12 (q, J = 7.0 Hz, 1H), 4.78 (td, J = 5.6, 3.5 Hz, 1H), 4.44 – 4.36 (m, 2H), 2.63 (td, J = 7.0, 3.6 Hz, 1H), 2.34 (s, 3H), 2.32 (s, 3H), 1.59 (d, J = 7.1 Hz, 3H), 1.00 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 7.0 Hz, 3H). HRMS(B) (M+H) 421.2348 Calc'd (M+H) 421.2352 2nd peak 326: ^{1}H NMR (400 MHz, MeOD) δ 8.18 (d, J = 5.8 Hz, 1H), 7.56 – 7.49 (m, 2H), 7.48 – 7.41 (m, 1H), 7.40 – 7.35 (m, 3H), 5.07 (q, J = 7.1 Hz, 1H), 4.78 (dt, J = 7.8, 3.8 Hz, 1H), 4.44 – 4.32 (m, 2H), 2.33 (s, 3H), 2.31 (br s, 1H) 2.29 (s, 3H), 1.59 (d, J = 7.1 Hz, 3H), 0.85 (br d, J = 7.0 Hz, 3H), 0.77 (br d, J = 6.9 Hz, 3H). HRMS(B) (M+H) 421.2347 Calc'd (M+H) 421.2352
327 & 328: (S)-3-(2-(1-(4-(1H-imidazol-1-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Separation was achieved by reverse HPLC (10-85% ACN/water 0.1% NH4OH modifier) to give (S)-3-(2-(((R)-1-(4-(1H-imidazol-1-yl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(4-(1H-imidazol-1-yl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one. 1st peak 327: ^{1}H NMR (400 MHz, MeOD) δ 8.25 – 8.00 (m, 2H), 7.53 (d, J = 0.7 Hz, 5H), 7.38 (d, J = 5.9 Hz, 1H), 7.15 (s, 1H), 5.04 (q, J = 7.1 Hz, 1H), 4.50 (br s, 1H), 4.40 – 4.19 (m, 2H), 2.68 (pd, J = 7.0, 3.6 Hz, 1H), 1.57 (d, J = 7.0 Hz, 3H), 1.02 (d, J = 7.0 Hz, 3H), 0.87 (d, J = 7.0 Hz, 3H). HRMS(B) (M+H) 393.2042 Calc'd (M+H) 393.2039 2nd peak 328: ^{1}H NMR (400 MHz, MeOD) δ 8.16 (d, J = 5.8 Hz, 1H), 8.10 (t, J = 1.2 Hz, 1H), 7.55 (t, J = 1.4 Hz, 1H), 7.52 (s, 4H), 7.38 (d, J = 5.8 Hz, 1H), 7.15 (t, J = 1.2 Hz, 1H), 5.12 (q, J = 7.0 Hz, 1H), 4.67 (br s, 1H), 4.44 – 4.23 (m, 2H), 1.84 (br s, 1H), 1.57 (d, J = 7.0 Hz, 3H), 0.71 (br s, 3H), 0.60 (br s, 3H). HRMS(B) (M+H) 393.2026 Calc'd (M+H) 393.2039
329 & 330: (S)-3-(2-(1-(3-fluoro-4-(pyridin-3-yloxy)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (Column AD-H 5mM 20x250mm column 15% MeOH+DEA) to give (S)-3-(2-(((R)-1-(3-fluoro-4-(pyridin-3-yloxy)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-fluoro-4-(pyridin-3-yloxy)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one. 1st peak 329: ^{1}H NMR (400 MHz, MeOD) δ 8.32 – 8.23 (m, 2H), 8.15 (d, J = 5.8 Hz, 1H), 7.45 – 7.35 (m, 3H), 7.31 (dd, J = 11.8, 2.0 Hz, 1H), 7.26 (dd, J = 8.5, 2.0 Hz, 1H), 7.19 (t, J = 8.2 Hz, 1H), 5.15 – 4.95 (m, 1H), 4.51 (s, 1H), 4.41 – 4.26 (m, 2H), 2.68 (pd, J = 7.1, 3.6 Hz, 1H), 1.56 (d, J = 7.0 Hz, 3H), 1.01 (d, J = 7.1 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H). HRMS(B) (M+H) 438.1935 Calc'd (M+H) 438.1941 2nd peak 330: ^{1}H NMR (400 MHz, MeOD) δ 8.28 (dd, J = 4.7, 1.4 Hz, 1H), 8.26 (d, J = 2.8 Hz, 1H), 8.17 (d, J =

	5.8 Hz, 1H), 7.43 – 7.40 (m, 2H), 7.36 (ddd, J = 8.4, 2.9, 1.5 Hz, 1H), 7.30 (dd, J = 11.8, 2.0 Hz, 1H), 7.25 (dd, J = 8.4, 2.0 Hz, 1H), 7.19 (t, J = 8.2 Hz, 1H), 5.10 (q, J = 7.1 Hz, 1H), 4.72 (br s, 1H), 4.43 – 4.29 (m, 2H), 1.93 (br s, 1H), 1.55 (d, J = 7.0 Hz, 3H), 0.78 (br s, 3H), 0.69 (br s, 3H). HRMS(B) (M+H) 438.1928 Calc'd (M+H) 438.1941
331 & 332: (4S)-4-isopropyl-3-(2-((1-(4-((tetrahydro-2H-pyran-4-yl)oxy)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (Column IA-H 5mM 20x250mm column 30% MeOH) to give (S)-4-isopropyl-3-(2-(((R)-1-(4-((tetrahydro-2H-pyran-4-yl)oxy)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(4-((tetrahydro-2H-pyran-4-yl)oxy)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one. 1st peak 331: HRMS(B) (M+) 426.2267, RT = 2.45min 2nd peak 332: HRMS(B) (M+) 426.2267, RT = 2.37min
333 & 334: (R)-3-(2-(1-(3,4-dichlorophenyl)ethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	Separation was achieved on a normal phase silica gel column with 10 to 40% ethylacetate / heptane to give (R)-3-(2-(((S)-1-(3,4-dichlorophenyl)ethyl)amino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one and (R)-3-(2-(((R)-1-(3,4-dichlorophenyl)ethyl)amino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one 1st peak 333: ^{1}H NMR (400 MHz, MeOD) δ 8.49 (d, J = 5.7 Hz, 1H), 7.85 – 7.74 (m, 5H), 7.74 – 7.68 (m, 1H), 7.66 – 7.61 (m, 2H), 7.55 (dd, J = 8.3, 2.1 Hz, 1H), 5.90 (dd, J = 8.9, 4.0 Hz, 1H), 5.14 (t, J = 8.7 Hz, 1H), 4.97 – 4.89 (m, 1H), 4.56 (dd, J = 8.8, 4.1 Hz, 1H), 1.60 (d, J = 7.0 Hz, 3H). HRMS(B) (M+H) 429.0899 Calc'd (M+H) 429.0885 2nd peak 334: ^{1}H NMR (400 MHz, MeOD) δ 8.50 (d, J = 5.7 Hz, 1H), 7.79 (d, J = 5.9 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.57 (dt, J = 4.6, 2.3 Hz, 3H), 7.45 (dd, J = 6.4, 2.9 Hz, 2H), 7.31 (dd, J = 8.3, 2.2 Hz, 1H), 6.16 (dd, J = 8.6, 3.5 Hz, 1H), 5.26 (q, J = 6.9 Hz, 1H), 5.16 (t, J = 8.6 Hz, 1H), 4.97 – 4.88 (m, 1H), 4.56 (dd, J = 8.8, 3.6 Hz, 1H), 1.80 (d, J = 7.0 Hz, 3H). HRMS(B) (M+H) 429.0887 Calc'd (M+H) 429.0885
335 & 336: (S)-4-isopropyl-3-(2-(1-(4-(pyridin-3-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (Column IA-H 5mM 20x250mm column 40% MeOH, 10mM NH4OH) to give (S)-4-isopropyl-3-(2-(((R)-1-(4-(pyridin-3-yl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(4-(pyridin-3-yl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one. 1st peak 335: ^{1}H NMR (400 MHz, MeOD) δ 8.81 (br s, 1H), 8.52 (br s, 1H), 8.14 (br s, 1H), 8.10 (dt, J = 8.2, 1.7 Hz, 1H), 7.71 – 7.59 (m, 2H), 7.58 – 7.46 (m, 3H), 7.37 (d, J = 5.8 Hz, 1H), 5.04 (dd, J = 11.2, 5.3 Hz, 1H), 4.50 (br s, 1H), 4.40 – 4.19 (m, 2H), 2.69 (ddd, J = 10.4, 7.0, 3.5 Hz, 1H), 1.58 (d, J = 7.0 Hz, 3H), 1.03 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 7.0 Hz, 3H). HRMS(B) (M+H) 404.2085 Calc'd (M+H) 404.2086 2nd peak 336: ^{1}H NMR (400 MHz, MeOD) δ 8.82 (br s,

	1H), 8.55 (br s, 1H), 8.17 (br s, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.70 – 7.59 (m, 2H), 7.54 (br s, 1H), 7.51 – 7.45 (m, 2H), 7.38 (d, J = 5.7 Hz, 1H), 5.11 (q, J = 7.0 Hz, 1H), 4.66 (br s, 1H), 4.36 – 4.30 (m, 2H), 1.80 (br s, 1H), 1.58 (d, J = 7.0 Hz, 3H), 0.67 (br s, 3H), 0.56 (br s, 3H). HRMS(B) (M+H) 404.2079 Calc'd (M+H) 404.2086
337 & 338: (S)-4-isopropyl-3-(2-(1-(4-(pyridin-4-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	Separation was achieved on a normal phase silica gel column with 20 to 100% ethylacetate / heptane to give (S)-4-isopropyl-3-(2-(((R)-1-(4-(pyridin-4-yl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(4-(pyridin-4-yl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one. 1st peak 337: ^{1}H NMR (400 MHz, MeOD) δ 8.58 (br s, 2H), 8.14 (d, J = 5.9 Hz, 1H), 7.83 – 7.66 (m, 4H), 7.60 – 7.46 (m, 2H), 7.37 (d, J = 5.8 Hz, 1H), 5.15 – 4.96 (m, 1H), 4.48 (br s, 1H), 4.38 – 4.15 (m, 2H), 2.69 (ddp, J = 10.5, 7.0, 3.5 Hz, 1H), 1.58 (d, J = 7.0 Hz, 3H), 1.03 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H). HRMS(B) (M+H) 404.2068 Calc'd (M+H) 404.2086 2nd peak 338: ^{1}H NMR (400 MHz, MeOD) δ 8.59 (br s, 2H), 8.17 (br s, 1H), 7.80 – 7.68 (m, 4H), 7.56 – 7.44 (m, 2H), 7.38 (d, J = 5.8 Hz, 1H), 5.11 (q, J = 7.0 Hz, 1H), 4.65 (br s, 1H), 4.31 (dt, J = 17.1, 9.0 Hz, 2H), 1.76 (br s, 1H), 1.58 (d, J = 7.1 Hz, 3H), 0.66 (br s, 3H), 0.55 (br s, 3H). HRMS(B) (M+H) 404.1939 Calc'd (M+H) 404.2086
339 & 340: (S)-4-isopropyl-3-(2-(1-(4-(methyl(phenyl)amino)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	Separation was achieved on a normal phase silica gel column with 40 to 100% ethylacetate / heptane to give (S)-4-isopropyl-3-(2-(((R)-1-(4-(methyl(phenyl)amino)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(4-(methyl(phenyl)amino)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one. 1st peak 339: ^{1}H NMR (400 MHz, MeOD) δ 8.12 (d, J = 5.8 Hz, 1H), 7.37 (d, J = 5.8 Hz, 1H), 7.31 – 7.18 (m, 4H), 7.03 – 6.94 (m, 4H), 6.91 (tt, J = 7.4, 1.1 Hz, 1H), 4.99 – 4.93 (m, 1H), 4.57 (br s, 1H), 4.42 – 4.27 (m, 2H), 3.28 (s, 3H), 2.68 (ddq, J = 10.5, 6.9, 3.4 Hz, 1H), 1.53 (d, J = 6.9 Hz, 3H), 1.01 (d, J = 7.1 Hz, 3H), 0.88 (d, J = 7.0 Hz, 3H). HRMS(B) (M+H) 432.2390 Calc'd (M+H) 432.2400 2nd peak 340: ^{1}H NMR (400 MHz, MeOD) δ 8.15 (d, J = 5.8 Hz, 1H), 7.37 (d, J = 5.8 Hz, 1H), 7.30 – 7.18 (m, 4H), 7.02 – 6.92 (m, 4H), 6.89 (tt, J = 7.3, 1.1 Hz, 1H), 5.04 (q, J = 7.0 Hz, 1H), 4.77 – 4.67 (m, 1H), 4.43 – 4.26 (m, 2H), 3.27 (s, 3H), 2.11 (br s, 1H), 1.52 (d, J = 7.0 Hz, 3H), 0.79 (br s, 3H), 0.68 (br s, 3H). HRMS(B) (M+H) 432.2386 Calc'd (M+H) 432.2400
341 & 342: S)-3-(2-(1-(3-fluoro-4-(4-methyl-1H-pyrazol-1-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column (IC 20x250nm 45% IPA in CO2, 75g/min Flow) to give (S)-3-(2-(((R)-1-(3-fluoro-4-(4-methyl-1H-pyrazol-1-yl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-fluoro-4-(4-methyl-1H-pyrazol-1-yl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-

	isopropyloxazolidin-2-one. 1st peak 341: ^{1}H NMR (400 MHz, MeOD) δ 8.15 (d, J = 5.8 Hz, 1H), 7.81 (dt, J = 2.9, 0.9 Hz, 1H), 7.66 (t, J = 8.3 Hz, 1H), 7.56 (s, 1H), 7.40 (d, J = 5.8 Hz, 1H), 7.36 – 7.25 (m, 2H), 5.01 (d, J = 7.5 Hz, 1H), 4.46 (br s, 1H), 4.38 – 4.25 (m, 2H), 2.68 (pd, J = 7.0, 3.5 Hz, 1H), 2.17 (d, J = 0.6 Hz, 3H), 1.56 (d, J = 7.0 Hz, 3H), 1.02 (d, J = 7.1 Hz, 3H), 0.87 (d, J = 6.9 Hz, 3H). HRMS(B) (M+H) 425.2089 Calc'd (M+H) 425.2101 2nd peak 342: ^{1}H NMR (400 MHz, MeOD) δ 8.17 (d, J = 5.8 Hz, 1H), 7.80 (d, J = 2.6 Hz, 1H), 7.66 (t, J = 8.3 Hz, 1H), 7.56 (s, 1H), 7.40 (d, J = 5.8 Hz, 1H), 7.35 – 7.26 (m, 2H), 5.10 (q, J = 7.0 Hz, 1H), 4.69 (br s, 1H), 4.43 – 4.24 (m, 2H), 2.17 (s, 3H), 1.80 (br s,1H), 1.56 (d, J = 7.1 Hz, 3H), 0.73 (br s, 3H), 0.62 (br s, 3H). HRMS(B) (M+H) 425.2081 Calc'd (M+H) 424.2101
343 & 344: (S)-3-(2-(1-(4-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (Column IA 20x250mm column 25% MeOH, 0.2% DEA) to give (S)-3-(2-(((R)-1-(4-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(4-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one. 1st peak 343: ^{1}H NMR (400 MHz, MeOD) δ 8.14 (d, J = 5.8 Hz, 1H), 7.56 – 7.48 (m, 2H), 7.41 – 7.34 (m, 3H), 6.06 (s, 1H), 5.07 – 5.02 (m, 1H), 4.46 (br s, 1H), 4.39 – 4.22 (m, 2H), 2.79 – 2.60 (m, 1H), 2.26 (s, 3H), 2.24 (s, 3H), 1.58 (d, J = 7.0 Hz, 3H), 1.02 (d, J = 7.1 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H). HRMS(B) (M+H) 421.2332 Calc'd (M+H) 421.2352 2nd peak 344: ^{1}H NMR (400 MHz, MeOD) δ 8.15 (d, J = 5.8 Hz, 1H), 7.55 – 7.47 (m, 2H), 7.41 – 7.33 (m, 3H), 6.06 (s, 1H), 5.17 (q, J = 7.0 Hz, 1H), 4.74 (br s, 1H), 4.45 – 4.19 (m, 2H), 2.26 (s, 3H), 2.25 (s, 3H), 2.07 (br s, 1H), 1.56 (d, J = 7.0 Hz, 3H), 0.80 (br s, 3H), 0.65 (br s, 3H). HRMS(B) (M+H) 421.2335 Calc'd (M+H) 421.2352
345 & 346: (S)-4-isopropyl-3-(2-((1-(5-methyl-1,3,4-oxadiazol-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 80 ml/min, 99 bar, eluting 10% MeOH/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(5-methyl-1,3,4-oxadiazol-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(5-methyl-1,3,4-oxadiazol-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one. 1st peak 345: HRMS(B) m/z 333.1668 (M + H)+. RT=1.96 min. 2nd peak 346: HRMS(B) m/z 333.1668 (M + H)+. RT=1.58 min.
347 & 348: (S)-4-isopropyl-3-(2-((1-(1-methyl-1H-1,2,4-triazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one.	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 80 ml/min, 99 bar, eluting 10% MeOH/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(1-methyl-1H-1,2,4-triazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(1-methyl-1H-1,2,4-triazol-5-

	yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one. 1st peak 347: HRMS(B) m/z 332.1831 (M + H)+. RT=1.68 min. 2nd peak 348: HRMS(B) m/z 332.1833 (M + H)+. RT=1.57 min.
349 & 350: (S)-3-(2-((1-(imidazo[2,1-b][1,3,4]thiadiazol-6-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 80 ml/min, 99 bar, eluting 10% MeOH/CO2) to give (S)-3-(2-(((R)-1-(imidazo[2,1-b][1,3,4]thiadiazol-6-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(imidazo[2,1-b][1,3,4]thiadiazol-6-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one. 1st peak 349: HRMS(B) m/z 374.1384 (M + H)+. RT=2.01 min. 2nd peak 350: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.12 (d, J = 5.8 Hz, 1H), 7.60 (s, 1H), 7.38 (d, J = 5.8 Hz, 1H), 5.13 (s, 1H), 4.60 (dt, J = 8.3, 3.3 Hz, 1H), 4.33 – 4.07 (m, 2H), 2.25 (b, 1H), 1.57 (d, J = 6.8 Hz, 3H), 0.84 – 0.52 (b, 6H). HRMS(B) m/z 373.1321 (M +), RT=1.88 min.
351 & 352: (S)-3-(2-((1-(1-ethyl-1H-1,2,4-triazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 80 ml/min, 99 bar, eluting 10% MeOH/CO2) to give (S)-3-(2-(((R)-1-(1-ethyl-1H-1,2,4-triazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(1-ethyl-1H-1,2,4-triazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 351: HRMS(B) m/z 346.1985 (M + H)+. RT=1.89 min. 2nd peak 352: HRMS(B) m/z 346.1983 (M + H)+, RT=1.75 min.
353 & 354: (S)-3-(2-((1-(4-ethyl-4H-1,2,4-triazol-3-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 80 ml/min, 99 bar, eluting 10% MeOH/CO2) to give (S)-3-(2-(((R)-1-(4-ethyl-4H-1,2,4-triazol-3-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(4-ethyl-4H-1,2,4-triazol-3-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 353: HRMS(B) m/z 346.1984 (M + H)+. RT=1.80 min. 2nd peak 354:HRMS(B) m/z 346.1982 (M + H)+, RT=1.77 min.
355 & 356: (S)-3-(2-((1-(imidazo[2,1-b]thiazol-6-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 75 ml/min, 120 bar, eluting 20-30% MeOH/CO2) to give (S)-3-(2-(((R)-1-(imidazo[2,1-b]thiazol-6-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(imidazo[2,1-b]thiazol-6-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 355: HRMS(B) m/z 373.1436 (M + H)+. RT=1.92 min.

	2nd peak 356: HRMS(B) m/z 373.1439 (M +H)+, RT=1.84 min.
357 & 358: N-(4-(1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)ethyl)phenyl)methanesulfonamide	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 80 ml/min, 96 bar, eluting 25% MeOH/CO2) to give N-(4-((R)-1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)ethyl)phenyl)methanesulfonamide and N-(4-((S)-1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)ethyl)phenyl)methanesulfonamide 1st peak 357: HRMS(B) m/z 420.1689 (M + H)+. RT=2.08 min. 2nd peak 358: HRMS(B) m/z 420.1687 (M +H)+, RT=1.98 min.
359 & 360: (S)-4-isopropyl-3-(2-((1-(3-(pyridin-2-yl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Separation was achieved by silica gel chromatography (10 to 40% EtOAc / heptane) to give (S)-4-isopropyl-3-(2-(((R)-1-(3-(pyridin-2-yl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-(pyridin-2-yl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 359: HRMS(B) m/z 396.1784 (M + H)+. RT=2.26 min. 2nd peak 360: HRMS(B) m/z 396.1784 (M +H)+, RT=2.20 min.
361 & 362: (S)-4-isopropyl-3-(2-((1-(3-(p-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Separation was achieved by silica gel chromatography (10 to 40% EtOAc / heptane) to give (S)-4-isopropyl-3-(2-(((R)-1-(3-(p-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-(p-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one. 1st peak 361: HRMS(B) m/z 409.1985 (M + H)+. RT=2.88 min. 2nd peak 362: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J = 5.8 Hz, 1H), 8.03 (d, J = 5.9 Hz, 2H), 7.59 (d, J = 5.8 Hz, 1H), 7.28 (d, J = 8.0 Hz, 2H), 5.41 (b, 1H), 4.67 (dt, J = 8.2, 3.3 Hz, 1H), 4.36 – 4.18 (m, 2H), 2.42 (s, 3H), 2.29 – 2.13 (m, 1H), 1.78 (d, J = 7.2 Hz, 3H), 0.81 (d, J = 7.1 Hz, 3H), 0.73 (d, J = 7.0 Hz, 3H). HRMS(B) m/z 409.1985 (M +H)+, RT=2.85 min.
363 & 364: (S)-4-isopropyl-3-(2-((1-(4-(methylsulfonyl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 74 ml/min, 100 bar, eluting 25% MeOH/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(4-(methylsulfonyl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(4-(methylsulfonyl)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 363: HRMS(B) m/z 405.1594 (M + H)+. RT=2.26 min. 2nd peak 364: HRMS(B) m/z 405.1595 (M +H)+, RT=2.14 min.
365 & 366: (S)-4-isopropyl-3-(2-((1-(3-methyl-1,2,4-oxadiazol-5-	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 80 ml/min, 100 bar, eluting 20% IPA/CO2) to give (S)-4-

yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	isopropyl-3-(2-(((R)-1-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 365: HRMS(B) m/z 333.1679 (M + H)+. RT=2.19 min. 2nd peak 366: HRMS(B) m/z 333.1680 (M +H)+, RT=2.12 min.
367 & 368: (S)-3-(2-((1-(3-ethylisoxazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 79 ml/min, 100 bar, eluting 20% IPA/CO2) to give (S)-3-(2-(((R)-1-(3-ethylisoxazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-ethylisoxazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 367: HRMS(B) m/z 346.1886 (M + H)+. RT=2.51 min. 2nd peak 368: HRMS(B) m/z 346.1882 (M +H)+, RT=2.45 min.
369 & 370: (S)-4-isopropyl-3-(2-((1-(3-propyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 75 ml/min, 100 bar, eluting 20% IPA/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(3-propyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-propyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 369: HRMS(B) m/z 361.1989 (M + H)+. RT=2.52 min. 2nd peak 370: HRMS(B) m/z 361.1985 (M +H)+, RT=2.49 min.
371 & 372: (S)-3-(2-((1-(3-cyclopropyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 80 ml/min, 100 bar, eluting 15% IPA/CO2) to give (S)-3-(2-(((R)-1-(3-cyclopropyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-cyclopropyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 371: HRMS(B) m/z 359.1830 (M + H)+. RT=2.42 min. 2nd peak 372: HRMS(B) m/z 359.1833 (M +H)+, RT=2.37 min.
373 & 374: (S)-4-isopropyl-3-(2-((1-(3-isopropyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 80 ml/min, 100 bar, eluting 20% IPA/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(3-isopropyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-isopropyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 373: HRMS(B) m/z 361.1990 (M + H)+. RT=2.58 min. 2nd peak 374: HRMS(B) m/z 361.1987 (M +H)+, RT=2.54 min.
375 & 376: (S)-3-(2-((1-(1-ethyl-1H-pyrazol-3-	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 78

yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	ml/min, 100 bar, eluting 20% IPA/CO2) to give (S)-3-(2-(((R)-1-(1-ethyl-1H-pyrazol-3-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(1-ethyl-1H-pyrazol-3-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 375: HRMS(B) m/z 345.2046 (M + H)+. RT=2.31 min. 2nd peak 376: HRMS(B) m/z 345.2050 (M +H)+, RT=2.26 min.
377 & 378: (S)-3-(2-((1-(2-hydroxyphenyl)ethyl) amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral column chromatography (OJ-H , 4.6x250 mm column , 1 ml/min, eluting 25% ethanol /Heptane) to give (S)-3-(2-(((R)-1-(2-hydroxyphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(2-hydroxyphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 377: HRMS(B) m/z 343.1767 (M + H)+. RT=2.41 min. 2nd peak 378: HRMS(B) m/z 343.1767 (M +H)+, RT=2.36 min.
379 & 380: (S)-4-isopropyl-3-(2-((1-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 874ml/min, 100 bar, eluting 30% IPA/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 379: HRMS(B) m/z 408.2135 (M + H)+. RT=2.37 min. 2nd peak 380: HRMS(B) m/z 408.2140 (M +H)+, RT=2.31 min.
381 & 382: (S)-4-isopropyl-3-(2-((1-(3-phenyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 74 ml/min, 100 bar, eluting 20% -35% IPA/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(3-phenyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-phenyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 381: HRMS(B) m/z 395.1792 (M + H)+. RT=2.63 min. 2nd peak 382: HRMS(B) m/z 395.1818(M +H)+, RT=2.58min.
383 & 384: (S)-3-(2-(((R)-1-(1H-pyrrolo[2,3-b]pyridin-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IA , 20x250 mm column , 74 ml/min, 99 bar, eluting 45% MeOH w ith 5mM NH4OH /CO2) to give (S)-3-(2-(((R)-1-(1H-pyrrolo[2,3-b]pyridin-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(1H-pyrrolo[2,3-b]pyridin-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 383: HRMS(B) m/z 367.1862 (M + H)+. RT=2.10 min. 2nd peak 384: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 2.2 Hz, 1H), 8.19 (d, J = 5.8 Hz, 1H), 7.94 (d, J = 2.1

	Hz, 1H), 7.47 (d, J = 5.8 Hz, 1H), 7.38 (d, J = 3.5 Hz, 1H), 6.46 (d, J = 3.5 Hz, 1H), 5.30 – 5.08 (m, 1H), 4.73 – 4.51 (m, 1H), 4.28 (t, J = 8.8 Hz, 1H), 4.19 (dd, J = 9.0, 3.1 Hz, 1H), 1.78 (dd, J = 31.8, 17.0 Hz, 1H), 1.66 (d, J = 6.9 Hz, 3H), 0.56 (s, 6H). HRMS(B) m/z 367.1870(M +H)+, RT=2.00min.
385 & 386: (S)-4-isopropyl-3-(2-((1-(1-methyl-1H-benzo[d]imidazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 80 ml/min, 99 bar, eluting 20% IPA/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(1-methyl-1H-benzo[d]imidazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(1-methyl-1H-benzo[d]imidazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 385: HRMS(B) m/z 381.2026 (M + H)+. RT=2.05 min. 2nd peak 386: HRMS(B) m/z 381.2022(M +H)+, RT=1.96min.
387 & 388: (S)-4-isopropyl-3-(2-((1-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 80 ml/min, 100 bar, eluting 25% IPA/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 387: HRMS(B) m/z 383.1811 (M + H)+. RT=1.90 min. 2nd peak 388: HRMS(B) m/z 383.1815(M +H)+, RT=1.85min.
389 & 390: (S)-3-(2-((1-(benzo[d]thiazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (ID, 5uM, 20x250 mm column , 74 ml/min, 100 bar, eluting 35%MeOH/CO2) to give (S)-3-(2-(((R)-1-(benzo[d]thiazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(benzo[d]thiazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 389: HRMS(B) m/z 384.1488 (M + H)+. RT=2.44 min. 2nd peak 390: HRMS(B) m/z 384.1473(M +H)+, RT=2.36min.
391 & 392: (S)-3-(2-((1-(indolizin-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (OJ , 5uM, 20x250 mm column , 75 ml/min, 120 bar, eluting 15-55% MeOH/CO2) to give (S)-3-(2-(((R)-1-(indolizin-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(indolizin-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 391: HRMS(B) m/z 366.1926 (M + H)+. RT=2.66 min. 2nd peak 392: HRMS(B) m/z 366.1918(M +H)+, RT=2.63min.
393 & 394: (S)-4-isopropyl-3-(2-((1-(3-(2-methoxyphenyl)-1,2,4-oxadiazol-5-	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 80 ml/min, 100 bar, eluting 5-55% MeOH/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(3-(2-methoxyphenyl)-1,2,4-

yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-(2-methoxyphenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 393: HRMS(B) m/z 425.1925 (M + H)+. RT=2.57 min. 2nd peak 394: HRMS(B) m/z 425.1916(M +H)+, RT=2.52min.
395 & 396: (S)-4-isopropyl-3-(2-((1-(3-(3-methoxyphenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IA, 5uM, 20x250 mm column , 74 ml/min, 100 bar, eluting m25% MeOH/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(3-(3-methoxyphenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-(3-methoxyphenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 395: HRMS(B) m/z 425.1924 (M + H)+. RT=2.60 min. 2nd peak 396: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dt, J = 7.7, 1.2 Hz, 1H), 7.49 (dt, J = 3.7, 1.8 Hz, 2H), 7.29 (t, J = 8.0 Hz, 2H), 6.96 (ddd, J = 8.3, 2.7, 0.9 Hz, 1H), 5.34 (b, 1H), 4.58 (dt, J = 8.2, 3.3 Hz, 1H), 4.37 – 4.03 (m, 2H), 3.78 (s, 3H), 2.12 (b, 1H), 1.68 (d, J = 7.1 Hz, 3H), 0.73 (d, J = 7.1 Hz, 3H), 0.65 (d, J = 7.0 Hz, 3H). HRMS(B) m/z 425.1924(M +H)+, RT=2.54min.
397 & 398: (S)-3-(2-((1-(3-(3-fluorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H , 5uM, 20x250 mm column , 75 ml/min, 100 bar, eluting 20% MeOH/CO2) to give (S)-3-(2-(((R)-1-(3-(3-fluorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-(3-fluorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 397: HRMS(B) m/z 413.1729 (M + H)+. RT=2.66 min. 2nd peak 398: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dt, J = 7.8, 1.2 Hz, 1H), 7.77 (ddd, J = 9.4, 2.7, 1.5 Hz, 2H), 7.60 (d, J = 5.3 Hz, 1H), 7.46 (td, J = 8.0, 5.7 Hz, 1H), 7.22 (tdd, J = 8.4, 2.6, 1.0 Hz, 1H), 5.44 (b, 1H), 4.68 (dt, J = 8.3, 3.3 Hz, 1H), 4.44 – 4.11 (m, 2H), 2.18 (d, J = 8.4 Hz, 1H), 1.78 (d, J = 7.1 Hz, 3H), 0.83 (d, J = 6.9 Hz, 3H), 0.75 (d, J = 6.9 Hz, 3H). HRMS(B) m/z 413.1732(M +H)+, RT=2.61min.
399 & 400: (S)-3-(2-((1-(3-cyclopentyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IA , 5uM, 20x250 mm column , 74 ml/min,99 bar, eluting 15% MeOH/CO2) to give (S)-3-(2-(((R)-1-(3-cyclopentyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-cyclopentyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 399: HRMS(B) m/z 387.2133 (M + H)+. RT=2.54 min. 2nd peak 400: HRMS(B) m/z 387.2117(M +H)+, RT=2.50min.

401 & 402: (S)-3-(2-((1-(3-cyclohexyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IA, 5uM, 20x250 mm column , 74 ml/min, 99 bar, eluting 30% MeOH/CO2) to give (S)-3-(2-(((R)-1-(3-cyclohexyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-cyclohexyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 401: HRMS(B) m/z 401.2277 (M + H)+. RT=2.71 min. 2nd peak 402: HRMS(B) m/z 401.2288(M +H)+, RT=2.68min.
403 & 404: (S)-3-(2-((1-(3-(tert-butyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrirnidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IA, 5uM, 20x250 mm column , 74 ml/min, 100 bar, eluting 15% MeOH/CO2) to give (S)-3-(2-(((R)-1-(3-(tert-butyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-(tert-butyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 403: HRMS(B) m/z 375.2131 (M + H)+. RT=2.47 min. 2nd peak 404: HRMS(B) m/z375.2130 (M +H)+, RT=2.44min.
405 & 406: (S)-3-(2-((1-(3-isobutyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IA, 5uM, 20x250 mm column , 74 ml/min, 100 bar, eluting 15% MeOH/CO2) to give (S)-3-(2-(((R)-1-(3-isobutyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-isobutyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 405: HRMS(B) m/z 375.2120 (M + H)+. RT=2.45 min. 2nd peak 406: HRMS(B) m/z 375.2135 (M +H)+, RT=2.44min.
407 & 408: (S)-3-(2-((1-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IA, 5uM, 20x250 mm column , 74 ml/min, 99 bar, eluting 30% IPA/CO2) to give (S)-3-(2-(((R)-1-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 407: HRMS(B) m/z 413.1713 (M + H)+. RT=2.31 min. 2nd peak 408: HRMS(B) m/z 413.1721 (M +H)+, RT=2.25min.
409 & 410: (S)-3-(2-((1-(benzo[d]oxazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IA, 5uM, 20x250 mm column , 74 ml/min, 99 bar, eluting 25% MeOH/CO2) to give (S)-3-(2-(((R)-1-(benzo[d]oxazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(benzo[d]oxazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one

	1st peak 409: HRMS(B) m/z 368.1729 (M + H)+. RT=2.66 min. 2nd peak 410: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.61 (m, 1H), 7.54 (s, 1H), 7.51 – 7.42 (m, 2H), 7.40 – 7.21 (m, 2H), 6.40 (b, 1H), 5.39 (s, 1H), 4.64 (dt, J = 8.1, 3.2 Hz, 1H), 4.36 – 4.17 (m, 2H), 2.11 (b, 1H), 1.77 (d, J = 6.9 Hz, 3H), 0.64 (b, 6H). HRMS(B) m/z 368.1727 (M +H)+, RT=2.60min.
411 & 412: (S)-3-(2-((1-(4-(4-chlorophenyl)-5-methylthiazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Separation was achieved by silica gel chromatography (10 to 50% EtOAc / heptane) to give (S)-3-(2-(((R)-1-(4-(4-chlorophenyl)-5-methylthiazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(4-(4-chlorophenyl)-5-methylthiazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 411: HRMS(B) m/z 458.1401 (M + H)+. RT=3.02 min. 2nd peak 412: HRMS(B) m/z 458.1401 (M +H)+, RT=2.92min.
413 & 414: (S)-3-(2-((1-(3-ethyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H column (80 g/min, 80 bar, 20 x 250 mm) eluting 15% MeOH/CO2) to give (S)-3-(2-(((R)-1-(3-ethyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-ethyl-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 413: HRMS(B) m/z 346.1753 RT=2.13 min. 2nd peak 414: HRMS(B) m/z 346.1753 RT=2.05 min.
415 & 416: (S)-4-isopropyl-3-(2-((1-(4-methylthiazol-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H column (75 ml/min, 120 bar, 20 x 250 mm) eluting 10-25% MeOH/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(4-methylthiazol-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(4-methylthiazol-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 415: HRMS(B) m/z 347.1416 RT=2.25 min. 2nd peak 416: HRMS(B) m/z 347.1416 RT=2.17 min.
417 & 418: (S)-4-isopropyl-3-(2-((1-(thiophen-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H column (75 ml/min, 120 bar, 20 x 250 mm) eluting 10-25% MeOH/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(thiophen-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(thiophen-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 417: HRMS(B) m/z 332.1307 RT=2.54 min. 2nd peak 418: HRMS(B) m/z 332.1307 RT=2.53 min.
419 & 420: (S)-3-(2-((1-(furan-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD-H column (75 ml/min, 120 bar, 20 x 250 mm) eluting 10-25% MeOH/CO2) to give (S)-3-(2-(((S)-1-(furan-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((R)-1-(furan-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 419: HRMS(B) m/z 316.1535 RT=2.37 min.

