

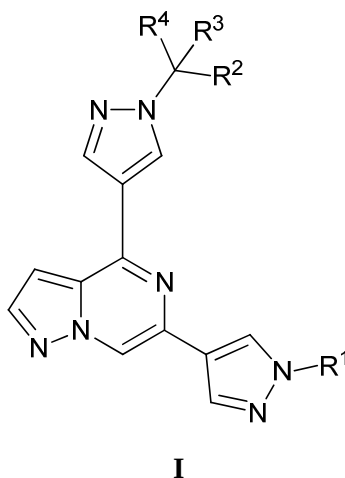
4,6-SUBSTITUTED-PYRAZOLO[1,5-a]PYRAZINES AS JANUS KINASE INHIBITORS

[0001] The present invention relates to novel compounds, to pharmaceutical compositions comprising the compounds, to processes for making the compounds, and to the use of the compounds in therapy. More particularly, it relates to 4,6-substituted-pyrazolo[1,5-a]pyrazine compounds which are inhibitors of JAK kinases. In particular, the compounds are inhibitors of Tyk2, JAK1, JAK2, and/or JAK3, and are useful in the treatment of JAK kinase-associated diseases such as autoimmune diseases, inflammatory diseases, organ, tissue and cell transplant rejection, and hematological disorders and malignancies.

[0002] The members of the Janus kinase (JAK) family of non-receptor, intracellular tyrosine kinases are components of cytokine signal transduction. Four family members have been identified: JAK1, JAK2, JAK3 and Tyk2. The JAKs play a key role in the intracellular signaling mediated through Type I and Type II cytokine receptors. Specific cytokine receptor chains are associated with particular JAK kinases (reviewed in O'Sullivan et al., *Mol. Immunol.*, 2007, 44:2497; Murray J., *Immunol.*, 2007, 178:2623). Upon binding of cytokines to their receptors, JAKs are activated and phosphorylate the receptors, creating docking sites for other signaling molecules, in particular members of the signal transducer and activator of transcription (STAT) family. Upon phosphorylation, STATs dimerize, translocate to the nucleus and activate expression of genes involved in development, growth, differentiation, and maintenance of a variety of cell types. The cytokine-induced responses mediated by JAK kinases are important in host defense and, when dysregulated, play a role in pathogenesis of immune or inflammatory diseases, immune deficiencies, and malignancy (O'Sullivan et al., *Mol. Immunol.*, 2007, 44:2497). Elevated or decreased levels of JAK/STAT-utilizing cytokines have been implicated in a number of disease states. In addition, mutations or polymorphisms in Type I and II cytokine receptors, JAK kinases, STAT proteins, and JAK/STAT regulatory proteins such as phosphotyrosine phosphatases, SOCS proteins, PIAS proteins have been reported in a variety of diseases. When dysregulated, JAK-mediated responses can positively or negatively affect cells leading to over-activation and malignancy or immune and hematopoietic deficiencies, respectively, and suggests the utility for use of inhibitors of JAK kinases. The JAK/STAT signaling pathway is involved in a variety of hyperproliferative and cancer-related processes including cell-cycle progression, apoptosis, angiogenesis, invasion, metastasis and evasion of the immune system (Haura et al., *Nature Clinical Practice Oncology*, 2005, 2(6), 315-324; Verna et al., *Cancer and Metastasis Reviews*, 2003, 22, 423-434). In addition, the JAK/STAT signaling pathway is important in the genesis and differentiation of hematopoietic cells and regulating both pro- and anti-inflammatory and immune responses (O'Sullivan et al., *Molecular Immunology* 2007, 44:2497). Because cytokines utilize different patterns of JAK kinases

CLAIMS

1. A compound of the general Formula I



or a stereoisomer or pharmaceutically acceptable salt or solvate thereof, wherein:

R¹ is hydroxy(1-6C)alkyl, HOCH₂(cyclopropylidene)CH₂-, (1-4C alkoxy)(1-6C)hydroxyalkyl, (hydroxy)trifluoro(1-6C)alkyl, dihydroxy(2-6C)alkyl, H₂N(3-6C)hydroxyalkyl, (1-3C alkyl)NH(3-6C)hydroxyalkyl, (1-3C alkyl)₂N(3-6C)hydroxyalkyl, H₂N(1-4C alkoxy)(3-6C)alkyl, Cyc¹(CH₂)_m-, hetCyc¹, hetCyc²CH₂-, R^aR^bNC(=O)CH₂-, hetCyc^{3a}(1-3C)alkyl, hetCyc^{3b}(2-3C)hydroxyalkyl, R^cR^dN(2-3C)alkyl, (1-3C alkyl)₂NSO₂(2-3C)alkyl, hetCyc⁴, (1-6C)alkyl or CH₃SO₂(1-6C)alkyl;

Cyc¹ is a 4-6 membered cycloalkyl substituted with 1-2 substituents independently selected from the group consisting of HO, HOCH₂-, (1-3C)alkyl, H₂NHC(=O)-, (1-3C alkyl)₂NC(=O)-, and HOCH₂CH₂NHC(=O)-;

m is 0 or 1;

hetCyc¹ is a 4-6 membered heterocyclic ring having a ring heteroatom selected from N, O and S wherein the S is optionally oxidized to SO₂, wherein said heterocyclic ring is optionally substituted with a substituent selected from the group consisting of OH, (1-3C alkyl)C(=O)-, (1-3C alkyl)SO₂-, (1-3C alkyl)NHC(=O)- and NH₂CH₂C(=O)-;

hetCyc² is a 4-6 membered heterocyclic ring having a ring S atom, wherein the S is oxidized to SO₂;

R^a and R^b are independently H or (1-3C)alkyl, or

R^a and R^b together with the nitrogen atom to which they are attached form a 4-6 membered ring optionally having a ring oxygen atom;

hetCyc^{3a} and hetCyc^{3b} are independently a 4-6 membered heterocyclic ring having 1-2 ring heteroatoms independently selected from N and O, wherein said heterocyclic ring is optionally

substituted with 1-2 substituents independently selected from the group consisting of halogen, OH, (1-4C)alkoxy, HOCH₂-, (1-3C alkyl)C(=O)- and oxo;

R^c is H or (1-3C)alkyl;

R^d is (1-3C)alkyl, (1-3C alkyl)SO₂-, hetCyc^a, or (3-6C)cycloalkyl optionally substituted with HOCH₂-;

hetCyc^a is a 5-6 membered azacyclic ring optionally substituted with 1-2 substituents independently selected from oxo and (1-3C)alkyl;

hetCyc⁴ is azetidiny substituted with ((CH₃)₂N)₂P(=O)- or Y-C(=O)-;

Y is R^eR^fN(CH₂)_n-, hetCyc^bCH₂-, Cyc², hydroxy(1-3C)alkyl, (1-3C alkyl)₂NC(=O)-, (1-3C)alkylSO₂- or (1-3C)alkyl;

n is 0 or 1;

R^e and R^f are independently H or (1-3C)alkyl;

hetCyc^b is a 4-5 membered azacyclic ring optionally substituted with OH;

Cyc² is a (3-6C)cycloalkyl optionally substituted with OH;

R² is (1-6C)alkyl, trifluoro(1-6C)alkyl, difluoro(1-6C)alkyl, fluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, (1-6C)alkoxy, (3-6C)cycloalkyl (optionally substituted with one or two halogens), (3-6C)cycloalkylCH₂-, HOC(=O)- or phenyl, and

R³ is (1-6C)alkyl or (3-6C)cycloalkyl, or

R² and R³ together with the carbon atom to which they are attached form a 3-7 membered cycloalkyl ring optionally substituted with one or two substituents independently selected from OH, (1-6C)alkyl and hydroxy(1-6C)alkyl, or

R² and R³ together with the carbon atom to which they are attached form a 4-membered saturated azacyclic ring substituted with SO₂CF₃; and

R⁴ is hydrogen or (1-6C)alkyl.

2. A compound according to claim 1, wherein R¹ is hydroxy(1-6C)alkyl, HOCH₂(cyclopropylidene)CH₂-, (1-4C alkoxy)(1-6C)hydroxyalkyl, (hydroxy)trifluoro(1-6C)alkyl, dihydroxy(2-6C)alkyl, H₂N(3-6C)hydroxyalkyl, (1-3C alkyl)NH(3-6C)hydroxyalkyl, (1-3C alkyl)₂N(3-6C)hydroxyalkyl, H₂N(1-4C alkoxy)(3-6C)alkyl, Cyc¹(CH₂)_m-, hetCyc¹, hetCyc²CH₂-, R^aR^bNC(=O)CH₂-, hetCyc^{3a}(1-3C)alkyl, hetCyc^{3b}(2-3C)hydroxyalkyl, R^cR^dN(2-3C alkyl)-, (1-3C alkyl)₂NSO₂(2-3C alkyl)- or hetCyc⁴.

3. A compound according to claim 1, wherein R¹ is hydroxy(1-6C)alkyl, HOCH₂(cyclopropylidene)CH₂-, (1-4C alkoxy)(1-6C)hydroxyalkyl, (hydroxy)trifluoro(1-6C)alkyl, dihydroxy(2-6C)alkyl, H₂N(3-6C)hydroxyalkyl, (1-3C alkyl)NH(3-6C)hydroxyalkyl, (1-3C alkyl)₂N(3-6C)hydroxyalkyl or H₂N(1-4C alkoxy)(3-6C)alkyl.

4. A compound according to claim 1, wherein R¹ is dihydroxy(2-6C)alkyl, H₂N(3-6C)hydroxyalkyl, (1-3C alkyl)NH(3-6C)hydroxyalkyl or (1-3C alkyl)₂N(3-6C)hydroxyalkyl.
5. A compound according to claim 1, wherein R¹ is dihydroxy(2-6C)alkyl.
6. A compound according to claim 1, wherein R¹ is H₂N(3-6C)hydroxyalkyl, (1-3C alkyl)NH(3-6C)hydroxyalkyl or (1-3C alkyl)₂N(3-6C)hydroxyalkyl.
7. A compound according to claim 1, wherein
R² is (1-6C)alkyl, trifluoro(1-6C)alkyl, difluoro(1-6C)alkyl, fluoro(1-6C)alkyl, hydroxy(1-6C)alkyl, (1-6C)alkoxy, (3-6C)cycloalkyl (optionally substituted with one or two halogens), (3-6C)cycloalkylCH₂-, HOC(=O)- or phenyl;
R³ is (1-6C)alkyl or (3-6C)cycloalkyl; and
R⁴ is hydrogen or (1-6C)alkyl.
8. A compound according to claim 7, wherein:
R² is (1-6C)alkyl;
R³ is (1-6C)alkyl; and
R⁴ is hydrogen.
9. A compound according to claim 1, wherein:
R² and R³ together with the carbon atom to which they are attached form a 3-7 membered cycloalkyl ring optionally substituted by one or two groups independently selected from OH, (1-6C)alkyl and hydroxy(1-6C)alkyl; and
R⁴ is hydrogen or (1-6C)alkyl.
10. A compound according to claim 1, wherein:
R² and R³ together with the carbon atom to which they are attached form a 4-membered saturated azacyclic ring substituted with SO₂CF₃; and
R⁴ is hydrogen or (1-6C)alkyl.
11. A compound according to claim 1, selected from
4-(1-(1-ethoxyethyl)-1H-pyrazol-4-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;
4-(1-cycloheptyl-1H-pyrazol-4-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;
4-(2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-

yl)ethyl)morpholine;

4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)-6-(1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

N,N-dimethyl-2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)acetamide;

1-morpholino-2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethanone;

6-(1-(3-(methylsulfonyl)propyl)-1H-pyrazol-4-yl)-4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

5-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)oxazolidin-2-one;

N-methyl-N-(2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethyl)methanesulfonamide;

N,N-dimethyl-2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethanamine;

4-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)tetrahydro-2H-thiopyran 1,1-dioxide;

N,N-dimethyl-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-amine;

3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)thietane 1,1-dioxide;

(R)-2-methyl-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-ol;

(S)-2-methyl-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-ol;

(3-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)oxetan-3-yl)methanol;

(S)-5-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)pyrrolidin-2-one;

(R)-5-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)pyrrolidin-2-one;

3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-ol;

2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethanol;

(R)-4-(4-(4-(1-(sec-butyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-

yl)tetrahydro-2H-thiopyran 1,1-dioxide;

6-(1-(2-(methylsulfonyl)ethyl)-1H-pyrazol-4-yl)-4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

N,N-dimethyl-2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethanesulfonamide;

2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethanesulfonamide;

4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)-6-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

4-(1-isopropyl-1H-pyrazol-4-yl)-6-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

(R)-4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)-6-(1-(pyrrolidin-2-ylmethyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

(S)-4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)-6-(1-(pyrrolidin-2-ylmethyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

(R)-4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)-6-(1-(piperidin-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

(S)-3-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)morpholine;

1-(4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)piperidin-1-yl)ethanone;

6-(1-(1-(methylsulfonyl)piperidin-4-yl)-1H-pyrazol-4-yl)-4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

2-methoxy-1-(4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)piperidin-1-yl)ethanone;

N-methyl-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)piperidine-1-carboxamide;

N,N-dimethyl-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)piperidine-1-carboxamide;

2-amino-1-(4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine-6-yl)-1H-pyrazol-1-yl)piperidin-1-yl)ethanone;

6-(1-(1-(methylsulfonyl)azetidin-3-yl)-1H-pyrazol-4-yl)-4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

1-(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)ethanone;

N-methyl-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-

1-yl)azetidine-1-carboxamide;

N,N-dimethyl-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidine-1-carboxamide;

Bis-N,N-dimethyl-P-(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)phosphonic amide;

2-methyl-1-(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)propan-1-one;

cyclopropyl(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)methanone;

2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine-4-yl)-1H-pyrazol-1-yl)butanoic acid;

2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)butan-1-ol;

2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)propan-1-ol;

3-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)pentan-1-ol;

4-(1-(3-ethyl-1-((trifluoromethyl)sulfonyl)azetidin-3-yl)-1H-pyrazol-4-yl)-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

6-(1-methyl-1H-pyrazol-4-yl)-4-(1-(1-methylcyclopentyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

6-(1-methyl-1H-pyrazol-4-yl)-4-(1-(3-methylpentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

(2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)cyclopentyl)methanol;

6-(1-methyl-1H-pyrazol-4-yl)-4-(1-(2-methylcycloheptyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

2-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)cyclopentanol;

(R)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(S)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(S)-3-methyl-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-2,3-diol;

(R)-3-methyl-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-2,3-diol;

3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(2R,3R)-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-2,3-diol;

2-methyl-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

2-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)propane-1,3-diol;

(S)-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-1,2-diol;

4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-1,3-diol;

(R)-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-1,2-diol;

(2S,3S)-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-2,3-diol;

(2R)-3-(4-(4-(1-(1-phenylpropyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(2R)-3-(4-(4-(1-(sec-butyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((S)-sec-butyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((R)-sec-butyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(S)-3-(4-(4-(1-((S)-sec-butyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(S)-3-(4-(4-(1-((R)-sec-butyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((S)-pentan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((R)-pentan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(S)-3-(4-(4-(1-((R)-pentan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((S)-4-methylpentan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(S)-3-(4-(4-(1-((S)-4-methylpentan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((R)-4-methylpentan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(S)-3-(4-(4-(1-((R)-4-methylpentan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(2R)-3-(4-(4-(1-(1-(3,3-difluorocyclobutyl)propyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((S)-3-methylbutan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,3-diol;

