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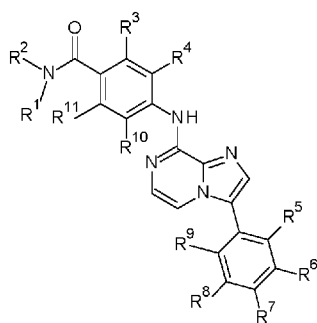
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(54) Title: NOVEL IMIDAZOPYRAZINE DERIVATIVES AS ANTIBACTERIALS



(I)

(57) Abstract: The invention provides novel imidazopyrazine derivatives having general formula (I), wherein R¹ to R¹¹ are as described herein, and pharmaceutically acceptable salts thereof. Further provided are pharmaceutical compositions including the compounds, processes of manufacturing the compounds and methods of using the compounds as medicaments, in particular methods of using the compounds as antibiotics for the treatment or prevention of bacterial infections and related diseases.

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NOVEL IMIDAZOPYRAZINE DERIVATIVES AS ANTIBACTERIALS

Field of the Invention

The present invention relates to novel imidazopyrazine derivatives which exhibit antibacterial properties. The invention also relates to methods of using the compounds for the treatment or
5 prevention of bacterial infections and resulting diseases, in particular for the treatment or prevention of infections with *Acinetobacter baumannii* and resulting diseases.

Background of the Invention

Acinetobacter baumannii is a Gram-negative, aerobic, nonfermenting bacterium recognized over the last decades as an emerging pathogen with very limited treatment options.

10 *A. baumannii* is considered to be a serious threat by the US Centers for Disease Control and Prevention and belongs to the so called ‘ESKAPE’ pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter species & E. coli*) that currently cause the majority of nosocomial infections and effectively “escape” the activity of antimicrobial agents.

15 *A. baumannii* is most often encountered in intensive care units and surgical wards, where extensive antibiotic use has enabled selection for resistance against all known antimicrobials and where it causes infections that include bacteremia, pneumonia, meningitis, urinary tract infection, and wound infection.

A. baumannii has an exceptional ability to upregulate and acquire resistance determinants and
20 shows an environmental persistence that allows its survival and spread in the nosocomial setting, making this organism a frequent cause of outbreaks of infection and an endemic, health care–associated pathogen.

Due to increasing antibiotic resistance to most if not all available therapeutic options, Multi-Drug Resistant (MDR) *A. baumannii* infections, especially those caused by Carbapenem resistant *A.*
25 *baumannii*, are extremely difficult or even impossible to treat with high mortality rate as well as increased morbidity and length of stay in intensive care unit.

Acinetobacter baumannii has been defined and still remains “a prime example of a mismatch between unmet medical needs and the current antimicrobial research and development pipeline” according to the Antimicrobial Availability Task Force (AATF) of the Infectious Diseases

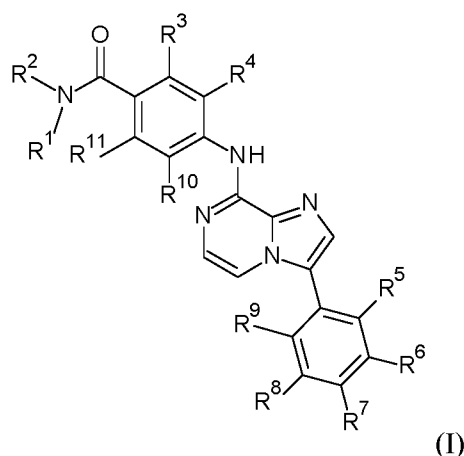
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Society of America (IDSA). Thus, there is a high demand and need to identify compounds suitable for the treatment of diseases and infections caused by *Acinetobacter baumannii*.

The present invention provides novel compounds which exhibit activity against drug-susceptible as well as drug-resistant strains of *Acinetobacter baumannii*.

5 Summary of the Invention

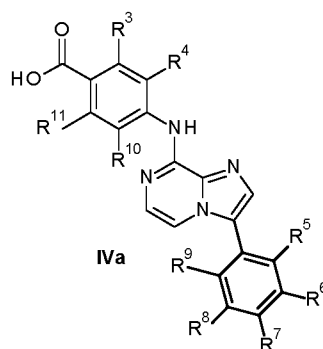
In a first aspect, the present invention provides a compound of formula (I)



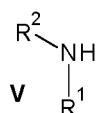
or a pharmaceutically acceptable salt thereof, wherein R^1 to R^{11} are as described herein.

In a further aspect, the present invention provides a process of manufacturing the compounds of formula (I) described herein, comprising:

(i) reacting an ester carboxylic acid **IVa**, wherein R^3 to R^{11} are as defined herein,



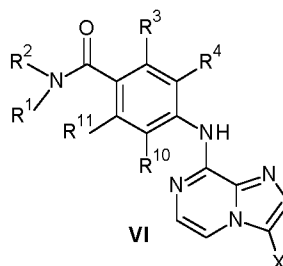
with an amine **V**, wherein R^1 and R^2 are as defined herein,



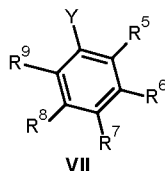
in the presence of a coupling reagent (such as HATU, TBTU, and the like) and a base (such as DIPEA, NEt_3 , and the like), to form said compound of formula (I); or

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- (ii) reacting a compound **VI**, wherein R^1 to R^4 , R^{10} and R^{11} are as defined herein and X is halogen,



- 5 with a boronic acid **VII**, wherein R^5 to R^9 are as defined herein and Y is a boronic acid or a boronic acid ester,



in the presence of a transition metal catalyst (such as $\text{PdCl}_2(\text{dppf})\text{-CH}_2\text{Cl}_2$ adduct, $\text{Pd}(\text{PPh}_3)_4$, and the like) and a base (such as K_3PO_4 , NaOtBu , and the like) to form said compound of formula (I).

- 10 In a further aspect, the present invention provides a compound of formula (I) as described herein, when manufactured according to the processes described herein.

In a further aspect, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for use as therapeutically active substance.

- 15 In a further aspect, the present invention provides a pharmaceutical composition comprising a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, and a therapeutically inert carrier.

In a further aspect, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for use as antibiotic.

- 20 In a further aspect, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of nosocomial infections and resulting diseases.

In a further aspect, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of infections and resulting diseases caused by Gram-negative bacteria.

In a further aspect, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of infections and resulting diseases caused by *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter species* or *E. coli*, or a combination thereof.

In a further aspect, the present invention provides a method for the treatment or prevention of infections and resulting diseases caused by *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter species* or *E. coli*, or a combination thereof, which method comprises administering a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, to a mammal.

In a further aspect, the present invention provides the use of a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, as an antibiotic.

In a further aspect, the present invention provides the use of a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for the treatment or prevention of infections and resulting diseases caused by *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter species* or *E. coli*, or a combination thereof.

In a further aspect, the present invention provides the use of a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for the preparation of medicaments useful for the treatment or prevention of infections and resulting diseases caused by *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter species* or *E. coli*, or a combination thereof.

Detailed Description of the Invention

Definitions

Features, integers, characteristics, compounds, chemical moieties or groups described in conjunction with a particular aspect, embodiment or example of the invention are to be understood to be applicable to any other aspect, embodiment or example described herein, unless

incompatible therewith. All of the features disclosed in this specification (including any accompanying claims, abstract and drawings), and/or all of the steps of any method or process so disclosed, may be combined in any combination, except combinations where at least some of such features and/or steps are mutually exclusive. The invention is not restricted to the details of any foregoing embodiments. The invention extends to any novel one, or any novel combination, of the features disclosed in this specification (including any accompanying claims, abstract and drawings), or to any novel one, or any novel combination, of the steps of any method or process so disclosed.

The term “alkyl” refers to a mono- or multivalent, e.g., a mono- or bivalent, linear or branched saturated hydrocarbon group of 1 to 6 carbon atoms (“C₁-C₆-alkyl”), e.g., 1, 2, 3, 4, 5, or 6 carbon atoms. In some embodiments, the alkyl group contains 1 to 3 carbon atoms, e.g., 1, 2 or 3 carbon atoms. Some non-limiting examples of alkyl include methyl, ethyl, propyl, 2-propyl (isopropyl), n-butyl, iso-butyl, sec-butyl, tert-butyl, and 2,2-dimethylpropyl. A particularly preferred, yet non-limiting example of alkyl is methyl.

The term “alkenyl” denotes a monovalent linear or branched hydrocarbon group of 2 to 6 carbon atoms with at least one double bond (“C₂-C₆-alkenyl”). In particular embodiments, alkenyl has 2 to 4 carbon atoms with at least one double bond. Examples of alkenyl include ethenyl, propenyl, prop-2-enyl, isopropenyl, n-butenyl and iso-butenyl. Particular alkenyl group is ethenyl.

The term “alkynyl” denotes a monovalent linear or branched hydrocarbon group of 2 to 6 carbon atoms with at least one triple bond (“C₂-C₆-alkynyl”). In particular embodiments, alkynyl has 2 to 4 carbon atoms with at least one triple bond. Examples of alkynyl include ethynyl, propynyl, n-butyne or isobutyne. Preferred alkenyl is propynyl.

The term “alkoxy” refers to an alkyl group, as previously defined, attached to the parent molecular moiety via an oxygen atom. Unless otherwise specified, the alkoxy group contains 1 to 6 carbon atoms (“C₁-C₆-alkoxy”). In some preferred embodiments, the alkoxy group contains 1 to 4 carbon atoms. In still other embodiments, the alkoxy group contains 1 to 3 carbon atoms. Some non-limiting examples of alkoxy groups include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy and tert-butoxy. A particularly preferred, yet non-limiting example of alkoxy is methoxy.

The term “alkynyloxy” refers to an alkynyl group, as previously defined, attached to the parent molecular moiety via an oxygen atom.

The term “halogen” or “halo” refers to fluoro (F), chloro (Cl), bromo (Br), or iodo (I). Preferably, the term “halogen” or “halo” refers to fluoro (F), chloro (Cl) or bromo (Br). Particularly preferred, yet non-limiting examples of “halogen” or “halo” are fluoro (F) and chloro (Cl).

- 5 The term “cycloalkyl” as used herein refers to a saturated or partly unsaturated monocyclic or bicyclic hydrocarbon group of 3 to 12 ring carbon atoms (“C₃-C₁₂-cycloalkyl”). In some preferred embodiments, the cycloalkyl group is a saturated monocyclic hydrocarbon group of 3 to 10 ring carbon atoms, in particular 3 to 8 ring carbon atoms. “Bicyclic cycloalkyl” refers to cycloalkyl moieties consisting of two saturated carbocycles having two carbon atoms in
- 10 common, i.e., the bridge separating the two rings is either a single bond or a chain of one or two ring atoms, and to spirocyclic moieties, i.e., the two rings are connected via one common ring atom. Preferably, the cycloalkyl group is a saturated monocyclic hydrocarbon group of 3 to 6 ring carbon atoms, e.g., of 3, 4, 5 or 6 carbon atoms. Some non-limiting examples of cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl.
- 15 The term “cycloalkyloxy” refers to a group cycloalkyl-O-, i.e. a cycloalkyl group substituted with an oxy group and attached to the parent molecular moiety via said oxy group.

The term “cyanocycloalkyloxy” refers to a cycloalkyloxy group, wherein at least one of the hydrogen atoms of the cycloalkyloxy group has been replaced by a cyano group. Preferably, “cyanocycloalkyloxy” refers to a cycloalkyloxy group wherein 1, 2 or 3 hydrogen atoms of the

20 cycloalkyloxy group have been replaced by a cyano group.

The term “aminoalkynyloxy” refers to an alkynyloxy group, wherein at least one of the hydrogen atoms of the alkynyloxy group has been replaced by an amino group. Preferably, “aminoalkynyloxy” refers to an alkynyloxy group wherein 1, 2 or 3 hydrogen atoms of the alkynyloxy group have been replaced by an amino group. A preferred, yet non-limiting example

25 of aminoalkynyloxy is 3-aminoprop-1-ynyl.

The term “aminoalkoxy” refers to an alkoxy group, wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by an amino group. Preferably, “aminoalkoxy” refers to an alkoxy group wherein 1, 2 or 3 hydrogen atoms of the alkoxy group have been replaced by an amino group. A preferred, yet non-limiting example of aminoalkoxy is aminomethoxy.

The term “aminoalkyl” refers to an alkyl group, wherein at least one of the hydrogen atoms of the alkyl group has been replaced by an amino group. Preferably, “aminoalkyl” refers to an alkyl group wherein 1, 2 or 3 hydrogen atoms of the alkyl group have been replaced by an amino group. A preferred, yet non-limiting example of aminoalkyl is aminomethyl.

- 5 The term “carboxyalkyl” refers to an alkyl group, wherein at least one of the hydrogen atoms of the alkyl group has been replaced by a carboxy group. Preferably, “carboxyalkyl” refers to an alkyl group wherein 1, 2 or 3 hydrogen atoms of the alkyl group have been replaced by a carboxy group. A preferred, yet non-limiting example of aminoalkyl is carboxymethyl.

- 10 The term “aminoalkoxyalkynyloxy” refers to an alkynyloxy group, wherein at least one of the hydrogen atoms of the alkynyloxy group has been replaced by an aminoalkoxy group. Preferably, “aminoalkoxyalkynyloxy” refers to an alkynyloxy group wherein 1, 2 or 3 hydrogen atoms of the alkynyloxy group have been replaced by an aminoalkoxy group.

- 15 The term “hydroxyalkynyloxy” refers to an alkynyloxy group, wherein at least one of the hydrogen atoms of the alkynyloxy group has been replaced by a hydroxy group. Preferably, “hydroxyalkynyloxy” refers to an alkynyloxy group wherein 1, 2 or 3 hydrogen atoms of the alkynyloxy group have been replaced by a hydroxy group. A preferred, yet non-limiting example of hydroxyalkynyloxy is 3-hydroxyprop-1-ynyl.

- The terms “heterocycloalkyl” and “heterocyclyl” are used interchangeably and refer to a saturated or partly unsaturated mono- or bicyclic, preferably monocyclic ring system of 3 to 10 ring atoms, preferably 3 to 8 ring atoms, wherein 1, 2, or 3 of said ring atoms are heteroatoms selected from N, O and S, the remaining ring atoms being carbon. Preferably, 1 to 2 of said ring atoms are selected from N and O, the remaining ring atoms being carbon. “Bicyclic heterocyclyl” refers to heterocyclic moieties consisting of two cycles having two ring atoms in common, i.e., the bridge separating the two rings is either a single bond or a chain of one or two ring atoms, and to spirocyclic moieties, i.e., the two rings are connected via one common ring atom. Some non-limiting examples of monocyclic heterocyclyl groups include azetidin-3-yl, azetidin-2-yl, oxetan-3-yl, oxetan-2-yl, 2-oxopyrrolidin-1-yl, 2-oxopyrrolidin-3-yl, 5-oxopyrrolidin-2-yl, 5-oxopyrrolidin-3-yl, 2-oxo-1-piperidyl, 2-oxo-3-piperidyl, 2-oxo-4-piperidyl, 6-oxo-2-piperidyl, 6-oxo-3-piperidyl, 1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-piperidinyl, morpholino, morpholin-2-yl, morpholin-3-yl, and 1,2,4-triazinan-4-yl.
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The term "heterocyclalkyl" refers to an alkyl group, wherein at least one of the hydrogen atoms of the alkyl group has been replaced by a heterocycl group. Preferably, "heterocyclalkyl" refers to an alkyl group wherein 1, 2 or 3 hydrogen atoms, most preferably 1 hydrogen atom of the alkyl group have been replaced by a heterocycl group.

- 5 The term "aryl" refers to a monocyclic, bicyclic, or tricyclic carbocyclic ring system having a total of 6 to 14 ring members ("C₆-C₁₄-aryl"), preferably, 6 to 12 ring members, and more preferably 6 to 10 ring members, and wherein at least one ring in the system is aromatic. Some non-limiting examples of aryl include phenyl and 9H-fluorenyl (e.g. 9H-fluoren-9-yl). A particularly preferred, yet non-limiting example of aryl is phenyl.
- 10 The term "heteroaryl" refers to a mono- or multivalent, monocyclic or bicyclic, preferably bicyclic ring system having a total of 5 to 14 ring members, preferably, 5 to 12 ring members, and more preferably 5 to 10 ring members, wherein at least one ring in the system is aromatic, and at least one ring in the system contains one or more heteroatoms. Preferably, "heteroaryl" refers to a 5-10 membered heteroaryl comprising 1, 2, 3 or 4 heteroatoms independently selected
- 15 from O, S and N. Most preferably, "heteroaryl" refers to a 5-10 membered heteroaryl comprising 1 to 2 heteroatoms independently selected from O and N. Some non-limiting examples of heteroaryl include 2-pyridyl, 3-pyridyl, 4-pyridyl, indol-1-yl, 1H-indol-2-yl, 1H-indol-3-yl, 1H-indol-4-yl, 1H-indol-5-yl, 1H-indol-6-yl, 1H-indol-7-yl, 1,2-benzoxazol-3-yl, 1,2-benzoxazol-4-yl, 1,2-benzoxazol-5-yl, 1,2-benzoxazol-6-yl, 1,2-benzoxazol-7-yl, 1H-indazol-3-yl, 1H-indazol-
- 20 4-yl, 1H-indazol-5-yl, 1H-indazol-6-yl, 1H-indazol-7-yl, pyrazol-1-yl, 1H-pyrazol-3-yl, 1H-pyrazol-4-yl, 1H-pyrazol-5-yl, imidazol-1-yl, 1H-imidazol-2-yl, 1H-imidazol-4-yl, 1H-imidazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl and [1,2,4]triazolo[4,3-a]pyridin-3-yl. A particularly preferred, yet non-limiting example of heteroaryl is indolyl, in particular 1H-indol-3-yl.

- The term "alkylheteroaryl" refers to a heteroaryl group, wherein at least one of the hydrogen atoms of the heteroaryl group has been replaced by an alkyl group. Preferably, "alkylheteroaryl" refers to a heteroaryl group wherein 1, 2 or 3 hydrogen atoms, most preferably 1 hydrogen atom of the heteroaryl group have been replaced by an alkyl group.
- 25

The term "heteroaryloxy" refers to a heteroaryl group attached to the parent molecular moiety via an oxygen atom.

- 30 The term "hydroxy" refers to an -OH group.

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The term “oxo” refers to an oxygen atom which is bound to the parent molecule via a double bond (=O).

The term “amino” refers to an -NH_2 group.

The term “imino” refers to a nitrogen atom which is bound to the parent molecule via a double bond (=N).

The term “thiono” refers to a sulfur atom which is bound to the parent molecule via a double bond (=S).

The term “cyano” refers to a -CN (nitrile) group.

The term “sulfamoyl” refers to a $\text{-SO}_2\text{-NH}_2$ group.

10 The term “alkylsulfamoyl” refers to a $\text{-SO}_2\text{-NH(alkyl)}$ group.

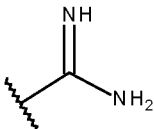
The term “dialkylsulfamoyl” refers to a $\text{-SO}_2\text{-N(alkyl)}_2$ group.

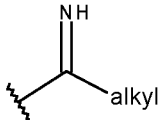
The term “alkylsulfonyl” refers to a $\text{-SO}_2\text{-alkyl}$ group.

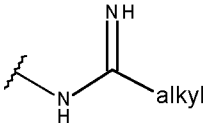
The term “alkylsulfonyloxy” refers to a $\text{-O-SO}_2\text{-alkyl}$ group.

The term “alkylsulfanyl” refers to a -S-alkyl group.

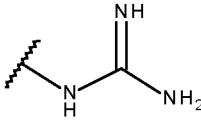
15 The term “carboxy” refers to a -COOH group.

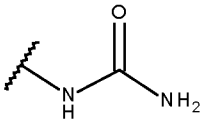
The term “carbamimidoyl” refers to a  group.

The term “alkylimidoyl” refers to a group .

The term “alkylimidoylamino” refers to a group .

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The term “guanidino” refers to a  group.

The term “ureido” refers to a  group.

The term “carbamoyl” refers to a $-\text{C}(\text{O})\text{NH}_2$ group.

The term “carbonyl” refers to a $-\text{C}(\text{O})-$ group.

- 5 The term “alkoxycarbonyl” refers to a $-\text{C}(\text{O})-\text{O}$ -alkyl group (i.e., an alkyl ester).

The term “haloalkyl” refers to an alkyl group, wherein at least one of the hydrogen atoms of the alkyl group has been replaced by a halogen atom, preferably fluoro. Preferably, “haloalkyl” refers to an alkyl group wherein 1, 2 or 3 hydrogen atoms of the alkyl group have been replaced by a halogen atom, most preferably fluoro. Particularly preferred, yet non-limiting examples of
10 haloalkyl are trifluoromethyl and trifluoroethyl.

The term “haloalkoxy” refers to an alkoxy group, wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by a halogen atom, preferably fluoro. Preferably, “haloalkoxy” refers to an alkoxy group wherein 1, 2 or 3 hydrogen atoms of the alkoxy group have been replaced by a halogen atom, most preferably fluoro. A particularly preferred, yet non-
15 limiting example of haloalkoxy is trifluoromethoxy ($-\text{OCF}_3$).

The term “cyanoalkoxy” refers to an alkoxy group, wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by a cyano group. Preferably, “cyanoalkoxy” refers to an alkoxy group wherein 1, 2 or 3 hydrogen atoms of the alkoxy group have been replaced by a cyano group. A particularly preferred, yet non-limiting example of cyanoalkoxy is
20 cyanomethoxy.

The term “cyanoalkyl” refers to an alkyl group, wherein at least one of the hydrogen atoms of the alkyl group has been replaced by a cyano group. Preferably, “cyanoalkyl” refers to an alkyl group wherein 1, 2 or 3 hydrogen atoms of the alkyl group have been replaced by a cyano group. A particularly preferred, yet non-limiting example of cyanoalkyl is cyanomethyl.

The term “alkoxyalkynyloxy” refers to an alkynyloxy group, wherein at least one of the hydrogen atoms of the alkynyloxy group has been replaced by an alkoxy group. Preferably, “alkoxyalkynyloxy” refers to an alkynyloxy group wherein 1, 2 or 3 hydrogen atoms of the alkynyloxy group have been replaced by an alkoxy group.

- 5 The term “cycloalkylalkoxy” refers to an alkoxy group, wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by a cycloalkyl group. Preferably, “cycloalkylalkoxy” refers to an alkoxy group wherein 1, 2 or 3 hydrogen atoms, most preferably 1 hydrogen atom of the alkoxy group have been replaced by a cycloalkyl group. A particularly preferred, yet non-limiting example of cycloalkylalkoxy is cyclopropylmethoxy.
- 10 The term “cyanocycloalkylalkoxy” refers to a cycloalkylalkoxy group, wherein at least one of the hydrogen atoms of the cycloalkylalkoxy group has been replaced by a cyano group. Preferably, “cyanocycloalkylalkoxy” refers to a cycloalkylalkoxy group wherein 1, 2 or 3 hydrogen atoms, most preferably 1 hydrogen atom of the cycloalkylalkoxy group have been replaced by a cyano group.
- 15 The term “hydroxyalkyl” refers to an alkyl group, wherein at least one of the hydrogen atoms of the alkyl group has been replaced by a hydroxy group. Preferably, “hydroxyalkyl” refers to an alkyl group wherein 1, 2 or 3 hydrogen atoms, most preferably 1 hydrogen atom of the alkyl group have been replaced by a hydroxy group. Preferred, yet non-limiting examples of hydroxyalkyl are hydroxymethyl and hydroxyethyl (e.g. 2-hydroxyethyl). A particularly preferred, yet non-limiting example of hydroxyalkyl is hydroxymethyl.
- 20

- The term “hydroxyalkoxy” refers to an alkoxy group, wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by a hydroxy group. Preferably, “hydroxyalkoxy” refers to an alkoxy group wherein 1, 2 or 3 hydrogen atoms, most preferably 1 hydrogen atom of the alkoxy group have been replaced by a hydroxy group. Preferred, yet non-limiting examples of hydroxyalkoxy are hydroxymethoxy and hydroxyethoxy (e.g. 2-hydroxyethoxy). A particularly preferred, yet non-limiting example of hydroxyalkoxy is hydroxymethoxy.
- 25

The term “hydroxyalkoxyalkyl” refers to an alkyl group, wherein at least one of the hydrogen atoms of the alkyl group has been replaced by a hydroxyalkoxy group. Preferably, “hydroxyalkoxyalkyl” refers to an alkyl group wherein 1, 2 or 3 hydrogen atoms, most

preferably 1 hydrogen atom of the alkyl group have been replaced by a hydroxyalkoxy group. A preferred, yet non-limiting example of hydroxyalkoxyalkyl is 2-hydroxyethoxymethyl.

The term "alkoxycarbonylalkoxy" refers to an alkoxy group, wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by an alkoxycarbonyl group. Preferably, "alkoxycarbonylalkoxy" refers to an alkoxy group wherein 1, 2 or 3 hydrogen atoms, most preferably 1 hydrogen atom of the alkoxy group have been replaced by an alkoxycarbonyl group. A preferred, yet non-limiting example of alkoxycarbonylalkoxy is 2-methoxy-2-oxo-ethoxy.

The term "arylalkoxy" refers to an alkoxy group, wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by an aryl group. Preferably, "arylalkoxy" refers to an alkoxy group wherein 1, 2 or 3 hydrogen atoms, most preferably 1 hydrogen atom of the alkoxy group have been replaced by an aryl group. A particularly preferred, yet non-limiting example of arylalkoxy is benzyloxy.

The term "heteroarylalkoxy" refers to an alkoxy group, wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by a heteroaryl group. Preferably, "heteroarylalkoxy" refers to an alkoxy group wherein 1, 2 or 3 hydrogen atoms, most preferably 1 hydrogen atom of the alkoxy group have been replaced by a heteroaryl group.

The term "alkoxyalkyl" refers to an alkyl group, wherein at least one of the hydrogen atoms of the alkyl group has been replaced by an alkoxy group. Preferably, "alkoxyalkyl" refers to an alkyl group wherein 1, 2 or 3 hydrogen atoms, most preferably 1 hydrogen atom of the alkyl group have been replaced by an alkoxy group. A particularly preferred, yet non-limiting example of alkoxyalkyl is 2-methoxyethyl.

The term "pharmaceutically acceptable salt" refers to those salts which retain the biological effectiveness and properties of the free bases or free acids, which are not biologically or otherwise undesirable. The salts are formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, in particular hydrochloric acid, and organic acids such as acetic acid, trifluoroacetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, lactic acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, N-acetylcystein and the like. In addition these salts may be prepared by addition of an inorganic base or an organic base to the

free acid. Salts derived from an inorganic base include, but are not limited to, the sodium, potassium, lithium, ammonium, calcium, magnesium salts and the like. Salts derived from organic bases include, but are not limited to salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion
5 exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, ethanolamine, lysine, arginine, N-ethylpiperidine, piperidine, polyimine resins and the like. Particular pharmaceutically acceptable salts of compounds of formula (I) are hydrochlorides, fumarates, lactates (in particular derived from L-(+)-lactic acid), tartrates (in particular derived from L-(+)-tartaric acid) and trifluoroacetates.

- 10 The term “protective group” (PG) denotes the group which selectively blocks a reactive site in a multifunctional compound such that a chemical reaction can be carried out selectively at another unprotected reactive site in the meaning conventionally associated with it in synthetic chemistry. Protective groups can be removed at the appropriate point. Exemplary protective groups are amino-protective groups, carboxy-protective groups or hydroxy-protective groups. Particular
15 protective groups are the tert-butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), fluorenylmethoxycarbonyl (Fmoc) and benzyl (Bn). Further particular protective groups are the tert-butoxycarbonyl (Boc) and the fluorenylmethoxycarbonyl (Fmoc). More particular protective group is the tert-butoxycarbonyl (Boc). Exemplary protective groups and their application in organic synthesis are described, for example, in “Protective Groups in Organic Chemistry” by T.
20 W. Greene and P. G. M. Wuts, 5th Ed., 2014, John Wiley & Sons, N.Y.

The compounds of formula (I) can contain several asymmetric centers and can be present in the form of optically pure enantiomers, mixtures of enantiomers such as, for example, racemates, optically pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates or mixtures of diastereoisomeric racemates.

- 25 According to the Cahn-Ingold-Prelog Convention, the asymmetric carbon atom can be of the "R" or "S" configuration.

- The term “treatment” as used herein includes: (1) inhibiting the state, disorder or condition (e.g. arresting, reducing or delaying the development of the disease, or a relapse thereof in case of maintenance treatment, of at least one clinical or subclinical symptom thereof); and/or (2)
30 relieving the condition (i.e., causing regression of the state, disorder or condition or at least one of its clinical or subclinical symptoms). The benefit to a patient to be treated is either statistically

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significant or at least perceptible to the patient or to the physician. However, it will be appreciated that when a medicament is administered to a patient to treat a disease, the outcome may not always be effective treatment.

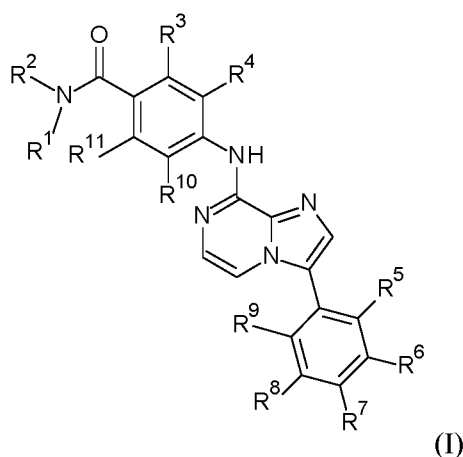
The term “prophylaxis” as used herein includes: preventing or delaying the appearance of clinical symptoms of the state, disorder or condition developing in a mammal and especially a human that may be afflicted with or predisposed to the state, disorder or condition but does not yet experience or display clinical or subclinical symptoms of the state, disorder or condition.

The term “mammal” as used herein includes both humans and non-humans and includes but is not limited to humans, non-human primates, canines, felines, murines, bovines, equines, and porcines. In a particularly preferred embodiment, the term “mammal” refers to humans.

The term “nosocomial infection” refers to a hospital-acquired infection (HAI), which is an infection that is acquired in a hospital or other health care facility. To emphasize both hospital and nonhospital settings, it is sometimes instead called a health care-associated infection (HAI or HCAI). Such an infection can be acquired in hospitals, nursing homes, rehabilitation facilities, outpatient clinics, or other clinical settings.

Compounds of the Invention

In a first aspect, the present invention provides a compound of formula (I)



or a pharmaceutically acceptable salt thereof, wherein:

- (i) R¹ is C₁-C₆-alkyl substituted with R¹², R¹³, R¹⁴, R¹⁵ and/or R¹⁶; and
R¹¹ is selected from hydrogen, halogen and C₁-C₆-alkyl; or

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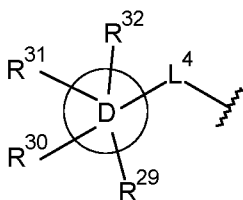
(ii) R^1 and R^{11} , taken together with the atoms to which they are attached, form a β -, γ -, δ - or ϵ -lactam;

R^2 is selected from hydrogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, cyano- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-, amino- C_1 - C_6 -alkyl-O- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-O- C_1 - C_6 -alkyl-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-O- C_1 - C_6 -alkyl- and C_3 - C_{12} -cycloalkyl;

R^3 is selected from hydrogen, halogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, NO_2 , CN, C_3 - C_{12} -cycloalkyl, hydroxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy and alkoxy- C_1 - C_6 -alkyl;

R^4 and R^{10} are each independently selected from hydrogen, halogen and C_1 - C_6 -alkyl;

each of R^5 , R^6 , R^7 , R^8 and R^9 is independently selected from hydrogen, halogen, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkoxy, amino, C_1 - C_6 -alkyl-NH-, (C_1 - C_6 -alkyl) $_2$ N-, hydroxy, C_1 - C_6 -alkoxy, C_1 - C_6 -alkylsulfanyl, C_1 - C_6 -alkylsulfonyloxy, halo- C_1 - C_6 -alkoxy, cyano- C_1 - C_6 -alkoxy, C_2 - C_6 -alkynyloxy, C_1 - C_6 -alkoxy- C_2 - C_6 -alkynyloxy, amino- C_2 - C_6 -alkynyloxy, hydroxy- C_2 - C_6 -alkynyloxy, halo- C_1 - C_6 -alkyl, sulfamoyl, C_1 - C_6 -alkylsulfamoyl, C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkoxy- C_2 - C_6 -alkynyloxy, amino- C_1 - C_6 -



alkoxy and a group

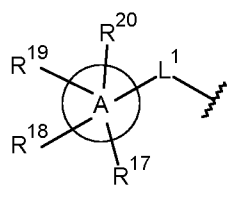
;

each of R^{12} , R^{13} , R^{14} , R^{15} and R^{16} is independently selected from hydrogen, halogen, cyano,

vinyl, hydroxy, amino, C_2 - C_6 -alkynyl, C_2 - C_6 -alkenyl, C_1 - C_6 -alkyl-NH-, (C_1 - C_6 -alkyl) $_2$ N-, carboxy, C_1 - C_6 -alkoxycarbonyl, C_1 - C_6 -alkoxycarbonyl-NH-, carbamoyl, C_1 - C_6 -alkyl-NH-C(O)-, (C_1 - C_6 -alkyl) $_2$ N-C(O)-, amino- C_1 - C_6 -alkyl-N(C_1 - C_6 -alkyl)-C(O)-, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-N(C_1 - C_6 -alkyl)-C(O)-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-N(C_1 - C_6 -alkyl)-C(O)-, amino- C_1 - C_6 -alkyl-NH-C(O)-, hydroxy- C_1 - C_6 -alkyl-NH-C(O)-, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-NH-C(O)-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-NH-C(O)-, amino- C_1 - C_6 -alkyl-C(O)-NH-, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-C(O)-NH-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-C(O)-NH-, amino- C_1 - C_6 -alkyl-C(O)-N(C_1 - C_6 -alkyl)-, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-C(O)-N(C_1 - C_6 -alkyl)-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-C(O)-N(C_1 - C_6 -alkyl)-, amino- C_1 - C_6 -alkyl-NH-C(O)-NH-, amino- C_1 - C_6 -alkyl-

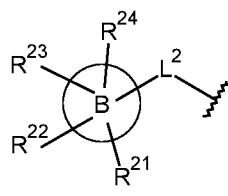
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CH(OH)-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-, guanidino,
 guanidino-C₁-C₆-alkyl-C(O)-NH-, guanidino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-,
 carboxy-C₁-C₆-alkyl-NH-C(=NH)-NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, ureido-C₁-
 C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-, hydroxy-
 C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-
 CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-
 CH(carboxy)-C₁-C₆-alkyl-C(O)-NH-, carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-
 CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-,
 amino-C₁-C₆-alkyl-, amino-C₂-C₆-alkenyl-, C₁-C₆-alkylimidoamino- and a group



or any two of R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶, taken together with the carbon atom(s) to which they are attached, form a C₃-C₁₂-cycloalkyl;

each of R¹⁷, R¹⁸, R¹⁹ and R²⁰ is independently selected from hydrogen, halogen, cyano, carboxy, carboxy-C₁-C₆-alkyl, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, oxo, imino, thiono, hydroxy-C₁-C₆-alkyl, cyano-C₁-C₆-alkyl, hydroxy, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-, amino-C₁-C₆-alkyl, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-, carbamimidoyl, C₁-C₆-alkyl-C(O)-, amino-C₁-C₆-alkyl-C(O)-, di-C₁-C₆-alkoxyphosphoryl, C₁-C₆-alkylsulfonyl, C₁-C₆-alkoxy, and a group



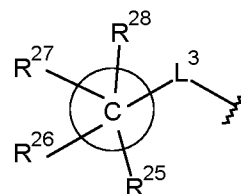
A, B and D are independently selected from C₆-C₁₄-aryl, C₃-C₁₂-cycloalkyl, C₂-C₉-heterocyclyl and C₁-C₁₃-heteroaryl;

L¹ is selected from a covalent bond, -O-, -S-, S=O, SO₂, carbonyl, -C(O)-O-, -O-C(O)-, -C(O)-NH-, -NH-C(O)-, -C₁-C₆-alkyl-C(O)-NH-, -C₁-C₆-alkyl-NH-C(O)-, -C₁-C₆-alkyl-NH-C(O)-C₁-C₆-alkyl-, -C₁-C₆-alkyl-C(O)-N(C₁-C₆-alkyl)-, -C₁-C₆-alkyl-CH(OH)-, -C(O)-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, -C(O)-C₁-C₆-alkyl-NH-C(O)- and -NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-;

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L^2 and L^4 are independently selected from a covalent bond, $-O-$, $-C_1-C_6\text{-alkyl-}$, $-C_1-C_6\text{-alkoxy-}$ and carbonyl;

each of R^{21} , R^{22} , R^{23} and R^{24} is independently selected from hydrogen, hydroxy, amino, halogen, cyano, $C_1-C_6\text{-alkyl}$, halo- $C_1-C_6\text{-alkyl}$, $C_1-C_6\text{-alkoxy}$, halo- $C_1-C_6\text{-alkoxy}$,



5 amino- $C_1-C_6\text{-alkyl-CH(OH)-C(O)-NH-}$ and a group ;

C is selected from $C_6-C_{14}\text{-aryl}$, $C_3-C_{12}\text{-cycloalkyl}$, $C_2-C_9\text{-heterocyclyl}$ and $C_1-C_{13}\text{-heteroaryl}$;

L^3 is selected from a covalent bond, $-O-$, $-C_1-C_6\text{-alkyl-}$, $-C_1-C_6\text{-alkoxy-}$ and carbonyl;

10 each of R^{25} , R^{26} , R^{27} and R^{28} is independently selected from hydrogen, hydroxy, amino, halogen, cyano, $C_1-C_6\text{-alkyl}$, halo- $C_1-C_6\text{-alkyl}$, $C_1-C_6\text{-alkoxy}$, halo- $C_1-C_6\text{-alkoxy}$ and amino- $C_1-C_6\text{-alkyl}$; and

each of R^{29} , R^{30} , R^{31} and R^{32} is independently selected from hydrogen, $C_1-C_6\text{-alkyl}$, $C_1-C_6\text{-alkoxy}$, halo- $C_1-C_6\text{-alkyl}$, halo- $C_1-C_6\text{-alkoxy}$, amino- $C_1-C_6\text{-alkyl}$, amino- $C_1-C_6\text{-alkoxy}$, amino- $C_1-C_6\text{-alkyl-NHC(O)-}$, halogen, cyano, hydroxy and amino.

15 In one embodiment, the present invention provides a compound of formula (I) or a pharmaceutically acceptable salt thereof, wherein:

(i) R^1 is $C_1-C_6\text{-alkyl}$ substituted with R^{12} , R^{13} , R^{14} , R^{15} and/or R^{16} ; and R^{11} is selected from hydrogen, halogen and $C_1-C_6\text{-alkyl}$; or

20 (ii) R^1 and R^{11} , taken together with the atoms to which they are attached, form a β -, γ -, δ - or ϵ -lactam;

R^2 is selected from hydrogen, $C_1-C_6\text{-alkyl}$, halo- $C_1-C_6\text{-alkyl}$, cyano- $C_1-C_6\text{-alkyl}$, hydroxy- $C_1-C_6\text{-alkyl}$, amino- $C_1-C_6\text{-alkyl}$, $C_1-C_6\text{-alkyl-NH-}$ $C_1-C_6\text{-alkyl-}$, $(C_1-C_6\text{-alkyl})_2\text{N-}$ $C_1-C_6\text{-alkyl-}$, amino- $C_1-C_6\text{-alkyl-O-}$ $C_1-C_6\text{-alkyl}$, $C_1-C_6\text{-alkyl-NH-}$ $C_1-C_6\text{-alkyl-O-}$ $C_1-C_6\text{-alkyl-}$, $(C_1-C_6\text{-alkyl})_2\text{N-}$ $C_1-C_6\text{-alkyl-O-}$ $C_1-C_6\text{-alkyl-}$ and $C_3-C_{12}\text{-cycloalkyl}$;

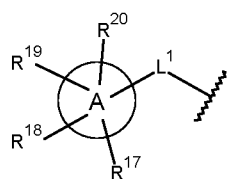
25 R^3 is selected from hydrogen, halogen, $C_1-C_6\text{-alkyl}$, halo- $C_1-C_6\text{-alkyl}$, hydroxy- $C_1-C_6\text{-alkyl}$, $C_2-C_6\text{-alkenyl}$, NO_2 , CN , $C_3-C_{12}\text{-cycloalkyl}$, hydroxy- $C_1-C_6\text{-alkoxy-}$ $C_1-C_6\text{-alkyl}$, $C_1-C_6\text{-alkoxy}$ and alkoxy- $C_1-C_6\text{-alkyl}$;

R^4 and R^{10} are each independently selected from hydrogen, halogen and $C_1-C_6\text{-alkyl}$;

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each of R⁵, R⁶, R⁷, R⁸ and R⁹ is independently selected from hydrogen, halogen, C₁-C₆-alkoxycarbonyl-C₁-C₆-alkoxy, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-, hydroxy, C₁-C₆-alkoxy, C₁-C₆-alkylsulfanyl, C₁-C₆-alkylsulfonyloxy, C₃-C₁₂-cycloalkyl-C₁-C₆-alkoxy, halo-C₁-C₆-alkoxy, C₆-C₁₄-aryl-C₁-C₆-alkoxy, C₁-C₁₃-heteroaryloxy, C₁-C₁₃-heteroaryl-C₁-C₆-alkoxy, cyano-C₁-C₆-alkoxy, C₃-C₁₂-cycloalkyloxy, C₂-C₆-alkynyloxy, C₁-C₆-alkoxy-C₂-C₆-alkynyloxy, cyano-C₃-C₁₂-cycloalkyloxy, cyano-C₃-C₁₂-cycloalkyl-C₁-C₆-alkoxy, amino-C₂-C₆-alkynyloxy, hydroxy-C₂-C₆-alkynyloxy, halo-C₁-C₆-alkyl, sulfamoyl, C₁-C₆-alkylsulfamoyl, C₁-C₆-alkyl, amino-C₁-C₆-alkoxy-C₂-C₆-alkynyloxy and amino-C₁-C₆-alkoxy;

R¹² is selected from hydrogen, halogen, cyano, vinyl, hydroxy, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-, carboxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkoxycarbonyl-NH-, carbamoyl, C₁-C₆-alkyl-NH-C(O)-, (C₁-C₆-alkyl)₂N-C(O)-, amino-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, amino-C₁-C₆-alkyl-NH-C(O)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-NH-C(O)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-NH-C(O)-, amino-C₁-C₆-alkyl-C(O)-NH-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-C(O)-NH-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-C(O)-N(C₁-C₆-alkyl)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-C(O)-N(C₁-C₆-alkyl)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-C(O)-N(C₁-C₆-alkyl)-, amino-C₁-C₆-alkyl-NH-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-, guanidino, guanidino-C₁-C₆-alkyl-C(O)-NH-, guanidino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-C₁-C₆-alkyl-NH-C(=NH)-NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, ureido-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-, hydroxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, C₁-C₆-alkylimidoamino- and



a group

;

R¹³ is selected from hydrogen, hydroxy, halogen, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N- and C₁-C₆-alkoxycarbonyl-NH-;

R¹⁴ is selected from hydrogen, halogen and hydroxy;

R¹⁵ is selected from hydrogen, halogen and hydroxy;

R¹⁶ is selected from hydrogen and hydroxy;

R¹⁷ is selected from hydrogen, carboxy, carboxy-C₁-C₆-alkyl, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, oxo, imino, hydroxy-C₁-C₆-alkyl, cyano-C₁-C₆-alkyl, hydroxy, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-, amino-C₁-C₆-alkyl, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-,
 5 (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-, carbamimidoyl, C₁-C₆-alkyl-C(O)-, di-C₁-C₆-alkoxyphosphoryl, C₁-C₆-alkylsulfonyl, and C₁-C₆-alkoxy;

R¹⁸ is hydrogen, hydroxy or C₁-C₆-alkyl;

R¹⁹ is hydrogen or hydroxy;

R²⁰ is hydrogen or hydroxy;

10 A is selected from C₆-C₁₄-aryl, C₃-C₁₂-cycloalkyl, C₂-C₉-heterocyclyl and C₁-C₁₃-heteroaryl; and

L¹ is selected from a covalent bond, -O-, -S-, S=O, SO₂, carbonyl, -C(O)-O-, -O-C(O)-, -C(O)-NH-, -NH-C(O)-, -C₁-C₆-alkyl-C(O)-NH-, -C₁-C₆-alkyl-C(O)-N(C₁-C₆-alkyl)-, -C₁-C₆-alkyl-CH(OH)-, -C(O)-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-,
 15 -C(O)-C₁-C₆-alkyl-NH-C(O)- and -NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

(i) R¹ is C₁-C₆-alkyl substituted with R¹², R¹³, R¹⁴, R¹⁵ and/or R¹⁶; and

R¹¹ is selected from hydrogen and halogen; or

20 (ii) R¹ and R¹¹, taken together with the atoms to which they are attached, form a δ- or ε-lactam.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

R¹ is C₁-C₆-alkyl substituted with R¹², R¹³, R¹⁴, R¹⁵ and/or R¹⁶; and

25 R¹¹ is hydrogen.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

R¹ is C₁-C₆-alkyl substituted with R¹², R¹³, R¹⁴, R¹⁵ and/or R¹⁶; and

R¹¹ is hydrogen;

30 wherein said C₁-C₆-alkyl is selected from methyl, ethyl, propyl, butyl, pentyl and 1-methyl-ethyl.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^2 is selected from hydrogen, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-, amino-C₁-C₆-alkyl-O-C₁-C₆-alkyl, and C₃-C₁₂-cycloalkyl.

- 5 In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^2 is hydrogen or C₁-C₆-alkyl.

In a particularly preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^2 is hydrogen or
10 methyl.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^3 is selected from hydrogen, halogen, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl, C₂-C₆-alkenyl, NO₂, cycloalkyl, and hydroxy-C₁-C₆-alkoxy-C₁-C₆-alkyl.

- 15 In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^3 is C₁-C₆-alkyl or halogen.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^3 is selected from
20 chloro, methyl and ethyl.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^4 is hydrogen.

- In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^5 is selected from hydrogen,
25 halogen and halo-C₁-C₆-alkyl.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^5 is hydrogen or halogen.

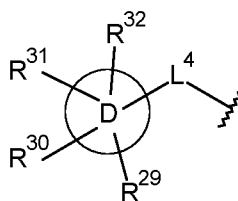
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In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^5 is selected from hydrogen, fluoro and chloro.

In one embodiment, the present invention provides a compound of formula (I) as described
5 herein, or a pharmaceutically acceptable salt thereof, wherein R^6 is hydrogen or halogen.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^6 is hydrogen or fluoro.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^7 is selected from halogen,
10 hydroxy, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy, cyano- C_1 - C_6 -alkoxy, amino- C_2 - C_6 -alkynyloxy,



amino- C_1 - C_6 -alkoxy- C_2 - C_6 -alkynyloxy; and a group , wherein:

D is C_1 - C_{13} -heteroaryl;

L^4 is selected from a covalent bond, $-O-$ and C_1 - C_6 -alkoxy;

R^{29} is selected from hydrogen, halogen, C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -
15 alkyl, amino- C_1 - C_6 -alkoxy and amino- C_1 - C_6 -alkyl- $NH-C(O)-$; and

R^{30} , R^{31} and R^{32} are all hydrogen.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^7 is selected from halogen,
hydroxy, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy, cyano- C_1 - C_6 -alkoxy, amino- C_2 - C_6 -alkynyloxy and
20 amino- C_1 - C_6 -alkoxy- C_2 - C_6 -alkynyloxy.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^7 is selected from C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy and cyano- C_1 - C_6 -alkoxy.

In a particularly preferred embodiment, the present invention provides a compound of formula
25 (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^7 is selected from methoxy, difluoromethoxy and cyanomethoxy.

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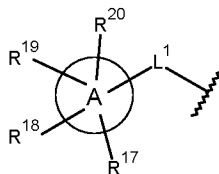
In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^8 is hydrogen.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^9 is hydrogen.