	2nd peak 420: HRMS(B) m/z 316.1535 RT=2.39 min.
421 & 422: (S)-4-isopropyl-3-(2-((1-(3-(pyridin-4-yl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IA column (75 ml/min, 120 bar, 20 x 250 mm) eluting 15-25% MeOH/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(3-(pyridin-4-yl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-(pyridin-4-yl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 421: HRMS(B) m/z 395.1706 RT=1.75 min. 2nd peak 422: HRMS(B) m/z 395.1706 RT=2.25 min.
423 & 424: (S)-3-(2-((1-(3-(2-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IA column (75 ml/min, 120 bar, 20 x 250 mm) eluting 15-25% MeOH/CO2) to give (S)-3-(2-(((R)-1-(3-(2-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-(2-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 423: HRMS(B) m/z 428.1364 RT=3.01 min. 2nd peak 424: HRMS(B) m/z 428.1364 RT=2.79 min.
425 & 426: (S)-3-(2-((1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IA column (75 rnl/rnin, 120 bar, 20 x 250 mm) eluting 15-25% MeOH/CO2) to give (S)-3-(2-(((R)-1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 425: HRMS(B) m/z 428.1364 RT=2.65 min. 2nd peak 426: ^{1}H NMR (400 MHz, MeOD) δ 8.22 (d, J = 5.8 Hz, 1.0H), 8.08 – 7.97 (m, 2.07 H), 7.63 – 7.40 (m, 3.09 H), 5.41 (q, J = 7.2 Hz, 1.04 H), 4.75 – 4.63 (m, 0.97 H), 4.33 (d, J = 6.3 Hz, 2.18 H), 1.76 (d, J = 7.2 Hz, 3.31 H), 1.07 – 0.85 (m, 0.95 H), 0.70 (d, J = 38.0 Hz, 5.81 H). HRMS(B) m/z 428.1364
427: (S)-4-isopropyl-3-(2-((1-(3-(pyridin-3-yl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IA column (75 ml/min, 120 bar, 20 x 250 mm) eluting 15-25% MeOH/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(3-(pyridin-3-yl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-(pyridin-3-yl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 2nd peak 427: HRMS(B) m/z 395.1706 RT=2.24 min.
428 & 429: (S)-3-(2-((1-(1-ethyl-1H-pyrazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD column (75 g/min, 120 bar, 20 x 250 mm) eluting 25% IPA/0.2% DEA/CO2) to give (S)-3-(2-(((R)-1-(1-ethyl-1H-pyrazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(1-ethyl-1H-pyrazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 428: HRMS(B) m/z 345.2005 (M+H) RT=2.28 min. 2nd peak 429: HRMS(B) m/z 345.2044 (M+H) RT=2.21 min.

430: (S)-4-isopropyl-3-(2-(((S)-1-(3-(m-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD column (75 g/min, 120 bar, 20 x 250 mm) eluting 25-35% IPA/0.2% DEA/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(3-(m-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-(m-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 2nd peak 430: HRMS(B) m/z 345.2044 (M+H) RT=2.82 min.
431 & 432: (S)-4-isopropyl-3-(2-((1-(2-phenylthiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD column (75 g/min, 120 bar, 20 x 250 mm) eluting 40% IPA/0.2% DEA/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(2-phenylthiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(2-phenylthiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 431: HRMS(B) m/z 409.1573 RT=2.33 min. 2nd peak 432: ^{1}H NMR (400 MHz, MeOD) δ 8.19 (d, J = 5.8 Hz, 1H), 7.92 – 7.78 (m, 2H), 7.65 (d, J = 1.1 Hz, 1H), 7.53 – 7.27 (m, 4H), 5.43 (q, J = 6.9 Hz, 1H), 4.74 (dt, J = 7.8, 3.7 Hz, 1H), 4.41 – 4.20 (m, 2H), 2.16 (s, 1H), 1.69 (d, J = 7.0 Hz, 3H), 1.15 (d, J = 6.1 Hz, 1H), 0.88 – 0.49 (m, 6H). HRMS(B) m/z 409.1573
433 & 434: (S)-4-isopropyl-3-(2-((1-(3-(o-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AD column (75 g/min, 120 bar, 20 x 250 mm) eluting 25-40% IPA/0.2% DEA/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(3-(o-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-(o-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 433: HRMS(B) m/z 409.1 (M+H) RT=2.25 min. 2nd peak 434: ^{1}H NMR (400 MHz, MeOD) δ 8.20 (d, J = 5.8 Hz, 1H), 7.90 (dd, J = 7.7, 1.4 Hz, 1H), 7.47 (d, J = 5.8 Hz, 1H), 7.41 – 7.25 (m, 3H), 5.40 (q, J = 7.2 Hz, 1H), 4.69 (s, 1H), 4.44 – 4.22 (m, 2H), 3.34 (s, 2H), 2.54 (s, 3H), 1.75 (d, J = 7.2 Hz, 3H), 1.15 (d, J = 6.1 Hz, 1H), 0.69 (d, J = 35.0 Hz, 6H). HRMS(B) m/z 409.1 (M+H)
435 & 436: 4-(1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)ethyl)-N,N-dimethylbenzenesulfonamide	Chiral separation was achieved by chiral SFC column chromatography (AS-H column (80 g/min, 120 bar, 20 x 250 mm) eluting 15% IPA/0.2% DEA/CO2) to give 4-((R)-1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)ethyl)-N,N-dimethylbenzenesulfonamide and 4-((S)-1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)ethyl)-N,N-dimethylbenzenesulfonamide 1st peak 435: HRMS(B) m/z 433.1784 RT=2.45 min. 2nd peak 436: HRMS(B) m/z 433.1784 RT=2.32 min.
437 & 438: (S)-4-isopropyl-3-(2-((1-(thiazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (IC column (75 g/min, 120 bar, 20 x 250 mm) eluting 25% IPA/0.2% DEA/CO2) to give (S)-4-isopropyl-3-(2-(((S)-1-(thiazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((R)-1-(thiazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one

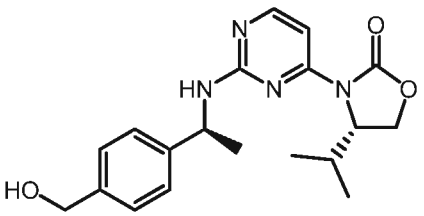
	1st peak 437: HRMS(B) m/z 333.1259 RT=1.88 min. 2nd peak 438: HRMS(B) m/z 333.1259 RT=1.98 min.
439 & 440: (S)-4-isopropyl-3-(2-((1-(3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AI column (70 g/min, 120 bar, 20 x 250 mm) eluting 20% IPA/0.2% DEA/CO2) to give (S)-4-isopropyl-3-(2-(((R)-1-(3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-(((S)-1-(3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one 1st peak 438: HRMS(B) m/z 425.1921 (M+H) RT=2.49 min. 2nd peak 439: HRMS(B) m/z 425.1923 (M+H) RT=2.42 min.
441 & 442: (S)-3-(2-((1-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (AI column (70 g/min, 120 bar, 20 x 250 mm) eluting 25% IPA/0.2% DEA/CO2) to give (S)-3-(2-(((R)-1-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 441: HRMS(B) m/z 413.1719 (M+H) RT=2.58 min. 2nd peak 442: HRMS(B) m/z 413.1719 (M+H) RT=2.52 min.
443: (S)-3-(2-(((S)-1-(5-(4-chlorophenyl)-1,2,4-oxadiazol-3-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (ID-H column (80 g/min, 120 bar, 20 x 250 mm) eluting 30% MeOH/CO2) to give (S)-3-(2-(((R)-1-(5-(4-chlorophenyl)-1,2,4-oxadiazol-3-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-(((S)-1-(5-(4-chlorophenyl)-1,2,4-oxadiazol-3-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 2nd peak 443: ^{1}H NMR (400 MHz, MeOD) δ 8.25 – 8.03 (m, 6H), 7.71 – 7.55 (m, 4H), 7.44 (d, J = 5.7 Hz, 2H), 5.26 (d, J = 5.6 Hz, 2H), 4.71 (d, J = 7.9 Hz, 2H), 4.46 – 4.26 (m, 4H), 3.37 (s, 1H), 2.66 (heptd, J = 7.0, 3.3 Hz, 2H), 1.69 (d, J = 7.1 Hz, 6H), 1.17 (d, J = 6.2 Hz, 1H), 1.04 (d, J = 7.1 Hz, 6H), 0.88 (d, J = 6.9 Hz, 6H). HRMS(B) m/z 428.1364 RT=2.77 min.
444 & 445: (S)-3-(2-(1-(5-(4-fluoro-3-methylphenyl)pyridin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Separation was achieved by silica gel chromatography (10 to 100% EtOAc / heptane) to give (S)-3-(2-((R)-1-(5-(4-fluoro-3-methylphenyl)pyridin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-((S)-1-(5-(4-fluoro-3-methylphenyl)pyridin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 444: HRMS(B) m/z 436.2126 (M + H)+, RT=2.78min 2nd peak 445: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (dd, J = 2.3, 0.9 Hz, 1H), 8.23 (d, J = 5.8 Hz, 1H), 7.78 (dd, J = 8.1, 2.4 Hz, 1H), 7.49 (d, J = 5.7 Hz, 1H), 7.41 – 7.27 (m, 3H), 7.12 (dd, J = 9.4, 8.4 Hz, 1H), 5.95 (d, J = 6.5 Hz, 1H), 5.16 (br s, 1H), 4.66 (br s, 1H), 4.34 – 4.19 (m,

	2H), 2.37 (d, J = 1.9 Hz, 3H), 1.93 (br s, 1H), 1.65 – 1.61 (m, 3H), 0.71 (br s, 6H). HRMS(B) m/z 436.2131 (M + H)+.
446 & 447: (S)-3-(2-(1-(5-(4-fluorophenoxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Chiral separation was achieved by chiral SFC column chromatography (Column IA 20x250mm column 30% IPA, 70% CO2) to give (S)-3-(2-((S)-1-(5-(4-fluorophenoxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-((R)-1-(5-(4-fluorophenoxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 446: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 8.21 (d, J = 5.8 Hz, 1H), 7.49 (d, J = 5.7 Hz, 1H), 7.18 – 6.99 (m, 4H), 6.18 (br s 1H), 5.28 (br s, 1H), 4.75 (dt, J = 8.2, 3.4 Hz, 1H), 4.39 – 4.25 (m, 2H), 2.34 (br s, 1H), 1.65 – 1.59 (m, 3H), 0.95 – 0.86 (d, J = 6.9 Hz, 3H), 0.82 (d, J = 6.9 Hz, 3H). HRMS(B) m/z 439.1876 (M + H)+. 2nd peak 447: HRMS(B) m/z 439.1883 (M + H)+, RT = 3.37min
448 & 449: (S)-3-(2-(1-(5-(4-fluorophenoxy)pyridin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	Separation was achieved by silica gel chromatography (20 to 100% EtOAc / heptane) to give (S)-3-(2-((R)-1-(5-(4-fluorophenoxy)pyridin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-((S)-1-(5-(4-fluorophenoxy)pyridin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st peak 448: HRMS(B) m/z 438.1922 (M + H)+. RT = 2.62min 2nd peak 449: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, J = 2.7, 0.8 Hz, 1H), 8.21 (d, J = 5.8 Hz, 1H), 7.49 (d, J = 5.8 Hz, 1H), 7.33 – 7.18 (m, 3H), 7.14 – 6.95 (m, 3H), 5.95 (d, J = 7.1 Hz, 1H), 5.14 (br s, 1H), 4.68 (d, J = 7.8 Hz, 1H), 4.36 – 4.22 (m, 2H), 1.75 (br s, 1H), 1.61 – 1.57 (m, 3H), 0.95 - 0.75 (m, 6H). HRMS(B) m/z 438.1950 (M + H)+.
450 & 451: (R)-3-(5-fluoro-2-(1-(5-(4-fluorophenoxy)pyridin-2-yl)ethylamino)pyrimidin-4-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one	Separation was achieved by silica gel chromatography (10 to 100% EtOAc / heptane) to give (R)-3-(5-fluoro-2-((S)-1-(5-(4-fluorophenoxy)pyridin-2-yl)ethylamino)pyrimidin-4-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one and (R)-3-(5-fluoro-2-((R)-1-(5-(4-fluorophenoxy)pyridin-2-yl)ethylamino)pyrimidin-4-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one 1st peak 450: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.17 (m, 1H), 8.08 (d, J = 2.8 Hz, 1H), 7.31 – 6.86 (m, 11H), 5.83 (d, J = 7.2 Hz, 1H), 5.28 (s, 1H), 4.69 (br s, 1H), 1.58 (s, 3H), 1.29 – 1.11 (m, 3H), 0.98 (s, 3H). HRMS(B) m/z 518.2005 (M + H)+. 2nd peak 451: HRMS(B) m/z 518.2003 (M + H)+, RT = 3.08min
452 & 453: (S)-3-(2-(1-(5-(4-fluorophenoxy)pyrazin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.	Separation was achieved by silica gel chromatography (25 to 100% EtOAc / heptane) to give (S)-3-(2-((R)-1-(5-(4-fluorophenoxy)pyrazin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-((S)-1-(5-(4-fluorophenoxy)pyrazin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one. 1st peak 452: HRMS(B) m/z 439.1877 (M + H)+, RT =

	2.66min 2nd peak 453: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 1.4 Hz, 1H), 8.20 (d, J = 5.8 Hz, 1H), 8.09 (s, 1H), 7.49 (d, J = 5.8 Hz, 1H), 7.12 (d, J = 6.3 Hz, 4H), 5.71 (s, 1H), 5.20 (br s, 1H), 4.66 (dt, J = 7.7, 2.9 Hz, 1H), 4.36 – 4.22 (m, 2H), 2.10 (br s, 1H), 1.61 (d, J = 6.9 Hz, 3H), 0.94 – 0.78 (m, 6H). HRMS(B) m/z 439.1882 (M + H)+.
454 & 455: (S)-3-(2-(1-(2-(4-fluorophenoxy)pyrimidin-5-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.	Separation was achieved by silica gel chromatography (25 to 100% EtOAc / heptane) to give (S)-3-(2-((R)-1-(2-(4-fluorophenoxy)pyrimidin-5-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-((S)-1-(2-(4-fluorophenoxy)pyrimidin-5-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one. 1st peak 454: HRMS(B) m/z 439.1904 (M + H)+, RT = 3.09 min 2nd peak 455: HRMS(B) m/z 439.1897 (M + H)+ , RT = 3.17 min
456: (S)-3-(2-(1-(5-(2,4-difluorophenoxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.	Separation was achieved on a normal phase silica gel column with 20 to 100% ethylacetate / heptane to give (S)-3-(2-((R)-1-(5-(2,4-difluorophenoxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-((S)-1-(5-(2,4-difluorophenoxy)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one. 2nd Peak 456: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 2H), 8.09 (d, J = 5.9 Hz, 1H), 7.42 (d, J = 5.9 Hz, 1H), 7.08 (td, J = 8.9, 5.4 Hz, 1H), 6.98 – 6.81 (m, 2H), 5.18 (br s, 1H), 4.64 (dt, J = 7.9, 3.1 Hz, 1H), 4.30 – 4.16 (m, 2H), 2.11 (br s, 1H), 1.53-1.49 (m, 3H), 0.85 – 0.77 (m, 3H), 0.71 (d, J = 6.8 Hz, 3H). HRMS(B) m/z 457.1797 (M + H)+.
457: (S)-4-isopropyl-3-(2-(1-(5-(3-(trifluoromethyl)phenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one.	Separation was achieved on a normal phase silica gel column with 25 to 100% gradient of (25% methanol in ethylacetate) and heptane to give (S)-4-isopropyl-3-(2-((R)-1-(5-(3-(trifluoromethyl)phenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-((S)-1-(5-(3-(trifluoromethyl)phenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one. Peak 2 457: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (s, 2H), 8.14 (d, J = 5.7 Hz, 1H), 7.77 – 7.54 (m, 4H), 7.40 (d, J = 5.7 Hz, 1H), 6.11 (br s, 1H), 5.25 (br s, 1H), 4.67 (dt, J = 7.8, 3.2 Hz, 1H), 4.33 – 4.15 (m, 2H), 2.92 2.15 (br s, 1H), 1.55 (d, J = 8.6 Hz, 3H), 0.85 – 0.76 (m, 3H), 0.70 (br s, 3H). HRMS(B) m/z 473.1897 (M + H)+.
458: (S)-3-(2-((S)-1-(5-(4-fluoro-2-methylphenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	The chiral separation was carried out with SFC (IA, 5µm, 20 x 250 mm) using 35% MeOH in CO2 to give (S)-3-(2-((S)-1-(5-(4-fluoro-2-methylphenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-((R)-1-(5-(4-fluoro-2-methylphenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one 1st Peak 458: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 2H), 8.24 (d, J = 5.8 Hz, 1H), 7.49 (d, J = 5.7 Hz, 1H), 7.17

	(dd, J = 8.4, 5.8 Hz, 1H), 7.10 – 6.98 (m, 2H), 6.28 (br s, 1H), 5.34 (br s, 1H), 4.78 (dt, J = 8.2, 3.3 Hz, 1H), 4.40 – 4.25 (m, 2H), 2.30 (s, 3H), 1.79 (br s, 1H), 1.73 (d, J = 7.1 Hz, 3H), 0.95 – 0.75 (m, 6H). HRMS(B) m/z 437.2086 (M + H)+.

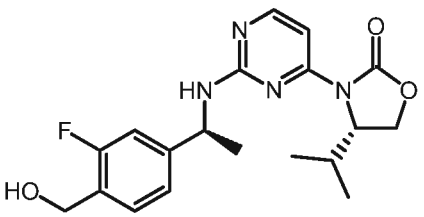
Example 459



A solution of (S)-(4-(1-aminoethyl)phenyl)methanol hydrochloride (4.0301 g, 21.47 mmol, purchased from NetChem), (S)-3-(2-fluoropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (5.3648 g, 23.82 mmol, 1.11 equiv) and DIPEA (38.0 mL, 218 mmol, 10.1 equiv) in DMSO (40 mL) was heated at 110 °C for 135 min. The reaction mixture was diluted with EtOAc (200 mL) and washed with water (200 mL). After separation, the aqueous phase was washed with EtOAc (2 x 150 mL). Combined organics were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (EtOAc/heptane 30 to 100%) provided (S)-3-(2-((S)-1-(4-(hydroxymethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (6.42 g) in 84% yield.

^{1}H NMR (400 MHz, CD_3OD) δ 8.13 (d, J = 5.8 Hz, 1 H), 7.36 - 7.28 (m, 5 H), 5.06 (q, J = 7.0 Hz, 1 H), 4.68 (br s, 1 H), 4.58 (s, 2 H), 4.37 - 4.29 (m, 2 H), 1.80 (br s, 1 H), 1.52 (d, J = 7.1 Hz, 3 H), 0.74 (br s, 3 H), 0.61 (br s, 3 H); MS *m/z* 355.1 (M - H)

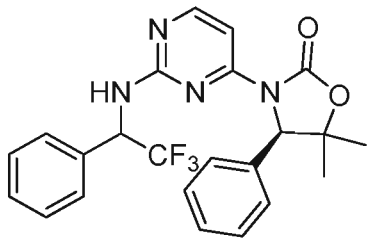
Example 460



S)-3-(2-((S)-1-(3-fluoro-4-(hydroxymethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one was prepared using a method similar to that described for the preparation of Example 459. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 5.9 Hz, 1 H), 7.51 - 7.49 (m, 1 H), 7.37 (t, J = 7.7 Hz, 1 H), 7.11 (d, J = 7.8 Hz, 1 H), 7.01 (d, J = 11, Hz, 1 H), 6.09 (br s, 1 H), 5.00 (br s, 1 H), 4.73 (s, 2 H), 4.61 - 4.55 (m, 1 H), 4.30 (t, J = 8.7

Hz, 1 H), 4.25 - 4.21 (m, 1 H), 3.00 (s, 1 H), 1.89 (br s, 1 H), 1.54 (d, J = 7.1 Hz, 3 H), 0.67 (br s, 6 H); MS *m/z* 375.0 (M + H)

Example 461

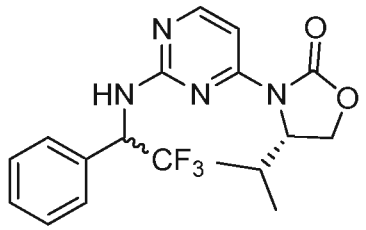


A solution of (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (50mg, 0.165mmol), 2,2,2-trifluoro-1-phenylethanamine (160mg, 0.913mmol) and pTsOH (78mg, 0.412mmol)in 2-BuOH was heated at 110°C for 2.5h. LCMS shows starting material as well as product. Another 78mg of pTsOH was added followed by 98mg of 2,2,2-trifluoro-1-phenylethanamine and heated at 110C for 1.5h. Mostly product some SM.

After cooling down mixture solidified. Added acetonitrial and sonicated. Filtered off solids (pTsOH salt of 2,2,2-trifluoro-1-phenylethanamine). The mother liquor was concentrated and purified by column chromatography (0-40% EtOAc/Hept followed by reverse HPLC (XBridge C18 5uM 10-85% ACN/Water over 12 minutes with 0.01%NH4OH modifier) to give (4R)-5,5-dimethyl-4-phenyl-3-(2-(2,2,2-trifluoro-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one (28mg, 0.063mmol).

^{1}H NMR (400 MHz, MeOD) δ 8.20 (d, J = 5.8 Hz, 1H), 7.58 (dd, J = 11.4, 5.8 Hz, 1H), 7.51 (br d, J = 6.8 Hz, 1H), 7.40 (dtd, J = 15.9, 9.2, 4.5 Hz, 5H), 7.33 – 7.22 (m, 3H), 7.10 (br s, 1H), 5.50 (s, 0.5H), 5.38 (s, 0.5H), 5.29 (br s, 1 H), 1.70 (s, 1.5H), 1.64 (s, 1.5H), 1.04 (s, 1.5H), 1.03 (s, 1.5H). HRMS(B) (M+H) 443.1682 Calc'd (M+H) 443.1695

Example 462 & 463



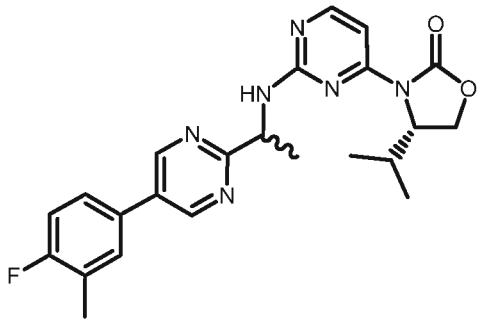
A solution of (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (163 mg, 0.674 mmol), 2,2,2-trifluoro-1-phenylethanamine (624 mg, 3.56 mmol, 5.3 equiv) and p-toluenesulfonic acid monohydrate (321 mg, 1.69 mmol, 2.5 equiv) in n-BuOH (3 mL) was

heated at 110 °C for 2 h and treated with additional p-toluenesulfonic acid monohydrate (321 mg, 1.69 mmol, 2.5 equiv), then heated at 110 °C for 1 ½ h. After cooling, the solid reaction mixture was treated with MeCN, sonicated and filtered. The filtrated was concentrated and purified by silica gel column chromatography (EtOAc/Heptane 0 to 30%) to give (4S)-4-isopropyl-3-(2-(2,2,2-trifluoro-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one (65 mg) in 25% yield. HRMS(B) m/z 381.1545 (M + H)+. Anal. RP-HPLC tR = 4.31//4.46 min (1.0 rnL/min flow rate with gradient from 5% to 15% acetonitrile with 0.05% formic acid in 5.00 min and then 15% to 95% acetonitrile with 0.05% formic acid from 5.00 min to 9.50 min, aqueous phase modified with 0.1% formic acid. Silica gel column chromatography separated the two diastereomers (S)-4-isopropyl-3-(2-((R)-2,2,2-trifluoro-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one and (S)-4-isopropyl-3-(2-((S)-2,2,2-trifluoro-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one.

1st Peak : ^{1}H NMR (400 MHz, MeOD) δ 8.23 (d, J = 5.8 Hz, 1H), 7.62 – 7.53 (m, 2H), 7.50 (d, J = 5.8 Hz, 1H), 7.42 (qt, J = 5.0, 2.2 Hz, 3H), 5.93 – 5.86 (m, 1H), 4.80 (dt, J = 7.5, 3.9 Hz, 1H), 4.48 – 4.33 (m, 2H), 2.65 (ddp, J = 10.4, 7.0, 3.4 Hz, 1H), 1.05 (d, J = 7.0 Hz, 3H), 0.89 (d, J = 7.0 Hz, 3H).

2nd Peak: ^{1}H NMR (400 MHz, MeOD) δ 8.23 (d, J = 5.8 Hz, 1H), 7.55 (dd, J = 7.3, 2.1 Hz, 2H), 7.49 (d, J = 5.8 Hz, 1H), 7.45 – 7.32 (m, 3H), 5.92 – 5.86 (m, 1H), 4.86 – 4.82 (m, 1H), 4.44 – 4.38 (m, 2H), 2.26 (br s, 1H), 0.94 (d, J = 7.0 Hz, 3H), 0.74 (br s, 3H).

Example 464

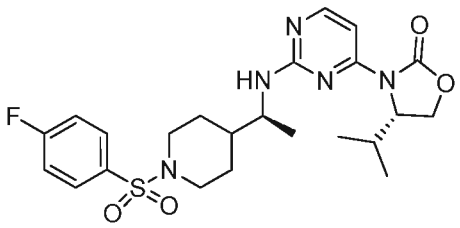


A solution of (*S*)-3-(2-fluoropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (1055 mg, 4.68 mmol), 1-(5-(4-fluoro-3-methylphenyl)pyrimidin-2-yl)ethanamine (1300 mg, 5.62 mmol, 1.2 equiv) and diisopropylethylamine (908mg, 7.03mmol, 1.5 equiv) in DMSO (20 mL) was heated at 110 °C for 1 h. The reaction mixture was poured into water (60 mL) and extracted with EtOAc (2x50 mL). Combined organics were washed with water (40mL), brine (40mL), dried over Na_2SO_4, filtered and concentrated directly onto silica gel. Silica gel chromatography provided the mixed distereomers of (S)-3-(2-(1-(5-(4-fluoro-3-methylphenyl)pyrimidin-2-yl)ethylamino) pyrimidin-4-yl)-4-isopropyloxazolidin-2-one

(560mg). Chiral separation was carried out with SFC (ID, 5µm, 20 x 250 mm) using 35% MeOH in CO2 to give (S)-3-(2-((S)-1-(5-(4-fluoro-3-methylphenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (S)-3-(2-((R)-1-(5-(4-fluoro-3-methylphenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

Example 464 first eluted product (302 mg) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 2H), 8.23 (d, J = 5.8 Hz, 1H), 7.49 (d, J = 5.7 Hz, 1H), 7.43 – 7.30 (m, 2H), 7.21 – 7.11 (m, 1H), 6.26 (br s, 1H), 5.31 (br s, 1H), 4.75 (dt, J = 7.9, 3.3 Hz, 1H), 4.39 – 4.24 (m, 2H), 2.38 (s, 3H), 2.09 (br s, 1H), 1.66-1.62 (m, 3H), 0.90 (dd, J = 9.8, 6.0 Hz, 3H), 0.78 (br s, 3H). HRMS(B) m/z 437.2093 (M + H)+.

Example 465



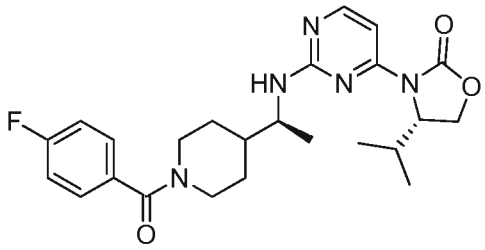
A solution of (S)-4-isopropyl-3-(2-((S)-1-(piperidin-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one (225mg, 0.675mmol), 4-fluorobenzene-1-sulfonyl chloride (146mg, 0.750mmol) and DIPEA (1ml) in CH_2Cl_2 was stirred at room temperature for 2h.

The reaction mixture was diluted with CH_2Cl_2 and washed with water. Aqueous layer was extracted with CH_2Cl_2. Combined organics were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography to give (S)-3-(2-((S)-1-(1-(4-fluorophenylsulfonyl)piperidin-4-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (4.5mg, 0.009mmol).

^{1}H NMR (400 MHz, MeOD) δ 8.45 (d, J = 6.0 Hz, 1H), 8.23 – 8.15 (m, 2H), 7.73 – 7.63 (m, 3H), 5.13 (dt, J = 7.4, 3.7 Hz, 1H), 4.78 – 4.69 (m, 2H), 4.26 (p, J = 6.7 Hz, 1H), 4.17 (dddd, J = 11.8, 6.4, 4.7, 2.3 Hz, 2H), 2.89 (ddq, J = 10.7, 7.1, 3.5 Hz, 1H), 2.69 (tdd, J = 11.6, 8.9, 2.6 Hz, 2H), 2.27 – 2.11 (m, 2H), 1.82 (dddt, J = 11.9, 9.0, 5.8, 2.9 Hz, 1H), 1.77 – 1.64 (m, 2H), 1.52 (d, J = 6.8 Hz, 3H), 1.30 (d, J = 7.1 Hz, 3H), 1.21 (d, J = 6.9 Hz, 3H). HRMS(B) (M+H) 492.2069 Calc'd (M+H) 492.2081

The following examples were prepared using methods substantially similar to those described for Example 465:

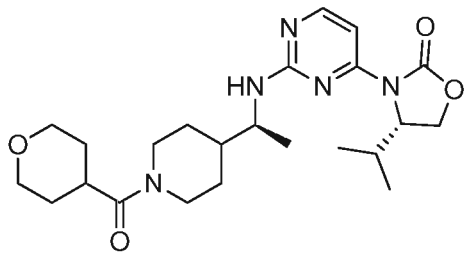
Example 466



Purified by column chromatography (20% to 100% EtOAc/Hept), followed by reverse phase preparative chromatography (C18 column, 10-85% ACN/Water 0.1% NH4OH modifier over 12 min.) to give (S)-3-(2-((S)-1-(1-(4-fluorobenzoyl)piperidin-4-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (12mg, 0.026mmol).

^{1}H NMR (400 MHz, MeOD) δ 8.12 (d, J = 5.8 Hz, 1H), 7.51 – 7.41 (m, 2H), 7.36 (d, J = 5.8 Hz, 1H), 7.25 – 7.15 (m, 2H), 4.82 (td, J = 5.9, 3.6 Hz, 1H), 4.68 (br s, 1H), 4.41 (d, J = 5.7 Hz, 2H), 3.98 (p, J = 6.7 Hz, 1H), 3.78 (br s, 1H), 3.12 (br s, 1H), 2.82 (br s, 1H), 2.60 (pd, J = 7.1, 6.5, 3.7 Hz, 1H), 1.92 (br s, 1H), 1.80 (dtd, J = 15.3, 9.4, 7.0, 3.6 Hz, 2H), 1.31 (br s, 2H), 1.22 (d, J = 6.8 Hz, 3H), 0.99 (d, J = 7.1 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H). HRMS(B) (M+H) 456.2384 Calc'd (M+H) 456.2411

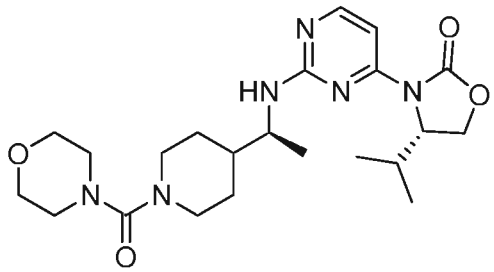
Example 467



Purified by column chromatography (MeOH/CH_2Cl_2 0 to 20%) to give (S)-4-isopropyl-3-(2-((S)-1-(1-(tetrahydro-2H-pyran-4-carbonyl)piperidin-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one (15mg, 0.034mmol).

^{1}H NMR (400 MHz, MeOD) δ 8.12 (d, J = 5.8 Hz, 1H), 7.36 (d, J = 5.8 Hz, 1H), 4.81 (td, J = 5.6, 3.3 Hz, 1H), 4.59 (br s, 1H), 4.41 (d, J = 5.7 Hz, 2H), 4.13 (br s, 1H), 3.96 (ddd, J = 11.6, 4.3, 2.2 Hz, 3H), 3.51 (tq, J = 11.8, 2.8 Hz, 2H), 3.15 – 2.89 (m, 2H), 2.69 – 2.48 (m, 2H), 1.99 – 1.68 (m, 5H), 1.61 (ddt, J = 10.7, 4.0, 2.3 Hz, 2H), 1.35 – 1.23 (m, 1H), 1.21 (d, J = 6.7 Hz, 3H), 1.19 – 1.09 (m, 1H), 0.98 (dd, J = 7.0, 1.5 Hz, 3H), 0.88 (d, J = 7.0 Hz, 3H). HRMS(B) (M+H) 446.2748 Calc'd (M+H) 446.2767

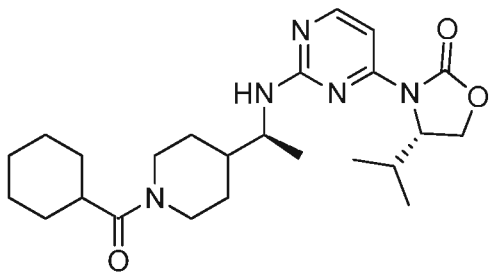
Example 468



Purified by column chromatography (50% to 100% EtOAc/Heptane follwed by 0% to 20% MeOH/CH_2Cl_2) to give (S)-4-isopropyl-3-(2-((S)-1-(1-(morpholine-4-carbonyl)piperidin-4-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one (21mg, 0.047mmol).