(S)-2-(4-(4-(1-(pentan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,3-diol;

(R)-2-(4-(4-(1-(pentan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,3-diol;

(S)-2-(4-(4-(1-(sec-butyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,3-diol;

(R)-2-(4-(4-(1-(sec-butyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,3-diol;

(S)-3-(4-(4-(1-((S)-pentan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(S)-2-(4-(4-(1-(4-methylpentan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,3-diol;

(R)-2-(4-(4-(1-(4-methylpentan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,3-diol;

(2S,3S)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-1,2-diol;

(2S,3R)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-1,2-diol;

(2R,3S)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-1,2-diol;

(2R,3R)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-1,2-diol;

(R)-3-(4-(4-(1-((1R,2S)-2-methylcyclopentyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((1S,2R)-2-methylcyclopentyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((S)-2,2-dimethylcyclopentyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((R)-2,2-dimethylcyclopentyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

N-isopropyl-2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)acetamide;

1-amino-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

(R)-1-(dimethylamino)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

(R)-1-(methylamino)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

(S)-1-(dimethylamino)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

(S)-1-(methylamino)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

(R)-1-(3-methoxyazetidin-1-yl)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

(S)-1-(3-methoxyazetidin-1-yl)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

(R)-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)-3-(pyrrolidin-1-yl)propan-2-ol;

(S)-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)-3-(pyrrolidin-1-yl)propan-2-ol;

(R)-1-methoxy-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

(S)-1-methoxy-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

(R)-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

(S)-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

4,4,4-trifluoro-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butan-2-ol;

3,3-dimethyl-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butan-2-ol;

3-methyl-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butan-2-ol;

(S)-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butan-2-ol;

(R)-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butan-2-ol;

4-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)tetrahydro-2H-pyran-4-ol;

2-methyl-1-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

trans-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclohexanol;

cis-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutanol;

(1s,3s)-3-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)cyclobutanol;

cis-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclohexanol;

((1s,3s)-3-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)cyclobutyl)methanol;

((1r,3r)-3-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)cyclobutyl)methanol;

2-methyl-2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-ol;

(S)-2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-ol;

(S)-2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-ol;

(S)-2-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)morpholine;

(R)-2-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)morpholine;

(S)-2-(dimethylamino)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-ol;

(R)-2-amino-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-ol;

(R)-2-(dimethylamino)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-ol;

(1R,2S,4s)-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclopentane-1,2-diol;

(1R,2S,4r)-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclopentane-1,2-diol;

N-(2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethyl)cyclopropanamine;

4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)-6-(1-(2-(pyrrolidin-1-yl)ethyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

(R)-6-(1-(2-(3-methoxypyrrolidin-1-yl)ethyl)-1H-pyrazol-4-yl)-4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

(S)-6-(1-(2-(3-methoxypyrrolidin-1-yl)ethyl)-1H-pyrazol-4-yl)-4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

6-(1-(2-(3-fluoroazetidin-1-yl)ethyl)-1H-pyrazol-4-yl)-4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazine;

1-(2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethyl)piperidin-4-ol;

(R)-1-(2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethyl)pyrrolidin-3-ol;

(S)-1-(2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethyl)pyrrolidin-3-ol;

(S)-1-methyl-3-((2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethyl)amino)pyrrolidin-2-one;

(R)-1-methyl-3-((2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethyl)amino)pyrrolidin-2-one;

4-(2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethyl)piperazin-2-one;

(3-((2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethyl)amino)cyclobutyl)methanol;

(1-(2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethyl)piperidin-4-yl)methanol;

1-(2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)ethyl)piperazin-2-one;

(R)-2-methoxy-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-amine;

(S)-2-methoxy-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-amine;

2-(4-(4-(1-((1R,2R)-2-methylcyclohexyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,3-diol;

(R)-3-(4-(4-(1-((1R,2R)-2-methylcyclohexyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(S)-3-(4-(4-(1-((1R,2R)-2-methylcyclohexyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(1R,2R)-2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclopentanol;

(1S,2S)-2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclopentanol;

(2S,3S)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butan-2-ol;

(2R,3R)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butan-2-ol;

(2R,3S)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butan-2-ol;

(2S,3R)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butan-2-ol;

(3S,4R)-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)tetrahydrofuran-3-ol;

(3R,4S)-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)tetrahydrofuran-3-ol;

trans-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutanol;

(1s,3s)-1-methyl-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutanol;

(1s,3s)-1-(hydroxymethyl)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutanol;

(1r,3r)-1-(hydroxymethyl)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutanol;

(trans-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutyl)methanol;

(cis-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutyl)methanol;

(1r,3r)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutanecarboxamide;

(1s,3s)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutanecarboxamide;

(1r,3r)-N,N-dimethyl-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutanecarboxamide;

(1s,3s)-N,N-dimethyl-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutanecarboxamide;

(1r,3r)-N-(2-hydroxyethyl)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutanecarboxamide;

(1s,3s)-N-(2-hydroxyethyl)-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclobutanecarboxamide;

(S)-2-hydroxy-1-(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)propan-1-one;

2-hydroxy-1-(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)ethanone;

(R)-2-hydroxy-1-(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)propan-1-one;

2-hydroxy-2-methyl-1-(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)propan-1-one;

(1-hydroxycyclopropyl)(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)methanone;

(cis-3-hydroxycyclobutyl)(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)methanone;

(trans-3-hydroxycyclobutyl)(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)methanone;

2-(3-hydroxyazetidin-1-yl)-1-(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)ethanone;

1-(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)-2-(pyrrolidin-1-yl)ethanone;

N,N-dimethyl-2-oxo-2-(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)acetamide;

(S)-3-amino-2-methyl-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butan-2-ol;

4-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)piperidin-4-ol;

1-(4-hydroxy-4-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)piperidin-1-yl)ethanone;

2-amino-1-(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)ethanone;

2-(methylamino)-1-(3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)azetidin-1-yl)ethanone;

(3R,4R)-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)piperidin-3-ol;

(1S,2R)-2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclopentanol;

(1R,2S)-2-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)cyclopentanol;

2,2-dimethyl-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-1-ol;

(1-((4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)methyl)cyclopropyl)methanol;

(2R)-3-(4-(4-(1-(1,1,1-trifluorobutan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((R)-4,4,4-trifluorobutan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((S)-4,4,4-trifluorobutan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((R)-1-cyclobutylpropyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((S)-1-cyclobutylpropyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((S)-2,2-difluoropentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((R)-2,2-difluoropentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(S)-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-1,3-diol;

(R)-4-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)butane-1,3-diol;

(R)-2-methyl-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(S)-2-methyl-3-(4-(4-(1-(pentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((R)-1-((S)-2,2-difluorocyclopropyl)propyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((S)-1-cyclopropylbutan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((R)-1-cyclopropylbutan-2-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((1S,2R)-2-ethylcyclopentyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((1R,2S)-2-ethylcyclopentyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((R)-1,1,1-trifluoropentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((S)-1,1,1-trifluoropentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-2-(4-(4-(1-(1,1,1-trifluoropentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,3-diol;

(S)-2-(4-(4-(1-(1,1,1-trifluoropentan-3-yl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,3-diol;

(R)-3-(4-(4-(1-((R)-1-cyclopropylpropyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-((S)-1-cyclopropylpropyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-2-(4-(4-(1-(1-cyclopropylpropyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,3-diol;

(R)-3-(4-(4-(1-(dicyclopropylmethyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol;

(R)-3-(4-(4-(1-(cis-2-methylcyclobutyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propane-1,2-diol; and

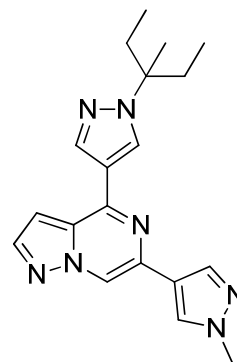
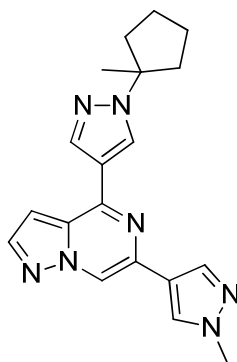
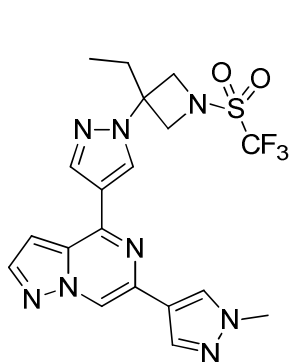
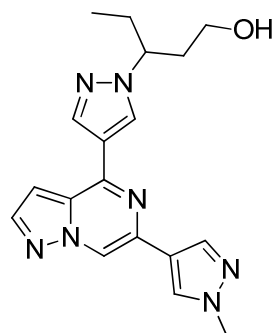
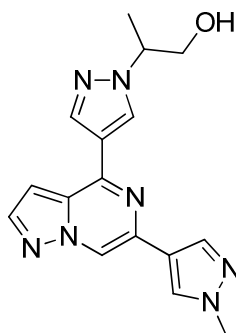
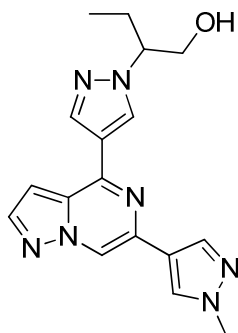
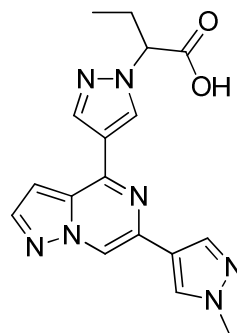
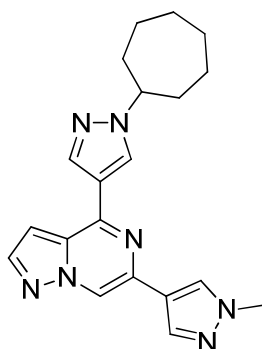
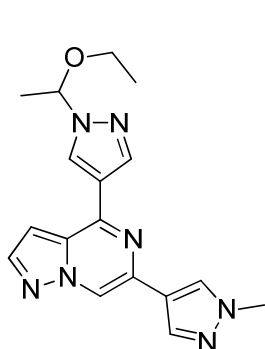
(S)-1-(4-(4-(1-((R)-1-cyclopropylpropyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazol-1-yl)propan-2-ol;

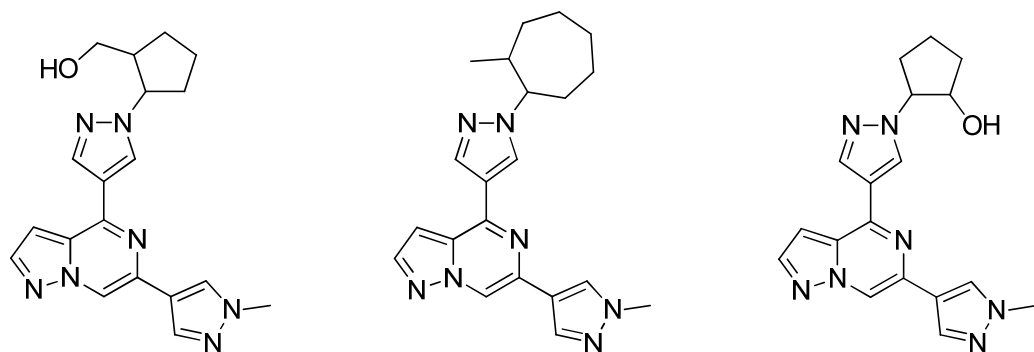
and pharmaceutically acceptable salts thereof.

12. The compound according to claim 11, wherein compound is a trifluoroacetic acid salt or a hydrochloric acid salt.

13. A pharmaceutical composition, which comprises a compound of Formula I as defined in claim 1 or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable diluent or carrier.

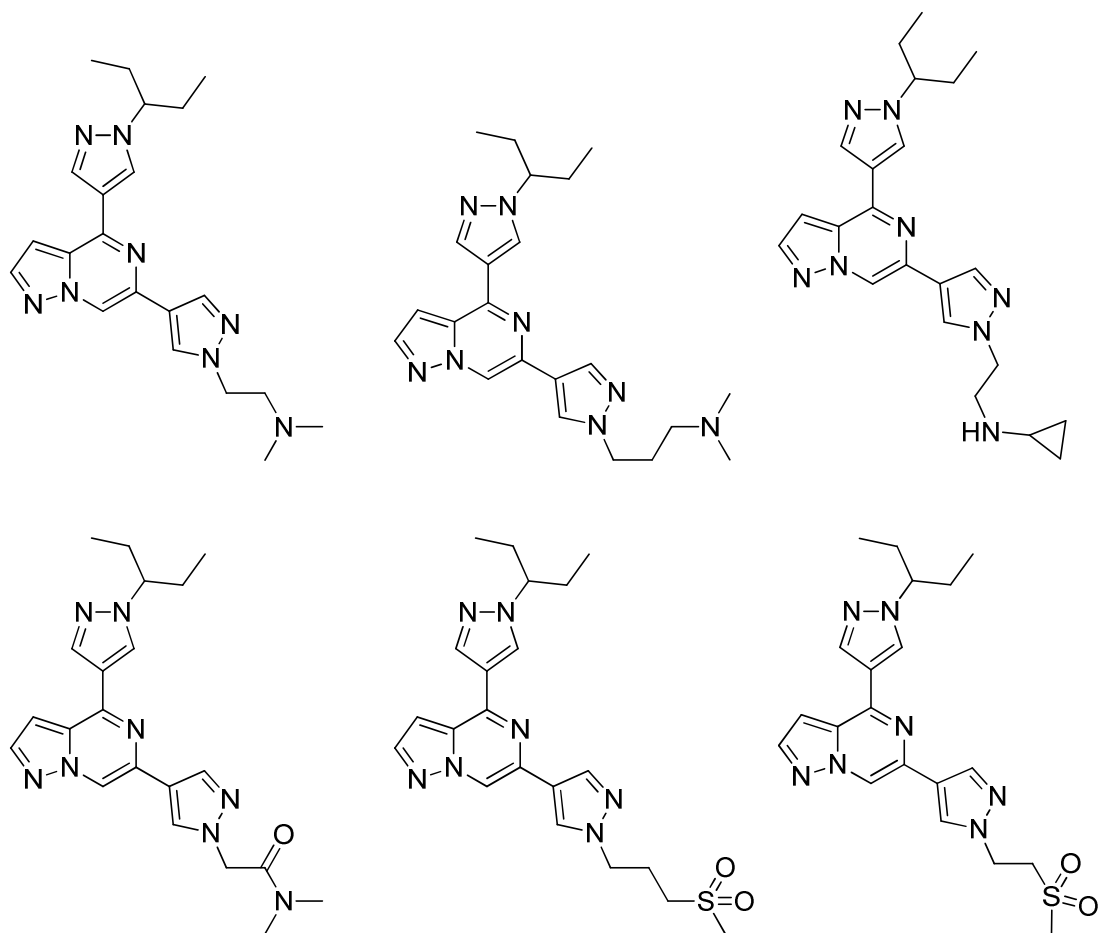
14. A compound according to claim 11, selected from:

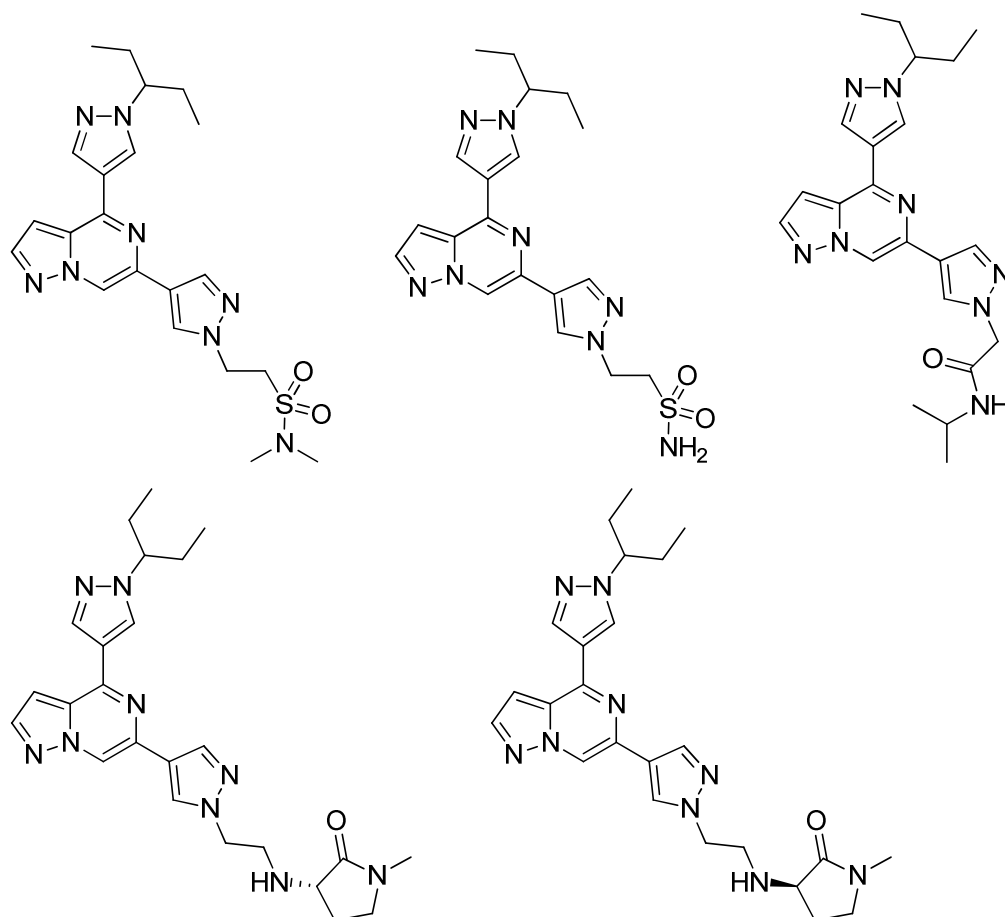




and pharmaceutically acceptable salts thereof.

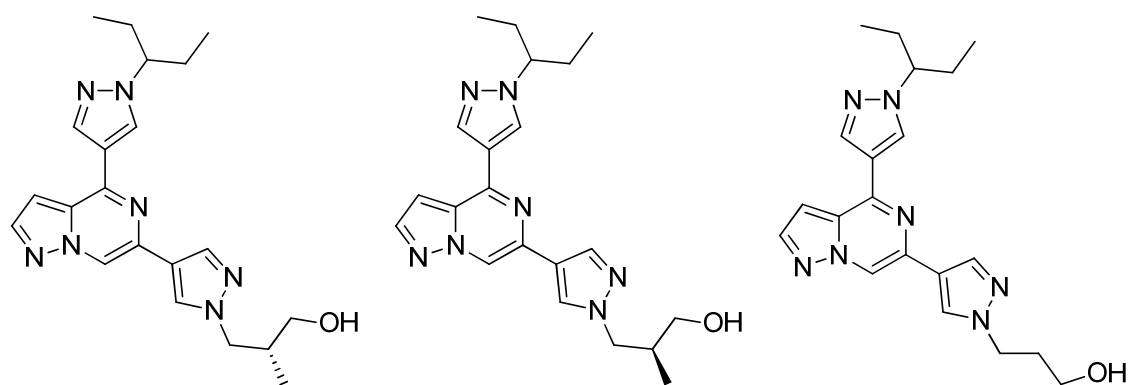
15. A compound according to claim 11, selected from:

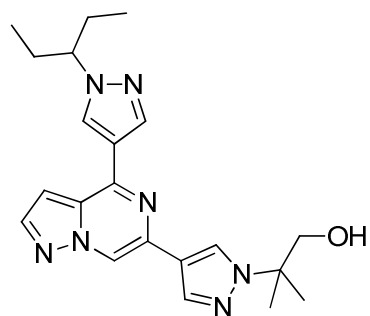
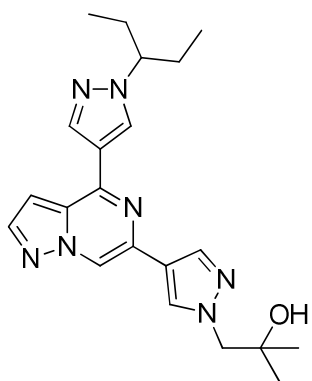
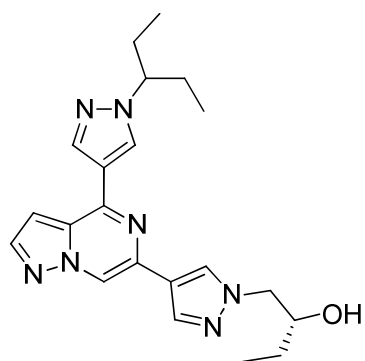
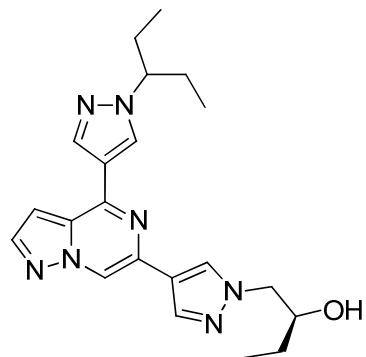
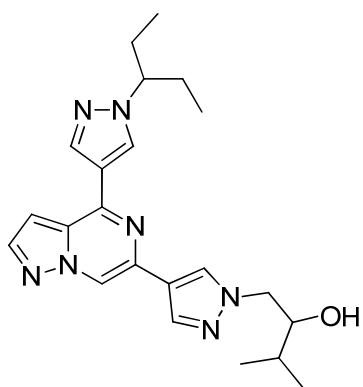
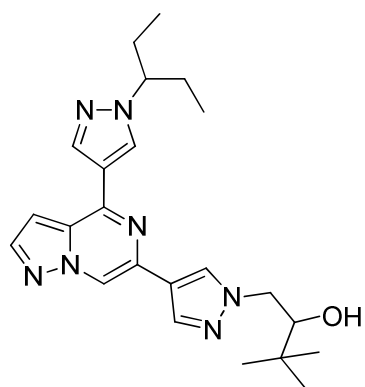
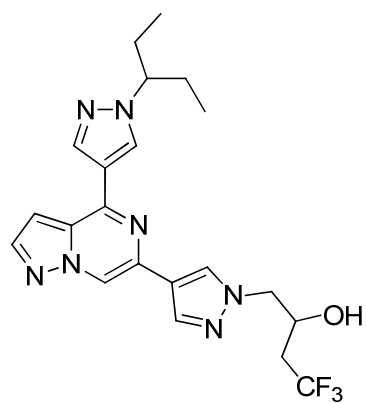
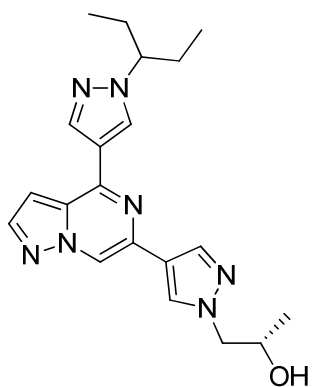
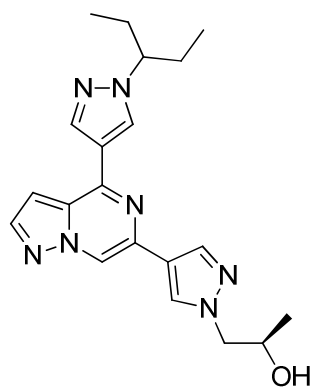
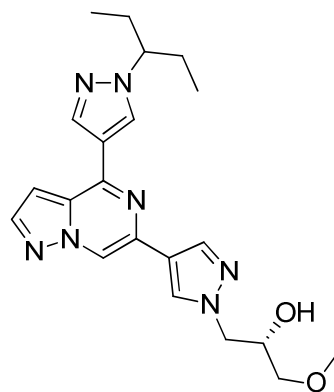
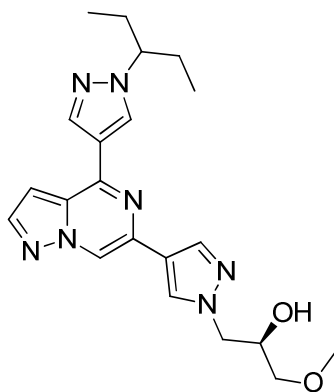
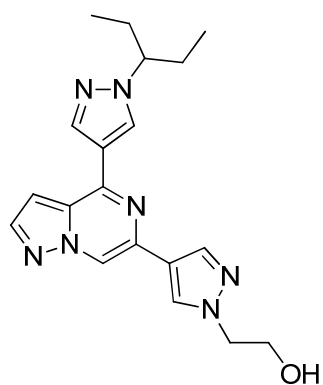


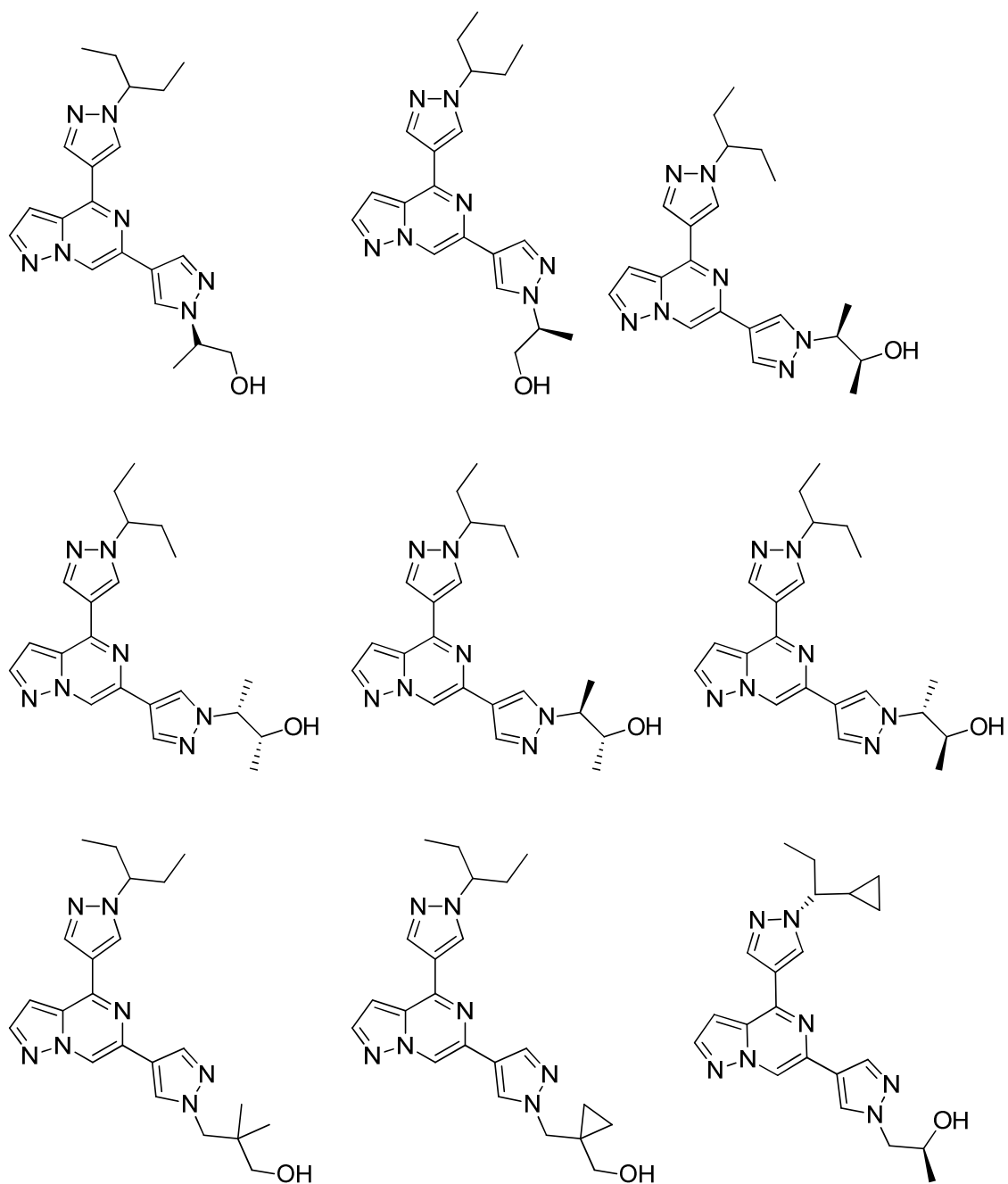


and pharmaceutically acceptable salts thereof.