- 5 In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^{10} is hydrogen.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

- R^{12} is selected from hydrogen, halogen, vinyl, hydroxy, amino, C_2 - C_6 -alkynyl, (C_1 - C_6 -alkyl) $_2$ N-, carboxy, C_1 - C_6 -alkoxycarbonyl, C_1 - C_6 -alkoxycarbonyl-NH-, carbamoyl, C_1 - C_6 -alkyl-NH-C(O)-, (C_1 - C_6 -alkyl) $_2$ N-C(O)-, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-NH-C(O)-, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-N(C_1 - C_6 -alkyl)-C(O)-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-NH-C(O)-, amino- C_1 - C_6 -alkyl-NH-C(O)-, amino- C_1 - C_6 -alkyl-C(O)-NH-, hydroxy- C_1 - C_6 -alkyl-NH-C(O)-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-C(O)-NH-, amino- C_1 - C_6 -alkyl-NH-C(O)-NH-, amino- C_1 - C_6 -alkyl-CH(OH)- C_1 - C_6 -alkyl-C(O)-NH-, amino- C_1 - C_6 -alkyl-CH(OH)-, guanidino, guanidino- C_1 - C_6 -alkyl-C(O)-NH-, guanidino- C_1 - C_6 -alkyl-CH(NH $_2$)-C(O)-NH-, carboxy- C_1 - C_6 -alkyl-NH-C(=NH)-NH- C_1 - C_6 -alkyl-CH(NH $_2$)-C(O)-NH-, ureido- C_1 - C_6 -alkyl-CH(NH $_2$)-C(O)-NH-, carboxy-CH(NH $_2$)- C_1 - C_6 -alkyl-C(O)-NH-, hydroxy- C_1 - C_6 -alkyl-CH(NH $_2$)-C(O)-NH-, amino- C_1 - C_6 -alkyl-CH(NH $_2$)-C(O)-NH-CH(carboxy)- C_1 - C_6 -alkyl-C(O)-NH-, carboxy-CH(NH $_2$)- C_1 - C_6 -alkyl-C(O)-NH-CH(guanidino- C_1 - C_6 -alkyl)-C(O)-NH-, carboxy- C_1 - C_6 -alkyl-CH(NH $_2$)-C(O)-NH-CH(guanidino- C_1 - C_6 -alkyl)-C(O)-NH-, amino- C_1 - C_6 -alkyl-CH(NH $_2$)-C(O)-NH-, amino- C_2 - C_6 -alkenyl, C_1 - C_6 -



alkylimidoamino- and a group

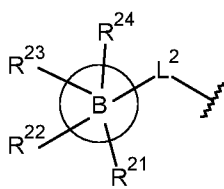
; wherein:

- 25 A is selected from C_6 - C_{14} -aryl, C_2 - C_9 -heterocyclyl and C_1 - C_{13} -heteroaryl;
 L^1 is selected from a covalent bond, -O-, -S-, SO $_2$, carbonyl, -C(O)-O-, -C(O)-NH-, - C_1 - C_6 -alkyl-C(O)-NH-, - C_1 - C_6 -alkyl-NH-C(O)-, - C_1 - C_6 -alkyl-NH-

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$C(O)-C_1-C_6\text{-alkyl-}$, $-C_1-C_6\text{-alkyl-CH(OH)-}$, $-C(O)-C_1-C_6\text{-alkyl-N}(C_1-C_6\text{-alkyl})-C(O)-$ and $-NH-C_1-C_6\text{-alkyl-CH(NH}_2)-C(O)-NH-$;

R^{17} is selected from hydrogen, halogen, carboxy, carboxy- $C_1-C_6\text{-alkyl}$, $C_1-C_6\text{-alkyl}$, halo- $C_1-C_6\text{-alkyl}$, oxo, imino, thiono, hydroxy- $C_1-C_6\text{-alkyl}$, cyano- $C_1-C_6\text{-alkyl}$, hydroxy, amino, $C_1-C_6\text{-alkyl-NH-}$, $(C_1-C_6\text{-alkyl})_2N-$, $C_1-C_6\text{-alkyl-NH-}C_1-C_6\text{-alkyl-}$, $(C_1-C_6\text{-alkyl})_2N-C_1-C_6\text{-alkyl-}$, carbamimidoyl, $C_1-C_6\text{-alkyl-C(O)-}$, amino- $C_1-C_6\text{-alkyl-C(O)-}$, di- $C_1-C_6\text{-alkoxyphosphoryl}$, $C_1-C_6\text{-alkylsulfonyl}$,



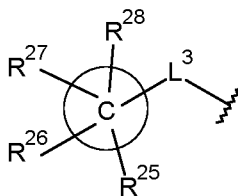
and a group

R^{18} is selected from hydrogen, hydroxy and $C_1-C_6\text{-alkyl}$;

R^{19} and R^{20} are both hydrogen or hydroxy;

B is selected from $C_3-C_{12}\text{-cycloalkyl}$, $C_2-C_9\text{-heterocyclyl}$ and $C_1-C_{13}\text{-heteroaryl}$;

L^2 is selected from $-O-$, $-C_1-C_6\text{-alkyl-}$ and carbonyl;



R^{21} is hydrogen or a group

R^{22} is hydrogen or amino- $C_1-C_6\text{-alkyl-CH(OH)-C(O)-NH-}$;

R^{23} and R^{24} are both independently selected from hydrogen, amino and hydroxy;

C is $C_2-C_9\text{-heterocyclyl}$;

L^3 is $-O-$;

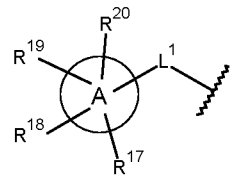
R^{25} is amino- $C_1-C_6\text{-alkyl-}$; and

R^{26} , R^{27} and R^{28} are all hydroxy.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^{12} is selected from hydrogen, halogen, vinyl, hydroxy, amino, $(C_1-C_6\text{-alkyl})_2N-$, carboxy, $C_1-C_6\text{-alkoxycarbonyl}$, $C_1-C_6\text{-alkoxycarbonyl-NH-}$, carbamoyl, $C_1-C_6\text{-alkyl-NH-C(O)-}$, $(C_1-C_6\text{-alkyl})_2N-C(O)-$, $C_1-C_6\text{-alkyl-NH-}C_1-C_6\text{-alkyl-N}(C_1-C_6\text{-alkyl})-C(O)-$, $(C_1-C_6\text{-alkyl})_2N-C_1-C_6\text{-alkyl-NH-C(O)-}$, amino- $C_1-C_6\text{-alkyl-C(O)-NH-}$, $(C_1-C_6\text{-alkyl})_2N-C_1-C_6\text{-alkyl-C(O)-NH-}$, amino- $C_1-C_6\text{-alkyl-NH-C(O)-NH-}$,

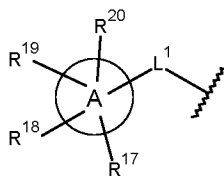
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amino-C₁-C₆-alkyl-CH(OH)-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-, guanidino,
 guanidino-C₁-C₆-alkyl-C(O)-NH-, guanidino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-C₁-C₆-
 alkyl-NH-C(=NH)-NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, ureido-C₁-C₆-alkyl-CH(NH₂)-C(O)-
 NH-, carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-, hydroxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-,
 5 carboxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-, amino-C₁-C₆-



alkyl-CH(NH₂)-C(O)-NH-, C₁-C₆-alkylimidoylamino- and a group
 wherein A, L¹ and R¹⁷ to R²⁰ are as defined herein.

In one embodiment, the present invention provides a compound of formula (I) as described
 herein, or a pharmaceutically acceptable salt thereof, wherein R¹² is selected from C₁-C₆-alkyl-
 10 NH-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, hydroxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, amino,
 amino-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, amino-C₁-C₆-alkyl-
 CH(OH)-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-NH-C(O)-NH-, guanidino-C₁-C₆-alkyl-
 CH(NH₂)-C(O)-NH-, guanidino, guanidino-C₁-C₆-alkyl-C(O)-NH- and a group



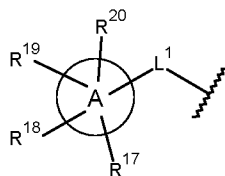
; wherein:

- 15 A is C₂-C₉-heterocyclyl;
- L¹ is selected from a covalent bond, -C(O)-NH- and carbonyl;
- R¹⁷ is selected from hydrogen, hydroxy, C₁-C₆-alkyl, carbamimidoyl, hydroxy-C₁-C₆-
 alkyl and imino;
- R¹⁸ is hydrogen or hydroxy; and
- 20 R¹⁹ and R²⁰ are both hydrogen.

In a preferred embodiment, the present invention provides a compound of formula (I) as
 described herein, or a pharmaceutically acceptable salt thereof, wherein R¹² is selected from C₁-
 C₆-alkyl-NH-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, hydroxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-,
 amino, amino-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, amino-C₁-C₆-
 25 alkyl-CH(OH)-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-NH-C(O)-NH-, guanidino-C₁-C₆-

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alkyl-CH(NH₂)-C(O)-NH-, guanidino, guanidino-C₁-C₆-alkyl-C(O)-NH- and a group



, wherein A, L¹ and R¹⁷ to R²⁰ are as defined herein.

In a particularly preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R¹² is selected from 4-piperidyl, piperazin-1-yl, [(2R)-2-amino-5-guanidino-pentanoyl]amino, [(2S)-2-amino-5-guanidino-pentanoyl]amino, 2-aminoethylcarbamoylamino, guanidino, 5-guanidinopentanoylamino, amino, 3-aminopropylcarbamoylamino, 1-carbamimidoyl-4-piperidyl, [(2S,4S)-4-hydroxy-4-methyl-pyrrolidine-2-carbonyl]amino, [(2S)-2-amino-3-hydroxy-propanoyl]amino, (2-aminoacetyl)amino, 3-aminopropanoylamino, [(2S,3R)-2-amino-3-hydroxy-butanoyl]amino, [(2S)-2,5-diaminopentanoyl]amino, (4-amino-3-hydroxy-butanoyl)amino, [(2S)-2,6-diaminohexanoyl]amino, [(2S)-2,4-diaminobutanoyl]amino, [(2S)-2,3-diaminopropanoyl]amino, (3S)-3-(hydroxymethyl)piperazine-1-carbonyl, methyl-[2-(methylamino)ethyl]carbamoyl, (2-iminoimidazolidine-4-carbonyl)amino, [(2S,4R)-4-hydroxypyrrolidine-2-carbonyl]amino and [(2S)-2-amino-3-guanidino-propanoyl]amino.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:
 R¹³ is selected from hydrogen, hydroxy, halogen, amino and C₁-C₆-alkoxycarbonyl-NH-; and
 R¹⁴ is selected from hydrogen, halogen and hydroxy; or
 R¹³ and R¹⁴, taken together with the carbon atom(s) to which they are attached, form a C₃-C₁₂-cycloalkyl.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R¹³ is selected from hydrogen, hydroxy, halogen, amino and C₁-C₆-alkoxycarbonyl-NH-.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R¹³ is hydrogen.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R¹⁴ is selected from hydrogen, halogen and hydroxy.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R¹⁴ is hydrogen.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R¹⁵ is selected from hydrogen, halogen and hydroxy.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R¹⁵ is hydrogen.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R¹⁶ is hydrogen or hydroxy.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R¹⁶ is hydrogen.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R¹⁷ is selected from hydrogen, carboxy, carboxy-C₁-C₆-alkyl, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, oxo, imino, hydroxy-C₁-C₆-alkyl, cyano-C₁-C₆-alkyl, hydroxy, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-, carbamimidoyl, C₁-C₆-alkyl-C(O)-, di-C₁-C₆-alkoxyphosphoryl and C₁-C₆-alkylsulfonyl.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R¹⁷ is selected from hydrogen, hydroxy, C₁-C₆-alkyl, carbamimidoyl, hydroxy-C₁-C₆-alkyl and imino.

In a particularly preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R¹⁷ is selected from hydrogen, hydroxy, methyl, carbamimidoyl, hydroxymethyl and imino.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^{18} is selected from hydrogen, hydroxy and C_1 - C_6 -alkyl.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^{18} is hydrogen or hydroxy.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^{19} is hydrogen or hydroxy.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^{19} is hydrogen.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^{20} is hydrogen or hydroxy.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein R^{20} is hydrogen.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein A is C_2 - C_9 -heterocyclyl.

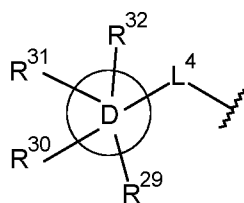
In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein A is selected from 4-piperidyl, piperazin-1-yl, pyrrolidin-2-yl and imidazolidin-4-yl.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein L^1 is selected from a covalent bond, $-O-$, $-S-$, SO_2 , carbonyl, $-C(O)-O-$, $-C(O)-NH-$, $-C_1-C_6$ -alkyl- $C(O)-NH-$, $-C_1-C_6$ -alkyl- $CH(OH)-$, $-C(O)-C_1-C_6$ -alkyl- $N(C_1-C_6$ -alkyl)- $C(O)-$ and $-NH-C_1-C_6$ -alkyl- $CH(NH_2)-C(O)-NH-$.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein L^1 is selected from a covalent bond, $-C(O)-NH-$ and carbonyl.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

- (i) R^1 is C_1 - C_6 -alkyl substituted with R^{12} , R^{13} , R^{14} , R^{15} and/or R^{16} ; and R^{11} is selected from hydrogen and halogen; or
- 5 (ii) R^1 and R^{11} , taken together with the atoms to which they are attached, form a δ - or ϵ -lactam;
- R^2 is selected from hydrogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-, amino- C_1 - C_6 -alkyl-O- C_1 - C_6 -alkyl, and C_3 - C_{12} -cycloalkyl;
- 10 R^3 is selected from hydrogen, halogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, NO_2 , cycloalkyl, and hydroxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl;
- R^4 , R^8 , R^9 and R^{10} are all hydrogen;
- R^5 is selected from hydrogen, halogen and halo- C_1 - C_6 -alkyl;
- R^6 is hydrogen or halogen;
- 15 R^7 is selected from halogen, hydroxy, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy, cyano- C_1 - C_6 -alkoxy, amino- C_2 - C_6 -alkynyloxy, amino- C_1 - C_6 -alkoxy- C_2 - C_6 -alkynyloxy; and a

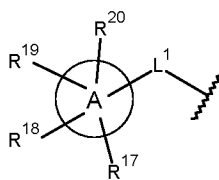


group, wherein:

- D is C_1 - C_{13} -heteroaryl;
- L^4 is selected from a covalent bond, -O- and C_1 - C_6 -alkoxy;
- 20 R^{29} is selected from hydrogen, halogen, C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkoxy and amino- C_1 - C_6 -alkyl-NH-C(O)-;
- R^{30} , R^{31} and R^{32} are all hydrogen;
- R^{12} is selected from hydrogen, halogen, vinyl, hydroxy, amino, C_2 - C_6 -alkynyl, (C_1 - C_6 -alkyl) $_2$ N-, carboxy, C_1 - C_6 -alkoxycarbonyl, C_1 - C_6 -alkoxycarbonyl-NH-, carbamoyl,
- 25 C_1 - C_6 -alkyl-NH-C(O)-, (C_1 - C_6 -alkyl) $_2$ N-C(O)-, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-NH-C(O)-, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-N(C(C_1 - C_6 -alkyl))-C(O)-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-NH-C(O)-, amino- C_1 - C_6 -alkyl-NH-C(O)-, amino- C_1 - C_6 -alkyl-C(O)-NH-, hydroxy- C_1 - C_6 -alkyl-NH-C(O)-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-C(O)-NH-, amino- C_1 -

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C₆-alkyl-NH-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-C₁-C₆-alkyl-C(O)-NH-,
 amino-C₁-C₆-alkyl-CH(OH)-, guanidino, guanidino-C₁-C₆-alkyl-C(O)-NH-,
 guanidino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-C₁-C₆-alkyl-NH-C(=NH)-NH-
 C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, ureido-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-,
 5 carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-, hydroxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-
 NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-CH(carboxy)-C₁-C₆-alkyl-C(O)-NH-,
 carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-,
 carboxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-,
 amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, amino-C₂-C₆-alkenyl, C₁-C₆-

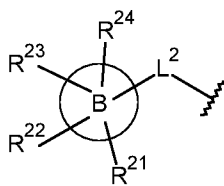


alkylimidoamino- and a group ; wherein:

A is selected from C₆-C₁₄-aryl, C₂-C₉-heterocyclyl and C₁-C₁₃-heteroaryl;

L¹ is selected from a covalent bond, -O-, -S-, SO₂, carbonyl, -C(O)-O-, -C(O)-
 NH-, -C₁-C₆-alkyl-C(O)-NH-, -C₁-C₆-alkyl-NH-C(O)-, -C₁-C₆-alkyl-NH-
 C(O)-C₁-C₆-alkyl-, -C₁-C₆-alkyl-CH(OH)-, -C(O)-C₁-C₆-alkyl-N(C₁-C₆-
 15 alkyl)-C(O)- and -NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-;

R¹⁷ is selected from hydrogen, halogen, carboxy, carboxy-C₁-C₆-alkyl, C₁-C₆-alkyl,
 halo-C₁-C₆-alkyl, oxo, imino, thiono, hydroxy-C₁-C₆-alkyl, cyano-C₁-C₆-alkyl,
 hydroxy, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-, C₁-C₆-alkyl-NH-C₁-C₆-
 alkyl-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-, carbamimidoyl, C₁-C₆-alkyl-C(O)-,
 20 amino-C₁-C₆-alkyl-C(O)-, di-C₁-C₆-alkoxyphosphoryl, C₁-C₆-alkylsulfonyl,



and a group ;

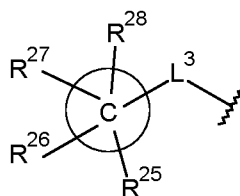
R¹⁸ is selected from hydrogen, hydroxy and C₁-C₆-alkyl;

R¹⁹ and R²⁰ are both hydrogen or hydroxy;

B is selected from C₃-C₁₂-cycloalkyl, C₂-C₉-heterocyclyl and C₁-C₁₃-heteroaryl;

L² is selected from -O-, -C₁-C₆-alkyl- and carbonyl;

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R^{21} is hydrogen or a group ;

R^{22} is hydrogen or amino- C_1 - C_6 -alkyl- $CH(OH)$ - $C(O)$ - NH -;

R^{23} and R^{24} are both independently selected from hydrogen, amino and hydroxy;

C is C_2 - C_9 -heterocyclyl;

5 L^3 is $-O-$;

R^{25} is amino- C_1 - C_6 -alkyl-; and

R^{26} , R^{27} and R^{28} are all hydroxy;

R^{13} is selected from hydrogen, hydroxy, halogen, amino and C_1 - C_6 -alkoxycarbonyl- NH -; and

10 R^{14} is selected from hydrogen, halogen and hydroxy; or

R^{13} and R^{14} , taken together with the carbon atom(s) to which they are attached, form a C_3 - C_{12} -cycloalkyl;

R^{15} is selected from hydrogen, halogen and hydroxy; and

R^{16} is hydrogen or hydroxy.

15 In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

(i) R^1 is C_1 - C_6 -alkyl substituted with R^{12} , R^{13} , R^{14} , R^{15} and/or R^{16} ; and R^{11} is hydrogen; or

(ii) R^1 and R^{11} , taken together with the atoms to which they are attached, form a β -, γ -, δ -
20 or ϵ -lactam;

R^2 is selected from hydrogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl- NH - C_1 - C_6 -alkyl-, $(C_1$ - C_6 -alkyl) $_2N$ - C_1 - C_6 -alkyl-, amino- C_1 - C_6 -alkyl- O - C_1 - C_6 -alkyl, and C_3 - C_{12} -cycloalkyl;

R^3 is selected from hydrogen, halogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -
25 alkyl, C_2 - C_6 -alkenyl, NO_2 , cycloalkyl, and hydroxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl;

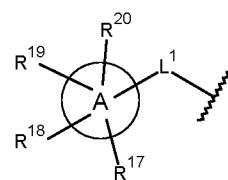
R^4 , R^8 , R^9 and R^{10} are all hydrogen;

R^5 and R^6 are each independently hydrogen or halogen;

R^7 is selected from halogen, hydroxy, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy, cyano- C_1 - C_6 -alkoxy, amino- C_2 - C_6 -alkynyloxy and amino- C_1 - C_6 -alkoxy- C_2 - C_6 -alkynyloxy;

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R^{12} is selected from hydrogen, halogen, vinyl, hydroxy, amino, $(C_1-C_6-alkyl)_2N-$,
 carboxy, $C_1-C_6-alkoxycarbonyl$, $C_1-C_6-alkoxycarbonyl-NH-$, carbamoyl, C_1-C_6-
 $alkyl-NH-C(O)-$, $(C_1-C_6-alkyl)_2N-C(O)-$, $C_1-C_6-alkyl-NH-C_1-C_6-alkyl-N(C_1-C_6-$
 $alkyl)-C(O)-$, $(C_1-C_6-alkyl)_2N-C_1-C_6-alkyl-NH-C(O)-$, amino- $C_1-C_6-alkyl-C(O)-$
 $NH-$, $(C_1-C_6-alkyl)_2N-C_1-C_6-alkyl-C(O)-NH-$, amino- $C_1-C_6-alkyl-NH-C(O)-NH-$,
 amino- $C_1-C_6-alkyl-CH(OH)-C_1-C_6-alkyl-C(O)-NH-$, amino- $C_1-C_6-alkyl-CH(OH)-$,
 guanidino, guanidino- $C_1-C_6-alkyl-C(O)-NH-$, guanidino- $C_1-C_6-alkyl-CH(NH_2)-$
 $C(O)-NH-$, carboxy- $C_1-C_6-alkyl-NH-C(=NH)-NH-C_1-C_6-alkyl-CH(NH_2)-C(O)-$
 $NH-$, ureido- $C_1-C_6-alkyl-CH(NH_2)-C(O)-NH-$, carboxy- $CH(NH_2)-C_1-C_6-alkyl-$
 $C(O)-NH-$, hydroxy- $C_1-C_6-alkyl-CH(NH_2)-C(O)-NH-$, carboxy- $C_1-C_6-alkyl-$
 $CH(NH_2)-C(O)-NH-CH(guanidino-C_1-C_6-alkyl)-C(O)-NH-$, amino- $C_1-C_6-alkyl-$



$CH(NH_2)-C(O)-NH-$, $C_1-C_6-alkylimidoylamino-$ and a group

R^{13} is selected from hydrogen, hydroxy, halogen, amino and $C_1-C_6-alkoxycarbonyl-NH-$;
 R^{14} and R^{15} are both independently selected from hydrogen, halogen and hydroxy;
 R^{16} , R^{19} and R^{20} are each independently hydrogen or hydroxy;
 R^{17} is selected from hydrogen, carboxy, carboxy- $C_1-C_6-alkyl$, $C_1-C_6-alkyl$, halo- C_1-C_6-
 $alkyl$, oxo, imino, hydroxy- $C_1-C_6-alkyl$, cyano- $C_1-C_6-alkyl$, hydroxy, amino, C_1-C_6-
 $alkyl-NH-$, $(C_1-C_6-alkyl)_2N-$, $C_1-C_6-alkyl-NH-C_1-C_6-alkyl-$, $(C_1-C_6-alkyl)_2N-C_1-C_6-$
 $alkyl-$, carbamimidoyl, $C_1-C_6-alkyl-C(O)-$, di- $C_1-C_6-alkoxyphosphoryl$ and C_1-C_6-
 $alkylsulfonyl$;
 R^{18} is selected from hydrogen, hydroxy and $C_1-C_6-alkyl$;
 A is selected from C_6-C_{14} -aryl, C_2-C_9 -heterocyclyl and C_1-C_{13} -heteroaryl; and
 L^1 is selected from a covalent bond, $-O-$, $-S-$, SO_2 , carbonyl, $-C(O)-O-$, $-C(O)-NH-$, $-$
 $C_1-C_6-alkyl-C(O)-NH-$, $-C_1-C_6-alkyl-CH(OH)-$, $-C(O)-C_1-C_6-alkyl-N(C_1-C_6-alkyl)-$
 $C(O)-$ and $-NH-C_1-C_6-alkyl-CH(NH_2)-C(O)-NH-$.

In a preferred embodiment, the present invention provides a compound of formula (I) as
 described herein, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is $C_1-C_6-alkyl$ substituted with R^{12} , R^{13} , R^{14} , R^{15} and/or R^{16} ;
 R^2 is hydrogen or $C_1-C_6-alkyl$;

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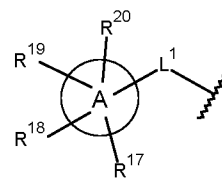
R^3 is halogen or C_1 - C_6 -alkyl;

R^4 , R^8 , R^9 , R^{10} , R^{11} , R^{13} , R^{14} , R^{15} , R^{16} , R^{19} and R^{20} are all hydrogen;

R^5 and R^6 are each independently hydrogen or halogen;

R^7 is selected from C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy and cyano- C_1 - C_6 -alkoxy;

5 R^{12} is selected from C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-N(C_1 - C_6 -alkyl)-C(O)-, hydroxy- C_1 - C_6 -alkyl-CH(NH₂)-C(O)-NH-, amino, amino- C_1 - C_6 -alkyl-C(O)-NH-, amino- C_1 - C_6 -alkyl-CH(NH₂)-C(O)-NH-, amino- C_1 - C_6 -alkyl-CH(OH)- C_1 - C_6 -alkyl-C(O)-NH-, amino- C_1 - C_6 -alkyl-NH-C(O)-NH-, guanidino- C_1 - C_6 -alkyl-CH(NH₂)-C(O)-NH-,



guanidino, guanidino- C_1 - C_6 -alkyl-C(O)-NH- and a group ;

10 R^{17} is selected from hydrogen, hydroxy, C_1 - C_6 -alkyl, carbamimidoyl, hydroxy- C_1 - C_6 -alkyl and imino;

R^{18} is hydrogen or hydroxy;

A is C_2 - C_9 -heterocyclyl; and

L^1 is selected from a covalent bond, -C(O)-NH- and carbonyl.

15 In a particularly preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is C_1 - C_6 -alkyl substituted with R^{12} , R^{13} , R^{14} , R^{15} and/or R^{16} ;

wherein said C_1 - C_6 -alkyl is selected from methyl, ethyl, propyl, butyl, pentyl and 1-methyl-ethyl;

20 R^2 is hydrogen or methyl;

R^3 is selected from chloro, methyl and ethyl;

R^4 , R^8 , R^9 , R^{10} , R^{11} , R^{13} , R^{14} , R^{15} , R^{16} , R^{19} and R^{20} are all hydrogen;

R^5 is selected from hydrogen, fluoro and chloro;

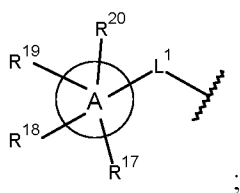
R^6 is hydrogen or fluoro;

25 R^7 is selected from methoxy, difluoromethoxy and cyanomethoxy;

R^{12} is selected from [(2R)-2-amino-5-guanidino-pentanoyl]amino, [(2S)-2-amino-5-guanidino-pentanoyl]amino, 2-aminoethylcarbamoylamino, guanidino, 5-guanidinopentanoylamino, amino, 3-aminopropylcarbamoylamino, [(2S)-2-amino-3-hydroxy-propanoyl]amino, (2-aminoacetyl)amino, 3-aminopropanoylamino,

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[(2S,3R)-2-amino-3-hydroxy-butanoyl]amino, [(2S)-2,5-diaminopentanoyl]amino, (4-amino-3-hydroxy-butanoyl)amino, [(2S)-2,6-diaminohexanoyl]amino, [(2S)-2,4-diaminobutanoyl]amino, [(2S)-2,3-diaminopropanoyl]amino, methyl-[2-(methylamino)ethyl]carbamoyl, [(2S)-2-amino-3-guanidino-propanoyl]amino and a



5

group

;

R^{17} is selected from hydrogen, hydroxy, methyl, carbamimidoyl, hydroxymethyl and imino;

R^{18} is hydrogen or hydroxy;

A is selected from 4-piperidyl, piperazin-1-yl, pyrrolidin-2-yl and imidazolidin-4-yl;
and

10

L^1 is selected from a covalent bond, $-C(O)-NH-$ and carbonyl.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is C_1 - C_6 -alkyl substituted with R^{12} , R^{13} , R^{14} , R^{15} and/or R^{16} ;

15

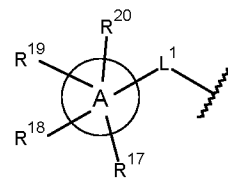
R^2 is selected from hydrogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl- NH - C_1 - C_6 -alkyl-, $(C_1$ - C_6 -alkyl) $_2N$ - C_1 - C_6 -alkyl-, amino- C_1 - C_6 -alkyl- O - C_1 - C_6 -alkyl, and C_3 - C_{12} -cycloalkyl;

R^{12} is selected from hydrogen, halogen, vinyl, hydroxy, amino, $(C_1$ - C_6 -alkyl) $_2N$ -, carboxy, C_1 - C_6 -alkoxycarbonyl, C_1 - C_6 -alkoxycarbonyl- NH -, carbamoyl, C_1 - C_6 -alkyl- NH - $C(O)$ -, $(C_1$ - C_6 -alkyl) $_2N$ - $C(O)$ -, C_1 - C_6 -alkyl- NH - C_1 - C_6 -alkyl- $N(C_1$ - C_6 -alkyl)- $C(O)$ -, $(C_1$ - C_6 -alkyl) $_2N$ - C_1 - C_6 -alkyl- NH - $C(O)$ -, amino- C_1 - C_6 -alkyl- $C(O)$ - NH -, $(C_1$ - C_6 -alkyl) $_2N$ - C_1 - C_6 -alkyl- $C(O)$ - NH -, amino- C_1 - C_6 -alkyl- NH - $C(O)$ - NH -, amino- C_1 - C_6 -alkyl- $CH(OH)$ - C_1 - C_6 -alkyl- $C(O)$ - NH -, amino- C_1 - C_6 -alkyl- $CH(OH)$ -, guanidino, guanidino- C_1 - C_6 -alkyl- $C(O)$ - NH -, guanidino- C_1 - C_6 -alkyl- $CH(NH_2)$ - $C(O)$ - NH -, carboxy- C_1 - C_6 -alkyl- NH - $C(=NH)$ - NH - C_1 - C_6 -alkyl- $CH(NH_2)$ - $C(O)$ - NH -, ureido- C_1 - C_6 -alkyl- $CH(NH_2)$ - $C(O)$ - NH -, carboxy- $CH(NH_2)$ - C_1 - C_6 -alkyl- $C(O)$ - NH -, hydroxy- C_1 - C_6 -alkyl- $CH(NH_2)$ - $C(O)$ - NH -, carboxy- C_1 - C_6 -alkyl-

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CH(NH₂)-C(O)-NH-CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-, amino-C₁-C₆-alkyl-



CH(NH₂)-C(O)-NH-, C₁-C₆-alkylimidoylamino- and a group

R¹³ is selected from hydrogen, hydroxy, halogen, amino and C₁-C₆-alkoxycarbonyl-NH-;

R¹⁴ and R¹⁵ are both independently selected from hydrogen, halogen and hydroxy;

5 R¹⁶ is hydrogen or hydroxy; and

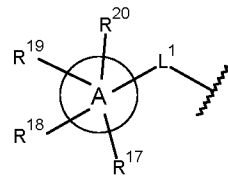
R¹⁷, R¹⁸, R¹⁹, R²⁰, A, and L¹ are as defined herein.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

R¹ is C₁-C₆-alkyl substituted with R¹², R¹³, R¹⁴, R¹⁵ and/or R¹⁶;

10 R² is hydrogen or C₁-C₆-alkyl;

R¹² is selected from C₁-C₆-alkyl-NH-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, hydroxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, amino, amino-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-NH-C(O)-NH-, guanidino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-,



15 guanidino, guanidino-C₁-C₆-alkyl-C(O)-NH- and a group

R¹³, R¹⁴, R¹⁵ and R¹⁶ are all hydrogen; and

R¹⁷, R¹⁸, R¹⁹, R²⁰, A, and L¹ are as defined herein.

In a particularly preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

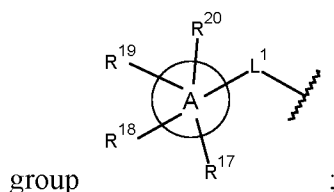
20 R¹ is C₁-C₆-alkyl substituted with R¹², R¹³, R¹⁴, R¹⁵ and/or R¹⁶;

wherein said C₁-C₆-alkyl is selected from methyl, ethyl, propyl, butyl, pentyl and 1-methyl-ethyl;

R² is hydrogen or methyl;

25 R¹² is selected from [(2R)-2-amino-5-guanidino-pentanoyl]amino, [(2S)-2-amino-5-guanidino-pentanoyl]amino, 2-aminoethylcarbamoylamino, guanidino, 5-

- guanidinopentanoylamino, amino, 3-aminopropylcarbamoylamino, [(2S)-2-amino-3-hydroxy-propanoyl]amino, (2-aminoacetyl)amino, 3-aminopropanoylamino, [(2S,3R)-2-amino-3-hydroxy-butanoyl]amino, [(2S)-2,5-diaminopentanoyl]amino, (4-amino-3-hydroxy-butanoyl)amino, [(2S)-2,6-diaminohexanoyl]amino, [(2S)-2,4-diaminobutanoyl]amino, [(2S)-2,3-diaminopropanoyl]amino, methyl-[2-(methylamino)ethyl]carbamoyl, [(2S)-2-amino-3-guanidino-propanoyl]amino and a



R^{13} , R^{14} , R^{15} and R^{16} are all hydrogen; and
 R^{17} , R^{18} , R^{19} , R^{20} , A, and L^1 are as defined herein.

- 10 In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:
- R^3 is selected from hydrogen, halogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, NO_2 , cycloalkyl, and hydroxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl; and
 R^4 , R^{10} and R^{11} are all hydrogen.
- 15 In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:
- R^3 is halogen or C_1 - C_6 -alkyl; and
 R^4 , R^{10} and R^{11} are all hydrogen.

- In a particularly preferred embodiment, the present invention provides a compound of formula
- 20 (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:
- R^3 is selected from chloro, methyl and ethyl; and
 R^4 , R^{10} and R^{11} are all hydrogen.

- In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:
- 25 R^5 and R^6 are each independently hydrogen or halogen;
 R^7 is selected from halogen, hydroxy, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy, cyano- C_1 - C_6 -alkoxy, amino- C_2 - C_6 -alkynyloxy and amino- C_1 - C_6 -alkoxy- C_2 - C_6 -alkynyloxy; and
 R^8 and R^9 are both hydrogen.

In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

R⁵ and R⁶ are each independently hydrogen or halogen;

R⁷ is selected from C₁-C₆-alkoxy, halo-C₁-C₆-alkoxy and cyano-C₁-C₆-alkoxy; and

5 R⁸ and R⁹ are both hydrogen.

In a particularly preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

R⁵ is selected from hydrogen, fluoro and chloro;

R⁶ is hydrogen or fluoro;

10 R⁷ is selected from methoxy, difluoromethoxy and cyanomethoxy; and

R⁸ and R⁹ are both hydrogen.

In one embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

15 R¹⁷ is selected from hydrogen, carboxy, carboxy-C₁-C₆-alkyl, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, oxo, imino, hydroxy-C₁-C₆-alkyl, cyano-C₁-C₆-alkyl, hydroxy, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-, carbamimidoyl, C₁-C₆-alkyl-C(O)-, di-C₁-C₆-alkoxyphosphoryl and C₁-C₆-alkylsulfonyl;

R¹⁸ is selected from hydrogen, hydroxy and C₁-C₆-alkyl;

20 R¹⁹ and R²⁰ are each independently hydrogen or hydroxy;

A is selected from C₆-C₁₄-aryl, C₂-C₉-heterocyclyl and C₁-C₁₃-heteroaryl; and

L¹ is selected from a covalent bond, -O-, -S-, SO₂, carbonyl, -C(O)-O-, -C(O)-NH-, -C₁-C₆-alkyl-C(O)-NH-, -C₁-C₆-alkyl-CH(OH)-, -C(O)-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)- and -NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-.

25 In a preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

R¹⁷ is selected from hydrogen, hydroxy, C₁-C₆-alkyl, carbamimidoyl, hydroxy-C₁-C₆-alkyl and imino;

R¹⁸ is hydrogen or hydroxy;

30 R¹⁹ and R²⁰ are both hydrogen;

A is C₂-C₉-heterocyclyl; and

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L^1 is selected from a covalent bond, $-C(O)-NH-$ and carbonyl.

In a particularly preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein:

R^{17} is selected from hydrogen, hydroxy, methyl, carbamimidoyl, hydroxymethyl and imino;

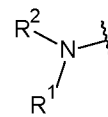
R^{18} is hydrogen or hydroxy;

R^{19} and R^{20} are both hydrogen;

A is selected from 4-piperidyl, piperazin-1-yl, pyrrolidin-2-yl and imidazolidin-4-yl; and

L^1 is selected from a covalent bond, $-C(O)-NH-$ and carbonyl.

In one embodiment, the present invention provides a compound of formula (I) as described



herein, or a pharmaceutically acceptable salt thereof, wherein the group is selected from:

dimethylamine; methylamin; ethylamin; 2-hydroxyethylamino; 2-(dimethylamino)ethyl-

methylamino; 2-aminoethylamino; 3-(dimethylamino)propylamino; diethylamine; 2-piperazin-1-ylethylamino; 2-aminoethyl(methyl)amino; [2-(methylamino)-2-oxoethyl]amino; [2-

(dimethylamino)-2-oxoethyl]amino; (2-amino-2-oxoethyl)amino; 2-hydroxyethyl(methyl)amino; [2-(4-hydroxypiperidin-1-yl)-2-oxoethyl]amino; 3-aminopropyl(methyl)amino; 2-(1-

methylpiperidin-4-yl)ethylamino; 2-(4-methylpiperazin-1-yl)ethylamino; 3-aminopropylamino;

pyridin-2-ylmethylamino; bis(2-hydroxyethyl)amino; (1-methylpiperidin-4-yl)methylamino; 4-

aminobutyl(methyl)amino; methyl(2-piperidin-4-ylethyl)amino; 5-[(2-methylpropan-2-yl)oxycarbonylamino]pentylamino; 5-aminopentylamino; 4-aminobutylamino; 2-piperidin-4-

ylethylamino; piperidin-4-ylmethylamino; 6-aminoethylamino; [(2-(R))-1-aminopropan-2-

yl]amino; pyrrolidin-3-ylmethylamino; methyl(2-piperazin-1-ylethyl)amino; [(5-(S))-6-methoxy-

5-[(2-methylpropan-2-yl)oxycarbonylamino]-6-oxohexyl]amino; morpholin-2-ylmethylamino;

2-(1-acetylpiperidin-4-yl)ethyl-methylamino; methyl-[2-(1-methylsulfonylpiperidin-4-

yl)ethyl]amino; [(2-(R))-2-aminopropyl]amino; 2-morpholin-4-ylethylamino; (1-hydroxy-3-

morpholin-4-ylpropan-2-yl)amino; (2-morpholin-4-yl-2-oxoethyl)amino; (2-methyl-1-

morpholin-4-ylpropan-2-yl)amino; 3-morpholin-4-ylpropylamino; 2-(3-oxomorpholin-4-

yl)ethylamino; methyl-(2-morpholin-4-yl-2-oxoethyl)amino; methyl(2-morpholin-4-

ylethyl)amino; 2-(2,2-dimethylmorpholin-4-yl)ethyl-methylamino; 2-[(2-(S),6-(R))-2,6-dimethylmorpholin-4-yl]ethyl-methylamino; 2-[(2-(S),6-(R))-2,6-dimethylmorpholin-4-yl]ethylamino; methyl-[2-(4-methylpiperazin-1-yl)-2-oxoethyl]amino; methyl-[2-[methyl-[2-(4-methylpiperazin-1-yl)-2-oxoethyl]amino]-2-oxoethyl]amino; methyl(2-piperidin-1-ylethyl)amino; [(5-(S))-5-amino-6-methoxy-6-oxohexyl]amino; 2-(1-diethoxyphosphorylpiperidin-4-yl)ethyl-methylamino; (4-hydroxypiperidin-4-yl)methylamino; 2-(3-oxopiperazin-1-yl)ethylamino; (1-carbamimidoylpiperidin-4-yl)methylamino; [(5-(S))-5-amino-5-carboxypentyl]amino; piperidin-3-ylmethylamino; piperidin-2-ylmethylamino; morpholin-3-ylmethylamino; (4-hydroxypiperidin-4-yl)methyl-methylamino; 4-morpholin-4-ylbutylamino; methyl-[2-oxo-2-(3-oxopiperazin-1-yl)ethyl]amino; methyl-(2-oxo-2-piperazin-1-ylethyl)amino; [2-(3-carboxypiperazin-1-yl)-2-oxoethyl]-methylamino; 3-(3-oxopiperazin-1-yl)propylamino; oxan-4-ylmethylamino; methyl(oxan-4-ylmethyl)amino; 3-(4-methyl-3-oxopiperazin-1-yl)propylamino; [2-(dimethylamino)-2-oxoethyl]-methylamino; piperazin-2-ylmethylamino; [2-[3-[(dimethylamino)methyl]pyrrolidin-1-yl]-2-oxoethyl]-methylamino; 3-(1,1-dioxo-1,4-thiazinan-4-yl)propylamino; 2-(oxan-4-yl)ethylamino; methyl(piperidin-4-ylmethyl)amino; 2-(2-oxopiperazin-1-yl)ethylamino; 1,3-dihydroxypropan-2-ylamino; 5-morpholin-4-ylpentylamino; methyl(4-morpholin-4-ylbutyl)amino; 3-piperazin-1-ylpropylamino; 3-carboxypropyl(methyl)amino; methyl(3-piperidin-1-ylpropyl)amino; 3-piperazin-1-ylsulfonylpropylamino; 2-[4-(2,2-difluoroethyl)piperazin-1-yl]ethyl-methylamino; methyl-(4-oxo-4-piperazin-1-ylbutyl)amino; methyl-(3-oxo-3-piperazin-1-ylpropyl)amino; thian-4-ylmethylamino; (5-amino-1,3-dioxan-2-yl)methylamino; (5-amino-1,3-dioxan-2-yl)methyl-methylamino; (1,1-dioxothian-4-yl)methylamino; 3-(2-oxopiperazin-1-yl)propylamino; methyl(3-piperazin-1-ylpropyl)amino; oxolan-3-ylmethylamino; methyl(oxolan-3-ylmethyl)amino; oxan-3-ylmethylamino; 3-(3-carboxypiperazin-1-yl)propylamino; 3-(5-amino-1,3-dioxan-2-yl)propyl-methylamino; [4-[2-(aminomethyl)morpholin-4-yl]-4-oxobutyl]-methylamino; 2-piperazin-1-ylethyl(2,2,2-trifluoroethyl)amino; methyl(pyridin-4-ylmethyl)amino; 2,2-difluoroethyl(2-piperazin-1-ylethyl)amino; [(2-(R))-1-hydroxy-3-(1~{H}-imidazol-5-yl)propan-2-yl]amino; methyl-[2-(triazolo[4,5-b]pyridin-3-yloxy)ethyl]amino; [(2-(R),3-(R),4-(S),5-(S))-2,3,4,5,6-pentahydroxyhexyl]amino; 2-(4-hydroxypiperidin-4-yl)ethylamino; (3-hydroxypyrrolidin-3-yl)methylamino; ethyl(methyl)amino; 2-pyridin-4-ylethylamino; 2-(dimethylamino)ethyl-ethylamino; methyl-(5-oxo-5-piperazin-1-ylpentyl)amino; 3-(azetidin-1-yl)propylamino; 5-piperazin-1-ylpentylamino; methyl(pyridin-3-ylmethyl)amino; methyl(pyrimidin-4-ylmethyl)amino; 2-(1~{H}-imidazol-2-yl)ethyl-methylamino; ethyl(2-

piperazin-1-ylethyl)amino; 2-[2-[(dimethylamino)methyl]morpholin-4-yl]ethyl-methylamino; (3-hydroxyazetidin-3-yl)methylamino; azetidin-3-ylmethyl(methyl)amino; 2-imidazol-1-ylethyl(methyl)amino; methyl-[2-[2-(methylaminomethyl)morpholin-4-yl]ethyl]amino; cyclopropyl(2-piperazin-1-ylethyl)amino; 3-pyridin-4-ylpropylamino; 2-[1-(2-cyanoethyl)piperidin-4-yl]ethyl-methylamino; 2-(piperidine-4-carbonylamino)ethylamino; 2-(piperazine-1-carbonylamino)ethylamino; 2-(1-methyltetrazol-5-yl)sulfanylethylamino; 2-(1-{H}-tetrazol-5-yl)ethylamino; methyl-[3-(1-methyltetrazol-5-yl)sulfanylpropyl]amino; 3-[1-[2-(dimethylamino)ethyl]tetrazol-5-yl]sulfanylpropyl-methylamino; 2-[1-(2-carboxyethyl)piperidin-4-yl]ethyl-methylamino; (2-oxo-1~{H}-pyridin-4-yl)methylamino; (1-methyl-2-oxopyridin-4-yl)methylamino; (1-methyl-6-oxopyridin-3-yl)methylamino; 2-[[2-(S))-2-amino-5-carbamimidamidopentanoyl]amino]ethylamino; 2-[(3-(S))-3-amino-2-oxopiperidin-1-yl]ethylamino; 3-[[2-(S))-2-amino-5-carbamimidamidopentanoyl]amino]propylamino; 2-(2-aminoethylcarbamoylethylamino)ethylamino; 2-[[3-(S))-3-carboxypiperazine-1-carbonyl]amino]ethylamino; 4-carbamimidamidobutylamino; 2-[1-(2-carboxyethyl)piperidin-4-yl]ethylamino; 2-(3-aminopropylcarbamoylethylamino)ethylamino; 3-(2-aminoethylcarbamoylethylamino)propylamino; 3-(3-aminopropylcarbamoylethylamino)propylamino; ethyl(2-hydroxyethyl)amino; 3-[[4-(S))-4-amino-4-carboxybutanoyl]amino]propylamino; 2-[3-[(2-(R))-1-methyl-3-oxoaziridin-2-yl]propanoylamino]ethylamino; 2-[3-[(2-(R))-3-oxoaziridin-2-yl]propanoylamino]ethylamino; ethyl-[2-(methylamino)ethyl]amino; 4-aminobutan-2-ylamino; ethyl(3-hydroxypropyl)amino; [(3-(R))-3-[(2-(S))-2-amino-5-carbamimidamidopentanoyl]amino]butylamino; [(2-(R))-2-[(2-(S))-2-amino-5-carbamimidamidopentanoyl]amino]propylamino; 4-[[2-(R),3-(R),4-(S),5-(S))-2,3,4,5,6-pentahydroxyhexyl]carbamoylethylamino]piperidin-1-yl; (4-amino-1,1-difluorobutan-2-yl)amino; 1-aminopentan-3-ylamino; 2-(5-methyl-4~{H}-1,2,4-triazol-3-yl)ethylamino; 3-pyrrolidin-1-ylpropylamino; methyl-[2-(1-methylpiperidin-4-yl)ethyl]amino; 3-aminopropyl(ethyl)amino; 2-[[2-(S))-2-amino-5-(carbamoylethylamino)pentanoyl]amino]ethylamino; (1-methylazetidin-3-yl)methylamino; (2-hydroxy-3-pyrrolidin-1-ylpropyl)amino; 3-imidazol-1-ylpropylamino; oxetan-3-ylmethylamino; 2-(5-carbamimidamidopentanoylamino)ethylamino; [(2-(R))-4-aminobutan-2-yl]amino; [(2-(S))-3-amino-1-methoxy-1-oxopropan-2-yl]amino; [(2-(S))-4-amino-1-methoxy-1-oxobutan-2-yl]amino; (3-amino-2,2-dimethylpropyl)amino; (1-amino-2-methylpropan-2-yl)amino; [(1-(R))-2-amino-1-phenylethyl]amino; (4-amino-1,1,1-trifluorobutan-2-yl)amino; (3-amino-2-hydroxypropyl)amino; 2-[[2-(R))-2-amino-5-(4,5-dihydro-1~{H}-imidazol-2-ylamino)pentanoyl]amino]ethylamino; 3-hydroxypropylamino; [(2-

- (S))-1-[[2-(S))-2-amino-5-carbamimidamidopentanoyl]amino]propan-2-yl]amino; 2-[[2-(S))-2-amino-4-carbamimidamidobutanoyl]amino]ethylamino; [3-[2-(dimethylamino)ethylamino]-3-oxopropyl]amino; (4-amino-2-methylbutan-2-yl)amino; 2-[[2-(S))-2-amino-3-hydroxypropanoyl]amino]ethylamino; 2-[(2-aminoacetyl)amino]ethylamino; 2-(3-aminopropanoylamino)ethylamino; 2-[[2-(S),3-(S))-2-amino-3-hydroxybutanoyl]amino]ethylamino; 2-[[2-(S),4-(S))-4-hydroxypyrrolidine-2-carbonyl]amino]ethylamino; 2-[[2-(dimethylamino)acetyl]amino]ethylamino; 3-[[2-(dimethylamino)acetyl]amino]propylamino; 2-[[2-(S))-2,5-diaminopentanoyl]amino]ethylamino; 2-(4-aminobutanoylamino)ethylamino; 2-[(4-amino-3-hydroxybutanoyl)amino]ethylamino; 3-[[2-(S))-2-amino-4-carbamimidamidobutanoyl]amino]propylamino; methyl-[3-(pyridine-4-carboxyloxy)propyl]amino; [(2-(S))-4-[[2-(S))-2-amino-5-carbamimidamidopentanoyl]amino]butan-2-yl]amino; 2-[[2-(S))-2,6-diaminohexanoyl]amino]ethylamino; 2-[[2-(S))-2,4-diaminobutanoyl]amino]ethylamino; 2-[[2-(S))-2,3-diaminopropanoyl]amino]ethylamino; 3-[[2-(S))-2-amino-3-carbamimidamidopropanoyl]amino]propylamino; [3-[[2-(S))-2-amino-3-carbamimidamidopropanoyl]amino]-2-hydroxypropyl]amino; 3-[(2-iminoimidazolidine-4-carbonyl)amino]propylamino; [3-(3-aminopropanoylamino)-2-hydroxypropyl]amino; [3-[(2-aminoacetyl)amino]-2-hydroxypropyl]amino; 3-[[2-(S))-2-[[2-(S))-2-amino-4-carboxybutanoyl]amino]-5-carbamimidamidopentanoyl]amino]propylamino; 2-[[2-(S),4-(S))-4-hydroxy-4-methylpyrrolidine-2-carbonyl]amino]ethylamino; 3-[[2-(S),4-(S))-4-hydroxypyrrolidine-2-carbonyl]amino]propylamino; 3-[[2-(S),4-(S))-4-hydroxy-4-methylpyrrolidine-2-carbonyl]amino]propylamino; 2-[[2-(S),4-(S))-4-ethyl-4-hydroxypyrrolidine-2-carbonyl]amino]ethylamino; 4-[[2-(S),4-(S))-4-hydroxy-4-methylpyrrolidine-2-carbonyl]piperazin-1-yl; 3-[(2-aminoacetyl)amino]propylamino; [2-[methyl-[2-(methylamino)ethyl]amino]-2-oxoethyl]amino; 3-[(2-(S),3-(S),4-(S),5-(R),6-(R))-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxypropylamino; 2-[[2-(S))-2-amino-5-[[~{N}-(3-carboxypropyl)carbamimidoyl]amino]pentanoyl]amino]ethylamino; 3-[[2-[[2-(S))-2-amino-4-carboxybutanoyl]amino]-3-carbamimidamidopropanoyl]amino]propylamino; [3-[(3-(S))-3-(hydroxymethyl)piperazin-1-yl]-3-oxopropyl]amino; [4-[(3-(S))-3-(hydroxymethyl)piperazin-1-yl]-4-oxobutyl]amino; [6-[(3-(S))-3-(hydroxymethyl)piperazin-1-yl]-6-oxohexyl]amino; [5-[(3-(S))-3-(hydroxymethyl)piperazin-1-yl]-5-oxopentyl]amino; 1-(ethanimidoylamino)propan-2-

ylamino; prop-2-enylamino; and [1-[(2-(S))-2,6-diaminohexanoyl]amino]-2-methylpropan-2-yl]amino.