^{1}H NMR (400 MHz, MeOD) δ 8.11 (d, J = 5.8 Hz, 1H), 7.36 (d, J = 5.8 Hz, 1H), 4.81 (td, J = 5.8, 3.4 Hz, 1H), 4.41 (d, J = 5.7 Hz, 2H), 3.95 (p, J = 6.8 Hz, 1H), 3.84 – 3.70 (m, 2H), 3.68 – 3.65 (m, 4H), 3.26 – 3.23 (m, 4H), 2.80 (tt, J = 12.9, 3.1 Hz, 2H), 2.60 (ddq, J = 10.4, 7.0, 3.5 Hz, 1H), 1.88 – 1.73 (m, 2H), 1.67 (ddt, J = 18.5, 10.4, 3.5 Hz, 1H), 1.37 – 1.23 (m, 2H), 1.21 (d, J = 6.8 Hz, 3H), 0.99 (d, J = 7.1 Hz, 3H), 0.88 (d, J = 7.0 Hz, 3H). HRMS(B) (M+H) 447.2690 Calc'd (M+H) 447.2720

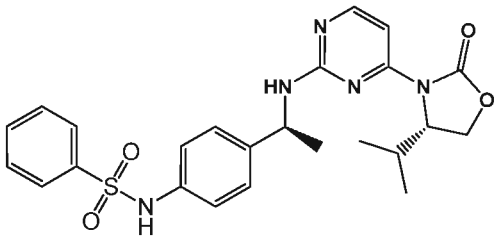
Example 469



Purified by column chromatography to give (S)-3-(2-((S)-1-(1-(cyclohexanecarbonyl) piperidin-4-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one

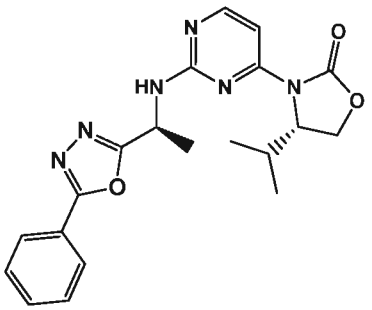
^{1}H NMR (400 MHz, MeOD) δ 8.12 (d, J = 5.7 Hz, 1H), 7.36 (d, J = 5.6 Hz, 1H), 4.80 (dt, J = 5.8, 2.9 Hz, 1H), 4.59 (br s, 1H), 4.40 (d, J = 5.6 Hz, 2H), 4.18 – 4.03 (m, 1H), 3.95 (p, J = 6.8 Hz, 1H), 3.05 (ddd, J = 14.1, 10.1, 6.6 Hz, 1H), 2.58 (td, J = 25.1, 23.5, 13.0 Hz, 3H), 1.97 – 1.63 (m, 8H), 1.54 – 1.08 (m, 7H), 1.21 (d, J = 6.8 Hz, 3H), 0.98 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H). HRMS(B) (M+H) 444.2953 Calc'd (M+H) 444.2975

Examples 470



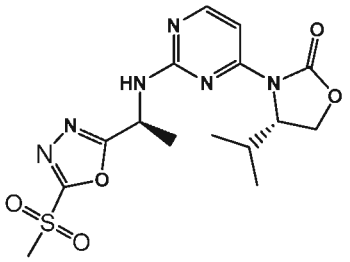
A solution of (S)-3-(2-(((S)-1-(4-aminophenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (100 mg, 0.30 mmol), benzenesulfonyl chloride (65 mg, 0.36 mmol, 1.2 equiv) and pyridine (35 mg, 0.45 mmol, 1.5 equiv) in DCM (5 mL) was stirred at room temperature for 15 h. The reaction mixture was quenched with MeOH, the solvent was removed to yield the crude product, which was purified by silica gel column chromatography (EA:MeOH=1:0 to 9:1), the solvent was removed to afford the pure product (46.8mg, white solid) in a 31.5% yield. N-(4-((S)-1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)ethyl)phenyl)benzenesulfonamide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 – 7.90 (m, 2H), 7.74 (d, *J* = 7.8 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.39 – 7.35 (m, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.96 (d, *J* = 8.0 Hz, 2H), 6.41 (s, 1H), 4.99 – 4.79 (m, 1H), 4.62 – 4.39 (m, 1H), 4.28 – 3.99 (m, 2H), 1.91 – 1.65 (b, 1H), 1.40 (d, *J* = 7.0 Hz, 3H), 0.53 (b, *J* = 21.1 Hz, 6H). HRMS(B) *m/z* 482.1847 $(M + H)^+$. RT=2.60 min.

Examples 471



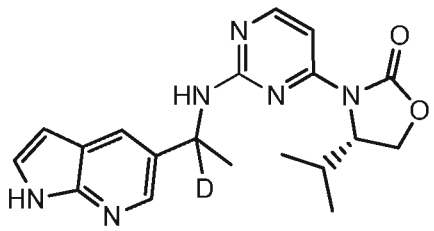
A solution of (triethoxymethyl)benzene (360 mg, 1.6 mmol, 5.0 equiv. in 5 mL of benzene and 0.5 mL of glacial AcOH) was added to (S)-2-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)propanehydrazide (99 mg, 0.30 mmol, 1.0 equiv.), the reaction mixture was stirred at reflux for 1.5 hours, the solvent was removed to yield the crude product. Silica gel column chromatography (ethyl acetate in heptane 10 to 90%) to yield (S)-4-isopropyl-3-(2-(((S)-1-(5-phenyl-1,3,4-oxadiazol-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one (21.2 mg, white solid) in 15.9% yield. HRMS(B) m/z 395.1820, (M+H)+, RT=2.42 min

Examples 472



To a solution of (S)-4-isopropyl-3-(2-(((S)-1-(5-(methylthio)-1,3,4-oxadiazol-2-yl)ethyl) amino)pyrimidin-4-yl)oxazolidin-2-one (102 mg, 0.28 mmol in 1.5 ml of CH_3COOH), was added a solution of $KMnO_4$ (66.4 mg, 0.42 mmol, 1.5 eq in 2.5 ml of water) dropwise. The solution was stirred at room temperature for 25 min, the mixture was decolorized with sodium bisulfite, the resulting solution was extracted with DCM, washed with sat. $NaHCO_3$, dried over Na_2SO_4, the solvent was removed to yield the pure desired product as a white solid. (S)-4-isopropyl-3-(2-(((S)-1-(5-(methylsulfonyl)-1,3,4-oxadiazol-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one (83 mg, white solid) in 71 % yield. HRMS(B) *m/z* 397.1281 $(M + H)^+$. RT=1.80 min.

Example 473 & 474



1-(1H-Pyrrolo[2,3-b]pyridin-5-yl)-ethanone (75 mg, 0.468 mmol), ammonium acetate (722 mg, 9.36 mmol, 20.0 eq) and sodium cyanoborodeuteride (131 mg, 1.999 mmol, 4.25 eq) were combined in propan-2-ol (5 ml) and heated under infrared irradiation at 130°C for 4 min. The reaction was diluted with EtOAc (15 ml) and water (15 ml) and treated with 6M NaOH solution (1 ml) to ~10 pH. The product, 1-deutero-1-(1H-pyrrolo[2,3-b]pyridin-5-yl)ethanamine, was carried to the next step without further purification.

A solution of 3-(2-fluoropyrimidin-4-yl)oxazolidin-2-one (99 mg, 0.441 mmol), 1-deutero-1-(1H-pyrrolo[2,3-b]pyridin-5-yl)ethanamine (72 mg, 0.441 mmol, 1.0 equiv), and DIEA (0.154 mL, 0.882 mmol, 2.0 equiv) in DMSO (1 mL) was heated at 130 °C for 120 min. The reaction mixture was diluted with EtOAc (20 mL) and washed with water (10 mL)

and concentrated in vacuo. Resolution of (4S)-3-(2-((1-deutero-1-(1H-pyrrolo[2,3-b]pyridin-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one via chiral SFC chromatography on a Al column (75 g/min, 120 bar, 20 x 250 mm) eluting 40-50% MeOH/0.2% DEA/CO2 (v/v) to give (4S)-3-(2-(((R)-1-deutero-1-(1H-pyrrolo[2,3-b]pyridin-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one and (4S)-3-(2-(((S)-1-deutero-1-(1H-pyrrolo[2,3-b]pyridin-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one

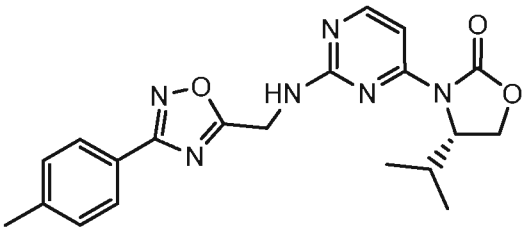
1st peak 473

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 8.33 (d, J = 2.2 Hz, 1H), 8.21 (d, J = 5.7 Hz, 1H), 7.92 (d, J = 2.3 Hz, 1H), 7.46 (d, J = 5.7 Hz, 1H), 7.35 (dd, J = 3.5, 2.0 Hz, 1H), 6.47 (dd, J = 3.4, 1.7 Hz, 1H), 5.82 (s, 1H), 1.66 – 1.58 (m, 3H), 4.59 (dt, J = 7.7, 3.2 Hz, 1H), 4.28 (t, J = 8.8 Hz, 1H), 4.19 (dd, J = 9.2, 3.1 Hz, 1H), 3.51 (s, 1H), 1.78 (d, J = 28.5 Hz, 2H), 1.30 – 1.15 (m, 1H), 0.57 (s, 6H). LCMS m/z 368.1 (M+H) RT=2.36 min.

2nd peak 474

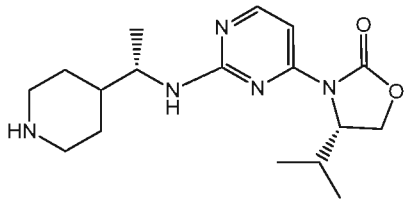
LCMS m/z 368.1 (M+H) RT=2.66 min.

Example 475



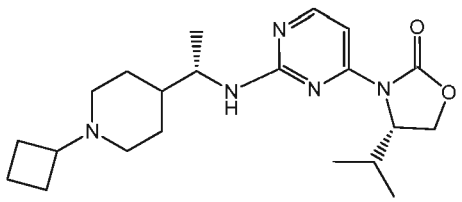
A solution of 3-(2-fluoropyrimidin-4-yl)oxazolidin-2-one (100 mg, 0.444 mmol), (3-(p-tolyl)-1,2,4-oxadiazol-5-yl)methanamine (84 mg, 0.444 mmol, 1.0 equiv), and TEA (0.186 mL, 1.332 mmol, 3.0 equiv) in butan-1-ol (2 mL) was heated at 100 °C for 90 min. Addition of propan-1-ol (1 ml) and heated at 150 °C for 60 min. The reaction mixture was concentrated in vacuo. Flash column (silica, 24 g) eluting w/ 0 - 30% EtOAc/DCM afforded (S)-4-Isopropyl-3-{2-[(3-p-tolyl-[1,2,4]oxadiazol-5-ylmethyl)-amino]-pyrimidin-4-yl}-oxazolidin-2-one (95 mg, white foam) in 54.2% yield. HRMS(B) m/z 394.1753 2.38 Min.

Example 476



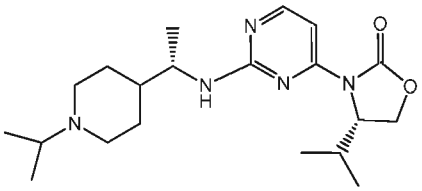
To a solution of 4-{(S)-1-[4-((S)-4-Isopropyl-2-oxo-oxazolidin-3-yl)-pyrimidin-2-ylamino]-ethyl}-piperidine-1-carboxylic acid benzyl ester (22 mg) in methanol (5 mL) was added palladium hydroxide on carbon (7 mg, 0.05 mmol). The reaction was then stirred at room temperature for 16 hours. The reaction is then filtered and then concentrated under vacuum. The crude material was then purified using reverse phase C18 ODB column water-acetonitrile 0.1% TFA modifier to give (S)-4-isopropyl-3-[2-((S)-1-piperidin-4-yl-ethylamino)-pyrimidin-4-yl]-oxazolidin-2-one (11 mg) in 70% yield.
HRMS(B) m/z 333.2165 (M + H)+; RT.: 1.09 min.

Example 477



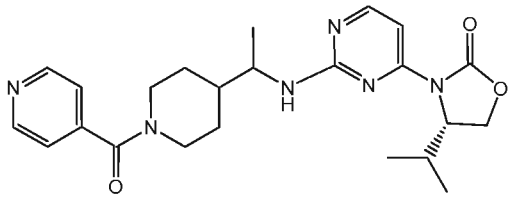
A solution of (S)-4-Isopropyl-3-[2-((S)-1-piperidin-4-yl-ethylamino)-pyrimidin-4-yl]-oxazolidin-2-one (28 mg, 0.084 mmol) in THF (2 mL) was added cyclobutanone (14 mg, 0.20 mmol) and sodium triacetoxyborohydride (28 mg, 0.13 mmol). The reaction was stirred at room temperature for 18 hours. The solvent is then removed under vacuum. The crude material was then purified using reverse phase C18 ODB column water-acetonitrile 0.1% TFA modifier to give (S)-3-{2-[(S)-1-(1-Cyclobutyl-piperidin-4-yl)-ethylamino]-pyrimidin-4-yl}-4-isopropyl-oxazolidin-2-one (20 mg) in 62% yield.
HRMS(B) m/z 388.2717 (M + H)+; RT.: 2.32 min.

Example 478



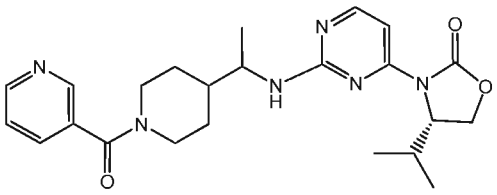
A solution of (S)-4-Isopropyl-3-[2-((S)-1-piperidin-4-yl-ethylamino)-pyrimidin-4-yl]-oxazolidin-2-one (20 mg, 0.060 mmol) in THF (2 mL) was added cyclobutanone (10 mg, 0.17 mmol) and sodium triacetoxyborohydride (20 mg, 0.09 mmol). The reaction was stirred at room temperature for 18 hours. The solvent is then removed under vacuum. The crude material was then purified using reverse phase C18 ODB column water-acetonitrile 0.1% TFA modifier to give (S)-4-Isopropyl-3-{2-[(S)-1-(1-isopropyl-piperidin-4-yl)-ethylamino]-pyrimidin-4-yl}-oxazolidin-2-one (20 mg) in 62% yield.
HRMS(B) m/z 376.2705 (M + H)+; RT.: 1.24 min.

Example 479



To a solution of S)-4-Isopropyl-3-[2-((S)-1-piperidin-4-yl-ethylamino)-pyrimidin-4-yl]-oxazolidin-2-one (20 mg, 0.48 mmol) in dichloromethane (1 mL) and DMF (1 mL) was added HATU (23 mg, 0.06 mmol) and DIPEA (0.03 mL, 0.18 mmol) The reaction was stirred at room temperature for 18 hours. The solvent is then removed under vacuum. The crude material was then purified using reverse phase C18 ODB column water-acetonitrile 0.1% TFA modifier to give (S)-4-Isopropyl-3-(2-{(S)-1-[1-(pyridine-4-carbonyl)-piperidin-4-yl]-ethylamino}-pyrimidin-4-yl)-oxazolidin-2-one (2 mg) in 8% yield.
HRMS(B) m/z 438.2379 (M + H)+; RT.: 1.82 min.

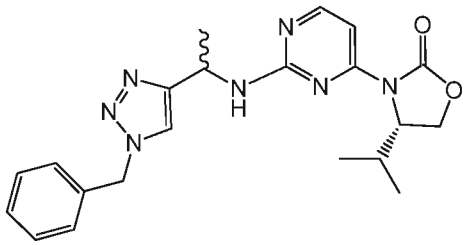
Example 480



To a solution of S)-4-Isopropyl-3-[2-((S)-1-piperidin-4-yl-ethylamino)-pyrimidin-4-yl]-oxazolidin-2-one (16 mg, 0.48 mmol) in dichloromethane (1 mL) and DMF (1 mL) was added HATU (20 mg, 0.05 mmol) and DiPEA (0.03 mL, 0.15 mmol) The reaction was stirred at room temperature for 18 hours. The solvent is then removed under vacuum. The crude material was then purified using reverse phase C18 ODB column water-acetonitrile 0.1% TFA modifier to give (S)-4-Isopropyl-3-(2-{(S)-1-[1-(pyridine-4-carbonyl)-piperidin-4-yl]-ethylamino}-pyrimidin-3-yl)-oxazolidin-2-one (2 mg) in 8% yield.

HRMS(B) m/z 438.2379 (M + H)+; RT.: 1.83 min.

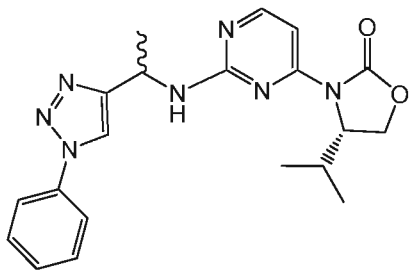
Example 481 & 482



To a solution of (S)-4-Isopropyl-3-[2-((S)-1-methyl-prop-2-ynylamino)-pyrimidin-4-yl]-oxazolidin-2-one (60 mg, 0.22 mmol) and benzyl azide (30 mg, 0.23 mmol) in water (0.5 mL) and DMSO (3 mL) was added copper sulfate pentahydrate (56 mg, 0.23 mmol) and L-ascorbic acid sodium salt (45 mg, 0.23 mmol). The reaction was stirred for 48 hours at room temperature. The reaction mixture was diluted with EtOAc (75 mL) and washed with water (15 mL) and 1N solution sodium bicarbonate (15 mL) . The organic layer was dried over MgSO4, filtered and concentrated. The crude material was then purified on reverse phase using a C18 columnn water-acetonitrile TFA as a modifier, which also effected separation of the two diastereomer products (S)-3-{2-[(S)-1-(1-benzyl-1H-[1,2,3]triazol-4-yl)-ethylamino]-pyrimidin-4-yl}-4-isopropyl-oxazolidin-2-one and (S)-3-{2-[(R)-1-(1-benzyl-1H-[1,2,3]triazol-4-yl)-ethylamino]-pyrimidin-4-yl}-4-isopropyl-oxazolidin-2-one

First Peak 481: HRMS(B) m/z 407.2070 (M + H)+; RT.: 2.26 min.
Second Peak 482: HRMS(B) m/z 407.2070 (M + H)+; RT.: 2.32 min.

Example 483 & 484



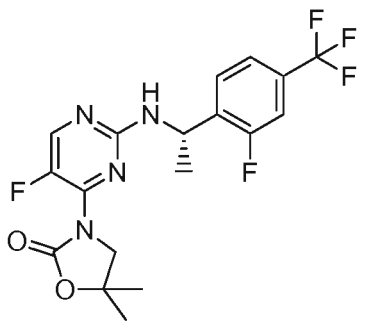
To a solution of (S)-4-Isopropyl-3-[2-((S)-1-methyl-prop-2-ynylamino)-pyrimidin-4-yl]-oxazolidin-2-one (82 mg, 0.30 mmol) and azidobenzene (36 mg, 0.30 mmol) in water (0.5 mL) and DMSO (3 mL) was added copper sulfate pentahydrate (75 mg, 0.23 mmol) and L-ascorbic acid sodium salt (60 mg, 0.23 mmol). The reaction was stirred for 48

hours at room temperature. The reaction mixture was diluted with EtOAc (75 mL) and washed with water (15 mL) and 1N solution sodium bicarbonate (15 mL) . The organic layer was dried over MgSO4, filtered and concentrated. The crude material was then purified on reverse phase using a C18 columnn water-acetonitrile TFA as a modifier , which also effected separation of the two diastereomer products (S)-4-isopropyl-3-{2-[(S)-1-(1-phenyl-1H-[1,2,3]triazol-4-yl)-ethylamino]-pyrimidin-4-yl}-oxazolidin-2-one and (S)-4-isopropyl-3-{2-[(R)-1-(1-phenyl-1H-[1,2,3]triazol-4-yl)-ethylamino]-pyrimidin-4-yl}-oxazolidin-2-one

First Peak 483: HRMS(B) m/z 393.1913 (M + H)+; RT.: 2.31 min.

Second Peak 484: HRMS(B) m/z 393.1913 (M + H)+; RT.: 2.40 min.

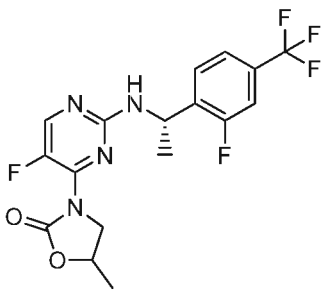
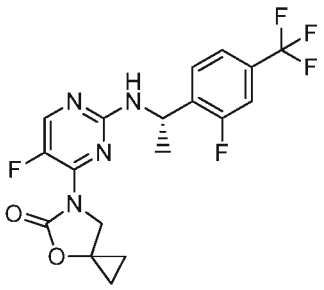
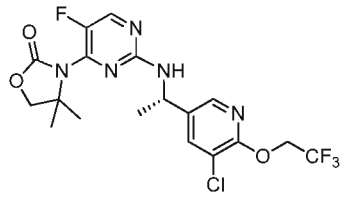
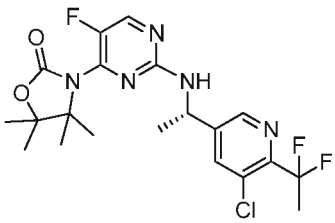
Example 485



To a room temperature solution of 3-(2-chloro-5-fluoropyrimidin-4-yl)-5,5-dimethyloxazolidin-2-one (30 mg, 0.122 mmol) in DMSO (300 µL) was treated with DIPEA (68 µL, 0.366 mmol) followed by addition of (S)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethanamine (41.4 mg, 0.2 mmol). The reaction was sealed, heated at 95°C for ~18 hr. . Purification by reverse phase HPLC provided the trifluoroacetate salt of (S)-3-(5-fluoro-2-(1-(2-fluoro-4-(trifluoromethyl) phenyl) ethylamino)pyrimidin-4-yl)-5,5-dimethyloxazolidin-2-one. (6.0 mg, white solid). ^{1}H NMR (400 MHz, METHANOL-*d*4) δ ppm 1.44 - 1.58 (m, 12 H) 3.50 - 3.74 (m, 1 H) 3.88 (d, *J*=9.8 Hz 1 H) 5.29 (d, *J*=7.04 Hz, 1 H) 7.38 - 7.45 (m, 2 H) 7.6 (t, *J*=8.22 Hz 1 H) 8.16 (d, *J*=3.13 Hz, 1 H); HRMS(A) *m/z* 417.1360 (M + H)$^+$, Rt 2.29 min.

The compounds in Table 11 were prepared using methods similar to those described for the preparation of Example 485.

Table 11.

486	487	
		
488	489	
		
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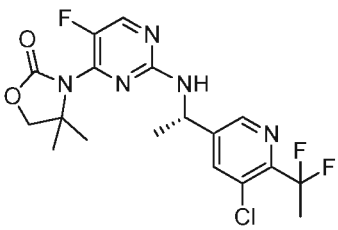	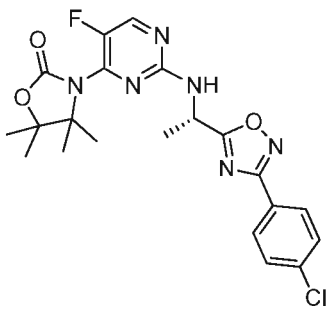	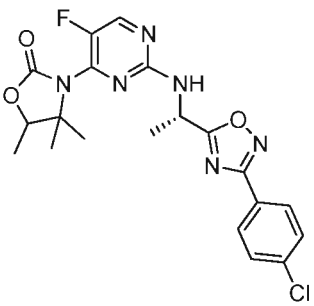
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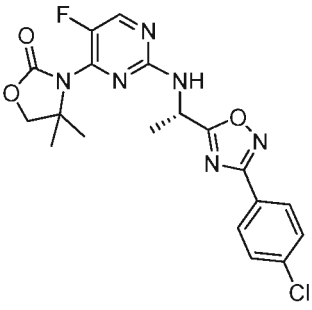
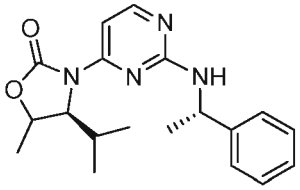
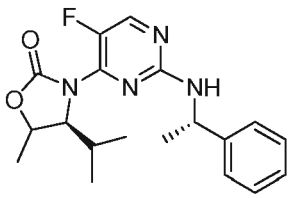
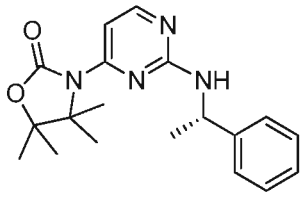
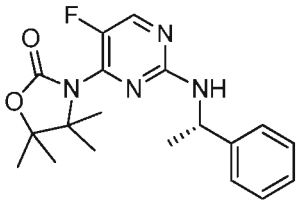
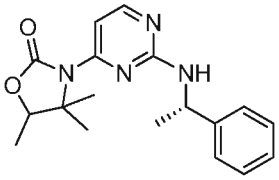
		

496	497	498
		
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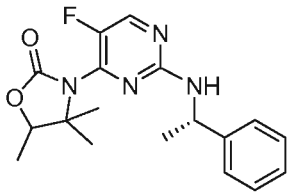	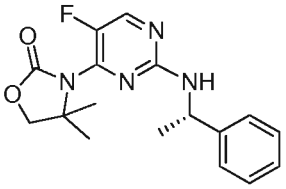	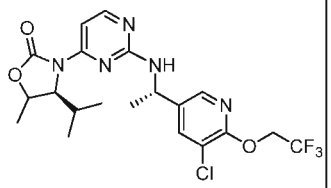
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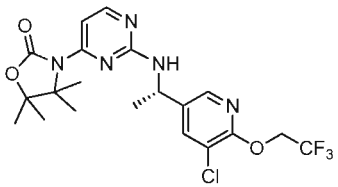	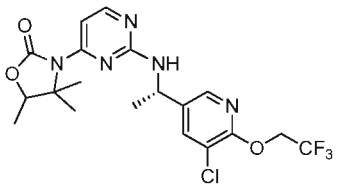	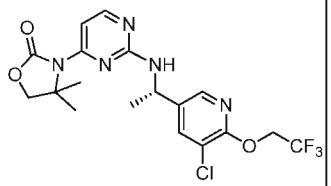
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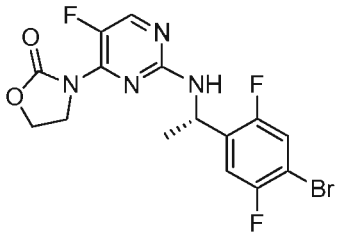
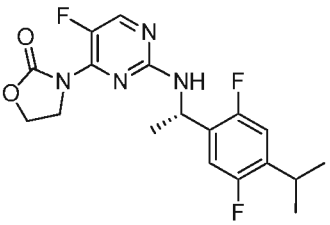
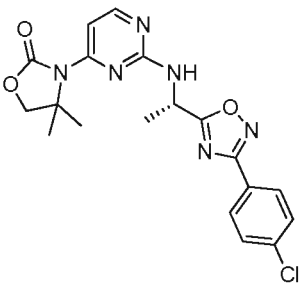
		

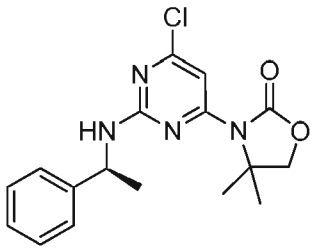
Table 12. Chemical name, NMR chemical shifts and LCMS signal for each compound listed in Table 11.

Example: Name	^{1}H NMR (400 MHz) ppm	LCMS
486: 3-(5-fluoro-2-((S)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethylamino)pyrimidin-4-yl)-5-methyloxazolidin-2-one	(CD_3OD) 1.41 - 1.58 (m, 8 H) 3.55 (br. s., 1 H) 3.74 - 3.80 (m, 1 H) 4.17 (dd, *J*=9.59, 7.63 Hz, 1 H) 5.26 - 5.33 (m, 1 H) 7.39 - 7.45 (m, 2 H) 7.60 (t, *J*=7.83 Hz, 1 H) 8.15 (d, *J*=3.52 Hz, 1 H)	HRMS(A) *m/z* 403.1198 $(M + H)^+$, Rt 2.20 min
487: (S)-6-(5-fluoro-2-(1-(2-fluoro-4-(trifluoromethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-oxa-6-azaspiro[2.4]heptan-5-one	(CD_3OD) 0.90 (m, 2 H) 1.18 - 1.27 (m, 2 H) 1.53 (d, *J*=7.04 Hz, 3 H) 4.21 (d, *J*=9.39 Hz, 1 H) 5.30 (d, *J*=7.04 Hz, 1 H) 7.38 - 7.45 (m, 2 H) 7.60 (t, *J*=7.83 Hz 1 H) 8.17 (d, *J*=3.52 Hz, 1 H)	HRMS(A) *m/z* 415.1204 $(M + H)^+$, Rt 2.31 min
488: (S)-3-(2-(1-(5-chloro-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)ethylamino)-5-fluoropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	(CD_3OD) 8.22 (d, *J*=3.13 Hz, 1 H) 8.08 (d, *J*=1.96 Hz, 1 H) 7.84 (d, *J*=1.96 Hz, 1 H) 5.26 - 5.27 (m, 1 H) 4.90 (q, *J*=8.61 Hz, 3 H) 4.13 - 4.22 (m, 2 H) 1.47 - 1.59 (m, 9 H)	HRMS(A) *m/z* 464.1125 $(M + H)^+$, Rt 2.28 min
489: (S)-3-(2-(1-(5-chloro-6-(1,1-difluoroethyl)pyridin-3-yl)ethylamino)-5-fluoropyrimidin-4-yl)-4,4,5,5-tetramethyloxazolidin-2-one	(CD_3OD) 8.51 (d, J=1.57 Hz, 1 H) 8.23 (d, J=2.35 Hz, 1 H) 7.93 (d, J=1.56 Hz, 1 H) 4.99 (q, J=6.52 Hz, 1 H) 2.02 (t, J=18.78 Hz, 3 H) 1.57 (d, J=7.43 Hz, 3 H) 1.34 - 1.42 (m, 12 H)	HRMS(A) *m/z* 458.1573 $(M + H)^+$, Rt 2.02 min
490: (S)-3-(2-(1-(5-chloro-6-(1,1-difluoroethyl)pyridin-3-yl)ethylamino)-5-fluoropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	(CD_3OD) 8.50 (d, J=1.17 Hz, 1 H) 8.24 (d, J=2.35 Hz, 1 H) 7.93 (d, J=1.57 Hz, 1 H) 4.99 (q, J=6.65 Hz, 1 H) 4.12 - 4.21 (m, 2 H) 2.01 (t, J=18.78 Hz, 3 H) 1.57 (d, J=7.04 Hz, 3 H) 1.47 (s, 6 H)	HRMS(A) *m/z* 430.1265 $(M + H)^+$, Rt 2.05 min
491: (S)-3-(2-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethylamino)-5-fluoropyrimidin-4-yl)-4,4,5,5-tetramethyloxazolidin-2-one	(CD_3OD) 8.27 (br. s., 1 H) 8.00 (d, *J*=8.61 Hz, 3 H) 7.52 (d, *J*=8.61 Hz, 4 H) 5.29 (d, *J*=7.04 Hz, 1 H) 1.73 (s, 3 H) 1.44 (s, 3 H) 1.38 (s, 3 H) 1.28 (s, 3 H)	HRMS(A) *m/z* 461.1512 $(M + H)^+$, Rt 2.37 min
492: 3-(2-((S)-1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethylamino)-5-fluoropyrimidin-4-yl)-4,4,5-trimethyloxazolidin-2-one (1:1 mixture of diastereomers)	(CD_3OD) 8.27 (d, *J*=1.57 Hz, 1 H) 8.00 (d, *J*=8.61 Hz, 2 H) 7.52 (d, *J*=8.61 Hz, 2 H) 5.29 (m, 1 H) 4.44(m, 1 H) 1.73 (d, *J*=7.43 Hz, 3 H) 1.44 (br. s., 3 H) 1.26 - 1.35 (m, 6 H)	HRMS(A) *m/z* 477.1349 $(M + H)^+$, Rt 2.3 min
493: (S)-3-(2-(1-(3-(4-chlorophenyl)-1,2,4-	(CD_3OD) 8.28 (d, J=2.35 Hz, 1 H) 8.00 (d, J=8.61 Hz, 2 H) 7.51 (d, J=8.61 Hz, 2 H)	HRMS(A) *m/z*

oxadiazol-5-yl)ethylamino)-5-fluoropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	5.29 (m, 1 H) 4.11 -4.24 (m, 2 H) 1.73 (d, J=7.04 Hz, 3 H) 1.53 (s, 3 H) 1.30 (br.s., 3 H)	433.1201 $(M + H)^+$, Rt 2.21 min
494: (4S)-4-isopropyl-5-methyl-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one (1:1 mixture of diastereomers)	(CD_3OD) 8.11 (d, *J*=6.26 Hz, 1 H) 7.71 (d, *J*=7.43 Hz, 1 H) 7.29 - 7.40 (m, 4 H) 7.22 - 7.28 (m, 1 H) 5.23 (br. s., 1 H) 4.82 - 4.91 (m, 1 H) 4.78 (br. s., 1 H) 2.01 (br. s., 1 H) 1.59 (d, *J*=7.04 Hz, 3 H) 1.54 (d, *J*=6.65 Hz, 3 H) 0.76 (br. s., 6 H)	HRMS(A) *m/z* 341.1985 $(M + H)^+$, Rt 1.78 min
495: (4S)-3-(5-fluoro-2-((S)-1-phenylethylamino)pyrimidin-4-yl)-4-isopropyl-5-methyloxazolidin-2-one (1:1 mixture of diastereomers)	(CD_3OD) 7.87 (d, *J*=3.13 Hz, 1 H) 6.95 - 7.02 (m, 2 H) 6.91 (t, *J*=7.63 Hz, 2 H) 6.75 - 6.85 (m, 1 H) 4.52 - 4.61 (m, 2H) 4.00 (br. s., 1 H) 1.49 (br. s., 1 H) 1.11 (dd, *J*=9.59, 6.85 Hz, 6 H) 0.38 (d, *J*=4.30 Hz, 6 H)	HRMS(A) *m/z* 359.1891 $(M + H)^+$, Rt 2.19 min
496: (S)-4,4,5,5-tetramethyl-3-(2-(1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 8.08 (d, *J*=6.26 Hz, 1 H) 7.28 - 7.40 (m, 5 H) 7.18 - 7.25 (m, 1 H) 5.05 (q, *J*=7.04 Hz, 1 H) 1.55 - 1.62 (m, 6H) 1.37 (s, 3 H) 1.32 (s, 3 H)	HRMS(A) *m/z* 341.1984 $(M + H)^+$, Rt 1.73 min
497: (S)-3-(5-fluoro-2-(1-phenylethylamino)pyrimidin-4-yl)-4,4,5,5-tetramethyloxazolidin-2-one	(CD_3OD) 8.18 (d, *J*=2.74 Hz, 1 H) 7.30 - 7.39 (m, 2 H) 7.23 - 7.30 (m, 2 H) 7.12 - 7.21 (m, 1 H) 4.90 (q, *J*=6.91 Hz, 1H) 1.50 (d, *J*=7.04 Hz, 3 H) 1.42 (s, 3 H) 1.36 (s, 3 H) 1.33 (s, 3 H)	HRMS(A) *m/z* 359.1891 $(M + H)^+$, Rt 2.16 min
498: 4,4,5-trimethyl-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one (1:1 mixture of diastereomers)	(CD_3OD) 8.09 (d, *J*=6.65 Hz, 1 H) 7.53 (d, *J*=7.04 Hz, 1 H) 7.45 (d, *J*=7.04 Hz, 1 H) 7.30 - 7.40 (m, 8 H) 7.20 - 7.28(m, 2 H) 5.09 (t, *J*=7.04 Hz, 2 H) 4.27 - 4.42 (m, 2 H) 1.52 - 1.69 (m, 12 H) 1.32 (dd, *J*=11.15, 6.46 Hz, 6 H) 0.82 - 1.20 (m, 6 H)	HRMS(A) *m/z* 327.1826 $(M + H)^+$, Rt 1.66 min
499: 3-(5-fluoro-2-((S)-1-phenylethylamino)pyrimidin-4-yl)-4,4,5-trimethyloxazolidin-2-one (1:1 mixture of diastereomers)	(CD_3OD) 8.18 (d, *J*=2.74 Hz, 1 H) 7.30 - 7.37 (m, 2 H) 7.24 - 7.30 (m, 2 H) 7.11 - 7.21 (m, 1 H) 4.87 - 4.97 (m, 1 H) 4.31 - 4.46 (m, 1 H) 1.50 (d, *J*=7.04 Hz, 3 H) 1.41 (d, *J*=10.96 Hz, 3 H) 1.29 (dd, *J*=6.46, 3.33 Hz, 3 H) 0.84 - 1.16 (br. s, 3 H)	HRMS(A) *m/z* 345.1735 $(M + H)^+$, Rt 2.09 min
500: (S)-3-(5-fluoro-2-(1-phenylethylamino)pyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	(CD_3OD) 8.19 (d, *J*=2.35 Hz, 1 H) 7.30 - 7.37 (m, 2 H) 7.24 - 7.30 (m, 2 H) 7.13 - 7.21 (m, 1 H) 4.91 (q, *J*=7.30 Hz, 1H) 4.12 (q, *J*=8.22 Hz, 2 H) 1.45 - 1.55 (m, 6 H) 1.08 (br. s., 3 H)	HRMS(A) *m/z* 331.1573 $(M + H)^+$, Rt 1.98 min
501: (4S)-3-(2-((S)-1-(5-chloro-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)ethylamino)pyrimidin-4-yl)-4-isopropyl-5-	^1H NMR (400 MHz, CD_3OD) δ ppm 8.14 (d, *J*=6.65 Hz, 1 H) 8.10 (d, *J*=1.96 Hz, 1 H) 7.86 (d, *J*=2.35 Hz, 1 H) 7.57 (d, *J*=6.26 Hz, 1 H) 5.17 (d, *J*=6.65 Hz, 1 H) 4.92 (q, *J*=8.87 Hz, 1 H) 4.80 - 4.84 (m, 1H) 2.04	HRMS(A) *m/z* 474.1523 $(M + H)^+$, Rt 2.18