16. A compound according to claim 11, selected from:

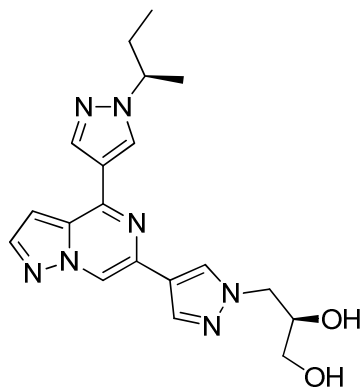
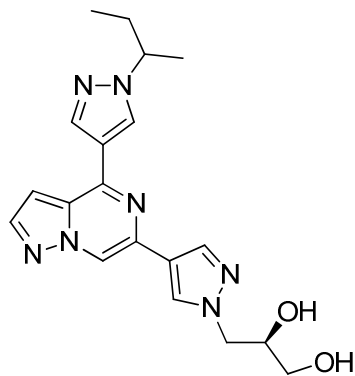
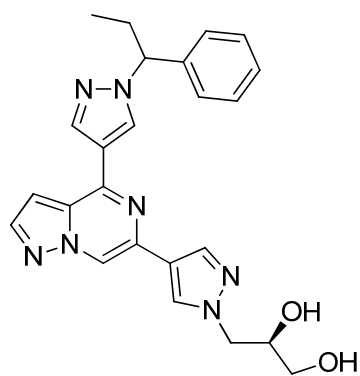
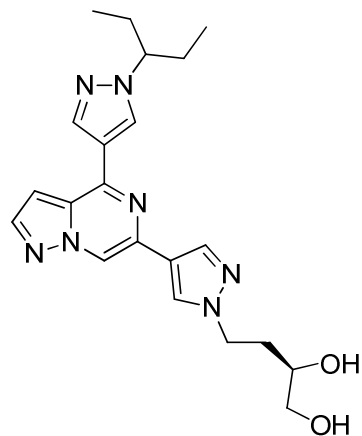
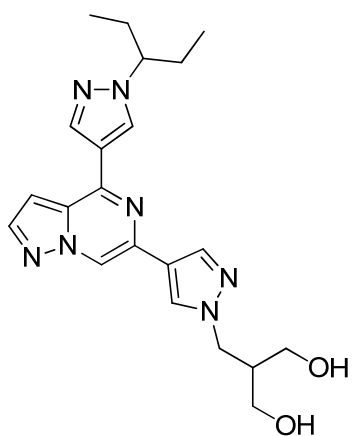
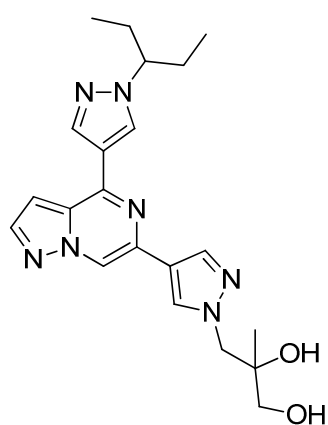
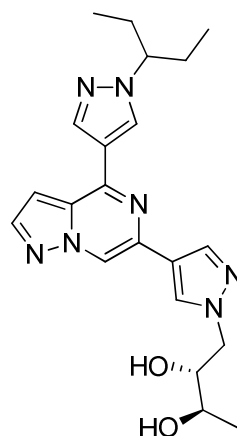
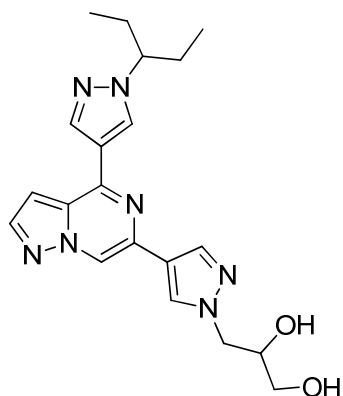
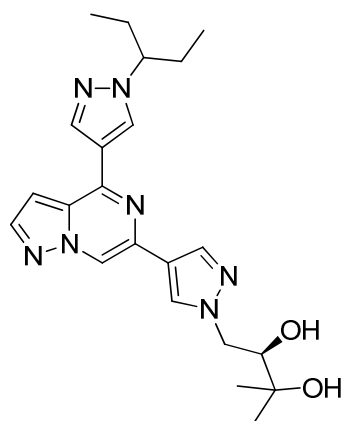
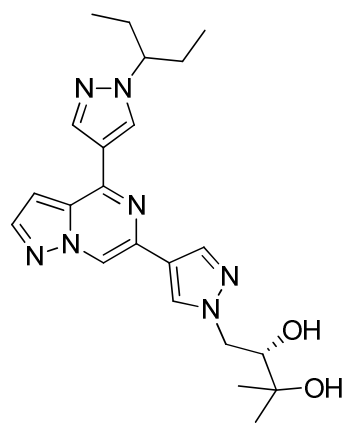
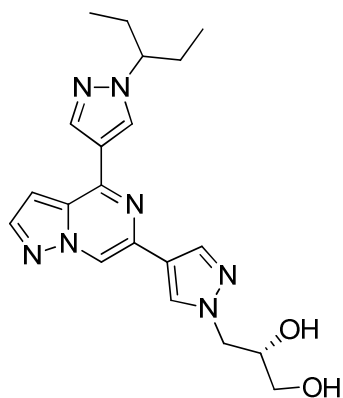
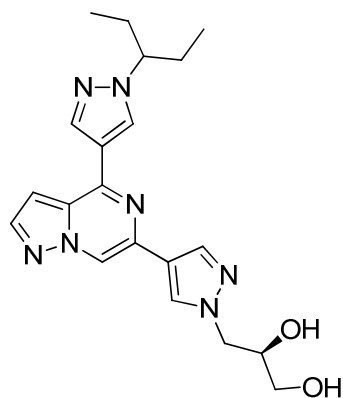


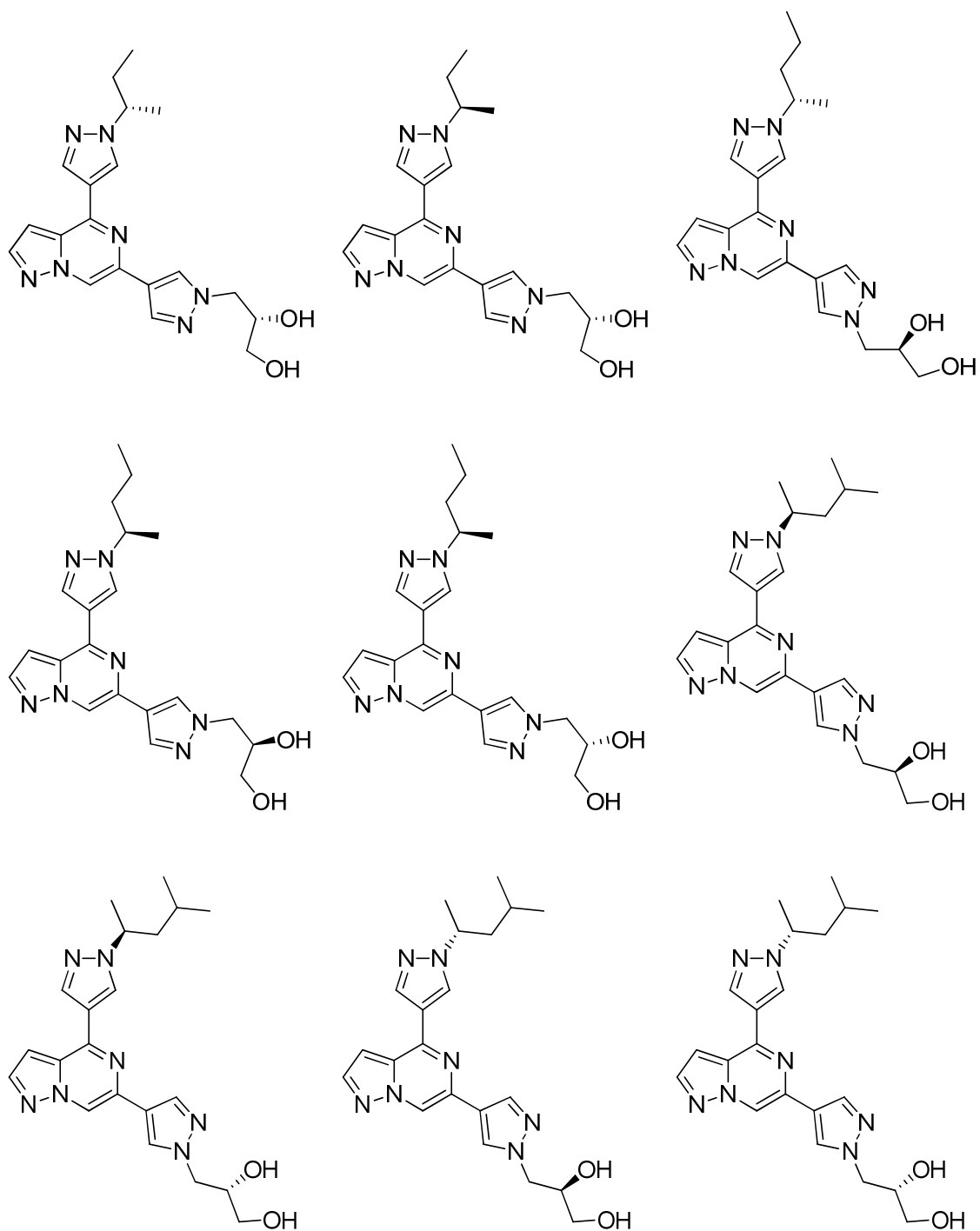


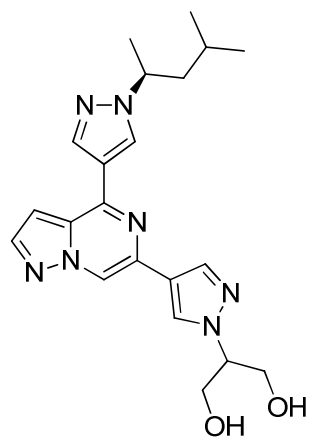
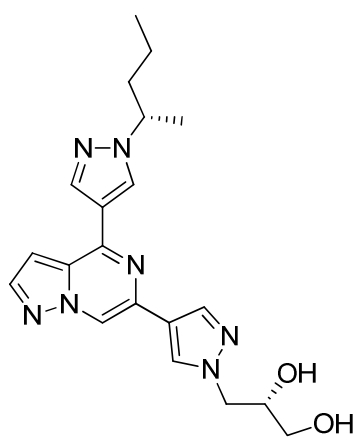
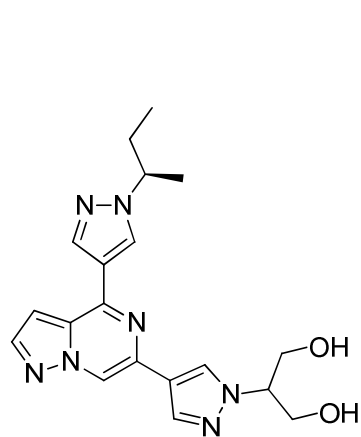
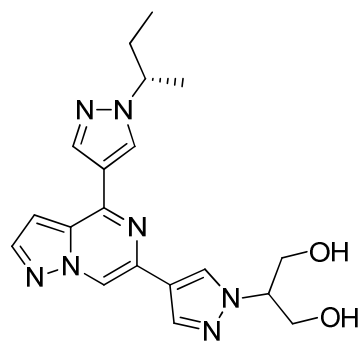
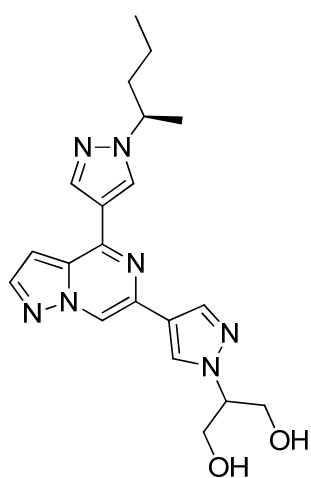
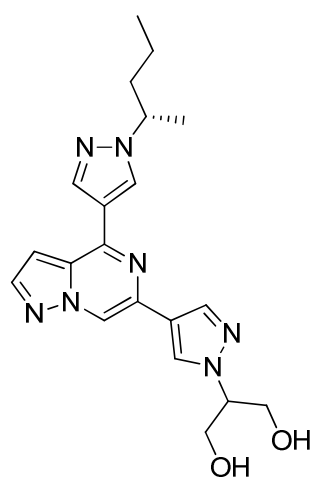
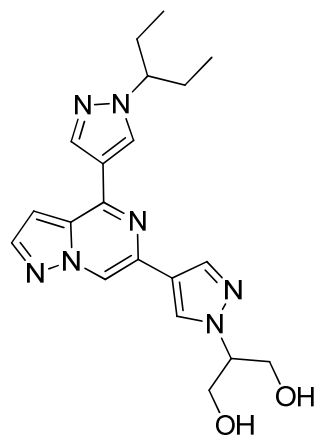
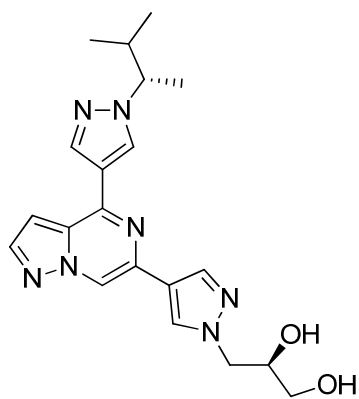
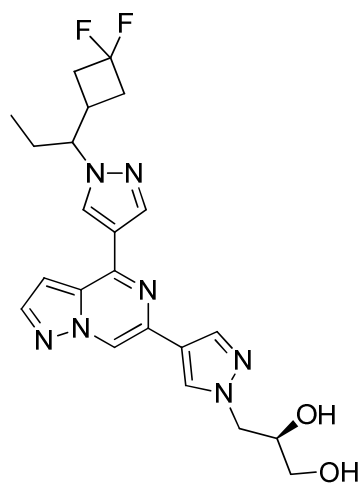


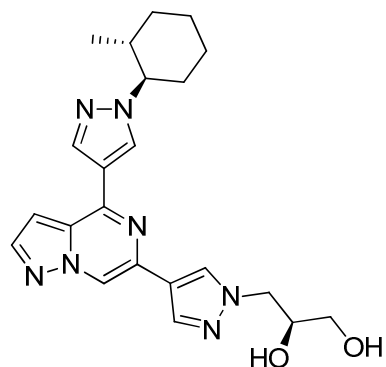
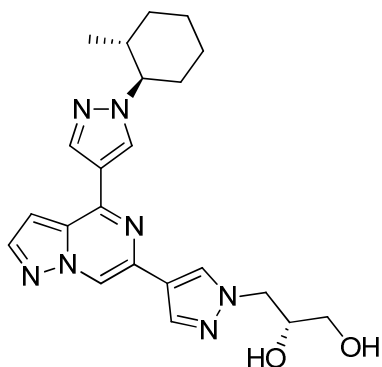
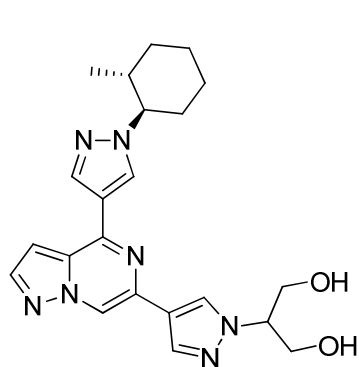
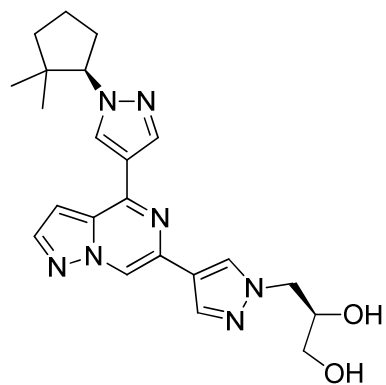
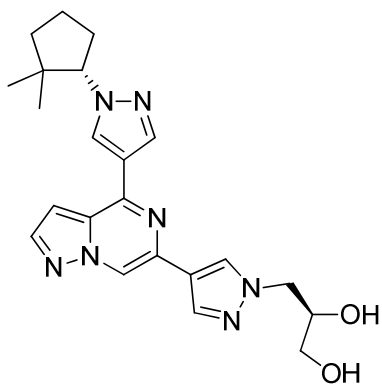
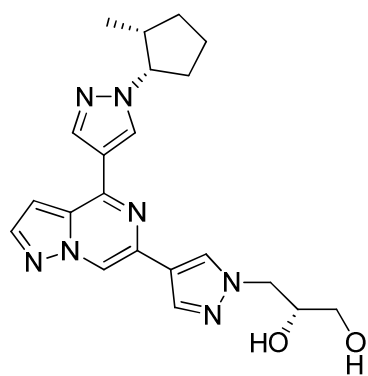
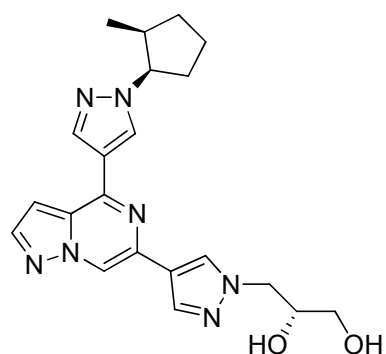
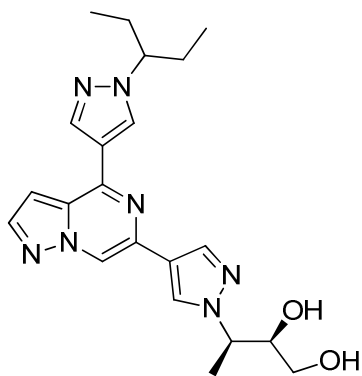
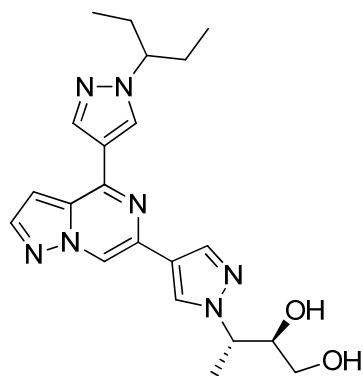
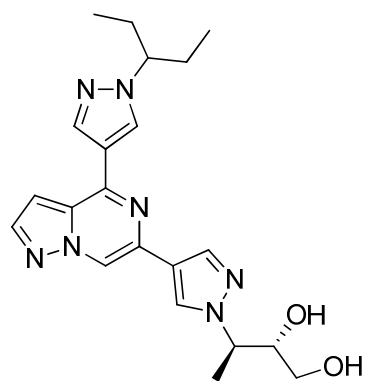
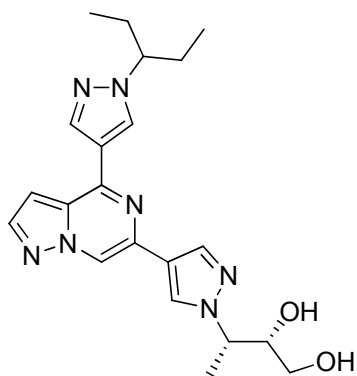
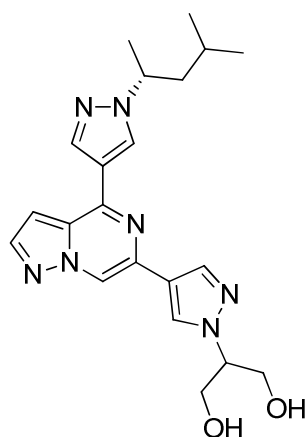
and pharmaceutically acceptable salts thereof.