In a particularly preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein the compound of

5 formula (I) is selected from:

2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-piperidylmethyl)benzamide;

4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-piperidyl)ethyl]benzamide;

10 N-(6-aminohexyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;

4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-piperidyl)ethyl]benzamide;

4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(3-15 piperazin-1-ylpropyl)benzamide;

4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N,2-trimethylbenzamide;

2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;

20 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethylbenzamide;

2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-[2-(4-piperidyl)ethyl]benzamide;

4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[3-25 (3-oxopiperazin-1-yl)propyl]benzamide;

4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide;

N-(6-aminohexyl)-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;

2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-30 piperazin-1-ylethyl)benzamide;

2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methylbenzamide;

- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(4-pyridylmethyl)benzamide;
- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1,1-dioxothian-4-yl)methyl]benzamide;
- 5 2-chloro-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(5-morpholinopentyl)benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(3-piperazin-1-ylsulfonylpropyl)benzamide;
- 10 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-piperidylmethyl)benzamide;
- 15 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(tetrahydropyran-4-ylmethyl)benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 20 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-piperazin-1-ylethyl)benzamide;
- 25 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-benzamide;
- 2-bromo-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 30 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-oxo-3-piperazin-1-yl-propyl)benzamide;

- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(1-methyl-4-piperidyl)ethyl]benzamide;
N-(5-aminopentyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
5 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(pyrrolidin-3-ylmethyl)benzamide;
2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;
4-[[3-[4-(difluoromethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-
10 dimethyl-N-[2-(4-piperidyl)ethyl]benzamide;
4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-
15 tetrahydropyran-4-ylethyl)benzamide;
4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-2-(trifluoromethyl)benzamide;
4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N,2-trimethyl-benzamide;
4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-
20 piperidyl)ethyl]benzamide;
2-chloro-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-piperazin-1-ylethyl)benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(1-
25 methyl-4-piperidyl)methyl]benzamide;
4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(1-methyl-4-piperidyl)ethyl]benzamide;
4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-iodo-N-methyl-
30 benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-piperidylmethyl)benzamide;

- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[3-(2-oxopiperazin-1-yl)propyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-morpholinobutyl)benzamide;
- 5 2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(4-oxo-4-piperazin-1-yl-butyl)benzamide;
- 10 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(pyrrolidin-3-ylmethyl)benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[3-(4-methyl-3-oxo-piperazin-1-yl)propyl]benzamide;
- 15 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-hydroxyethyl)-N-methyl-benzamide;
- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- N-[(1-carbamimidoyl-4-piperidyl)methyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 20 N-[3-(5-amino-1,3-dioxan-2-yl)propyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-piperazin-1-ylethyl)benzamide;
- 25 4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- N-(4-aminobutyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 30 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-morpholinobutyl)benzamide;
- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethyl-benzamide;

- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- N-(4-aminobutyl)-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 5 4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(1-methyl-4-piperidyl)ethyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-iodo-N-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- N-[3-(1,1-dioxo-1,4-thiazinan-4-yl)propyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 10 N-(4-aminobutyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 2-chloro-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 15 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(4-methylpiperazin-1-yl)ethyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- N-[2-(1-acetyl-4-piperidyl)ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 20 2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(4-piperidylmethyl)benzamide;
- N-[(5-amino-1,3-dioxan-2-yl)methyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 25 N-[(5-amino-1,3-dioxan-2-yl)methyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- N-(4-aminobutyl)-4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- N-(2-amino-2-oxo-ethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 30 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(4-morpholinobutyl)benzamide;

- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(3-morpholinopropyl)benzamide;
- N,N-diethyl-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-2-vinyl-
5 benzamide;
- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(tetrahydropyran-4-ylmethyl)benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(4-piperidylmethyl)benzamide;
- 10 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-piperidylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-
15 oxo-2-(3-oxopiperazin-1-yl)ethyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-oxo-2-piperazin-1-yl-ethyl)benzamide;
- N-[2-(4-hydroxy-1-piperidyl)-2-oxo-ethyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 20 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-piperidylmethyl)benzamide;
- 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-diethyl-benzamide;
- N-(2-hydroxyethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-
25 dimethyl-benzamide;
- N-(3-aminopropyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(tetrahydrofuran-3-ylmethyl)benzamide;
- 30 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(1-methyl-4-piperidyl)methyl]benzamide;
- 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethyl-benzamide;

- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(1-methyl-4-piperidyl)methyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(3-oxopiperazin-1-yl)ethyl]benzamide;
- 5 N-[2-(dimethylamino)-2-oxo-ethyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-2-nitro-benzamide;
- N-[2-hydroxy-1-(hydroxymethyl)ethyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 10 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)-2-vinyl-benzamide;
- N-[2-[3-[(dimethylamino)methyl]pyrrolidin-1-yl]-2-oxo-ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 15 N-[2-(1-diethoxyphosphoryl-4-piperidyl)ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(tetrahydrothiopyran-4-ylmethyl)benzamide;
- N-[4-[2-(aminomethyl)morpholin-4-yl]-4-oxo-butyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 20 N-(3-aminopropyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-isopropyl-N-methyl-benzamide;
- 25 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(tetrahydropyran-3-ylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-piperazin-1-ylpropyl)benzamide;
- N-(2-hydroxyethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
- 30 4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(1-methyl-4-piperidyl)methyl]benzamide;

- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(3-oxopiperazin-1-yl)ethyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(1,1-dimethyl-2-morpholino-ethyl)-2-methyl-benzamide;
- 5 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(tetrahydrofuran-3-ylmethyl)benzamide;
- tert-butyl N-[5-[[4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]pentyl]carbamate;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(3-piperidylmethyl)benzamide;
- 10 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(methylamino)-2-oxo-ethyl]benzamide;
- 15 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-2-propylbenzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(hydroxymethyl)-N-methyl-benzamide;
- N-(3-aminopropyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 20 methyl (2S)-2-amino-6-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]hexanoate;
- N-(2-aminoethyl)-4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 25 N,N-diethyl-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;
- N-(3-aminopropyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- N-(3-aminopropyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-morpholinoethyl)benzamide;

- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-morpholinoethyl)benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(tetrahydropyran-4-ylmethyl)benzamide;
- 5 2-cyclopropyl-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(morpholin-2-ylmethyl)benzamide;
- 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-
- 10 benzamide;
- 2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(morpholin-2-ylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(1-methylsulfonyl-4-piperidyl)ethyl]benzamide;
- 15 N-(3-aminopropyl)-4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-[rac-(2R,6S)-2,6-dimethylmorpholin-4-yl]ethyl]benzamide;
- 2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-
- 20 N-[2-(1-piperidyl)ethyl]benzamide;
- 6-[[3-(2-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3,4-dihydro-2H-isoquinolin-1-one;
- N-(2-aminoethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 25 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(pyrrolidin-3-ylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)-2-vinyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-
- 30 (morpholin-3-ylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-[rac-(2R,6S)-2,6-dimethylmorpholin-4-yl]ethyl]benzamide;

- N-(2-aminoethyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-methylpiperazin-1-yl)-2-oxo-ethyl]benzamide;
- 5 N-[2-(dimethylamino)-2-oxo-ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-hydroxyethoxymethyl)-N-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-morpholino-2-oxo-ethyl)benzamide;
- 10 N-[2-[4-(2,2-difluoroethyl)piperazin-1-yl]ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(morpholin-2-ylmethyl)benzamide;
- 15 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-2-[(E)-prop-1-enyl]benzamide;
- 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-hydroxyethyl)benzamide;
- 2-chloro-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-pyridylmethyl)benzamide;
- 20 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(2,2-dimethylmorpholin-4-yl)ethyl]-N,2-dimethyl-benzamide;
- methyl (2S)-2-(tert-butoxycarbonylamino)-6-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]hexanoate;
- 25 N-[2-(dimethylamino)ethyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(piperazin-2-ylmethyl)benzamide;
- 30 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(3-oxomorpholin-4-yl)ethyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(2-oxopiperazin-1-yl)ethyl]benzamide;

- N-(2-aminoethyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperidylmethyl)benzamide;
- 5 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[1-(hydroxymethyl)-2-morpholino-ethyl]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-morpholino-2-oxo-ethyl)benzamide;
- 4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-piperidylmethyl)benzamide;
- 10 N-(2-aminoethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- N-[(2S)-2-aminopropyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 15 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(morpholin-3-ylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-morpholino-2-oxo-ethyl)benzamide;
- 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(dimethylamino)ethyl]-N-methyl-benzamide;
- 20 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[3-(1-piperidyl)propyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-[methyl-[2-(4-methylpiperazin-1-yl)-2-oxo-ethyl]amino]-2-oxo-ethyl]benzamide;
- 25 N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(hydroxymethyl)-N,N-dimethyl-benzamide;
- 30 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(dimethylamino)ethyl]-N,2-dimethyl-benzamide;

- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(4-hydroxy-4-piperidyl)methyl]-N,2-dimethyl-benzamide;
- 4-[3-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]piperazine-2-carboxylic acid;
- 5 N-(3-aminopropyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(4-hydroxy-4-piperidyl)methyl]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-bis(2-hydroxyethyl)-2-methyl-benzamide;
- 10 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-(dimethylamino)propyl]benzamide;
- N-(2-aminoethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
- 15 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(1-piperidyl)ethyl]benzamide;
- N-(2-aminoethyl)-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(1-piperidyl)ethyl]benzamide;
- 20 N-[(2R)-2-aminopropyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)-N-(2,2,2-trifluoroethyl)benzamide;
- 25 N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- N-[(1R)-2-amino-1-methyl-ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]acetyl]piperazine-2-carboxylic acid;
- 30 4-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]butanoic acid;

- (2S)-2-amino-6-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]hexanoic acid;
- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 5 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(4-pyridyl)ethyl]benzamide;
- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(3-piperazin-1-ylpropyl)benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(5-piperazin-1-ylpentyl)benzamide;
- 10 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(5-oxo-5-piperazin-1-yl-pentyl)benzamide;
- 15 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-pyridylmethyl)benzamide;
- 6-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-3,4-dihydroisoquinolin-1-one;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(pyrimidin-4-ylmethyl)benzamide;
- 20 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-piperazin-1-ylpropyl)benzamide;
- N-(3-aminopropyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(pyrrolidin-3-ylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-ethyl-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-imidazol-1-ylethyl)-N,2-dimethyl-benzamide;
- 30 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1S)-1-(hydroxymethyl)-2-(1H-imidazol-5-yl)ethyl]-2-methyl-benzamide;

- N-(azetidin-3-ylmethyl)-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- N-(3-aminopropyl)-2-ethyl-4-[[3-(2-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 5 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(4-hydroxy-4-piperidyl)ethyl]-2-methyl-benzamide;
- 2-[2-(dimethylamino)ethyl]-6-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3,4-dihydroisoquinolin-1-one;
- N-[3-(azetidin-1-yl)propyl]-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(1H-imidazol-2-yl)ethyl]-N,2-dimethyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-[2-(methylaminomethyl)morpholin-4-yl]ethyl]benzamide;
- 15 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(3-hydroxyazetidin-3-yl)methyl]-2-methyl-benzamide;
- N-[2-[2-[(dimethylamino)methyl]morpholin-4-yl]ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- N-(3-aminopropyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-benzamide;
- 20 N-(3-aminopropyl)-4-[[3-(4-chloro-2-fluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-cyclopropyl-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 25 N-(2,2-difluoroethyl)-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(4-hydroxy-4-piperidyl)methyl]-2-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(3-hydroxypyrrolidin-3-yl)methyl]-2-methyl-benzamide;
- 30 4-[[3-[4-(4-aminobut-2-ynoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(3-aminopropyl)-2-ethyl-benzamide;

- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-
[(2R,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]benzamide;
N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-hydroxy-phenyl)imidazo[1,2-a]pyrazin-8-
yl]amino]-2-ethyl-benzamide;
- 5 N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2-chloro-4-
(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-
benzamide;
- N-[2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-
phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-
difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-
phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[3-(2-aminoethylcarbamoylamino)propyl]-4-[[3-(2,3-difluoro-4-methoxy-
phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2-chloro-3-fluoro-4-
methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(difluoromethoxy)-2,3-
difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 N-[2-[[[(2S)-2-amino-5-(4,5-dihydro-1H-imidazol-2-ylamino)pentanoyl]amino]ethyl]-4-
[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-
benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-
guanidinobutyl)-2-methyl-benzamide;
- 25 N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2-chloro-3-fluoro-4-
methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(1-carbamimidoyl-4-piperidyl)methyl]-4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-
a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-
phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 N-[(2R)-2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-
methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-[(2S)-2-[(2S)-2-amino-5-guanidino-pentanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 3-[4-[2-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]ethyl]-1-piperidyl]propanoic acid;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(3-imidazol-1-ylpropyl)benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-(5-guanidinopentanoylamino)ethyl]benzamide;
- 10 N-(5-aminopentyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(2-oxo-1H-pyridin-4-yl)methyl]benzamide;
- 15 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1-methyl-6-oxo-3-pyridyl)methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(oxetan-3-ylmethyl)benzamide;
- N-[2-[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2-chloro-4-
- 20 (cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(1-carbamimidoyl-4-piperidyl)methyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-
- 25 ethyl-N-(3-hydroxypropyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[2-(dimethylamino)acetyl]amino]ethyl]-2-ethyl-benzamide;
- 2-chloro-4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(4-pyridyl)ethyl]benzamide;
- 30 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-(5-methyl-4H-1,2,4-triazol-3-yl)ethyl]benzamide;
- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1-methyl-2-oxo-4-pyridyl)methyl]benzamide;

- N-[3-(3-aminopropylcarbamoylamino)propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(1-carbamimidoyl-4-piperidyl)methyl]-2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 5 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(1-methylazetidin-3-yl)methyl]benzamide;
- N-[(1-carbamimidoyl-4-piperidyl)methyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-(4-pyridyl)propyl]benzamide;
- 10 N-(3-aminopropyl)-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(3-pyrrolidin-1-ylpropyl)benzamide;
- 15 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-[2-(methylamino)ethyl]-3,4-dihydroisoquinolin-1-one;
- 3-[4-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethyl]-1-piperidyl]propanoic acid;
- 20 2-chloro-4-[[3-[3-chloro-4-(cyanomethoxy)-2-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(4-pyridyl)ethyl]benzamide;
- 2-(3-aminopropyl)-6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3,4-dihydroisoquinolin-1-one;
- 25 N-(4-aminobutyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-hydroxyethyl)-3,4-dihydroisoquinolin-1-one;
- N-[(1R)-2-[(2S)-2-amino-5-guanidino-pentanoyl]amino]-1-methyl-ethyl-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 N-[2-[(2S)-2-amino-5-ureido-pentanoyl]amino]ethyl-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-[2-[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(3-amino-2-hydroxy-propyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 N-[(1R)-3-amino-1-methyl-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(2-amino-1,1-dimethyl-ethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(2-hydroxy-3-pyrrolidin-1-yl-propyl)benzamide;
- N-(3-amino-1,1-dimethyl-propyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-(3-aminopropylcarbamoylamino)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 2-chloro-4-[[3-[4-(1-cyanoethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)benzamide;
- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(3S)-3-[(2S)-2-amino-5-guanidino-pentanoyl]amino]butyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 N-(3-aminopropyl)-4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(triazolo[4,5-b]pyridin-3-yloxy)ethyl]benzamide;
- 25 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-[3-[(2S)-3-oxoaziridin-2-yl]propanoylamino]ethyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(1-methyltetrazol-5-yl)sulfanylethyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-[3-[(2S)-1-methyl-3-oxo-aziridin-2-yl]propanoylamino]ethyl]benzamide;
- 30 N-[2-(2-aminoethylcarbamoylamino)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-(2-aminoethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 1-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-N-[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]piperidine-4-carboxamide;
- 5 N-[(3R)-3-[(2S)-2-amino-5-guanidino-pentanoyl]amino]butyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(3-hydroxyazetidin-3-yl)methyl]benzamide;
- 10 methyl (2S)-3-amino-2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propanoate;
- N-[2-[1-(2-cyanoethyl)-4-piperidyl]ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 15 N-[(1S)-2-[(2S)-2-amino-5-guanidino-pentanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[3-[(2S)-2-amino-5-guanidino-pentanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(3-amino-2,2-dimethyl-propyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 (2S)-2-amino-6-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]hexanoic acid;
- methyl (2R)-3-amino-2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propanoate;
- 25 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(3-hydroxypyrrolidin-3-yl)methyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-[1-[2-(dimethylamino)ethyl]tetrazol-5-yl]sulfanylpropyl]-N,2-dimethyl-benzamide;
- N-[2-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]piperazine-1-carboxamide;
- 30 N-[2-[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,4-dichlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[3-(1-methyltetrazol-5-yl)sulfanylpropyl]benzamide;
- N-[2-[(3S)-3-amino-2-oxo-1-piperidyl]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(1H-tetrazol-5-yl)ethyl]benzamide;
- (2S)-4-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethylcarbamoyl]piperazine-2-carboxylic acid;
- (2S)-2-amino-6-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]hexanoic acid;
- 10 (2S)-4-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethylcarbamoyl]piperazine-2-carboxylic acid;
- N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 4-[[3-[4-(4-aminobut-2-ynoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,N,2-trimethyl-benzamide;
- N-[(1S)-3-amino-1-methyl-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[3-[[2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]propyl]piperazine-2-carboxylic acid;
- 20 N-[3-amino-1-(difluoromethyl)propyl]-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,4-dichlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 (2R)-4-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethylcarbamoyl]piperazine-2-carboxylic acid;
- (2R)-4-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethylcarbamoyl]piperazine-2-carboxylic acid;
- N-[2-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]piperidine-4-carboxamide;
- 30 N-(3-aminopropyl)-2-(2,2-difluoroethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;

- N-(3-amino-1-ethyl-propyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(3-amino-1-methyl-propyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 5 (2S)-2-amino-5-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propylamino]-5-oxo-pentanoic acid;
- 4-[[3-[4-(4-aminobut-2-ynoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(1-methyl-4-piperidyl)ethyl]benzamide;
- N-[3-amino-1-(trifluoromethyl)propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 N-[(1R)-2-amino-1-phenyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- methyl (2S)-4-amino-2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]butanoate;
- 15 (2S,4S)-N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-hydroxy-4-methyl-pyrrolidine-2-carboxamide;
- (2S,4S)-N-[3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-4-methyl-pyrrolidine-2-
- 20 carboxamide;
- N-[2-[(2S)-2-amino-3-hydroxy-propanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[(2-aminoacetyl)amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[(2S,3R)-2-amino-3-hydroxy-butanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[N-[(4S)-4-amino-5-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethylamino]-5-oxo-
- 30 pentyl]carbamidoyl]amino]butanoic acid;

rac-(4S)-4-amino-5-[[2-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propylamino]-1-(guanidinomethyl)-2-oxo-ethyl]amino]-5-oxo-pentanoic acid;

N-[2-[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[(2S)-2,5-diaminopentanoyl]amino]ethyl]-2-ethyl-benzamide;

N-[2-(4-aminobutanoylamino)ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

N-[2-[(4-amino-3-hydroxy-butanoyl)amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[(2S)-2,6-diaminohexanoyl]amino]ethyl]-2-ethyl-benzamide;

4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[(2S)-2,4-diaminobutanoyl]amino]ethyl]-2-ethyl-benzamide;

4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[(2S)-2,3-diaminopropanoyl]amino]ethyl]-2-ethyl-benzamide;

N-[(1R)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

N-[3-(3-aminopropanoylamino)-2-hydroxy-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

(4S)-4-amino-5-[(1S)-1-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propylcarbamoyl]-4-guanidino-butyl]amino]-5-oxo-pentanoic acid;

N-[3-[(2-aminoacetyl)amino]propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[3-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-3-oxo-propyl]benzamide;

4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[4-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-4-oxo-butyl]benzamide;

- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[6-
[(3S)-3-(hydroxymethyl)piperazin-1-yl]-6-oxo-hexyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[5-
[(3S)-3-(hydroxymethyl)piperazin-1-yl]-5-oxo-pentyl]benzamide;
- 5 4-[[3-[4-[4-(2-aminoethoxy)but-2-ynoxy]-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-
yl]amino]-N-(3-aminopropyl)-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-
[methyl-[2-(methylamino)ethyl]amino]-2-oxo-ethyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-
ethyl-N-[3-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-
yl]oxypropyl]benzamide;
- 10 N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-
yl]amino]-2-(difluoromethyl)benzamide;
- N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-
benzoyl]amino]propyl]-2-imino-imidazolidine-4-carboxamide;
- 15 (2S,4R)-N-[3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-
yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- (2S,4R)-N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-
2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- 20 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(2-
piperazin-1-ylethyl)benzamide;
- N-[3-[[[(2S)-2-amino-3-guanidino-propanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-
methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-(4-aminobutanoylamino)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-
a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 (2S,4S)-N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-
2-methyl-benzoyl]amino]propyl]-4-hydroxy-4-methyl-pyrrolidine-2-carboxamide;
- [4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-
phenyl]-[4-[(2S,4R)-4-hydroxy-4-methyl-pyrrolidine-2-carbonyl]piperazin-1-
yl]methanone;
- 30 (2S,4R)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-
2-methyl-benzoyl]amino]ethyl]-4-hydroxy-pyrrolidine-2-carboxamide;

- N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- (2S,4R)-N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- 5 (2S,4S)-N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-ethyl-4-hydroxy-pyrrolidine-2-carboxamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(ethanimidoylamino)-1-methyl-ethyl]-2-ethyl-benzamide;
- 10 N-[3-[(2S)-2-amino-4-guanidino-butanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-[[2-(dimethylamino)acetyl]amino]propyl]-2-ethyl-benzamide;
- N-[2-[(2-aminoacetyl)amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2-amino-3-guanidino-propanoyl]amino]propyl]benzamide;
- (2S,4R)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- 20 (2S,4S)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-ethyl-4-hydroxy-pyrrolidine-2-carboxamide;
- (2S,4S)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-hydroxy-4-methyl-pyrrolidine-2-carboxamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-[[2-(dimethylamino)ethylamino]-3-oxo-propyl]-2-ethyl-benzamide;
- 25 N-[2-[(2S)-2-amino-3-hydroxy-propanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 3-[[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]-methyl-amino]propyl pyridine-4-carboxylate;
- 30 N-[3-[(2-aminoacetyl)amino]-2-hydroxy-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(1R)-3-[(2S)-2-amino-5-guanidino-pentanoyl]amino]-1-methyl-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-[2-[(4-amino-3-hydroxy-butanoyl)amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2S)-2,6-diaminohexanoyl]amino]-1,1-dimethyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(3-hydroxypropyl)-3,4-dihydroisoquinolin-1-one;
- N-allyl-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 2-chloro-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-piperidylmethyl)benzamide;
- 10 N-[(2-aminothiazol-5-yl)methyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 2-[4-[[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]methyl]-1-piperidyl]-2-methyl-propanoic acid;
- 15 N-[[1-(azetidin-3-ylmethyl)-4-piperidyl]methyl]-4-[[3-[2,3-difluoro-4-[3-(trifluoromethyl)-1H-pyrazol-4-yl]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 1-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethyl]pyrrolidine-3-carboxamide;
- 2-[4-[[[4-[[3-[2,3-difluoro-4-(3-methyl-1H-pyrazol-4-yl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]methyl]-1-piperidyl]acetic acid;
- 20 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(4-pyridylmethyl)benzamide;
- N-[[1-(azetidin-3-ylmethyl)-4-piperidyl]methyl]-4-[[3-[2,3-difluoro-4-(3-methyl-1H-pyrazol-4-yl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 2-[4-[[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]methyl]-1-piperidyl]acetic acid;
- 2-[4-[[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]methyl]-1-piperidyl]acetic acid;
- N-(5-aminopentyl)-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 4-[[3-[2,3-difluoro-4-(1H-triazol-5-yloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[1-(pyrrolidin-3-ylmethyl)-4-piperidyl]methyl]benzamide;

- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[1-(2-pyrrolidin-2-ylethyl)-4-piperidyl]methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(1-methylpyrazol-4-yl)methyl]benzamide;
- 5 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[1-(3-pyridylmethyl)-4-piperidyl]methyl]benzamide;
- 1-(azetidin-3-ylmethyl)-N-[(2S)-2-[[4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propyl]piperidine-4-carboxamide;
- 10 N-[(2S)-2-[[4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propyl]piperidine-4-carboxamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[1-[2-oxo-2-(pyrrolidin-3-ylmethylamino)ethyl]-4-piperidyl]methyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(pyrrolidin-3-ylmethyl)benzamide;
- 15 4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[1-(pyrrolidin-3-ylmethyl)-4-piperidyl]methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(4-piperidylmethyl)benzamide;
- 20 N-[[1-(azetidin-3-ylmethyl)-4-piperidyl]methyl]-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[1-(piperidine-4-carbonyl)-4-piperidyl]methyl]benzamide;
- N-[3-[[4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propyl]-1-(pyrrolidin-3-ylmethyl)piperidine-4-carboxamide;
- 25 N-[3-[[4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propyl]piperidine-4-carboxamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(4-piperidylmethyl)benzamide;
- 30 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(3-oxo-3-piperazin-1-yl-propyl)benzamide;

- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-prop-
2-ynyl-benzamide;
- N-(8-aminooctyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-
yl]amino]-2-ethyl-benzamide;
- 5 N-[(1R)-1-(aminomethyl)-2-hydroxy-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-
phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-
benzamide;
- 2-ethyl-4-[[3-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-
10 methyl-benzamide;
- N-[(E)-4-aminobut-2-enyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-
8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(6-
imidazol-1-ylhexyl)benzamide;
- 15 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[6-(1-
piperidyl)hexyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[5-
([1,2,4]triazolo[4,3-a]pyridin-3-yl)pentyl]benzamide;
- N-[[1-(2-aminoacetyl)azetidin-3-yl]methyl]-4-[[3-(2,3-difluoro-4-methoxy-
20 phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
[[3S,4R)-4-hydroxypyrrolidin-3-yl]methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
[(3S)-pyrrolidin-3-yl]methyl]benzamide;
- 25 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
[(3R)-pyrrolidin-3-yl]methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(3-
hydroxypyrrolidin-3-yl)methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
30 (pyrrolidin-2-ylmethyl)benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(3-
fluoroazetidin-3-yl)methyl]benzamide;

- N-(2-amino-3-hydroxy-propyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(2-amino-2-methyl-propyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 N-(2-aminobutyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(2S)-2-aminopropyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 N-(7-aminoheptyl)-2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- N-[3-[(2R,3R,4R,5R,6R)-3-amino-4,5-dihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl]oxypropyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(4-aminobutyl)-2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 15 N-(7-aminoheptyl)-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- N-(7-aminoheptyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 N-(7-aminoheptyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- N-(4-aminobutyl)-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- N-(4-aminobutyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 N-(4-aminobutyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-[4-[[5-(2-aminoethoxy)-2-pyridyl]oxy]-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-benzamide;
- 30 4-[[3-[4-[[5-(3-aminopropoxy)-2-pyridyl]oxy]-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-benzamide;
- 4-[[3-[4-[[5-(3-aminopropoxy)-2-pyridyl]oxy]-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N,N-dimethyl-benzamide;

- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-
[(1R)-1-methyl-2-(2-methylpropanimidoylamino)ethyl]benzamide;
N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-
a]pyrazin-8-yl]amino]-2-methyl-benzamide;
5 N-(3-aminopropyl)-6-[4-[8-[3-ethyl-4-(methylcarbamoyl)anilino]imidazo[1,2-a]pyrazin-3-
yl]-2,3-difluoro-phenoxy]pyridine-3-carboxamide;
N-[(1R)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-
a]pyrazin-8-yl]amino]-2-methyl-benzamide;
N-[(1S)-2-amino-1-methyl-ethyl]-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-
10 phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
N-[(1R)-2-amino-1-methyl-ethyl]-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-
phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(1S)-
1-methyl-2-(2-methylpropanimidoylamino)ethyl]benzamide;
15 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(1R)-
1-methyl-2-(2-methylpropanimidoylamino)ethyl]benzamide;
2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-
[(1R)-2-(ethanimidoylamino)-1-methyl-ethyl]benzamide;
2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-
20 [(1S)-1-methyl-2-(2-methylpropanimidoylamino)ethyl]benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-
[(1S)-1-methyl-2-(2-methylpropanimidoylamino)ethyl]benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-
[(1R)-1-methyl-2-(2-methylpropanimidoylamino)ethyl]benzamide;
25 N-(6-aminohexyl)-2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-
a]pyrazin-8-yl]amino]benzamide;
N-(5-aminopentyl)-2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-
a]pyrazin-8-yl]amino]benzamide;
N-(6-aminohexyl)-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-
30 8-yl]amino]benzamide;
N-(6-aminohexyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-
yl]amino]-2-ethyl-benzamide;

- N-(6-aminoethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- N-(5-aminopentyl)-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 5 N-(5-aminopentyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- N-(2-aminoethyl)-6-[4-[8-[3-ethyl-4-(methylcarbamoyl)anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]pyridine-3-carboxamide;
- N-[(1S)-1-(aminomethyl)propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1S)-2-(ethanimidoylamino)-1-methyl-ethyl]-2-methyl-benzamide;
- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1S)-2-(ethanimidoylamino)-1-methyl-ethyl]benzamide;
- 15 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1R)-2-(ethanimidoylamino)-1-methyl-ethyl]-2-methyl-benzamide;
- N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-[2,3-difluoro-4-(1H-pyrazol-3-ylmethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[1-[[[(2S)-2,6-diaminohexanoyl]amino]methyl]cyclopropyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2,3-dihydroxypropyl)-2-ethyl-benzamide;
- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-thiazol-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-pent-4-ynyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1S)-2-(ethanimidoylamino)-1-methyl-ethyl]-2-ethyl-benzamide;
- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3-fluoro-2-methyl-benzamide;
- 30 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[6-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-6-oxo-hexyl]benzamide;

- 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
[5-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-5-oxo-pentyl]benzamide;
- 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
[4-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-4-oxo-butyl]benzamide;
- 5 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
[3-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-3-oxo-propyl]benzamide;
- 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
[2-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-2-oxo-ethyl]benzamide;
- (2S,4R)-N-[(2R)-2-amino-3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-
10 a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-
carboxamide;
- 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
methyl-benzamide;
- 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-
15 N,N-dimethyl-benzamide;
- (2S,4R)-N-[(2S)-2-amino-3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-
a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-
carboxamide;
- (2S,4R)-N-[(2S)-2-amino-3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-
20 a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-
carboxamide;
- (2S,4R)-N-[(2R)-2-amino-3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-
a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-
carboxamide;
- 25 N-(2-aminoethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-
yl]amino]-2-fluoro-6-methyl-benzamide;
- N-(2-aminoethyl)-4-[[3-[2,3-difluoro-4-(4-methoxypyrimidin-2-yl)oxy-
phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(1R)-2-[(2S)-2,6-diaminohexanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-
30 methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-
[(3S)-3-(hydroxymethyl)piperazin-1-yl]-2-oxo-ethyl]benzamide;

- N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-[2,3-difluoro-4-(6-methoxypyrimidin-4-yl)oxy-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-[2,3-difluoro-4-(4-methoxypyrimidin-2-yl)oxy-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 rac-(4S)-4-amino-5-[[2-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethylamino]-1-(guanidinomethyl)-2-oxo-ethyl]amino]-5-oxo-pentanoic acid;
- N-[(1R)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-prop-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 (3R,4R)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-3-hydroxy-piperidine-4-carboxamide;
- N-[(1S)-2-[(2R)-2-amino-4-guanidino-butanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 N-[(1S)-2-[(2S)-2-amino-4-guanidino-butanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(1S)-2-[(2S)-2-amino-4-guanidino-butanoyl]amino]-1-methyl-ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-
- 20 benzamide;
- N-[(1S)-2-[(2S)-2-amino-4-guanidino-butanoyl]amino]-1-methyl-ethyl]-4-[[3-[2,3-difluoro-4-(4-methylpyrimidin-2-yl)oxy-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[5-[(2R,3S,4S,5R,6R)-4-amino-6-[(1S,2S,3R,4S,6R)-4-amino-6-[(2S)-4-amino-2-hydroxy-butanoyl]amino]-3-[(2R,3R,4S,5S,6R)-6-(aminomethyl)-3,4,5-trihydroxy-tetrahydropyran-2-yl]oxy-2-hydroxy-cyclohexoxy]-3,5-dihydroxy-tetrahydropyran-2-yl]methylamino]-5-oxo-pentyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 N-[(1S)-2-[(2S)-2,6-diaminohexanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-prop-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- (3R,4R)-N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-3-hydroxy-piperidine-4-carboxamide;
N-[2-[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-methoxy-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
5 N-[2-[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-methoxy-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[2,3-difluoro-4-[(5-methoxy-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-methoxy-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
10 N-[2-[2-(azetidin-1-yl)ethylamino]-2-oxo-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(4-methylpyrimidin-2-yl)oxy-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
15 4-[4-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethyl]piperazin-1-yl]butanoic acid;
4-[4-[2-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]ethyl]-1-piperidyl]butanoic acid;
20 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[3-[(2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl]oxypropyl]benzamide;
N-[2-[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
25 N-[2-[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
30 N-[2-[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-(3-aminopropyl)-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-6-fluoro-benzamide;
- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2,6-difluoro-benzamide;
- 5 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[2-(dimethylamino)ethylamino]-2-oxo-ethyl]-2-ethyl-benzamide;
- N-[2-[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-(2-aminoethylamino)-2-oxo-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 N-[2-[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-fluoro-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-[2-(methylamino)ethylamino]-2-oxo-ethyl]benzamide;
- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-fluoro-6-methyl-benzamide;
- 20 N-[2-[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[2,3-difluoro-4-[(5-fluoro-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 N-[2-[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-fluoro-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-(2-hydroxyethylamino)-2-oxo-ethyl]benzamide;
- N-[2-[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-[2-[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(3-aminopropyl)-4-[[3-[2,3-difluoro-4-(4-hydroxybut-2-ynoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 N-(5-aminopentyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2-amino-4-guanidino-butanoyl]amino]propyl]benzamide;
- 10 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2,3-diaminopropanoyl]amino]propyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2,4-diaminobutanoyl]amino]propyl]benzamide;
- 15 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2,5-diaminopentanoyl]amino]propyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2,6-diaminohexanoyl]amino]propyl]benzamide;
- N-[3-[(4-amino-3-hydroxy-butanoyl)amino]-2-hydroxy-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 N-[3-(4-aminobutanoylamino)-2-hydroxy-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[4-(hydroxymethyl)-2-oxo-oxazolidin-4-yl]methyl]benzamide;
- 25 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-methyl-3-[[rac-(2S)-2-amino-3-guanidino-propanoyl]amino]propyl]benzamide;
- (2S)-2-amino-5-[[[(1S)-1-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propyl]carbamoyl]-4-guanidino-butyl]amino]-5-oxo-pentanoic acid;
- 30 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-methyl-3-[[rac-(2S)-2-amino-5-guanidino-pentanoyl]amino]propyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2-amino-5-guanidino-pentanoyl]amino]propyl]benzamide;

- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(2-(dimethylamino)ethylamino)-2-oxo-ethyl]-2-ethyl-benzamide;
- (2S)-2-[[[(2S)-2,6-diaminohexanoyl]amino]-5-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propylamino]-5-oxo-pentanoic acid;
- 5 N-(3-amino-1-methyl-propyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-methyl-3-[[rac-(2S)-2-amino-4-guanidino-butanoyl]amino]propyl]benzamide;
- 10 N-[2-[[[(2S)-2,3-diaminopropanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2S)-2,4-diaminobutanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2S)-2,6-diaminohexanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 N-[2-[[[(2S)-2,5-diaminopentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-[3-(2-methyl-5,6-dioxo-3-thioxo-1,2,4-triazinan-4-yl)propyl]benzamide;
- 20 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-[3-[(2-methyl-5,6-dioxo-1H-1,2,4-triazin-3-yl)sulfanyl]propyl]benzamide;
- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 N-[2-[[[(2S,3R)-2-amino-3-hydroxy-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-fluoroethyl)benzamide;
- 30 6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-3,4-dihydroisoquinolin-1-one; and
- 7-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2,3,4,5-tetrahydro-2-benzazepin-1-one.

In a further particularly preferred embodiment, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, wherein the compound of formula (I) is selected from:

- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-
5 piperidylmethyl)benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-
piperazin-1-ylethyl)benzamide;
- 2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-
piperazin-1-ylethyl)benzamide;
- 10 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-
methyl-N-(2-piperazin-1-ylethyl)benzamide;
- N-[2-[[2(R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2-chloro-4-(cyanomethoxy)-3-
fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[2(S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-
15 difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[2(R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-
phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[3-(2-aminoethylcarbamoylamino)propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-
a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 N-[2-[[2(S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2-chloro-3-fluoro-4-methoxy-
phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-guanidinobutyl)-2-
methyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-(5-
25 guanidinopentanoylamino)ethyl]benzamide;
- N-(5-aminopentyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-
yl]amino]-2-ethyl-benzamide;
- N-[3-(3-aminopropylcarbamoylamino)propyl]-4-[[3-(2,3-difluoro-4-methoxy-
phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 N-[(1-carbamimidoyl-4-piperidyl)methyl]-2-chloro-4-[[3-(3-fluoro-4-methoxy-
phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- (2S,4S)-N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-
yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-hydroxy-4-methyl-pyrrolidine-2-carboxamide;

- (2S,4S)-N-[3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-4-methyl-pyrrolidine-2-carboxamide;
N-[2-[[[(2S)-2-amino-3-hydroxy-propanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
5 N-[2-[(2-aminoacetyl)amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[[[(2S,3R)-2-amino-3-hydroxy-butanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
10 N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,5-diaminopentanoyl]amino]ethyl]-2-ethyl-benzamide;
15 N-[2-(4-aminobutanoylamino)ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[(4-amino-3-hydroxy-butanoyl)amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,6-diaminohexanoyl]amino]ethyl]-2-ethyl-benzamide;
20 4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,4-diaminobutanoyl]amino]ethyl]-2-ethyl-benzamide;
4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,3-diaminopropanoyl]amino]ethyl]-2-ethyl-benzamide;
25 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[3-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-3-oxo-propyl]benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[4-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-4-oxo-butyl]benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[6-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-6-oxo-hexyl]benzamide;
30 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[5-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-5-oxo-pentyl]benzamide;

- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-[methyl-
[2-(methylamino)ethyl]amino]-2-oxo-ethyl]benzamide;
N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-
benzoyl]amino]propyl]-2-imino-imidazolidine-4-carboxamide;
5 (2S,4R)-N-[3-[[4-[[3-(4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-
yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide;
(2S,4R)-N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-
methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide; and
N-[3-[[2S)-2-amino-3-guanidino-propanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxy-
10 phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide.

In one embodiment, the present invention provides pharmaceutically acceptable salts of the compounds of formula (I) as described herein, especially pharmaceutically acceptable salts selected from hydrochlorides, fumarates, lactates (in particular derived from L-(+)-lactic acid), tartrates (in particular derived from L-(+)-tartaric acid) and trifluoroacetates. In yet a further
15 particular embodiment, the present invention provides compounds according to formula (I) as described herein (i.e., as “free bases” or “free acids”, respectively).

In some embodiments, the compounds of formula (I) are isotopically-labeled by having one or more atoms therein replaced by an atom having a different atomic mass or mass number. Such isotopically-labeled (i.e., radiolabeled) compounds of formula (I) are considered to be within the
20 scope of this disclosure. Examples of isotopes that can be incorporated into the compounds of formula (I) include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, sulfur, fluorine, chlorine, and iodine, such as, but not limited to, ^2H , ^3H , ^{11}C , ^{13}C , ^{14}C , ^{13}N , ^{15}N , ^{15}O , ^{17}O , ^{18}O , ^{31}P , ^{32}P , ^{35}S , ^{18}F , ^{36}Cl , ^{123}I , and ^{125}I , respectively. Certain isotopically-labeled compounds of formula (I), for example, those incorporating a radioactive isotope, are useful in drug and/or
25 substrate tissue distribution studies. The radioactive isotopes tritium, i.e. ^3H , and carbon-14, i.e., ^{14}C , are particularly useful for this purpose in view of their ease of incorporation and ready means of detection. For example, a compound of formula (I) can be enriched with 1, 2, 5, 10, 25, 50, 75, 90, 95, or 99 percent of a given isotope.

Substitution with heavier isotopes such as deuterium, i.e. ^2H , may afford certain therapeutic
30 advantages resulting from greater metabolic stability, for example, increased *in vivo* half-life or reduced dosage requirements.

Substitution with positron emitting isotopes, such as ^{11}C , ^{18}F , ^{15}O and ^{13}N , can be useful in Positron Emission Topography (PET) studies for examining substrate receptor occupancy. 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

5 Examples as set out below using an appropriate isotopically-labeled reagent in place of the non-labeled reagent previously employed.

Processes of Manufacturing

The preparation of compounds of formula (I) of the present invention may be carried out in sequential or convergent synthetic routes. Syntheses of the compounds of the invention are

10 shown in the following schemes. The skills required for carrying out the reactions and purifications of the resulting products are known to those skilled in the art. The substituents and indices used in the following description of the processes have the significance given herein before unless indicated to the contrary. In more detail, the compounds of formula (I) can be manufactured by the methods given below, by the methods given in the examples or by

15 analogous methods. Appropriate reaction conditions for the individual reaction steps are known to a person skilled in the art. Also, for reaction conditions described in literature affecting the described reactions see for example: *Comprehensive Organic Transformations: A Guide to Functional Group Preparations, 3rd Edition, Richard C. Larock. John Wiley & Sons, New York, NY. 2018*). We find it convenient to carry out the reactions in the presence or absence of a

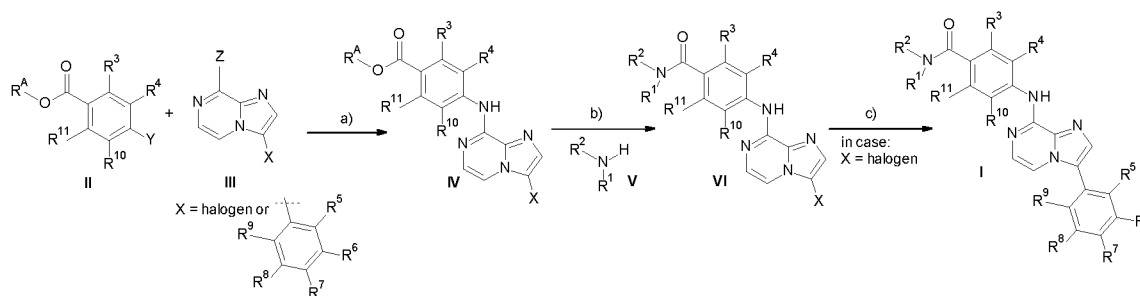
20 solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve the reagents, at least to some extent. The described reactions can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. It is convenient to carry out the described reactions in a temperature range between $-78\text{ }^{\circ}\text{C}$ to reflux temperature.

25 The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents. However, a period of from 0.5 h to several days will usually suffice to yield the described intermediates and compounds. The reaction sequence is not limited to the one displayed in the schemes, however, depending on the starting materials and their respective reactivity the sequence of reaction steps can be freely altered.

30 Starting materials are either commercially available or can be prepared by methods analogous to the methods given below, by methods described in references cited in the description or in the examples, or by methods known in the art.

The synthesis of the compounds of formula (I) may, for example, be accomplished according to the general synthesis outlined in the following Scheme 1.

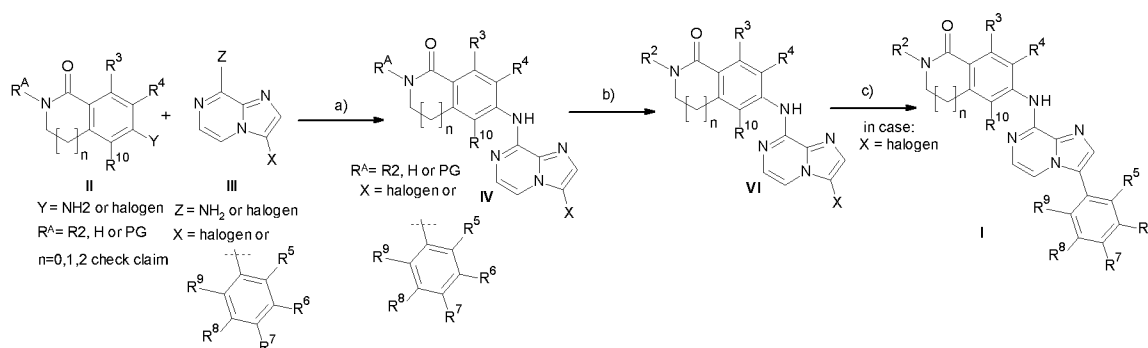
Scheme 1



- 5 a) Acids or esters **II**, wherein Y is NH₂ or halogen and R^A is H or alkyl, are commercially available, can be accessed by methods known in the art or in literature and can conveniently be reacted with imidazopyrazine derivatives **III** to access intermediates **IV**. Depending on the varying substitution (**II**: Y= NH₂ or halogen) it is convenient to react acids / esters **II** with the appropriate imidazopyrazine derivative **III** (Z= NH₂ or halogen and X= halogen or appropriately substituted aryl moiety) under metal catalysis reaction conditions or nucleophilic aromatic substitution reaction conditions (as appropriate) to yield acids / esters **IV**.
- 10 b) Acid derivatives **IV** (R^A = H), can be accessed from esters **IV** (R^A = alkyl) upon saponification in the presence of a base. Examples of bases include: LiOH, NaOH and the like. In addition, acid derivatives are accessible by treatment of a suitable ester such as a tBu-ester with an acid such as HCl, TFA or the like. Acid derivatives **IV** are conveniently reacted with an amine **V** under varying coupling reaction conditions (coupling reaction conditions include: HATU, TBTU, and the like in the presence of a base, such as DIPEA, NEt₃, and the like) to afford amides **VI**. Amines **V** (and their protected congeners) are commercially available, known in the art or prepared according to methods known in the art. In case X = appropriately substituted aryl ring, these derivatives **VI** might be the final desired imidazopyrazines derivatives **I**, or any protecting group might have to be cleaved under appropriate conditions to afford final imidazopyrazines derivatives **I**. These imidazopyrazines **I** might be the final desired compounds however might be further derivatised to yield final imidazopyrazines derivatives **I**.
- 15 c) Amides **VI** are conveniently reacted under metal catalysis (catalysts include: PdCl₂(dppf)-CH₂Cl₂ adduct, Pd(PPh₃)₄, and the like and in the presence of a base, such as K₃PO₄, NaOtBu, sodium carbonate and the like) with the appropriate boronic acid or ester to afford imidazopyrazines derivatives **I**. These imidazopyrazines derivatives **I** might be the final desired
- 20
- 25

compounds however any protecting group will have to be cleaved under appropriate conditions to afford final imidazopyrazines **I**. These imidazopyrazines **I** might be the final desired compounds however might be further derivatised to yield final imidazopyrazines derivatives **I**. The synthesis of the compounds of formula (I), wherein R^1 and R^{11} , taken together with the atoms to which they are attached, form a β -, γ -, δ - or ϵ -lactam may, for example, be accomplished according to the general synthesis outlined in the following Scheme 2.

Scheme 2



a) Heterocycles **II**, wherein Y is NH₂ or halogen and R^A is H or R², are commercially available, can be accessed by methods known in the art or in literature and can conveniently be reacted with imidazopyrazine derivatives **III** to access intermediates **IV**. Depending on the varying substitution (**II**: Y = NH₂ or halogen) it is convenient to react heterocycles **II** with the appropriate imidazopyrazine derivative **III** (Z = NH₂ or halogen and X = halogen or appropriately substituted aryl moiety) under metal catalysis reaction conditions or nucleophilic aromatic substitution reaction conditions (as appropriate) to yield amides **IV**.

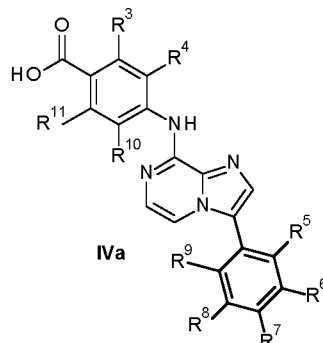
b) Amides **IV** (R^A = H), can be assessed from amides **IV** (R^A = protecting group) through appropriate deprotection reactions methods as described in literature and are reacted with appropriate electrophile in presence of bases, such as NaH, NEt₃ and the like to yield intermediates **VI**. These amides **VI** might be the final desired imidazopyrazines **I**, however might be further derivatised to yield final imidazopyrazines derivatives **I**.

c) Amides **VI** (X = halogen) are conveniently reacted under metal catalysis, such as PdCl₂(dppf)-CH₂Cl₂ adduct, Pd(PPh₃)₄, and the like and in the presence of a base, such as K₃PO₄, NaOtBu, sodium carbonate and the like with the appropriate boronic acid or ester to afford imidazopyrazines derivatives **I**. These imidazopyrazines derivatives **I** might be the final desired compounds however any protecting group will have to be cleaved under appropriate conditions

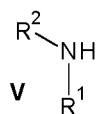
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to afford final imidazopyrazines **I**. These imidazopyrazines **I** might be the final desired compounds however might be further derivatised to yield final imidazopyrazines derivatives **I**. In one aspect, the present invention provides a process of manufacturing the compounds of formula (I) described herein, comprising:

- 5 (i) reacting an ester carboxylic acid **IVa**, wherein R^3 to R^{11} are as defined herein,

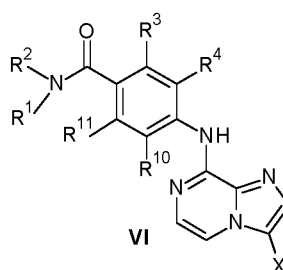


with an amine **V**, wherein R^1 and R^2 are as defined herein,

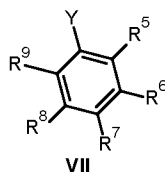


10 in the presence of a coupling reagent (such as HATU, TBTU, and the like) and a base (such as DIPEA, NEt_3 , and the like), to form said compound of formula (I); or

- (ii) reacting a compound **VI**, wherein R^1 to R^4 , R^{10} and R^{11} are as defined herein and X is halogen,



15 with a boronic acid **VII**, wherein R^5 to R^9 are as defined herein and Y is a boronic acid or a boronic acid ester,



in the presence of a transition metal catalyst (such as PdCl₂(dppf)-CH₂Cl₂ adduct, Pd(PPh₃)₄, and the like) and a base (such as K₃PO₄, NaOtBu, and the like) to form said compound of formula (I).

In a further aspect, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, when manufactured according to the processes disclosed herein.

Using the Compounds of the Invention

As illustrated in the example section below, the compounds of formula (I) and their pharmaceutically acceptable salts possess valuable pharmacological properties for the treatment or prevention of infections and resulting diseases, particularly bacteremia, pneumonia, meningitis, urinary tract infection, and wound infection, caused by pathogens, particularly by bacteria, more particularly by *Acinetobacter* species, most particularly by *Acinetobacter baumannii*.

The compounds of formula (I) and their pharmaceutically acceptable salts exhibit activity as antibiotics, particularly as antibiotics against *Acinetobacter* species, more particularly as antibiotics against *Acinetobacter baumannii*, most particularly as pathogen-specific antibiotics against *Acinetobacter baumannii*.

The compounds of formula (I) and their pharmaceutically acceptable salts can be used as antibiotics, i.e. as antibacterial pharmaceutical ingredients suitable in the treatment and prevention of bacterial infections, particularly in the treatment and prevention of bacterial infections caused by *Acinetobacter* species, more particularly in the treatment and prevention of bacterial infections caused by *Acinetobacter baumannii*.

The compounds of the present invention can be used, either alone or in combination with other drugs, for the treatment or prevention of infections and resulting diseases, particularly bacteremia, pneumonia, meningitis, urinary tract infection, and wound infection, caused by pathogens, particularly by bacteria, more particularly caused by *Acinetobacter* species, most particularly by *Acinetobacter baumannii*.

In one aspect, the present invention provides compounds of formula (I) or their pharmaceutically acceptable salts as described herein for use as therapeutically active substances.

In a further aspect, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for use as antibiotic.