methyloxazolidin-2-one (1:1 mixture of diastereomers)	(br. s., 2 H) 1.55 (dd, *J*=15.85, 6.85 Hz, 6 H) 0.79 (br.s., 6 H)	min
502: (S)-3-(2-(1-(5-chloro-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)ethylamino)pyrimidin-4-yl)-4,4,5,5-tetramethyloxazolidin-2-one	(CD_3OD) 8.07 - 8.16 (m, 1 H) 7.89 (d, *J*=1.96 Hz, 1 H) 7.32 (d, *J*=6.26 Hz, 1 H) 5.08 (q, *J*=6.78 Hz, 1 H) 1.55 - 1.65 (m, 8 H) 1.37 (d, *J*=11.35 Hz, 6 H) 1.20 (d, *J*=11.35 Hz, 3 H)	HRMS(A) *m/z* 474.1534 $(M + H)^+$, Rt 2.16 min
503: 3-(2-((S)-1-(5-chloro-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)ethylamino)pyrimidin-4-yl)-4,4,5-trimethyloxazolidin-2-one (1:2 mixture of diastereomers)	(CD_3OD) 8.47 (d, *J*=5.87 Hz, 1 H) 8.11 (d, *J*=2.35 Hz, 3H) 7.99 (d, *J*=6.26 Hz, 1 H) 7.88 (d, *J*=1.96 Hz, 3 H) 7.39 (d,*J*=6.26 Hz, 2 H) 7.32 (d, *J*=6.65 Hz, 2 H) 5.04 - 5.13 (m, 1 H) 4.87 - 4.98 (m, 2 H) 4.45 (d, *J*=6.65 Hz, 1 H) 4.35 (dd, *J*=13.69, 6.65 Hz, 2 H) 1.67(d, *J*=4.70 Hz, 9 H) 1.59 (d, *J*=7.04 Hz, 12 H) 1.39 (d, *J*=6.65 Hz, 3 H) 1.33 (t, *J*=6.06 Hz, 6 H) 0.99 - 1.27 (m, 9 H)	HRMS(A) *m/z* 460.1375 $(M + H)^+$, Rt 2.08, 2.11 min
504: (S)-3-(2-(1-(5-chloro-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)ethylamino)pyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	(CD_3OD) 8.09 - 8.17 (m, 1 H) 7.88 (d, *J*=2.35 Hz, 1 H) 7.38 (d, *J*=6.26 Hz, 1 H) 4.91 (q, *J*=8.61 Hz, 1 H) 4.06 - 4.16(m, 2 H) 1.71 (m, 5 H) 1.58 (d, *J*=7.04 Hz, 3 H) 1.28 (br. s., 3 H)	HRMS(A) *m/z* 446.1219 $(M + H)^+$, Rt 2.01 min
505: (S)-3-(2-(1-(2,5-difluoro-4-isopropylphenyl)ethylamino)-5-fluoropyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 8.15 (d, *J*=3.13 Hz, 1 H) 6.92 - 7.08 (m, 2 H) 5.21 (q, *J*=6.78 Hz, 1 H) 4.44 - 4.58 (m, 2 H) 4.10 - 4.22 (m, 1H) 3.96 (m, 1 H) 3.07 - 3.23 (m, 1 H) 1.48 (d, *J*=7.04 Hz, 5 H) 1.21 (m, 6 H)	HRMS(A) *m/z* 381.1544 $(M + H)^+$, Rt 2.26 min
506: (S)-3-(2-(1-(4-bromo-2,5-difluorophenyl)ethylamino)-5-fluoropyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 8.15 (d, *J*=3.52 Hz, 1 H) 7.39 (dd, *J*=9.00, 5.48 Hz, 1 H) 7.24 (dd, *J*=9.19, 6.46 Hz, 1 H) 5.19 (q, *J*=7.04 Hz,1 H) 4.44 - 4.58 (m, 2 H) 4.09 - 4.23 (m, 1 H) 3.94 (br. s., 1 H) 1.48 (d, *J*=7.04 Hz, 3 H)	HRMS(A) *m/z* 417.018 $(M + H)^+$, t 2.07 min
507: (S)-3-(2-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethylamino)pyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	(CD_3OD) 8.09 (d, *J*=6.26 Hz, 1 H) 7.91 (d, *J*=8.61 Hz, 2 H) 7.43 (d, *J*=8.61 Hz, 3 H) 5.35 (q, *J*=7.30 Hz, 1 H) 3.97 -4.09 (m, 2 H) 1.69 (d, *J*=7.43 Hz, 3 H) 1.62 (s, 3 H) 1.14 - 1.45 (m, 3 H)	HRMS(A) *m/z* 415.1287 $(M + H)^+$, Rt 2.14 min

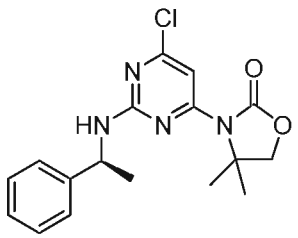
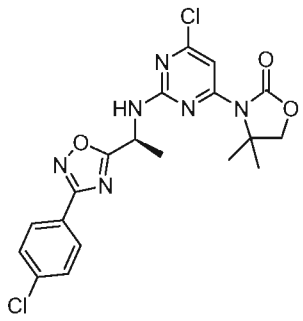
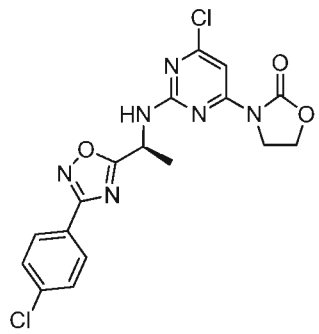
Example 508



A solution of 3-(2,6-dichloropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one (70.0 mg, 0.267 mmol), (*S*)-(-)-1-phenylethanamine (0.034 mL, 0.267 mmol, 1.0 equiv), and N-ethyl-N-isopropylpropan-2-amine (0.070 mL, 0.401 mmol, 1.5 equiv) in DMSO (1.5 mL) was heated at 85 °C for 2-4 h. Purification by reverse phase HPLC provided the trifluoroacetate salt of (S)-3-(6-chloro-2-(1-phenylethylamino)pyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one (20.0 mg, white solid) in 16% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (s, 1H), 7.33 – 7.31 (m, 4H),7.26 – 7.21 (m, 1H), 5.48 (br m, 1H), 4.02 – 3.94 (m, 2H), 1.65 (s, 3H), 1.55 (d, J = 6.9 Hz, 3H), 1.26 (s, 3H); HRMS(A) *m/z* 347.1274 $(M + H)^+$, Rt 2.32 min.

The compounds in Table 13 were prepared using methods similar to those described for the preparation of Example 508.

Table 13.

509	510	511
		
512	513	

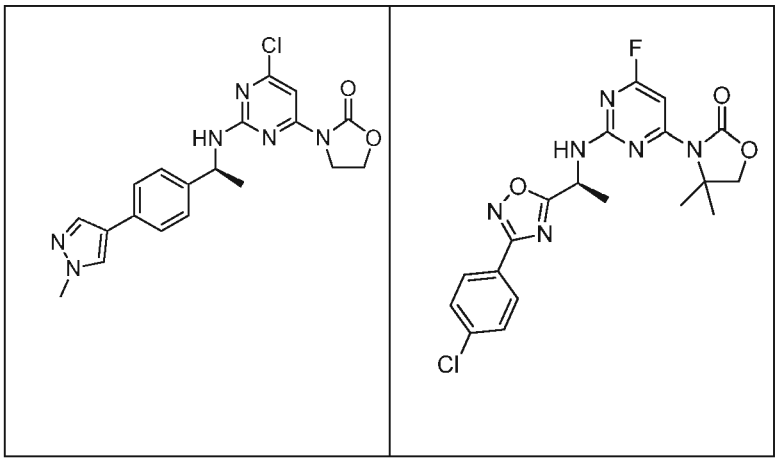
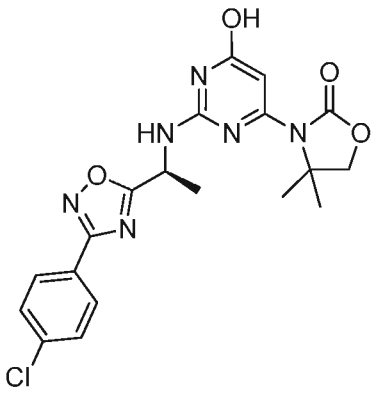


Table 14. Chemical name, NMR chemical shifts and LCMS signal for each compound listed in Table 13.

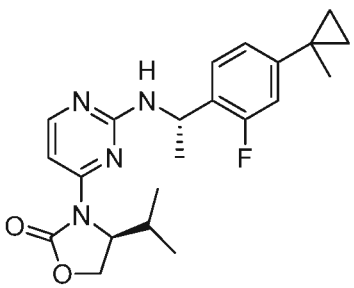
Example: Name	^{1}H NMR **(400 MHz)** δ **ppm**	**LCMS**
509: (S)-3-(6-chloro-2-(1-phenylethylamino)pyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	($CDCl_3$) 7.36 (s, 1H), 7.33 – 7.31 (m, 4H),7.26 – 7.21 (m, 1H), 5.48 (br m, 1H), 4.02 – 3.94 (m, 2H), 1.65 (s, 3H), 1.55 (d, J = 6.9 Hz, 3H), 1.26 (s, 3H)	HRMS(A) *m/z* 347.1274 $(M + H)^+$, Rt 2.32 min
510: (S)-3-(6-chloro-2-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethylamino)pyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	($CDCl_3$) 8.00 (d, J = 8.4 Hz, 2 H), 7.53 (s, 1H), 7.47 (d, J = 8.4 Hz, 2H), 5.44 – 5.29 (br m, 1H), 4.09 – 4.02 (m, 2H), 1.78 (d, J = 7.1 Hz, 3H), 1.72 (s, 3H), 1.40 (br s, 3H)	HRMS(A) *m/z* 449.0905 $(M + H)^+$, Rt 2.51 min
511: (S)-3-(6-chloro-2-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 8.00 (d, J = 8.7 Hz, 2H), 7.62 (s, 1H), 7.47 (d, J = 8.7 Hz, 2H), 5.32 (br m, 1H), 4.49 – 4.43 (m, 2H), 4.17 – 4.14 (m, 1H), 3.95 – 3.60 (br m, 1H), 1.77 (d, J = 7.1 Hz, 3H)	HRMS(A) *m/z* 421.0585 $(M + H)^+$, Rt 2.32 min
512: (S)-3-(6-chloro-2-(1-(2-fluoro-4-(1-methyl-1H-pyrazol-4-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	($CDCl_3$) 7.76 (s, 1H), 7.60 (s, 1H), 7.50 (s, 1H), 7.34 – 7.28 (m, 1H), 7.20 (dd, J = 7.8, 1.6 Hz, 1H), 7.15 – 7.09 (m, 1H), 5.30 (br m, 1H), 4.49 – 4.42 (m, 2H), 4.28 – 4.23 (m, 1H), 3.97 (s, 3H), 3.92 (br m, 1H), 1.56 (d, J = 6.7 Hz, 3H)	LCMS m/z 417.2 (M+H)+
513: (S)-3-(2-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethylamino)-6-fluoropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one	($CDCl_3$) 7.99 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 7.11 (s, 1H), 5.38 (br m, 1H), 4.08 – 4.03 (m, 2H), 1.78 (d, J = 7.0 Hz, 3H), 1.73 (s, 3H), 1.38 (br s, 3H)	HRMS(A) *m/z* 433.1201 $(M + H)^+$, Rt 2.42 min

Example 514:



A solution of (S)-3-(2-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethylamino)-6-fluoropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one (29.0 mg, 0.053 mmol) and 1 N aqueous hydrochloric acid (0.70 mL) in 1,4-dioxane (0.7 mL) was heated at 100 °C for 4 h. After cooling to room temperature, the reaction mixture was diluted with dichloromethane (10 mL), washed with saturated aqueous sodium bicarbonate solution (10 mL), dried over Na_2SO_4, filtered and concentrated. Purification by reverse phase HPLC provided the trifluoroacetate salt of (S)-3-(2-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethylamino)-6-hydroxypyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one (16 mg, white solid) in 55% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.5 Hz, 2H), 7.46 (d, J = 8.5 Hz, 2H), 6.71 (br s, 1H), 5.33 (br m, 1H), 4.02 – 3.99 (m, 2H), 1.83 (d, J = 7.1 Hz, 3H), 1.68 (s, 3H), 1.31 (s, 3H); HRMS(A) *m/z* 431.1245 $(M + H)^+$, Rt 1.80 min.

Example 515



Step 1

To round bottom flask containing (R)-N-((S)-1-(2-fluoro-4-(1-methylcyclopropyl)phenyl)ethyl)-2-methylpropane-2-sulfinamide (87 mg, 0.29 mmol) was added dioxane (2 mL). To this solution was added hydrochloric acid in dioxane (4.0M, 0.15 ml, 0.59 mmol) and the solution allowed to stir 10 min at room temperature.

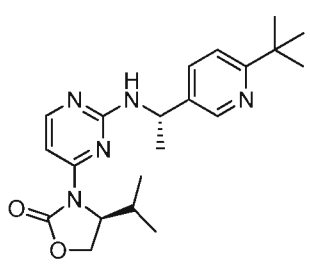
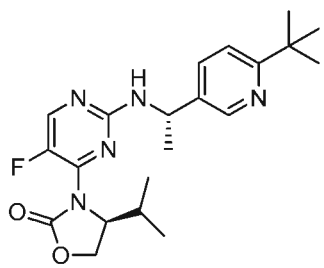
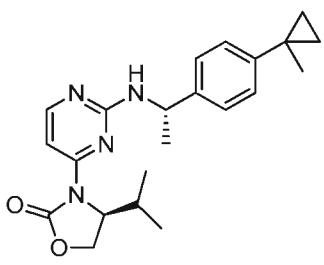
Volatiles were removed. Et_2O (10 mL) was added and the reaction mixture sonnicated. The volatiles were removed again. Et_2O (10 ml) was again added and the suspension sonnicated. Solid material was collected and washed with Et_2O to afford an HCl salt of (S)-1-(2-fluoro-4-(1-methylcyclopropyl)phenyl)ethanamine (42 mg, 0.18 mmol, 63 % yield) as a white solid. LCMS *m/z* 194.1 $(M + H)^+$, Rt 0.60 min.

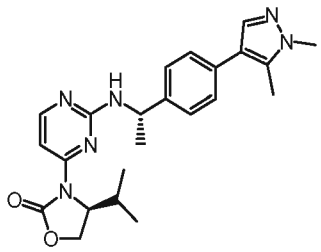
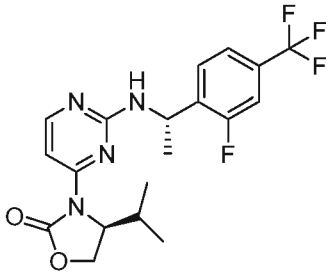
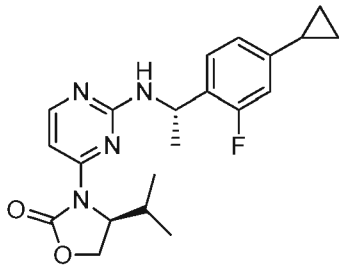
Step 2

To a microwave vial with stir bar was added (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (30 mg, 0.12 mmol) and DMSO (1 mL). To this reaction mixture was added (S)-1-(2-fluoro-4-(1-methylcyclopropyl) phenyl)ethanamine (51 mg, 0.22 mmol) and DIEA (0.09 ml, 0.50 mmol). The vial was capped and the reaction mixture was heated in a preheated oil bath at 110 °C for 18 hr. Solution was purified by reverse phase HPLC. Product fractions combined, frozen and lyophilized to afford (S)-3-(2-((S)-1-(2-fluoro-4-(1-methylcyclopropyl) phenyl) ethylamino) pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (3.3 mg, 6.3 µmol, 5 % yield) as a TFA salt. ^1H NMR (400 MHz, CD_3OD) δ 0.58 (br. s., 3 H) 0.77 (td, *J*=5.23, 1.76 Hz, 5 H) 0.80 - 0.86 (m, 2 H) 1.38 (s, 3 H) 1.57 (d, *J*=6.94 Hz, 3 H) 4.34 - 4.41 (m, 2 H) 4.67 (br. s., 1 H) 5.33 (d, *J*=7.97 Hz, 1 H) 6.95 - 7.05 (m, 2 H) 7.22 (t, *J*=7.97 Hz, 1 H) 7.67 (d, *J*=6.85 Hz, 1 H) 8.14 (d, *J*=6.65 Hz, 1 H). LCMS *m/z* 399.4 $(M + H)^+$, Rt 0.93 min. HRMS(A) *m/z* 399.2202 $(M + H)^+$, Rt 2.23 min.

The compounds in Table 15 were prepared using methods similar to those described for the preparation of Examples 515.

Table 15.

516	517	518
		
519	520	521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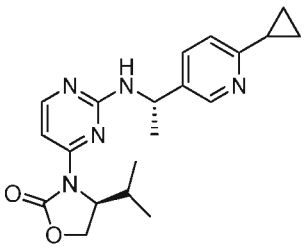	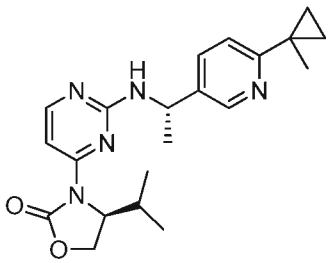	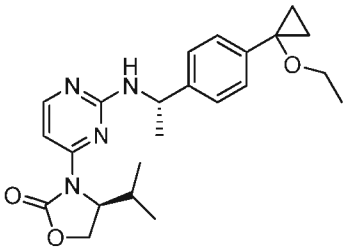
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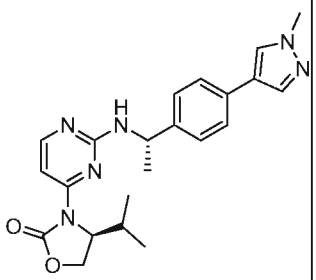	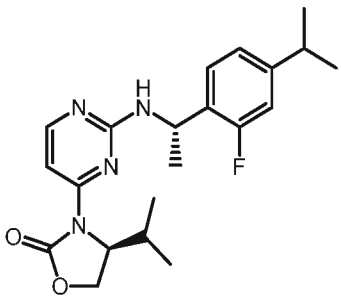	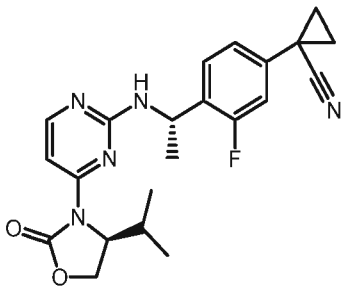
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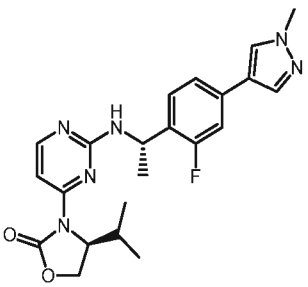	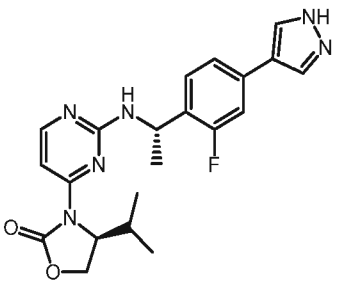	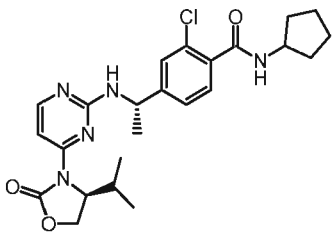
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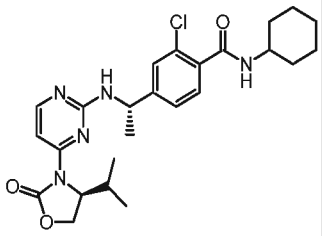	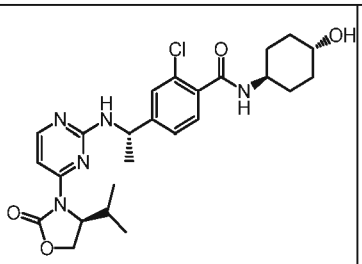	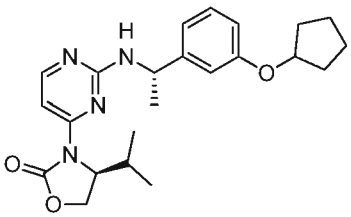
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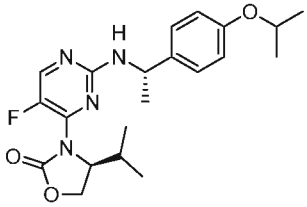	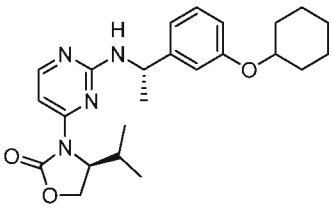	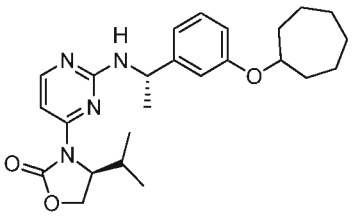
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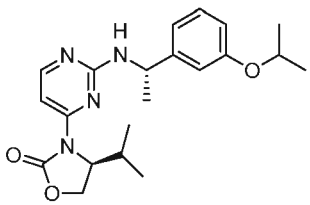	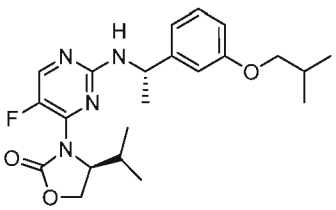	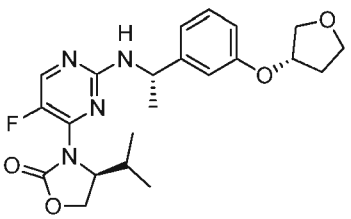
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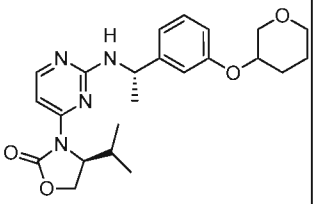	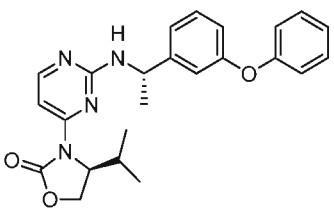	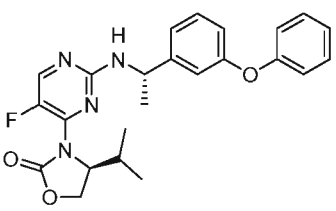
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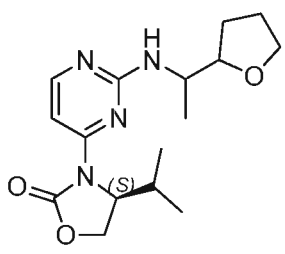	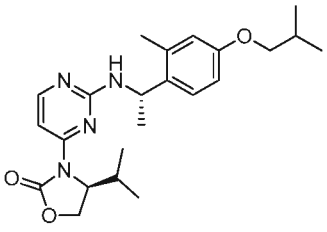	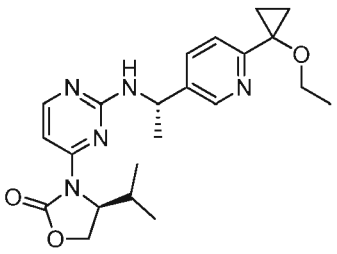
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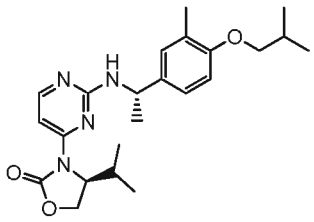
		

Table 16. Chemical name, NMR chemical shifts and LCMS signal for each compound listed in Table 15.

Table 16.

Example: Name	^{1}H NMR **(400 MHz)** δ **ppm**	**LCMS**
516: (S)-3-(2-((S)-1-(6-tert-butylpyridin-3-yl) ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO) 0.46 (br. s., 3 H) 0.63 (br. s., 3 H) 1.35 (s, 9 H) 1.50 (d, *J*=6.99 Hz, 3 H) 4.34 (d, *J*=7.92 Hz, 2 H) 4.59 (br. s., 1 H) 5.14 (br. s., 1 H) 7.32 (d, *J*=5.92 Hz, 1 H) 7.70 (br. s., 1 H) 8.03 (br. s., 1 H) 8.24 (br. s., 2 H) 8.59 (br. s., 1 H)	HRMS(A) *m/z* 384.2410 $(M + H)^+$, Rt 1.34
517: (S)-3-(2-((S)-1-(6-tert-butylpyridin-3-yl)ethylamino)-5-fluoropyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO) 0.55 (br. s., 6 H) 1.25 - 1.38 (s, 9 H) 1.47 (d, *J*=7.04 Hz, 3 H) 4.26 (br. s., 1 H) 4.45 - 4.59 (m, 2 H) 4.98 (br. s., 1 H) 7.66 (br. s., 1 H) 8.11 (br. s., 2 H) 8.41 (br. s., 1 H) 8.60 (br. s., 1 H)	HRMS(A) *m/z* 402.2314 $(M + H)^+$, Rt 1.45
518: (S)-4-isopropyl-3-(2-((S)-1-(4-(1-methyl cyclopropyl) phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one		HRMS(A) *m/z* 381.2295 $(M + H)^+$, Rt 2.10
519: (S)-3-(2-((S)-1-(4-(1,5-dimethyl-1H-pyrazol-4-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO) 0.49 (br. s., 3 H) 0.68 (br. s., 3 H) 1.48 (d, *J*=7.04 Hz, 6 H) 2.33 (s, 3 H) 3.76 (s, 3 H) 4.63 (br. s., 1 H) 4.75 - 4.82 (m, 1 H) 5.03 (br. s., 2 H) 7.30 - 7.37 (m, 4 H) 7.50 (s, 1 H) 8.22 (br. s., 1 H) 8.36 (br. s., 1 H)	HRMS(A) *m/z* 421.2362 $(M + H)^+$, Rt 1.58

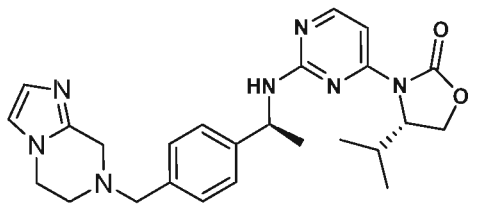
520: (S)-3-(2-((S)-1-(2-fluoro -4-(trifluoromethyl) phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO) 0.40 (br. s., 3 H) 0.57 (br. s., 3 H) 1.40 (br. s., 1 H) 1.47 (d, *J*=7.04 Hz, 3 H) 4.24 - 4.37 (m, 2 H) 4.49 (br. s., 1 H) 5.23 (br. s., 1 H) 7.30 (d, *J*=5.82 Hz, 1 H) 7.48 - 7.59 (m, 2 H) 7.65 (d, *J*=10.56 Hz, 1 H) 8.21 (d, *J*=18.58 Hz, 2 H)	HRMS(A) *m/z* 413.1602 $(M + H)^+$, Rt 2.16
521: (S)-3-(2-((S)-1-(4-cyclopropyl-2-fluorophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 0.61 (br. s., 3 H) 0.64 - 0.69 (m, 3 H) 0.77 (br. s., 3 H) 0.96 - 1.04 (m, 2 H) 1.57 (d, *J*=6.99 Hz, 3 H) 1.88 - 1.95 (m, 1 H) 4.39 (d, *J*=5.97 Hz, 2 H) 4.69 (br. s., 1 H) 5.33 (br. s., 1 H) 6.82 (dd, *J*=12.08, 1.71 Hz, 1 H) 6.88 (d, *J*=7.97 Hz, 1 H) 7.19 (t, *J*=8.31 Hz, 1 H) 7.70 (d, *J*=6.90 Hz, 1 H) 8.14 (d, *J*=7.04 Hz, 1 H)	HRMS(A) *m/z* 385.2042 $(M + H)^+$, Rt 2.06
522: (S)-3-(2-((S)-1-(6-cyclopropylpyridin-3-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 0.65 - 0.83 (m, 6 H) 1.14 - 1.20 (m, 2 H) 1.37 - 1.43 (m, 2 H) 1.64 (d, *J*=7.09 Hz, 3 H) 2.26 - 2.37 (m, 1 H) 4.36 - 4.39 (m, 2 H) 4.68 (br. s., 1 H) 5.25 (q, *J*=6.75 Hz, 1 H) 7.57 (d, *J*=8.51 Hz, 1 H) 7.63 (br. s., 1 H) 8.18 (d, *J*=5.92 Hz, 1 H) 8.33 (d, *J*=7.24 Hz, 1 H) 8.57 (d, *J*=2.10 Hz, 1 H)	HRMS(A) *m/z* 368.2097 $(M + H)^+$, Rt 1.12
523: (S)-4-isopropyl-3-(2-((S)-1-(6-(1-methylcyclopropyl)pyridin-3-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 0.59 - 0.84 (m, 6 H) 1.08 - 1.15 (m, 2 H) 1.22 - 1.28 (m, 2 H) 1.56 (s, 3 H) 1.64 (d, *J*=7.09 Hz, 3 H) 4.35 - 4.39 (m, 2 H) 4.69 (br. s., 1 H) 5.21 - 5.32 (m, 1 H) 7.62 (br. s., 1 H) 7.79 (d, *J*=8.46 Hz, 1 H) 8.18 (d, *J*=6.11 Hz, 1 H) 8.33 (d, *J*=7.14 Hz, 1 H) 8.57 (d, *J*=2.20 Hz, 1 H)	HRMS(A) *m/z* 382.2247 $(M + H)^+$, Rt 1.30
524: (S)-3-(2-((S)-1-(4-(1-ethoxycyclopropyl)-2-fluorophenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 0.60 (br. s., 3 H) 0.78 (br. s., 3 H) 0.92 - 0.98 (m, 2 H) 1.15 (t, *J*=7.07 Hz, 3 H) 1.19 - 1.26 (m, 2 H) 1.59 (d, *J*=6.99 Hz, 3 H) 1.78 (br. s., 1 H) 3.43 (q, *J*=7.09 Hz, 2 H) 4.40 (d, *J*=5.72 Hz, 2 H) 4.70 (d, *J*=3.91 Hz, 1 H) 5.38 (br. s., 1 H) 7.06 (s, 1 H) 7.07 - 7.12 (m, 1 H) 7.31 (t, *J*=7.95 Hz, 1 H) 7.73 (d, *J*=7.04 Hz, 1 H) 8.15 (d, *J*=6.90 Hz, 1 H)	HRMS(A) *m/z* 429.2310 $(M + H)^+$, Rt 2.08
525: (S)-4-isopropyl-3-(2-((S)-1-(4-(1-methyl-1H-pyrazol-4-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	(DMSO) 0.47 (br. s., 3 H) 0.69 (br. s., 3 H) 1.45 (d, *J*=6.99 Hz, 3 H) 1.81 (br. s., 1 H) 3.84 (s, 3 H) 4.33 (d, *J*=13.45 Hz, 2 H) 4.62 (br. s., 1 H) 4.99 (br. s., 1 H) 7.24 - 7.33 (m, 3 H) 7.46 (d, *J*=8.27 Hz, 2 H) 7.79 (d, *J*=0.73 Hz, 1 H) 8.06 (s, 1 H) 8.18 (br. s., 1 H)	HRMS(B) *m/z* 407.2179 $(M + H)^+$, Rt 2.44min
526: (S)-3-(2-((S)-1-(2-fluoro-4-isopropylphenyl)ethylamin	(CD_3OD) 0.59 (br. s., 3 H) 0.78 (br. s., 3 H) 1.23 (dd, *J*=6.90, 1.03 Hz, 6 H) 1.58 (d, *J*=6.99 Hz, 3 H) 2.91 (dt, *J*=13.78, 6.93 Hz,	HRMS(A) *m/z* 387.2207

o)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	1 H) 4.39 (d, *J*=5.97 Hz, 2 H) 4.69 (br. s., 1 H) 5.35 (br. s., 1 H) 6.97 - 7.06 (m, 2 H) 7.20 - 7.28 (m, 1 H) 7.73 (d, *J*=6.99 Hz, 1 H) 8.15 (d, *J*=6.90 Hz, 1 H)	$(M + H)^+$, Rt 2.20
527: 1-(3-fluoro-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino) ethyl)phenyl)cyclopropane carbonitrile	(CD_3OD) 0.61 (br. s., 3 H) 0.75 (br. s., 3 H) 1.40 - 1.50 (m, 2 H) 1.57 (d, *J*=6.94 Hz, 3 H) 1.71 - 1.79 (m, 2 H) 4.37 (d, *J*=6.50 Hz, 2 H) 4.66 (br. s., 1 H) 5.34 (d, *J*=6.55 Hz, 1 H) 7.07 - 7.18 (m, 2 H) 7.36 (t, *J*=8.19 Hz, 1 H) 7.64 (d, *J*=6.65 Hz, 1 H) 8.15 (d, *J*=6.60 Hz, 1 H)	HRMS(A) *m/z* 410.1999 $(M + H)^+$, Rt 1.82
528: (S)-3-(2-((S)-1-(2-fluoro-4-(1-methyl-1H-pyrazol-4-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 0.58 (br. s., 3 H) 0.78 (br. s., 3 H) 1.62 (d, *J*=7.04 Hz, 3 H) 1.82 (br. s., 1 H) 3.92 (s, 3 H) 4.40 (d, *J*=6.26 Hz, 2 H) 4.70 (br. s., 1 H) 5.39 (br. s., 1 H) 7.29 - 7.39 (m, 3 H) 7.78 (d, *J*=7.04 Hz, 1 H) 7.82 (s, 1 H) 7.99 (s, 1 H) 8.16 (d, *J*=7.04 Hz, 1 H)	HRMS(A) *m/z* 425.2112 $(M + H)^+$, Rt 1.64
529: (S)-3-(2-((S)-1-(2-fluoro-4-(1H-pyrazol-4-yl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 0.59 (br. s., 3 H) 0.79 (br. s., 3 H) 1.63 (d, *J*=6.94 Hz, 3 H) 1.84 (br. s., 1 H) 4.40 (d, *J*=6.26 Hz, 2 H) 4.71 (br. s., 1 H) 5.40 (br. s., 1 H) 7.29 - 7.36 (m, 1 H) 7.37 - 7.43 (m, 2 H) 7.78 (d, *J*=7.09 Hz, 1 H) 7.99 (s, 2 H) 8.17 (dd, *J*=6.36, 1.86 Hz, 1 H)	HRMS(A) *m/z* 411.1949 $(M + H)^+$, Rt 1.52
530: 2-chloro-N-cyclopentyl-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide	(DMSO) 0.55 (br. s., 3 H) 0.78 (br. s., 3 H) 1.42 (d, *J*=7.09 Hz, 3 H) 1.50 (d, *J*=4.65 Hz, 4 H) 1.64 (br. s., 2 H) 1.83 (d, *J*=6.46 Hz, 3 H) 4.14 (dd, *J*=12.72, 6.60 Hz, 1 H) 4.34 (br. s., 2 H) 4.64 (br. s., 1 H) 5.03 (br. s., 1 H) 7.25 (d, *J*=5.77 Hz, 1 H) 7.31 (s, 2 H) 7.42 (s, 1 H) 8.19 (br. s., 1 H) 8.27 (br. s., 1 H)	HRMS(A) *m/z* 472.2117 $(M + H)^+$, Rt 1.82
531: 2-chloro-N-cyclohexyl-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide	(DMSO) 0.55 (br. s., 3 H) 0.78 (br. s., 4 H) 1.18 - 1.34 (m, 4 H) 1.42 (d, *J*=7.04 Hz, 3 H) 1.56 (d, *J*=12.08 Hz, 1 H) 1.69 (d, *J*=12.86 Hz, 3 H) 1.81 (br. s., 3 H) 4.34 (br. s., 2 H) 4.63 (br. s., 1 H) 5.03 (br. s., 1 H) 7.26 (d, *J*=5.82 Hz, 1 H) 7.31 (s, 2 H) 7.43 (s, 1 H) 8.03 (br. s., 1 H) 8.18 (br. s., 2 H)	HRMS(A) *m/z* 486.2275 $(M + H)^+$, Rt 1.94
532: 2-chloro-N-((1r,4S)-4-hydroxycyclohexyl)-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide	(DMSO) 0.54 (br. s., 3 H) 0.77 (br. s., 3 H) 1.18 - 1.30 (m, 5 H) 1.36 (s, 1 H) 1.42 (d, *J*=7.04 Hz, 3 H) 1.81 (d, *J*=9.19 Hz, 5 H) 3.36 (br. s., 1 H) 4.33 (br. s., 2 H) 4.63 (br. s., 1 H) 5.02 (br. s., 1 H) 7.25 (d, *J*=5.77 Hz, 1 H) 7.30 (s, 2 H) 7.42 (s, 1 H) 8.17 (br. s., 2 H)	HRMS(A) *m/z* 502.2226 $(M + H)^+$, Rt 1.40
533: (S)-3-(2-((S)-1-(3-(cyclopentyloxy)phenyl)ethylamino)pyrimidin-4-yl)-	(DMSO) 0.40 - 0.73 (m, 6 H) 1.40 (d, *J*=6.99 Hz, 3 H) 1.47 - 1.70 (m, 6 H) 1.83 (dd, *J*=16.80, 6.72 Hz, 3 H) 4.31 (d,*J*=8.75	HRMS(A) *m/z* 411.2402