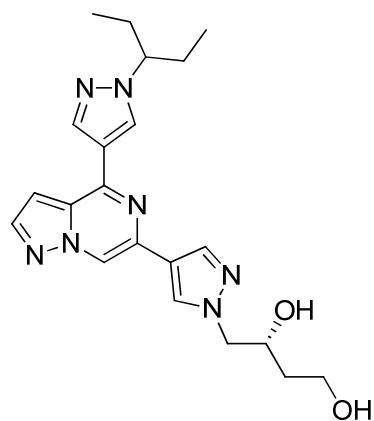
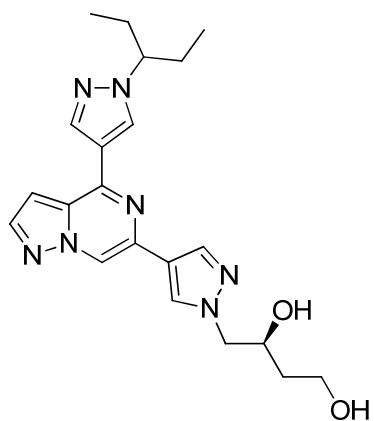
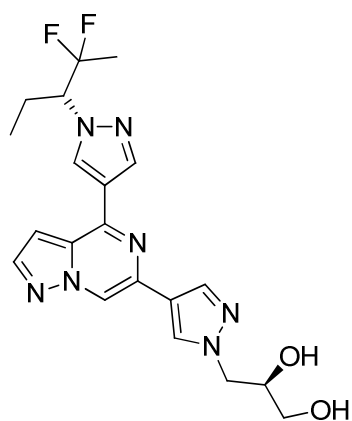
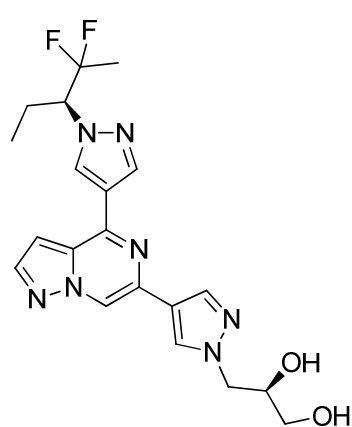
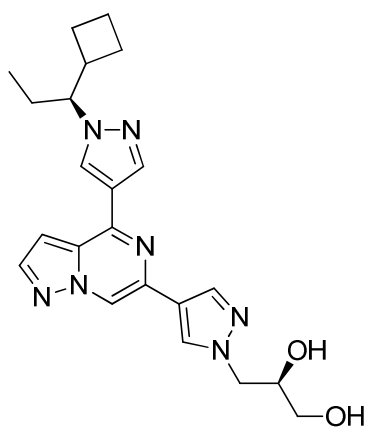
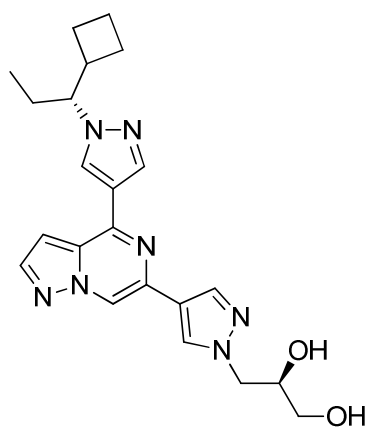
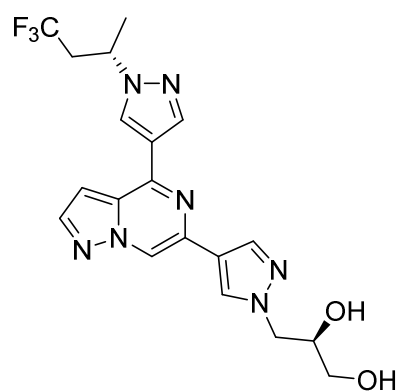
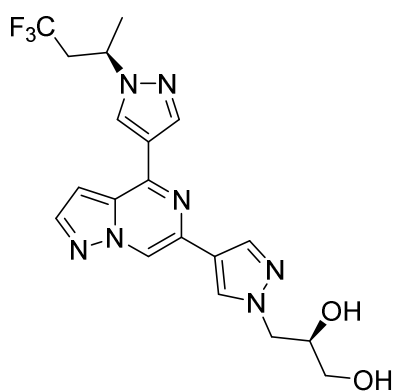
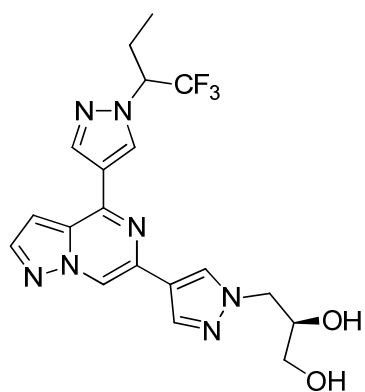
17. A compound according to claim 11, selected from:

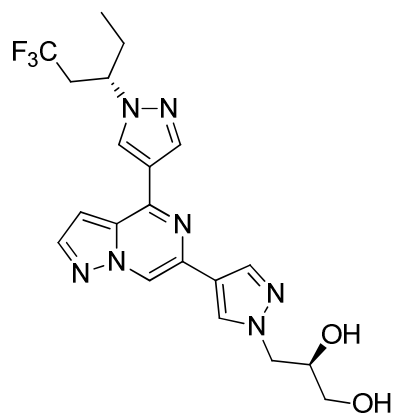
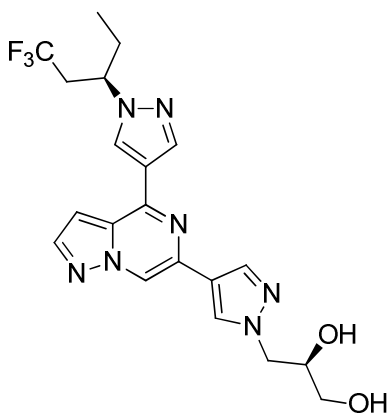
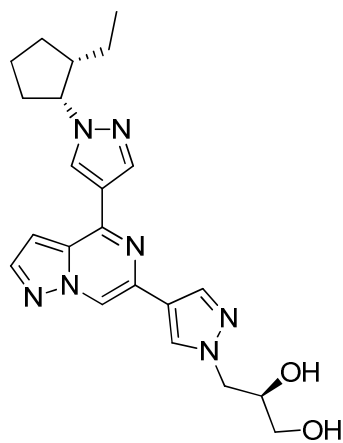
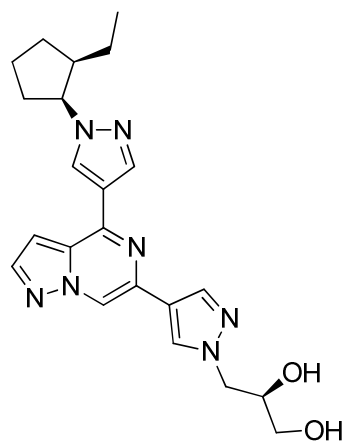
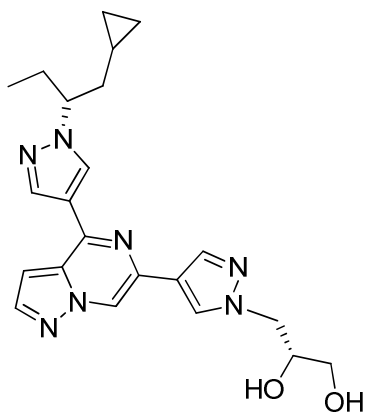
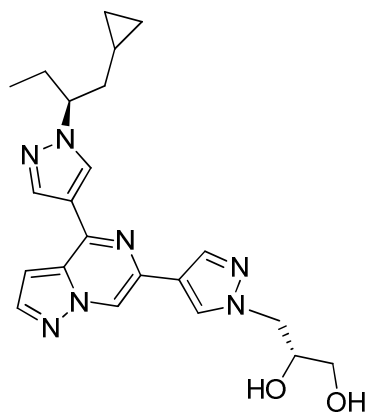
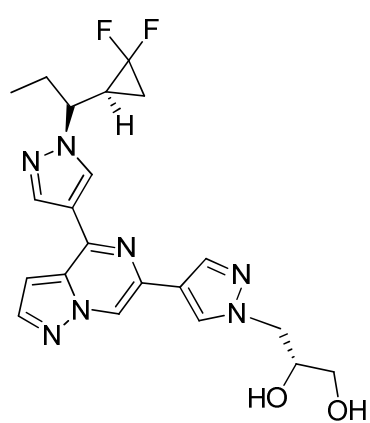
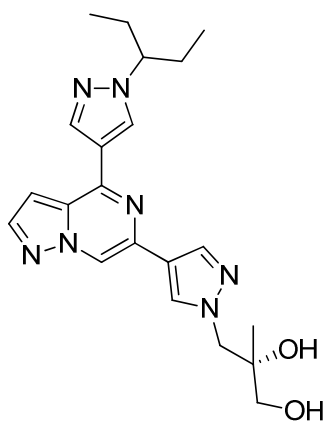
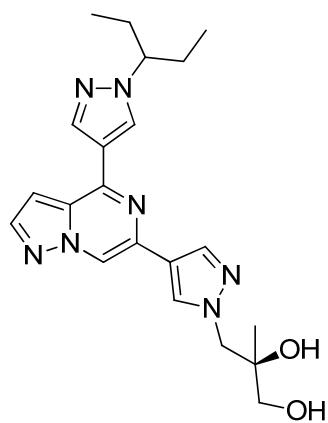