In a further aspect, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of
5 nosocomial infections and resulting diseases.

In a particular embodiment, said nosocomial infections and resulting diseases are selected from bacteremia, pneumonia, meningitis, urinary tract infection and wound infection, or a combination thereof.

In a further aspect, the present invention provides a compound of formula (I) as described herein,
10 or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of infections and resulting diseases caused by Gram-negative bacteria.

In a particular embodiment, said infections and resulting diseases caused by Gram-negative bacteria are selected from bacteremia, pneumonia, meningitis, urinary tract infection and wound infection, or a combination thereof.

15 In a further aspect, the present invention provides a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of infections and resulting diseases caused by *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter species* or *E. coli*, or a combination thereof.

20 In a further aspect, the present invention provides a method for the treatment or prevention of infections and resulting diseases caused by *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter species* or *E. coli*, or a combination thereof, which method comprises administering a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, to a mammal.

25 In a further aspect, the present invention provides the use of a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, as an antibiotic.

In a further aspect, the present invention provides the use of a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for the treatment or prevention of infections and resulting diseases caused by *Enterococcus faecium*, *Staphylococcus aureus*,

Klebsiella pneumoniae, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter species* or *E. coli*, or a combination thereof.

In a further aspect, the present invention provides the use of a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for the preparation of
5 medicaments useful for the treatment or prevention of infections and resulting diseases caused by *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter species* or *E. coli*, or a combination thereof.

In a particular embodiment, said infections and resulting diseases caused by *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*,
10 *Pseudomonas aeruginosa*, *Enterobacter species* or *E. coli*, or a combination thereof, are selected from bacteremia, pneumonia, meningitis, urinary tract infection and wound infection, or a combination thereof.

In a further aspect, the present invention provides compounds of formula (I) or their pharmaceutically acceptable salts as defined above for use in the treatment or prevention of
15 infections and resulting diseases, particularly bacteremia, pneumonia, meningitis, urinary tract infection, and wound infection, caused by pathogens, particularly by bacteria, more particularly caused by *Acinetobacter species*, most particularly by *Acinetobacter baumannii*.

In a further aspect, the present invention provides a method for the treatment or prevention of infections and resulting diseases, particularly bacteremia, pneumonia, meningitis, urinary tract
20 infection, and wound infection, caused by pathogens, particularly by bacteria, more particularly caused by *Acinetobacter species*, most particularly by *Acinetobacter baumannii*, which method comprises administering a compound of formula (I) or a pharmaceutically acceptable salt thereof as defined above to a mammal.

In a further aspect, the present invention provides the use of compounds of formula (I) or their
25 pharmaceutically acceptable salts as defined above for the treatment or prevention of infections and resulting diseases, particularly bacteremia, pneumonia, meningitis, urinary tract infection, and wound infection, caused by pathogens, particularly by bacteria, more particularly caused by *Acinetobacter species*, most particularly by *Acinetobacter baumannii*.

In a further aspect, the present invention provides the use of compounds of formula (I) or their
30 pharmaceutically acceptable salts as defined above for the preparation of medicaments for the

treatment or prevention of infections and resulting diseases, particularly bacteremia, pneumonia, meningitis, urinary tract infection, and wound infection, caused by pathogens, particularly by bacteria, more particularly caused by *Acinetobacter* species, most particularly by *Acinetobacter baumannii*. Such medicaments comprise compounds of formula (I) or their pharmaceutically acceptable salts as defined above.

Pharmaceutical Compositions and Administration

In one aspect, the present invention provides pharmaceutical compositions comprising compounds of formula (I) or their pharmaceutically acceptable salts as defined above and one or more pharmaceutically acceptable excipients. Exemplary pharmaceutical compositions are described in Examples 570 to 573.

In a further aspect, the present invention relates to pharmaceutical compositions comprising compounds of formula (I) or their pharmaceutically acceptable salts as defined above and one or more pharmaceutically acceptable excipients for the treatment or prevention of infections and resulting diseases, particularly bacteremia, pneumonia, meningitis, urinary tract infection, and wound infection, caused by pathogens, particularly by bacteria, more particularly caused by *Acinetobacter* species, most particularly by *Acinetobacter baumannii*.

The compounds of formula (I) and their pharmaceutically acceptable salts can be used as medicaments (e.g. in the form of pharmaceutical preparations). The pharmaceutical preparations can be administered internally, such as orally (e.g. in the form of tablets, coated tablets, dragées, hard and soft gelatin capsules, solutions, emulsions or suspensions), nasally (e.g. in the form of nasal sprays) or rectally (e.g. in the form of suppositories). However, the administration can also be effected parentally, such as intramuscularly or intravenously (e.g. in the form of injection solutions or infusion solutions).

The compounds of formula (I) and their pharmaceutically acceptable salts can be processed with pharmaceutically inert, inorganic or organic excipients for the production of tablets, coated tablets, dragées and hard gelatin capsules. Lactose, corn starch or derivatives thereof, talc, stearic acid or its salts etc. can be used, for example, as such excipients for tablets, dragées and hard gelatin capsules.

Suitable excipients for soft gelatin capsules are, for example, vegetable oils, waxes, fats, semi-solid substances and liquid polyols, etc.

Suitable excipients for the production of solutions and syrups are, for example, water, polyols, saccharose, invert sugar, glucose, etc.

Suitable excipients for injection solutions are, for example, water, alcohols, polyols, glycerol, vegetable oils, etc.

- 5 Suitable excipients for suppositories are, for example, natural or hardened oils, waxes, fats, semi-solid or liquid polyols, etc.

Moreover, the pharmaceutical preparations can contain preservatives, solubilizers, viscosity-increasing substances, stabilizers, wetting agents, emulsifiers, sweeteners, colorants, flavorants, salts for varying the osmotic pressure, buffers, masking agents or antioxidants. They can also
10 contain still other therapeutically valuable substances.

The dosage can vary in wide limits and will, of course, be fitted to the individual requirements in each particular case. In general, in the case of oral administration a daily dosage of about 0.1 mg to 20 mg per kg body weight, preferably about 0.5 mg to 4 mg per kg body weight (e.g. about 300 mg per person), divided into preferably 1-3 individual doses, which can consist, for
15 example, of the same amounts, should be appropriate. It will, however, be clear that the upper limit given herein can be exceeded when this is shown to be indicated.

Examples

The invention will be more fully understood by reference to the following examples. The claims should not, however, be construed as limited to the scope of the examples.

- 20 In case the preparative examples are obtained as a mixture of enantiomers, the pure enantiomers can be separated by methods described herein or by methods known to the man skilled in the art, such as e.g., chiral chromatography (e.g., chiral SFC) or crystallization.

All reaction examples and intermediates were prepared under an argon atmosphere if not specified otherwise.

- 25 The following abbreviations are used in the present text:

(R)-BINAP = (R)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, ACN = acetonitrile, aq. = aqueous, Boc = tert-butyloxycarbonyl, Boc-Glu-OtBu = Boc-L-glutamic acid 1-tert-butyl ester, Boc-Glu(OtBu)-OH = N- α -t.-Boc-L-glutamic acid γ -t.-butyl ester, Boc-Orn(Z)-OH = N α -Boc-N δ -Cbz-L-ornithine, N α -Boc-N δ -Z-L-ornithine, N δ -Z-N α -Boc-L-ornithine, BrettPhos-Pd-G3

= [(2-Di-cyclohexylphosphino-3,6-dimethoxy-2',4',6'- triisopropyl-1,1'-biphenyl)-2-(2'-amino-1,1' -biphenyl)]palladium(II) methanesulfonate methanesulfonate, CAS = chemical abstracts registration number, Cs₂CO₃ = cesium carbonate, DCM = dichloromethane, DIAD = diisopropyl azodicarboxylate, DIPEA = ethyl diisopropylamine, DMA = N,N-dimethylacetamide, DMAP =

5 4-(dimethylamino)-pyridine, DMF = N,N-dimethylformamide, DMSO = dimethylsulfoxide, DMSO-d₆ = deuterated dimethylsulfoxide, EA = ethyl acetate, EDC = 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, EDCI = 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, EI = electron impact, ESI = electrospray ionization, ESI⁺ = electrospray ionization positive (mode), ESP = electrospray ionization positive (mode), Et₂O = diethylether, Et₃N =

10 triethylamine, EtOAc = ethyl acetate, EtOH = ethanol, FA = formic acid, Fmoc-AgP(Boc)₂-OH = N- α -Fmoc-N,N'- γ -di-t.-butoxycarbonyl-L-diaminobutanoic acid, Fmoc-Arg(Boc)₂-OH = N- α -Fmoc-N- ω ,N- ω -bis-t-butoxycarbonyl-L-arginine, H₂ = hydrogen, h = hour(s), HATU = 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium-3-oxide hexafluorophosphate, HCl = hydrochloric acid, HFIP = 1,1,1,3,3,3-hexafluoroisopropanol, H₂O

15 = water, HOBt = 1-hydroxy-1H-benzotriazole, HPLC = high performance liquid chromatography, HV = high vacuum, ISN = ion spray negative (mode), K₂CO₃ = potassium carbonate, KI = potassium iodide, KOH = potassium hydroxide, K₃PO₄ = potassium phosphate tribasic, LC-MS = liquid chromatography coupled with mass spectroscopy, LiOH = lithium hydroxide, MeOH = methanol, MgSO₄ = magnesium sulphate, min = minute(s), mL = milliliter,

20 MS = mass spectrometry, MTBE = tert.-butyl methyl ether, N₂ = nitrogen, Na₂CO₃ = sodium carbonate, Na₂SO₃ = sodium sulfite, Na₂SO₄ = sodium sulfate, Na₂S₂O₃ = sodium thiosulfate, NEt₃ = triethylamine, NaHCO₃ = sodium hydrogen carbonate, NaOH = sodium hydroxide, NH₄Cl = ammonium chloride, NiCl₂.6H₂O = nickel(II)chloride hexahydrate, NMO = N-methylmorpholine N-oxide, NMP = N-methyl-2-pyrrolidone, Pd/C = palladium on activated

25 carbon, Pd₂(dba)₃ = tris(dibenzylideneacetone)dipalladium(0), PdCl₂(PPh₃)₂ = bis(triphenylphosphine)palladium(II) dichloride, Pd(dppf)Cl₂ = [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), PdCl₂(dppf)-CH₂Cl₂ = [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) dichloromethane complex, PE = petroleum ether, PhI(OAc)₂ = (diacetoxyiodo)benzene, PPA = polyphosphoric acid, pTsOH =

30 para toluenesulfonic acid, Rf = retention factor, RM = reaction mixture, RT = room temperature, SOCl₂ = thionyl chloride, SFC = supercritical fluid chromatography, TBTU = 2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethylaminium tetrafluoroborate, T₃P = propylphosphonic anhydride, t-Bu-X-phos = 2-di-tert-butylphosphino-2',4',6'-triisopropylbiphenyl, TEA =

triethylamine, TEMPO = (2,2,6,6-tetramethylpiperidin-1-yl)oxyl, TFA = trifluoroacetic acid, THF = tetrahydrofuran, prep-TLC = preparative thin layer chromatography, UV = ultraviolet.

Intermediate 1

4-((3-Iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid

- 5 A mixture of 8-chloro-3-iodoimidazo[1,2-a]pyrazine (100 mg, 358 μ mol) and 4-amino-2-methylbenzoic acid (108 mg, 716 μ mol) in 1,4-dioxane (2 mL) and acetic acid (2 mL) was stirred at 90 °C for 48 h. The mixture was allowed to cool to room temperature and filtered. The residue was washed with diethyl ether and dried *in vacuo* to give the title compound (139 mg) as a white solid. MS (ESI, m/z): 395.1 [M+H]⁺.

10 Intermediate 2

2-Chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid

- To 8-chloro-3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazine (Intermediate 3, 50 mg, 180 μ mol) in acetonitrile (0.9 mL) and acetic acid (100 μ L) was added 4-amino-2-chlorobenzoic acid (46.3 mg, 270 μ mol), followed by stirring at 80 °C overnight. The reaction mixture was filtered
15 to give the title compound (70 mg) as a light brown solid. MS (ESI, m/z): 411.3 [M-H]⁻.

The following intermediates were prepared in analogy:

Int.	Name	MS ESI [M+H] ⁺	Starting Material
4	4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid	375.2	4-amino-2-methylbenzoic acid and Intermediate 5
6	4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid	393.3	4-amino-2-methylbenzoic acid and Intermediate 3
7	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid	411	4-amino-2-methylbenzoic acid and Intermediate 8
9	2-chloro-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid	395.2	4-amino-2-chlorobenzoic acid and Intermediate 5
10	2-bromo-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid	475.1	4-amino-2-bromobenzoic acid and Intermediate 8

11	2-chloro-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid	431.2	4-amino-2-chlorobenzoic acid and Intermediate 8
12	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzoic acid	425.1	methyl 4-amino-2-ethylbenzoate and Intermediate 13 followed by ester hydrolysis
14	4-((3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid	409.3	methyl 4-amino-2-methylbenzoate and Intermediate 15 followed by ester hydrolysis
16	4-((3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid	395.1	4-aminobenzoic acid and Intermediate 15
17	4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid	360	4-aminobenzoic acid and Intermediate 5
18	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-(trifluoromethyl)benzoic acid	465.2	4-amino-2-(trifluoromethyl)benzoic acid and Intermediate 8
19	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-nitrobenzoic acid	442.2	4-amino-2-nitrobenzoic acid and Intermediate 8
20	2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid	431	4-amino-2-chlorobenzoic acid and Intermediate 21
22	2-chloro-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid	467.1	4-amino-2-chlorobenzoic acid and Intermediate 23
24	2-chloro-4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid	471.2	4-amino-2-chlorobenzoic acid and Intermediate 25
26	4-[[3-(2-chloro-5-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoic acid	427.1	methyl 4-amino-2-methylbenzoate and Intermediate 27
28	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoic acid	411.0	4-amino-2-methylbenzoic acid and Intermediate 21

20	2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid	431	4-amino-2-chlorobenzoic acid and Intermediate 21
29	2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid	456.1	4-amino-2-chlorobenzoic acid and Intermediate 30
31	4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoic acid	436.1	Intermediate 30 and 4-amino-2-methylbenzoic acid
32	4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoic acid	450.1	Intermediate 33 and Intermediate 30

34	4-((3-(2-chloro-3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid	427.2	Intermediate 1 and 2-(2-chloro-3-fluoro-4-methoxy-phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane
35	2-chloro-4-[[3-[3-chloro-4-(cyanomethoxy)-2-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid	472.0	Intermediate 36 and 4-amino-2-chlorobenzoic acid
37	2-chloro-4-[[3-[5-chloro-4-(cyanomethoxy)-2-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid	471.9	Intermediate 38 and 4-amino-2-chlorobenzoic acid
39	4-[[3-[5-chloro-4-(cyanomethoxy)-2-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoic acid	452.1	Intermediate 38 and 4-amino-2-methylbenzoic acid

40	4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoic acid	466.1	Intermediate 41 and Intermediate 33
42	methyl 2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoate	423.2	8-chloro-3-iodoimidazo[1,2-a]pyrazine and methyl 4-amino-2-ethyl-benzoate (CAS No 1211589-24-0)
43	4-((3-(4-(difluoromethoxy)-3-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid	429.2	Intermediate 44 and 4-amino-2-methylbenzoic acid
45	2-cyano-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid	422.2	methyl 4-amino-2-cyanobenzoate and Intermediate 8 followed by ester hydrolysis with LiOH
46	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-iodobenzoic acid	523.1	methyl 4-amino-2-iodobenzoate and Intermediate 8 followed by ester hydrolysis with LiOH

47	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-vinylbenzoic acid	423.1	Intermediate 48 and Intermediate 8 followed by ester hydrolysis with LiOH
49	methyl 4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoate	409.1	From 8-chloro-3-iodoimidazo[1,2-a]pyrazine and methyl 4-amino-2-methylbenzoate

Intermediate 3**8-Chloro-3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazine**

To 8-chloro-3-iodoimidazo[1,2-a]pyrazine (500 mg, 1.79 mmol) in dioxane (6.5 mL) and water (3.25 mL) was added 2-(3-fluoro-4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (474 mg, 1.88 mmol), 1,1'-bis(diphenylphosphino)ferrocenedichloro palladium(II) dichloromethane complex (65.5 mg, 89.5 μ mol) and sodium carbonate (379 mg, 3.58 mmol, Eq: 2) followed by stirring at 50 °C for 2 d. The reaction mixture was partitioned between ethyl acetate and water. The organic layers were dried over Na₂SO₄, filtered and concentrated to give a red solid, which was purified by column chromatography (silica gel, DCM/MeOH, 0-5%) to give the title compound (359 mg) as a pink-brown solid. MS (ESI, m/z): 278.1 [M+H]⁺.

The following intermediates were prepared in analogy to Intermediate 3:

Int.	Name	ESI MS [M+H] ⁺	Starting Material
5	8-Chloro-3-(4-methoxyphenyl)imidazo[1,2-a]pyrazine	260.1	(4-methoxyphenyl) boronic acid

8	8-chloro-3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazine	296	2-(4-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane
50	4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)phenol	246.0	4-hydroxyphenylboronic acid
13	8-chloro-3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazine	299.9	(4-chloro-2,3-difluorophenyl)boronic acid
15	8-chloro-3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazine	294.1	(3-chloro-4-methoxyphenyl)boronic acid
51	8-chloro-3-(2-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazine	293.1	(2-chloro-4-methoxyphenyl)boronic acid
21	8-chloro-3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazine	296.0	(2,3-difluoro-4-methoxyphenyl)boronic acid
30	2-[4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2,3-difluoro-phenoxy]acetonitrile	321.0	Intermediate 52

36	2-[2-chloro-4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-3-fluoro-phenoxy]acetonitrile	337.0	Intermediate 53
38	2-[5-chloro-4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenoxy]acetonitrile	337.0	Intermediate 53
44	8-chloro-3-[4-(difluoromethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazine	314.0	2-[4-(difluoromethoxy)-3-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane
25	2-[3-chloro-4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenoxy]acetonitrile	339.0	2-[3-chloro-2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetonitrile
54	4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2,3-difluoro-phenol	281.0	(2,3-difluoro-4-hydroxyphenyl)boronic acid

Intermediate 52

2-[2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetonitrile

Step 1:**2-(4-bromo-2,3-difluoro-phenoxy)acetonitrile**

To a solution of 4-bromo-2,3-difluorophenol (5.2 g, 25 mmol, Eq: 1), bromoacetonitrile (6.0 g, 50 mmol, Eq: 2) in DMF (25 mL) was added potassium carbonate (6.9 g, 50 mmol, Eq: 2) and then the resultant mixture was stirred overnight at room temperature.

The mixture was poured into water (50 mL) and the aqueous solution was extracted with ethyl acetate (100 mL×2). The organic layers were combined and washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by prep. HPLC to give the title compound (5.2 g, 84 % yield) as white solid.

MS (ESI, m/z): 248.0 [M+H]⁺.

Step 2:**2-[2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetonitrile**

To a solution of 2-(4-bromo-2,3-difluorophenoxy)acetonitrile (6.2 g, 25 mmol, Eq: 1) in dioxane (50 mL) and was added (4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (6.35 g, 25 mmol, Eq: 1), Pd(dppf)Cl₂ (1.6g, 2 mmol, Eq: 0.08) and potassium acetate (4.9 g, 50 mmol, Eq: 2) and then the resultant mixture was degassed for 5 min with nitrogen and then stirred overnight at 80°C. After cooling to room temperature, the mixture was poured into water (100 mL) and the aqueous solution was extracted with ethyl acetate (100 mL×2). The organic layers were combined and washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give a red oil which was purified by silica gel column chromatography to provide the desired compound (4 g, 54% yield) as an off-white solid.

Intermediate 55**2-[3-chloro-2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetonitrile**

Prepared in analogy to Intermediate 52 starting from 4-bromo-3-chloro-2-fluoro-phenol [CAS#1360745-16-9].

Intermediate 33**4-amino-2-ethyl-benzoic acid****Step 1: methyl 4-nitro-2-vinyl-benzoate & ethyl 4-nitro-2-vinyl-benzoate**

- 5 A mixture of methyl 2-bromo-4-nitro-benzoate (5.2 g, 20 mmol, 1 eq), 2,4,6-trivinylcyclotriboroxane pyridine complex (5.78 g, 24 mmol, 1.2 eq), tetrakis(triphenylphosphine)palladium(0) (1.16 g, 1 mmol, 0.050 eq) and potassium carbonate (11.05 g, 79.99 mmol, 4 eq) in toluene (50 mL) and ethanol (50 mL) was stirred at 90 °C under nitrogen for 2 h. The mixture was filtered over Celite. The filtrate was concentrated to dryness.
- 10 To the crude was added water (50 mL). The mixture was extracted with ethyl acetate (50 mL × 3). The combined organic layers were concentrated to dryness. The crude was then purified by flash column chromatography eluting 10% ethyl acetate in petrol ether to afford methyl 4-nitro-2-vinyl-benzoate (1.58 g) as a brown oil.

Step 2: ethyl 4-amino-2-ethyl-benzoate

- 15 A mixture of ethyl 4-nitro-2-vinyl-benzoate (392.0 mg, 1.77 mmol, 1 eq) and Pd/C (10%) (50.0 mg) in MeOH (10 mL) was stirred at 25 °C for 5 h under a hydrogen atmosphere. The mixture was filtered over Celite to afford ethyl 4-amino-2-ethyl-benzoate (331 mg, 1.71 mmol, 96.66% yield) as brown oil. MS (ESI⁺): 194.1 [(M+H)⁺].

Step 3: 4-amino-2-ethyl-benzoic acid

- 20 To a solution of methyl 4-amino-2-ethylbenzoate (540 mg, 3.0 mmol) in THF (5 mL) and methanol (25 mL) was added 2.0 M LiOH (3.0 mL) aqueous solution. The resultant mixture was stirred for 15 h at room temperature and then acidified to pH=5-6 with 3.0 M hydrochloric acid. The resulting suspension was filtered, the solid was washed with water and then dried to give the title compound (0.3 g, 60.5% yield) as a white solid
- 25 MS (ESI, m/z): 166.0 [M+H]⁺.

Intermediate 56**2-(dimethylamino)-1-piperazin-1-yl-ethanone di-trifluoroacetate**

Step 1: tert-butyl 4-[2-(dimethylamino)acetyl]piperazine-1-carboxylate

To a solution of tert-butyl piperazine-1-carboxylate (500mg, 2.68 mmol) in DMF (20mL) was added dimethylglycine (277 mg, 2.68 mmol), triethylamine (815 mg, 1.12 mL, 8.05 mmol) and 1-propanephosphonic anhydride (1.71 g, 5.37 mmol,), the reaction was stirred for 20 minutes at room temperature. The reaction mixture was quenched with water and washed with brine. The mixture was extracted in DCM. The organic layer was concentrated in vacuum to give crude product (530 mg), which was used in the next step without further purification. MS (ESI, m/z): [Ms+1]⁺ 272

Step 2: 2-(dimethylamino)-1-piperazin-1-yl-ethanone di-trifluoroacetate

A solution of tert-butyl 4-(dimethylglycyl)piperazine-1-carboxylate (530 mg) in DCM (5 mL) and TFA (5 mL) was stirred for one hour at room temperature. The reaction mixture was concentrated *in vacuo* to give the crude product (680 mg), which was used without further purification. MS (ESI, m/z): [M+H]⁺ 172

Intermediate 57**4-(3-aminopropyl)piperazin-2-one****Step 1:****2-[3-(3-oxopiperazin-1-yl)propyl]isoindoline-1,3-dione**

A mixture of 3-(1,3-dioxoisoindolin-2-yl)propyl methanesulfonate (1.34 g, 5 mmol, Eq: 1), piperazin-2-one (600 mg, 6 mmol, Eq: 1.2) and potassium carbonate (1.38 g, 10 mmol, Eq: 2) in N,N-dimethylformamide (25 mL) was stirred at room temperature overnight. The mixture was diluted with H₂O and extracted with DCM. The DCM layer was dried and concentrated *in vacuo* to give a yellow oil, which was purified by flash column chromatography to provide the desired compound (1.2 g, 83.5 % yield) as a white solid. MS (ESI, m/z): 278.1 [M+H]⁺.

Step 2:**4-(3-aminopropyl)piperazin-2-one**

To a mixture of 2-(3-(3-oxopiperazin-1-yl)propyl)isoindoline-1,3-dione (1.15 g, 4 mmol) in EtOH (25 mL) was added hydrazine hydrate (2.0 mL) and then the mixture was stirred at room temperature overnight. The suspension was filtered and the filtrate was concentrated to give the title compound (0.5 g, 80 % yield) as a yellow oil. MS (ESI, m/z): 158.1 [M+H]⁺.

- 5 The following intermediates were prepared in analogy to intermediate 57

Int.	Name	ESI MS [M+H] ⁺	Starting Material
58	4-(3-aminopropyl)-1-methyl-piperazin-2-one	172.1	1-methylpiperazin-2-one
59	tert-butyl 4-(3-aminopropyl)-3-oxo-piperazine-1-carboxylate	258.1	tert-butyl 3-oxopiperazine-1-carboxylate
60	1-tert-butyl 2-methyl 4-(3-aminopropyl)piperazine-1,2-dicarboxylate	302.2	1-tert-butyl 2-methyl piperazine-1,2-dicarboxylate
61	2-(2-imidazol-1-ylethoxy)ethanamine	156.1	Intermediate 62 and imidazole

Intermediate 63

2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoic acid

10 Step 1: methyl 2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoate

To a solution of 8-chloro-3-iodo-imidazo[1,2-a]pyrazine (6.0 g, 21.47 mmol, 1 eq) in ACN (60 mL) was added methyl 4-amino-2-ethyl-benzoate [CAS#1211589-24-0] (4.72 g, 26.31 mmol, 1.23 eq) and acetic acid (6.0 mL, 21.47 mmol, 1 eq). The reaction mixture was stirred at 80 °C for 60 h. After cooling to room temperature, the reaction mixture was filtered and washed with

- 15 (ACN:MeOH=10:1, V:V), and then dried to provide methyl 2-ethyl-4-[(3-iodoimidazo[1,2-

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a]pyrazin-8-yl)amino]benzoate (9.37 g, crude) as off-white solid. ^1H NMR (400 MHz, DMSO- d_6) δ 10.14 (br s, 1H), 7.98-8.06 (m, 2H), 7.89 (s, 1H), 7.86 (d, $J=4.77$ Hz, 1H), 7.82 (d, $J=8.53$ Hz, 1H), 7.62 (d, $J=4.77$ Hz, 1H), 3.80 (s, 3H), 2.93 (q, $J=7.40$ Hz, 2H), 1.18 (t, $J=7.40$ Hz, 3H)

Step 2: 2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoic acid

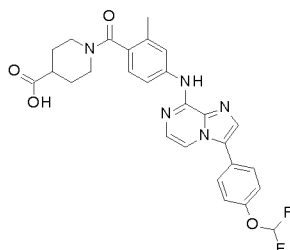
- 5 To a solution of methyl 2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoate (9.37 g, 22.19 mmol, 1 eq) in THF (80 mL) was added sodium hydroxide (80.0 mL, 320 mmol, 14.42 eq) and then stirred at 60 °C for 60 h. The reaction mixture was adjusted to pH=1~2 by 3N HCl, filtered and dried to 2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoic acid (8.2 g, 20.09 mmol, 90.52 % yield) as white solid. ^1H NMR (400 MHz, DMSO- d_6) δ 12.48 (br s, 1H),
 10 9.86 (s, 1H), 8.05 (dd, $J=2.13, 8.66$ Hz, 1H), 7.99 (d, $J=2.01$ Hz, 1H), 7.78-7.86 (m, 3H), 7.61 (d, $J=4.64$ Hz, 1H), 2.95 (q, $J=7.40$ Hz, 2H), 1.18 (t, $J=7.47$ Hz, 3H).

The following intermediates were prepared in analogy to Intermediate 63

Int.	Name	ESI MS [M+H] $^+$	Starting Material
64	2-chloro-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoic acid	415.1	methyl 4-amino-2-chlorobenzoate

15 Reference Example 1

1-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxylic acid



Step 1

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methyl 1-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxylate

A mixture of Intermediate 7, DIPEA (94.5 mg, 128 μ L, 731 μ mol) and HATU (185 mg, 487 μ mol) in DMF (2 mL) was stirred for 30 min. Methyl piperidine-4-carboxylate (52.3 mg, 366 μ mol) was added and stirring continued overnight. The mixture was purified by prep. HPLC to yield the title compound as a light brown solid (93 mg).

MS (ESI, m/z): 536.3 [M+H]⁺.

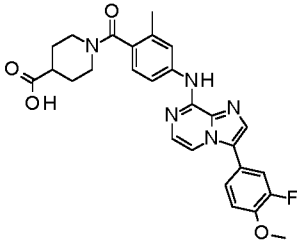
Step 2

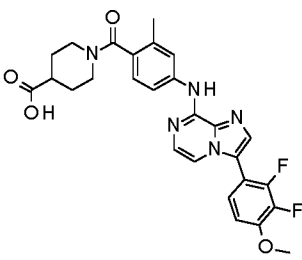
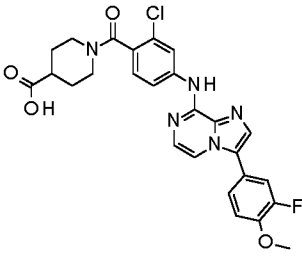
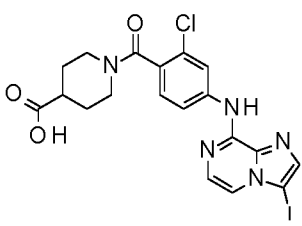
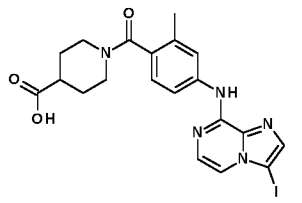
1-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxylic acid

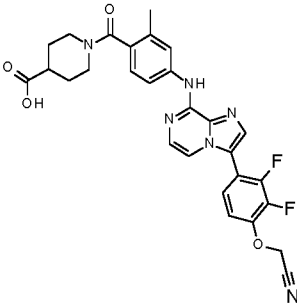
A mixture of methyl 1-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxylate (93 mg), 1M aq LiOH (0.8 mL) in THF(1 mL)/water (0.5 mL) was stirred at 60 °C for 5 h. The reaction mixture was concentrated and acidified by addition of 1M aq HCl. Water (1 mL) was added and the mixture was extracted with DCM. The combined organic layers were dried over sodium sulphate and then concentrated *in vacuo* to give the title compound (91 mg) as a white solid.

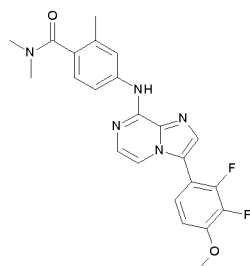
MS (ESI, m/z): 522.2 [M+H]⁺.

The following Examples and Intermediates were prepared in analogy to Reference Example 1

Ex.	Name	Structure	ESI MS [M+H] ⁺	Starting Material
REF 2	1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxylic acid		504.2	Intermediate 6

65	1-[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperidine-4-carboxylic acid		522.4	Intermediate 28
66	1-(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperidine-4-carboxylic acid		524.3	Intermediate 2
67	1-[2-chloro-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoyl]piperidine-4-carboxylic acid		526.3	Intermediate 64
68	1-[4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]-2-methylbenzoyl]piperidine-4-carboxylic acid		506.1	Intermediate 1

69	1-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxylic acid		547.3	Intermediate 31 and piperidine-4-carboxylic acid (no hydrolysis step)
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Example 1**4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,N,2-trimethylbenzamide**

5

Step 1:**4-amino-N,N,2-trimethyl-benzamide**

To a solution 4-amino-2-methylbenzoic acid (2.7g, 18 mmol), dimethylamine hydrochloride (1.76g, 21.6 mmol) in DCM (350 mL) was added TEA (3.6 g, 36 mmol) and then the resultant mixture was stirred for 30 min at room temperature, EDCI (4 g, 21mmol) was added in the mixture and stirred for extra 10 h. The mixture was poured into water (500 mL) and the aqueous solution was extracted with DCM (100 mL×2). The organic layers were combined and washed with water and brine, dried over anhydrous sodium sulphate and concentrated under reduced pressure to give a yellow oil which was purified by flash column chromatography to provide the desired compound (2.5 g, 78% yield) as an off-white solid

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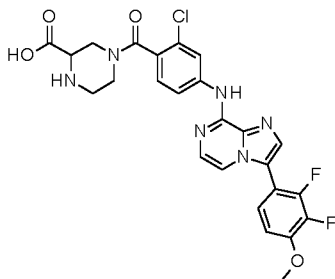
MS (ESI, m/z): 179.1 [M+H]⁺.**Step 2:**

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4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,N,2-trimethylbenzamide

To a solution of Intermediate 21 (295 mg, 1 mmol) in acetonitrile (10 mL) and acetic acid (1 mL) was added 4-amino-N,N,2-trimethyl-benzamide (178 mg, 1 mmol). The mixture was stirred overnight at 85 °C. The mixture was poured into water (50 mL) and the aqueous solution was extracted with DCM (75 mL×2). The organic layers were combined and washed with water and brine, dried over anhydrous sodium sulphate and concentrated under reduced pressure to give a red oil which was purified by prep. HPLC to provide the desired compound (200 mg, 45.7 % yield) as an off-white solid.

MS (ESI, m/z): 438.1 [M+H]⁺.

Reference Example 3**4-(2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperazine-2-carboxylic acid****Step 1:****1-tert-butyl 2-methyl 4-[2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperazine-1,2-dicarboxylate**

To a solution of 2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid (215 mg, 0.5 mmol), 1-tert-butyl 2-methyl piperazine-1,2-dicarboxylate (146 mg, 0.6 mmol) in anhydrous DMF (5 mL) was added DIPEA (129 mg, 1.0 mmol) and then the resultant mixture was stirred for 30 min at room temperature, HATU (380 mg, 1.0 mmol) was added in the mixture and stirred for extra 10 h. The mixture was poured into water (50 mL) and the aqueous solution was extracted with ethyl acetate (50 mL×2). The organic layers were

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combined and washed with water and brine, dried and concentrated under reduced pressure to give a red oil, which was used in next step without purification. MS (ESI, m/z): 657.1 [M+H]⁺.

Step 2:**5 methyl 4-[2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperazine-2-carboxylate**

To a solution of 1-tert-butyl 2-methyl 4-(2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperazine-1,2-dicarboxylate (200 mg, 0.3 mmol) in ethyl acetate (5 mL) was added 1 M hydrochloric acid in ethyl acetate (5.0 mL) at room temperature. The resultant mixture was stirred for 4 h and then adjusted to pH=7-8
10 with 2M aq. Na₂CO₃. The mixture was extracted with DCM (75 mL×2), the combined organic layers were washed with water and brine, dried and concentrated to give a red solid, which was used in the next step without purification.

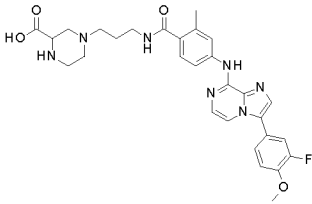
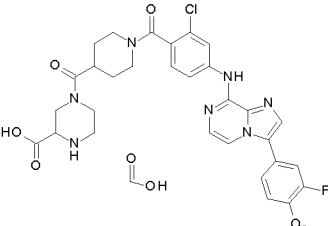
MS (ESI, m/z): 557.1 [M+H]⁺.

Step 3:**15 4-[2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperazine-2-carboxylic acid**

To a solution of methyl 4-(2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperazine-2-carboxylate (167 mg, 0.3 mmol) in THF (5 mL) and MeOH ethyl acetate (5 mL) was added 1M aq. LiOH (3 mL) dropwise at room temperature. The
20 resultant mixture was stirred for 4 h, and then acidified to pH 5-6 with 2 M hydrochloric acid. The mixture was extracted with DCM (50 mL x 2), and the combined organic layers were washed with brine, and then dried and then concentrated to give a light yellow oil, which was purified by prep. HPLC to provide the desired compound (200 mg, 45.7 % yield) as an off-white solid.

25 MS (ESI, m/z): 438.1 [M+H]⁺

The following Examples were prepared in analogy to Reference Example 3

Ex.	Name	Structure	ESI MS [M+H] ⁺	Starting Material
2	4-(3-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamido)propyl)piperazine-2-carboxylic acid		562.2	Intermediate 6 and Intermediate 60
REF 4	4-(1-(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperidine-4-carbonyl)piperazine-2-carboxylic acid, formate salt		636.4	Intermediate 66 and 1-(tert-butyl) 2-methyl piperazine-1,2-dicarboxylate

Intermediate 23

8-chloro-3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazine

5 Step 1: 1-bromo-4-(difluoromethoxy)-2,3-difluoro-benzene

A mixture of 4-bromo-2,3-difluorophenol (1 g, 4.78 mmol), sodium chlorodifluoroacetate (1.09 g, 7.18 mmol) and potassium carbonate (1.32 g, 9.57 mmol) in DMF (10 mL) was heated to 100 °C with stirring overnight. The mixture was diluted with saturated aq. NaHCO₃ solution and

extracted with DCM. The DCM layer was dried and concentrated. The residue was purified by column chromatography (eluting with PE/EA=50/1) to give the title compound (1 g) as colorless oil.

Step 2: 2-[4-(difluoromethoxy)-2,3-difluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

A mixture of 1-bromo-4-(difluoromethoxy)-2,3-difluorobenzene (850 mg), bis(pinacolato)diboron (833 mg, 3.28 mmol), potassium acetate (644 mg, 6.56 mmol) and PdCl₂(PPh₃)₂ (115 mg, 164 μmol) in dioxane (20 mL) was heated to 100 °C with stirring overnight. The mixture was concentrated in vacuo and the residue was purified by column chromatography (eluting with PE/EA=30/1) to give the title compound (800 mg, 2.61 mmol) as colorless oil.

Step 3: 8-chloro-3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazine

A mixture of 8-chloro-3-iodoimidazo[1,2-a]pyrazine (730 mg, 2.61 mmol), 2-(4-(difluoromethoxy)-2,3-difluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (800 mg, 2.61 mmol), PdCl₂(dppf)-CH₂Cl₂ adduct (95.6 mg, 131 μmol) and K₃PO₄ (1.66 g, 7.84 mmol) in THF (40 mL) and H₂O (10 mL) was heated to 50 °C with stirring overnight. The mixture was diluted with H₂O and extracted with DCM. The DCM layer was dried and concentrated. The residue was purified by silica gel column chromatography (eluting with PE/EA=5/1) to give the title compound (400 mg, 1.21 mmol) as a brown solid. MS (ESI, m/z): 332.2 [M+H]⁺

Intermediate 41

2-[3-chloro-4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenoxy]acetonitrile

Step 1: 4-bromo-3-chloro-2-fluoro-phenol

To a stirred solution of 3-chloro-2-fluorophenol (10.00 g, 68.24 mmol) in DCM (200 mL) was added bromine (13.09 g, 81.88 mmol) dropwise at -10 °C. The reaction mixture was warmed up to 20 °C and stirred for 16 h. The reaction was quenched with sat. aq. Na₂SO₃ (100 mL) and extracted with DCM (150 mL). The organic phase was washed with sat. NaHCO₃ (100 mL) and brine (100 mL), dried and concentrated under reduced pressure to give 4-bromo-3-chloro-2-

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fluoro-phenol (13.7 g) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ : 7.31 (dd, 1H), 6.86 (t, 1H)

Step 2: 2-(4-bromo-3-chloro-2-fluoro-phenoxy)acetonitrile

A mixture of 4-bromo-3-chloro-2-fluoro-phenol (13.70 g, 60.77 mmol), potassium carbonate (12.60 g, 91.16 mmol) and bromoacetonitrile (8.75 g, 72.92 mmol) in acetonitrile (200 mL) was stirred at 60 °C for 16 h. The reaction mixture was cooled and filtered. The filtrate was concentrated under reduced pressure, purified by the flash column chromatography (eluting with PE/EA=10/1) to give 2-(4-bromo-3-chloro-2-fluoro-phenoxy) acetonitrile (13.0 g) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ : 7.43 (dd, 1H), 6.96 (dd, 1H), 4.84 (s, 2H)

Step 3: 2-[3-chloro-2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetonitrile

A mixture of 2-(4-bromo-3-chloro-2-fluoro-phenoxy)acetonitrile (13.00 g, 49.15 mmol), bis(pinacolato)diboron (14.98 g, 58.98 mmol), potassium acetate (14.47 g, 147.46 mmol) and Pd(dppf)Cl₂·CH₂Cl₂ adduct (3.60 g, 4.92 mmol) in 1,4-dioxane (280 mL) was stirred at 70 °C under nitrogen for 16 h. The reaction was cooled and the mixture was filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (eluting with PE: EA=10:1) to afford desired product (11.6 g) as a light yellow solid.

Step 4: 2-[3-chloro-4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenoxy]acetonitrile

Intermediate 41

A mixture of 8-chloro-3-iodo-imidazo[1,2-a]pyrazine (6.50 g, 23.26 mmol), 2-[3-chloro-2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy] acetonitrile (11.59 g, 23.26 mmol), sodium carbonate (7.40 g, 69.77 mmol) and Pd(dppf)Cl₂·CH₂Cl₂ adduct (1.7 g, 2.33 mmol) in 1,4-dioxane (150 mL) and water (30 mL) was stirred under nitrogen at 60 °C for 16 h. The reaction mixture was cooled and filtered. The filtrate was concentrated and the residue was diluted with H₂O (100 mL) and extracted with DCM (200 mLx3). The organic phase was washed with brine (100 mL), concentrated under reduced pressure and purified by flash column chromatography (PE/EA=1/1) to give crude product. It was re-purified by trituration (PE/EA=3/1) and dried in vacuo to afford the title compound (5.0 g) as a light red solid.

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MS obsd. (ESI⁺) [(M+H)⁺]: 337.2

Intermediate 27

8-chloro-3-(2-chloro-5-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazine

5 Step 1: 1-chloro-4-fluoro-5-methoxy-2-nitro-benzene

Sodium (712 mg, 30.97 mmol) was added to MeOH (50 mL) and the mixture was stirred for 10 min. To the resulting mixture was added a solution of 1-chloro-4, 5-difluoro-2-nitro-benzene (5.0 g, 25.83 mmol) in MeOH (20 mL) at 0 °C. The reaction was stirred at 15 °C for 2 h. The mixture was quenched with water (30 mL) and then extracted with DCM (100 mL). The DCM layer was
10 washed with brine (30 mL), dried and concentrated under reduced pressure to give 1-chloro-4-fluoro-5-methoxy-2-nitro-benzene (4.2 g) as a yellow solid. ¹H NMR (400 MHz, CDCl₃) □: 7.86 (d, 1H), 7.08 (d, 1H), 4.00 (s, 3H)

Step 2: 2-chloro-5-fluoro-4-methoxy-aniline

To a stirred suspension of nickel(ii) chloride hexahydrate (2.44 g, 10.25 mmol) and sodium
15 borohydride (380 mg, 10.04 mmol) in methanol (100 mL) was added a solution of 1-chloro-4-fluoro-5-methoxy-2-nitro-benzene (4.2 g, 20.43 mmol) in THF (40 mL) at 0 °C drop wise. Then additional sodium borohydride (2.31 g, 61.06 mmol) was added at 0 °C and the reaction mixture was stirred for 1 h at 15 °C. The reaction was quenched by addition of water (20 mL). The solid was filtered and the filtrate was extracted with DCM. The organic phase was washed with brine,
20 dried and concentrated under reduced pressure. The residue was purified by column chromatography (eluting with PE/EA=5/1) to give the title compound (2.8 g) as a yellow solid.

Step 3: 1-bromo-2-chloro-5-fluoro-4-methoxy-benzene

To a solution of 2-chloro-5-fluoro-4-methoxy-aniline (1.7 g, 9.68 mmol) in aq. HBr (20 mL) was added sodium nitrite (735 mg, 10.65 mmol) in water (8 mL) at 0 °C. The mixture was stirred at 0
25 °C for 30 min. Then a solution of copper (I) bromide (2.08 g, 14.52 mmol) and copper (II) bromide (3.24 g, 14.52 mmol) in aq. HBr (20 mL) was added to the mixture. The reaction was stirred at 60 °C for 2 h. The mixture was diluted with DCM (100 mL), washed with water (30

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mL) and brine (30 mL), dried and concentrated under reduced pressure. The residue was purified by column chromatography (PE/EA=20/1) to give the title compound (530 mg) as a white solid.

Step 4: 2-(2-chloro-5-fluoro-4-methoxy-phenyl)-4, 4, 5, 5-tetramethyl-1, 3, 2-dioxaborolane

A mixture of 1-bromo-2-chloro-5-fluoro-4-methoxy-benzene (530 mg, 2.21 mmol),
5 bis(pinacolato)diboron (843 mg, 3.32 mmol), potassium acetate (652 mg, 6.64 mmol) and Pd(dppf)Cl₂ · CH₂Cl₂ adduct (181 mg, 0.22 mmol) in 1,4-dioxane (2 mL) was stirred at 80 °C under nitrogen for 16 h. The reaction was cooled and the mixture was filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (PE/EA=100/1) to give desired compound (250 mg) as a white solid.

10 **Step 5: 8-chloro-3-(2-chloro-5-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazine**

A mixture of intermediate 8-chloro-3-iodo-imidazo[1,2-a]pyrazine (400 mg, 1.43 mmol), 2-(2-chloro-5-fluoro-4-methoxy-phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (420 mg, 1.47 mmol), sodium carbonate (455 mg, 4.29 mmol) and Pd(dppf)Cl₂ · CH₂Cl₂ adduct (117 mg, 0.14 mmol) in 1,4-dioxane (8 mL) and water (2 mL) was stirred under nitrogen at 50 °C for 16 h. The
15 reaction mixture was cooled and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (PE/EA=3/1) to give the desired product (375 mg) as a brown solid. MS obsd. (ESI⁺) [(M+H)⁺]: 312.2

Intermediate 70

8-chloro-3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazine

20

Step 1: 1-bromo-2-chloro-3-fluoro-4-methoxy-benzene

To a stirred solution of 1-chloro-2-fluoro-3-methoxy-benzene (2.00 g, 12.46 mmol) in chloroform (20 mL) was added bromine (1.89 g, 11.83 mmol) drop wise. The reaction mixture was stirred at 15 °C for 2 h. The reaction was quenched with aq. Na₂SO₃ solution and extracted
25 with DCM. The organic phase was washed with brine (20 mL), dried over anhydrous sodium sulphate, concentrated under reduced pressure to give the desired compound (2.00 g) as a white solid.

Step 2: 2-(2-chloro-3-fluoro-4-methoxy-phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

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A mixture of 1-bromo-2-chloro-3-fluoro-4-methoxy-benzene (1.00 g, 2.8 mmol), bis(pinacolato)diboron (710 mg, 2.8 mmol), potassium acetate (824 mg, 8.39 mmol) and Pd(dppf)Cl₂·CH₂Cl₂ adduct (228 mg, 0.28 mmol) in 1,4-dioxane (20 mL) was stirred at 80 °C under nitrogen for 2 h. The reaction was cooled and the mixture was filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (eluting with PE/EA=50/1) to give the desired compound (200 mg) as a white solid.

Step 3: 8-chloro-3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazine

A mixture of 2-(2-chloro-3-fluoro-4-methoxy-phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (195 mg, 0.68 mmol), 8-chloro-3-iodo-imidazo[1,2-a]pyrazine (190 mg, 0.68 mmol), sodium carbonate (216 mg, 2.04 mmol) and Pd(dppf)Cl₂·CH₂Cl₂ adduct (55 mg, 0.07 mmol) in 1,4-dioxane (4 mL) and water (1 mL) was stirred under nitrogen at 50 °C for 16 h. The reaction was cooled to RT and concentrated under reduced pressure. The residue was purified by prep-TLC (PE/EA=2/1) to afford desired compound (67 mg) as a white solid. MS obsd. (ESI⁺) [(M+H)⁺] : 312.

Intermediate 71

2-[5-chloro-2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetonitrile

Step 1: 5-chloro-2-fluoro-4-nitro-phenol

A mixture of 1-chloro-4,5-difluoro-2-nitro-benzene (5.0 g, 25.83 mmol) and 15% aqueous KOH (2.9 g, 7.75 mmol) was stirred at 100 °C for 14 h. The mixture was added HCl (1N) until pH 4~5 and extracted with DCM (100 mL × 3). The mixture was then concentrated to dryness and purified by flash column chromatography (PE/EA = 100% ~ 10%) to afford 5-chloro-2-fluoro-4-nitro-phenol (4.1 g, 21.41 mmol) as a yellow solid. MS obsd. (ESI⁻): 190.0 [(M-H)-].

Step 2: 4-amino-5-chloro-2-fluoro-phenol

To a mixture of 5-chloro-2-fluoro-4-nitro-phenol (4.0 g, 20.88 mmol) and ammonium chloride (5.59 g, 104.42 mmol) in ethanol (60 mL) and water (30 mL) was added iron (5.83 g, 104.42 mmol). The mixture was stirred at 25 °C for 2 h. The mixture was filtered by celite. The filtrate

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was concentrated *in vacuo* to remove EtOH. The mixture was extracted with EA (30 mL × 3). The combined organic layers were concentrated to dryness. The crude product was purified by flash column chromatography to (PE/EA = 100% to 90%) afford 4-amino-5-chloro-2-fluoro-phenol (1.68 g) as a brown solid. MS obsd. (ESI⁻): 162.1 [(M-H)⁻].

5 **Step 3: 4-bromo-5-chloro-2-fluoro-phenol**

To a mixture of 4-amino-5-chloro-2-fluoro-phenol (1.55 g, 9.57 mmol) in hydrobromic acid (19.69 mL, 145.02 mmol) was added a solution of sodium nitrite (0.79 g, 11.48 mmol) in water (8 mL) at 0 °C. The mixture was kept at the same temperature for 30 min. Then a mixture of copper(II) bromide (0.67 mL, 14.35 mmol) and copper(I) bromide (2.06 g, 14.35 mmol) in
10 hydrobromic acid (19.69 mL, 145.02 mmol) was added. The mixture was stirred at 60 °C for 14 h. The mixture was diluted with water (50 mL) and extracted with DCM (50 mL×3). The combined organic layers were concentrated to dryness. The crude was purified by flash column chromatography (PE/EA = 100% to 90%) to afford 4-bromo-5-chloro-2-fluoro-phenol (1.89 g) as a white solid.