4-isopropyloxazolidin-2-one	Hz, 2 H) 4.58 (br. s., 1 H) 4.71 (br. s., 1 H) 4.94 (br. s., 1 H) 6.69 (dd, *J*=7.95, 2.03 Hz, 1 H) 6.81 (d, *J*=8.31 Hz, 2 H) 7.09 - 7.19 (m, 1 H) 7.27 (d, *J*=6.06 Hz, 1 H) 8.16 (br. s., 2 H)	$(M + H)^+$, Rt 2.15 min
534: (S)-3-(2-((S)-1-(3-(cyclohexyloxy)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO) 0.47 (br. s., 3 H) 0.65 (br. s., 3 H) 1.14 - 1.36 (m, 5 H) 1.40 (d, *J*=7.04 Hz, 3 H) 1.44 - 1.54 (m, 1 H) 1.65 (d, *J*=9.34 Hz, 2 H) 1.72 - 1.91 (m, 3 H) 4.11 - 4.39 (m, 3 H) 4.57 (br. s., 1 H) 4.94 (br. s., 1 H) 6.71 (dd, *J*=7.85, 1.88 Hz, 1 H) 6.80 (br. s., 2 H) 7.14 (t, *J*=8.07 Hz, 1 H) 7.26 (d, *J*=6.02 Hz, 1 H) 8.16 (br. s., 2 H)	HRMS(A) *m/z* 425.2565 $(M + H)^+$, Rt 2.26 min
535: (S)-3-(2-((S)-1-(3-(cycloheptyloxy)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO) 0.50 (br. s., 3 H) 0.68 (br. s., 3 H) 1.43 (d, *J*=7.04 Hz, 5 H) 1.53 (d, *J*=2.98 Hz, 4 H) 1.58 - 1.71 (m, 4 H) 1.73 - 1.97 (m, 3 H) 4.34 (d, *J*=8.46 Hz, 2 H) 4.38 - 4.46 (m, 1 H) 4.60 (br. s., 1 H) 4.98 (br. s., 1 H) 6.70 (dd, *J*=8.14, 2.03 Hz, 1 H) 6.76 - 6.89 (m, 2 H) 7.18 (t, *J*=7.87 Hz, 1 H) 7.30 (d, *J*=6.02 Hz, 1 H) 8.20 (br. s., 2 H)	HRMS(A) *m/z* 439.2712 $(M + H)^+$, Rt 2.41 min
536: (S)-3-(2-((S)-1-(3-isopropoxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO) 0.49 (br. s., 3 H) 0.67 (br. s., 3 H) 1.09 - 1.28 (m, 7 H) 1.32 - 1.50 (m, 3 H) 4.23 - 4.39 (m, 2 H) 4.52 (dt, *J*=12.04, 6.08 Hz, 1 H) 4.60 (br. s., 1 H) 4.96 (br. s., 1 H) 6.71 (dd, *J*=8.00, 1.98 Hz, 1 H) 6.82 (br. s., 2H) 7.15 (t, *J*=8.09 Hz, 1 H) 7.30 (d, *J*=6.02 Hz, 1 H) 8.18 (br. s., 1 H) 8.28 (br. s., 1 H)	HRMS(A) *m/z* 385.2248 $(M + H)^+$, Rt 1.92 min
537: (S)-3-(5-fluoro-2-((S)-1-(3-isobutoxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO) 0.49 (br. s., 6 H) 0.92 (d, *J*=6.7 Hz, 6 H) 1.37 (d, *J*=7.04 Hz, 3 H) 1.93 (dquin, *J*=13.25, 6.60, 6.60, 6.60, 6.60 Hz, 1 H) 3.59 - 3.70 (m, 2 H) 3.94 - 4.31 (m, 3 H) 4.45 (br. s., 1 H) 6.69 (dd, *J*=8.17, 1.76 Hz, 1 H) 6.80 - 6.89 (m, 2 H) 7.13 (t, *J*=7.83 Hz, 1H) 7.92 (br. s., 1 H) 8.34 (br. s., 1 H)	HRMS(A) *m/z* 417.231 $(M + H)^+$, Rt 2.53 min
538: (S)-3-(5-fluoro-2-((S)-1-(3-((S)-tetrahydrofuran-3-yloxy)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO) 1.41 (d, *J*=7.04 Hz, 6 H) 1.83 - 1.93 (m, 1 H) 2.11 - 2.23 (m, 1 H) 3.68 - 4.04 (m, 8 H) 4.25 (br. s., 1 H) 4.49 (br. s., 2 H) 4.80 (br. s., 1 H) 4.95 (dd, *J*=6.06, 4.65 Hz, 1 H) 6.72 (dd, *J*=8.02, 2.10 Hz, 1 H) 6.83 - 6.94 (m, 2 H) 7.19 (t, *J*=7.87 Hz, 1 H) 7.96 (br. s., 1 H) 8.38 (br. s., 1 H)	HRMS(A) *m/z* 431.2098 $(M + H)^+$, Rt 2.01 min
539: (4S)-4-isopropyl-3-(2-((1S)-1-(3-(tetrahydro-2H-pyran-3-yloxy)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one	(DMSO) 0.47 (br. s., 3 H) 0.66 (br. s., 3 H) 1.39 (d, *J*=6.99 Hz, 3 H) 1.44 - 2.00 (m, 5 H) 3.32 - 3.50 (m, 2 H) 3.54 - 3.88 (m, 3 H) 4.23 - 4.37 (m, 2 H) 4.61 (br. s., 1H) 4.90 (br. s., 1H) 6.74 (d, *J*=8.36 Hz, 1 H) 6.85 (d, *J*=13.55 Hz, 2 H) 7.15 (t, *J*=7.87 Hz, 1 H) 7.25 (d, *J*=5.97 Hz, 1 H) 8.06 (br. s.,1 H) 8.16 (br. s., 1 H)	HRMS(A) *m/z* 427.2353 $(M + H)^+$, Rt 1.75 min
540: (S)-4-isopropyl-3-(2-((S)-1-(3-phenoxyphenyl)ethylamin	(DMSO) 0.50 (br. s., 3 H) 0.66 (br. s., 3 H) 1.42 (d, *J*=7.04 Hz, 3 H) 1.75 (br. s., 1 H) 4.27 - 4.37 (m, 2 H) 4.55 - 4.62 (m, 1 H)	HRMS(A) *m/z* 419.2092

o)pyrimidin-4-yl)oxazolidin-2-one	4.97 -5.07 (m, 1 H) 6.78 (dd, *J*=8.02, 1.81 Hz, 1 H) 6.87 (d, *J*=7.53 Hz, 2 H) 6.96 (br. s., 1 H) 7.04 - 7.14 (m, 2 H) 7.25 - 7.37 (m, 4 H) 8.17 (d, *J*=4.99 Hz, 1 H) 8.36 (br. s., 1 H)	$(M + H)^+$, Rt 2.12 min
541: (S)-3-(5-fluoro-2-((S)-1-(3-phenoxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO) 0.44 - 0.65 (m, 6 H) 1.37 (d, *J*=6.99 Hz, 3 H) 4.08 - 4.40 (m, 2 H) 4.45 (br. s., 1 H) 4.82 (br. s., 1 H) 6.75 (dd, *J*=8.07, 1.37 Hz, 1 H) 6.86 (d, *J*=7.48 Hz, 2 H) 6.95 (br. s., 1 H) 7.03 - 7.11 (m, 2 H) 7.28 (dt, *J*=19.78, 7.86 Hz, 3 H) 7.94 (br. s., 1 H) 8.33 (br. s.,1 H)	HRMS(A) *m/z* 437.1992 $(M + H)^+$, Rt 2.45 min
542: (S)-3-(5-fluoro-2-((S)-1-(4-isopropoxyphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(DMSO) 0.56 (br. s., 6 H) 1.18 (d, *J*=2.35 Hz, 3 H) 1.20 (d, *J*=2.30 Hz, 3 H) 1.36 (d, *J*=7.04 Hz, 3 H) 4.21 (br. s., 1H) 4.36 - 4.58 (m, 3 H) 4.75 (br. s., 1H) 6.77 (d, *J*=8.71 Hz, 2 H) 7.18 (d, *J*=8.56 Hz, 2 H) 7.87 (br. s., 1 H) 8.33 (d, *J*=2.74 Hz, 1 H)	HRMS(A) *m/z* 403.2156 $(M + H)^+$, Rt 2.30 min
543: (4S)-4-isopropyl-3-(2-((1-(tetrahydrofuran-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 8.00 - 8.17 (m, 1H), 7.71 (d, J = 7.04 Hz, 1H), 4.78 - 4.85 (m, 1H), 4.41 - 4.55 (m, 2H), 3.98 - 4.14 (m, 1H), 3.84 - 3.97 (m, 1H), 3.67 - 3.82 (m, 1H), 2.55 - 2.70 (m, 1H), 1.86 - 2.13 (m, 3H), 1.56 - 1.82 (m, 1H), 1.24 - 1.34 (m, 3H), 1.00 - 1.06 (m, 3H), 0.91 (t, J= 6.06 Hz, 3H)	HRMS(A) *m/z* 321.1935 (M + H)+, Rt 1.32 min
544: (S)-3-(2-((S)-1-(4-isobutoxy-3-methylphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(400 MHz, DMSO) δ ppm 0.54 (br. s., 3 H) 0.72 (br. s., 3 H) 0.96 (d, J=6.70 Hz, 6 H) 1.41 (d, J=6.99 Hz, 3 H) 1.89 (br. s., 1 H) 1.99 (dt, J=13.24, 6.61 Hz, 1 H) 2.11 (s, 3 H) 3.68 (d, J=6.41 Hz, 2 H) 4.31 - 4.41 (m, 2 H) 4.62 (dd, J=6.99, 3.72 Hz, 1 H) 4.94 (quin, J=6.94 Hz, 1 H) 6.80 (d, J=8.31 Hz, 1 H) 7.00 - 7.13 (m, 2 H) 7.34 (d, J=6.06 Hz, 1 H) 8.19 (d, J=4.94 Hz, 1 H) 8.42 (br. s., 1 H)	HRMS(A) m/z 413.2561 (M + H)+, Rt 2.34 min
545: (S)-3-(2-((S)-1-(6-(1-ethoxycyclopropyl)pyridin-3-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	^1H NMR (400 MHz, CD_3OD) d 0.65 (br. s., 3 H) 0.75 (br. s., 3 H) 1.23 (t, J=7.04 Hz, 3 H) 1.28 - 1.45 (m, 4 H) 1.64 (d, J=7.09 Hz, 3 H) 3.55 (q, J=7.04 Hz, 2 H) 4.36 - 4.43 (m, 2 H) 4.70 (br. s., 1 H) 5.20 - 5.28 (m, 1 H) 7.66 (d, J=8.41 Hz, 2 H) 8.04 (br. s., 1 H) 8.16 (d, J=6.41 Hz, 1 H)	HRMS(A) m/z 412.2349 (M + H)+, Rt 1.55 min
546: (S)-3-(2-((S)-1-(4-isobutoxy-3-methylphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	^1H NMR (400 MHz, DMSO) d ppm 0.54 (br. s., 3 H) 0.72 (br. s., 3 H) 0.96 (d, J=6.70 Hz, 6 H) 1.41 (d, J=6.99 Hz, 3 H) 1.89 (br. s., 1 H) 1.99 (dt, J=13.24, 6.61 Hz, 1 H) 2.11 (s, 3 H) 3.68 (d, J=6.41 Hz, 2 H) 4.31 - 4.41 (m, 2 H) 4.62 (dd, J=6.99, 3.72 Hz, 1 H) 4.94 (quin, J=6.94 Hz, 1 H) 6.80 (d, J=8.31 Hz, 1 H) 7.00 - 7.13 (m, 2 H) 7.34 (d, J=6.06 Hz, 1 H) 8.19 (d, J=4.94 Hz, 1 H) 8.42 (br. s., 1 H)	HRMS m/z 413.2561 (M + H)+; Rt-2.34 min.

Example 547

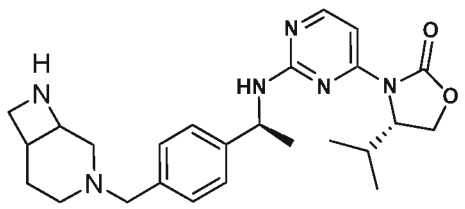


A solution of (S)-3-(2-((S)-1-(4-(chloromethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (75 mg, 0.2 mmol) and 5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine (25 mg, 0.2 mmol) in DMSO (2 mL) was heated at 80 °C for 16 h. The reaction mixture was diluted with EtOAc (20 mL) and washed with water (20 mL). After separation, the aqueous phase was washed with EtOAc (2 x 15 mL). Combined organics were dried over Na2SO4, filtered and concentrated. Silica gel column chromatography (MeOH in CH_2Cl_2 0 to 10%) provided (S)-3-(2-((S)-1-(4-((5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (58 mg, white solid) in 62.8% yield.

^{1}H NMR (400 MHz, MeOD) δ 8.12 (d, J = 6.0 Hz, 1H), 7.34 (d, J = 5.9 Hz, 1H), 7.33 (s, 4H), 6.99 (d, J = 1.3 Hz, 1H), 6.89 (d, J = 1.4 Hz, 1H), 5.07 (q, J = 7.0 Hz, 1H), 4.68 (br s, 1H), 4.37 – 4.25 (m, 2H), 4.02 (t, J = 5.5 Hz, 2H), 3.72 (s, 2H), 3.63 (s, 2H), 2.90 (td, J = 5.4, 2.6 Hz, 2H), 1.84 (br s, 1H), 1.51 (d, J = 7.0 Hz, 3H), 0.72 (br s, 3H), 0.57 (br s, 3H); HRMS m/z 462.2606 (M + H)+.

The following compounds were prepared using methods similar to those described for the preparation of **Example 205.**

Example 548

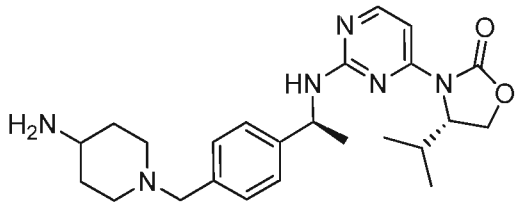


(4S)-3-(2-((1S)-1-(4-(3,8-diazabicyclo[4.2.0]octan-3-ylmethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

^{1}H NMR (400 MHz, MeOD) δ 8.12 – 8.08 (m, 1H), 7.37 – 7.22 (m, 5H), 5.10 – 5.01 (m, 1H), 4.66 (br s, 1H), 4.37 – 4.23 (m, 2H), 3.92 – 3.89 (m, 1H), 3.63 – 3.54 (m, 1H), 3.54 – 3.47 (m, 1H), 3.24 – 3.20 (m, 1H), 3.11 – 2.95 (m, 1H), 2.95 – 2.73 (m, 1H), .2.67 – 2.59

(m, 2H), 2.49 (ddd, J = 16.2, 12.8, 5.3 Hz, 1H), 2.20 – 2.08 (m, 1H), 1.99 – 1.68 (m, 3H), 1.50 (d, J = 7.0 Hz, 3H), 0.72 (br s, 1H), 0.56 (br s, 1H) ; HRMS m/z 451.2810 (M + H)+.

Example 549

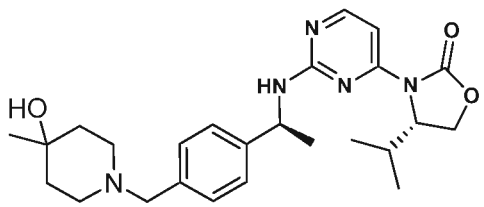


(S)-3-(2-((S)-1-(4-((4-aminopiperidin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

^{1}H NMR (400 MHz, MeOD) d 8.12 (d, J = 5.8 Hz, 1H), 7.34 (d, J = 5.8 Hz, 1H), 7.27 (q, J = 8.2 Hz, 4H), 5.05 (q, J = 7.0 Hz, 1H), 4.67 (s, 1H), 4.38 - 4.25 (m, 2H), 3.48 (s, 2H), 2.86 (br d, J = 11.8 Hz, 2H), 2.71 (tt, J = 10.9, 4.2 Hz, 1H), 2.05 (tt, J = 12.0, 2.5 Hz, 2H), 1.90 - 1.75 (m, 3H), 1.54 - 1.37 (m, 5H), 0.72 (br s, 4H), 0.55 (br s, 3H); HRMS m/z 439.2805 (M + H)+.

The following compounds were prepared using methods similar to those described for the preparation of **Example 210**.

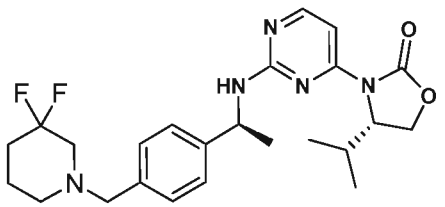
Example 550



(S)-3-(2-((S)-1-(4-((4-hydroxy-4-methylpiperidin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

^{1}H NMR (400 MHz, MeOD) δ 8.12 (d, J = 5.7 Hz, 1H), 7.34 (d, J = 5.9 Hz, 1H), 7.27 (t, J = 6.6 Hz, 4H), 5.06 (q, J = 6.8 Hz, 1H), 4.67 (br s, 1H), 4.37 – 4.25 (m, 2H), 3.51 (d, J = 3.2 Hz, 2H), 2.52 (br s, 2H), 2.44 (br s, 2H), 1.81 (br s, 1H), 1.59 (br s, 4H), 1.50 (d, J = 7.0 Hz, 3H), 1.19 (s, 3H), 0.72 (br s, 3H), 0.56 (br s, 3H); HRMS m/z 454.2816 (M + H)+.

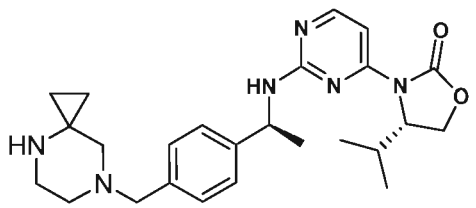
Example 552



(S)-3-(2-((S)-1-(4-((3,3-difluoropiperidin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

^{1}H NMR (400 MHz, MeOD) δ 8.12 (d, J = 5.8 Hz, 1H), 7.35 (d, J = 5.8 Hz, 1H), 7.28 (q, J = 8.2 Hz, 4H), 5.06 (q, J = 7.0 Hz, 1H), 4.67 (br s, 1H), 4.39 – 4.25 (m, 2H), 3.55 (d, J = 2.2 Hz, 2H), 2.56 (t, J = 11.5 Hz, 2H), 2.51 – 2.40 (m, 2H), 1.91 – 1.81 (m, 3H), 1.78 – 1.70 (m, 2H), 1.50 (d, J = 7.0 Hz, 3H), 0.71 (br s, 3H), 0.56 (br s, 3H) ; HRMS m/z 460.2537 (M + H)+.

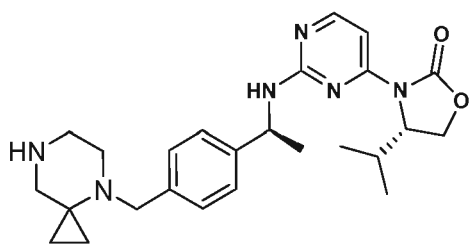
Example 553



(S)-3-(2-((S)-1-(4-(4,7-diazaspiro[2.5]octan-7-ylmethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one

^{1}H NMR (400 MHz, MeOD) δ 8.12 (d, J = 5.8 Hz, 1H), 7.34 (d, J = 5.8 Hz, 1H), 7.32 – 7.24 (m, 4H), 5.06 (q, J = 7.0 Hz, 1H), 4.68 (br s, 1H), 4.37 – 4.26 (m, 2H), 3.49 (s, 2H), 2.89 (t, J = 5.0 Hz, 2H), 2.47 (br s, 2H), 2.28 (br s, 2H), 1.86 (br s, 1H), 1.49 (d, J = 7.0 Hz, 3H), 0.72 (br s, 3H), 0.64 – 0.49 (m, 5H), 0.45 (t, J = 3.2 Hz, 2H) ; HRMS m/z 451.2809 (M + H)+.

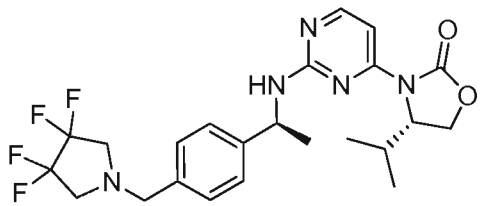
Example 554



(S)-3-(2-((S)-1-(4-(4,7-diazaspiro[2.5]octan-4-ylmethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

^{1}H NMR (400 MHz, MeOD) δ 8.11 (d, J = 5.8 Hz, 1H), 7.33 (d, J = 5.8 Hz, 1H), 7.24 (q, J = 8.3 Hz, 4H), 5.03 (q, J = 7.0 Hz, 1H), 4.67 (br s, 1H), 4.37 – 4.25 (m, 2H), 3.85 (s, 2H), 2.85 – 2.65 (m, 6H), 1.87 (br s, 1H), 1.48 (d, J = 7.0 Hz, 3H), 0.85 – 0.63 (m, 5H), 0.63 – 0.46 (m, 5H) ; HRMS m/z 451.2810 (M + H)+.

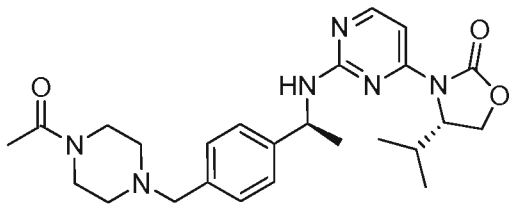
Example 555



(S)-4-isopropyl-3-(2-((S)-1-(4-((3,3,4,4-tetrafluoropyrrolidin-1-yl)methyl)phenyl) ethylamino)pyrimidin-4-yl)oxazolidin-2-one.

HRMS m/z 482.2161 (M + H)+; RT=2.78 min.

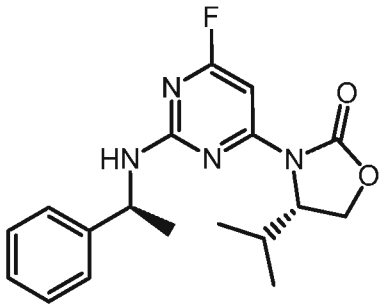
Example 556



(S)-3-(2-((S)-1-(4-((4-acetylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one.

HRMS m/z 467.2752 (M + H)+; RT=1.92 min.

Example 557



(S)-4,6-difluoro-N-(1-phenylethyl)pyrimidin-2-amine (48.8 mg, 0.21 mmol) was added to NaH (95 %, 6.1 mg, 0.25 mmol, 1.2 equiv) in DMF (2 mL) at 0 °C. After 5 min, (S)-4-isopropyl-2-oxazolidinone (27.9 mg, 0.22 mmol, 1.0 equiv) was added. The reaction was stirred for 10 min at 0 °C and then warmed to room temperature. After 4h, the reaction mixture was quenched with water and poured into dilute brine (1:1 sat. brine:water) and EtOAc. The aqueous phase was extracted with EtOAc and the combined organic layers were washed with diluted brine. The organic layer was dried over Na_2SO_4, filtered and concentrated to a pink oil. Purification by reverse phase HPLC followed by lyopholization of the fractions containing product provided (S)-3-(6-fluoro-2-(((S)-1-phenylethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one as a white solid (22.5 mg TFA salt) in 31% yield. ^{1}H NMR (400 MHz, CD_3OD) δ 7.27 - 7.39 (m, 4H), 7.17 - 7.26 (m, 1H), 6.92 (s, 1H), 5.05 (q, *J* = 7.04 Hz, 1H), 4.63 (br. s., 1H), 4.19 - 4.41 (m, 2H), 1.77 (br. s., 1H), 1.51 (d, *J* = 7.04 Hz, 3H), 0.44 - 0.78 (m, 6H); LCMS *m/z* 345.1 $(M + H)^+$., R_t 1.00 min; UPLC R_t 5.038 min.

The compounds in Table 17 were prepared using methods similar to those described for the preparation of Example 557.

Table 17.

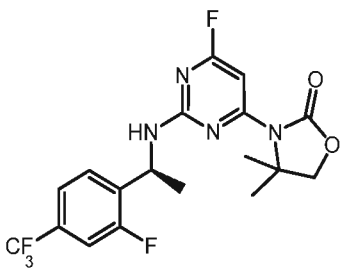
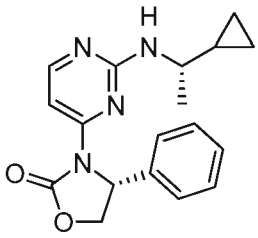
558


Table 18: Chemical name, NMR chemical shifts and LCMS signal for each compound listed in Table **17**.

Example: Name	^{1}H NMR (400 MHz) δ ppm	LCMS
558: (*S*)-5,5-dimethyl-4-phenyl-3-(2-((*S*)-1-phenylethylamino)pyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 8.06 (d, J = 5.8 Hz, 1 H), 7.43 (d, J = 5.8 Hz, 1 H), 7.31 – 7.24 (m, 3 H), 7.19 – 7.11 (m, 5 H), 7.01 (br s 2 H), 5.48 (s, 1 H), 4.86 – 4.80 (m, 1 H), 1.65 (s, 3 H), 1.43 (d, J = 7.0 Hz, 3 H), 0.98 (s, 3 H)	HRMS(A) *m/z* 389.1987 $(M + H)^+$

Example 559



A mixture of (R)-3-(2-chloropyrimidin-4-yl)-4-phenyloxazolidin-2-one (55.3 mg, 0.20 mmol), (S)-1-cyclopropylethylamine (40 μL, 0.26 mmol, 1.3 equiv) and *i*Pr_2Net (0.20 mL, 1.15 mmol, 5.7 equiv) in NMP (1 mL) was heated in the microwave at 180 °C for 20min. The reaction mixture was filtered and purified by reverse phase HPLC to give (R)-3-(2-(((S)-1-cyclopropylethyl)amino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one as a white solid (8.8 mg) in 10 % yield. ^{1}H NMR (400 MHz, CD_3OD) δ 7.72 (d, J = 6.26 Hz, 1H), 7.29 - 7.43 (m, 6H), 5.76 (dd, J = 4.11, 8.80 Hz, 1H), 4.28 (dd, J = 4.30, 8.61 Hz, 1H), 3.06 - 3.19 (m, 1H), 1.39 (dd, J = 3.52, 6.65 Hz, 1H), 0.88 - 0.97 (m, 1H), 0.83 (br. s., 3H), 0.53 - 0.62 (m, 1H), 0.50 (dt, J = 4.11, 8.51 Hz, 1H), 0.33 (qd, J = 4.78, 9.54 Hz, 1H), 0.26 (td, J = 4.60, 9.59 Hz, 1H); HRMS(A) *m/z* 325.1667 $(M + H)^+$, Rt 1.54 min; UPLC 2.807 min.

The compounds in Table 19 were prepared using methods similar to those described for the preparation of Example 559.

Table 19.

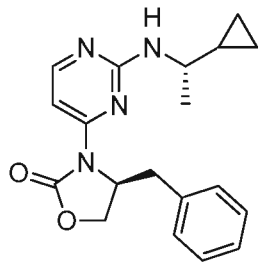
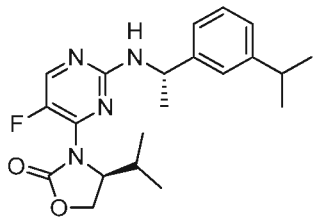
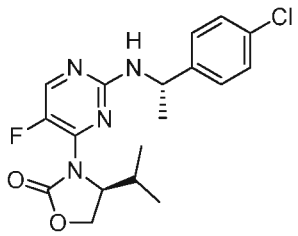
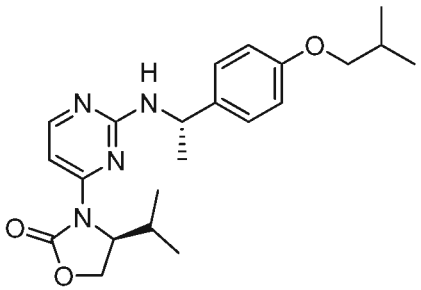
560	561	562
		

Table 20. Chemical name, NMR chemical shifts and LCMS signal for each compound listed in Table 19.

Example: Name	^{1}H NMR (400 MHz) δ ppm	LCMS
560: (S)-4-benzyl-3-(2-(((S)-1-cyclopropylethyl)amino)pyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 8.13 (d, J = 7.04 Hz, 1H), 7.71 (d, J = 7.04 Hz, 1H), 7.22 - 7.38 (m, 5H), 5.11 (tt, J = 3.03, 8.12 Hz, 1H), 4.23 -4.53 (m, 2H), 3.08 (dd, J = 8.41, 13.50 Hz, 1H), 1.42 (d, J = 6.65 Hz, 3H), 1.04 - 1.23 (m, 1H), 0.47 - 0.73 (m, 2H), 0.17 - 0.47 (m, 2H).	HRMS(A) *m/z* 339.1822 $(M + H)^+$, Rt 1.64 min
561: (S)-3-(5-fluoro-2-(((S)-1-(3-isopropylphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one		HRMS(A) *m/z* 387.2203 $(M + H)^+$, Rt 2.52 min
562: (S)-3-(2-(((S)-1-(4-chlorophenyl)ethyl)amino)-5-fluoropyrimidin-4-yl)-4-isopropyloxazolidin-2-one		HRMS(A) *m/z* 379.1341 $(M + H)^+$, Rt 2.30 min

Example 563



A mixture of (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (43.2 mg, 0.18 mmol), (1S)-1-[4-(2-Methylpropoxy)phenyl]ethan-1-amine (84.0 mg, 0.37 mmol, 2.0 equiv) and *i*Pr_2Net (0.30 mL, 1.72 mmol, 4.7 equiv) in NMP (1 mL) was heated at 105 °C for 24 h. The reaction mixture was filtered and purified by reverse phase HPLC to give (S)-3-(2-(((S)-1-(4-isobutoxyphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one as a white solid (5.3 mg, TFA salt) in 4 % yield. ^{1}H NMR (400 MHz, CD_3OD) δ 7.68 (d, J = 6.65 Hz, 1H), 7.25 (d, J = 8.61 Hz, 2H), 6.90 (d, J = 8.61 Hz, 2H), 4.41 (d, J = 5.87 Hz, 2H), 3.74 (d, J = 6.26 Hz, 2H), 1.96 - 2.15 (m, 1H), 1.58 (d, J = 7.04 Hz, 3H), 1.03 (d, J = 6.65 Hz, 6H); HRMS(A) *m/z* 399.2399 $(M + H)^+$, Rt 2.60 min; UPLC 4.223 min.

The compounds in Table 21 were prepared using methods similar to those described for the preparation of Example 563.

Table 21.