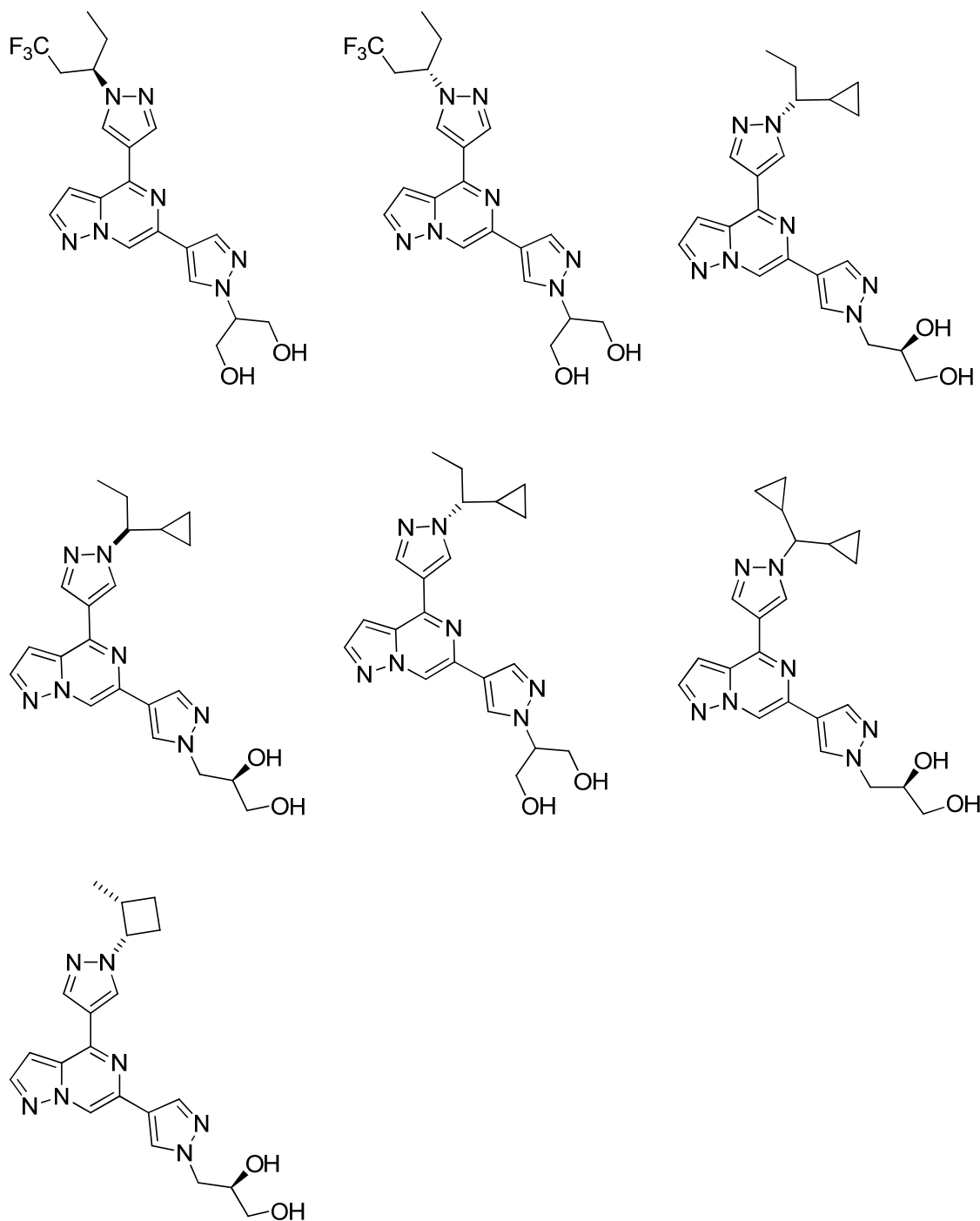






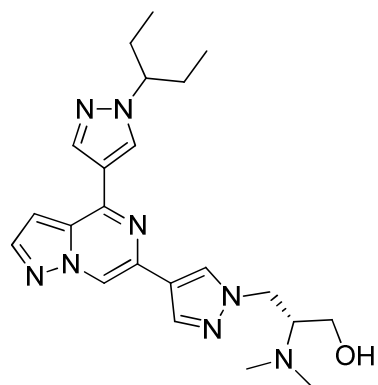
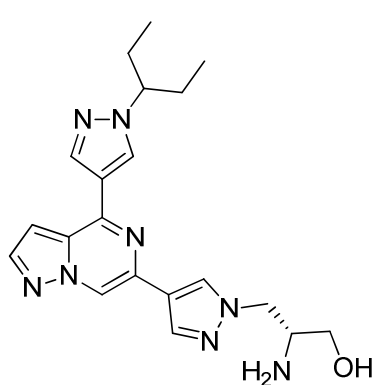
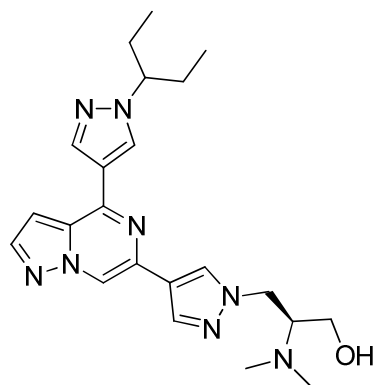
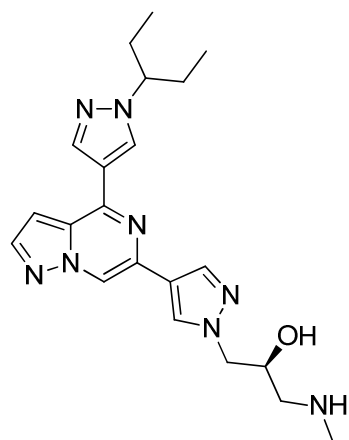
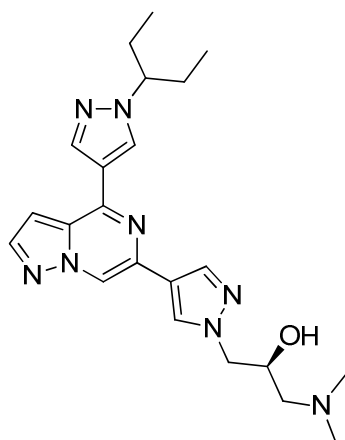
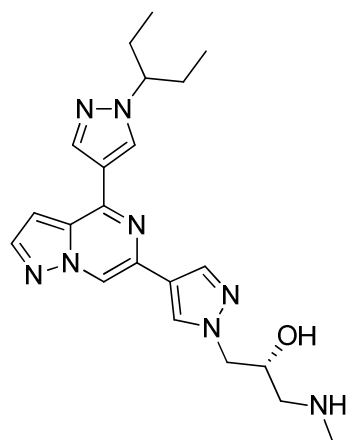
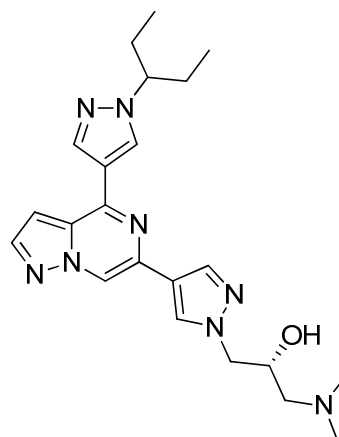
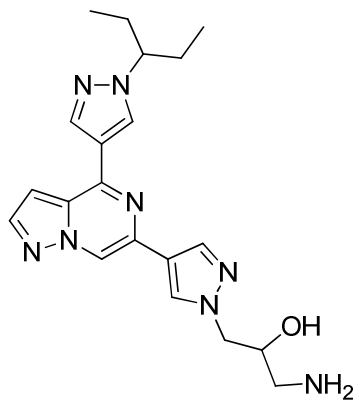
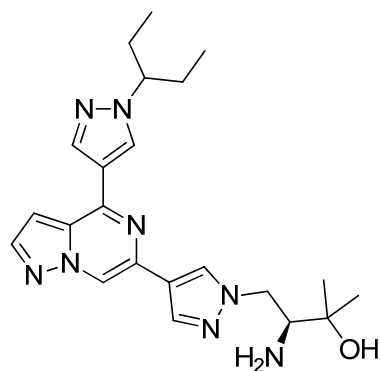


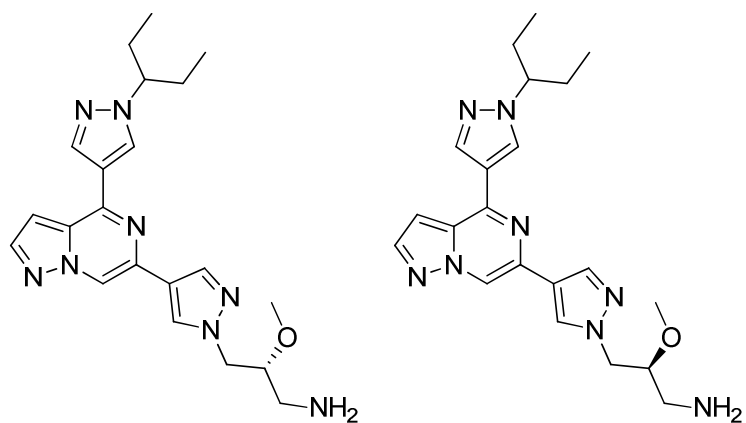




and pharmaceutically acceptable salts thereof.

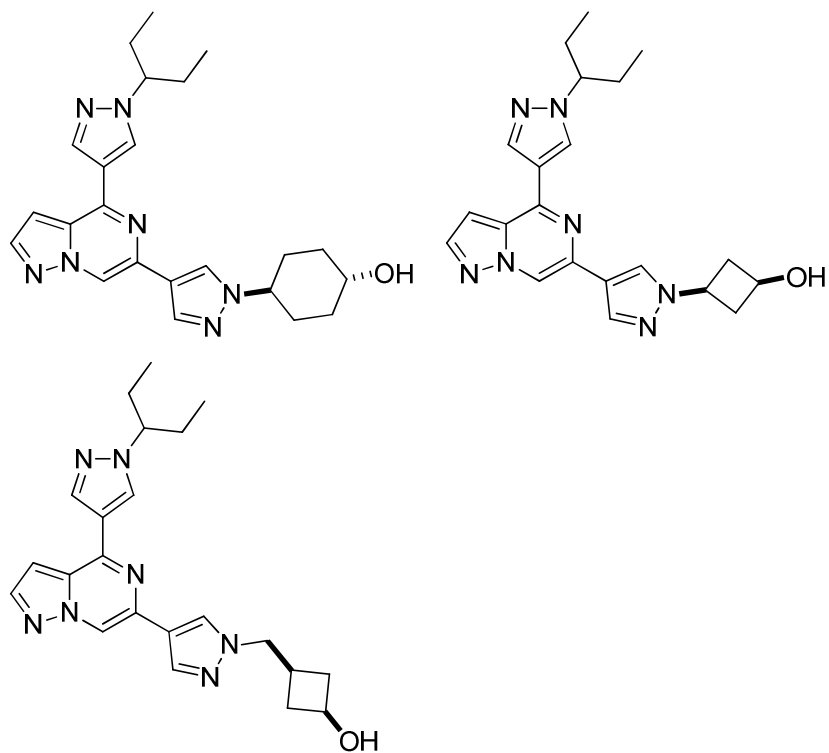
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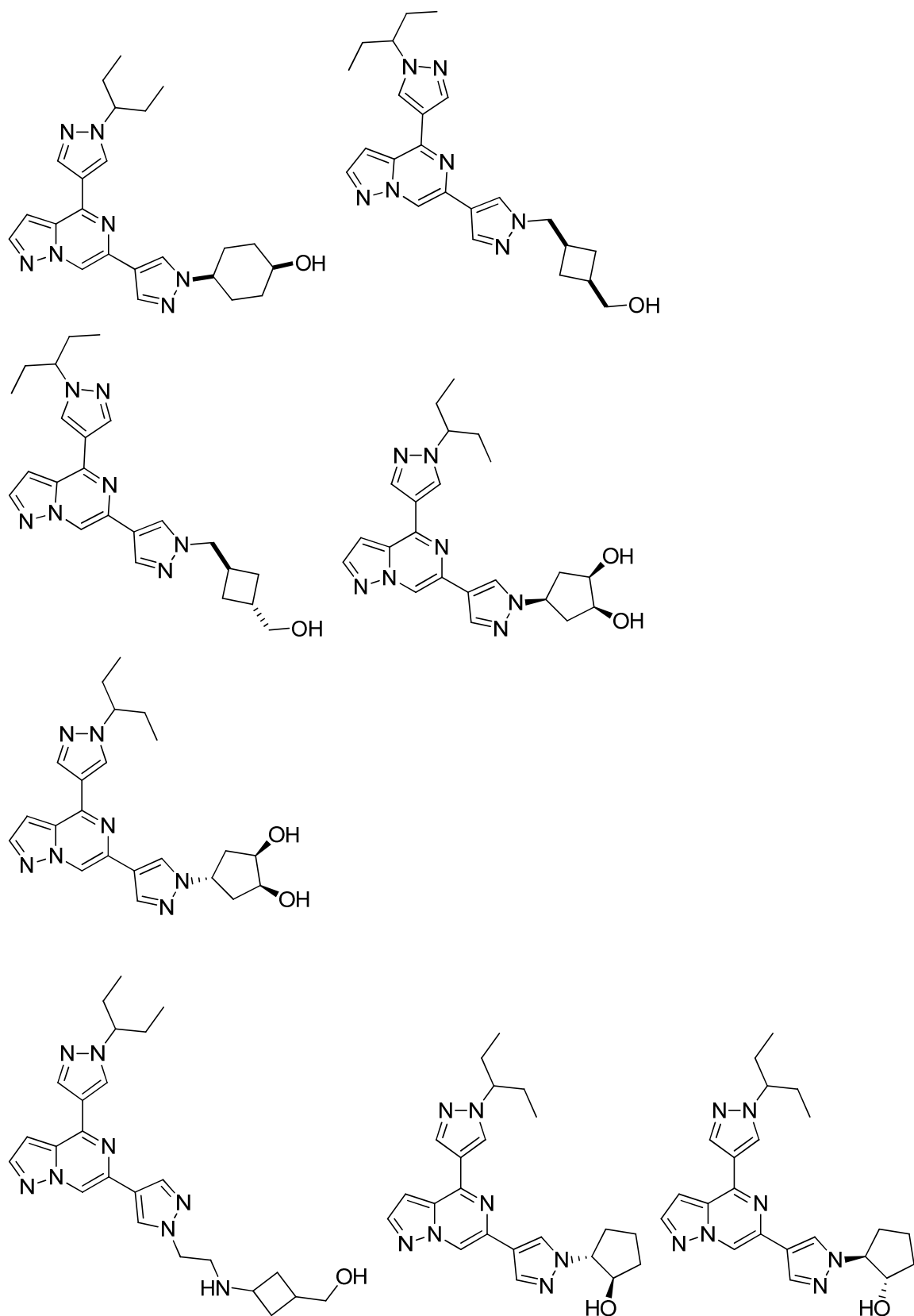