15 MS obsd. (ESI⁻): 223.0 [(M-H)⁻].

Step4: 2-(4-bromo-5-chloro-2-fluoro-phenoxy)acetonitrile

A mixture of 4-bromo-5-chloro-2-fluoro-phenol (1.89 g, 8.38 mmol) and potassium carbonate (3.48 g, 25.15 mmol) in acetone (150 mL) was stirred at 25 °C for 10 min. Then bromoacetonitrile (0.63 mL, 10.06 mmol) was added. The mixture was then stirred at 25 °C for
20 14 h. The mixture was concentrated to dryness and added water (20 mL). The mixture was extracted with ethyl acetate (10 mL × 3). The combined organic layers were concentrated to dryness. The crude was purified by flash column chromatography (EA/PE = 10%) to afford 2-(4-bromo-5-chloro-2-fluoro-phenoxy)acetonitrile (1.96 g) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ: 7.44 (d, 1H), 7.23 (d, 1H), 4.83 (s, 2H)

25 **Step 5: 2-[5-chloro-2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetonitrile**

A mixture of 2-(4-bromo-5-chloro-2-fluoro-phenoxy)acetonitrile (1.96 g, 7.41 mmol), bis(pinacolato)diboron (2.26 g, 8.89 mmol), potassium acetate (1.39 mL, 22.23 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (542.26 mg, 0.740 mmol) in 1,4-dioxane
30 (20 mL) was stirred at 100 °C under nitrogen for 14 h. The mixture was filtered over celite. The filtrate was concentrated to dryness. The crude product was then purified by flash column

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chromatography (EA/PE = 5%) to afford 2-[5-chloro-2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetonitrile (2.12 g) as a white solid.

¹H NMR (400 MHz, CDCl₃) δ ppm: 1.36 (s, 12H) 4.84 (s, 2H) 7.07 (d, *J* = 7.0 Hz, 1H) 7.49 (d, *J* = 11.3 Hz, 1H)

5 *Intermediate 72*

2-(2-(2-hydroxyethoxy)ethyl)isoindoline-1,3-dione

A mixture of 2-(2-aminoethoxy)ethanol (3.51 g, 33.4 mmol) and isobenzofuran-1,3-dione (4.5 g, 30.4 mmol) in toluene (40 mL) was heated to 110 °C with stirring overnight. The mixture was concentrated *in vacuo*. The residue was diluted with water and extracted with DCM. The DCM layer was dried and concentrated to give crude 2-(2-(2-hydroxyethoxy)ethyl)isoindoline-1,3-dione (5.8 g, 81 % yield) as yellow solid which was used in next step directly. MS obsd. (ESI⁺) [(M+H)⁺] : 236.

Intermediate 62

2-[2-(1,3-dioxoisindolin-2-yl)ethoxy]ethyl 4-methylbenzenesulfonate

To a solution of 2-(2-(2-hydroxyethoxy)ethyl)isoindoline-1,3-dione (2.5 g, 10.6 mmol) and TEA (2.15 g, 2.96 mL, 21.2 mmol) in DCM (40 mL) cooled at 0 °C was added 4-methylbenzene-1-sulfonyl chloride (4.05 g, 21.3 mmol). The mixture was warmed slowly to RT and stirred at RT overnight. The mixture was purified by column chromatography (eluting with PE/EA=2/1) to give 2-(2-(1,3-dioxoisindolin-2-yl)ethoxy)ethyl 4-methylbenzenesulfonate (3.2 g, 78 % yield) as white solid. MS obsd. (ESI⁺) [(M+H)⁺]: 390.

Intermediate 73

tert-butyl N-[[1-[4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate

A mixture of 4-(Boc-aminomethyl)piperidine (1.77 g, 8.25 mmol), 4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid (Intermediate 1, 2.5 g, 6.34 mmol), HATU (3.62 g, 9.51 mmol) and Et₃N (1.93 g, 2.65 mL, 19 mmol) in DMF (30 mL) was stirred at room temperature overnight. The mixture was poured into water. The aqueous phase was extracted with DCM. The organic phase was washed with saturated NaCl solution and water. The organic

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phase was dried and concentrated *in vacuo*. The residue was purified by flash column to afford the title compound (3 g) as an orange oil. MS (ESI, m/z): 591 [M+H]⁺

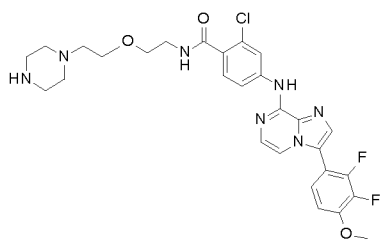
The following intermediates were prepared in analogy:

Int.	Name	MS ESI [M+H] ⁺	Starting Material
74	tert-butyl rac-(3R)-3-[[1-[2-chloro-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoyl]piperidine-4-carbonyl]amino]pyrrolidine-1-carboxylate	694.4	Intermediate 67 and tert-butyl (R)-3-aminopyrrolidine-1-carboxylate
75	tert-butyl (2S,4R)-4-hydroxy-2-(4-(4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carbonyl)pyrrolidine-1-carboxylate	676.2	Intermediate 76 and (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid

5

Reference Example 5

2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(2-piperazin-1-ylethoxy)ethyl]benzamide; 2,2,2-trifluoroacetic acid



10 Step 1: tert-butyl 4-[2-[2-(1,3-dioxoisindolin-2-yl)ethoxy]ethyl]piperazine-1-carboxylate

A mixture of Intermediate 62 (650 mg, 1.67 mmol), *tert*-butyl piperazine-1-carboxylate (466 mg, 2.5 mmol) and potassium carbonate (461 mg, 3.34 mmol) in DMF (10 mL) was stirred at RT

overnight. The mixture was diluted with H₂O and extracted with DCM. The DCM layer was combined and washed with brine, concentrated and the residue was purified by column (silica gel, eluting with PE/EA=3/1) to give *tert*-butyl 4-(2-(2-(1,3-dioxoisindolin-2-yl)ethoxy)ethyl)piperazine-1-carboxylate (700 mg) which was used in next step directly.

5 **Step 2: *tert*-butyl 4-[2-(2-aminoethoxy)ethyl]piperazine-1-carboxylate**

To a solution of *tert*-butyl 4-(2-(2-(1,3-dioxoisindolin-2-yl)ethoxy)ethyl)piperazine-1-carboxylate (700 mg, 1.73 mmol) in EtOH (10 mL) was added hydrazine hydrate (510 mg, 0.5 mL, 10.2 mmol). The mixture was stirred at rt overnight. The volatiles were removed and the residue was suspended in DCM and an insoluble solid was filtered off. The filtrate was
10 concentrated *in vacuo* to give crude *tert*-butyl 4-(2-(2-aminoethoxy)ethyl)piperazine-1-carboxylate (500 mg) as light yellow oil which was used in next step directly.

Step 3: *tert*-butyl 4-[2-[2-[[2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]ethoxy]ethyl]piperazine-1-carboxylate

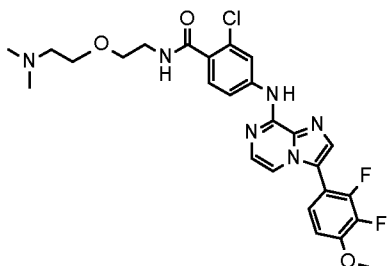
A mixture of *tert*-butyl 4-(2-(2-aminoethoxy)ethyl)piperazine-1-carboxylate (127 mg, 464
15 μ mol), intermediate 20 (100 mg, 232 μ mol), HATU (177 mg, 464 μ mol) and TEA (363 mg, 0.5 mL) in DMF (5 mL) was stirred at rt overnight. The reaction was diluted with H₂O (50 mL) and extracted with DCM. The DCM layer was dried and concentrated *in vacuo* to give crude *tert*-butyl 4-(2-(2-(2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamido)ethoxy)ethyl)piperazine-1-carboxylate (200 mg) as yellow oil which was
20 used in the next step directly.

Step 4: 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(2-piperazin-1-ylethoxy)ethyl]benzamide

To a solution of *tert*-butyl 4-(2-(2-(2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamido)ethoxy)ethyl)piperazine-1-carboxylate (200 mg, 291 μ mol) in
25 MeOH (10 mL) was added TFA (2.96 g, 2 mL, 26 mmol). The mixture was heated to 50 °C with stirring overnight. The volatiles were removed and the residue was purified by prep-HPLC to give 2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(2-(2-(piperazin-1-yl)ethoxy)ethyl)benzamide (30 mg) as light yellow solid. MS obsd. (ESI+) [(M+H)+] : 586.

Reference Example 6

2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[2-(dimethylamino)ethoxy]ethyl]benzamide; 2,2,2-trifluoroacetic acid



5 **Step 1: 2-[2-[2-(dimethylamino)ethoxy]ethyl]isoindoline-1,3-dione**

A mixture of Intermediate 62 (400 mg, 1.03 mmol), dimethylamine (770 μ L, 1.54 mmol) and potassium carbonate (284 mg, 2.05 mmol) in acetonitrile (10 mL) was stirred at RT overnight. The mixture was diluted with H₂O and extracted with DCM. The DCM layer was combined and washed with brine, concentrated to give crude 2-(2-(2-(dimethylamino)ethoxy)ethyl)isoindoline-1,3-dione (300 mg) which was used in next step directly.

10 **Step 2: 2-[2-(dimethylamino)ethoxy]ethanamine**

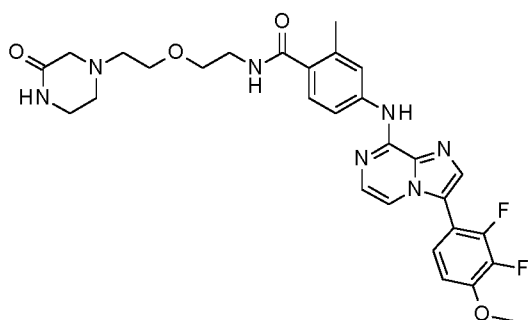
To a solution of 2-(2-(2-(dimethylamino)ethoxy)ethyl)isoindoline-1,3-dione (300 mg, 1.14 mmol) in EtOH (10 mL) was added hydrazine hydrate (57.3 mg, 1.14 mmol). The reaction was stirred at RT overnight. The solid was filtered and the filtrate was concentrated *in vacuo* to give 2-(2-aminoethoxy)-N,N-dimethylethanamine (150 mg) as light yellow oil which was used in next step directly.

15 **Step 3: 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[2-(dimethylamino)ethoxy]ethyl]benzamide**

A mixture of Intermediate 20 (100 mg, 232 μ mol), 3-(2-(dimethylamino)ethoxy)propan-1-amine (33.9 mg, 232 μ mol), HATU (177 mg, 464 μ mol) and TEA (363 mg, 0.5 mL, 3.59 mmol) in DMF (5 mL) was stirred at rt overnight. The mixture was diluted with H₂O (50 mL) and extracted with DCM (50 mL) for three times. The DCM layer was dried and concentrated *in vacuo*. The residue was purified by prep-HPLC to give the title compound (40 mg) as light yellow solid. MS (ESI⁺) [M+H]⁺: 545.1.

Reference Example 7

4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-[2-(3-oxopiperazin-1-yl)ethoxy]ethyl]benzamide; 2,2,2-trifluoroacetic acid



5 Step 1: 2-[2-(1,3-dioxisoindolin-2-yl)ethoxy]ethyl methanesulfonate

To a solution of Intermediate 72 (2 g, 8.5 mmol) and TEA (1.45 g, 2 mL) in CH₂Cl₂ (50 mL) cooled at 0 °C was added MsCl (1.07 g, 9.35 mmol). The mixture was warmed to RT and stirred at RT for 4 h. The mixture was concentrated *in vacuo* and the residue was purified by column chromatography (eluting with PE/EA=1/1) to give 2-(2-(1,3-dioxisoindolin-2-yl)ethoxy)ethyl methanesulfonate

Step 2: 2-[2-[2-(3-oxopiperazin-1-yl)ethoxy]ethyl]isoindoline-1,3-dione

A mixture of 2-(2-(1,3-dioxisoindolin-2-yl)ethoxy)ethyl methanesulfonate (500 mg, 1.6 mmol), piperazin-2-one (192 mg, 1.91 mmol) and K₂CO₃ (441 mg, 3.19 mmol) in DMF (5 mL) was heated to 100 °C with stirring overnight. The mixture was diluted with H₂O and extracted with DCM. The DCM layer was dried and concentrated *in vacuo* to give crude 2-(2-(2-(3-oxopiperazin-1-yl)ethoxy)ethyl)isoindoline-1,3-dione (550 mg) as yellow oil which was used in next step directly.

Step 3: 4-[2-(2-(2-(3-oxopiperazin-1-yl)ethoxy)ethyl]piperazin-2-one

A mixture of crude 2-(2-(2-(3-oxopiperazin-1-yl)ethoxy)ethyl)isoindoline-1,3-dione (550 mg, 1.73 mmol, Eq: 1) and hydrazine monohydrate (104 mg, 2.08 mmol) in EtOH (5 mL) was stirred at RT overnight. The mixture was concentrated *in vacuo* and the solid residue was suspended in DCM. The mixture was stirred at RT for 30 min and filtered. The filtrate was

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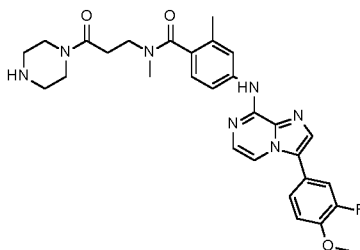
concentrated *in vacuo* to give crude 4-(2-(2-aminoethoxy)ethyl)piperazin-2-one (350 mg) as a yellow oil which was used in next step directly.

Step 4: 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-[2-(3-oxopiperazin-1-yl)ethoxy]ethyl]benzamide

- 5 A mixture of Intermediate 28 (150 mg, 366 μmol), 4-(2-(2-aminoethoxy)ethyl)piperazin-2-one (137 mg, 731 μmol), TEA (363 mg, 0.5 mL) and HATU (278 mg, 731 μmol) in DMF (5 mL) was stirred at rt. The mixture was diluted with H₂O (30 mL) and extracted with ethyl acetate. The ethyl acetate layer was concentrated and the residue was purified by prep-HPLC to give the title compound (36 mg) as light yellow solid. (ESI+) [(M+H)⁺]: 580.

10 **Example 3**

4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-oxo-3-piperazin-1-yl-propyl)benzamide



Step 1: ethyl 3-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]propanoate

- 15 To a stirred solution of ethyl 3-(methylamino) propanoate (100 mg, 0.76 mmol), Intermediate 6 (200 mg, 0.51 mmol) and triethylamine (0.2 mL, 1.53 mmol) in DMF (3 mL) was added 1-propanephosphonic anhydride (487 mg, 0.76 mmol, 50% in ethyl acetate) slowly. The reaction was stirred at 15 °C for 4 h. The reaction mixture was diluted with H₂O (10 mL) and extracted with ethyl acetate. The organic phase was washed with brine, dried over anhydrous sodium sulphate and concentrated under reduced pressure to give the title compound (250 mg) as a yellow oil. MS (ESI, m/z): 506 [M+H]⁺.

Step 2: 3-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]propanoic acid

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To a stirred solution of ethyl 3-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]propanoate (250 mg, 0.49 mmol) in ethanol (3 mL) was added a solution of sodium hydroxide (40 mg, 0.99 mmol) in water (0.5 mL) slowly. The reaction was stirred at 30 °C for 4 h. Aq. HCl (1.0 M) was added drop wise until pH=4-5. The reaction mixture was concentrated under reduced pressure and the residue was purified by prep-HPLC to afford the title compound (59.4 mg) as a white solid. MS obsd. (ESI⁺) [(M+H)⁺] : 478

Step 3: tert-butyl 4-[3-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]propanoyl]piperazine-1-carboxylate

To a stirred mixture of 3-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]propanoic acid (140 mg, 0.29 mmol), Boc-piperazine hydrochloride (98 mg, 0.44 mmol) and triethylamine (0.12 mL, 0.88 mmol) in DMF (2 mL) was added 1-propanephosphonic anhydride (280 mg, 0.44 mmol, 50% in ethyl acetate) slowly at 15 °C. The reaction was stirred for 4 h. The reaction mixture was diluted with H₂O (10 mL) and extracted with ethyl acetate. The organic phase was washed with brine (10 mL), dried and concentrated under reduced pressure to give the title compound (170 mg) as a yellow oil. MS obsd. (ESI⁺) [(M+H)⁺] : 646

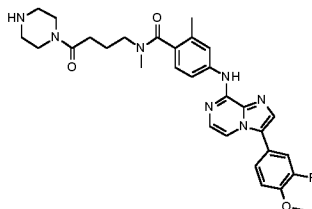
Step 4: 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-oxo-3-piperazin-1-yl-propyl)benzamide

A mixture of tert-butyl 4-[3-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]propanoyl]piperazine-1-carboxylate (170 mg, 0.26 mmol) and a solution of HCl in MeOH (0.2 mL, 0.79 mmol) in methanol (2 mL) was stirred at 15 °C for 4 h. The reaction mixture was concentrated under reduced pressure and purified by prep-HPLC to give the title compound (7.7 mg) as a white solid. MS obsd. (ESI⁺) [(M+H)⁺]: 546.1.

Example 4

4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(4-oxo-4-piperazin-1-yl-butyl)benzamide

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Example 4 was prepared using same procedure as for Example 3, changing ethyl 3-(methylamino) propanoate to methyl 4-(methylamino) butanoate hydrochloride. The title compound was purified by prep-HPLC. MS (ESI, m/z): 560.1 [M+H]⁺.

5 *Intermediate 77:*

2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]acetic acid

Step 1: methyl 2-[methyl-(2-methyl-4-nitro-benzoyl)amino]acetate

- 10 A mixture of 2-methyl-4-nitro-benzoic acid (2.00 g, 11.04 mmol), EDC hydrochloride (3.17 g, 16.56 mmol), HOBt (2.24 g, 16.56 mmol) and DIPEA (5.77 mL, 33.12 mmol) in DMF (40 mL) was stirred at 15 °C for 0.5 h. Then sarcosine methyl ester hydrochloride (2.31 g, 16.56 mmol) was added and the mixture was stirred at 15°C for 16 h. The reaction mixture was diluted with H₂O (50 mL) and extracted with ethyl acetate. The organic phase was washed with brine, dried,
- 15 concentrated under reduced pressure and purified by flash column chromatography (eluting with PE:EA=3:1) to afford the title compound (1.00 g) as brown oil. MS obsd. (ESI⁺) [M+H]⁺ : 267

Step 2: methyl 2-[(4-amino-2-methyl-benzoyl)-methyl-amino]acetate

- A mixture of methyl 2-[methyl-(2-methyl-4-nitro-benzoyl)amino]acetate (1.00 g, 3.76 mmol) and palladium (200 mg, 1.88 mmol, 10 wt% on charcoal) in methanol (20 mL) was stirred under
- 20 hydrogen (15 psi) at 15 °C for 16 h. The mixture was filtered and the filtrate was concentrated under reduced pressure to give the title compound (850 mg) as a crude product which was used directly in the next step.

Step 3: methyl 2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]acetate

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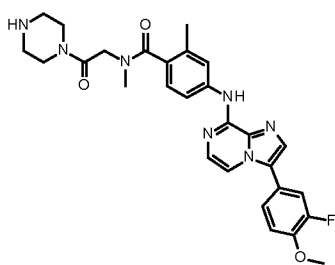
A mixture of Intermediate 3 (950 mg, 3.42 mmol) and methyl 2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]acetate (808 mg, 3.42 mmol) in acetonitrile (18 mL) and acetic acid (2 mL) was stirred at 100 °C for 4 h. The reaction was cooled and concentrated under reduced pressure. The residue was purified by flash
 5 column chromatography (eluting with DCM/MeOH=50/1) to afford the title compound (1.20 g) as a yellow solid. MS obsd. (ESI⁺) [(M+H)⁺] : 478

Step 4: 2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]acetic acid

Into a stirred solution of methyl 2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]acetate (1.10 g, 2.3 mmol) in methanol (20 mL) was
 10 added a solution of sodium hydroxide (276 mg, 6.91 mmol) in water (3.5 mL). The reaction was stirred at 30 °C for 4 h and then cooled and concentrated. The residue was diluted with H₂O (20 mL) and acidified with aq. HCl (1.0 M) until pH=5-6. The precipitate was collected by filtration and then triturated (acetonitrile) to afford the title compound (1.02 g) as a white solid, which was
 15 used without further purification in the subsequent steps. (ESI⁺) [(M+H)⁺] : 464.1

Example 5

2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methyl-methyl-amino]-1-piperazin-1-yl-ethanone hydrochloride



20 **Step 1: tert-butyl 4-[2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]acetyl]piperazine-1-carboxylate**

Into a stirred solution of Intermediate 77 (206. mg, 0.44 mmol), Boc-piperazine hydrochloride (119 mg, 0.53 mmol) and triethylamine (0.19 mL, 1.33 mmol) in DMF (3 mL) was added 1-propanephosphonic anhydride (425 mg, 0.67 mmol, 50% in ethyl acetate) slowly. The reaction
 25 was stirred at 15 °C for 4h. The reaction mixture was diluted with H₂O (10 mL) and extracted

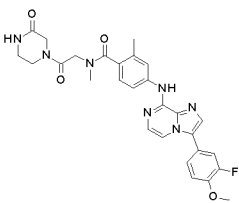
-124-

with ethyl acetate. The organic phase was washed with brine, dried over anhydrous sodium sulphate and concentrated under reduced pressure to give the title compound (300 mg) as a yellow oil which was used directly in the next step. MS obsd. (ESI⁺) [(M+H)⁺] : 632

Step 2: 2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methyl-methyl-amino]-1-piperazin-1-yl-ethanone hydrochloride

A mixture of tert-butyl 4-[2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]acetyl]piperazine-1-carboxylate (200 mg, 0.32 mmol) and a solution of HCl in 1,4-dioxane (0.4 mL, 1.58 mmol) in methanol (2 mL) was stirred at 15 °C for 4 h. The reaction mixture was concentrated under reduced pressure and the residue was purified by prep-HPLC to afford the title compound (88 mg) as a white solid. MS obsd. (ESI⁺) [(M+H)⁺]: 532

The following intermediates were prepared in analogy:

Ex#	Name	Structure	MS ESI [M+H] ⁺	Starting Material
6	4-[2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methyl-methyl-amino]acetyl]piperazin-2-one		546.1	Intermediate 77 and piperazin-2-one

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7	N-[2-(dimethylamino)-2-oxo-ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide		491.1	Intermediate 77 and dimethylamine
8	4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-morpholino-2-oxo-ethyl)benzamide		533.1	Intermediate 77 and morpholine
9	N-[2-[3-[(dimethylamino)methyl]pyrrolidin-1-yl]-2-oxo-ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide		574.1	Intermediate 77 and N, N-dimethyl-1-pyrrolidin-3-ylmethanamine dihydrochloride

Intermediate 78**tert-Butyl N-[2-[2-[(4-amino-2-methyl-benzoyl)amino]ethoxy]ethyl]carbamate****5 Step 1****tert-Butyl N-[2-[2-[(2-methyl-4-nitro-benzoyl)amino]ethoxy]ethyl]carbamate**

To a mixture of 2-methyl-4-nitro-benzoic acid (3.45 g, 19.04 mmol, 1 eq), N-Boc-2-(2-aminoethoxy)-ethylamine (3.89 g, 19.04 mmol, 1 eq) and triethylamine (7.96 mL, 57.13 mmol, 3 eq) in THF (50 mL) was added 1-propanephosphonic anhydride in ethyl acetate (18.18 g, 28.57 mmol, 1.5 eq) at 25 °C. The mixture was stirred at 25 °C for 16 h. The reaction was concentrated to

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dryness and the residue was taken up in ethyl acetate (50 mL) and washed with 2 x 50 mL water then 1 x 50 mL brine. The combined organic layers were then separated and dried (MgSO₄) before concentration to dryness to afford the crude product. The product was purified by silica gel column chromatography (30% ethyl acetate / PE) to afford the desired product (5.08 g) as a colorless oil.

Step 2

tert-Butyl N-[2-[2-[(4-amino-2-methyl-benzoyl)amino]ethoxy]ethyl]carbamate

A mixture of tert-butyl N-[2-[2-[(2-methyl-4-nitro-benzoyl)amino]ethoxy]ethyl]carbamate (2.0 g, 4.35 mmol, 1 eq) and palladium/C (1.5 mmol, 0.350 eq) in methanol (20 mL) was stirred under H₂ (775 mmHg) at 25 °C for 16 h. The mixture was filtered and purified by flash column chromatography to afford the title product (1.12 g) as a light yellow oil. MS (ESI, m/z): 238 [M+H-Boc]⁺.

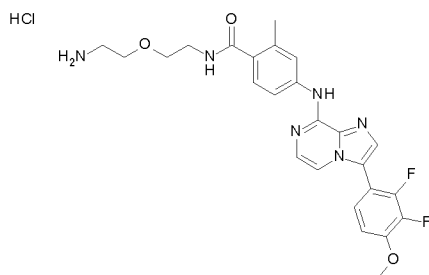
Intermediate 79

tert-Butyl (2-(2-(4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamido)ethoxy)ethyl)carbamate

The title compound was prepared in analogy to Reference Example 8 step 1 from Intermediate 1 and tert-butyl (2-(2-aminoethoxy)ethyl)carbamate. MS (ESI, m/z): 581.3[M+H]⁺

Reference Example 9

N-(2-(2-aminoethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride



Step 1:

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tert-Butyl (2-(2-(4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamido)ethoxy)ethyl) carbamate

tert-Butyl (2-(2-aminoethoxy)ethyl)carbamate (104 mg, 510 μ mol), diisopropylethylamine (132 mg, 178 μ l, 1.02 mmol) and HATU (259 mg, 680 μ mol) were added to a solution of 4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid (intermediate 1, 134 mg, 340 μ mol) in DMF (5 mL). The mixture was stirred overnight at room temperature. The reaction mixture was poured into 5 mL H₂O and extracted with acetonitrile. The organic layers were dried over sodium sulphate and concentrated *in vacuo*. The crude material was purified by flash chromatography (silica gel, 50% to 100% ethyl acetate in heptane) to give the title compound (112 mg) as a yellow solid. MS (ESI, m/z): 581.3 [M+H]⁺.

Step 2:

tert-Butyl (2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamido)ethoxy)ethyl)carbamate

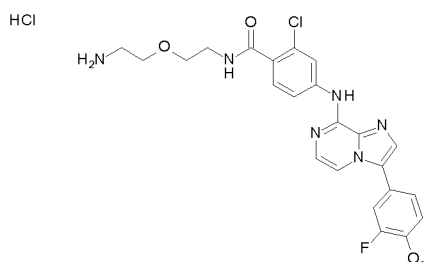
tert-butyl (2-(2-(4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamido)ethoxy)ethyl) carbamate (50 mg, 86.1 μ mol), (2,3-difluoro-4-methoxyphenyl)boronic acid (24.3 mg, 129 μ mol), Na₂CO₃ (18.3 mg, 172 μ mol) and 1,1'-bis(diphenylphosphino)ferrocenedichloro palladium(II) dichloromethane complex (7.03 mg, 8.61 μ mol) in dioxane (1000 μ l) and water (100 μ l) was heated in a microwave at 80 °C for 30 min. The crude reaction mixture was purified by prep. HPLC to give the title compound (28 mg) as a white solid. MS (ESI, m/z): 597.4 [M+H]⁺.

Step 3:

N-(2-(2-(2-aminoethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride

tert-Butyl (2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamido)ethoxy)ethyl)carbamate (28 mg, 46.9 μ mol) was combined with 3M HCl in MeOH (235 μ l, 704 μ mol) to give a light yellow solution. The reaction mixture was stirred at room temperature overnight. After removal of the volatiles, the solid obtained was dried *in vacuo* to give the title product (23.3 mg) as a light yellow solid. MS (ESI, m/z): 497.2 [M+H]⁺.

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Reference Example 8**N-(2-(2-aminoethoxy)ethyl)-2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide hydrochloride****5 Step 1:****tert-Butyl (2-(2-(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamido)ethoxy)ethyl) carbamate.**

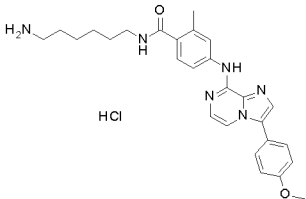
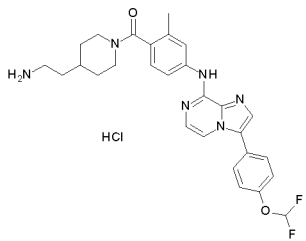
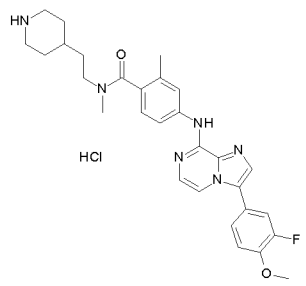
To 2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid (intermediate 2, 35 mg, 84.8 μ mol) in DMF (1 mL) was added tert-butyl (2-(2-aminoethoxy)ethyl)carbamate (26 mg, 127 μ mol), HATU (64.5 mg, 170 μ mol) and diisopropylethylamine (32.9 mg, 44.4 μ L, 254 μ mol) followed by stirring at room temperature for 1 h. The crude reaction mixture was purified by prep. HPLC to give the title compound (31 mg) as an orange solid. MS (ESI, m/z): 599.4 [M+H]⁺.

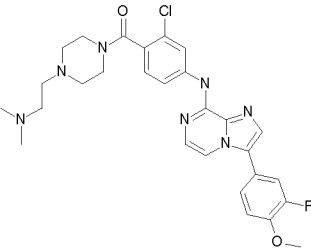
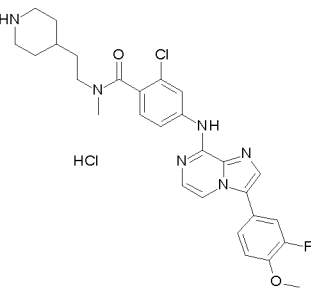
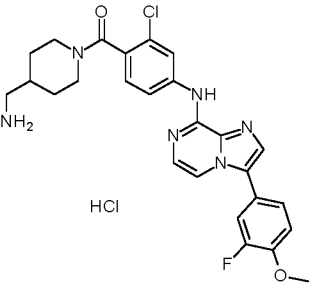
Step 2:**15 N-(2-(2-aminoethoxy)ethyl)-2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide hydrochloride**

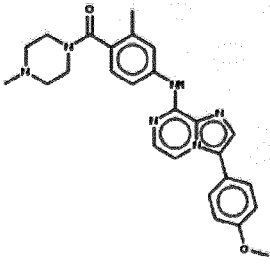
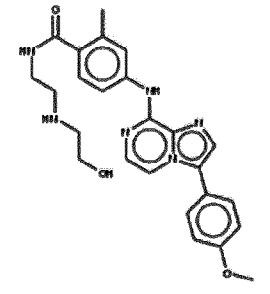
The title compound was obtained as a white solid (31 mg) in analogy to Reference Example 9, step 3 from tert-butyl (2-(2-(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamido)ethoxy)ethyl) carbamate. MS (ESI, m/z): 500.3 [M+H]⁺.

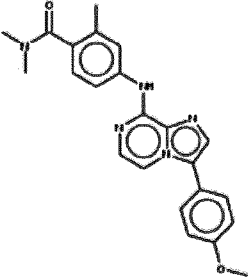
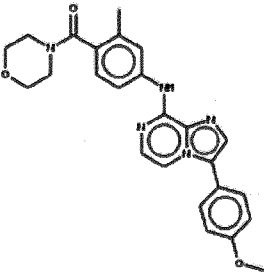
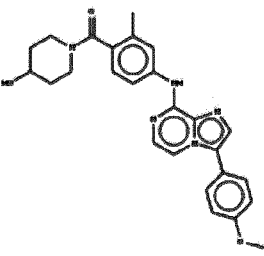
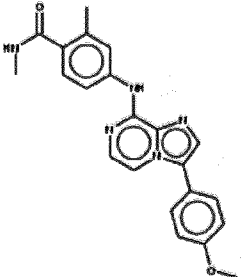
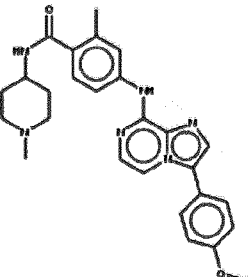
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The following examples were prepared in analogy to Reference Example 8, the deprotection step 2 was only applied for intermediates derived from Boc-protected amines.

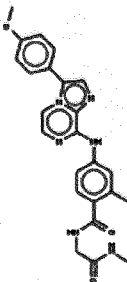
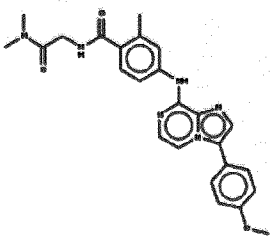
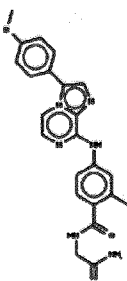
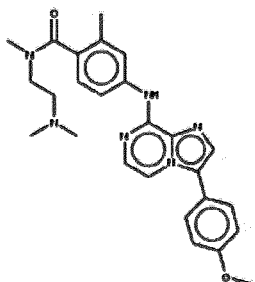
Ex.	Name	Structure	MS ESI [M+H] ⁺	Starting Material
10	N-(6-aminohexyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride		473.3	Intermediate 4 and tert-butyl (6-aminohexyl)carbamate hydrochloride
REF 10	(4-(2-Aminoethyl)piperidin-1-yl)(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone hydrochloride		521.1	Intermediate 7 and tert-butyl (2-(piperidin-4-yl)ethyl)carbamate
11	4-((3-(3-Fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethyl-N-(2-(piperazin-1-yl)ethyl)benzamide hydrochloride		517.3	Intermediate 6 and tert-butyl 4-(2-(methylamino)ethyl)piperidine-1-carboxylate

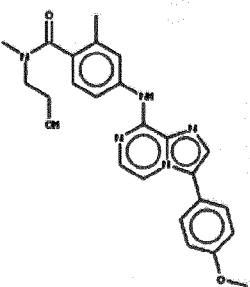
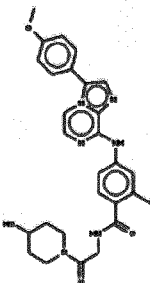
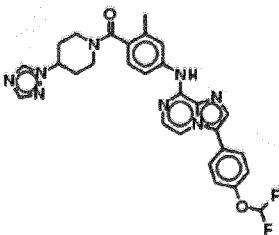
REF 11	(2-Chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)(4-(dimethylamino)ethyl)piperazin-1-yl)methanone		553.3	Intermediate 2 and N,N-dimethyl-2-(piperazin-1-yl)ethanamine
12	2-Chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methyl-N-(2-(piperazin-1-yl)ethyl)benzamide hydrochloride		537.0	Intermediate 2 and tert-butyl 4-(2-(methylamino)ethyl)piperazine-1-carboxylate
REF 12	(4-(Aminomethyl)piperidin-1-yl)(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)methanone hydrochloride		510.1	Intermediate 2 and tert-butyl (piperidin-4-ylmethyl)carbamate

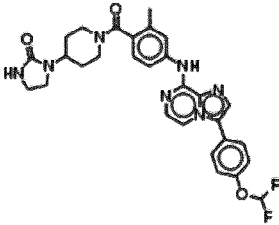
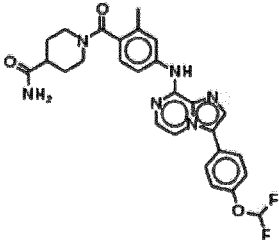
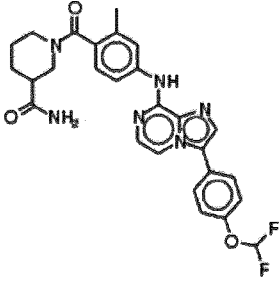
REF 13	N-(2-(2-aminoethoxy)ethyl)-2-chloro-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide hydrochloride		481.2	Intermediate 9 and tert-butyl (2-(2-aminoethoxy)ethyl)carbamate
REF 14	1-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamide		521.7	Intermediate 7 and piperidine-4-carboxamide
REF 15	(4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(4-methylpiperazin-1-yl)methanone		456	Intermediate 4 and 1-methylpiperazine
REF 16	N-(2-((2-hydroxyethyl)amino)ethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		460	Intermediate 4 and 2-((2-aminoethyl)amino)ethanol

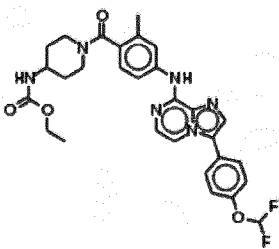
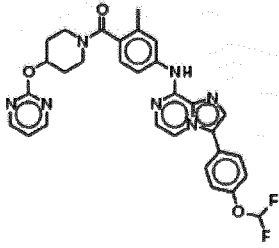
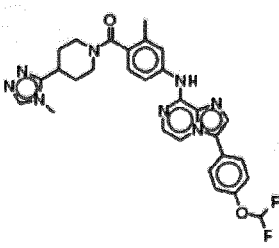
13	4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,N,2-trimethylbenzamide		401	Intermediate 4 and dimethylamine hydrochloride
REF 17	(4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(morpholino)methanone		443	Intermediate 4 and morpholine
REF 18	(4-hydroxypiperidin-1-yl)(4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone		457	Intermediate 4 and piperidin-4-ol hydrochloride
14	4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamide		387	Intermediate 4 and methanamine hydrochloride
REF 19	4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(1-methylpiperidin-4-yl)benzamide		470	Intermediate 4 and 1-methylpiperidin-4-amine hydrochloride

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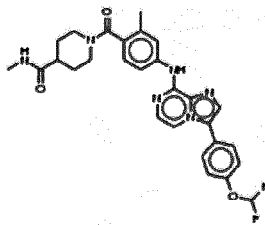
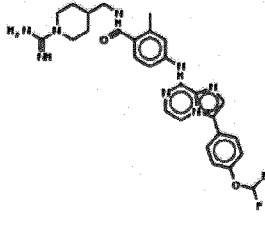
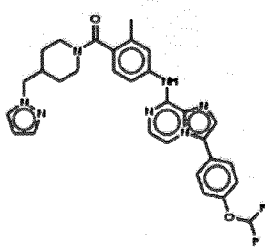
15	4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(2-(methylamino)-2-oxoethyl)benzamide		444	Intermediate 4 and 2-amino-N-methylacetamide hydrochloride
16	N-(2-(dimethylamino)-2-oxoethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		458	Intermediate 4 and 1,1-dimethylurea hydrochloride
17	N-(2-amino-2-oxoethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		430	Intermediate 4 and 2-aminoacetamide hydrochloride
18	N-(2-(dimethylamino)ethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamide		458	Intermediate 4 and N1,N1,N2-trimethylethane-1,2-diamine

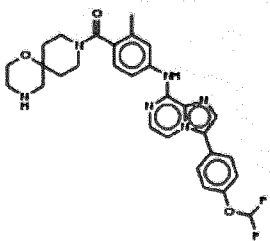
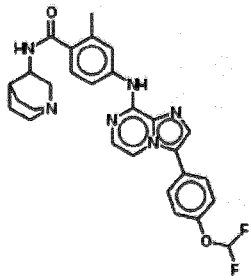
19	N-(2-hydroxyethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamide		431	Intermediate 4 and 2-(methylamino)ethanol 1
20	N-(2-(4-hydroxypiperidin-1-yl)-2-oxoethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		514	Intermediate 4 and 2-amino-1-(4-hydroxypiperidin-1-yl)ethanone
21	N-(6-aminohexyl)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride		509.2	Intermediate 7 and tert-butyl (6-aminohexyl)carbamate
REF 20	(4-(1H-1,2,4-triazol-1-yl)piperidin-1-yl)(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-		545.6	Intermediate 7 and 4-(1H-1,2,4-triazol-1-yl)piperidine

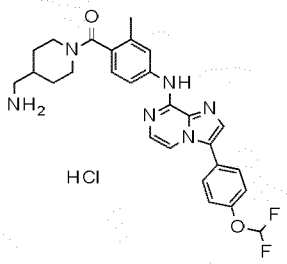
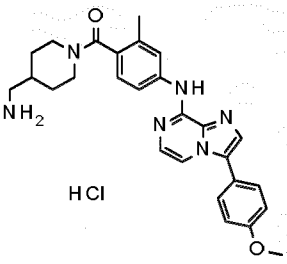
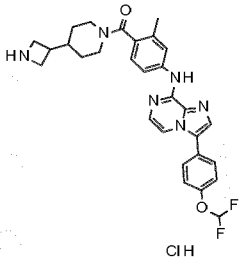
	methyphenyl)methanone			
REF 21	1-(1-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)imidazolidin-2-one		562.7	Intermediate 7 and 1-(piperidin-4-yl)imidazolidin-2-one
REF 14	1-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamide		521.7	Intermediate 7 and piperidine-4-carboxamide
REF 22	1-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-3-carboxamide		521.2	Intermediate 7 and piperidine-3-carboxamide

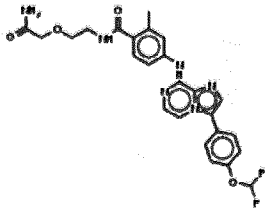
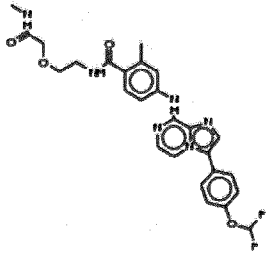
REF 23	ethyl (1-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)carbamate		565.4	Intermediate 7 and ethyl piperidin-4-ylcarbamate
REF 24	(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(4-(pyrimidin-2-yloxy)piperidin-1-yl)methanone		572.5	Intermediate 7 and 2-(piperidin-4-yloxy)pyrimidine dihydrochloride
REF 25	(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(4-(4-methyl-4H-1,2,4-triazol-3-yl)piperidin-1-yl)methanone		559.5	Intermediate 7 and 4-(4-methyl-4H-1,2,4-triazol-3-yl)piperidine

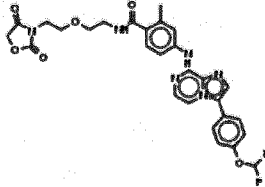
22	2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methylbenzamide		426.3	Intermediate 2 and methylamine hydrochloride
REF 26	(1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)(piperazin-1-yl)methanone hydrochloride		572.3	Intermediate 6 and tert-butyl piperazine-1-carboxylate
REF 27	(4-(aminomethyl)piperidin-1-yl)(2-bromo-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)methanone hydrochloride		573.3	Intermediate 10 and tert-butyl (piperidin-4-ylmethyl)carbamate

23	2-chloro-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methyl-N-(2-(piperidin-4-yl)ethyl)benzamide hydrochloride		555.2	Intermediate 11 and tert-butyl 4-(2-(methylamino)ethyl)piperidine-1-carboxylate
REF 28	1-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-methylpiperidine-4-carboxamide		535.3	Intermediate 7 and N-methylpiperidine-4-carboxamide
24	N-((1-carbamimidoylpiperidin-4-yl)methyl)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		549.3	Intermediate 7 and 4-(aminomethyl)piperidine-1-carboximidamide hydrochloride
REF 29	(4-((1H-pyrazol-1-yl)methyl)piperidin-1-yl)(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-		558.2	Intermediate 7 and 4-((1H-pyrazol-1-yl)methyl)piperidine

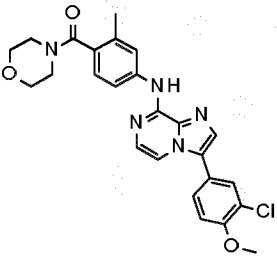
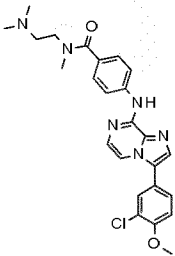
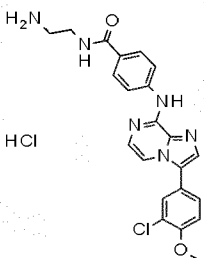
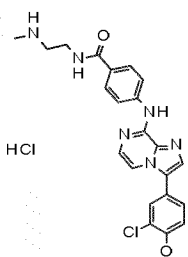
	yl)amino)-2-methylphenyl)methanone			
REF 30	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(1-oxa-4,9-diazaspiro[5.5]undecan-9-yl)methanone		549.2	Intermediate 7 and 1-oxa-4,9-diazaspiro[5.5]undecane
REF 31	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(quinuclidin-3-yl)benzamide		519.3	Intermediate 7 and quinuclidin-3-amine dihydrochloride
REF 32	N-(2-(2-chloroethoxy)ethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		480.3	Intermediate 4 and 2-(2-chloroethoxy)ethanamine hydrochloride

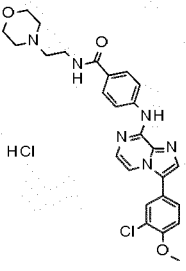
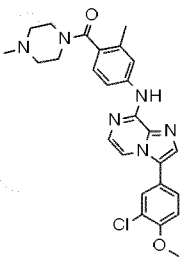
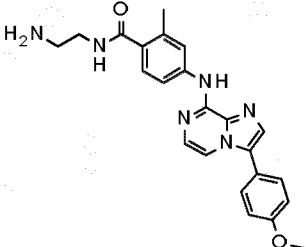
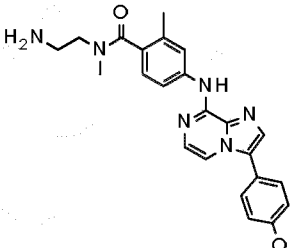
REF 33	(4-(aminomethyl)piperidin-1-yl)(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone hydrochloride		505.4 [M-H] ⁻	Intermediate 7 and tert-butyl (piperidin-4-ylmethyl)carbamate
REF 34	(4-(aminomethyl)piperidin-1-yl)(4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone hydrochloride		508.0	Intermediate 4 and tert-butyl (piperidin-4-ylmethyl)carbamate
REF 35	(4-(azetidin-3-yl)piperidin-1-yl)(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone hydrochloride		533.2	Intermediate 7 and tert-butyl 3-(piperidin-4-yl)azetidine-1-carboxylate

REF 36	N-(2-(2-aminoethoxy)ethyl)-4-((3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		515.1	Intermediate 12 and tert-butyl (2-(2-aminoethoxy)ethyl)carbamate
25	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(5-morpholinopentyl)benzamide		565.2	Intermediate 7 and 5-morpholinopentan-1-amine
REF 37	N-(2-(2-amino-2-oxoethoxy)ethyl)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		511.4	Intermediate 7 and 2-(2-aminoethoxy)acetamide
REF 38	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(2-(2-(methylamino)-2-		525.4	Intermediate 7 and 2-(2-aminoethoxy)-N-methylacetamide

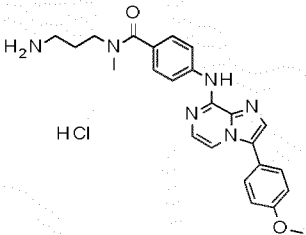
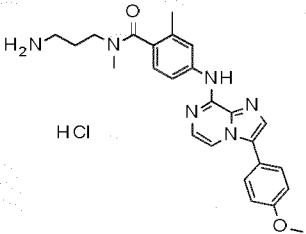
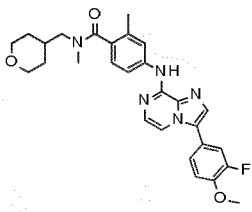
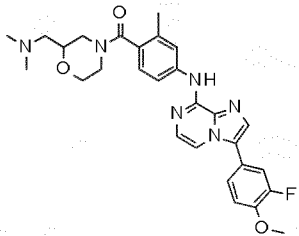
	oxoethoxy)ethyl)benzamide			
REF 39	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(2-(2-(2,4-dioxooxazolidin-3-yl)ethoxy)ethyl)-2-methylbenzamide		581.4	Intermediate 7 and 3-(2-(2-aminoethoxy)ethyl)oxazolidine-2,4-dione
26	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)methyl)-N,2-dimethylbenzamide		422 [M-H] ⁻	Intermediate 7 and methylamine hydrochloride
27	4-((3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamide		422.3	Intermediate 14 and methylamine (2M in THF)

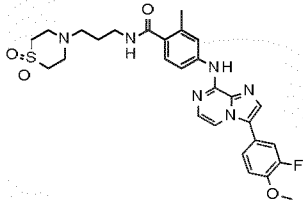
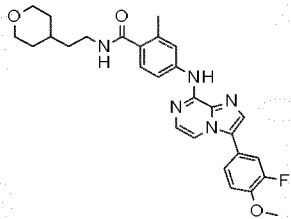
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REF 40	4-((3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl(morpholino)methanone		478.2	Intermediate 14 and morpholine
28	4-((3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(2-(dimethylamino)ethyl)-N-methylbenzamide		479.7	Intermediate 16 and N1,N1,N2-trimethylethane-1,2-diamine
29	N-(2-aminoethyl)-4-[[3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;hydrochloride		435.3	Intermediate 16 and tert-butyl (2-aminoethyl)carbamate
REF 41	4-[[3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(methylamino)ethyl]benzamide;hydrochloride		449.3	Intermediate 16 and tert-butyl (2-aminoethyl)(methyl)carbamate

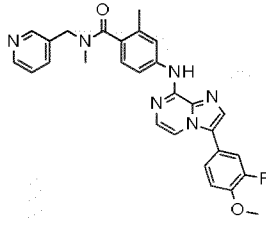
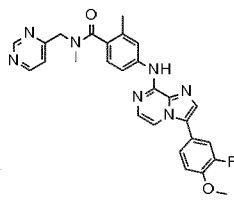
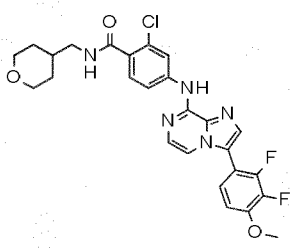
30	4-((3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(2-(piperazin-1-yl)ethyl)benzamide hydrochloride		506.2	Intermediate 16 and tert-butyl 4-(2-aminoethyl)piperazine-1-carboxylate
REF 42	(4-((3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(4-methylpiperazin-1-yl)methanone		389.4 [M-H] ⁻	Intermediate 14 and 1-methylpiperazine
31	N-(2-aminoethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		417.2	Intermediate 4 and tert-butyl (2-aminoethyl)carbamate
32	N-(2-aminoethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamide		431.2	Intermediate 4 and tert-butyl (2-(methylamino)ethyl)carbamate

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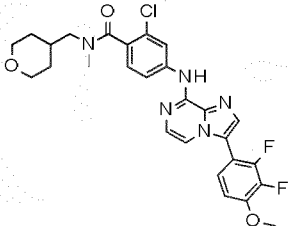
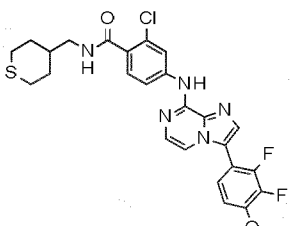
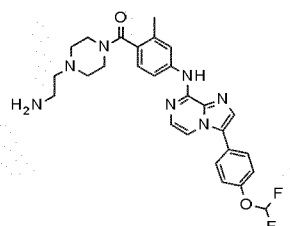
33	N-(3-aminopropyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methylbenzamide hydrochloride		431.2	Intermediate 17 and tert-butyl (3-(methylamino)propyl)carbamate hydrochloride
34	N-(3-aminopropyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamide hydrochloride		445.2	Intermediate 4 and tert-butyl (3-(methylamino)propyl)carbamate hydrochloride
35	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(tetrahydropyran-4-ylmethyl)benzamide ;2,2,2-trifluoroacetic acid		504.1	Intermediate 6 and N-methyl-1-(tetrahydro-2H-pyran-4-yl)methanamine
REF 43	[2-[(dimethylamino)methyl]morpholin-4-yl]-[4-[[3-(3-fluoro-4-methoxy-		519.1	Intermediate 6 and N,N-dimethyl-1-(morpholin-2-yl)methanamine

	phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone ;2,2,2-trifluoroacetic acid			
36	N-[3-(1,1-dioxo-1,4-thiazinan-4-yl)propyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;2,2,2-trifluoroacetic acid		567.2	Intermediate 6 and 4-(3-aminopropyl)thiomorpholine 1,1-dioxide
37	4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-tetrahydropyran-4-ylethyl)benzamide;2,2,2-trifluoroacetic acid		504.2	Intermediate 6 and 2-(tetrahydro-2H-pyran-4-yl)ethanamine