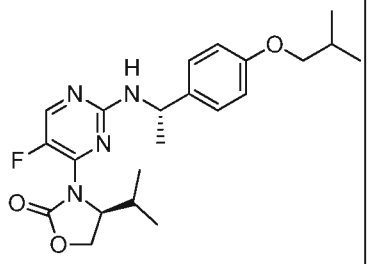
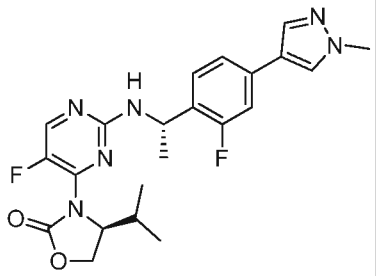
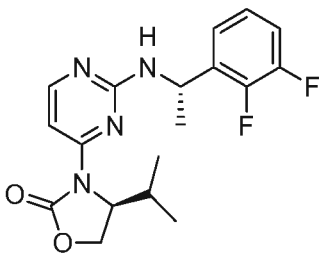
564	565
	

Table 22. Chemical name, NMR chemical shifts and LCMS signal for each compound listed in Table 21.

Example: Name	^{1}H NMR (400 MHz) δ ppm	LCMS
564: (S)-3-(5-fluoro-2-(((S)-1-(4-isobutoxyphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one		HRMS(A) *m/z* 417.2314 $(M + H)^+$, Rt 2.53 min
565: (S)-3-(5-fluoro-2-(((S)-1-(2-fluoro-4-(1-methyl-1H-pyrazol-4-yl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one		HRMS(A) *m/z* 443.2012 $(M + H)^+$, Rt 1.92 min

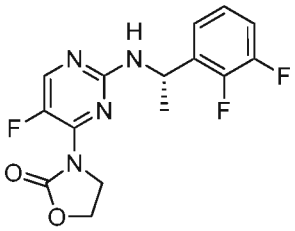
Example 566



To a microwave vial with stir bar was added (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (24.96 mg, 0.103 mmol) in DMSO (1653 µL). To this reaction mixture was added (S)-1-(2,3-difluorophenyl)ethanamine (40 mg, 0.207 mmol) and DIEA (144 µL, 0.826 mmol). The vial capped and heated at 110 °C over the weekend. The solution was filtered, then purified by reverse phase HPLC. Product fractions combined, frozen and lyopholyzed to afford ((S)-3-(2-((S)-1-(2,3-difluorophenyl)ethylamino) pyrimidin-4-yl)-4-isopropyloxazolidin-2-one (10.2 mg, 0.021 mmol, 10.26 % yield) as a

TFA salt. ^{1}H NMR (400 MHz, CD_3OD) δ ppm 0.59 (br. s., 3 H) 0.75 (br. s., 3 H) 1.59 (d, *J*=6.99 Hz, 3 H) 1.69 (br. s., 1 H) 4.37 (d, *J*=5.67 Hz, 2 H) 4.66 (br. s., 1 H) 5.40 (d, *J*=7.38 Hz, 1 H) 7.06 - 7.23 (m, 3 H) 7.70 (d, *J*=6.90 Hz, 1 H) 8.14 (d, *J*=6.46 Hz, 1 H); LCMS *m/z* 363.3 $(M + H)^+$, Rt 0.77 min.; HRMS(A) *m/z* 363.1642 $(M + H)^+$, Rt 1.89 min.

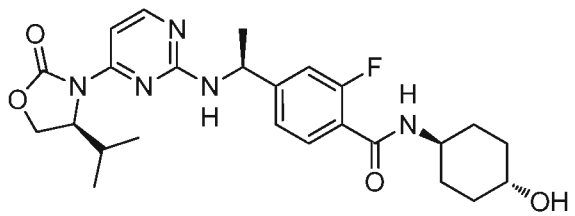
Example 567



(S)-3-(2-(1-(2,3-difluorophenyl)ethylamino)-5-fluoropyrimidin-4-yl)oxazolidin-2-one was prepared using a method similar to that described for the preparation of Example 566. ^{1}H NMR (400 MHz, CD_3OD) δ ppm 1.50 (d, J=7.04 Hz, 3 H) 3.91 (br. s., 1 H) 4.09 - 4.20 (m, 1 H) 4.42 - 4.56 (m, 2 H) 5.26 (q, J=6.68 Hz, 1 H) 6.99 - 7.12 (m, 2 H) 7.16 (t, J=7.48 Hz, 1 H) 8.13 (d, J=3.37 Hz, 1 H). HRMS(A) m/z 339.1075 (M + H)+, Rt 1.86 min.

Example 568

2-fluoro-N-(*trans*-4-hydroxycyclohexyl)-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide



Step 1: Preperation of (S)-4-(1-(tert-butoxycarbonylamino)ethyl)-2-fluorobenzoic acid:

To (S)-4-(1-aminoethyl)-2-fluorobenzoic acid (900 mg, 4.10 mmol) was added, DCM (11 ml), Hunig's Base (2.147 ml, 12.29 mmol) and BOC-Anhydride (1.998 ml, 8.61 mmol). Then NMP (11.00 ml) was added to help solubility. The reaction was sonicated for 10 minutes and was stirred at room temperature for 22 hours, followed by LCMS. The DCM was mostly concentrated off. Then to the crude reaction was added 120 ml of water and basified with 10 ml of 5M NaOH. The basic aqueous solution was extracted with 2 x 50 ml of (15% ethyl acetate in heptane) solution. Then to the basic aqueous solution (with

the product) was added 150 ml of ethyl acetate and with stirring acidified with 2M aqueous HCl solution to about pH 3. Then the ethyl acetate was extracted, saved and the acidic water extracted again with 100 ml of ethyl acetate. The organic layers were combined and washed with 0.5M aqueous HCl solution 1 x 40 ml, with water 3 x 40 ml, and concentrated to constant mass to give 1104 mg of (S)-4-(1-(tert-butoxycarbonylamino)ethyl)-2-fluorobenzoic acid, used as is. LCMS *m/z* BOC pattern of 269.0 (M+H-15 fragment) and weak 228.0 (M+H-56 fragment) compared to expected 284.0 $(M + H)^+$, Rt 0.72 min.

Step 2: Preperation of tert-butyl (S)-1-(3-fluoro-4-(*trans*-4-hydroxycyclohexylcarbamoyl)phenyl)ethylcarbamate:
To (S)-4-(1-(tert-butoxycarbonylamino)ethyl)-2-fluorobenzoic acid (40.8 mg, 0.144 mmol) was added NMP (0.5 ml), *trans*-4-aminocyclohexanol (41.5 mg, 0.360 mmol), Hunig's Base (0.101 ml, 0.576 mmol) and HATU (110 mg, 0.288 mmol) The reaction was stirred at room temperature for 6 hours, followed by LCMS. To the reaction was added 0.5 ml of NMP, filtered, purified by prep LC and lyophilized to give 33 mg of tert-butyl (S)-1-(3-fluoro-4-(*trans*-4-hydroxycyclohexylcarbamoyl)phenyl)ethylcarbamate as the TFA Salt. LCMS *m/z* 381.1 (M + H)+, Rt 0.70 min.

Step 3: Preperation of 4-((S)-1-aminoethyl)-2-fluoro-N-(*trans*-4-hydroxycyclohexyl)benzamide:
To tert-butyl (S)-1-(3-fluoro-4-(*trans*-4-hydroxycyclohexylcarbamoyl)phenyl)ethylcarbamate (33 mg, 0.087 mmol) was added, HCl 4M in Dioxane (2 mL, 8.00 mmol) and MeOH (0.2 ml). The reaction was stirred at room temperature for 1 hour, followed by LCMS. The solvent was concentrated off to residue to give 4-((S)-1-aminoethyl)-2-fluoro-N-(*trans*-4-hydroxycyclohexyl)benzamide in quantitative yield (0.087 mmol) as HCl salt. LCMS *m/z* 281.1 $(M + H)^+$, Rt 0.33 min.

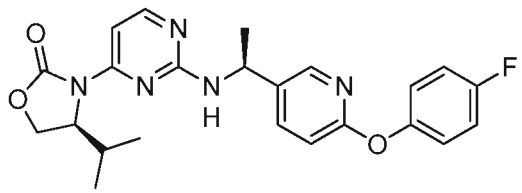
Step 4: Preperation of 2-fluoro-N-(*trans*-4-hydroxycyclohexyl)-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide:
To 4-((S)-1-aminoethyl)-2-fluoro-N-((1r,4S)-4-hydroxycyclohexyl)benzamide (0.024 g, 0.087 mmol) was added (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (0.034 g, 0.139 mmol), DMSO (0.6 ml) and Hunig's Base (0.053 ml, 0.305 mmol). The reaction was heated at 100-105 °C for 16 hours or until done by LCMS. The reaction was let cool, 0.5 ml of DMSO added, filtered, purified by prep LC and lyophilized to give 10.1 mg of 2-fluoro-N-(*trans*-4-hydroxycyclohexyl)-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-

yl)pyrimidin-2-ylamino)ethyl)benzamide as the TFA Salt. LCMS *m/z* 486.2 $(M + H)^+$, Rt 0.57 min.

^{1}H NMR (400 MHz, CD_3OD) δ ppm 8.13 (d, J = 6.7 Hz, 1H), 7.70 (d, J = 6.7 Hz, 1H), 7.64 (t, J = 7.8 Hz, 1H), 7.13 - 7.28 (m, 2H), 5.16 (br. s., 1H), 4.67 (br. s., 1H), 4.37 (d, J = 5.5 Hz, 2H), 3.82 (br. s., 1H), 3.53 (d, J = 3.9 Hz, 1H), 1.97 (dd, J = 5.1, 3.1 Hz, 4H), 1.57 (d, J = 7.0 Hz, 3H), 1.38 (t, J = 8.6 Hz, 4H), 0.50 - 0.88 (m, 6H); HRMS(A) *m/z* 486.2523 $(M + H)^+$.

Example 569

(S)-3-(2-((S)-1-(6-(4-fluorophenoxy)pyridin-3-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one

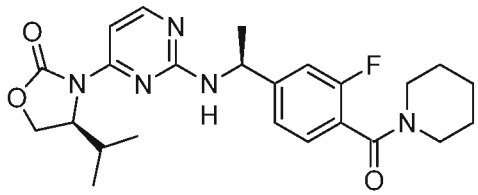


To (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (28 mg, 0.116 mmol) was added (S)-1-(6-(4-fluorophenoxy)pyridin-3-yl)ethanamine (46.7 mg, 0.174 mmol), DMSO (0.6 ml) and Hunig's Base (0.071 ml, 0.406 mmol). The reaction was heated at 105-110 °C for 24 hours or until done by LCMS. The reaction was let cool, 0.5 ml of DMSO was added, filtered, purified by prep LC and lyophilized to give 7.1 mg of (S)-3-(2-((S)-1-(6-(4-fluorophenoxy)pyridin-3-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one as the TFA Salt. LCMS *m/z* 438.2 $(M + H)^+$, Rt 0.82 min.

^{1}H NMR (400 MHz, CD_3OD) δ ppm 8.04 (d, J = 6.3 Hz, 1H), 8.01 (d, J = 2.0 Hz, 1H), 7.73 (dd, J = 8.6, 2.3 Hz, 1H), 7.53 (d, J = 6.3 Hz, 1H), 6.94 - 7.10 (m, 4H), 6.84 (d, J = 8.6 Hz, 1H), 5.05 (d, J = 7.0 Hz, 1H), 4.61 (d, J = 3.9 Hz, 1H), 4.28 (d, J = 5.5 Hz, 2H), 1.49 (d, J = 7.0 Hz, 3H), 0.51 - 0.78 (m, 6H); HRMS(A) *m/z* 438.1946 $(M + H)^+$.

Example 570

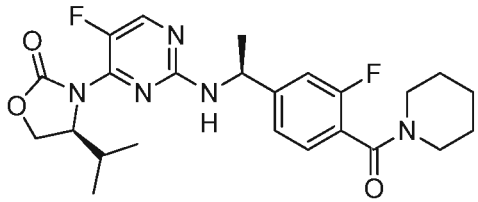
(S)-3-(2-((S)-1-(3-fluoro-4-(piperidine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one



To (S)-(4-(1-aminoethyl)-2-fluorophenyl)(piperidin-1-yl)methanone (0.019 g, 0.076 mmol) was added (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (0.028 g, 0.114 mmol), NMP (0.5 ml) and Hunig's Base (0.033 ml, 0.190 mmol). The reaction was heated at 105-110 °C for 16 hours or until done by LCMS. The reaction was let cool, 0.5 ml of NMP was added, filtered, purified by prep LC and lyophilized to give 4.0 mg of (S)-3-(2-((S)-1-(3-fluoro-4-(piperidine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one as TFA Salt. LCMS *m/z* 456.1 $(M + H)^+$, rt 0.74 min. ^{1}H NMR (400 MHz, CD_3OD) δ ppm 8.13 (d, J = 6.7 Hz, 1H), 7.69 (d, J = 7.0 Hz, 1H), 7.30 - 7.38 (m, 1H), 7.23 - 7.28 (m, 1H), 7.20 (d, J = 10.6 Hz, 1H), 5.18 (br. s., 1H), 4.63 - 4.74 (m, 1H), 4.33 - 4.42 (m, 2H), 3.61 - 3.79 (m, 2H), 1.61 - 1.76 (m, 5H), 1.57 (d, J = 7.0 Hz, 3H), 1.51 (br. s., 2H), 0.77 (br. s., 3H), 0.62 (br. s., 3H); HRMS(A) *m/z* 456.2416 $(M + H)^+$.

Example 571

(S)-3-(5-fluoro-2-((S)-1-(3-fluoro-4-(piperidine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one

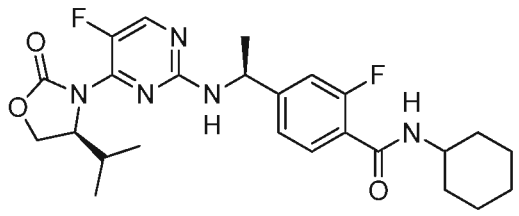


To (S)-(4-(1-aminoethyl)-2-fluorophenyl)(piperidin-1-yl)methanone (0.019 g, 0.076 mmol) was added (S)-3-(2-chloro-5-fluoropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (0.030 g, 0.114 mmol), NMP (0.5 ml) and Hunig's Base (0.033 ml, 0.190 mmol). The reaction was heated at 105-110 °C for 8 hours or until done by LCMS. The reaction was let cool, 0.5 ml of NMP added, filtered, purified by prep LC and lyophilized to give 4.5 mg of (S)-3-(5-fluoro-2-((S)-1-(3-fluoro-4-(piperidine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one as TFA Salt. LCMS *m/z* 474.2 $(M + H)^+$, Rt 0.91 min. ^{1}H NMR (400 MHz, CD_3OD) δ ppm 8.21 (d, J = 2.7 Hz, 1H), 7.22 - 7.33 (m, 2H), 7.17 (d, J = 11.0 Hz, 1H), 4.97 (q, J = 7.0 Hz, 1H), 4.59 (br. s., 1H), 4.47 (t, J = 8.8 Hz, 1H), 4.20

- 4.32 (m, 1H), 3.68 (br. s., 2H), 1.57 - 1.75 (m, 5H), 1.48 (d, J = 7.0 Hz, 5H), 0.69 (br. s., 3H), 0.62 (br. s., 3H) ; HRMS(A) *m/z* 474.2330 $(M + H)^+$.

Example 572

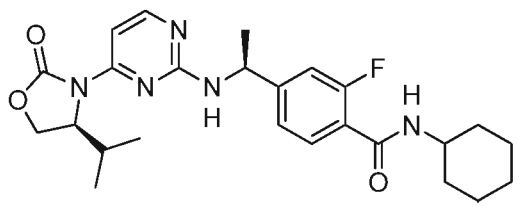
N-cyclohexyl-2-fluoro-4-((S)-1-(5-fluoro-4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide



To (S)-4-(1-aminoethyl)-N-cyclohexyl-2-fluorobenzamide (16 mg, 0.061 mmol) was added (S)-3-(2-chloro-5-fluoropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (31.4 mg, 0.121 mmol), NMP (0.5 ml) and Hunig's Base (0.032 ml, 0.182 mmol). The reaction was heated at 125 °C for 4 hours or until done by LCMS. The reaction was let cool, 0.5 ml of NMP added, filtered, purified by prep LC and lyophilized to give 2.5 mg of N-cyclohexyl-2-fluoro-4-((S)-1-(5-fluoro-4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide as the TFA Salt. LCMS *m/z* 488.2 $(M + H)^+$, Rt 0.99 min. ^{1}H NMR (400 MHz, CD_3OD) δ ppm 8.21 (br. s., 1H), 7.62 (t, J = 7.8 Hz, 1H), 7.24 (dd, J = 8.0, 1.4 Hz, 1H), 7.16 (d, J = 12.1 Hz, 1H), 4.39 - 4.54 (m, 2H), 4.23 (t, J = 7.2 Hz, 1H), 3.83 (t, J = 10.4 Hz, 1H), 1.86 - 1.97 (m, 2H), 1.76 (d, J = 12.9 Hz, 2H), 1.64 (d, J = 12.9 Hz, 1H), 1.48 (d, J = 7.0 Hz, 3H), 1.12 - 1.42 (m, 6H), 0.61 (br. s., 6H); HRMS(A) *m/z* 488.2484 $(M + H)^+$

Example 573

N-cyclohexyl-2-fluoro-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide



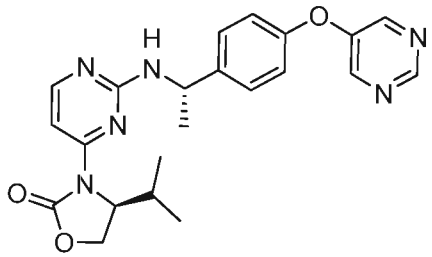
To (S)-4-(1-aminoethyl)-N-cyclohexyl-2-fluorobenzamide (16 mg, 0.061 mmol) was added (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (29.3 mg, 0.121 mmol),

NMP (0.5 ml) and Hunig's Base (0.032 ml, 0.182 mmol). The reaction was heated at 125 °C for 4 hours or until done by LCMS. The reaction was let cool, 0.5 ml of NMP added, filtered, purified by prep LC and lyophilized to give 5.6 mg of N-cyclohexyl-2-fluoro-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide as the TFA Salt. LCMS *m/z* 470.2 (M + H)+, Rt 0.83 min.

^{1}H NMR (400 MHz, CD_3OD) δ ppm 8.12 (br. s., 1H), 7.57 - 7.73 (m, 2H), 7.13 - 7.27 (m, 2H), 5.15 (br. s., 1H), 4.66 (br. s., 1H), 4.36 (d, J = 5.5 Hz, 2H), 3.76 - 3.94 (m, 1H), 1.87 - 1.99 (m, 2H), 1.77 (d, J = 12.9 Hz, 2H), 1.65 (d, J = 13.7 Hz, 1H), 1.57 (d, J = 7.0 Hz, 3H), 1.12 - 1.50 (m, 6H), 0.73 (br. s., 3H), 0.62 (br. s., 3H); HRMS(A) *m/z* 470.2572 (M + H)$^+$

Example 574

(S)-4-Isopropyl-3-(2-(((S)-1-(4-(pyrimidin-5-yloxy)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one



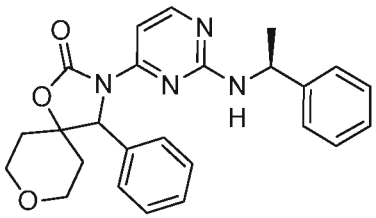
To the solution of (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (43 mg, 0.169 mmol) in NMP (0.7 mL) was added (S)-1-(4-(pyrimidin-5-yloxy)phenyl)ethanamine (41 mg, 0.169 mmol) and DIEA (88 µL, 0.507 mmol). The brown reaction mixture was stirred at 110 °C for 2 days. The reaction mixture was diluted with ethyl acetate and aqueous sodium bicarbonate solution. The separated organic layer was washed with saturated aqueous sodium bicarbonate solution, water and brine. The organic phase was dried over sodium sulfate, filtered off and concentrated under reduced pressure. The residue was purified by reverse phase column chromatography [C-18] to provide (S)-4-isopropyl-3-(2-(((S)-1-(4-(pyrimidin-5-yloxy)phenyl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one (7 mg) as its trifluoroacetic acid salt.

MS *m/z* 421.3 (M + H)$^+$, Rt 0.68 min.

HRMS(A) *m/z* 421.1996 (M + H)$^+$, Rt 1.54 min.

Example 575

4-Phenyl-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)-1,8-dioxa-3-azaspiro[4.5]decan-2-one

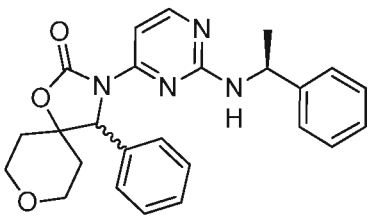


A mixture of crude 3-(2-chloropyrimidin-4-yl)-4-phenyl-1,8-dioxa-3-azaspiro[4.5]decan-2-one (330 mg, 0.954 mmol), (S)-1-phenylethanamine (810 mg, 6.68 mmol), Hunig's base (1.17 mL, 6.68 mmol) in DMA (3.5 mL) was heated in a sealed tube at 80 °C for ~16 hours. The mixture was allowed to cool to room temperature, diluted with DMSO and purified by reverse phase HPLC. Selected fractions were combined and lyophilized, providing 4-phenyl-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)-1,8-dioxa-3-azaspiro[4.5]decan-2-one as its trifluoroacetic acid salt as a white solid. LCMS *m/z* 431.2 $(M + H)^+$, Rt 0.83 min.

The solid was dissolved in ethyl acetate/saturated aqueous $NaHCO_3$ solution. The separated organic layer was washed with saturated aqueous $NaHCO_3$ solution (2x), brine, dried over sodium sulfate, filtered off and concentrated under reduced pressure providing 4-phenyl-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)-1,8-dioxa-3-azaspiro[4.5]decan-2-one (120 mg).

Examples 576 & 577

(S)-4-phenyl-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)-1,8-dioxa-3-azaspiro[4.5]decan-2-one and (R)-4-phenyl-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)-1,8-dioxa-3-azaspiro[4.5]decan-2-one



120 mg of 4-phenyl-3-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)-1,8-dioxa-3-azaspiro[4.5]decan-2-one were dissolved in EtOH (10 mL).

Analytical separation:

Column: CHIRALPAK AD-H (5 um) 100 x 4.6 mm (Daicel Chemical Industries, LTD.).

Solvent: n-heptane : ethyl alcohol = 70 : 30

Flow rate: 1.0 mL/min; detection: UV = 220 nm.

Fraction 1: Retention time: 5.84 min.

Fraction 2: Retention time: 10.18 min.

Preparative separation:

Column: CHIRALPAK AD-prep (10 um) 2 x 25 cm.

Solvent: n-heptane : ethyl alcohol = 70 : 30

Flow rate: 20 mL/min; 530 psi; injection: 4 mL; detection: UV = 210 nm.

Fractions were concentrated under reduce pressure. The residue was dissolved in acetonitrile and filtered through a syringe filter, diluted with water and lyophilized.

Example 576: Peak 1: white powder. Yield: 52.0 mg; de = 99% (UV, 220 nm).

LCMS *m/z* 431.3 $(M + H)^+$, Rt 0.81 min.

Example 577: Peak 2: white powder. Yield: 47.8 mg; de = 99% (UV, 220 nm).

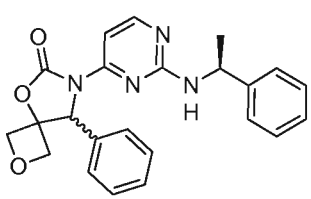
LCMS *m/z* 431.3 $(M + H)^+$, Rt 0.81 min.

Examples 578 and 579

(R)-8-phenyl-7-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)-2,5-dioxa-7-azaspiro[3.4]octan-6-one and

(S)-8-phenyl-7-(2-((S)-1-phenylethylamino)pyrimidin-4-yl)-2,5-dioxa-7-azaspiro[3.4]octan-6-one were prepared using methods similar to those described for the preparation of Example 576 & 577.

Table 23.

Example No.	Structure	Chiral column for separation/ conditions	Chiral column for quality control/ conditions	Retention time
578 (Peak 1)		AD column; 56 mg/ 6 mL EtOH; heptane:EtOH 75:25; 20 mL/min, 400 psi	AD-H column; heptane:EtOH 75:25; 1 mL/min	5.4 min
579 (Peak 2)			AD-H column; heptane:EtOH 75:25; 1 mL/min	8.9 min

The compounds in Table 24 were prepared using methods similar to those described for the preparation of Example 569

Table 24.

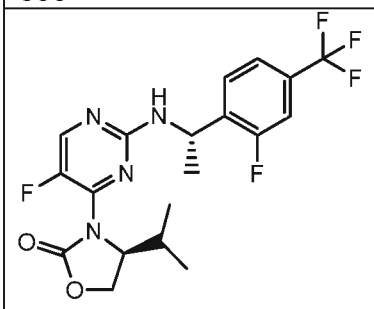
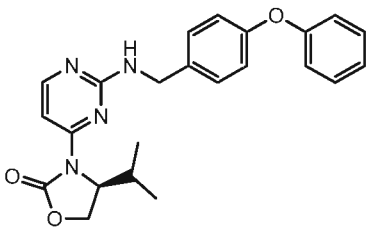
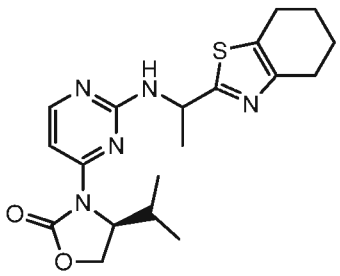
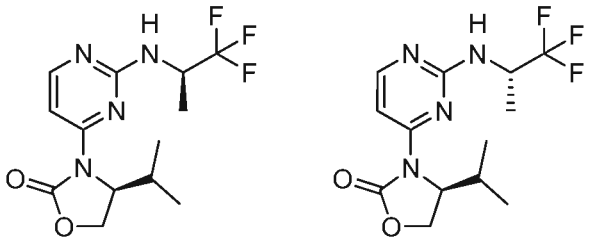
580	581	582
		

Table 25. Chemical name, NMR chemical shifts and LCMS signal for each compound listed in Table 24.

Example: Name	^{1}H NMR (400 MHz) δ ppm	LCMS
580: (S)-3-(5-fluoro-2-((S)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 0.46 - 0.69 (m, 6 H) 0.81 - 0.91 (m, 1 H) 1.53 (d, J=3.00 Hz, 3 H) 4.21 - 4.29 (m, 1 H) 4.43 - 4.53 (m, 2 H) 5.25 (m, J=7.00, 7.00, 7.00 Hz, 1 H) 7.43 (m, J=7.40 Hz, 2 H) 7.52 - 7.59 (m, 1 H) 8.21 - 8.27 (m, 1 H)	HRMS(A) m/z 431.1516 (M + H)+; Rt-2.40 min
581: (S)-4-isopropyl-3-(2-(4-phenoxybenzylamino)pyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 0.63 - 1.00 (m, 7 H) 4.37 - 4.49 (m, 2 H) 4.58 - 4.65 (m, 1 H) 4.66 - 4.78 (m, 2 H) 6.95 - 7.02 (m, 4 H) 7.10 - 7.16 (m, 1 H) 7.32 - 7.40 (m, 4 H) 7.75 (d, J=7.04 Hz, 1 H) 8.16 (d, J=6.65 Hz, 1 H)	HRMS(A) m/z 405.1935 (M + H)+; Rt-2.02 min
582: (4S)-4-isopropyl-3-(2-(1-(4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one		HRMS(A) m/z 388.1814 (M + H)+; Rt-1.82/1.88 min

Examples 583 & 584

(S)-4-isopropyl-3-(2-((R)-1,1,1-trifluoropropan-2-ylamino)pyrimidin-4-yl)oxazolidin-2-one
(S)-4-isopropyl-3-(2-((S)-1,1,1-trifluoropropan-2-ylamino)pyrimidin-4-yl)oxazolidin-2-one



To a solution of (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (40 mg, 0.166 mmol) in 2-butanol was added 1,1,1-trifluoropropan-2-amine (74.9 mg, 0.662 mmol) and para-toluenesulfonic acid monohydrate (74.9 mg, 0.662 mmol). The mixture was heated under argon in a sealed vial for ~7 days at 115 °C. Independently, to a solution of (S)-3-(2-chloropyrimidin-4-yl)-4-isopropyloxazolidin-2-one (100 mg, 0.414 mmol) in 2-butanol was added 1,1,1-trifluoropropan-2-amine (187 mg, 1.655 mmol) and para-toluenesulfonic acid monohydrate (157 mg, 0.828 mmol). The mixture was heated under argon in a sealed vial at 115 °C for ~4 days. The two reaction mixtures was combined and concentrated under reduced pressure. The residue was diluted with DMSO and water (~10 vol.% of DMSO), filtered through a syringe filter and purified by reverse phase HPLC. Selected fractions were collected and lyophilized providing two isomers as white solids as their trifluoroacetic acid salts.

1st Peak 583: Yield: 29.1mg.

^{1}H NMR (400 MHz, CD_3OD) δ ppm 0.90 (d, *J*=7.04 Hz, 3 H) 0.98 - 1.02 (m, 3 H) 1.45 (d, *J*=7.04 Hz, 3 H) 2.59 (dtd, *J*=13.89, 6.95, 6.95, 3.52 Hz, 1 H) 4.43 - 4.47 (m, 2 H) 4.76 - 4.83 (m, 2 H) 7.70 (d, *J*=5.87 Hz, 1 H) 8.20 (d, *J*=6.26 Hz, 1 H)

LCMS *m/z* 319.3 $(M + H)^+$, Rt 0.73 min. HRMS(A) *m/z* 319.1391 (M + H)+, Rt 1.89 min

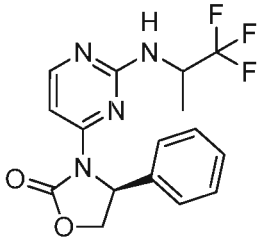
2nd Peak 584: Yield: 38.5 mg.

^{1}H NMR (400 MHz, CD_3OD) δ ppm 0.87 (d, *J*=7.04 Hz, 3 H) 0.98 (d, *J*=7.04 Hz, 3 H) 1.45 (d, *J*=7.04 Hz, 3 H) 2.48 - 2.60 (m, 1 H) 4.40 - 4.49 (m, 2 H) 4.88 - 4.95 (m, 2 H) 7.69 (d, *J*=5.87 Hz, 1 H) 8.20 (d, *J*=6.65 Hz, 1 H)

LCMS *m/z* 319.3 $(M + H)^+$, Rt 0.73 min. HRMS(A) *m/z* 319.1385 (M + H)+, Rt 1.88 min

Example 585

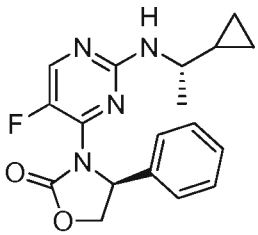
(4S)-4-phenyl-3-(2-(1,1,1-trifluoropropan-2-ylamino)pyrimidin-4-yl)oxazolidin-2-one



A mixture of (S)-3-(2-chloropyrimidin-4-yl)-4-phenyloxazolidin-2-one (40 mg, 0.145 mmol), 1,1,1-trifluoropropan-2-amine (82 mg, 0.725 mmol), Hunig's Base (0.038 mL, 0.218 mmol) in DMSO (0.4 mL) was heated under argon at 115 °C for ~3 days. Then mixture was allowed to cool to room temperature. The mixture was diluted with DMSO and water (~10 vol.% of DMSO), filtered through a syringe filter and purified by reverse phase HPLC. Selected fractions were collected and lyophilized providing (4S)-4-phenyl-3-(2-(1,1,1-trifluoropropan-2-ylamino)pyrimidin-4-yl)oxazolidin-2-one (ratio of two isomers: 7/3) as white solid as its trifluoroacetic acid salt. LCMS *m/z* 353.2 (M + H)+, Rt 0.78 min. HRMS(A) *m/z* 353.1231 (M + H)+, Rt 1.92/1.96 min.

Example 586

(S)-3-(2-((S)-1-cyclopropylethylamino)-5-fluoropyrimidin-4-yl)-4-phenyloxazolidin-2-one



A mixture of (S)-3-(2-chloro-5-fluoropyrimidin-4-yl)-4-phenyloxazolidin-2-one (40 mg, 0.136 mmol), (S)-1-cyclopropylethanamine (34.8 mg, 0.409 mmol), Hunig's Base (0.119 mL, 0.681 mmol) in DMSO (0.4 mL) was heated under argon at 105-115 °C for ~18 hrs (alternative: 120-135 °C for ~90 min). Then mixture was allowed to cool to room temperature. The mixture was diluted with DMSO and water (~10 vol.% of DMSO), filtered through a syringe filter and purified by reverse phase HPLC. Selected fractions were collected and lyophilized providing (S)-3-(2-((S)-1-cyclopropylethylamino)-5-fluoropyrimidin-4-yl)-4-phenyloxazolidin-2-one (26 mg) as a white solid as its trifluoroacetic acid salt.

^{1}H NMR (400 MHz, CD_3OD) δ ppm -0.14 - -0.05 (m, 1 H) 0.01 - 0.08 (m, 1 H) 0.23 - 0.31 (m, 1 H) 0.36 - 0.44 (m, 1 H) 0.78 - 0.86 (m, 1 H) 1.19 (d, J=6.65 Hz, 3 H) 3.05 - 3.14 (m,

1 H) 4.25 - 4.32 (m, 1 H) 4.89 - 4.90 (m, 1 H) 5.77 (t, J=8.61 Hz, 1 H) 7.32 - 7.39 (m, 5 H) 8.15 (d, J=3.52 Hz, 1 H).

LCMS *m/z* 343.1 $(M + H)^+$, Rt 0.88 min. HRMS(A) *m/z* 343.1577 $(M + H)^+$, Rt 2.09 min

The compounds in Table 26 were prepared using methods similar to those described for the preparation of Example **586.**

Table 26.