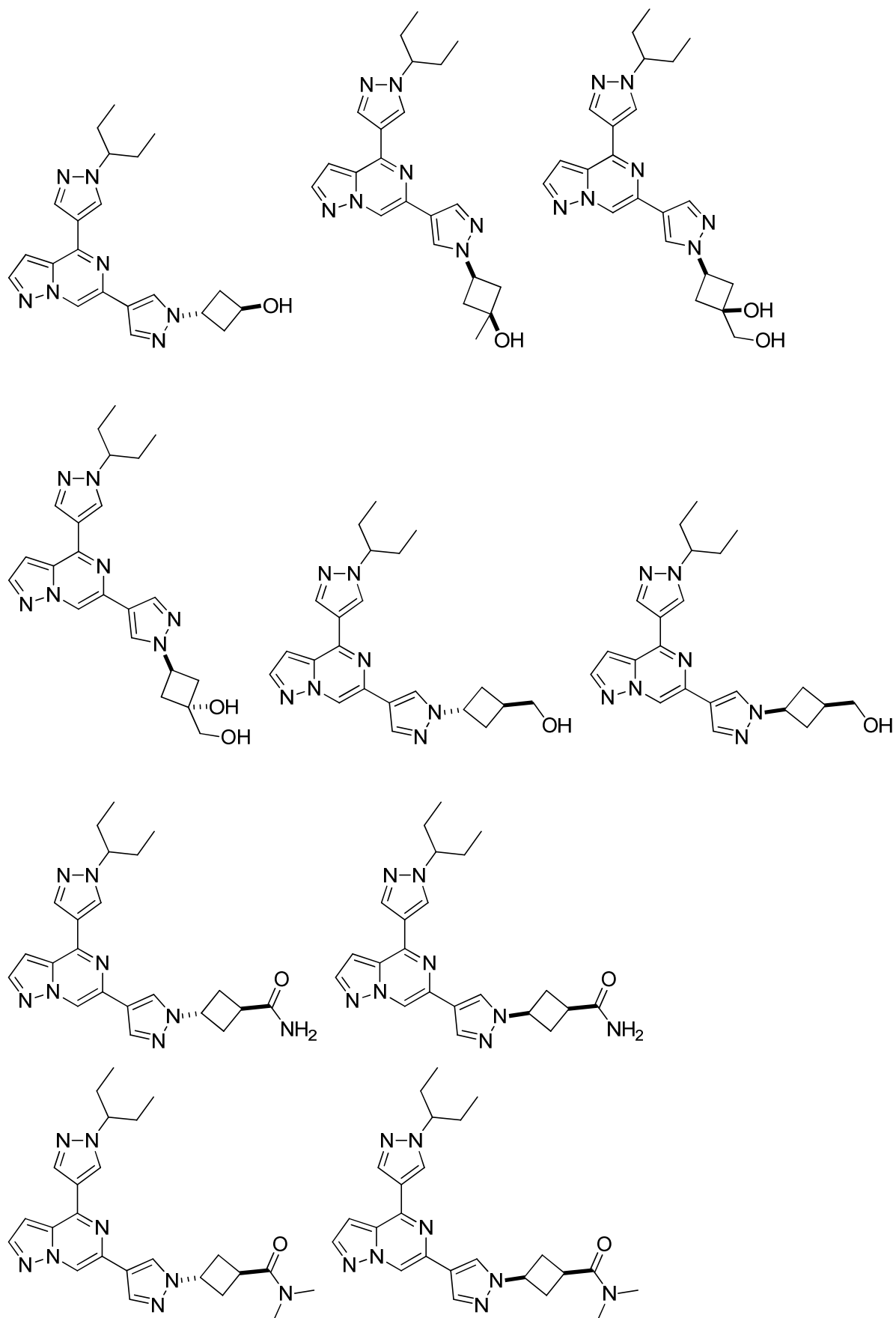


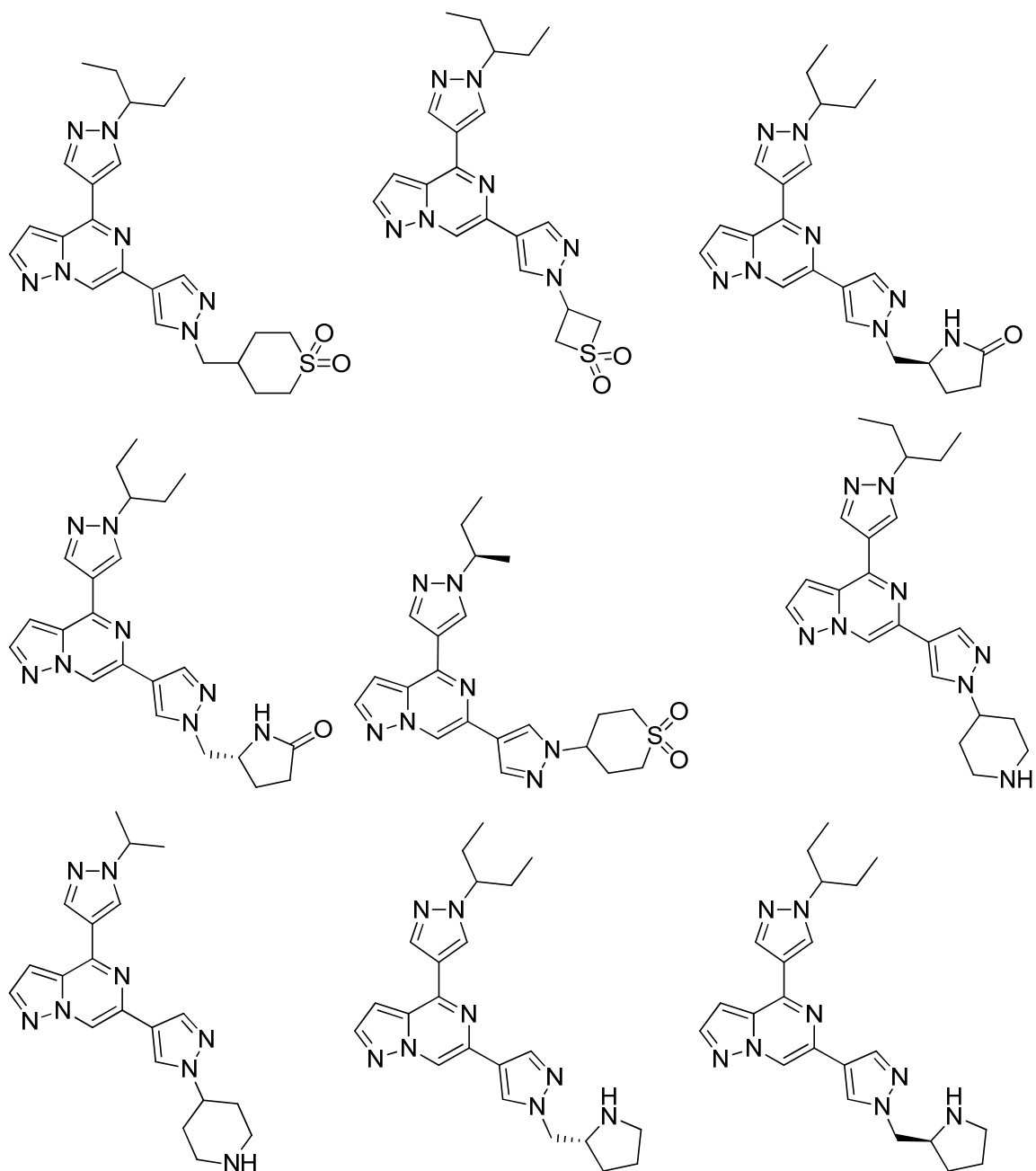
and pharmaceutically acceptable salts thereof.

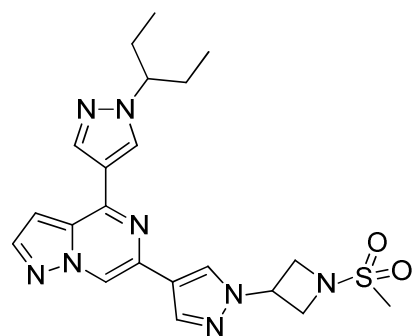
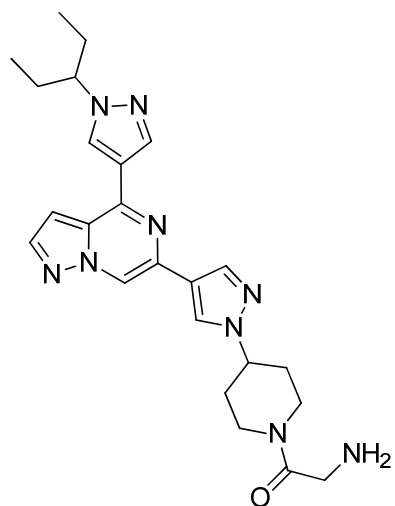
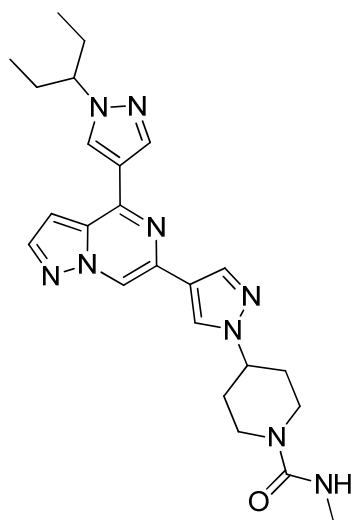
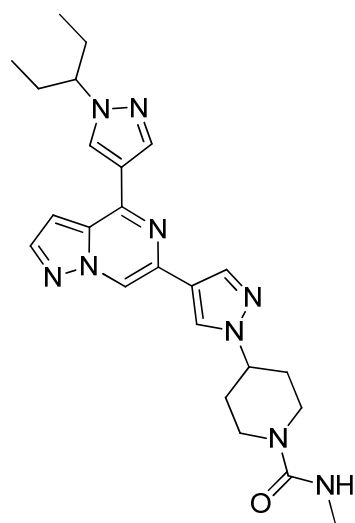
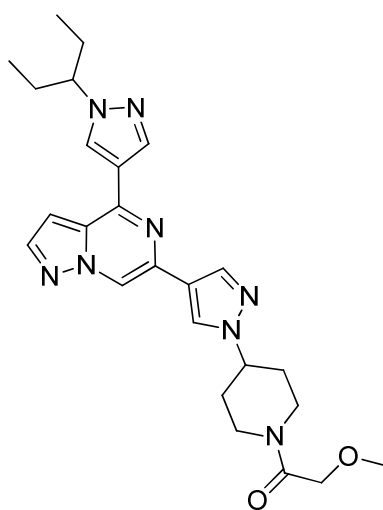
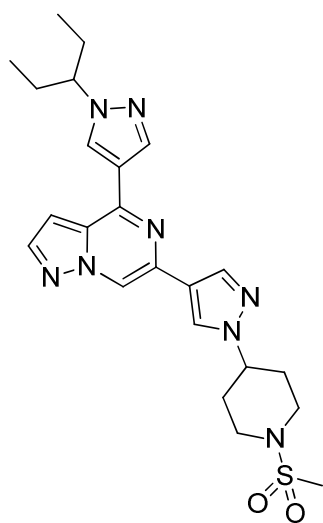
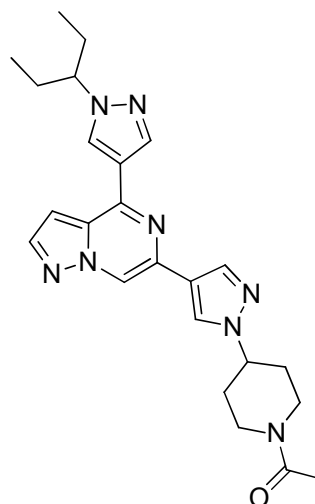
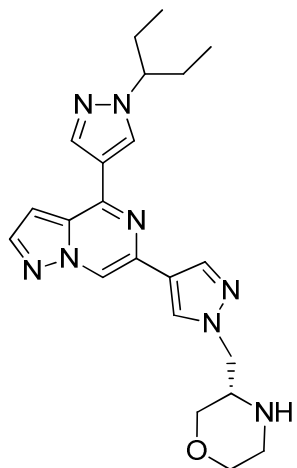
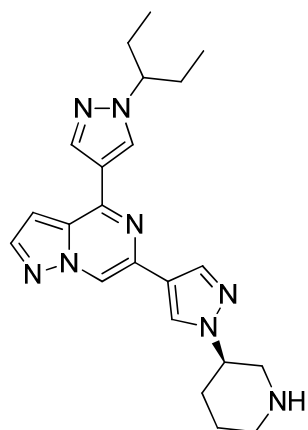
19. A compound according to claim 11, selected from:

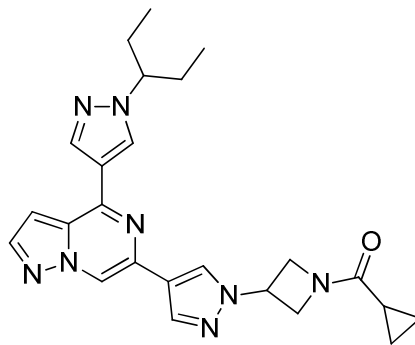
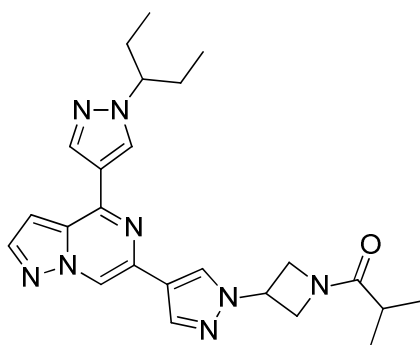
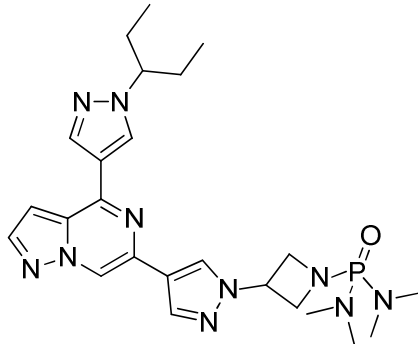
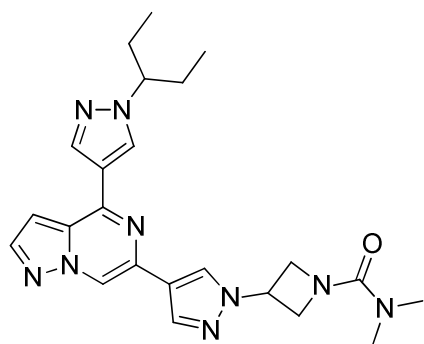
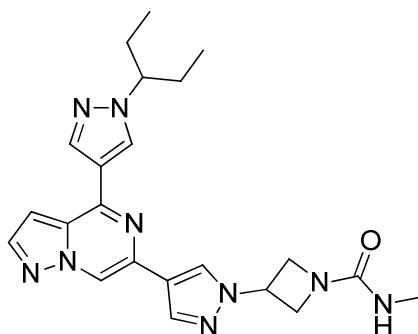
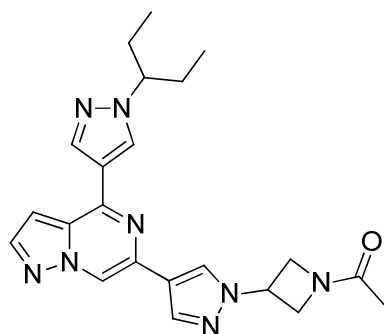


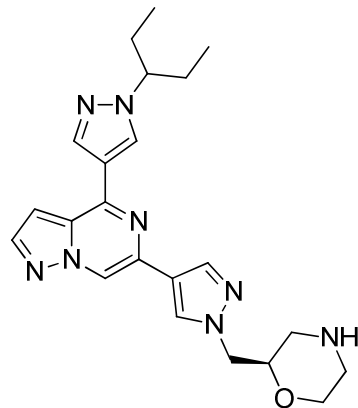
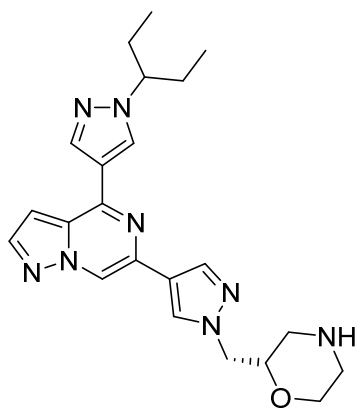
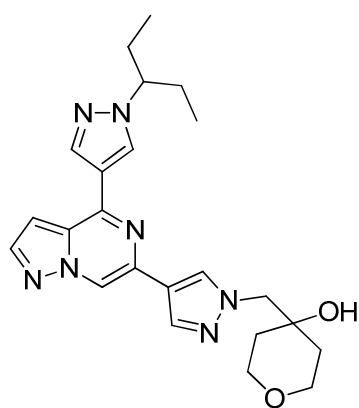
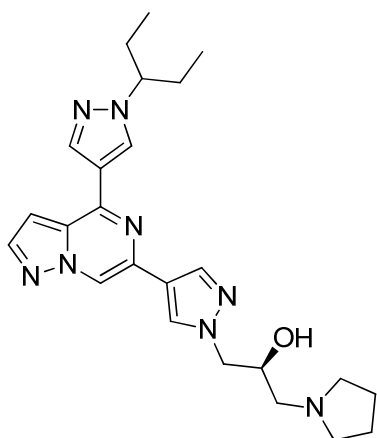
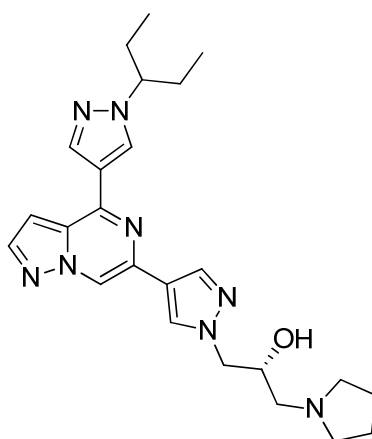
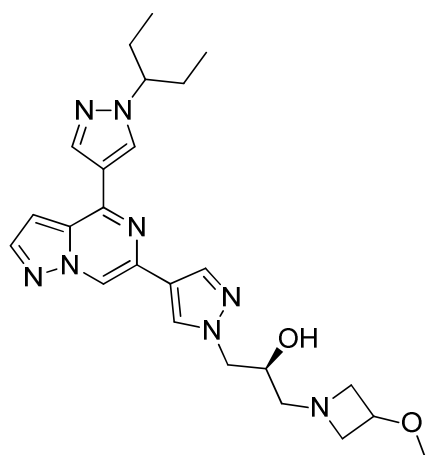