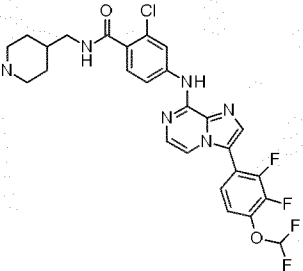
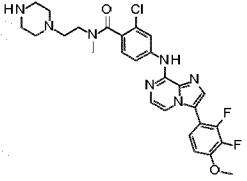
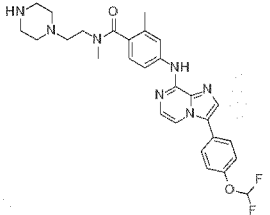
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38	4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-pyridylmethyl)benzamide		497.3	Intermediate 6 and N-methyl-N-(3-pyridylmethyl)amine
39	4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(pyrimidin-4-ylmethyl)benzamide		498.0	Intermediate 6 and N-methyl-1-pyrimidin-4-yl-methanamine
40	2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(tetrahydropyran-4-ylmethyl)benzamide; 2,2,2-trifluoroacetic acid		528.1	Intermediate 20 and (tetrahydro-2H-pyran-4-yl)methanamine

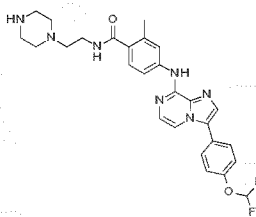
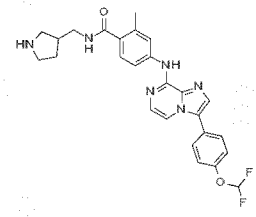
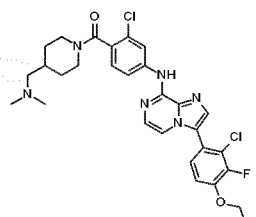
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41	2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(tetrahydropyran-4-ylmethyl)benzamide; 2,2,2-trifluoroacetic acid		542.1	Intermediate 20 and N-methyl-1-(tetrahydro-2H-pyran-4-yl)methanamine
42	2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(tetrahydrothiopyran-4-ylmethyl)benzamide		544.2	Intermediate 20 and (tetrahydro-2H-thiopyran-4-yl)methanamine
REF 44	[4-(2-aminoethyl)piperazin-1-yl]-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]methanone		522.2	Intermediate 7 and 2-(piperazin-1-yl)ethanamine

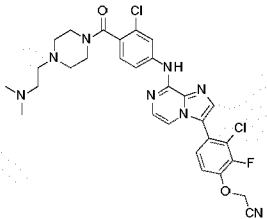
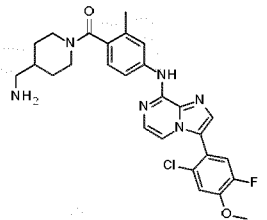
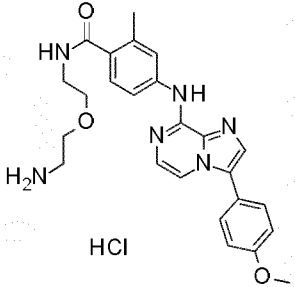
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43	2-chloro-4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-piperidylmethyl)benzamide; 2,2,2-trifluoroacetic acid		563.1	Intermediate 22 and piperidin-4-ylmethanamine
44	2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)benzamide; 2,2,2-trifluoroacetic acid		556.2	Intermediate 20 and tert-butyl 4-(2-(methylamino)ethyl)piperazine-1-carboxylate
45	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-piperazin-1-ylethyl)benzamide		536.3	Intermediate 7 and tert-butyl 4-(2-(methylamino)ethyl)piperazine-1-carboxylate

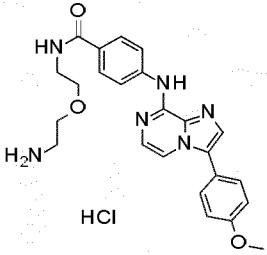
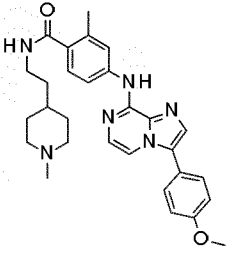
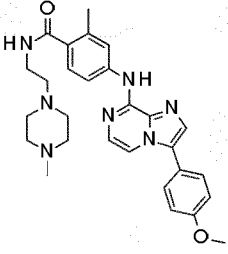
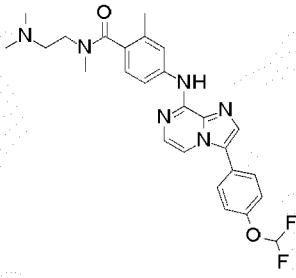
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46	tert-butyl 4-[2-[[4- [[3-[4- (difluoromethoxy)ph enyl]imidazo[1,2- a]pyrazin-8- yl]amino]-2-methyl- benzoyl]amino]ethyl]piperazine-1- carboxylate		522.2	Intermediate 7 and tert-butyl 4-(2- aminoethyl)piperazin e-1-carboxylate
47	tert-butyl 3-[[[4-[[3- [4- (difluoromethoxy)ph enyl]imidazo[1,2- a]pyrazin-8- yl]amino]-2-methyl- benzoyl]amino]meth yl]pyrrolidine-1- carboxylate		492.3	Intermediate 7 and tert-butyl 3- (aminomethyl)pyrroli dine-1-carboxylate
REF 45	2-[3-chloro-4-[8-[3- chloro-4-[4- [(dimethylamino)me thyl]piperidine-1- carbonyl]anilino]imi dazo[1,2-a]pyrazin- 3-yl]-2-fluoro- phenoxy] acetonitrile; formic acid		596.2	Intermediate 80 and N,N-dimethyl-1-(4- piperidyl) methanamine

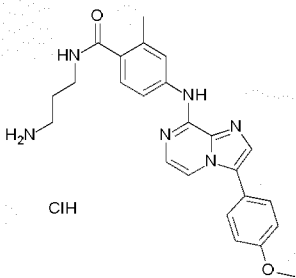
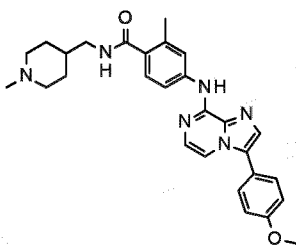
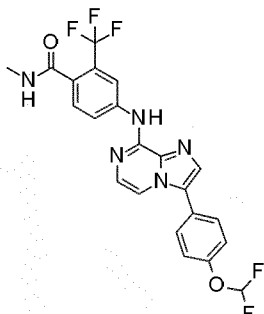
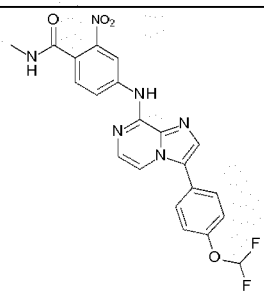
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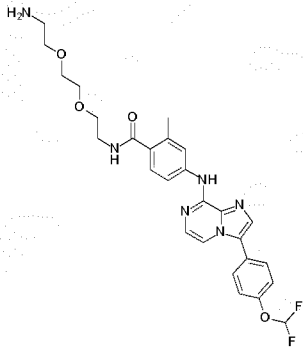
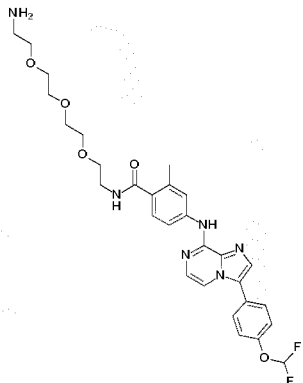
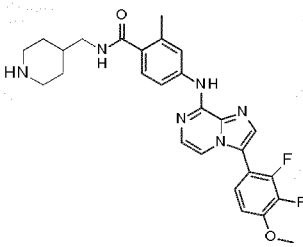
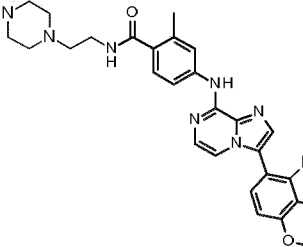
REF 46	2-[3-chloro-4-[8-[3-chloro-4-[4-[2-(dimethylamino)ethyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2-fluorophenoxy]acetonitrile		611.2	Intermediate 80 and 1-(2-dimethylaminoethyl) piperazine
REF 47	[4-(aminomethyl)-1-piperidyl]-[4-[[3-(2-chloro-5-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]methanone hydrochloride		523.2	Intermediate 26 and 4-(tert-butoxy carbonyl aminomethyl) piperidine
REF 48	N-(2-(2-aminoethoxy)ethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride		461.2	Intermediate 4 and tert-butyl (2-(2-aminoethoxy)ethyl)ca rbamate

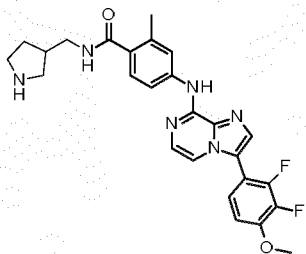
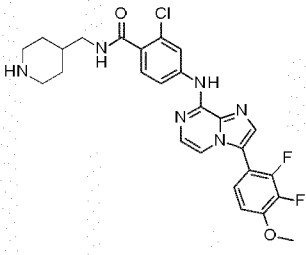
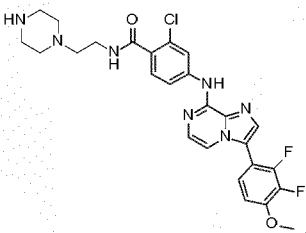
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REF 49	N-(2-(2-aminoethoxy)ethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide hydrochloride		447.2	Intermediate 17 and tert-butyl (2-(2-aminoethoxy)ethyl)carbamate
48	4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)methyl)-2-methyl-N-(2-(1-methylpiperidin-4-yl)ethyl)benzamide		497 [M-H] ⁻	Intermediate 4 and 2-(1-methylpiperidin-4-yl)ethanamine
49	4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)methyl)-2-methyl-N-(2-(4-methylpiperazin-1-yl)ethyl)benzamide		500	Intermediate 4 and 2-(4-methylpiperazin-1-yl)ethanamine hydrochloride
50	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(2-(dimethylamino)ethyl)-N,2-dimethylbenzamide		495	Intermediate 7 and N1,N1,N2-trimethylethane-1,2-diamine

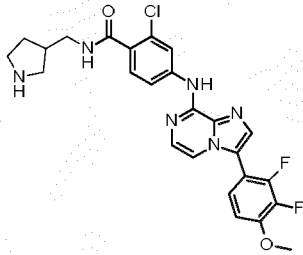
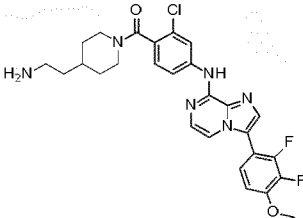
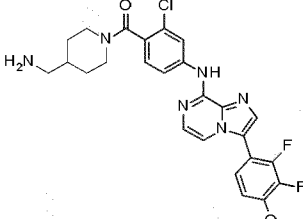
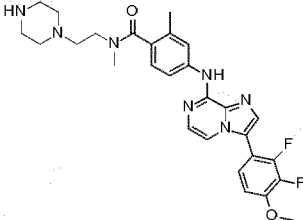
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51	N-(3-aminopropyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride		431	Intermediate 4 and tert-butyl (3-aminopropyl)carbamate
52	4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(1-methylpiperidin-4-yl)methyl]benzamide		483.3 [M-H] ⁻	Intermediate 4 and N,1-dimethylpiperidin-4-amine
53	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methyl-2-(trifluoromethyl)benzamide		448.3	Intermediate 18 and methanamine hydrochloride
54	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methyl-2-nitrobenzamide		455.3	Intermediate 19 and methanamine hydrochloride

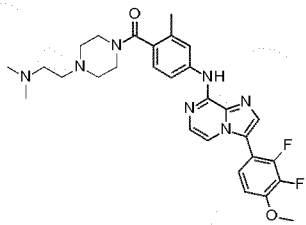
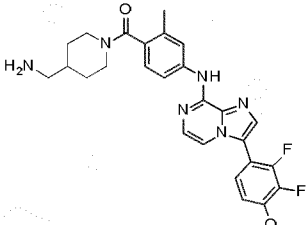
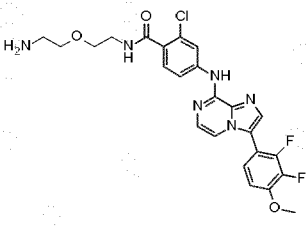
REF 50	N-(2-(2-(2-aminoethoxy)ethoxy)ethyl)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		539.5 [M-H] ⁻	Intermediate 7 and tert-butyl (2-(2-(2-aminoethoxy)ethoxy)ethyl)carbamate
REF 51	N-(2-(2-(2-(2-aminoethoxy)ethoxy)ethoxy)ethyl)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		583.5 [M-H] ⁻	Intermediate 7 and tert-butyl (2-(2-(2-(2-aminoethoxy)ethoxy)ethoxy)ethyl)carbamate
55	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-piperidylmethyl)benzamide		507.2	Intermediate 28 and tetrahydropyridyl tert-butyl 4-(aminomethyl)piperidine-1-carboxylate
56	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(2-(piperazin-1-		522.2	Intermediate 28 and 2-(piperazin-1-yl)ethanamine

	yl)ethyl)benzamide hydrochloride			
57	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(pyrrolidin-3-ylmethyl)benzamide		493.2	Intermediate 28 and tert-butyl 3-(aminomethyl)pyrrolidine-1-carboxylate
58	2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-piperidylmethyl)benzamide		527.1	Intermediate 20 and tert-butyl 4-(aminomethyl)piperidine-1-carboxylate
59	2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)benzamide		542.1	Intermediate 20 and tert-butyl 4-(2-aminoethyl)piperazine-1-carboxylate

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60	2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(pyrrolidin-3-ylmethyl)benzamide		513.1	Intermediate 20 and tert-butyl 3-(aminomethyl)pyrrolidine-1-carboxylate
REF 52	(4-(2-aminoethyl)piperidin-1-yl)(2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)methanone		541.1	Intermediate 20 and tert-butyl (2-(piperidin-4-yl)ethyl)carbamate
REF 53	(4-(aminomethyl)piperidin-1-yl)(2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)methanone		527.1	Intermediate 20 and piperidin-4-ylmethanamine
61	4-(((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethyl-N-(2-		536.2	Intermediate 28 and tert-butyl 4-(2-(methylamino)ethyl)piperazine-1-carboxylate

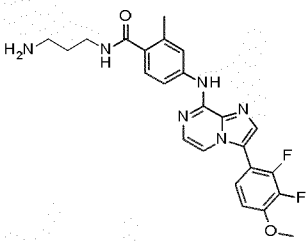
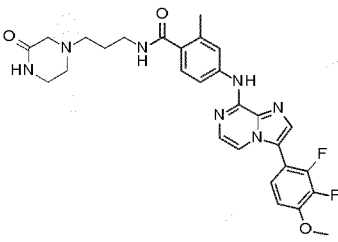
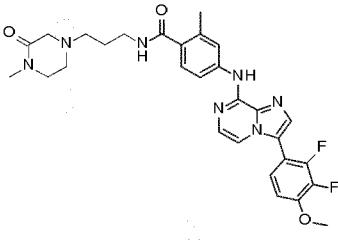
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	(piperazin-1-yl)ethyl)benzamide			
REF 54	(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(4-(2-(dimethylamino)ethyl)piperazin-1-yl)methanone		550.2	Intermediate 28 and N,N-dimethyl-2-(piperazin-1-yl)ethanamine
REF 55	(4-(aminomethyl)piperidin-1-yl)(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone		507.2	Intermediate 28 and piperidin-4-ylmethanamine
REF 56	N-(2-(2-aminoethoxy)ethyl)-2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide		517.1	Intermediate 20 and piperidin-4-ylmethanamine

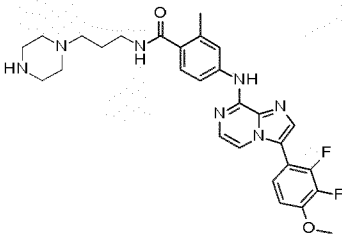
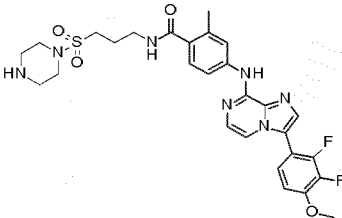
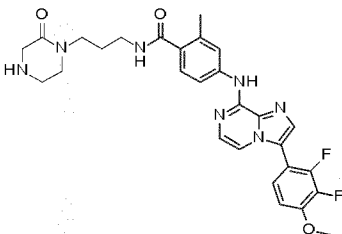
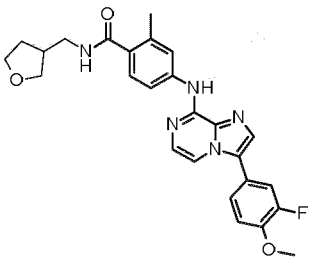
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REF 57	(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(4-((dimethylamino)methyl)piperidin-1-yl)methanone		535.2	Intermediate 28 and N,N-Dimethyl-1-(piperidin-4-yl)methanamine dihydrochloride
62	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-((1-methylpiperidin-4-yl)methyl)benzamide		521.2	Intermediate 28 and (1-methylpiperidin-4-yl)methanamine
REF 58	aziridin-1-yl(2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)methanone		456.0	Intermediate 20 and 2-chloroethanamine hydrochloride
63	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethyl-N-(2-		535.2	Intermediate 28 and tert-butyl 4-[2-(methylamino)ethyl]piperidine-1-carboxylate

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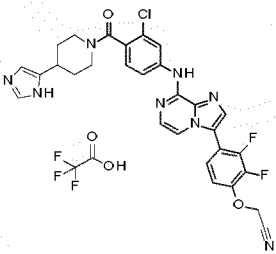
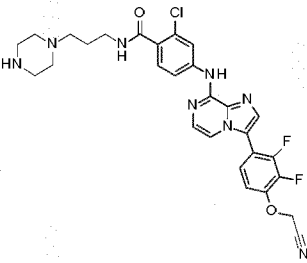
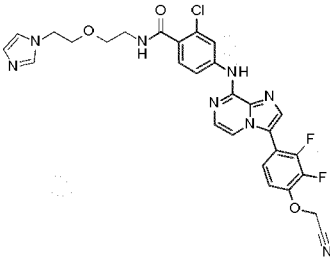
	(piperidin-4-yl)ethyl)benzamide			
64	N-(3-aminopropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		467.1	Intermediate 28 and tert-butyl (3-aminopropyl)carbamate
65	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(3-(3-oxopiperazin-1-yl)propyl)benzamide		550.2	Intermediate 28 and Intermediate 57-P1
66	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(3-(4-methyl-3-oxopiperazin-1-yl)propyl)benzamide		564.2	Intermediate 28 and Intermediate 58

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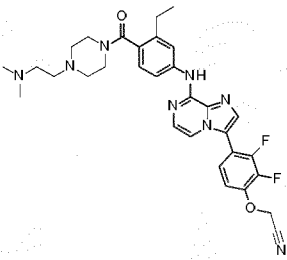
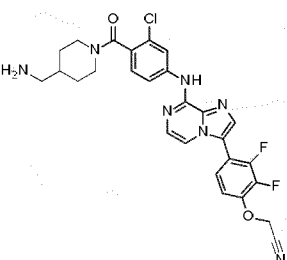
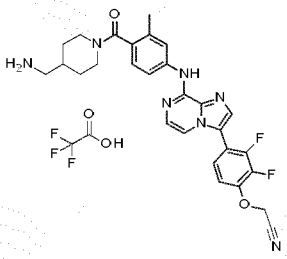
67	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(3-(piperazin-1-yl)propyl)benzamide		536.2	Intermediate 28 and tert-butyl 4-(3-aminopropyl)piperazine-1-carboxylate
68	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(3-(piperazin-1-ylsulfonyl)propyl)benzamide		600.2	Intermediate 28 and tert-butyl 4-((3-aminopropyl)sulfonyl)piperazine-1-carboxylate
69	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(3-(2-oxopiperazin-1-yl)propyl)benzamide		550.2	Intermediate 28 and Intermediate 59
70	4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-((tetrahydrofuran-3-yl)methanamine		476.2	Intermediate 6 and (tetrahydrofuran-3-yl)methanamine

	yl)methyl)benzamide			
71	4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethyl-N-((tetrahydrofuran-3-yl)methyl)benzamide		490.2	Intermediate 6 and N-methyl-1-(tetrahydrofuran-3-yl)methanamine
72	4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-((tetrahydro-2H-pyran-3-yl)methyl)benzamide		490.2	Intermediate 6 and (tetrahydrofuran-3-yl)methanamine
73	4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethyl-N-(pyridin-4-yl)methyl)benzamide		497.2	Intermediate 6 and N-methyl-1-(pyridin-4-yl)methanamine

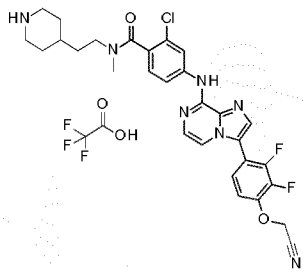
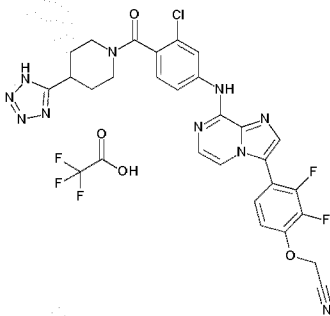
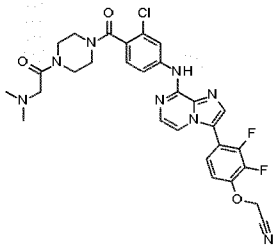
REF 59	2-(4-(8-((3-chloro-4-(4-(2-(dimethylamino)ethyl)piperazine-1-carbonyl)phenyl)amino)imidazo[1,2-a]pyrazin-3-yl)-2,3-difluorophenoxy)acetonitrile		595.2	Intermediate 29 and N,N-dimethyl-2-(piperazin-1-yl)ethanamine
74	2-chloro-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methyl-N-(2-(piperazin-1-yl)ethyl)benzamide		581.2	Intermediate 29 and tert-butyl 4-(2-(methylamino)ethyl)piperazine-1-carboxylate
75	2-chloro-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(2-(pyridin-4-yl)ethyl)benzamide		560.1	Intermediate 29 and 2-(pyridin-4-yl)ethanamine
76	2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-(4-pyridyl)propyl]benza		574.1	Intermediate 29 and 3-(pyridin-4-yl)propan-1-amine

	mide;2,2,2-trifluoroacetic acid			
REF 60	2-[4-[8-[3-chloro-4-[4-(1H-imidazol-5-yl)piperidine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile;2,2,2-trifluoroacetic acid		589.1	Intermediate 29 and 4-(1H-imidazol-5-yl)piperidine
77	2-chloro-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(3-(piperazin-1-yl)propyl)benzamide		581.1	Intermediate 29 and tert-butyl 4-(3-aminopropyl)piperazine-1-carboxylate
REF 61	N-(2-(2-(1H-imidazol-1-yl)ethoxy)ethyl)-2-chloro-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide		593.1	Intermediate 29 and 61

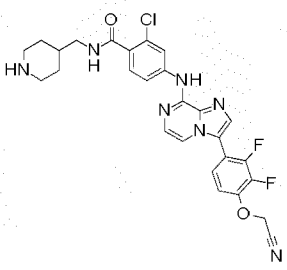
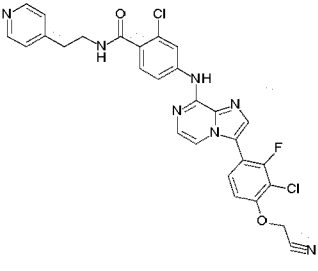
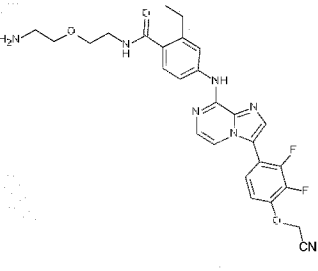
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REF 62	2-(4-(8-((4-(4-(2-(dimethylamino)ethyl)piperazine-1-carbonyl)-3-ethylphenyl)amino)imidazo[1,2-a]pyrazin-3-yl)-2,3-difluorophenoxy)acetonitrile		589.2	Intermediate 32 and N,N-dimethyl-2-(piperazin-1-yl)ethanamine
REF 63	2-(4-(8-((4-(4-(aminomethyl)piperidine-1-carbonyl)-3-chlorophenyl)amino)imidazo[1,2-a]pyrazin-3-yl)-2,3-difluorophenoxy)acetonitrile		552.1	Intermediate 29 and tert-butyl (piperidin-4-ylmethyl)carbamate
REF 64	2-[4-[8-[4-[4-(aminomethyl)piperidine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile; 2,2,2-trifluoroacetic acid		532.2	Intermediate 31 and tert-butyl (piperidin-4-ylmethyl)carbamate

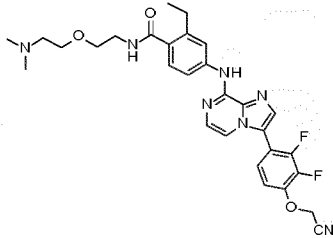
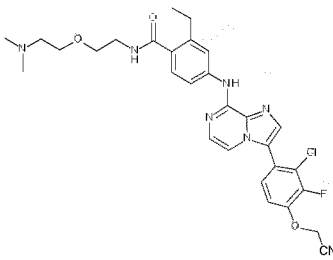
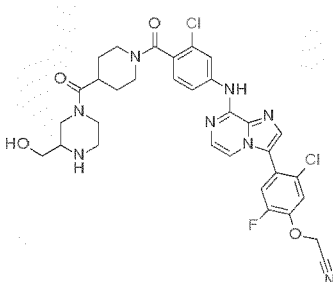
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78	2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-[2-(4-piperidyl)ethyl]benzamide; 2,2,2-trifluoroacetic acid		580.1	Intermediate 29 and tert-butyl 4-(2-(methylamino)ethyl)piperidine-1-carboxylate
REF 65	2-[4-[8-[3-chloro-4-[4-(1H-tetrazol-5-yl)piperidine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile; 2,2,2-trifluoroacetic acid		591.1	Intermediate 29 and 4-(2H-tetrazol-5-yl)piperidine hydrochloride
REF 66	2-[4-[8-[3-chloro-4-[4-[2-(dimethylamino)acetyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile; 2,2,2-trifluoroacetic acid		609.2	Intermediate 29 and intermediate 56

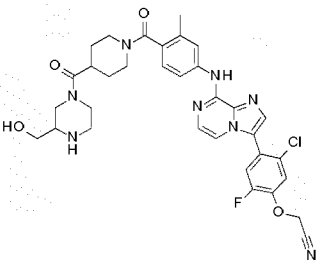
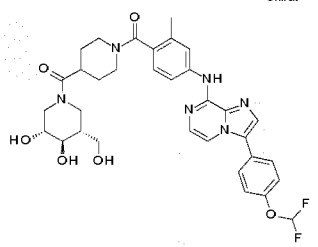
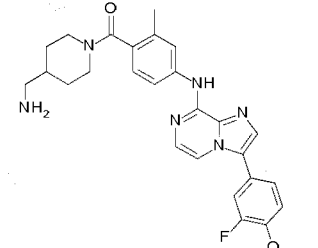
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79	2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-piperidylmethyl)benzamide		552.1	Intermediate 29 and 4-piperidyl methanamine
80	2-chloro-4-[[3-[3-chloro-4-(cyanomethoxy)-2-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(4-pyridyl)ethyl]benzamide		576.2	Intermediate 35 and 2-(pyridin-4-yl)ethanamine
REF 67	N-[2-(2-aminoethoxy)ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide; 2,2,2-trifluoroacetic acid		536.2	Intermediate 32 and N-BOC-2-(2-amino-ethoxy)-ethylamine

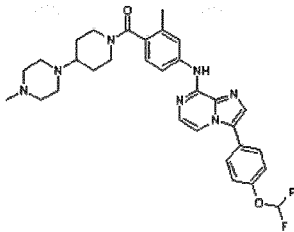
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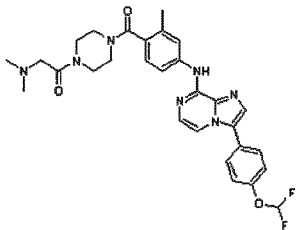
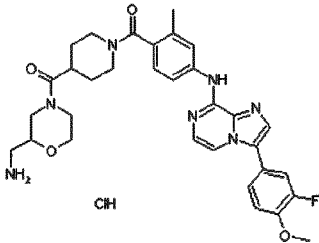
REF 68	4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[2-(dimethylamino)ethoxy]ethyl]-2-ethylbenzamide		564.2	Intermediate 32 and 2-[2-(dimethylamino)ethoxy]ethanamine
REF 69	4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[2-(dimethylamino)ethoxy]ethyl]-2-ethylbenzamide		580.2	Intermediate 40 and 2-[2-(dimethylamino)ethoxy]ethanamine
REF 70	2-[5-chloro-4-[8-[3-chloro-4-[4-[3-(hydroxymethyl)piperazine-1-carbonyl]piperidine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2-fluorophenoxy]acetonitrile ; 2,2,2-trifluoroacetic		681.1	Intermediate 37 and 81

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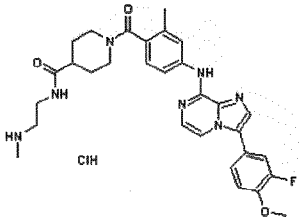
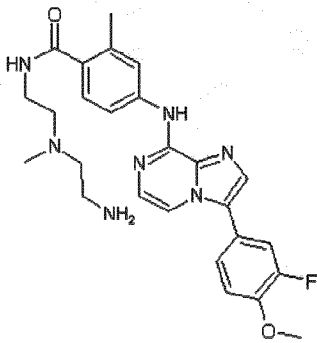
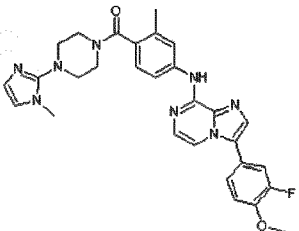
REF 71	2-[5-chloro-2-fluoro-4-[8-[4-[4-[3-(hydroxymethyl)piperazine-1-carbonyl]piperidine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile; 2,2,2-trifluoroacetic acid		661.3	Intermediate 39 and 81
REF 72	(1-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)((3R,4R,5R)-3,4-dihydroxy-5-(hydroxymethyl)piperidin-1-yl)methanone		651.5	Intermediate 7 and (3R,4R,5R)-5-(hydroxymethyl)piperidine-3,4-diol hydrochloride
REF 73	(4-(aminomethyl)piperidin-1-yl)(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-		489.2	Intermediate 6 and tert-butyl (piperidin-4-ylmethyl)carbamate

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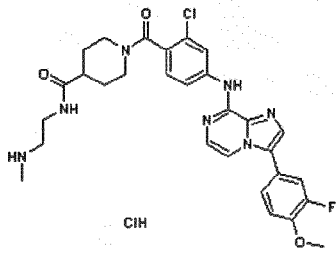
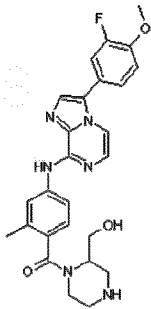
	yl)amino)-2-methylphenyl)methanone hydrochloride			
REF 74	(4-(2-(dimethylamino)ethyl)piperazin-1-yl)(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone		532.6	Intermediate 6 and N,N-dimethyl-2-(piperazin-1-yl)ethanamine
REF 75	(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(4-(4-methylpiperazin-1-yl)piperidin-1-yl)methanone		576.2	Intermediate 7 and 1-methyl-4-(piperidin-4-yl)piperazine
REF 76	2-amino-1-(4-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piper		536.2	Intermediate 7 and tert-butyl (2-oxo-2-(piperazin-1-yl)ethyl)carbamate

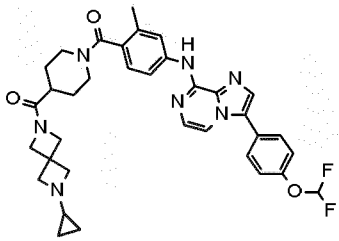
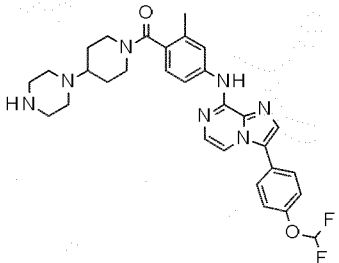
	azin-1-yl)ethanone hydrochloride			
REF 77	1-(4-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)-2-(dimethylamino)ethanone		564.1	Intermediate 7 and 2-(dimethylamino)-1-(piperazin-1-yl)ethanone dihydrochloride
REF 78	(4-(2-(aminomethyl)morpholine-4-carbonyl)piperidin-1-yl)(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone hydrochloride		602.3	Intermediate 6 and tert-butyl (morpholin-2-ylmethyl)carbamate

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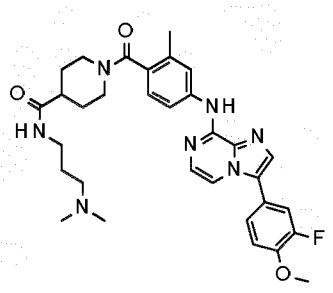
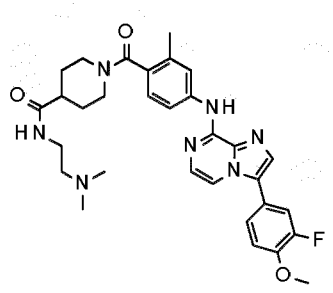
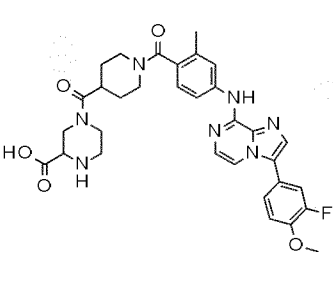
REF 79	1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-(2-(methylamino)ethyl)piperidine-4-carboxamide hydrochloride		560.3	Intermediate 6 and tert-butyl (2-aminoethyl)(methyl)carbamate
REF 80	N-(2-((2-aminoethyl)(methylamino)ethyl)-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		492.3	Intermediate 6 and N1-(2-aminoethyl)-N1-methylethane-1,2-diamine
REF 81	(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(4-(1-methyl-1H-imidazol-2-yl)piperazin-1-yl)methanone		541.3	Intermediate 6 and 1-(1-methyl-1H-imidazol-2-yl)piperazine

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REF 82	1-(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)-N-(2-(methylamino)ethyl)piperidine-4-carboxamide hydrochloride		580.2	Intermediate 2 and tert-butyl (2-aminoethyl)(methyl)carbamate
REF 83	(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(2-(hydroxymethyl)piperazine-1-yl)methanone		489.4	Intermediate 6 and tert-butyl 2-(hydroxymethyl)piperazine-1-carboxylate
REF 84	(4-(2-(aminomethyl)morpholine-4-carbonyl)piperidin-1-yl)(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone hydrochloride		678.7	Reference Example 1 and tert-butyl (2-aminoethyl)(methyl)carbamate

REF 85	(4-(6-cyclopropyl-2,6-diazaspiro[3.3]heptane-2-carbonyl)piperidin-1-yl)(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone		642.5	Reference Example 1 and 2-cyclopropyl-2,6-diazaspiro[3.3]heptane
REF 86	(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(4-(piperazin-1-yl)piperidin-1-yl)methanone hydrochloride		562.3	Intermediate 7 and tert-butyl 4-(piperidin-4-yl)piperazine-1-carboxylate

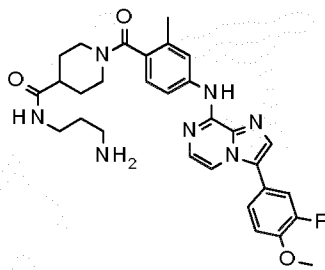
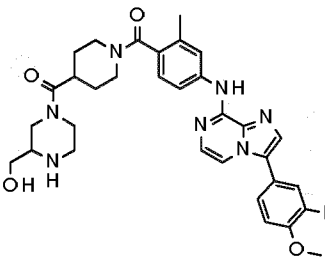
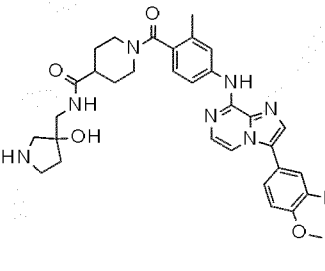
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REF 87	N-[3-(dimethylamino)propyl]-1-[4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperidine-4-carboxamide		588.3	Reference Example 2 and N1,N1-dimethylpropane-1,3-diamine
REF 88	N-[2-(dimethylamino)ethyl]-1-[4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperidine-4-carboxamide		574.7	Reference Example 2 and N1,N1-dimethylethane-1,2-diamine
REF 89	4-[1-[4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperidine-4-carbonyl]piperazine-2-carboxylic acid;hydrochloride		616.3	Reference Example 2 and 1-tert-butyl 2-methyl piperazine-1,2-dicarboxylate, the intermediate ester was hydrolyzed with LiOH in THF/MeOH/H2O as described previously

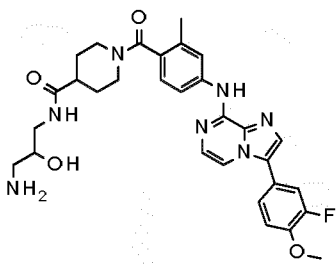
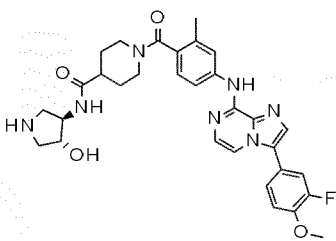
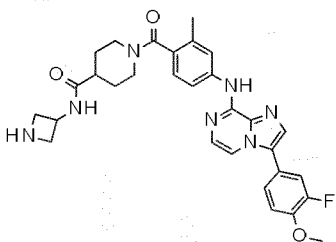
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REF 90	1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-(3-(methylamino)propyl)piperidine-4-carboxamide hydrochloride		574.4	Reference Example 2 and tert-butyl (3-aminopropyl)(methyl)carbamate
REF 91	(R)-(1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)(3-(methylamino)pyrrolidin-1-yl)methanone hydrochloride		586.4	Reference Example 2 and (R)-tert-butyl methyl(pyrrolidin-3-yl)carbamate
REF 92	1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-(4-(methylamino)butyl)piperidine-4-carboxamide hydrochloride		588.5	Reference Example 2 and tert-butyl (4-aminobutyl)(methyl)carbamate

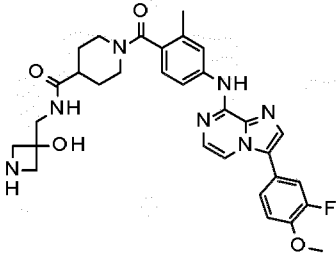
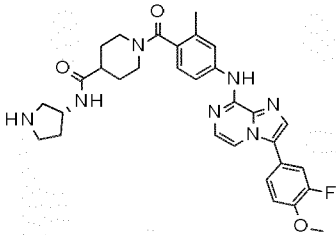
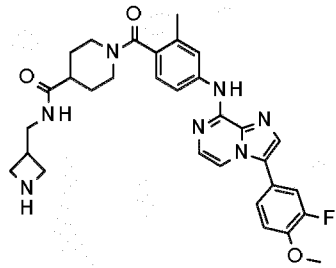
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REF 93	N-(3-aminopropyl)-1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamide hydrochloride		560.4	Reference Example 2 and tert-butyl (3-aminopropyl)carbamate
REF 94	(1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)(3-(hydroxymethyl)piperazine-1-yl)methanone 2,2,2-trifluoroacetate		602.4	Reference Example 2 and tert-butyl 2-(hydroxymethyl)piperazine-1-carboxylate
REF 95	1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-((3-(hydroxypyrrolidin-3-yl)methyl)piperidine-4-carboxamide 2,2,2-trifluoroacetate		602.4	Reference Example 2 and tert-butyl 3-(aminomethyl)-3-hydroxypyrrolidine-1-carboxylate

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REF 96	N-(3-amino-2-hydroxypropyl)-1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamide 2,2,2-trifluoroacetate		576.3	Reference Example 2 and tert-butyl (3-amino-2-hydroxypropyl)carbamate
REF 97	1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-((3R,4R)-4-hydroxypyrrolidin-3-yl)piperidine-4-carboxamide 2,2,2-trifluoroacetate		588.3	Reference Example 2 and (3R,4R)-tert-butyl 3-amino-4-hydroxypyrrolidine-1-carboxylate
REF 98	N-(azetidin-3-yl)-1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamide 2,2,2-trifluoroacetate		558.3	Reference Example 2 and tert-butyl 3-aminoazetidine-1-carboxylate

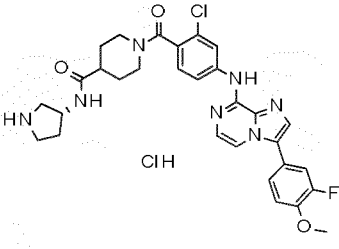
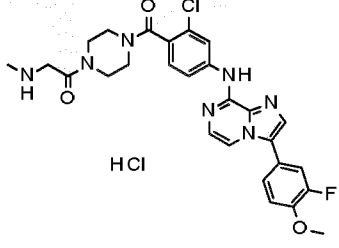
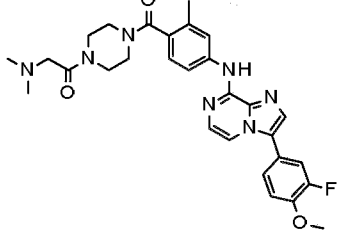
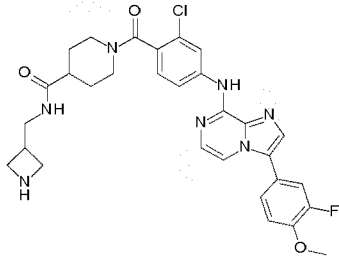
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REF 99	1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-((3-hydroxyazetidin-3-yl)methyl)piperidine-4-carboxamide 2,2,2-trifluoroacetate		588.3	Reference Example 2 and tert-butyl 3-(aminomethyl)-3-hydroxyazetidine-1-carboxylate
REF 100	(R)-1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-(pyrrolidin-3-yl)piperidine-4-carboxamide 2,2,2-trifluoroacetate		572.3	Reference Example 2 and (R)-tert-butyl 3-aminopyrrolidine-1-carboxylate
REF 101	N-(azetidin-3-ylmethyl)-1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamide 2,2,2-trifluoroacetate		572.4	Reference Example 2 and tert-butyl 3-(aminomethyl)azetidine-1-carboxylate

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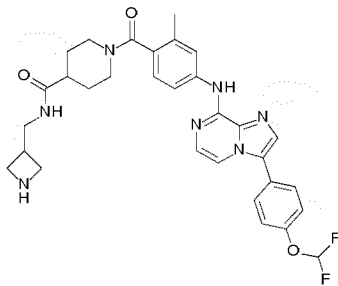
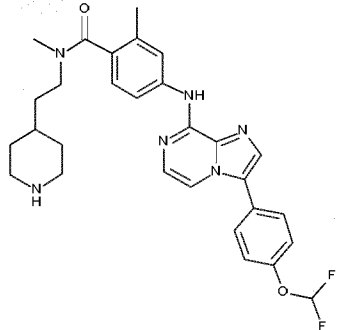
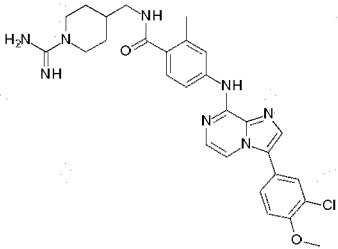
REF 102	N-(2-(azetidin-1-yl)ethyl)-1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamide		586.3	Reference Example 2 and 2-(azetidin-1-yl)ethanamine
REF 103	N-(3-(azetidin-1-yl)propyl)-1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamide		600.3	Reference Example 2 and 3-(azetidin-1-yl)propan-1-amine
REF 104	(R)-1-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-(pyrrolidin-3-yl)piperidine-4-carboxamide hydrochloride		590.3	Intermediate 65 and tert-butyl (R)-3-aminopyrrolidine-1-carboxylate

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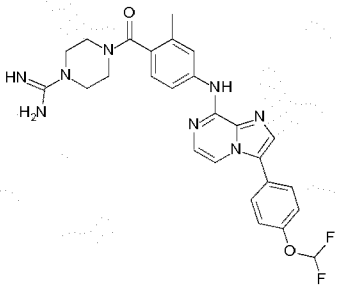
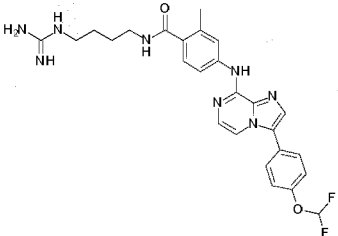
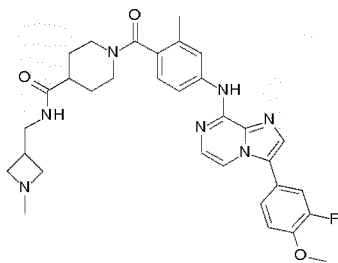
REF 105	(R)-1-(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)-N-(pyrrolidin-3-yl)piperidine-4-carboxamide hydrochloride	 ClH	593.3	Intermediate 66 and tert-butyl (R)-3-aminopyrrolidine-1-carboxylate
REF 106	1-(4-(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperazin-1-yl)-2-(methylamino)ethan-1-one hydrochloride	 HCl	553.3	Intermediate 2 and tert-butyl methyl(2-oxo-2-(piperazin-1-yl)ethyl)carbamate
REF 107	2-(dimethylamino)-1-(4-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)ethanone		546.3	Intermediate 6 and 2-(dimethylamino)-1-(piperazin-1-yl)ethanone dihydrochloride
REF 108	N-(azetidin-3-ylmethyl)-1-(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-		590.6 (M-H)	Intermediate 66 and tert-butyl 3-(aminomethyl)azetidine-1-carboxylate.