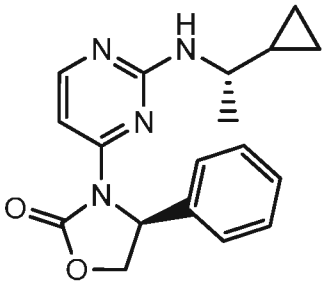
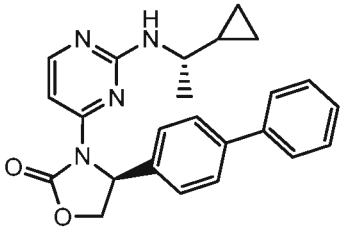
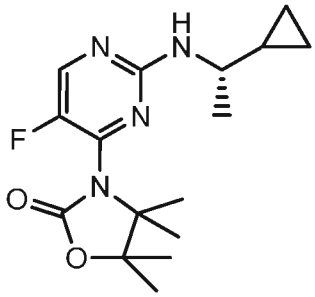
587	588	589
		

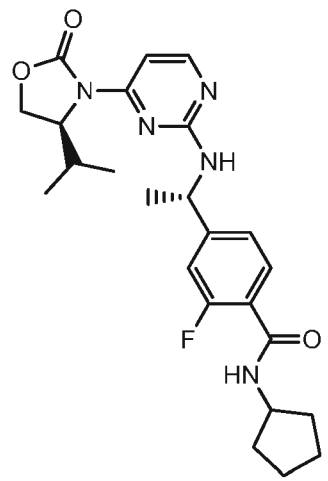
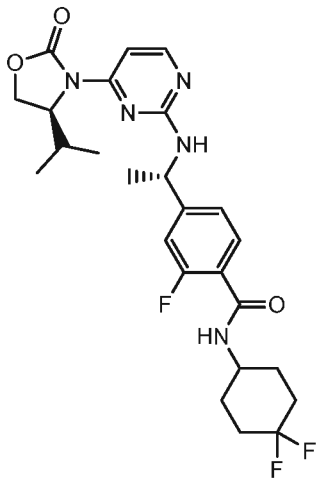
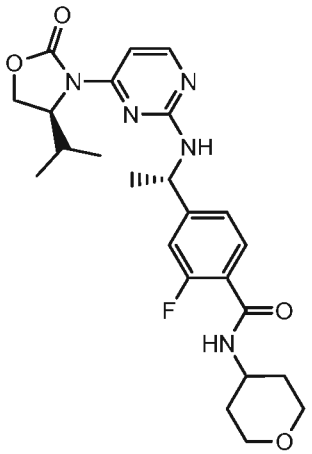
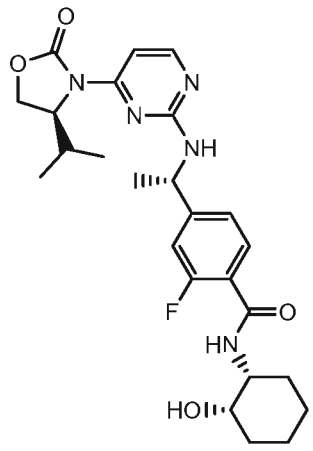
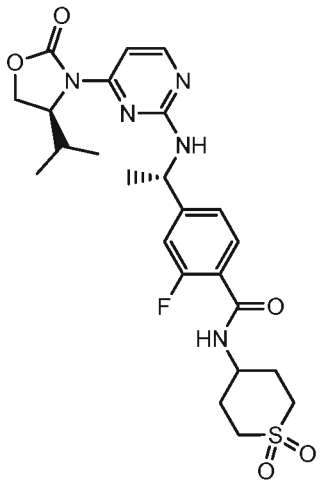
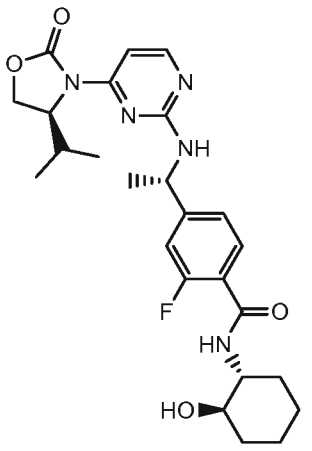
Table 27. Chemical name, NMR chemical shifts and LCMS signal for each compound listed in Table 26.

Example: Name	^{1}H NMR (400 MHz) δ ppm	LCMS
587: (S)-3-(2-((S)-1-cyclopropylethylamino)pyrimidin-4-yl)-4-phenyloxazolidin-2-one	(CD_3OD) -0.55 - -0.27 (m, 1 H), -0.01 (m, J=9.00, 4.30 Hz, 1 H), 0.12 - 0.32 (m, 1 H) 0.35 - 0.50 (m, 1 H) 0.64 - 0.93 (m, 1 H) 1.28 (d, J=1.00 Hz, 3 H) 2.77 - 3.00 (m, 1 H) 4.26 (dd, J=1.00 Hz, 1 H) 4.76 - 4.95 (m, 1-2 H; overlay with solvent) 5.75 (dd, J=1.00 Hz, 1 H) 7.17 - 7.52 (m, 5 H) 7.78 (d, J=1.00 Hz, 1 H) 8.08 (d, J=7.04 Hz, 1 H)	MS m/z 325.2 (M + H)+; Rt-0.77 min. HRMS(A) m/z 325.1664 (M + H)+; Rt-1.53 min
588: (S)-4-(biphenyl-4-yl)-3-(2-((S)-1-cyclopropylethylamino)pyrimidin-4-yl)oxazolidin-2-one	(CD_3OD) 0.01 (m, J=4.30 Hz, 1 H) 0.14 - 0.26 (m, 1 H) 0.33 - 0.45 (m, 1 H) 0.73 - 0.85 (m, 1 H) 1.28 (d, J=6.65 Hz, 3 H) 2.91 - 3.02 (m, 1 H) 4.32 (dd, J=9.00, 4.30 Hz, 1 H) 4.89 - 4.96 (m, 1 H) 5.81 (dd, J=9.00, 4.30 Hz, 1 H) 7.34 - 7.42 (m, 3 H) 7.45 (t, J=7.63 Hz, 2 H) 7.59 - 7.64 (m, 2 H) 7.67 (m, J=8.20 Hz, 2 H) 7.79 (d, J=7.04 Hz, 1 H) 8.10 (d, J=7.04 Hz, 1 H)	MS m/z 401.3 (M + H)+; Rt-0.89 min. HRMS(A) m/z 401.1988 (M + H)+; Rt-1.89 min
589: (S)-3-(2-(1-cyclopropylethylamino)-5-fluoropyrimidin-4-yl)-	(CD_3OD) 0.17 - 0.24 (m, 1 H) 0.31 (dq, J=9.34, 4.71 Hz, 1 H) 0.41 - 0.55 (m, 2 H) 0.93 - 1.04 (m, 1 H) 1.26 (d, J=6.65 Hz, 3	HRMS(A) *m/z* 464.1125

4,4,5,5-tetramethyloxazolidin-2-one	H) 1.42 (s, 6 H) 1.49 (s, 6 H) 3.34 - 3.42 (m, 1 H) 8.17 (d, J=3.13 Hz, 1 H) MS m/z 323.6 (M + H)+; Rt-0.89 min. HRMS m/z 323.1891 (M + H)+; Rt-2.10 min	$(M + H)^+$, Rt 2.28 min

The compounds in Table 28 were prepared using methods similar to those described for the preparation of Example 568

Table 28.

590	591	592
		
593	594	595
		
596	597	598

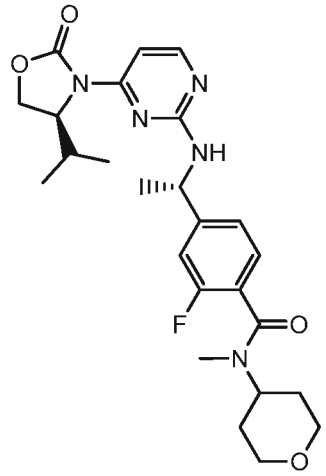
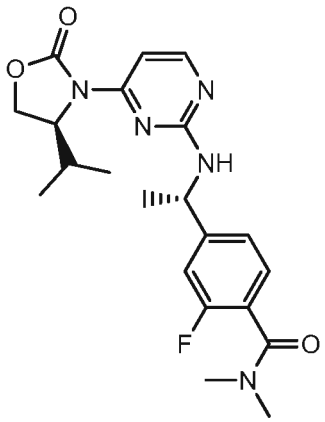
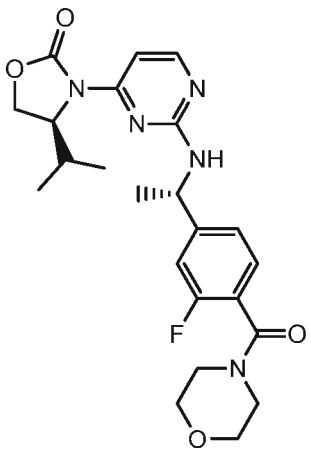
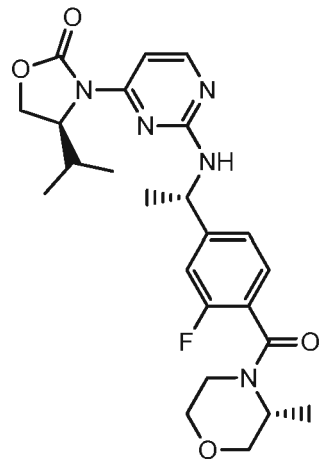
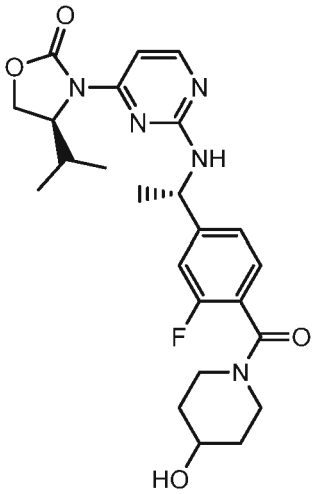
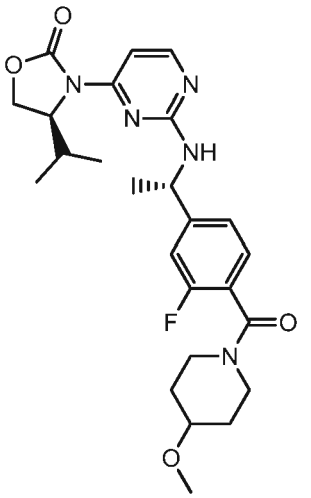
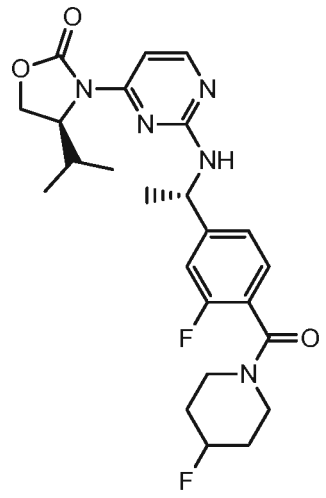
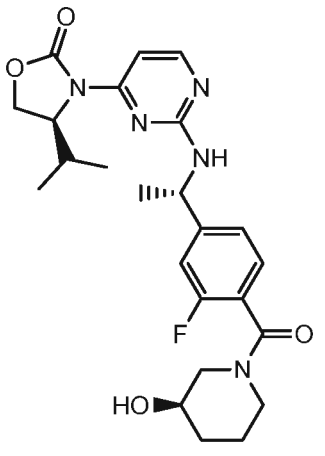
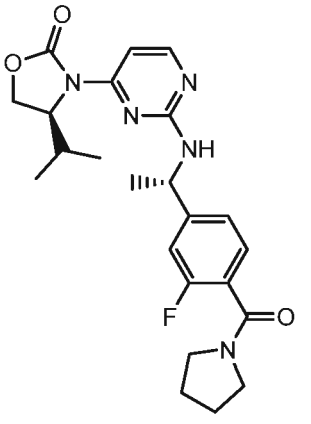
		
599	600	601
		
602	603	604
		

Table 29. Chemical name, NMR chemical shifts and LCMS signal for each compound listed in Table 28.

Example: Name	^{1}H NMR (400 MHz) δ ppm	LCMS
590: N-cyclopentyl-2-fluoro-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide	(CD_3OD) 8.14 (d, J = 6.3 Hz, 1H), 7.72 (d, J = 7.0 Hz, 1H), 7.64 (t, J = 7.6 Hz, 1H), 7.13 - 7.31 (m, 2H), 5.17 (br. s., 1H), 4.67 (br. s., 1H), 4.34 - 4.41 (m, 2H), 4.24 - 4.33 (m, 1H), 1.99 (dt, J = 11.7, 5.9 Hz, 2H), 1.73 (d, J = 6.7 Hz, 2H), 1.49 - 1.66 (m, 8H), 0.74 (br. s., 3H), 0.61 (br. s., 3H)	HRMS(A) m/z (M + H)+ 456.2422
591: N-(4,4-difluorocyclohexyl)-2-fluoro-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide	(CD_3OD) 8.14 (d, J = 6.3 Hz, 1H), 7.70 (d, J = 7.0 Hz, 1H), 7.64 (t, J = 7.8 Hz, 1H), 7.12 - 7.32 (m, 2H), 5.16 (br. s., 1H), 4.67 (br. s., 1H), 4.37 (d, J = 5.9 Hz, 2H), 4.00 (t, J = 10.0 Hz, 1H), 1.82 - 2.13 (m, 6H), 1.61 - 1.77 (m, 2H), 1.57 (d, J = 7.0 Hz, 3H), 0.73 (br. s., 3H), 0.61 (br. s., 3H)	HRMS(A) m/z (M + H)+ 506.2388
592: 2-fluoro-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)-N-(tetrahydro-2H-pyran-4-yl)benzamide	(CD_3OD) 8.13 (d, J = 5.9 Hz, 1H), 7.58 - 7.71 (m, 2H), 7.13 - 7.29 (m, 2H), 5.16 (br. s., 1H), 4.67 (br. s., 1H), 4.36 (d, J = 5.5 Hz, 2H), 4.01 - 4.16 (m, 1H), 3.94 (d, J = 11.3 Hz, 2H), 3.50 (td, J = 11.7, 2.0 Hz, 2H), 1.82 - 1.94 (m, 2H), 1.59 - 1.69 (m, 2H), 1.57 (d, J = 7.0 Hz, 3H), 0.73 (br. s., 3H), 0.61 (br. s., 3H)	HRMS(A) m/z (M + H)+ 472.2366
593: 2-fluoro-N-((1R,2S)-2-hydroxycyclohexyl)-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide	(CD_3OD) 8.14 (d, J = 6.3 Hz, 1H), 7.83 (t, J = 7.8 Hz, 1H), 7.69 (d, J = 7.0 Hz, 1H), 7.14 - 7.36 (m, 2H), 5.15 (d, J = 6.3 Hz, 1H), 4.65 (br. s., 1H), 4.36 (d, J = 5.5 Hz, 2H), 3.96 - 4.05 (m, 1H), 3.94 (d, J = 2.3 Hz, 1H), 1.79 (dd, J = 10.4, 4.5 Hz, 1H), 1.69 (d, J = 5.9 Hz, 4H), 1.54 - 1.64 (m, 5H), 1.28 - 1.48 (m, 2H), 0.70 (br. s., 3H), 0.60 (br. s., 3H)	HRMS(A) m/z (M + H)+ 486.2526
594: N-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-2-fluoro-4-((S)-1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)ethyl)benzamide	(CD_3OD) 8.14 (d, J = 6.3 Hz, 1H), 7.69 (d, J = 7.0 Hz, 1H), 7.64 (t, J = 7.6 Hz, 1H), 7.15 - 7.31 (m, 2H), 5.16 (br. s., 1H), 4.67 (br. s., 1H), 4.36 (d, J = 5.9 Hz, 2H), 4.13 - 4.27 (m, 1H), 3.08 (d, J = 13.7 Hz, 2H), 2.25 - 2.36 (m, 2H), 2.07 - 2.24 (m, 2H), 1.57 (d, J = 7.0 Hz, 3H), 0.73 (br. s., 3H), 0.61 (br. s., 3H)	HRMS(A) m/z (M + H)+ 520.203
595: 2-fluoro-N-((1R,2R)-2-hydroxycyclohexyl)-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide	(CD_3OD) 8.13 (d, J = 6.3 Hz, 1H), 7.63 - 7.78 (m, 2H), 7.14 - 7.30 (m, 2H), 5.15 (br. s., 1H), 4.67 (br. s., 1H), 4.36 (d, J = 5.5 Hz, 2H), 3.67 - 3.83 (m, 1H), 3.38 - 3.51 (m, 1H), 2.01 (d, J = 9.0 Hz, 2H), 1.64 - 1.81 (m, 3H), 1.57 (d, J = 7.0 Hz, 3H), 1.17 - 1.46 (m, 4H), 0.74 (br. s., 3H), 0.61 (br. s., 3H)	HRMS(A) m/z (M + H)+ 486.2521
596: 2-fluoro-4-((S)-1-(4-	(CD_3OD) 8.14 (d, J = 6.7 Hz, 1H), 7.76 (d,	HRMS(A)

((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)-N-methyl-N-(tetrahydro-2H-pyran-4-yl)benzamide	J = 7.4 Hz, 1H), 7.32 - 7.42 (m, 1H), 7.17 - 7.31 (m, 2H), 5.22 (br. s., 1H), 4.60 - 4.76 (m, 2H), 4.33 - 4.44 (m, 2H), 4.02 (dd, J = 11.3, 4.3 Hz, 1H), 3.91 (d, J = 8.6 Hz, 1H), 3.45 - 3.65 (m, 2H), 3.07 - 3.21 (m, 1H), 2.99 (s, 1H), 2.80 (s, 2H), 1.81 - 2.05 (m, 3H), 1.52 - 1.71 (m, 5H), 0.78 (br. s., 3H), 0.63 (br. s., 3H)	m/z (M + H)+ 486.2528
597: 2-fluoro-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)-N,N-dimethylbenzamide	(CD_3OD) 8.14 (d, J = 7.0 Hz, 1H), 7.75 (d, J = 7.0 Hz, 1H), 7.32 - 7.43 (m, 1H), 7.13 - 7.31 (m, 2H), 5.20 (br. s., 1H), 4.70 (br. s., 1H), 4.33 - 4.45 (m, 2H), 3.09 (s, 3H), 2.92 (d, J = 0.8 Hz, 3H), 1.76 (br. s., 1H), 1.59 (d, J = 7.0 Hz, 3H), 0.78 (br. s., 3H), 0.62 (br. s., 3H)	HRMS(A) m/z (M + H)+ 416.2106
598: (S)-3-(2-((S)-1-(3-fluoro-4-(morpholine-4-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 8.14 (d, J = 6.7 Hz, 1H), 7.73 (d, J = 6.7 Hz, 1H), 7.35 - 7.43 (m, 1H), 7.28 (d, J = 7.8 Hz, 1H), 7.22 (d, J = 10.6 Hz, 1H), 5.18 (br. s., 1H), 4.69 (br. s., 1H), 4.30 - 4.42 (m, 2H), 3.73 (d, J = 3.1 Hz, 4H), 3.59 (t, J = 4.7 Hz, 2H), 1.58 (d, J = 7.0 Hz, 3H), 0.76 (br. s., 3H), 0.62 (br. s., 3H)	HRMS(A) m/z (M + H)+ 458.2209
599: (S)-3-(2-((S)-1-(3-fluoro-4-((R)-3-methylmorpholine-4-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 8.14 (d, J = 6.7 Hz, 1H), 7.76 (d, J = 7.0 Hz, 1H), 7.36 (d, J = 6.7 Hz, 1H), 7.14 - 7.31 (m, 2H), 5.20 (br. s., 1H), 4.70 (br. s., 1H), 4.65 (br. s., 1H), 4.34 - 4.45 (m, 2H), 4.29 (d, J = 13.3 Hz, 1H), 3.96 (d, J = 10.6 Hz, 1H), 3.75 (d, J = 11.3 Hz, 1H), 3.51 - 3.67 (m, 2H), 3.43 - 3.51 (m, 1H), 3.07 - 3.19 (m, 1H), 1.76 (br. s., 1H), 1.59 (d, J = 7.0 Hz, 3H), 1.36 (d, J = 6.7 Hz, 2H), 1.28 (br. s., 1H), 0.77 (br. s., 3H), 0.62 (br. s., 3H)	HRMS(A) m/z (M + H)+ 472.2366
600: (S)-3-(2-((S)-1-(3-fluoro-4-(4-hydroxypiperidine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 8.14 (d, J = 6.7 Hz, 1H), 7.73 (d, J = 7.0 Hz, 1H), 7.31 - 7.40 (m, 1H), 7.16 - 7.29 (m, 2H), 5.18 (br. s., 1H), 4.70 (br. s., 1H), 4.31 - 4.45 (m, 2H), 4.16 (dd, J = 12.9, 5.5 Hz, 1H), 3.87 (br. s., 1H), 3.48 (d, J = 14.1 Hz, 1H), 3.35 (d, J = 3.5 Hz, 1H), 3.05 - 3.22 (m, 1H), 1.85 - 1.98 (m, 1H), 1.70 - 1.83 (m, 2H), 1.58 (d, J = 7.0 Hz, 3H), 1.49 - 1.55 (m, 1H), 1.43 (br. s., 1H), 0.76 (br. s., 3H), 0.62 (br. s., 3H)	HRMS(A) m/z (M + H)+ 472.2369
601: (S)-3-(2-((S)-1-(3-fluoro-4-(4-methoxypiperidine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 8.13 (d, J = 6.7 Hz, 1H), 7.70 (d, J = 6.7 Hz, 1H), 7.31 - 7.41 (m, 1H), 7.26 (d, J = 7.8 Hz, 1H), 7.21 (d, J = 10.6 Hz, 1H), 5.17 (br. s., 1H), 4.69 (br. s., 1H), 4.33 - 4.42 (m, 2H), 3.98 (dd, J = 10.8, 6.5 Hz, 1H), 3.40 - 3.60 (m, 3H), 3.34 (s, 3H), 3.18 (d, J = 8.6 Hz, 1H), 1.88 - 2.03 (m, 1H), 1.79 (br. s., 1H), 1.62 (br. s., 1H), 1.58 (d, J = 7.0 Hz, 3H), 1.49 (br. s., 1H), 0.76 (br. s., 3H), 0.62 (br. s., 3H)	HRMS(A) m/z (M + H)+ 486.2523
602: (S)-3-(2-((S)-1-(3-fluoro-4-(4-	(CD_3OD) 8.14 (d, J = 6.7 Hz, 1H), 7.73 (d, J = 7.0 Hz, 1H), 7.34 - 7.44 (m, 1H), 7.16 -	HRMS(A) m/z (M +

fluoropiperidine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	7.31 (m, 2H), 5.18 (br. s., 1H), 4.93 (br. s., 1H), 4.70 (br. s., 1H), 4.29 - 4.43 (m, 2H), 3.91 (d, J = 11.3 Hz, 1H), 3.70 (br. s., 1H), 3.40 - 3.53 (m, 1H), 1.93 - 2.06 (m, 1H), 1.83 - 1.93 (m, 2H), 1.77 (dd, J = 10.2, 4.7 Hz, 2H), 1.58 (d, J = 7.0 Hz, 3H), 0.76 (br. s., 3H), 0.62 (br. s., 3H)	H)+ 474.2324
603: (S)-3-(2-((S)-1-(3-fluoro-4-((R)-3-hydroxypiperidine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 8.13 (d, J = 6.7 Hz, 1H), 7.72 (d, J = 7.0 Hz, 1H), 7.36 (t, J = 7.4 Hz, 1H), 7.14 - 7.30 (m, 2H), 5.19 (br. s., 1H), 4.70 (br. s., 1H), 4.30 - 4.44 (m, 2H), 3.71 (br. s., 1H), 3.38 - 3.52 (m, 1H), 3.08 - 3.19 (m, 1H), 3.02 (br. s., 1H), 1.96 (br. s, 1H), 1.87 (br. s., 1H), 1.66 - 1.81 (m, 1H), 1.49 - 1.62 (m, 5H), 1.43 (br. s., 1H), 0.78 (br. s., 3H), 0.63 (br. s., 3H)	HRMS(A) m/z (M + H)+ 472.2362
604: (S)-3-(2-((S)-1-(3-fluoro-4-(pyrrolidine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one	(CD_3OD) 8.13 (d, J = 6.3 Hz, 1H), 7.71 (d, J = 7.0 Hz, 1H), 7.34 - 7.43 (m, 1H), 7.14 - 7.30 (m, 2H), 5.18 (br. s., 1H), 4.70 (br. s., 1H), 4.28 - 4.43 (m, 2H), 3.57 (t, J = 6.8 Hz, 2H), 1.93 - 2.07 (m, 2H), 1.83 - 1.93 (m, 2H), 1.58 (d, J = 7.0 Hz, 3H), 0.77 (br. s., 3H), 0.63 (br. s., 3H)	HRMS(A) m/z (M + H)+ 442.2263

Biological Data

Mutant IDH1 biochemical assay: LC-MS detection of 2-HG.

Mutant IDH1 R132H catalytic activity was monitored using the quantitative liquid chromatography/mass spectrometry (LC-MS) detection of 2-HG, a product of the NADPH-dependent alpha-KG reduction reaction.

More specifically, the biochemical reactions were performed at room temperature in 384-well Greiner flat-bottom plates (Costar, Cat. No. 781201) using a final reaction volume of 30 μL and the following assay buffer conditions: 50 mM HEPES pH 7.4, 10 mM $MgCl_2$, 50 mM KCl, 1 mM DTT, 0.02% BSA, 5 uM NADPH and 100 uM alpha-KG.

The final reaction mixture contained 3.3% DMSO and inhibitors with concentrations ranging 0.02 – 50 μM. The IDH1 enzyme was used at a final concentration of 0.25 nM. Following 45 minutes incubation, the reaction mixtures were quenched by the addition of 10 μL of 16% formic acid containing 800 nM of 5-carbon labeled ^{13}C-2-HG). The protein was then precipitated by the addition of 2.5 volumes of acetonitrile followed by centrifugation (3000 x g, 20 minutes). The concentration of 2-HG in the resulting supernatants was measured by LC-MS (see below).

LC-MS method. Reaction mixture supernatants were submitted to chromatographic separation on a BiobasicAX column (2.1 mm x 20 mm, 5 μm particle,

Thermo Scientific Inc.). The chromatographic mobile phases were A) 25 mM ammonium biocarbonate and B) acetonitrile (0.1% ammonium hydroxide). Nicotinamide was eluted at 1 ml/min using a 85-5% B gradient over 0.9 minutes (Agilent 1200SL LC system, Thermofisher LX-4 autosampler) and analyzed by multiple reaction monitoring (MRM) on a API4000 QTrap mass spectrometer (ABSciex, Framingham, MA) in the positive electrospray ionization (ESI+) mode. The mass transition for 2-HG and ^{13}C-2-HG were 147→129 and 152→134, respectively. The relative responses (2-HG/^{13}C-2-HG) were measured at varied inhibitor concentrations and used to calculate inhibitory IC50 values (normalized IC50 regression curves).

R132 protein expression and purification.

IDH1 R132H was cloned into the pET47b vector using the restriction sites XmaI/XhoI which yields an in frame, N-terminal His_6 site cleavable with Prescission protease. This plasmid was transformed into Rosetta™ 2(DE3) (Novagen) cells. In shake flasks, 8L of cells were grown in Terrific Broth (Teknova) (plus kanamycin 50µg/mL and chloramphenicol 34µg/mL) at 37°C to an OD_{600} of 0.8 and protein expression was induced by addition of IPTG to a concentration of 0.20mM. The cells were subsequently grown for 18 hours at 18°C.

His_6-IDH1 (R132H) Uncut protein

MAHHHHHHSAALEVLFQGPGMSKKISGGSVVEMQGDEMTRIIWELIKEKLIFPYVELDL
HSYDLGIENRDATNDQVTKDAAEAIKKHNVGVKCATITPDEKRVEEFKLKQMWKSPNGT
IRNILGGTVFREAIICKNIPRLVSGWVKPIIIGHHAYGDQYRATDFVVPGPGKVEITYTPSD
GTQKVTYLVHNFEEGGGVAMGMYNQDKSIEDFAHSSFQMALSKGWPLYLSTKNTILKK
YDGRFKDIFQEIYDKQYKSQFEAQKIWYEHRLIDDMVAQAMKSEGGFIWACKNYDGDV
QSDSVAQGYGSLGMMTSVLVCPDGKTVEAEAAHGTVTRHYRMYQKGQETSTNPIASIF
AWTRGLAHRAKLDNNKELAFFANALEEVSIETIEAGFMTKDLAACIKGLPNVQRSDYLNT
FEFMDKLGENLKIKLAQAKL (stop) (SEQ ID NO: 1)

IDH1 (R132H) Prescission Cut Protein (N-term gpg is cloning artifact)

*GPG*MSKKISGGSVVEMQGDEMTRIIWELIKEKLIFPYVELDLHSYDLGIENRDATNDQVT
KDAAEAIKKHNVGVKCATITPDEKRVEEFKLKQMWKSPNGTIRNILGGTVFREAIICKNIP
RLVSGWVKPIIIGHHAYGDQYRATDFVVPGPGKVEITYTPSDGTQKVTYLVHNFEEGGG
VAMGMYNQDKSIEDFAHSSFQMALSKGWPLYLSTKNTILKKYDGRFKDIFQEIYDKQYK
SQFEAQKIWYEHRLIDDMVAQAMKSEGGFIWACKNYDGDVQSDSVAQGYGSLGMMTS
VLVCPDGKTVEAEAAHGTVTRHYRMYQKGQETSTNPIASIFAWTRGLAHRAKLDNNKE

LAFFANALEEVSIETIEAGFMTKDLAACIKGLPNVQRSDYLNTFEFMDKLGENLKIKLAQA KL (stop) (SEQ ID NO: 2)

Purification

The cells were homogenized in Lysis Buffer with protease inhibitors (cOmplete EDTA-free protease inhibitor tablets (Roche), 1 tablet per 50mL of buffer), DNAse, and to 200 μM PMSF and lysed in a Microfluidizer. After lysis, Triton X-100 was added to 0.1% and stirred at 4ºC for 30 minutes.

The cleared lysate was loaded onto 2 x 5mL HisTrap FF crude columns (GE), washed extensively with Lysis Buffer until the A_{280} stabilized and eluted with Ni Elution Buffer. Peak eluted fractions were concentrated to 30mL, EDTA was added to 1mM and GST-Prescission protease was added to 3U/100μg of protein. The sample was dialyzed against 2L Dialysis Buffer I (MWCO 50kDa) for 6 hours at 4°C then dialyzed against 2L of Dialysis Buffer II for at least 6 more hours. GST-Prescission cleaved sample was rocked with Glutathione Agarose Beads, spun down and then the supernatant was loaded through a 5mL HisTrap HP column and the flow through was collected.

Flow through was then diluted with ice cold 20mM Tris pH 7.4 and 1mM TCEP until the conductivity dropped to less than 5 mS/cm (a roughly three fold dilution). This sample was then flowed through a HiTrap Q column and the flow through was concentrated to 10mL and loaded onto an equilibrated 26/60 Superdex 200 column using SEC Buffer as the mobile phase. Peak fractions were collected, concentrated and aliquoted.

Lysis Buffer: 50mM Tris pH=7.4, 500mM NaCl, 20mM Imidazole, and 1mM TCEP

Ni Elution Buffer: 50mM Tris pH=7.4, 150mM NaCl, 200mM Imidazole, and 1mM TCEP

Dialysis Buffer I: 20mM Tris pH=7.4, 150mM NaCl, 1mM TCEP, and 50mM Imidazole

Dialysis Buffer II:20mM Tris pH=7.4, 150mM NaCl, and 1mM TCEP

SEC Buffer: 20mM Tris pH=7.4, 150mM NaCl, and 1mM TCEP

The results of the mutant IDH1 biochemical assay (mIDH R132H) are given in Table 30. Some of the examples were run in the assay multiple times and therefore the IC_{50} values are expressed as a range of activity.

Fluorescence biochemical assay

The IDH1 (R132H) mutant catalyzes the reduced form of NADP+ (NADPH) and α-ketoglutarate (α-KG) to form nicotinamide adenine dinucleotide phosphate (NADP+) and R (-)-2-hydroxyglutarate (2HG). The reaction can be monitored kinetically by following the oxidation of NADPH to NADP+ which is measured using fluorescence, excitation at 355 nm and emission at 530 nm. Reactions were monitored using the Perkin-Elmer Envision, Model 2101. More specifically, the biochemical reactions were performed at room temperature in 384-well Greiner flat-bottom plates (Cat. No. 781076) using a final reaction volume of 20 μL and the following assay buffer conditions: 50 mM HEPES pH 7.5, 10 mM $MgCl_2$, 1 mM DTT, 0.02% BSA, 0.02% Tween-20, 10 μM NADPH and 100 μM α-KG. The final reaction mixture contained 2.5% DMSO and test compounds with concentrations ranging 0.0000008 – 25 μM. The IDH1 (R132H) enzyme was used at a final concentration of 10 nM. Curve fitting for dose response IC50 determinations was done in the Helios module of the software package DAVID. The 4-parameter logistic model was used: $y = min + ((max - min) / 1 + (x / IC_{50})^{slope})$

Table 30. Results of the LC-MS and fluorescence biochemical assays.