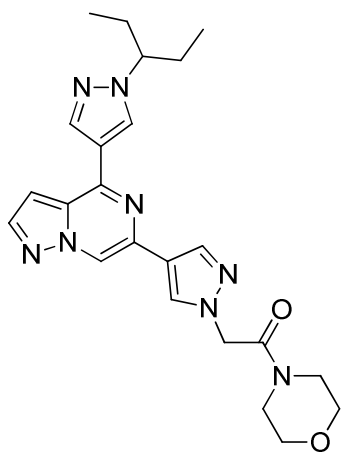
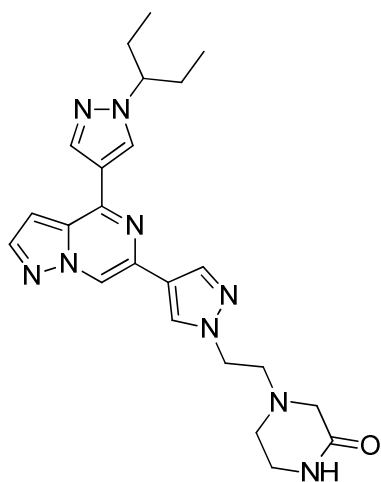
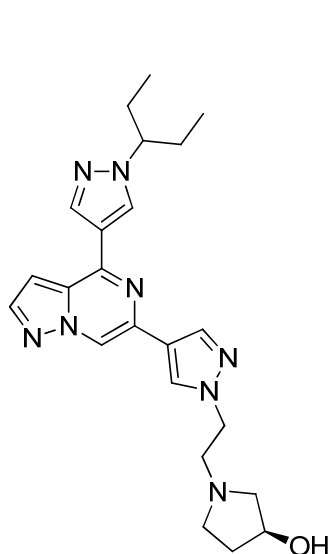
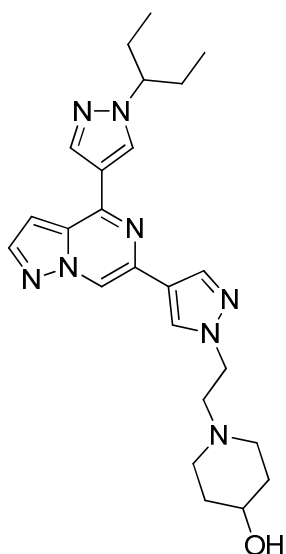
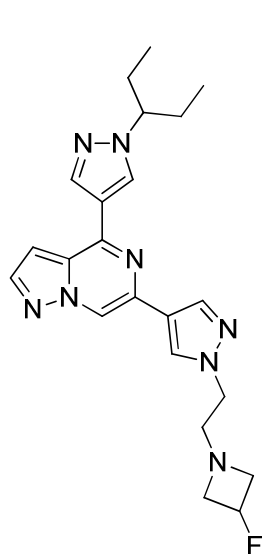
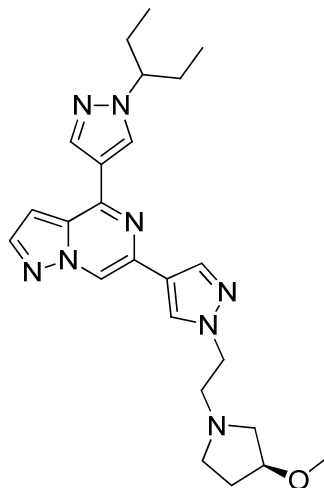
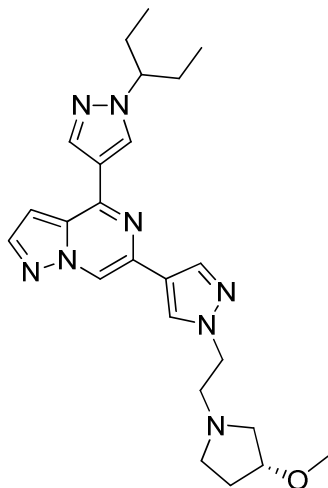
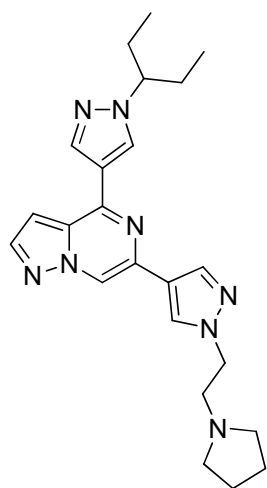


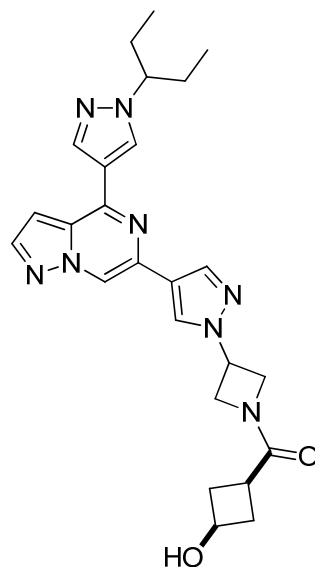
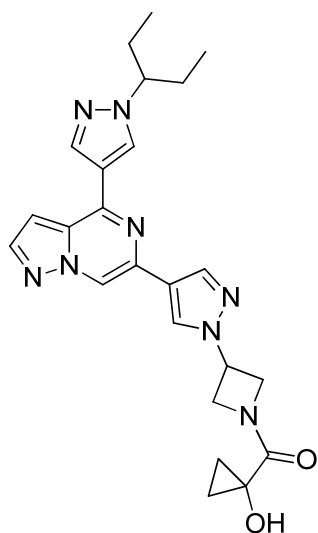
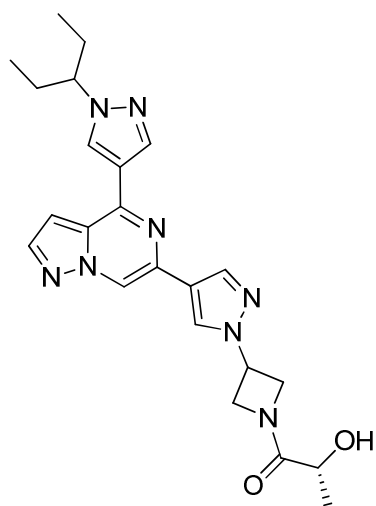
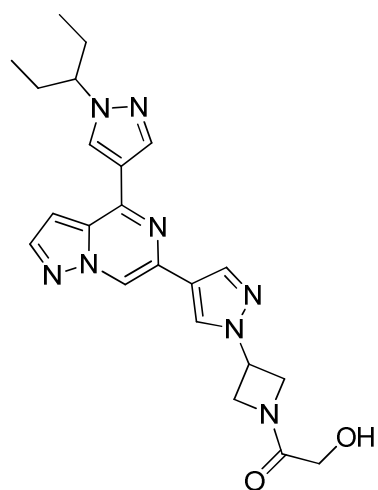
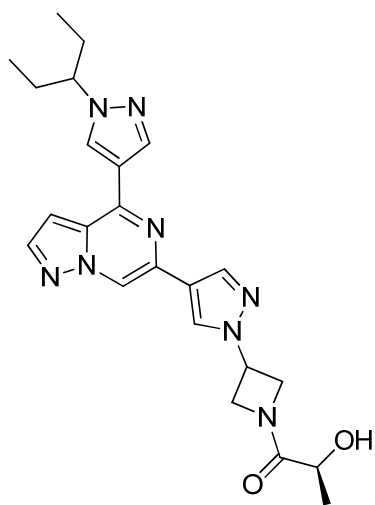
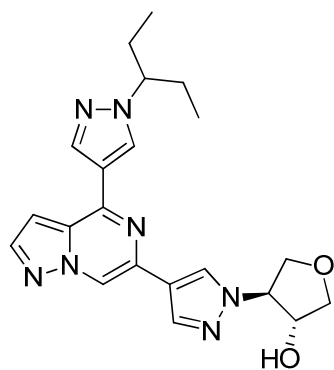
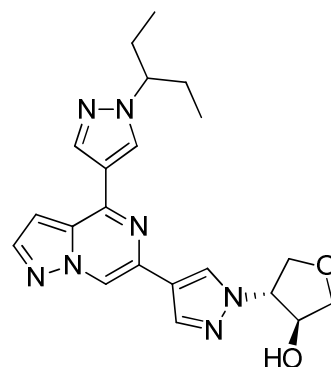
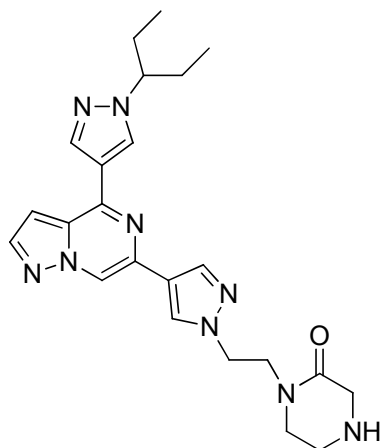
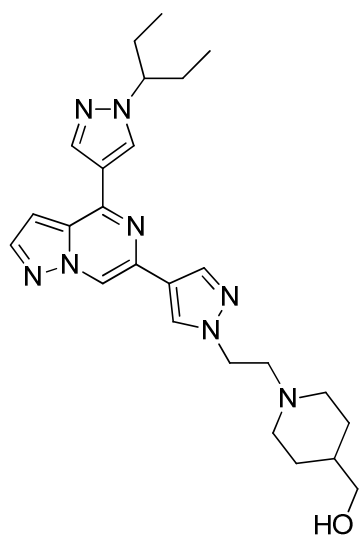


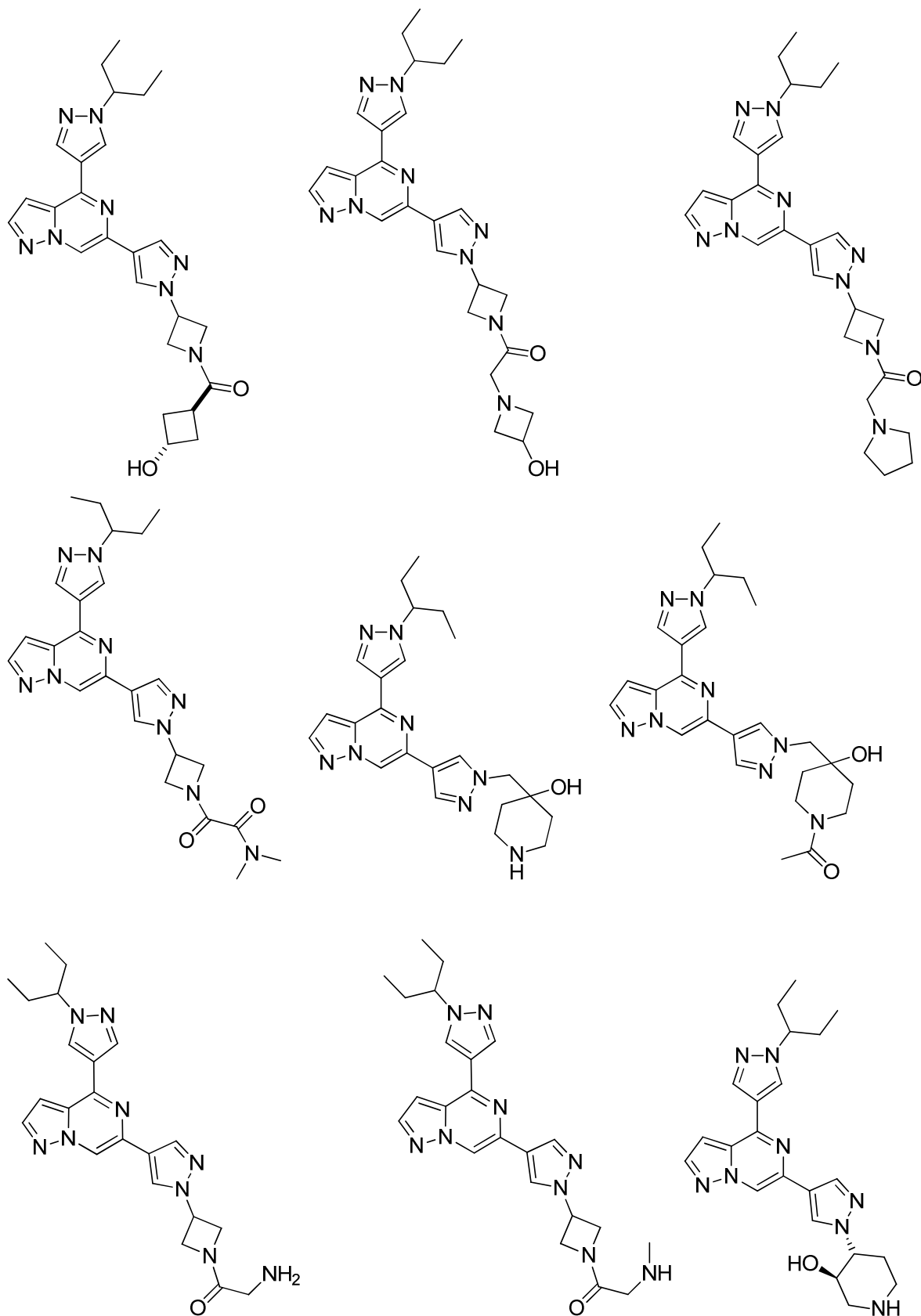


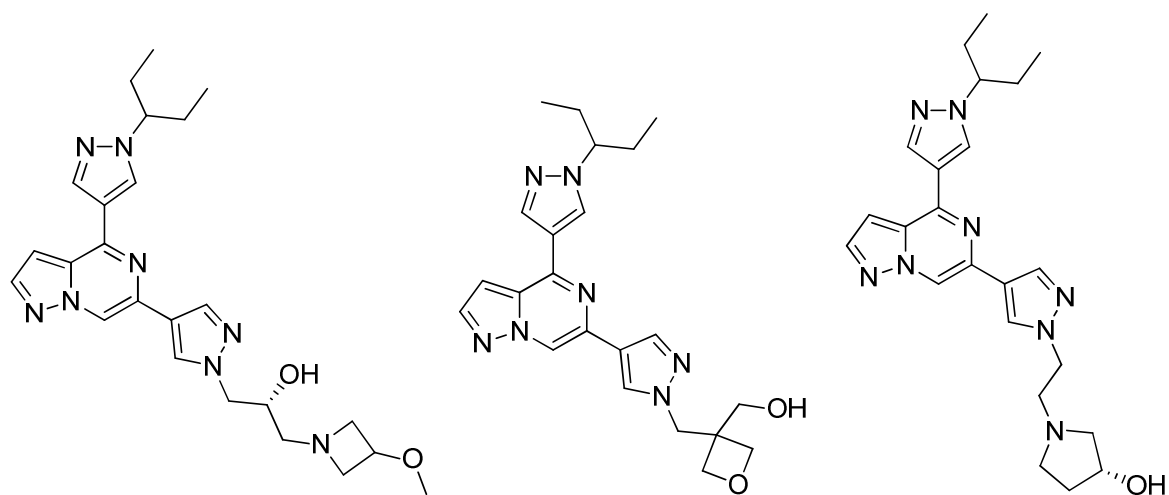












and pharmaceutically acceptable salts thereof.