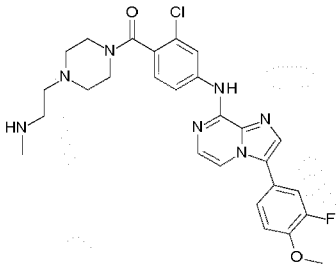
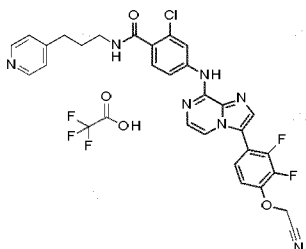
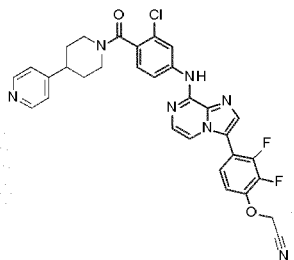
	yl)amino)benzoyl)piperidine-4-carboxamide			
REF 109	N-(azetidin-3-ylmethyl)-1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamide		572.5	Reference Example 2 and tert-butyl 3-(aminomethyl)azetidine-1-carboxylate.
REF 110	(S)-1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-(pyrrolidin-3-yl)piperidine-4-carboxamide hydrochloride		572.3	Reference Example 2 and tert-butyl (S)-3-aminopyrrolidine-1-carboxylate
REF 111	(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(4-(4,5-dihydro-1H-imidazol-2-		547.2	Intermediate 7 and 1-(4,5-dihydro-1H-imidazol-2-yl)piperazine hydroiodide (CAS 295341-59-2)

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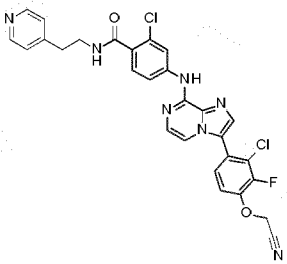
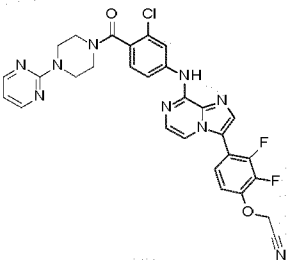
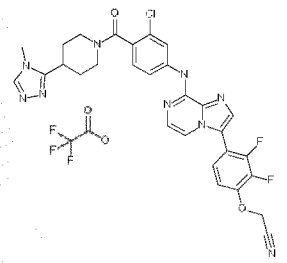
	yl)piperazin-1-yl)methanone			
REF 112	N-(azetidin-3-ylmethyl)-1-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamide		590.4	Reference Example 1 and tert-butyl 3-(aminomethyl)azetidine-1-carboxylate
81	4-[[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-piperidyl)ethyl]benzamide;hydrochloride		535.5	Intermediate 7 and tert-butyl 4-(2-(methylamino)ethyl)piperidine-1-carboxylate
82	N-((1-carbamimidoylpiperidin-4-yl)methyl)-4-((3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		547.4	Reference Example 2 and 4-(aminomethyl)piperidine-1-carboximidamide

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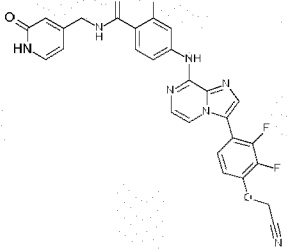
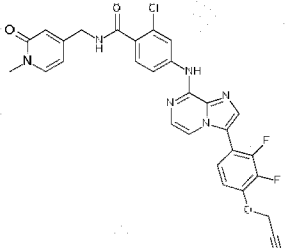
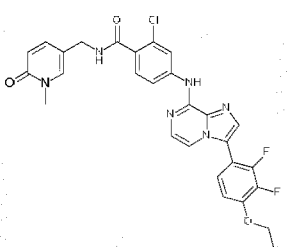
REF 113	4-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carboximidamide		521.2	Intermediate 7 and piperazine-1-carboximidamide
83	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(4-guanidinobutyl)-2-methylbenzamide		523.2	Intermediate 7 and 1-(4-aminobutyl)guanidine sulfate
REF 114	1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-((1-methylazetidin-3-yl)methyl)piperidine-4-carboxamide		586.3	Reference Example 2 and (1-methylazetidin-3-yl)methanamine

REF 115	(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)(4-(2-(methylamino)ethyl)piperazin-1-yl)methanone		538.2	Intermediate 2 and (9H-fluoren-9-yl)methyl methyl(2-(piperazin-1-yl)ethyl)carbamate hydrochloride. In situ deprotection with piperidine.
76	2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-(4-pyridyl)propyl]benzamide; 2,2,2-trifluoroacetic acid		574.1	Intermediate 29 and 3-(pyridin-4-yl)propan-1-amine
REF 116	2-[4-[8-[3-chloro-4-[4-(4-pyridyl)piperidine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile		600.1	Intermediate 29 and 4-(piperidin-4-yl)pyridine

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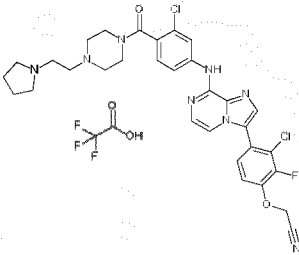
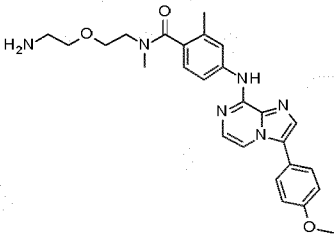
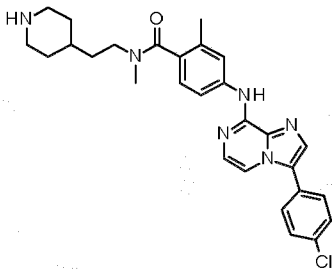
84	2-chloro-4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(4-pyridyl)ethyl]benzamide		576.1	Intermediate 24 and 2-(pyridin-4-yl)ethan-1-amine
REF 117	2-[4-[8-[3-chloro-4-(4-pyrimidin-2-yl)piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile		602.1	Intermediate 29 and 2-(piperazin-1-yl)pyrimidine hydrochloride
REF 118	2-[4-[8-[3-chloro-4-[4-(4-methyl-1,2,4-triazol-3-yl)piperidine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile; 2,2,2-trifluoroacetic acid		604.1	Intermediate 29 and 4-(4-methyl-4H-1,2,4-triazol-3-yl)piperidine hydrochloride

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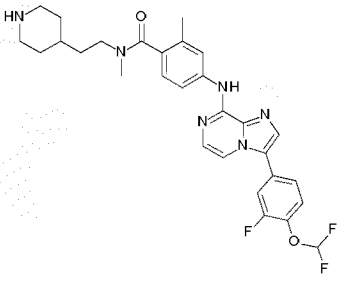
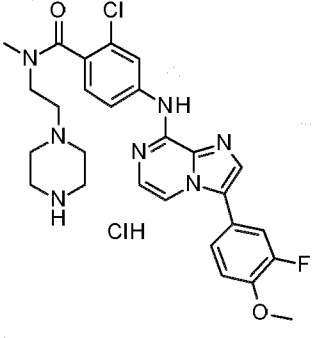
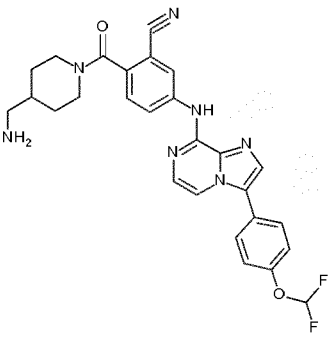
85	2-chloro-4-[[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(2-oxo-1H-pyridin-4-yl)methyl]benzamide		562.1	Intermediate 29 and 4-(aminomethyl)pyridin-2(1H)-one hydrochloride
86	2-chloro-4-[[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1-methyl-2-oxo-4-pyridyl)methyl]benzamide		576.1	Intermediate 29 and 4-(aminomethyl)-1-methylpyridin-2(1H)-one hydrochloride
87	2-chloro-4-[[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1-methyl-6-oxo-3-pyridyl)methyl]benzamide		576.1	Intermediate 29 and 5-(aminomethyl)-1-methylpyridin-2(1H)-one hydrochloride

REF 119	2-[4-[8-[3-chloro-4-[4-(1,2,4-triazol-4-yl)piperidine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile		590.1	Intermediate 29 and 4-(4H-1,2,4-triazol-4-yl)piperidine
REF 60	2-[4-[8-[3-chloro-4-[4-(1H-imidazol-4-yl)piperidine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile ;2,2,2-trifluoroacetic acid		589.1	Intermediate 29 and 4-cyclohexyl-1H-imidazole
REF 120	2-[3-chloro-4-[8-[3-chloro-4-[4-[2-(dimethylamino)ethylamino]piperidine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2-fluorophenoxy]acetonitrile ;2,2,2-trifluoroacetic acid		625.1	Intermediate 24 and N,N-dimethyl-3-(piperazin-1-yl)propan-1-amine

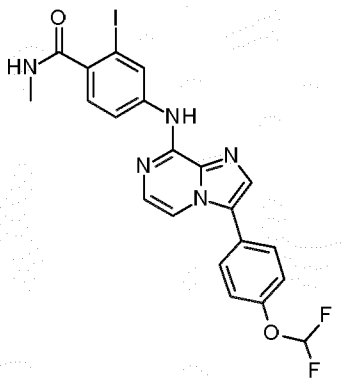
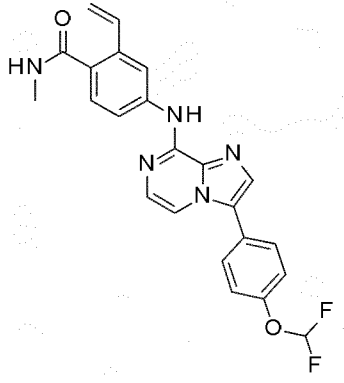
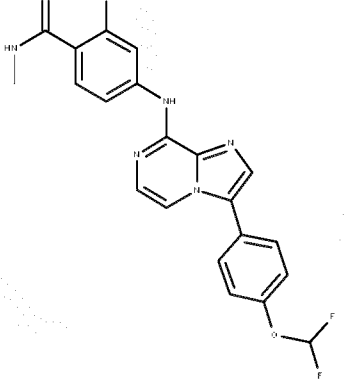
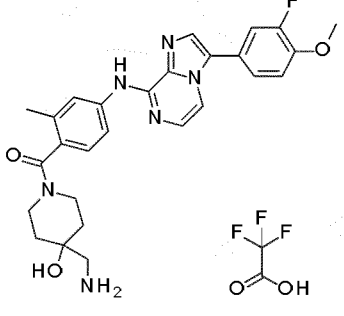
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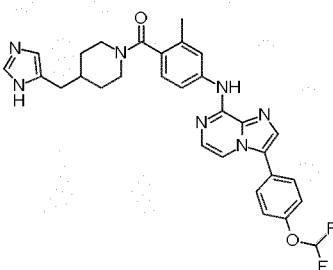
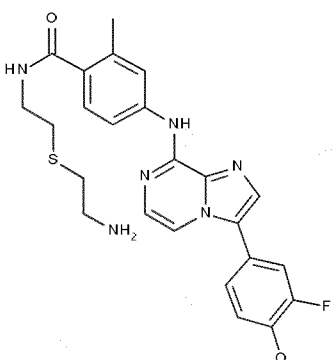
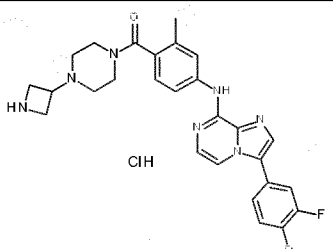
REF 121	2-[4-[8-[3-chloro-4-[4-(2-pyrrolidin-1-ylethyl)piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile; 2,2,2-trifluoroacetic acid		637.2	Intermediate 24 and 1-(2-(pyrrolidin-1-yl)ethyl)piperazine
REF 122	N-(2-(2-aminoethoxy)ethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamide hydrochloride		475.3	Intermediate 4 and tert-butyl (2-(2-(methylamino)ethoxy)ethyl)carbamate hydrochloride
88	4-((3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethyl-N-(2-(piperidin-4-yl)ethyl)benzamide hydrochloride		503.4	Intermediate 82 and tert-butyl 4-(2-(methylamino)ethyl)piperidine-1-carboxylate

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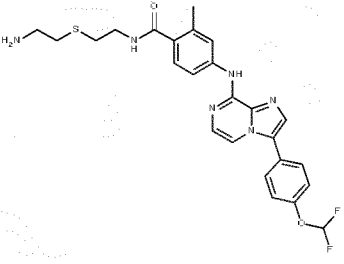
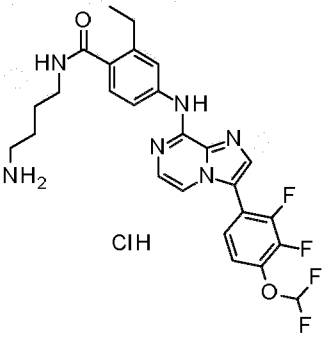
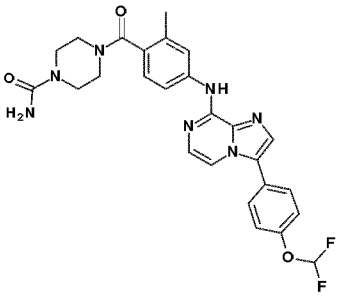
89	4-((3-(4-(difluoromethoxy)-3-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethyl-N-(2-(piperidin-4-yl)ethyl)benzamide hydrochloride		551.5(M-H)	Intermediate 43 tert-butyl 4-(2-(methylamino)ethyl)piperidine-1-carboxylate
90	2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methyl-N-(2-(piperazin-1-yl)ethyl)benzamide hydrochloride		539.7	Intermediate 2 and tert-butyl 4-(2-(methylamino)ethyl)piperazine-1-carboxylate
REF 123	2-(4-(aminomethyl)piperidine-1-carbonyl)-5-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzonitrile		518.2	Intermediate 45 and tert-butyl (piperidin-4-ylmethyl)carbamate (Deprotection with TFA)

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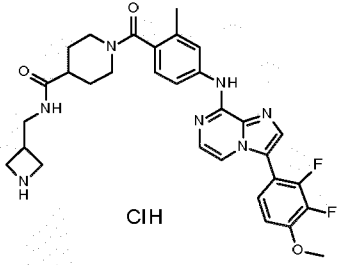
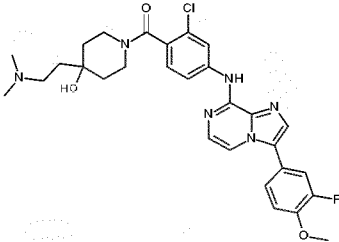
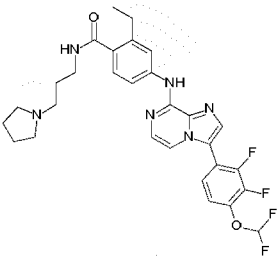
91	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-iodo-N-methylbenzamide		536	Intermediate 46 and methanamine hydrochloride
92	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methyl-2-vinylbenzamide		436.2	Intermediate 47 and methanamine hydrochloride
93	2-bromo-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methylbenzamide		488.1	Intermediate 10 and methanamine hydrochloride
REF 124	[4-(aminomethyl)-4-hydroxypiperidin-1-yl]-[4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-		505.3	Intermediate 6 and tert-butyl ((4-hydroxypiperidin-4-yl)methyl)carbamate

	methylphenyl]methane; 2,2,2-trifluoroacetic acid			
REF 125	(4-((1H-imidazol-4-yl)methyl)piperidin-1-yl)(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methane		558.1	Intermediate 7 and 4-((1H-imidazol-4-yl)methyl)piperidine dihydrobromide
REF 126	N-(2-((2-aminoethyl)thio)ethyl)-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		495.2	Intermediate 6 and 2,2'-thiodiethanamine
REF 127	(4-(azetidin-3-yl)piperazin-1-yl)(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-		516.3	Intermediate 6 and tert-butyl 3-(piperazin-1-yl)azetidine-1-carboxylate

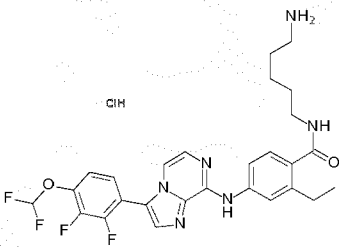
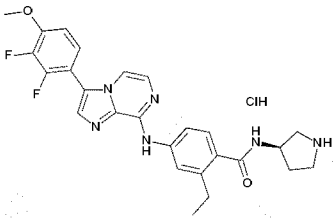
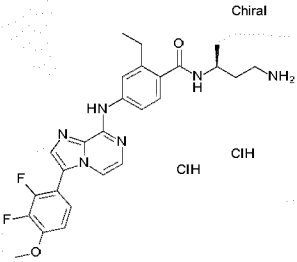
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	methylphenyl)methanone hydrochloride			
84	N-(2-((2-aminoethyl)thio)ethyl)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		513.3	Intermediate 7 and 2,2'-thiodiethanamine
94	N-(4-aminobutyl)-4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		531.3	Intermediate 85 and tert-butyl (4-aminobutyl)carbamate
REF 128	4-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carboxamide		522.2	Intermediate 7 and piperazine-1-carboximidamide

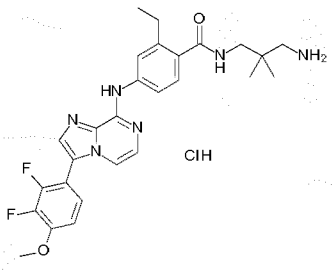
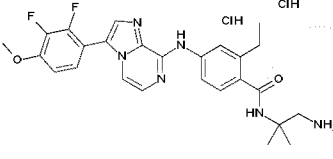
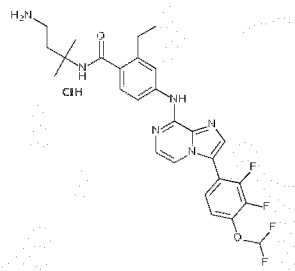
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REF 129	N-(azetidin-3-ylmethyl)-1-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamide hydrochloride	 ClH	590.3	Intermediate 65 and benzyl 3-(aminomethyl)azetidine-1-carboxylate
REF 130	(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)(4-(2-(dimethylamino)ethyl)-4-hydroxypiperidin-1-yl)methanone		567.2	Intermediate 2 and 4-(2-(dimethylamino)ethyl)piperidin-4-ol
95	4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(3-(pyrrolidin-1-yl)propyl)benzamide		571.4	Intermediate 85 and 3-(pyrrolidin-1-yl)propan-1-amine

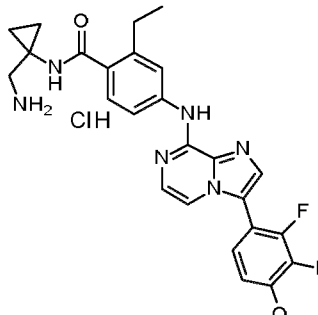
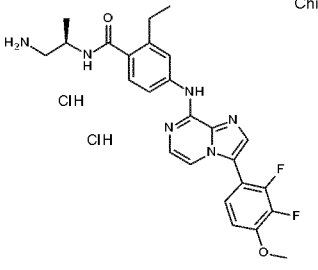
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96	N-(5-aminopentyl)-4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		545.3	Intermediate 85 and tert-butyl (5-aminopentyl)carbamate
REF 131	(R)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(pyrrolidin-3-yl)benzamide hydrochloride			Intermediate 86 and rac-tert-butyl (R)-3-aminopyrrolidine-1-carboxylate
97	(S)-N-(4-aminobutan-2-yl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride			Intermediate 86 and rac-tert-butyl (R)-(3-aminobutyl)carbamate

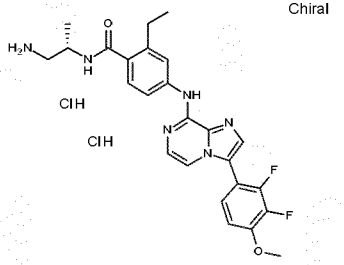
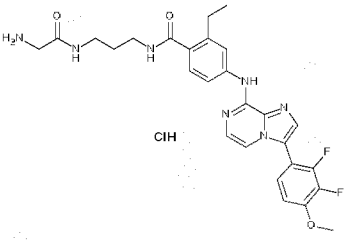
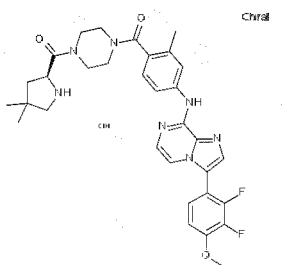
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98	N-(3-amino-2,2-dimethylpropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		509.4	Intermediate 86 and tert-butyl (3-amino-2,2-dimethylpropyl)carbamate
99	N-(1-amino-2-methylpropan-2-yl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		495.4	Intermediate 86 and tert-butyl (2-amino-2-methylpropyl)carbamate hydrochloride
100	N-(4-amino-2-methylbutan-2-yl)-4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		545.2	Intermediate 85 and tert-butyl (3-amino-3-methylbutyl)carbamate

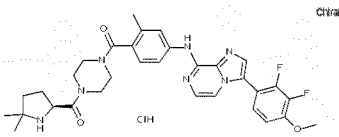
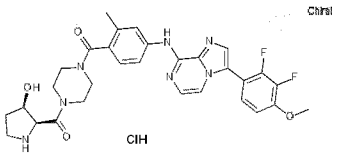
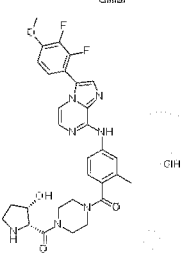
-196-

REF 132	N-(1-(aminomethyl)cyclopropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		493.3	Intermediate 86 and tert-butyl ((1-aminocyclopropyl)methyl)carbamate
101	(R)-N-(1-aminopropan-2-yl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide dihydrochloride		481.3	Intermediate 86 and tert-butyl (R)-(2-aminopropyl)carbamate

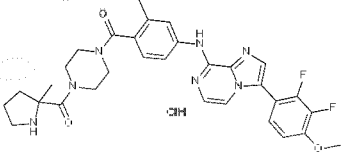
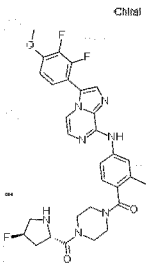
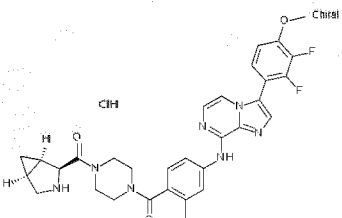
-197-

102	(S)-N-(1-aminopropan-2-yl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide dihydrochloride	 Chiral	481.3	Intermediate 86 and tert-butyl (S)-(2-aminopropyl)carbamate
103	N-(3-(2-aminoacetamido)propyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride	 ClH	538.3	Intermediate 87 and (tert-butoxycarbonyl)glycine
REF 133	(S)-(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)(4,4-dimethylpyrrolidin-2-yl)methanone hydrochloride	 Chiral ClH	604.4	Intermediate REF 134 and (S)-1-(tert-butoxycarbonyl)-4,4-dimethylpyrrolidine-2-carboxylic acid

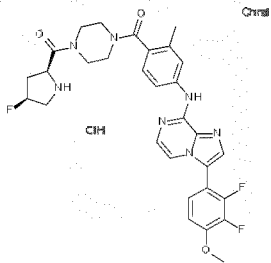
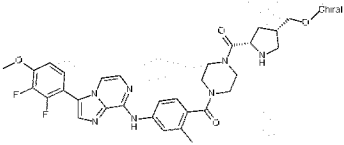
-198-

REF 135	(S)-(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)(5,5-dimethylpyrrolidin-2-yl)methanone hydrochloride		604.4	Intermediate REF 134 and (S)-1-(tert-butoxycarbonyl)-5,5-dimethylpyrrolidine-2-carboxylic acid
REF 136	(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)((2S,3R)-3-hydroxypyrrolidin-2-yl)methanone hydrochloride		592.4	Intermediate REF 134 and (2S,3R)-1-(tert-butoxycarbonyl)-3-hydroxypyrrolidine-2-carboxylic acid
REF 137	[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[(2R,3S)-3-hydroxypyrrolidine-2-carbonyl]piperazin-1-		592.4	Intermediate REF 134 and (2R,3S)-1-(tert-butoxycarbonyl)-3-hydroxypyrrolidine-2-carboxylic acid

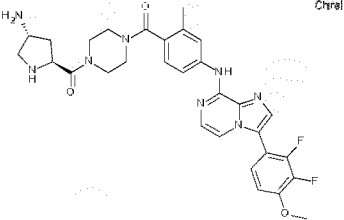
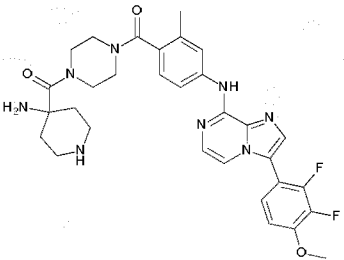
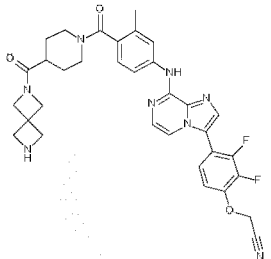
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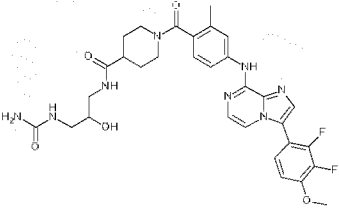
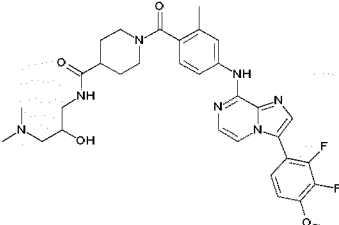
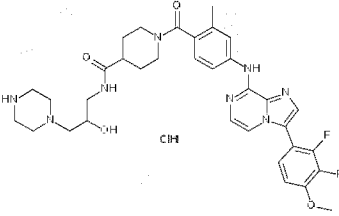
	yl]methanone;hydrochloride			
REF 138	(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)(2-methylpyrrolidin-2-yl)methanone hydrochloride		590.4	Intermediate REF 134 and 1-(tert-butoxycarbonyl)-2-methylpyrrolidine-2-carboxylic acid
REF 139	(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)((2S,4R)-4-fluoropyrrolidin-2-yl)methanone hydrochloride		594.4	Intermediate REF 134 and (2S,4R)-1-(tert-butoxycarbonyl)-4-fluoropyrrolidine-2-carboxylic acid
REF 140	(4-((1R,2S,5S)-3-azabicyclo[3.1.0]hexane-2-carbonyl)piperazin-1-yl)(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)methanone hydrochloride		588.4	Intermediate REF 134 and rac-(1R,2S,5S)-3-(tert-butoxycarbonyl)-3-

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	methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone hydrochloride			azabicyclo[3.1.0]hexane-2-carboxylic acid
REF 141	(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)((2S,4S)-4-fluoropyrrolidin-2-yl)methanone hydrochloride		594.4	Intermediate REF 134 and (2S,4S)-1-(tert-butoxycarbonyl)-4-fluoropyrrolidine-2-carboxylic acid
REF 142	(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)((2S,4S)-4-(methoxymethyl)pyrrolidin-2-yl)methanone hydrochloride		620.4	Intermediate REF 134 and (2S,4S)-1-(tert-butoxycarbonyl)-4-(methoxymethyl)pyrrolidine-2-carboxylic acid

-201-

REF 143	[4-[(2S,4R)-4-aminopyrrolidine-2-carbonyl]piperazin-1-yl]-[4-[[3-(2,3difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]methanone		591.4	Intermediate REF 134 and (2S,4R)-4-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-1-(tert-butoxycarbonyl)pyrrolidine-2-carboxylic acid. Final Fmoc removal with 4-methylpiperidine
REF 144	(4-aminopiperidin-4-yl)(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)methanone		605.3	Intermediate REF 134 and 4-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-1-(tert-butoxycarbonyl)piperidine-4-carboxylic acid. Final Fmoc removal with piperidine
REF 145	2-(4-(8-((4-(4-(2,6-diazaspiro[3.3]heptane-2-carbonyl)piperidine-1-carbonyl)-3-methylphenyl)amino)imidazo[1,2-a]pyrazin-3-yl)-2,3-		625.4(M-H)	Intermediate 69 and tert-butyl 2,6-diazaspiro[3.3]heptane-2-carboxylate

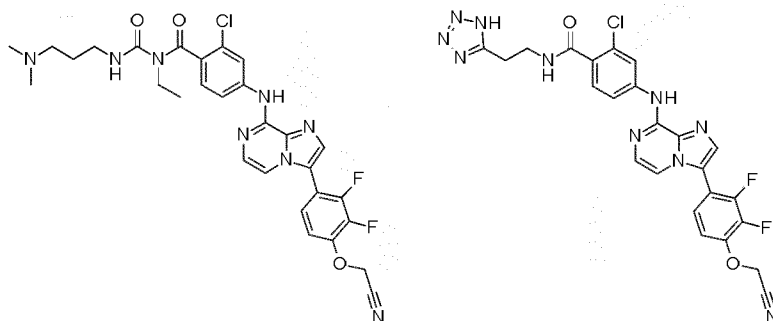
	difluorophenoxy)acetone nitrile			
REF 146	1-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-(2-hydroxy-3-ureidopropyl)piperidine-4-carboxamide		637.3	Intermediate 65 and 1-(3-amino-2-hydroxypropyl)urea
REF 147	1-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-(3-(dimethylamino)-2-hydroxypropyl)piperidine-4-carboxamide		622.2	Intermediate 65 and 1-amino-3-(dimethylamino)propan-2-ol
REF 148	1-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-		663.3	Intermediate 65 and tert-butyl 4-(3-amino-2-

-203-

	methylbenzoyl)-N-((2-hydroxy-3-((piperazin-1- yl)propyl)piperidine- 4-carboxamide hydrochloride			hydroxypropyl)pipera zine-1-carboxylate
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Reference Example 149 and Example 104

2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-
 N-[3-(dimethylamino)propylcarbamoyl]-N-ethyl-benzamide and 2-chloro-4-[[3-[4-
 5 (cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(1H-tetrazol-
 5-yl)ethyl]benzamide



To a solution of Intermediate 29 (230 mg, 0.5 mmol), 4-(4-methyl-4H-1,2,4-triazol-3-
 yl)piperidine hydrochloride (122 mg, 0.6 mmol) in anhydrous DMF (10 mL) was added DIPEA
 10 (129 mg, 1.0 mmol) and DMAP (73 mg, 0.6 mmol). Followed by the resultant mixture was stirred
 for 30 min at room temperature, EDCI (115 mg, 0.6 mmol) was added in the mixture and stirred
 for extra 10 h.

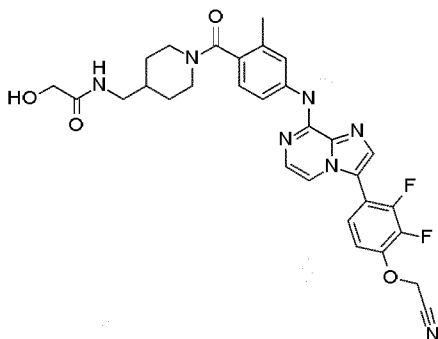
The mixture was poured into water (50 mL) and the aqueous solution was extracted with DCM
 (50 mL×2). The organic layers were combined and washed with water and brine, dried over
 15 anhydrous sodium sulphate and concentrated under reduced pressure to give a red oil, which was
 purified by prep.HPLC to give Reference Example 149 (50 mg, 16% yield) as a white powder

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MS (ESI, m/z): 611.2 [M+H]⁺ and Example 104 (60 mg, 21.3% yield) as a white powder. MS (ESI, m/z): 551.1 [M+H]⁺

Reference Example 150

N-[[1-[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]-2-hydroxy-acetamide

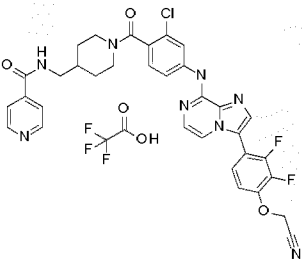


To a solution of Reference Example 64 (106 mg, 0.2 mmol), 2-hydroxyacetic acid (16 mg, 0.2 mmol) in anhydrous DMF (5 mL) was added DIPEA (52 mg, 0.4 mmol) and then the resultant mixture was stirred for 30 min at room temperature, HATU (152 mg, 0.4 mmol) was added in the mixture and stirred for extra 10 h. The mixture was poured into water (50 mL) and the aqueous solution was extracted with DCM (50 mL x2). The organic layers were combined and washed with water and brine, dried over anhydrous sodium sulphate and concentrated under reduced pressure to give a red oil, which was purified by prep.HPLC to give Reference Example 150 (5 mg, 4.2 % yield) as a white powder MS (ESI, m/z): 590.2 [M+H]⁺

The following example was prepared in analogy to Reference Example 150

Ex.	Name	Structure	ESI MS [M+H] ⁺	Starting Material

-205-

RE F 15 1	N-[[1-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]-4-piperidyl]methyl]pyridine-4-carboxamide 2,2,2-trifluoroacetate		657.1	Reference Example 63 and isonicotinic acid
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Intermediate 81:**tert-butyl 2-(hydroxymethyl)-4-(piperidine-4-carbonyl)piperazine-1-carboxylate****5 Step 1: tert-butyl 4-(1-benzyloxycarbonylpiperidine-4-carbonyl)-2-(hydroxymethyl)piperazine-1-carboxylate**

A mixture of 1-[(benzyloxy)carbonyl]piperidine-4-carboxylic acid (2.89 g, 10.99 mmol, 1.1 eq), tert-butyl 2-(hydroxymethyl)piperazine-1-carboxylate (2.16 g, 9.99 mmol, 1 eq), O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (5.7 g, 14.98 mmol, 1.5 eq) and N,N-diisopropylethylamine (5.22 mL, 29.96 mmol, 3 eq) in DMF (25 mL) was stirred at 25 °C for 14 h. The mixture was added water (50 mL) and extracted with ethyl acetate (50 mL × 3). The combined organic layers were washed with saturated NH₄Cl solution (50 mL) and concentrated to dryness. The crude product was purified by prep. HPLC. To the desired fractions were added NaHCO₃ (s) until pH 7~8 and extracted with ethyl acetate (100 mL × 3).

15 The combined organic layers were dried over sodium sulphate and concentrated *in vacuo* to afford tert-butyl 4-(1-benzyloxycarbonylpiperidine-4-carbonyl)-2-(hydroxymethyl)piperazine-1-carboxylate (2.28 g) as a brown oil. MS obsd. (ESI⁺): 461.9 [(M+H)⁺].

Step 2: tert-butyl 2-(hydroxymethyl)-4-(piperidine-4-carbonyl)piperazine-1-carboxylate

20 A mixture of tert-butyl 4-(1-benzyloxycarbonylpiperidine-4-carbonyl)-2-(hydroxymethyl)piperazine-1-carboxylate (2.08 g, 4.51 mmol, 1 eq) and Pd/C (10%, 300 mg) in

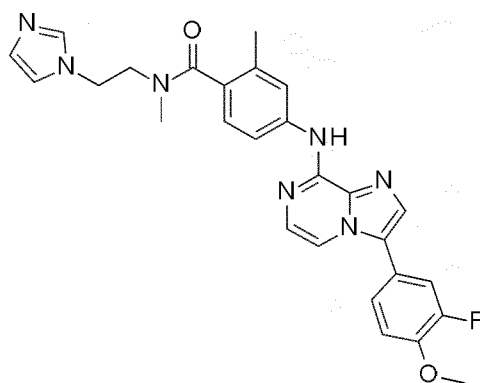
-206-

ethyl acetate (20 mL) was stirred at 25 °C for 72 h under hydrogen atmosphere. The mixture was filtered over celite and the filtrate was concentrated to dryness to afford tert-butyl 2-(hydroxymethyl)-4-(piperidine-4-carbonyl)piperazine-1-carboxylate (Intermediate 81) (1.29 g, 3.94 mmol, 87.43 % yield) as black oil. The crude product was used in next step without any purification.

MS obsd. (ESI⁺): 328.2 [(M+H)⁺].

Example 105:

4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-imidazol-1-ylethyl)-N,2-dimethyl-benzamide



Step 1: 2-imidazol-1-ylethyl methanesulfonate

A mixture of 1-(2-hydroxyethyl)imidazole (1.0 g, 8.92 mmol) in DCM (10 mL) was added methanesulfonyl chloride (1.02 g, 8.92 mmol) and triethylamine (2.5 mL, 17.84 mmol). After stirring at 20 °C for 4h, the reaction was quenched with H₂O (10 mL) and concentrated to dryness. The residue was diluted with EA (30 mL) and washed with water (30 mL) and brine (30 mL), dried over anhydrous sodium sulphate, concentrated under reduced pressure to afford the crude title product (500 mg) as yellow oil which was used in next step directly.

Step 2: 2-imidazol-1-yl-N-methyl-ethanamine

A mixture of 2-imidazol-1-ylethyl methanesulfonate (250 mg, 1.31 mmol) and a solution of monomethylamine in EtOH (2 mL) was stirred at 70 °C for 12 h. The reaction mixture was

-207-

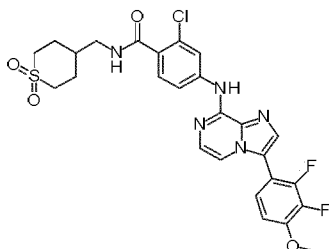
concentrated under reduced pressure to afford crude product (150 mg) as yellow oil which was used directly in next step.

Step 3: 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-imidazol-1-ylethyl)-N,2-dimethyl-benzamide

- 5 Into a stirred solution of intermediate 6 (200 mg, 0.51 mmol), 2-imidazol-1-yl-N-methyl-ethanamine (96 mg, 0.76 mmol) and triethylamine (0.2 mL, 1.53 mmol) in DMF (2 mL) was added 1-propanephosphonic anhydride (486 mg, 0.76 mmol) slowly. The reaction was stirred at 25°C for 12h and then concentrated to dryness. The residue was diluted with ethyl acetate (10 mL) and the resulting mixture was washed with water (3 mL) and brine (3 mL), dried over
- 10 anhydrous sodium sulphate, concentrated under reduced pressure to afford crude product. The residue was purified by prep-HPLC to afford the title compound (50 mg) as yellow solid. MS obsd. (ESI⁺) [(M+H)⁺]: 500.3

Example 106

- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1,1-dioxothian-4-yl)methyl]benzamide; 2,2,2-trifluoroacetic acid**
- 15

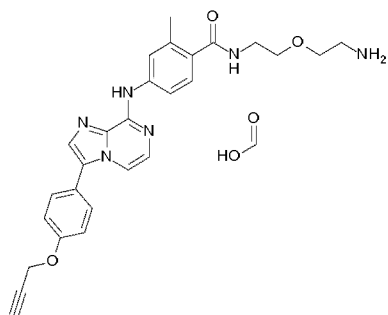


- A mixture of Example 42 (200 mg, 368 μmol) and oxone (678 mg, 1.1 mmol) in DMF (5 mL) was stirred at rt for 4 hrs. The mixture was diluted with H₂O (40 mL) and extracted with DCM. The organic layer was dried and concentrated *in vacuo*. The residue was purified by prep-HPLC
- 20 to give the title compound (56 mg) as light yellow solid. MS (ESI, m/z): 576.1.

Reference Example 152

N-[2-(2-Aminoethoxy)ethyl]-2-methyl-4-[[3-(4-prop-2-yloxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide; formic acid

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**Step 1:****8-Chloro-3-(4-prop-2-ynoxyphenyl)imidazo[1,2-a]pyrazine**

A mixture of 4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)phenol (intermediate 50, 100 mg, 0.410 mmol, 1 eq) and potassium carbonate (169 mg, 1.22 mmol, 3 eq) in DMF (3 mL) was added propargyl bromide (145 mg, 1.22 mmol, 3 eq) at 20 °C and stirred at 20 °C for 16 h. The mixture was filtered, poured into water, extracted with ethyl acetate, concentrated and purified by prep-TLC (PE/ethyl acetate=1:1) to afford the desired product (61 mg) as a yellow solid.

Step 2:

tert-Butyl N-[2-[2-[[2-methyl-4-[[3-(4-prop-2-ynoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]ethoxy]ethyl]carbamate

A mixture of tert-butyl N-[2-[2-[(4-amino-2-methyl-benzoyl)amino]ethoxy]ethyl]carbamate (intermediate 78, 45.0 mg, 0.130 mmol, 1 eq), 8-chloro-3-(4-prop-2-ynoxyphenyl)imidazo[1,2-a]pyrazine (37.84 mg, 0.130 mmol, 1 eq), cesium carbonate (130.36 mg, 0.400 mmol, 3 eq), tris(dibenzylideneacetone)dipalladium (0) (12.21 mg, 0.010 mmol, 0.100 eq) and 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (7.72 mg, 0.010 mmol, 0.100 eq) in 1,4-dioxane (5 mL) was stirred under N₂ at 115 °C on microwave for 2 h. The mixture was filtered and concentrated, purified by prep-TLC(DCM/MeOH/MeCN=10:1:1) to afford product (20 mg) as a light yellow solid.

Step 3:

N-[2-(2-Aminoethoxy)ethyl]-2-methyl-4-[[3-(4-prop-2-ynoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide formate

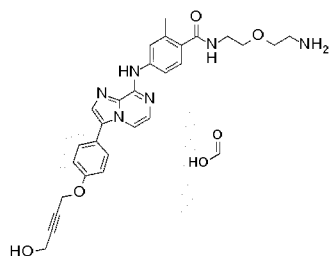
-209-

A solution of tert-butyl N-[2-[2-[[2-methyl-4-[[3-(4-prop-2-ynoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]ethoxy]ethyl]carbamate (50.0 mg, 0.090 mmol, 1 eq) in DCM (4 mL) was added trifluoroacetic acid (0.39 mL, 5.11 mmol, 59.78 eq) and stirred at 20 °C for 16 h. The solution was concentrated and purified by prep-HPLC to afford 13.4 mg product as white solid.

5 MS (ESI, m/z): 485.4

Reference Example 153

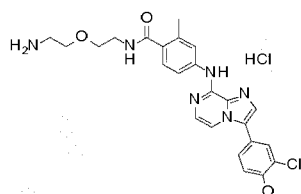
N-[2-(2-aminoethoxy)ethyl]-4-[[3-[4-(4-hydroxybut-2-ynoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide formate



10 The title compound was obtained in analogy to Reference Example 152 using 4-hydroxybut-2-ynyl methanesulfonate instead of propargyl bromide. MS (ESI, m/z): 515.3

Reference Example 154

N-(2-(2-aminoethoxy)ethyl)-4-((3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride



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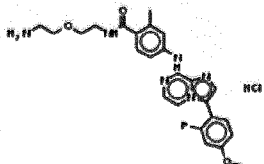
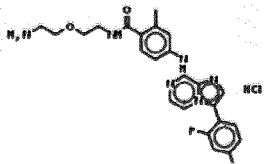
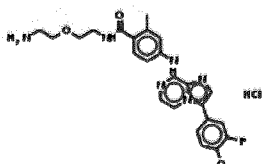
To Intermediate 79 (24 mg) in dioxane (900 µl) and water (100 µl) was added (3-chloro-4-methoxyphenyl)boronic acid (11.6 mg), 1,1'-bis(diphenylphosphino)ferrocenedichloro palladium(II) dichloromethane complex (3.03 mg, 4.13 µmol) and potassium carbonate (14.3 mg, 103 µmol) followed by stirring at 105 °C overnight. The reaction mixture was concentrated and purified by prep. HPLC to give a Boc-protected intermediate, which was deprotected to the

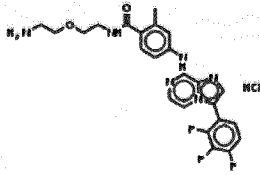
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title compound (11 mg, colorless solid) by addition of 4M HCl in dioxane (1 h), followed by concentration and drying *in vacuo*. MS (ESI, m/z): 495.3

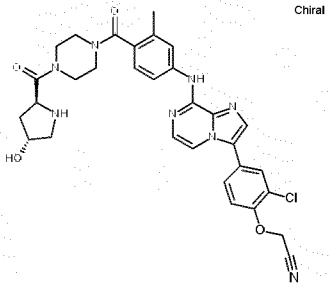
The following examples were prepared in analogy to Reference Example 154:

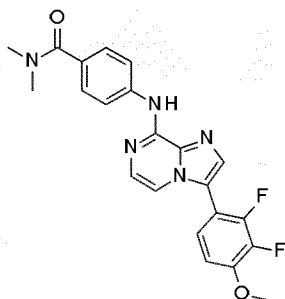
Ex.	Name	Structure	MS ESI [M+H] ⁺	Starting Material
REF 155	N-(2-(2-aminoethoxy)ethyl)-4-((3-(4-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride		449.7	Intermediate 79 and (4-fluorophenyl)boronic acid
REF 156	N-(2-(2-aminoethoxy)ethyl)-4-((3-(4-chloro-3-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride		483.1	Intermediate 79 and (4-chloro-3-fluorophenyl)boronic acid
REF 157	N-(2-(2-aminoethoxy)ethyl)-4-((3-(3,4-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride		467.9	Intermediate 79 and (3,4-difluorophenyl)boronic acid

	methylbenzamide hydrochloride			
REF 158	N-(2-(2-aminoethoxy)ethyl)- 4-((3-(2-fluoro-4-methoxyphenyl)imid azo[1,2-a]pyrazin-8-yl)amino)-2- methylbenzamide hydrochloride		479.4	Intermediate 79 and (2-fluoro-4-methoxyphenyl)boronic acid
REF 159	N-(2-(2-aminoethoxy)ethyl)- 4-((3-(2,4-difluorophenyl)imid azo[1,2-a]pyrazin-8-yl)amino)-2- methylbenzamide hydrochloride		467.2	Intermediate 79 and (2,4-difluorophenyl)boronic acid
REF 160	N-(2-(2-aminoethoxy)ethyl)- 4-((3-(3-fluoro-4-methoxyphenyl)imid azo[1,2-a]pyrazin-8-yl)amino)-2- methylbenzamide hydrochloride		479.1	Intermediate 79 and (3-fluoro-4-methoxyphenyl)boronic acid

REF 161	N-(2-(2-aminoethoxy)ethyl)-2-methyl-4-((3-(2,3,4-trifluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide hydrochloride		485.2	Intermediate 79 and (2,3,4-trifluorophenyl)boronic acid
REF 162	(4-(4-((3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)((2S,4R)-4-hydroxypyrrolidin-2-yl)methanone hydrochloride		590.2	Intermediate 75 and (3-chloro-4-methoxyphenyl)boronic acid
REF 163	(4-(4-((3-(3-chloro-2-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)((2S,4R)-4-hydroxypyrrolidin-2-yl)methanone hydrochloride		609.1	Intermediate 75 and (3-chloro-2-fluoro-4-methoxyphenyl)boronic acid

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REF 164	2-(2-chloro-4-(8-((4-(4-((2S,4R)-4-hydroxypyrrolidin-2-carbonyl)piperazine-1-carbonyl)-3-methylphenyl)amino)imidazo[1,2-a]pyrazin-3-yl)phenoxy)acetonitrile		615.2	Intermediate 75 and (2-(2-chloro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)acetonitrile (Intermediate 88)
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Example 107**4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethylbenzamide**

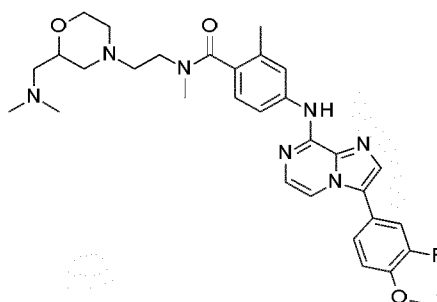
5

A mixture of 4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-N,N-dimethylbenzamide (150 mg, 368 μ mol), (2,3-difluoro-4-methoxyphenyl)boronic acid (69.2 mg, 368 μ mol), K_3PO_4 (235 mg, 1.11 mmol) and $PdCl_2(dppf)-CH_2Cl_2$ adduct (13.5 mg, 18.4 μ mol) in THF (5 mL) and H_2O (1 mL) was heated to 50 $^{\circ}C$ with stirring overnight. The reaction mixture was diluted with H_2O and
 10 extracted with DCM (30 mL) twice. The combined DCM layer was dried and concentrated in vacuo. The residue was purified by prep-HPLC to give 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,N-dimethylbenzamide (20 mg) as white solid. (ESI+) $[(M+H)^+]$: 424.

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Example 108

N-[2-[2-[(dimethylamino)methyl]morpholin-4-yl]ethyl]-4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide; formic acid



5 Step 1: N-(2-chloroethyl)-N,2-dimethyl-4-nitro-benzamide

To a solution of (2-chloroethyl)methylamine (310 mg, 3.31 mmol), 2-methyl-4-nitro-benzoic acid (500 mg, 2.76 mmol), triethylamine (1.15 mL, 8.28 mmol) in DMF (8 mL) was added T3P (2.63 g, 4.14 mmol). The mixture was stirred at 20 °C for 16 h. The mixture was diluted with ethyl acetate (100 mL), washed with water (30 mL), brine (30 mL), dried over sodium sulphate and concentrated. The residue was purified by column chromatography to give N-(2-chloroethyl)-N,2-dimethyl-4-nitro-benzamide (480 mg) as a colorless oil.

Step 2: N-[2-[2-[(dimethylamino)methyl]morpholin-4-yl]ethyl]-N,2-dimethyl-4-nitro-benzamide

A mixture of N,N-dimethyl-2-morpholinmethanamine (148 mg, 1.03 mmol), N-(2-chloroethyl)-N,2-dimethyl-4-nitro-benzamide (220 mg, 0.860 mmol), N,N-diisopropylethylamine (0.6 mL, 3.43 mmol) in DMSO (3 mL) was stirred at 100 °C for 16 h. After cooling to room temperature, the mixture was diluted with ethyl acetate (100 mL), washed with water (30 mL), brine (30 mL x 2), dried over sodium sulphate and concentrated under reduced pressure. The residue was purified by prep-HPLC (TFA). The fraction was concentrated. The residue was neutralized by aq. NaHCO₃, extracted with ethyl acetate (100 mL), dried over sodium sulphate and concentrated to give N-[2-[2-[(dimethylamino)methyl]morpholin-4-yl]ethyl]-N,2-dimethyl-4-nitro-benzamide (60 mg) as a light-yellow oil.

Step 3: 4-amino-N-[2-[2-[(dimethylamino)methyl]morpholin-4-yl]ethyl]-N,2-dimethyl-benzamide

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To a solution of N-[2-[2-[(dimethylamino)methyl]morpholin-4-yl]ethyl]-N,2-dimethyl-4-nitro-benzamide (60 mg, 0.160 mmol) in ethyl acetate (3 mL) was added Pd/C (10%, 20 mg). The mixture was stirred at 20 °C under H₂ for 16 h. The mixture was filtered and the filtrate was concentrated under reduced pressure to give crude 4-amino-N-[2-[2-

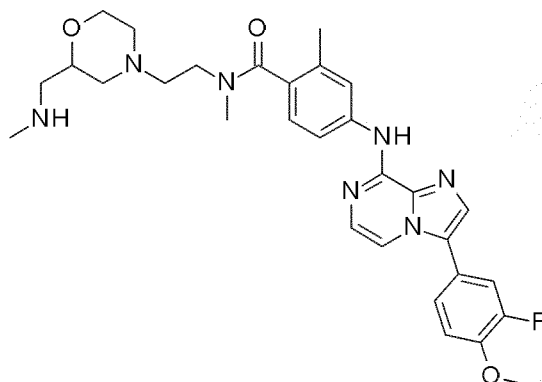
5 [(dimethylamino)methyl]morpholin-4-yl]ethyl]-N,2-dimethyl-benzamide (50 mg) as a yellow oil, which was used directly for the next step without further purification.

Step 4: N-[2-[2-[(dimethylamino)methyl]morpholin-4-yl]ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide; formic acid

A mixture of 8-chloro-3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazine (50 mg, 0.180
10 mmol, 3), 4-amino-N-[2-[2-[(dimethylamino)methyl]morpholin-4-yl]ethyl]-N,2-dimethyl-benzamide (50 mg, 0.150 mmol), Brettphos Pd G3 (14 mg, 0.020 mmol, CAS# 1470372-59-8), potassium carbonate (62 mg, 0.450 mmol) in tert-butanol (1 mL) was stirred at 100 °C for 16 h. The mixture was diluted with ethyl acetate (100 mL), washed with water (30 mL), brine (30 mL), dried over sodium sulphate and concentrated under reduced pressure. The residue was
15 purified by prep-TLC (DCM:MeOH=10:1), then further purified by prep-HPLC (FA) to give N-[2-[2-[(dimethylamino)methyl]morpholin-4-yl]ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide (25.5 mg) as a white solid. MS obsd. (ESI⁺) [(M+H)⁺]: 576.2

Example 109

20 **4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-[2-(methylaminomethyl)morpholin-4-yl]ethyl]benzamide hydrochloride**



Step 1: tert-butyl N-methyl-N-[[4-[2-[methyl-(2-methyl-4-nitro-benzoyl)amino]ethyl]morpholin-2-yl]methyl]carbamate

A mixture of N-(2-chloroethyl)-N,2-dimethyl-4-nitro-benzamide (230 mg, 0.900 mmol), tert-butyl N-methyl-N-(morpholin-2-ylmethyl)carbamate (250 mg, 1.09 mmol), N,N-diisopropylethylamine (0.62 mL, 3.58 mmol) in DMSO (5 mL) was stirred at 100 °C for 16 h. After cooling to room temperature, the mixture was diluted with ethyl acetate (100 mL), washed with water (30 mL), brine (30 mL x 2), dried over sodium sulphate and concentrated under reduced pressure. The residue was purified by prep-HPLC to give tert-butyl N-methyl-N-[[4-[2-[methyl-(2-methyl-4-nitro-benzoyl)amino]ethyl]morpholin-2-yl]methyl]carbamate (160 mg) as a light-yellow oil.

Step 2: tert-butyl N-[[4-[2-[(4-amino-2-methyl-benzoyl)-methyl-amino]ethyl]morpholin-2-yl]methyl]-N-methyl-carbamate

To a solution of N-methyl-N-[[4-[2-[methyl-(2-methyl-4-nitro-benzoyl)amino]ethyl]morpholin-2-yl]methyl]carbamate (160 mg, 0.360 mmol) in ethyl acetate (3 mL) was added Pd/C (10%, 20 mg). The mixture was hydrogenated at 20 °C under H₂ for 16 h. The mixture was filtered and the filtrate was concentrated under reduced pressure to give crude tert-butyl N-[[4-[2-[(4-amino-2-methyl-benzoyl)-methyl-amino]ethyl]morpholin-2-yl]methyl]-N-methyl-carbamate (120 mg) as a yellow solid.