Example Number	**LC-MS biochemical assay IC_{50} (μM)**	**Fluorescence biochemical assay IC50 (μM)**
1	0.084 – 0.236	
2	>50	
3	0.086 – 0.575	0.091-0.501
4	4.612	
5	0.410-0.600	
6	12.175	
7	2.527	
8	13.011	
9	6.444	
10	0.355-0.419	
11	0.770 – 4.552	
12	1.990 – 2.391	9.55
13	18.344 – 29.100	
14	2.333 – 2.814	

15	5.383	
16	>50	
17	7.625	
18	>50	
19	>50	
20	>50	
21	4.169	
22	19.671	
23	0.502 –0.591	
24	3.564	
25	18.182 – >50	
26	>50	
27	2.486 – 2.730	
28	4.427 – 4.625	
29	4.630 – 11.566	
30	1.072	
31	1.721	
32	9.797	
33	3.483	
34	7.588	
35	0.222 – 0.273	
36	17.576	
37	4.595	
38	>50	
39	8.806	
40	20.34	
41	0.291 – 0.581	
42	0.584	
43	7.686	
44	0.125	
45	>50	
46	0.234	
47	7.481	
48	2.090 – 2.601	1.91
49	2.803	
50	0.076 – 0.100	

51	19.457	
52	23.847	
53	3.852	
54	0.141	
55	3.494	
56	9.502	
57	1.393-3.153	7.58
58	>50	
59	0.575	
60	0.052	0.094
61	12.729	
62	0.117 – 0.178	
63	0.085 – 0.124	
64	6.79	
65	0.25	
66	0.073	
67	5.342	
68	6.302	
69	0.127 – 0.390	
70	0.195 – 0.230	
71	20.503	
72	37.361	
73	0.316	
74	2.569	
75	1.338	4.27
76	8.008	
77	11.26	
78	28.611	
79	0.09	
80	0.679	
81	0.103	
82	0.163 – 0.217	
83	0.238 – 0.462	
84	0.075	
85	1.061	17.9
86	9.767	

87	0.126	0.245
88	0.148 – 0.344	
89	0.203	0.308
90	0.272	0.275
91	2.875	
92	0.211 – 0.544	0.598
93	0.405 – 0.905	
94	4.487	
95	0.655	0.571
96	>50	
97	0.195	0.166
98	0.628	
99	0.184	
100	0.169	
101	2.382	
102	0.401	
103	3.184	
104	0.207	
105	0.352	0.352
106	1.918	
107	3.445	
108	>50	
109	0.542	0.939
110	0.188	0.284
111	0.125	
112	7.768	
113	1.925	
114	0.697	1.14
115	0.092	0.126
116	2.038	
117	0.163 – 0.217	
118	1.302 – 2.152	
119	0.117	0.149
120	0.258-0.847	
121	0.081-0.448	
122	0.157-0.379	

123	0.112	0.162
124	0.081 – 0.298	0.791
125	1.012	
126	0.118	
127	0.158	0.215
128	0.565	
129	0.467	
130	0.549 – 0.615	
131	14.319	
132	31.016	
133	7.115	
134	3.102	
135	11.6	
136	6.455	
137	3.14	
138	1.061	
139	1.252	2.5
140	0.089	0.114-0.181
141	0.095	
142	0.390 – 0.512	
143	>50	
144	>50	
145	6.807	
146	11.362	
147	6.445	
148	3.544	
149	0.647	
150	0.53	0.538
151	1.363	
152	0.385	0.598
153	0.759	0.582
154	0.049	0.091
155	0.04	
156	0.232	0.248
157	>50	
158	0.873	1.41

159	0.287	
160	6.078	
161	6.502	
162	0.009-0.035	0.020-0.043
163	0.149	
164	0.067	0.0339
165	0.183	0.143
166	0.637	1.56
167	0.254	
168	0.102	
169	0.195	
170	1.083	
171	6.161	
172	0.245 – 0.274	
173	2.908	
174	0.056 – 0.118	0.283
175	8.156	
176	0.125	0.138
177	4.333	
178	0.097	0.0687
179	5.973	
180	0.194	
181	10.232	
182	0.309-0.370	
183	36.818	
184	0.696	
185	6.066	
186	0.04	
187	3.899	
188	0.089	0.17
189	0.117	
190	2.134	
191	6.969	
192	0.221	0.294
193	0.097	
194	4.333	

195	5.748	
196	0.083	
197	15.05	
198	0.173	0.179
199	2.435	
200	0.08	0.0665
201	0.927	
202	0.025	0.0541
203	1.856	
204	0.062	0.0955
205	0.199	0.219
206	1.458	0.81
207	0.069	0.0169
208	0.085	0.108-0.183
209	0.088	0.0881
210	0.576	0.343
211		0.439
212	0.132	0.024
213	2.913	
214	0.298	0.791
215	0.390	0.419
216	0.031	0.0206
217	0.177 - 0.206	0.079-0.146
218	1.373	0.625
219	0.613	
220	0.529	0.247
221	0.098	0.0476
222	0.505	0.296
223	0.293	0.14
224	<0.022	0.0166
225	0.026	0.0173
226	0.114	0.0832
227	0.065	0.0339
228	0.067	0.0463
229	0.113	0.0662
230	0.072	0.0415

231	0.327	0.242
232	0.251	0.755
233	0.147	0.0684
234	> 50	> 25
235	0.039	0.0141
236	0.372	0.338
237	0.877	0.219
238		9.8
239	0.038	0.073
240	0.030	0.0506
241	0.155	0.213
242	0.048	0.242
243	0.260 - 0.914	1.21-1.6
244	0.863	0.774
245	0.184	0.103
246	0.497 - 0.589	0.236-0.316
247	1.373	1.79
248	0.687	0.842
249	0.585	0.616
250	0.031	0.0468
251	0.064	0.0878
252	0.033	0.0608
253		0.559
254	0.656	1.12
255	10.369	
256	0.197	
257	0.242 - 0.282	0.221-0.27
258	0.378	
259	2.569	
260	0.186	
261	0.040	0.0639
262	0.058	0.0991
263		0.679
264	0.108	
265	<0.022	0.0232
266	0.152	

267	3.308	
268	20.567	
269	0.467	
270	0.463	
271	0.100	0.108
272	1.717	2.28
273	0.202	0.143
274	0.104	0.0524
275	0.261	0.273
276	0.298	0.175
277	0.094	0.0899
278	0.241	0.29
279	0.312	
280	7.823	
281	<0.022	
282	0.180	
283	0.538	0.635
284	2.023	1.38
285	0.390	0.375
286	1.807	2.54
287	34.794	> 25
288	0.053	0.269
289	0.316	0.19
290	2.222	0.414-0.975
291		4.64
292	0.049	0.0645
293	2.696	
294	0.095	0.648
295	0.342	0.252
296	0.085	
297		0.848
298	0.188	1.04
299	4.052	10.4
300	1.639	1.84
301		0.0887
302	0.131	

303		0.326
304	2.107	
305	0.065	0.0413
306	4.043	12.5
307		0.225
308	0.259	0.703
309	0.868	1.66
310	36.281	> 25
311	4.139	
312	0.051	0.024
313	0.073	0.0799
314	1.311	1.59
315	5.916	
316	0.131	
317	0.050	
318	5.007	
319	0.705	
320	2.410	
321	1.214	
322	0.026	0.0666
323		17.1
324		0.483
325	15.718	18.5-21.4
326	0.115	0.268-0.369
327		19.2
328	0.329 - 1.144	0.558-0.843
329	2.164	5.62
330	0.026	0.0545
331	6.083	7.65
332	0.052 - 0.072	0.0693
333	0.128	0.335
334	0.646	
335		6.53
336		0.236
337		7.22
338	0.148	0.145

339	3.101	4.4
340	<0.022	0.0276
341		2.13
342	0.029	0.0278
343		4.08
344		0.265
345	> 50	
346	32.256	
347	> 50	
348	> 50	
349	4.010	24.2
350	0.583	0.731
351	> 50	
352	> 50	
353	> 50	
354	> 50	
355	33.589	> 25
356	1.642	4.53
357	13.229	
358	0.864	1.53
359	> 50	> 25
360	3.035	4.37-11.9
361	0.781	0.736
362	0.063	0.0621
363	14.441	23.3
364	0.964	1.06
365	> 50	> 25
366	2.602	20.2-21.7
367	20.809	> 25
368	0.706	0.862
369	> 50	> 25
370	6.649	3.01
371	25.036	> 25
372		4.19
373	39.696	> 25
374	1.617	1.89-2.42

375	> 50	> 25
376	2.321	3.27-4.33
377		>25
378		4.19
379		> 25
380		0.839
381		20
382	0.203	0.349
383		5.16
384	0.068	0.107
385		22.5
386		4.74
387		20.6
388		4.37
389		1.83
390	0.140	0.213
391		2.35-5.33
392	0.694	0.355-0.697
393		12.1
394	0.268	0.34
395		9.36
396	0.189	0.224
397		7.14
398	0.094 - 0.123	0.189
399		> 25
400		0.648
401		19
402	0.362	0.39
403		> 25
404		0.964
405		21.1
406		1.82
407		6.39
408	0.237	0.349
409		1.35
410	0.340 - 0.440	0.098-0.521

411	2.907	
412	0.190	
413	21.616	
414	6.026 - 7.675	5.47-8.32
415	26.674	
416	1.592	
417	20.287	
418	0.808	
419	2.833	
420	> 50	
421	27.999	> 25
422	2.136	3.81
423	7.595	14.8
424	0.162	0.491-0.747
425	0.909	2.45
426	<0.022 - 0.038	0.019-0.058
427	1.229	2.09
428	> 50	> 25
429	6.407	9.78
430	0.133	0.0908
431	0.568	0.811
432	0.040	0.0448
433	6.675	5.31
434	0.153	2.19-3.96
435		> 25
436	0.291	0.364-0.373
437		2.69-3.18
438		> 25
439		6.155
440	0.125	0.105-0.122
441	4.229	1.63-10.6
442	0.136	0.225
443	0.063 - 0.077	0.0414
444	0.040	0.0266
445	2.526	2.46
446	0.079 - 0.081	0.039

447	3.876	
448	0.034	0.0373
449		5.43
450	0.062	0.0518
451	0.207	0.386
452	0.063 - 0.065	0.134
453	11.400	14.5
454	0.401	0.601
455	6.218	> 25
456	0.082	0.041
457	<0.022	0.013
458	0.069	0.0588
459	0.991	1.16
460		
461	2.275	
462	1.924	2.87
463	> 50	
464	<0.022	0.020-0.055
465		0.164
466	0.665	0.821
467		9.82
468		3.03-11.8
469	0.077	0.185-0.198
470	0.075	0.172
471	0.925	0.78
472		14.8
473		0.0986
474		7.1
475	0.341	0.355
476	> 50	
477	> 50	
478	> 50	
479	> 50	
480	> 50	
481	0.780	2.52
482	>50	>25

483	0.096	0.202
484	5.160	21.3
485		2.12
486		0.873
487		1
488	0.311	0.437
489		4.15
490		2.61
491		0.821
492		0.249
493	0.067	0.139
494	1.649	0.595
495	0.712	0.734
496	0.751	0.723
497		1.13
498		5.27
499		2.39
500		1.45
501		0.494
502		0.305
503	0.546	0.96
504	0.268	0.243
505		0.275
506		0.46
507		0.0773
508	0.553	0.484
509	0.553	0.484
510		0.0294
511	0.062	
512	0.450	0.38
513		0.0336
514		
515		0.0287
516	0.082	0.0592
517		1.58
518		0.0785

519	0.123	0.363
520	0.080	0.053-0.321
521		0.23
522		0.745
523		0.165
524	0.026	0.0211
525	0.085	0.108-0.183
526	0.088	0.0427
527		0.0851
528	0.077	0.0613
529	0.117	0.0622
530	<0.022	0.00835
531		0.00812
532		0.0727
533	0.307	0.227
534	0.188	0.331
535		0.183
536		0.104
537	0.400	0.257
538	0.416	0.268
539		2.66
540	0.878	0.573
541	0.266	0.0899
542	0.090	0.0877
543		> 25
544	0.075	0.0477
545		0.0943
546	0.059	0.0423
547	0.158	0.146
548	0.184	
549	1.840	
550	0.791	0.276
552	<0.022	0.0199
553	0.521	0.41
554	0.075	0.217
555	<0.022	

556	<0.072	
557	0.246	0.237
558		0.283
559		17.6
560		25
561		0.552
562		0.364
563		0.04
564		0.0501
565		0.309
566	0.135	0.13
567		5.41
568	0.086 - 0.141	0.067-0.161
569		0.0575
570		0.0446
571		0.0742
572		0.0781
573		0.00786
574	0.204	0.324
575		1.91
576		2.37
577		1.65
578		1.07
579	0.911	0.591
580	0.153	0.193
581	0.260	0.432
582		0.204
583		> 25
584		10.6
585		6.7
586	2.797	1.02
587		1.95
588	0.764	0.85
589		2.92
590	<0.022	0.006-0.009
591	<0.022	0.018

592	0.138	0.077
593	0.077	0.036
594	0.257	0.178
595	0.121	0.053
596	0.161	0.154
597	0.457	0.741
598	0.519	0.715
599	0.155	0.265
600	0.488	0.729
601	0.042	0.042
602	0.049	0.034
603	0.244	0.336
604	0.112	0.161

IDH Cellular Assay

The IDH cellular assay consists of two side-by-side comparator assays: 1) 2HG oncometabolite detection assay using LC-MS (See Mutant IDH1 biochemical assay for LC-MS detection details) and 2) Cell proliferation assay to monitor off-target killing of cells and to normalize 2HG level change. IDH1 cellular screens were run with the HCT-116 cell line (express endogenous level of IDH1mut R132H, available from Horizon Discoveries X-Man isogenic human cell lines, catalog # HD104-013). The cells were grown in DMEM (LONZA Cat# 12-540F) with 10% Fetal bovine serum (Gibco cat# 10099) and 1X non-essential amino acids (NEAA LONZA cat# 13-114E). Panel assays were run periodically to test compound activity in cell lines with different endogenous mutations – HT1080 (IDH1mut R132C, EMEM + 10% FBS), SNU-1079 (IDH1mut R132C, RPMI + 10%FBS + 1% sodium pyruvate), and SW1353 (IDH2mut R172S, RPMI + 10%FBS + 1% sodium pyruvate).

The assay process is as follows:

Day 1: cells were seeded in 384-well plates (Corning Cat# 3707) in triplicates for both the cell proliferation and 2HG assay, and incubated at 37C, 95% Rh, 5% CO2 overnight.

Day 2: compounds were serially diluted 1:3 (10 point dilution from 10mM solutions in DMSO) and delivered to the cell assay plates via acoustic dispenser, with final concentration ranging from 30uM to 1.5nM. The plates were returned to the incubator after treatment and incubated for 48 hours.

Day 4 Proliferation assay: CTG (cell titer-glo, Promega part # G755B) was added to the assay plates and luminescence signal was read on the plate reader.

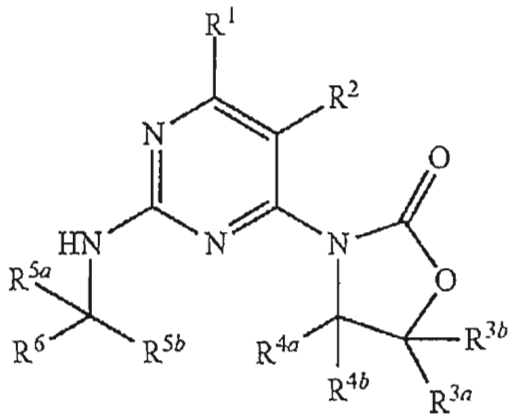
Day 4 2HG assay : Extraction sample preparation consisted of aspirating all media from the assay plates, adding 70 ul of 90% methanol in water, dry ice incubation for 15 minutes, centrifuging at 2000 rpm for 30 min to ensure all particulates have settled, and transferring 30 ul of the supernatant into LC-MS ready plates. LC-MS analysis follows.

Certain compounds of the invention have been tested in the IDH Cellular Assay.

What is claimed is:

1. A compound of formula (I)

(I)



wherein:

R^1 and R^2 are each independently hydrogen, deuterium, halo, hydroxyl, NH_2, aryl, heteroaryl, or optionally substituted C_{1-4} alkyl,

wherein said C_{1-4} alkyl is optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, and NH_2;

R^{3a} is hydrogen, deuterium, C_{1-6} alkyl, phenyl, or benzyl and

R^{3b} is hydrogen, deuterium, or C_{1-6} alkyl; or

R^{3a} and R^{3b} are joined together forming an optionally substituted 3-7 membered cycloalkyl ring or an optionally substituted 4-7 membered heterocyclic ring,

wherein said cycloalkyl and heterocyclic rings are each optionally substituted with one or two substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl;

R^{4a} is hydrogen, C_{1-6} alkyl, optionally substituted phenyl, optionally substituted benzyl, optionally substituted heteroaryl, or methylene-dibenzene,

wherein said phenyl, benzyl, and heteroaryl rings are optionally substituted with one to three substituents

each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-4} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, phenyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, —$COOR^b$, —SO_2R^b, —$NHC(O)R^b$, and —NR^bR^b and

R^{4b} is hydrogen, deuterium, or C_{1-3} alkyl; or

R^{4a} and R^{4b} are joined together forming an optionally substituted 3-7 membered cycloalkyl ring or an optionally substituted 4-7 membered heterocyclic ring,

wherein said cycloalkyl and heterocyclic rings are optionally substituted with one or two substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl,

provided that only one of R^{3a} and R^{3b} and R^{4a} and R^{4b} are joined together forming a ring;

R^{5a} is hydrogen or deuterium;

R^{5b} is hydrogen, deuterium, methyl, ethyl, CD_3, CF_3, CH_2F, or CHF_2 and

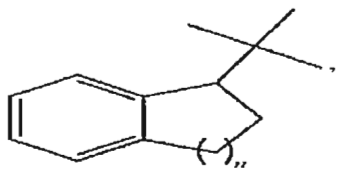
R^6 is optionally substituted C_{1-6} alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclic, or optionally substituted C_{3-10} cycloalkyl,

wherein said C_{1-6} alkyl is optionally substituted with one substituent selected from the group consisting of hydroxyl, C_{1-3} alkoxy and $-OR^a$,

wherein said aryl, heteroaryl, heterocyclic and C_{3-10} cycloalkyl are optionally substituted with one to three substituents each independently selected from the group consisting of: halo; hydroxyl; cyano; nitro; C_{1-4} alkoxy; C_{1-3} haloalkyl; C_{1-3} haloalkoxy; C_{1-6} alkyl; C_{3-6} cycloalkyl optionally substituted with one to three substituents each independently selected from the group consisting of: hydroxyl, cyano, C_{1-3} alkyl, C_{1-3} alkoxy, and C_{1-3} haloalkyl; phenyl optionally substituted with one to three substituents each independently selected from the group consisting of: halo,

hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, —COOR^b, —SO_2R^b, —NHC(O)R^b, and NR^{b}R^b; 5-6 membered heteroaryl optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, C_{1-3} alkyl, C_{1-3} alkoxy; 5-6 membered heterocyclic optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl; —CH_2R^a; —OR^a; —C(O)R^a; —NR^{a}R^b; —COOR^a; —SO_2R^a; —SO_2R^b; —NHC(O)R^a; —NHC(O)R^b; —C(O)NR^{a}R^b; —C(O)NHR^b; and —SO_2NR^{b}R^b; or R^{5b} and R^6 are joined together forming an optionally substituted C_{3-7} cycloalkyl group or an optionally substituted group of formula (a):

(a)



wherein n is 1, 2, or 3 and

said C_{3-7} cycloalkyl and group of formula (a) are optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, benzyloxy, —COOR^b, —SO_2R^b, —NHC(O)R^b, and —NR^{b}R^b;

each R^a is independently optionally substituted phenyl, optionally substituted heteroaryl, optionally substituted heterocyclic, or optionally substituted C_{3-7} cycloalkyl,

wherein said phenyl and heteroaryl are optionally substituted with one to three substituents each independently selected from the group consisting of halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, and C_{1-3} alkyl,

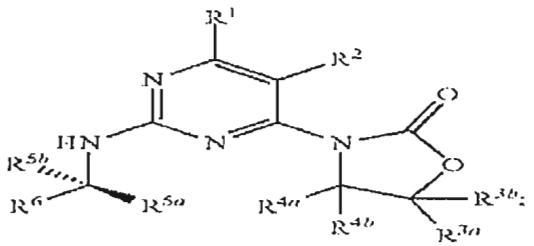
wherein said heterocyclic is optionally substituted with one to three substituents each independently selected from the group consisting of halo, hydroxyl, oxo, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-4} alkyl, C_{3-5} cycloalkyl, —C(O)R^b, and —NR^{b}R^b, and

wherein said C_{3-7} cycloalkyl is optionally substituted with one to three substituents each independently selected from the group consisting of halo, hydroxyl, oxo, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, and C_{1-3} alkyl; and

each R^b is independently hydrogen or C_{1-6} alkyl; or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1 of the formula (III)

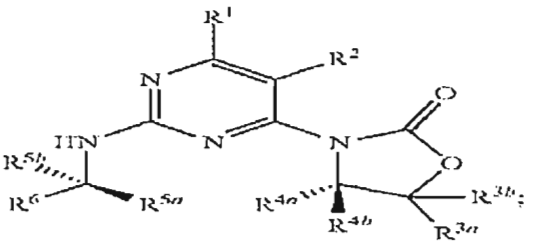
(III)



or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 2 of the formula (IV)

(IV)



or a pharmaceutically acceptable salt thereof.

4. The compound according to claim 3 wherein R^{3a} and R^{3b} are both hydrogen; or a pharmaceutically acceptable salt thereof.

5. The compound according to claim 4 wherein R^{5a} is hydrogen and R^{5b} is hydrogen, methyl, ethyl, or CF_3; or a pharmaceutically acceptable salt thereof.

6. The compound according to claim 5 wherein R^{5b} is methyl; or a pharmaceutically acceptable salt thereof.

7. The compound according to claim 6 wherein R^1 is hydrogen, fluoro or chloro and R^2 is hydrogen, fluoro, chloro, or methyl; or a pharmaceutically acceptable salt thereof.

8. The compound according to claim 7 wherein R^1 and R^2 are both hydrogen; or a pharmaceutically acceptable salt thereof.

9. The compound according to claim 8 wherein R^{4a} is hydrogen, C_{1-6} alkyl, optionally substituted phenyl, optionally substituted benzyl, optionally substituted heteroaryl, or methylene-dibenzene,

wherein said phenyl, benzyl, and heteroaryl rings are optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, —$COOR^b$, —SO_2R^b, —$NHC(O)R^b$, and —NR^bR^b and R^{4b} is hydrogen or C_{1-3} alkyl; or a pharmaceutically acceptable salt thereof.

10. The compound according to claim 9 wherein R^{4b} is hydrogen or methyl; or a pharmaceutically acceptable salt thereof.

11. The compound according claim 10 wherein R^{4b} is hydrogen; or a pharmaceutically acceptable salt thereof.

12. The compound according to claim 11 R^{4a} is hydrogen, methyl, ethyl, isopropyl, phenyl, 4-fluorophenyl, 4-methoxyphenyl, biphenyl, benzyl, or pyridinyl; or a pharmaceutically acceptable salt thereof.

13. The compound according to claim 12 wherein R^{4a} is isopropyl; or a pharmaceutically acceptable salt thereof.

14. The compound according to claim 1 wherein R^6 is methyl, C_{5-10} cycloalkyl, optionally substituted phenyl, optionally substituted pyridinyl, optionally substituted pyrimidinyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted triazolyl, optionally substituted pyrazolyl, optionally substituted thiazolyl, optionally substituted 1,3,4-oxadiazolyl, optionally substituted 1,2,4-oxadiazolyl, optionally substituted isoxazolyl, thienyl, oxazolyl, quinolinyl, optionally substituted benzimidazolyl, benzthiazolyl, benzoxazolyl, tetrazolo[1,5-a]pyridinyl, imidazo[2,1-b][1,3,4]thiadiazolyl, optionally substituted piperidinyl, optionally substituted piperazinyl, tetrahydrofuranyl, tetrahydropyranyl, optionally substituted tetrahydrothiopyran1,1-dioxide, 1H-pyrrolo[2,3-b]pyridinyl, 2,3-dihydro-benzo[1,4]dioxinyl, 5,6,7,8-tetrahydro-[1,2,4]trazolo[4,3-a]pyrazinyl, 4,5,6,7-tetrahydro-benzothiazolyl, indolizinyl, cyclopropyl, cyclopentyl, or cyclohexyl, wherein said phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, triazolyl, pyrazolyl, thiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, isoxazolyl, benzimidazolyl, piperidinyl, piperazinyl, and tetrahydro-thiopyran1,1-dioxide are each optionally substituted with one or two substituents as defined in formula (I).

15. The compound according to claim 14 wherein R^6 is optionally substituted with one or two substituents each independently selected from the group consisting of: halo; hydroxy; nitro; C_{1-4} alkoxy; C_{1-3} haloalkyl; C_{1-3} haloalkoxy; C_{1-6} alkyl; C_{3-6} cycloalkyl optionally substituted with one substituent selected from the group consisting of: cyano, C_{1-3} alkyl, and C_{1-3} alkoxy; phenyl optionally substituted with one or two substituents each independently selected from the group consisting of: fluoro, chloro, methyl, cyano, and methoxy; and 5-6 membered heteroaryl optionally substituted with one or two methyl groups; or a pharmaceutically acceptable salt thereof.

16. The compound according to claim 15 wherein R^6 is optionally substituted 1,3,4-oxadiazolyl or optionally substituted 1,2,4-oxadiazolyl; or a pharmaceutically acceptable salt thereof.

17. The compound according to claim 14 wherein R^6 is substituted with one $—CH_2R^a$, $—C(O)R^a$, $—NHC(O)R^a$, $—NHC(O)R^b$, $—C(O)NHR^a$, $C(O)NHR^b$, $—OR^a$, $—NR^aR^b$, $—SO_2NR^bR^b$, $—SO_2R^a$, or $—SO_2R^b$ group; or a pharmaceutically acceptable salt thereof.

18. The compound according to claim 17 wherein Ra is

(a) phenyl optionally substituted with one or two substituents each independently selected from the group consisting of fluoro, chloro and bromo;

(b) optionally substituted 5-6 membered heteroaryl;

(c) C_{5-7} cycloalkyl optionally substituted with one or two substituents each independently selected from the group consisting of fluoro, hydroxy, methyl, and C_{1-3} haloalkoxy; or

(d) a heterocyclic group selected from the group consisting of: piperidinyl, piperazinyl, morpholinyl, tetrahydropyranyl, tetrahydro-thiopyran1,1-dioxide, 1,4-diazepanyl, 4,7-diaza-spiro[2.5]octanyl, 3,8-diaza-bicyclo[3.2.1]octanyl, 3,8-diaza-bicyclo[4.2.0]octanyl, octahydropyrrolo[1,2-a]pyrazinyl, octahydro-pyrido[1,2-a]pyrazinyl, octahydro-pyrrolo[3,4-c]pyrrolyl, and 5,6,7,8-tetrahydro-imidazo[1,2-a]pyrazinyl each of which is optionally substituted with one to three substituents each independently selected from the group consisting of: hydroxy, fluoro, amino, dimethylamino, C_{1-3}

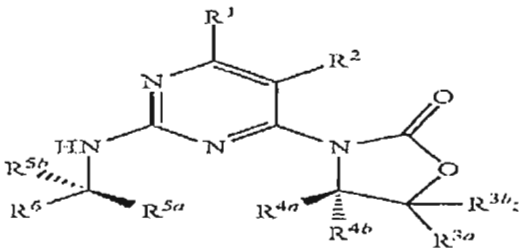
haloalkoxy, C_{1-3} alkyl, and C_{3-5} cycloalkyl; or a pharmaceutically acceptable salt thereof.

19. The compound according to claim **18** wherein R^6 is optionally substituted phenyl; or a pharmaceutically acceptable salt thereof.

20. The compound according to claim **19** wherein the phenyl is substituted with one —CH_2R^a, —C(O)R^a, or —C(O)NHR^a group in the para position; or a pharmaceutically acceptable salt thereof.

21. The compound according to claim **2** of the formula (V)

(V)



wherein R^{4a} is phenyl and R^{4b} is hydrogen; or a pharmaceutically acceptable salt thereof.

22. The compound according to claim **1** selected from the group consisting of:

(S)-4-isopropy-3-(2-(((S)-1-(4-(2-yl)phenyl)ethyl)amino) pyrimidin-4-yl)oxazolidin-2-one;

N-(4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl) pyrimidin-2-ylamino)ethyl)phenyl)cyclohexanecarboxamide;

(S)-3-(2-(((S)-1-(3-fluoro-4-((4-methylpiperazin-1-yl) methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-4-isopropyl-3-(2-(((S)-1-(4-((3,3,4-trimethylpiperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl) oxazolidin-2-one;

2-fluoro-N-(4-hydroxy-4-methylcyclohexyl)-4-((S)-1-((4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-yl)amino)ethyl)benzamide;

(S)-3-(2-((S)-1-(4-((4-amino-4-methylpiperidin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-((S)-1-(4-((4-(dimethylamino)piperidin-1-yl) methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-4-isopropyl-3-(2-((S)-1-(4-((4-methylpiperazin-1-yl) methyl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;

(S)-4-isopropyl-4-methyl-3-(2-((S)-1-(4-((4-methylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl) oxazolidin-2-one;

(S)-4-isopropyl-3-(2-((S)-1-(6-phenylpyridin-3-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;

(S)-3-(2-((S)-1-(4-benzoylphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-4-isopropyl-3-(2-(((S)-1-(5-phenyl-1,3,4-thiadiazol-2-yl)ethyl)amino) pyrimidin-4-yl)oxazolidin-2-one;

(4S)-4-isopropyl-3-(2-(1-(5-phenylpyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;

3-(5-fluoro-2-((1-(5-(4-fluoro-3-methylphenyl)pyridin-2-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one;

(S)-4-isopropyl-3-(2-(((S)-1-(1-(3-methoxyphenyl)-1H-pyrazol-4-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one;

(S)-3-(2-(((S)-1-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-(((S)-1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-4-isopropyl-3-(2-(((S)-1-(3-(m-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)oxazolidin-2-one;

(S)-3-(2-(((S)-1-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-((S)-1-(5-(4-fluoro-2-methylphenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-4-Isopropyl-3-{2-[(3-p-tolyl-[1,2,4]oxadiazol-5-ylmethyl)-amino]-pyrimidin-4-yl}-oxazolidin-2-one;

(S)-4-isopropyl-3-(2-((S)-1-(4-(1-methyl-1H-pyrazol-4-yl)phenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;

(S)-3-(2-((S)-1-(2-fluoro-4-isopropylphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-((S)-1-(4-isobutoxy-3-methylphenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-(((S)-1-(4-isobutoxyphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(5-fluoro-2-(((S)-1-(4-isobutoxyphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

2-fluoro-N-(trans-4-hydroxycyclohexyl)-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide;

(S)-3-(5-fluoro-2-((S)-1-(3-fluoro-4-(piperidine-1-carbonyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

N-cyclohexyl-2-fluoro-4-((S)-1-(5-fluoro-4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide;

N-cyclohexyl-2-fluoro-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide; and

(S)-3-(5-fluoro-2-((S)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethylami no)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one; or a pharmaceutically acceptable salt thereof.

23. The compound according to claim **1** selected from the group consisting of:

(S)-3-(2-(((S)-1-(3-fluoro-4-((3,3,4-trimethylpiperazin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-(((S)-1-(4-((4,4-difluoropiperidin-1-yl)methyl)phenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(5-fluoro-2-(1-(4-phenoxyphenyl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;

(S)-3-(2-((S)-1-(4-(4-fluorophenoxy)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-((S)-1-(4-(((2S,6R)-2,6-dimethylmorpholino)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-(((S)-1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-(((S)-1-(5-(4-chlorophenyl)-1,2,4-oxadiazol-3-yl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-((S)-1-(5-(4-fluoro-3-methylphenyl)pyridin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-((S)-1-(5-(4-fluorophenoxy)pyrimidin-2-yl) ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-((S)-1-(5-(4-fluorophenoxy)pyrazin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-4-isopropyl-3-(2-((S)-1-(5-(3-(trifluoromethyl)phenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one; and

(S)-3-(2-((S)-1-(5-(4-fluoro-3-methylphenyl)pyrimidin-2-yl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one; or a pharmaceutically acceptable salt thereof.

24. The compound according to claim 1 selected from the group consisting of:

(S)-3-(2-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl) ethylamino)-5-fluoropyrimidin-4-yl)-4,4-dimethyloxazolidin-2-one;

(S)-3-(6-chloro-2-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethylamino)pyrimidin-4-yl)oxazolidin-2-one;

(S)-3-(2-((S)-1-(2-fluoro-4-(1-methylcyclopropyl)phenyl)ethylamino) pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-((S)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

2-chloro-N-cyclopentyl-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide;

(S)-3-(2-((S)-1-(4-((3,3-difluoropiperidin-1-yl)methyl) phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-((S)-1-(4-(4,7-diazaspiro[2.5]octan-4-ylmethyl) phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-((S)-1-(4-((4-acetylpiperazin-1-yl)methyl)phenyl)ethylamino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(2-(((S)-1-(4-isobutoxyphenyl)ethyl)amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one;

(S)-3-(5-fluoro-2-(((S)-1-(4-isobutoxyphenyl)ethyl) amino)pyrimidin-4-yl)-4-isopropyloxazolidin-2-one; and

2-fluoro-N-(trans-4-hydroxycyclohexyl)-4-((S)-1-(4-((S)-4-isopropyl-2-oxooxazolidin-3-yl)pyrimidin-2-ylamino)ethyl)benzamide; or a pharmaceutically acceptable salt thereof.

25. The compound according to claim 1 wherein

each R^1 and R^2 is independently hydrogen, deuterium, halo, hydroxyl, NH_2, aryl, heteroaryl, or optionally substituted C_{1-4} alkyl,

wherein said C_{1-4} alkyl is optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, and NH_2;

R^{3a} is hydrogen, deuterium, C_{1-6} alkyl, phenyl, or benzyl and

R^{3b} is hydrogen, deuterium, or C_{1-6} alkyl; or

R^{3a} and R^{3b} are joined together forming an optionally substituted 3-7 membered cycloalkyl ring or an optionally substituted 4-7 membered heterocyclic ring,

wherein said cycloalkyl and heterocyclic rings are each optionally substituted with one or two substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl;

R^{4a} is hydrogen, C_{1-6} alkyl, optionally substituted phenyl, optionally substituted benzyl, optionally substituted heteroaryl, or methylene-dibenzene,

wherein said phenyl, benzyl, and heteroaryl rings are optionally substituted with one to three substituents

each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, $COOR^b$, SO_2R^b, $NHC(O)R^b$, and NR^bR^b and

R^{4b} is hydrogen, deuterium, or C_{1-3} alkyl; or

R^{4a} and R^{4b} are joined together forming an optionally substituted 3-7 membered cycloalkyl ring or an optionally substituted 4-7 membered heterocyclic ring,

wherein said cycloalkyl and heterocyclic rings are optionally substituted with one or two substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl,

provided that only one of R^{3a} and R^{3b} and R^{4a} and R^{4b} are joined together forming a ring;

R^{5a} is hydrogen or deuterium;

R^{5b} is hydrogen, deuterium, methyl, ethyl, CD_3, CF_3, CH_2F, or CHF_2 and

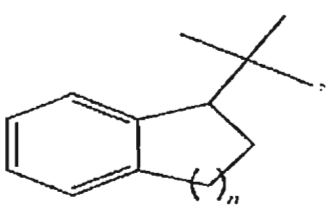
R^6 is optionally substituted C_{1-6} alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclic, or optionally substituted C_{5-10} cycloalkyl,

wherein said C_{1-6} alkyl is optionally substituted with one substituent selected from the group consisting of hydroxyl, C_{1-3} alkoxy and $-OR^a$;

wherein said aryl, heteroaryl, heterocyclic and C_{5-10} cycloalkyl are optionally substituted with one to three substituents each independently selected from the group consisting of: halo; hydroxyl; cyano; nitro; C_{1-3} alkoxy; C_{1-3} haloalkyl; C_{1-3} haloalkoxy; C_{1-6} alkyl; C_{3-6} cycloalkyl; phenyl optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, phenoxy, $COOR^b$, SO_2R^b, $NHC(O)R^b$, and NR^bR^b; 5-6 membered heteroaryl; 5-6 membered heterocyclic optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, oxo, NH_2, and C_{1-3} alkyl; $—CH_2R^a$; $—OR^a$; $—C(O)R^a$; $—NR^aR^b$; $—COOR^a$; $—SO_2R^a$; $NHC(O)R^a$; and $—SO_2NR^bR^b$; or

R^{5b} and R^6 are joined together forming an optionally substituted C_{3-7} cycloalkyl group or an optionally substituted group of formula (a):

(a)



wherein n is 1, 2, or 3 and

said C_{3-7} cycloalkyl and group of formula (a) are optionally substituted with one to three substituents each independently selected from the group consisting of: halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, 5-6 membered heterocyclic, benzyloxy, $COOR^b$, SO_2R^b, NHC(O) R^b, and NR^bR^b;

each R^a is independently optionally substituted phenyl, optionally substituted heteroaryl, or optionally substituted 4-7 membered heterocyclic,

wherein said phenyl and heteroaryl are optionally substituted with one to three substituents each independently selected from the group consisting of halo, hydroxyl, cyano, nitro, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, and C_{1-3} alkyl,

wherein said 4-7 membered heterocyclic is optionally substituted with one to three substituents each independently selected from the group consisting of halo, hydroxyl, oxo, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, and C_{1-3} alkyl; and

each R^b is independently hydrogen or C_{1-6} alkyl; or a pharmaceutically acceptabble salt thereof.

26. The compound according to claim **25** wherein

R^1 is hydrogen, fluoro, chloro, or methyl;

R^2 is hydrogen;

R^{3a} is hydrogen, methyl, or phenyl;

R^{3b} is hydrogen or methyl;

R^{4a} is hydrogen, C_{1-4} alkyl, optionally substituted phenyl, optionally substituted benzyl, optionally substituted heteroaryl, or methylene-dibenzene;

R^{4b} is hydrogen or methyl;

R^{5a} is H; and

R^{5b} is hydrogen, methyl, ethyl, or CF_3; or a pharmaceutically acceptable salt thereof.

27. The compound according to claim **26** wherein R^6 is isopropyl, optionally substituted aryl, optionally substituted pyrazolyl, optionally substituted pyridinyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzo[b][1,4]dioxinyl, or optionally substituted C_{5-10} cycloalkyl; or a pharmaceutically acceptable salt thereof.

28. A pharmaceutical composition comprising a compound according to claim **1**, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

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