Step 3: tert-butyl N-[[4-[2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]ethyl]morpholin-2-yl]methyl]-N-methyl-carbamate

A mixture of 8-chloro-3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazine (80 mg, 0.290 mmol), N-[[4-[2-[(4-amino-2-methyl-benzoyl)-methyl-amino]ethyl]morpholin-2-yl]methyl]-N-methyl-carbamate (120 mg, 0.290 mmol), Brettphos Pd G3 (27 mg, 0.030 mmol, cas# 1470372-59-8), potassium carbonate (118 mg, 0.850 mmol) in t-BuOH (1.5 mL) was stirred at 100 °C for 16 h. The mixture was diluted with ethyl acetate (100 mL), washed with water (30 mL), brine (30 mL), dried over sodium sulphate and concentrated under reduced pressure. The residue was purified by prep-TLC (DCM/MeOH=15/1) to give tert-butyl N-[[4-[2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]ethyl]morpholin-2-yl]methyl]-N-methyl-carbamate (120 mg) as a yellow oil.

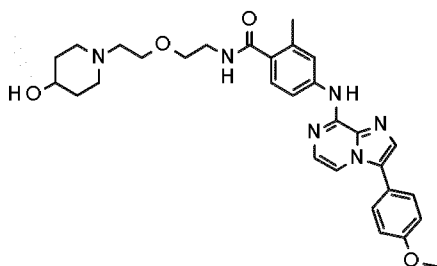
-217-

Step 4: 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-[2-(methylaminomethyl)morpholin-4-yl]ethyl]benzamide

To a solution of tert-butyl N-[[4-[2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]ethyl]morpholin-2-yl]methyl]-N-methyl-carbamate (120 mg, 0.180 mmol) in DCM (3 mL) was added HCl in dioxane (1.6 mL, 6.4 mmol). The mixture was stirred at 20 °C for 16 h. The mixture was concentrated under reduced pressure. The residue was purified by prep-HPLC to give the title compound (21 mg) as a white solid. MS obsd. (ESI⁺) [(M+H)⁺]: 562.1

Reference Example 165

10 N-(2-(2-(4-hydroxypiperidin-1-yl)ethoxy)ethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide



A mixture of N-(2-(2-chloroethoxy)ethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide (Reference Example 32, 30 mg, 62.5 µmol, Eq: 1), piperidin-4-ol (9.5 mg), sodium carbonate (9.94 mg, 93.8 µmol, Eq: 1.50) and potassium iodide (519 µg, 3.13 µmol, Eq: 0.05) in n-BuOH (0.5 mL) was heated at 105 °C for 48 h. Water was added to the reaction mixture and extracted with DCM. The combined organic layers were dried over sodium sulphate and concentrated to an oil. The product was purified by prep. HPLC to give the title compound (19 mg). MS (ESI, m/z): 547.4.

20 The following examples were prepared in analogy to Reference Example 165, Boc-protected intermediates were deprotected using HCl (4M in dioxane).

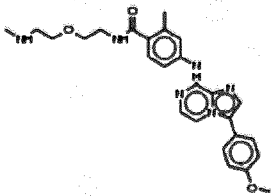
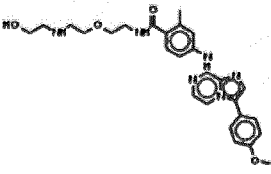
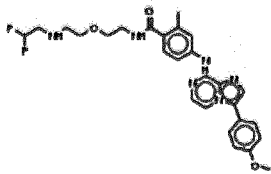
Intermediate 89

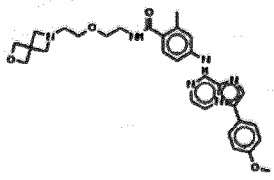
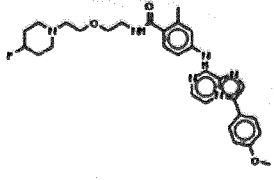
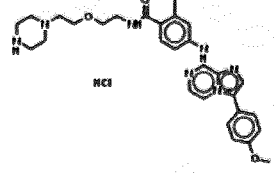
N-(2-(2-chloroethoxy)ethyl)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide

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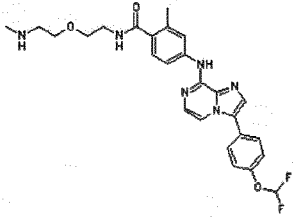
The title compound was prepared in analogy to Reference Example 32 from Intermediate 7 and 2-(2-chloroethoxy)ethanamine hydrochloride. MS (ESI⁺) [(M+H)⁺]: 516.3

The following examples were prepared in analogy to Reference Example 165

Ex.	Name	Structure	MS ESI [M+H] ⁺	Starting Material
REF 166	4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(2-(2-(methylamino)ethoxy)ethyl)benzamide		475.4	Reference Example 32 and methanamine
REF 167	N-(2-(2-((2-hydroxyethyl)amino)ethoxy)ethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		505.4	Reference Example 32 and 2-aminoethanol
REF 168	N-(2-(2-((2,2-difluoroethyl)amino)ethoxy)ethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		525.4	Reference Example 32 and 2,2-difluoroethanamine

	yl)amino)-2-methylbenzamide			
REF 169	N-(2-(2-(2-oxa-6-azaspiro[3.3]heptan-6-yl)ethoxy)ethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		543.5	Reference Example 32 and 2-oxa-6-azaspiro[3.3]heptane
REF 170	N-(2-(2-(4-fluoropiperidin-1-yl)ethoxy)ethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		547.4	Reference Example 32 and 4-fluoropiperidine
REF 171	4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(2-piperazin-1-ylethoxy)ethyl]benzamide; dihydrochloride		530.5	Reference Example 32 and tert-butyl piperazine-1-carboxylate

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REF 172	4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methyl-N-(2-(2-(methylamino)ethoxy)ethyl)benzamide		511.4	Intermediate 89 and methylamine
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Intermediate 90**1-(4-amino-2-chloro-benzoyl)piperidine-4-carboxylic acid****Step 1:****5 methyl 1-(4-amino-2-chloro-benzoyl)piperidine-4-carboxylate**

To a solution of 4-amino-2-chlorobenzoic acid (1.70 g, 10 mmol), methyl piperidine-4-carboxylate (2.85 g, 20 mmol) in anhydrous DCM (50 mL) was added DIPEA (2.58 g, 20 mmol) and then the resultant mixture was stirred for 30 min at room temperature, HATU (7.6 g, 20 mmol) was added in the mixture and stirred for extra 10 h. The mixture was poured into water (100 mL) and the aqueous solution was extracted with DCM (100 mL×2). The organic layers were combined and washed with water and brine, dried over anhydrous sodium sulphate and concentrated under reduced pressure to give a red oil, which was purified by flash column chromatography to provide the desired compound (1.82 g, 61.3 % yield) as a white solid. MS (ESI, m/z): 297.1 [M+H]⁺.

15 Step 2:**1-(4-amino-2-chloro-benzoyl)piperidine-4-carboxylic acid**

To a solution of methyl 1-(4-amino-2-chlorobenzoyl)piperidine-4-carboxylate (890 mg, 3.0 mmol) in THF (5 mL) and methanol (25 mL) was added 2.0 M aq. LiOH (3.0 mL). The resultant mixture was stirred for 15 h at room temperature and then acidified to pH=5-6 with 3.0 M hydrochloric acid. The resulting suspension was filtered, the solid was washed with water and

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then dried to give the title compound (0.6 g, 70.7% yield) as a white solid. MS (ESI, m/z): 283.0 [M+H]⁺.

Intermediate 91

1-(4-amino-2-methyl-benzoyl)piperidine-4-carboxylic acid

5

Step 1:

methyl 1-(2-methyl-4-nitro-benzoyl)piperidine-4-carboxylate

To a solution of 2-methyl-4-nitrobenzoic acid (1.8 g, 10 mmol), methyl piperidine-4-carboxylate (2.85 g, 20 mmol) in anhydrous DCM (50 mL) was added DIPEA (2.58 g, 20 mmol) and then the resultant mixture was stirred for 30 min at room temperature, HATU (7.6 g, 20 mmol) was added in the mixture and stirred for extra 10 h. The mixture was poured into water (100 mL) and the aqueous solution was extracted with DCM (100 mL×2). The organic layers were combined and washed with water and brine, dried over anhydrous sodium sulphate and concentrated under reduced pressure to give a red oil, which was purified by flash column chromatography to provide the desired compound (2.86 g, 93.4 % yield) as a yellow solid. MS (ESI, m/z): 307.1 [M+H]⁺.

Step 2:

methyl 1-(4-amino-2-methyl-benzoyl)piperidine-4-carboxylate

To a solution of methyl 1-(2-methyl-4-nitro-benzoyl)piperidine-4-carboxylate (3.0 g, 9.3 mmol) in EtOH (50 mL) was added palladium on carbon (254 mg, 0.1 mol). The mixture was degassed and charged with a H₂ balloon. The reaction was stirred at room temperature overnight. The catalyst was filtered off and the filtrate was concentrated. The residue was purified by column chromatography to give the final compound (1.93 g, 70 % yield) as a red oil. MS (ESI, m/z): 277.1 [M+H]⁺.

Step 3:

1-(4-amino-2-methyl-benzoyl)piperidine-4-carboxylic acid

25

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To a solution of methyl 1-(4-amino-2-methylbenzoyl)piperidine-4-carboxylate (830 mg, 3.0 mmol) in THF (5 mL) and methanol (25 mL) was added 2.0 M aq LiOH (6.0 mL). The resultant mixture was stirred for 15 h at room temperature and then acidified to pH=5-6 with 3.0 M hydrochloric acid. The resulting suspension was filtered, the solid was washed with water and then dried to give the title compound (0.6 g, 76.2% yield) as a white solid. MS (ESI, m/z): 263.1 [M+H]⁺.

Intermediate 92**1-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperidine-4-carboxylic acid**

To a solution of intermediate 30 (0.96 g, 3.0 mmol) in acetonitrile (30 mL) and acetic acid (3.0 mL) was added intermediate 90 (0.85 g, 3.0 mmol) and then stirred overnight at 95 °C. The mixture was poured into water (50 mL) and the resulting suspension filtered. The solid was washed with acetonitrile and water, dried to give the title compound (1.0 g, 58.8 % yield) as a light red solid which was used in next step without purification. MS (ESI, m/z): 567.1 [M+H]⁺.

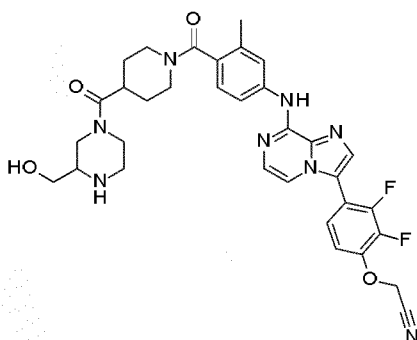
The following intermediates were prepared in analogy to intermediate 92

Int.	Name	ESI MS [M+H] ⁺	Starting Material
93	1-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperidine-4-carboxylic acid	583.1	Intermediate 90 and intermediate 41
94	1-[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperidine-4-carboxylic acid	547.1	Intermediate 91 and intermediate 30
95	1-[4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperidine-4-carboxylic acid	563.1	Intermediate 90 and intermediate

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Reference Example 173

2-[2,3-difluoro-4-[8-[4-[4-[3-(hydroxymethyl)piperazine-1-carbonyl]piperidine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile; 2,2,2-trifluoroacetic acid



5

Step 1:

tert-butyl 4-[1-[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperidine-4-carbonyl]-2-(hydroxymethyl)piperazine-1-carboxylate

- 10 To a solution of intermediate 94 (273 mg, 0.5 mmol), tert-butyl 2-(hydroxymethyl)piperazine-1-carboxylate (130 mg, 0.6 mmol) in anhydrous DMF (10 mL) was added DIPEA (258 mg, 2.0 mmol) and then the resultant mixture was stirred for 30 min at room temperature, T₃P (0.5 mL, 0.75 mmol) was added to the mixture and stirred for extra 10 h. The mixture was poured into water (50 mL) and the aqueous solution was extracted with DCM (50 mL×2). The organic layers
- 15 were combined and washed with water and brine, dried over anhydrous sodium sulphate and concentrated under reduced pressure to give a red oil which was used in next step without purification. MS (ESI, m/z): 745.3 [M+H]⁺.

Step 2:

- 20 **2-[2,3-difluoro-4-[8-[4-[4-[3-(hydroxymethyl)piperazine-1-carbonyl]piperidine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile; 2,2,2-trifluoroacetic acid**

To a solution of tert-butyl 4-(1-(4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carbonyl)-2-(hydroxymethyl)piperazine-1-carboxylate (300 mg, 0.4 mmol) in THF (5 mL) was added 3M hydrochloric acid (2.0 mL) at room temperature. The resultant mixture was stirred for 10 h and then adjusted to pH=7-8 with 5 2M Na₂CO₃ aqueous solution. The mixture was extracted with DCM (50 mL×2), the combined organic layers were washed with water and brine, dried over anhydrous sodium sulphate, and concentrated to give a red oil which was purified by prep. HPLC to provide the desired compound (215 mg, 79.2 % yield) as an off-white powder. MS (ESI, m/z): 645.2 [M+H]⁺.

The following examples were prepared in analogy to Reference Example 173

Int.	Name	ESI MS [M+H] ⁺	Starting Material
REF 174	piperazin-2-ylmethyl 1-[2-chloro-4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperidine-4-carboxylate trifluoroacetate	681.1	Intermediate 93 and tert-butyl 3-(hydroxymethyl)piperazine-1-carboxylate
REF 54	piperazin-2-ylmethyl 1-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperidine-4-carboxylate trifluoroacetate	665.2	Intermediate 92 and tert-butyl 3-(hydroxymethyl)piperazine-1-carboxylate
REF 175	2-[4-[8-[3-chloro-4-[4-[2-(hydroxymethyl)piperazine-1-carbonyl]piperidine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]acetonitrile trifluoroacetate	665.2	Intermediate 92 and tert-butyl 3-(hydroxymethyl)piperazine-1-carboxylate

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REF 176	2-[3-chloro-2-fluoro-4-[8-[4-[4-[3-(hydroxymethyl)piperazine-1-carbonyl]piperidine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile trifluoroacetate	661.2	Intermediate 95 and tert-butyl 2-(hydroxymethyl)piperazine-1-carboxylate
REF 177	piperazin-2-ylmethyl 1-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperidine-4-carboxylate trifluoroacetate	661.2	Intermediate 95 and tert-butyl 3-(hydroxymethyl)piperazine-1-carboxylate
REF 178	2-[3-chloro-4-[8-[3-chloro-4-[4-[2-(hydroxymethyl)piperazine-1-carbonyl]piperidine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2-fluoro-phenoxy]acetonitrile trifluoroacetate	681.1	Intermediate 93 and tert-butyl 3-(hydroxymethyl)piperazine-1-carboxylate
REF 173	2-[2,3-difluoro-4-[8-[4-[4-[3-(hydroxymethyl)piperazine-1-carbonyl]piperidine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile trifluoroacetate	645.2	Intermediate 94 and tert-butyl 2-(hydroxymethyl)piperazine-1-carboxylate
REF 179	1-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide trifluoroacetate	623.2	Intermediate 92 and tert-butyl (2-aminoethyl)(methyl)carbamate
REF 180	1-[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-N-[2-(1H-tetrazol-5-	642.2	Intermediate 94 and 2-(2H-tetrazol-

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	yl)ethyl]piperidine-4-carboxamide trifluoroacetate		5-yl)ethan-1-amine hydrochloride
REF 181	1-[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-N-methylsulfonyl-piperidine-4-carboxamide trifluoroacetate	624.1	Intermediate 94 and methanesulfonamide
REF 182	N-(2-amino-3-hydroxypropyl)-1-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamide hydrochloride	576.3	Reference Example 2 and tert-butyl (1-amino-3-hydroxypropan-2-yl)carbamate

Intermediate 96

2-[4-[8-[3-chloro-4-(piperazine-1-carbonyl)anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]acetonitrile

5

Step 1:

tert-butyl 4-[1-[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperidine-4-carbonyl]-2-(hydroxymethyl)piperazine-1-carboxylate

- 10 To a solution of intermediate 29 (1.82 g, 4 mmol), tert-butyl piperazine-1-carboxylate (0.9 g, 4.8 mmol) in anhydrous DMF (35 mL) was added DIPEA (2.6 g, 20 mmol) and then the resultant mixture was stirred for 30 min at room temperature, T₃P (4 mL, 6.4 mmol) was added in the mixture and stirred for extra 10 h. The mixture was poured into water (50 mL) and the aqueous solution was extracted with DCM (50 mL×2). The organic layers were combined and washed
- 15 with water and brine, dried over anhydrous sodium sulphate and concentrated under reduced

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pressure to give a red oil which was used in next step without purification. MS (ESI, m/z): 624.1 [M+H]⁺.

Step 2:

2-[4-[8-[3-chloro-4-(piperazine-1-carbonyl)anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]acetonitrile

To a solution of tert-butyl 4-[1-[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperidine-4-carbonyl]-2-(hydroxymethyl)piperazine-1-carboxylate (1.8 g, 3 mmol) in THF (15 mL) was added 3M hydrochloric acid aqueous solution (10 mL) at room temperature. The resultant mixture was stirred for 10 h and then adjusted to pH=7-8 with ammonia solution. The mixture was poured into water (25 mL) and then extracted with dichloromethane / isopropanol (100 /10 mL), the organic layer was concentrated to give a red oil, which was purified by prep. HPLC to provide the title compound (1.2 g, 79.4 % yield) as a light red solid. MS (ESI, m/z): 524.1 [M+H]⁺.

The following intermediates were prepared in analogy to intermediate 96

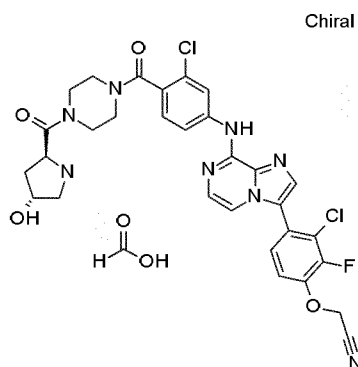
Int.	Name	ESI MS [M+H] ⁺	Starting Material
97	2-[3-chloro-4-[8-[3-chloro-4-(piperazine-1-carbonyl)anilino]imidazo[1,2-a]pyrazin-3-yl]-2-fluoro-phenoxy]acetonitrile	539.1	Intermediate 24 and tert-butyl piperazine-1-carboxylate
98	[2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]-piperazin-1-yl-methanone	499.1	Intermediate 20 and tert-butyl piperazine-1-carboxylate

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76	(4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(piperazin-1-yl)methanone hydrochloride	463.3	Intermediate 1 and tert-butylpiperazine-1-carboxylate
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Reference Example 183

2-[3-chloro-4-[8-[3-chloro-4-[4-[(2S,4R)-4-hydroxypyrrolidine-2-carbonyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2-fluoro-phenoxy]acetonitrile formate



5

Step 1:

tert-butyl (2S,4R)-2-[4-[2-chloro-4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperazine-1-carbonyl]-4-hydroxypyrrolidine-1-carboxylate

- 10 To a solution of intermediate 97 (162 mg, 0.3 mmol), (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid (83 mg, 0.36 mmol) was added DIPEA (78 mg, 0.6 mmol), the resultant mixture was stirred for 10 min at room temperature, and then HATU (228 mg, 0.6 mmol) was added in the mixture and stirred for extra 10 h at room temperature. The mixture was poured into water (50 mL) and the aqueous solution was extracted with DCM (50
- 15 mL×2). The organic layers were combined and washed with water and brine, dried over anhydrous sodium sulphate and concentrated under reduced pressure to give a red oil which was used in next step without purification. MS (ESI, m/z): 753.2 [M+H]⁺.

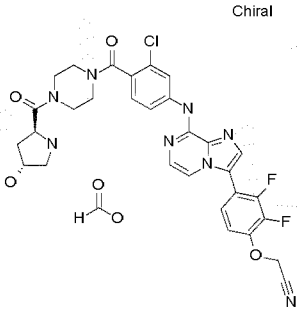
Step 2:

2-[3-chloro-4-[8-[3-chloro-4-[4-[(2S,4R)-4-hydroxypyrrolidine-2-carbonyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2-fluoro-phenoxy]acetonitrile formate

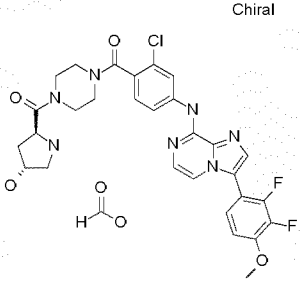
To a solution of tert-butyl (2S,4R)-2-(4-(2-chloro-4-((3-(2-chloro-4-(cyanomethoxy)-3-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperazine-1-carbonyl)-4-

- 5 hydroxypyrrolidine-1-carboxylate (200 mg, 0.265 mmol) in THF (5 mL) was added 3M hydrochloric acid aqueous solution (1 mL) at room temperature. The resultant mixture was stirred for 10 h and then adjusted to pH=7-8 with ammonia solution. The mixture was poured into water (25 mL) and then extracted with dichloromethane / isopropanol (50 / 5 mL), the organic layer was concentrated to give a red oil, which was purified by prep. HPLC to provide
- 10 the title compound (20 mg, 11.3 % yield) as a white powder. MS (ESI, m/z): 653.2 [M+H]⁺.

The following examples were prepared in analogy to Reference Example 183

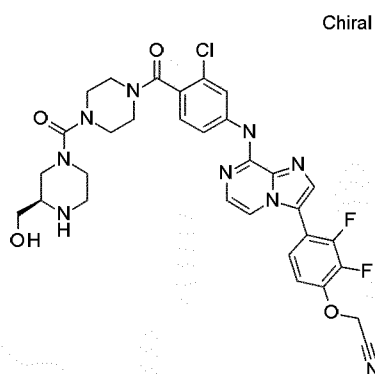
Ex.	Name	Structure	ESI MS [M+H] ⁺	Starting Material
REF 184	2-[4-[8-[3-chloro-4-[4-[(2S,4R)-4-hydroxypyrrolidine-2-carbonyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]acetonitrile formate		637.1	Intermediate 96 and (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid

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REF 185	[2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]-[4-[(2S,4R)-4-hydroxypyrrolidine-2-carbonyl]piperazin-1-yl]methanone formate		612.1	Intermediate 98 and (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid
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Reference Example 186

2-[4-[8-[3-chloro-4-[4-[(3R)-3-(hydroxymethyl)piperazine-1-carbonyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]acetonitrile



5

Step 1:

tert-butyl (2R)-4-[4-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperazine-1-carbonyl]-2-(hydroxymethyl)piperazine-1-carboxylate

- 10 To a solution of intermediate 96 (210 mg, 0.4 mmol), DIPEA (258 mg, 2.0 mmol) in anhydrous DCM (10 mL) was added triphosgene (104 mg, 0.2 mmol) and then the resultant mixture was stirred for 1.0 h at 0°C, and then treated with tert-butyl (R)-2-(hydroxymethyl)piperazine-1-carboxylate (104 mg, 0.48 mmol), the reaction mixture was allowed to warm to room temperature. The mixture was poured into saturated aq. sodium bicarbonate (50 mL) and the

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aqueous solution was extracted with DCM (50 mL×2). The organic layers were combined and washed with water and brine, dried over anhydrous sodium sulphate and concentrated under reduced pressure to give a red oil which was used in next step without purification. MS (ESI, m/z): 766.2 [M+H]⁺.

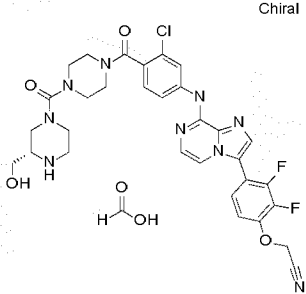
5 Step 2:

2-[4-[8-[3-chloro-4-[4-[(3R)-3-(hydroxymethyl)piperazine-1-carbonyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]acetonitrile

To a solution of tert-butyl (2R)-4-[4-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperazine-1-carbonyl]-2-

- 10 (hydroxymethyl)piperazine-1-carboxylate (153 mg, 0.2 mmol) in THF (10 mL) was added 3M hydrochloric acid (2 mL) at room temperature. The resultant mixture was stirred for 10 h and then adjusted to pH=7-8 with ammonia solution. The mixture was poured into water (30 mL) and then extracted with dichloromethane / isopropanol (100 / 10 mL), the organic layer was concentrated to give a red oil, which was purified by prep. HPLC to provide the title compound
- 15 (18 mg, 13.3 % yield) as a white powder. MS (ESI, m/z): 666.2 [M+H]⁺.

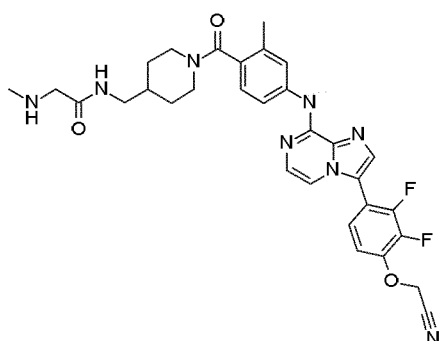
The following example was prepared in analogy to Reference Example 186

Ex.	Name	Structure	ESI MS [M+H] ⁺	Starting Material
REF 187	2-[4-[8-[3-chloro-4-[4-[(3S)-3-(hydroxymethyl)piperazine-1-carbonyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-	 Chiral	666.2	Intermediate 96 and tert-butyl (S)-2-(hydroxymethyl)piperazine-1-carboxylate

	phenoxy]acetonitrile formate			
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Reference Example 188

N-[[1-[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]-2-(methylamino)acetamide



5

Step 1:

tert-butyl N-[2-[[1-[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methylamino]-2-oxo-ethyl]-N-methyl-carbamate

To a solution of intermediate REF 64 (106 mg, 0.2 mmol), N-(tert-butoxycarbonyl)-N-methylglycine (57 mg, 0.3 mmol) in anhydrous DMF (10 mL) was added DIPEA (52 mg, 0.4 mmol) and then the resultant mixture was stirred for 30 min at room temperature, HATU (152 mg, 0.4 mmol) was added in the mixture and stirred for extra 10 h. The mixture was poured into water (50 mL) and the aqueous solution was extracted with DCM (50 mL×2). The organic layers were combined and washed with water and brine, dried over anhydrous sodium sulphate and concentrated under reduced pressure to give a red oil, which was used in next step without purification. MS (ESI, m/z): 703.2 [M+H]⁺.

15

Step 2:

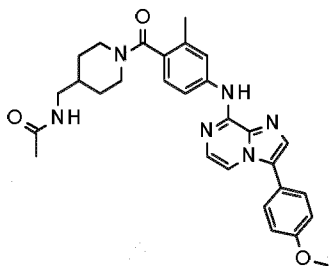
N-[[1-[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]-2-(methylamino)acetamide

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To a solution of tert-butyl (2-(((1-(4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)methyl)amino)-2-oxoethyl)(methyl)carbamate (140 mg, 0.2 mmol) in THF (5 mL) was added 3M aq. hydrochloric acid (2.0 mL) at room temperature. The resultant mixture was stirred for 10 h and then adjusted to pH=7-8 with aq. ammonia. The mixture was poured into water (25 mL) and then extracted with dichloromethane / isopropanol (50 / 5 mL), the organic layer was concentrated to give a red oil, which was purified by prep. HPLC to provide the title compound (25 mg, 20.3 % yield) as a white powder. MS (ESI, m/z): 603.2 [M+H]⁺.

Reference Example 189

10 N-((1-(4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)methyl)acetamide

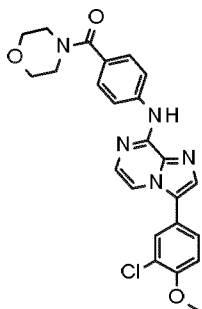


tert-Butyl ((1-(4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)methyl)carbamate (Intermediate obtained in the preparation of Reference Example 34, 200 mg) was treated with 1.05eq acetyl chloride (0.032 mL) in 5 mL AcOEt/EtOH (9/1) the mixture was stirred overnight at room temperature. A mixture of Reference Example 34 and the title compound was obtained, which was separated by prep. HPLC. White powder (44 mg), MS (ESI, m/z): 513.4.

Reference Example 190

20 (4-((3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)(morpholino)methanone

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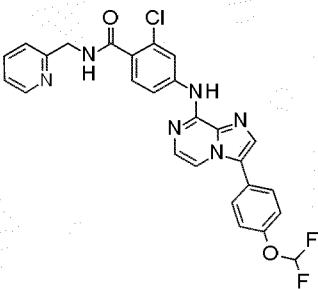
A mixture of (4-aminophenyl)(morpholino)methanone (31 mg), Intermediate 15 (29.4 mg), potassium carbonate (27.6 mg), t-Bu-X-phos (2 mg) and Pd₂(dba)₃ (1 mg) in dioxane was stirred at 100 °C overnight. DMSO was added, the mixture was filtered over Celite and purified by prep. HPLC to give the title compound (9 mg) as a colorless solid.

MS (ESI, m/z): 464.2

The following examples were prepared in analogy:

Ex.	Name	Structure	MS ESI [M+H] ⁺	Starting material
110	2-chloro-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methylbenzamide		444.3	Intermediate 8 and 4-amino-2-chloro-N-methylbenzamide

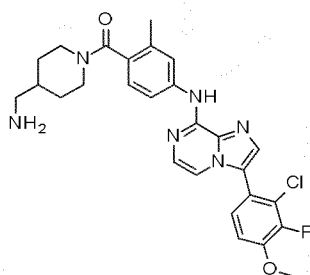
-235-

111	2-chloro-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(pyridin-2-ylmethyl)benzamide		521.2	Intermediate 8 and 4-amino-2-chloro-N-(pyridin-2-ylmethyl)benzamide
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Reference Example 191

[4-(aminomethyl)-1-piperidyl]-[4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone hydrochloride

5

**Step 1: tert-butyl N-[[1-(2-methyl-4-nitro-benzoyl)-4-piperidyl]methyl]carbamate**

A mixture of 2-methyl-4-nitro-benzoic acid (1.00 g, 5.52 mmol), HATU (2.52 g, 6.62 mmol) and DIPEA (2.88 mL, 16.56 mmol) in DMF (25 mL) was stirred at 15°C for 0.5h. Then 4-(tert-butoxycarbonylaminomethyl) piperidine (1.42 g, 6.62 mmol) was added and the reaction was stirred at 15 °C for 16 h. The reaction mixture was diluted with H₂O (50 mL) and extracted with ethyl acetate. The organic phase was washed with brine, dried over anhydrous sodium sulphate, concentrated under reduced pressure and purified by flash column chromatography (eluting with DCM/MeOH=50/1) to afford desired compound (2.00 g) as a light yellow solid. MS obsd. (ESI⁺)

15 [(M+Na)⁺]: 400

Step 2: tert-butyl N-[[1-(4-amino-2-methyl-benzoyl)-4-piperidyl]methyl]carbamate

A mixture of tert-butyl N-[[1-(2-methyl-4-nitro-benzoyl)-4-piperidyl]methyl]carbamate

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(1.00 g, 2.65 mmol) and palladium on charcoal (100 mg, 10 wt.%) in methanol (10 mL) was stirred at 15 °C under H₂ for 16 h. The catalyst was filtered off and the filtrate was concentrated under reduced pressure to give desired compound (900 mg) as a red oil which was used directly for the next step.

5 **Step 3: tert-butyl N-[[1-[4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate**

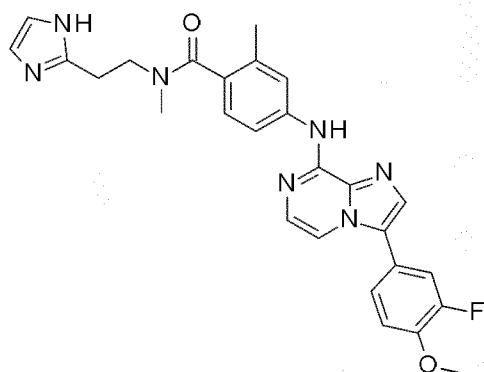
A mixture of intermediate 70 (50 mg, 0.16 mmol) and tert-butyl N-[[1-(4-amino-2-methyl-benzoyl)-4-piperidyl]methyl]carbamate (100 mg, 0.29 mmol) in acetonitrile (0.9 mL) and acetic acid (0.1 mL) was stirred at 90 °C for 16 h. The mixture was cooled to RT and concentrated under reduced pressure. The residue was purified by prep-TLC (DCM/MeOH=20/1) to afford desired compound (20 mg) as a white oil. MS obsd. (ESI⁺) [(M+H)⁺] : 623.1

10 **Step 4: [4-(aminomethyl)-1-piperidyl]-[4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone hydrochloride**

To a stirred solution of tert-butyl N-[[1-[4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate (20 mg, 0.03 mmol) in methanol (0.5 mL) was added a solution of HCl in dioxane (0.04 mL 4.0 M) drop wise. The reaction mixture was stirred at 15 °C for 2 h. The reaction mixture was concentrated under reduced pressure and the residue was purified by prep. HPLC to give the title compound (5.8 mg) as a white solid. MS obsd. (ESI⁺) [(M+H)⁺]: 523.2.

20 **Example 112**

4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(1H-imidazol-2-yl)ethyl]-N,2-dimethyl-benzamide



Step 1: N-(3-hydroxypropyl)-N,2-dimethyl-4-nitro-benzamide

To a solution of 2-methyl-4-nitro-benzoic acid (1.0 g, 5.52 mmol) in DMF (10 mL) was added HATU (2.73 g, 7.18 mmol), 3-(methylamino)propan-1-ol (590 mg, 6.62 mmol) and triethylamine (1.68 g, 16.6 mmol). The mixture was stirred at 25 °C for 12 h and then diluted
5 with ethyl acetate. The resulting mixture was washed with water and brine successively, dried over anhydrous sodium sulphate, concentrated under reduced pressure. The residue was purified by flash column chromatography (eluted with DCM/MeOH=20) to give the title compound (1.2 g) as a light yellow oil.

Step 2: N,2-dimethyl-4-nitro-N-(3-oxopropyl)benzamide

10 To a stirred solution of N-(3-hydroxypropyl)-N,2-dimethyl-4-nitro-benzamide (900 mg, 3.57 mmol) and TEMPO (56 mg, 0.36 mmol) in DCM (10 mL) was added $\text{PhI}(\text{OAc})_2$ (1.38 g, 4.28 mmol) slowly. The reaction was stirred at 20 °C for 1 h and then quenched with sat. Na_2SO_3 solution. The resulting mixture was extracted with DCM. The DCM layer was washed with brine, dried over anhydrous sodium sulphate, concentrated under reduced pressure and purified
15 by flash column chromatography to afford the title compound (460 mg) as a light yellow oil.

Step 3: N-[2-(1H-imidazol-2-yl)ethyl]-N,2-dimethyl-4-nitro-benzamide

To a stirred solution of N,2-dimethyl-4-nitro-N-(3-oxopropyl)benzamide (450 mg, 1.8 mmol) and ammonium hydroxide (1.76 g, 12.6 mmol) in methanol (5 mL) was added glyoxal (230 mg, 3.96 mmol) slowly. The reaction was stirred at 20 °C for 12 h. The mixture was diluted with H_2O
20 (20 mL) and extracted with DCM (30 mL). The organic phase was washed with brine, dried over anhydrous sodium sulphate, concentrated under reduced pressure to afford the title compound (450 mg) as a light yellow oil.

Step 4: 4-amino-N-[2-(1H-imidazol-2-yl)ethyl]-N,2-dimethyl-benzamide

Into a stirred solution of N-[2-(1H-imidazol-2-yl)ethyl]-N,2-dimethyl-4-nitro-benzamide (200
25 mg, 0.69 mmol) in methanol (5 mL) was added Pd on charcoal (74 mg, 10 wt.%). The reaction was stirred under H_2 balloon at 20 °C for 1 h. The catalyst was filtered off and the filtrate was concentrated under reduced pressure to afford the title compound (60 mg) as a light yellow oil which was used directly in next step.

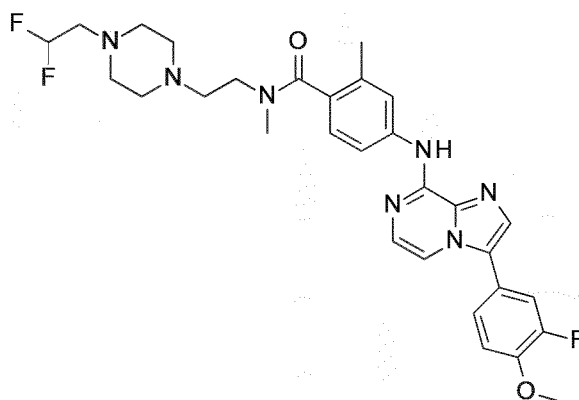
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Step 5: 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(1H-imidazol-2-yl)ethyl]-N,2-dimethyl-benzamide

To a solution of Intermediate 3 (60 mg, 0.22 mmol) in tert-butanol (2 mL) was added BrettPhos-Pd-G3 (196 mg, 0.22 mmol, CAS#1470372-59-8), 4-amino-N-[2-(1H-imidazol-2-yl)ethyl]-N,2-dimethyl-benzamide (59 mg, 0.23 mmol), and potassium carbonate (30 mg, 0.22 mmol). The mixture was stirred at 100 °C for 12 h under N₂. After cooled to RT, the reaction mixture was diluted with ethyl acetate (100 mL). The resulting mixture was washed with water and brine successively, dried over anhydrous Na₂SO₄, concentrated under reduced pressure to afford crude product as a yellow oil. It was purified by prep-HPLC to give the title compound (37 mg) as a white solid. MS obsd. (ESI⁺) [(M+H)⁺]: 500.1

Example 113:

N-[2-[4-(2,2-difluoroethyl)piperazin-1-yl]ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide; formic acid



15

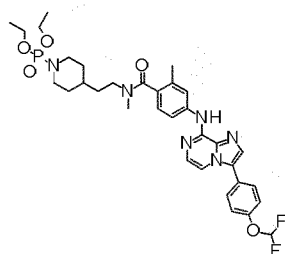
To a solution of 114 (50 mg, 0.09 mmol) in DMF (1 mL) was added potassium carbonate (37 mg, 0.27 mmol) and 1,1-difluoro-2-iodoethane (21 mg, 0.11 mmol). The reaction was stirred at 50 °C for 12 h and then was diluted with ethyl acetate. The resulting mixture was washed with water and brine successively, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to afford crude product as a yellow oil. It was purified by prep-HPLC to give the title compound (11 mg) as a white solid. MS obsd. (ESI⁺) [(M+H)⁺]: 582.

20

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Example 115:

N-[2-(1-diethoxyphosphoryl-4-piperidyl)ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide

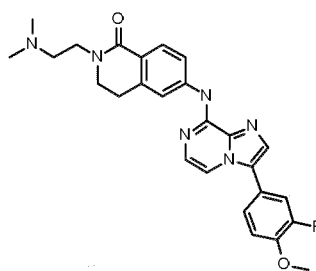


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Into a stirred solution of Example 81 (200 mg, 0.35 mmol) and triethylamine (0.15 mL, 1.05 mmol) in DCM (4 mL) was added diethyl chlorophosphate (200 mg, 1.16 mmol) slowly. The reaction was stirred at 15 °C for 2 h. The reaction was quenched with H₂O (5 mL) and extracted with DCM (10 mL x 3). The organic phase was washed with brine (10 mL), dried over anhydrous Na₂SO₄, concentrated under reduced pressure and purified by prep-HPLC to afford the title compound (81.4 mg) as a white solid. MS obsd. (ESI⁺) [(M+23)⁺] : 671.1.

Example 116:

2-[2-(dimethylamino)ethyl]-6-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3,4-dihydroisoquinolin-1-one



15

Step 1: 6-bromo-2-[2-(dimethylamino)ethyl]-3,4-dihydroisoquinolin-1-one

Into a stirred solution of 6-bromo-3, 4-dihydro-2H-isoquinolin-1-one (200 mg, 0.88 mmol) in DMF (5 mL) was added sodium hydride (53 mg, 1.33 mmol, 60 wt%) portion wise at 15 °C. The mixture was stirred for 0.5 h. Then (2-bromoethyl)dimethylamine hydrobromide (309 mg,

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1.33 mmol) was added and the reaction was stirred at 15 °C for 16 h. Sat. aq. NH₄Cl was added to quench the reaction. The obtained mixture was diluted with H₂O (10 mL) and extracted with ethyl acetate. The organic phase was washed with brine, dried over anhydrous Na₂SO₄, concentrated under reduced pressure and purified by prep-TLC (DCM/MeOH=20, R_f=0.1) to give the title compound (120 mg) as a light yellow oil.

Step 2: 3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-amine

A mixture of 8-chloro-3-iodo-imidazo[1,2-a]pyrazine (500 mg, 1.8 mmol) and a solution of ammonium hydroxide (10 mL, 17.83 mmol) in 1,4-dioxane (5 mL) was stirred at 100 °C for 16 h in a sealed vessel. The reaction mixture was cooled and concentrated under reduced pressure. The residue was diluted with H₂O (20 mL) and extracted with DCM. The organic phase was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give 3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-amine (300 mg) as a brown solid.

Step 3: 2-[2-(dimethylamino)ethyl]-6-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3,4-dihydroisoquinolin-1-one

A mixture of 3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-amine (100 mg, 0.39 mmol), 6-bromo-2-[2-(dimethylamino)ethyl]-3,4-dihydroisoquinolin-1-one (115 mg, 0.39 mmol), cesium carbonate (378 mg, 1.16 mmol), (R)-BINAP (48 mg, 0.08 mmol) and Pd₂(dba)₃ (22 mg, 0.04 mmol) in 1,4-dioxane (3 mL) was stirred under nitrogen at 100 °C for 16 h. The reaction mixture was cooled and filtered. The filtrate was concentrated under reduced pressure and purified by prep-TLC (DCM/MeOH=20, R_f = 0.2) to get a crude product. It was re-purified by trituration (CH₃OH, 2 mL) to afford the title compound (17.9 mg) as a white solid. MS obsd. (ESI⁺) [(M+H)⁺] : 475.1.

Reference Example 192

7-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2,3,4,5-tetrahydro-2-benzazepin-1-one hydrochloride

Step 1: 6-aminotetralin-1-one oxime

A mixture of 6-amino-1,2,3,4-tetrahydronaphthalen-1-one (1.0 g, 6.2 mmol), hydroxylamine hydrochloride (474 mg, 6.82 mmol), sodium acetate (1.12 g, 13.65 mmol) in ethanol (10 mL) and water (3.3 mL) was stirred at 90 °C for 4 h. The mixture was cooled to RT and diluted with

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H₂O (20 mL). The precipitate was collected by filtration and washed with water and dried over high vacuum to give 6-aminotetralin-1-one oxime (880 mg) as a white solid.

Step 2: 7-amino-2,3,4,5-tetrahydro-2-benzazepin-1-one

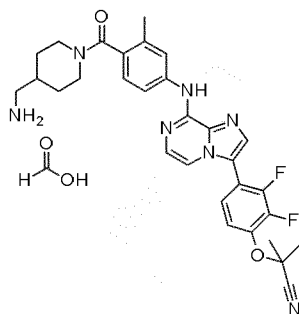
A mixture of 6-aminotetralin-1-one oxime (880 mg, 4.99 mmol) in PPA (10 mL) was stirred at 120 °C for 2 h. The mixture was cooled to 90 °C and then poured onto ice. The resulting mixture was neutralized with 4N aq. NaOH and extracted with ethyl acetate. The ethyl acetate layer was washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure to give crude compound (850 mg) (mixed of another isomer) as brown solid.

Step 3: 7-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2,3,4,5-tetrahydro-2-benzazepin-1-one hydrochloride

A mixture of Intermediate 3 (150 mg, 0.540 mmol), crude 7-amino-2,3,4,5-tetrahydro-2-benzazepin-1-one (105 mg, 0.600 mmol) in acetonitrile (1.8 mL) and acetic acid (0.200 mL) was stirred at 90 °C for 16 h. The mixture was concentrated under reduced pressure and the residue was purified by prep. HPLC to give 7-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2,3,4,5-tetrahydro-2-benzazepin-1-one (18.7 mg) as a red solid. (ESI⁺) [(M+H)⁺]: 418

Reference Example 193

2-[4-[8-[4-[4-(aminomethyl)piperidine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]-2-methyl-propanenitrile;formic acid



Step 1:

Ethyl 2-(4-bromo-2,3-difluoro-phenoxy)-2-methyl-propanoate

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4-Bromo-2,3-difluorophenol (6 g, 28.7 mmol), ethyl 2-bromo-2-methylpropanoate (6.72 g, 34.5 mmol), Cs_2CO_3 (9.35 g, 28.7 mmol) and tetrabutylammoniumiodide (530 mg, 1.44 mmol) were suspended in DMF (30 mL). The resulting mixture was heated at 80 °C overnight. Then the mixture was cooled, diluted with water and extracted with ethyl ether. The combined organic phases were dried and concentrated. The residue was purified by flash column chromatography to give the title compound (6 g, 64.7 % yield).

Step 2:**2-(4-bromo-2,3-difluoro-phenoxy)-2-methyl-propanoic acid**

Ethyl 2-(4-bromo-2,3-difluorophenoxy)-2-methyl-propanoate (4.3 g, 13.3 mmol) and NaOH (1.06 g, 26.6 mmol) was dissolved in a mixed solution of MeOH (36 mL), THF (18 mL) and water (12 mL). The reaction solution was stirred at room temperature for 2 h. Then the solution was acidified by 12 N HCl aqueous solution to pH 2-3. The water layer was extracted with ethyl acetate, dried over anhydrous MgSO_4 and concentrated to give the title compound as a white solid (3.5 g, 89.1 % yield).

Step 3:**2-(4-bromo-2,3-difluoro-phenoxy)-2-methyl-propanamide**

A mixture of 2-(4-bromo-2,3-difluorophenoxy)-2-methyl-propanoic acid (3.3 g, 11.2 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.57 g, 13.4 mmol), 1-hydroxybenzotriazole (2.27 g, 16.8 mmol) and DIPEA (2.17 g, 2.93 mL, 16.8 mmol) in THF (30 mL) was stirred at room temperature for 2 h. Then aq. 25% NH_3 (10 mL) was added. The mixture was stirred overnight and then quenched with water. The aqueous layer was extracted with DCM. The combined organic layers were washed with saturated aq. NaHCO_3 , brine, dried and concentrated. The residue was purified by flash column chromatography to give the title compound as a yellow solid (2 g, 60.8 % yield).

Step 4:**2-(4-bromo-2,3-difluoro-phenoxy)-2-methyl-propanenitrile**

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To a solution of 2-(4-bromo-2,3-difluorophenoxy)-2-methyl-propanamide (2 g, 6.8 mmol) and Et₃N (4.13 g, 5.69 mL, 40.8 mmol) in dichloromethane (40 mL) was added trifluoroacetic anhydride (8.57 g, 5.76 mL, 40.8 mmol) at 0 °C. After the addition, the solution was allowed to reach room temperature and stirred for 2 h. Then the mixture was heated at 70 °C overnight. The reaction was concentrated and diluted with water. The water phase was adjusted to pH 8-9 by NaHCO₃ aqueous solution. The water phase was extracted with DCM, dried and concentrated. The residue was used into next step reaction without further purification.

Step 5:**2-[2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]-2-methyl-propanenitrile**

A mixture of 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (2.48 g, 9.78 mmol), 2-(4-bromo-2,3-difluorophenoxy)-2-methylpropanenitrile (1.8 g, 6.52 mmol), 1,1'-

Bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (532 mg, 652 μmol) and potassium acetate (1.28 g, 13 mmol) in 1,4-dioxane (20 mL) was stirred at 80 °C overnight. Then the mixture was filtered and then concentrated. The residue was used in the next step reaction directly without further purification.

Step 6:**tert-butyl N-[[1-[4-[[3-[4-(1-cyano-1-methyl-ethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate**

To a solution of tert-butyl ((1-(4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)methyl)carbamate (intermediate 73, 600 mg, 1.02 mmol) in water (5 mL) and THF (10 mL) was added 2-(2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)-2-methylpropanenitrile (the crude product from step 5), 1,1'-

Bis(diphenylphosphino)ferrocene-palladium(II) dichloride dichloromethane complex (166 mg, 203 μmol) and potassium phosphate tribasic (647 mg, 616 μl, 3.05 mmol) and then the mixture was degassed for 5 min with nitrogen and then stirred overnight at 70 °C. The mixture was filtered. The solution was concentrated and the water layer was extracted with DCM. The organic layer was concentrated and the residue was purified by prep. HPLC to give the title compound (400 mg). MS (ESI, m/z): 660.3 [M+H]⁺

Step 7:**2-[4-[8-[4-[4-(aminomethyl)piperidine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]-2-methyl-propanenitrile formate**

tert-butyl ((1-(4-((3-(4-((2-cyanopropan-2-yl)oxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)methyl)carbamate (400 mg, 606 μ mol) in TFA (5 mL) and DCM (10 mL) was stirred at room temperature for 2 h. Then the mixture was neutralized by NaHCO₃ aqueous solution. The water layer was extracted with DCM. The organic layer was dried and concentrated. The residue was purified by prep-HPLC to give the title compound as a white powder (120 mg). MS (ESI, m/z): 560.3 [M+H]⁺

10 Intermediate 99**1-[2,3-Difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]cyclopropanecarbonitrile****Step 1:****15 methyl 4-bromo-2-(4-bromo-2,3-difluoro-phenoxy)butanoate**

K₂CO₃ (6.61 g, 47.8 mmol) was added into a solution of 4-bromo-2,3-difluorophenol (5 g, 23.9 mmol) in dry DMF (20 mL). The mixture was stirred at RT for 10 min. To the mixture was added methyl 2,4-dibromobutanoate (6.22 g, 23.9 mmol) dropwise. The resulting mixture was stirred at RT for 3h. The mixture was diluted with ethyl acetate (60 mL), removed inorganic solid by filtration, then washed with water and brine. The organic phase was dried over flash column chromatography and concentrated. The residue was purified by flash column chromatography to give the title compound as an oil (4.7 g, 50 % yield).

Step 2:**Methyl 1-(4-bromo-2,3-difluoro-phenoxy)cyclopropanecarboxylate**

25 Methyl 4-bromo-2-(4-bromo-2,3-difluorophenoxy)butanoate (4.7 g, 12.1 mmol) was dissolved in dry THF (30 mL) under N₂ protection, cooled with ice-acetone bath. To the mixture was added solid potassium tert-butoxide (1.36 g, 12.1 mmol) in portions. The resulting mixture was stirred

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at -10°C for 30 min, then at room temperature for 2 h. The reaction was dried *in vacuo*, the residue was directly purified by flash column chromatography to afford the title compound (2 g, 53.8 % yield).

Step 3:

5 **1-[2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]cyclopropanecarbonitrile**

The title compound was prepared in similar procedures to the step2, step 3, step 4 and step 5 of Reference Example 193 using methyl 1-(4-bromo-2,3-difluorophenoxy)cyclopropanecarboxylate as the starting materials.

10 **Intermediate 100**

2-[[2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]methyl]cyclopropanecarbonitrile

Step 1:

15 **ethyl 2-(p-tolylsulfonyloxymethyl)cyclopropanecarboxylate**

To a solution of ethyl 2-(hydroxymethyl)cyclopropane-1-carboxylate (4 g, 27.7 mmol) in DCM (30 mL) was added Et₃N (5.62 g, 7.73 mL, 55.5 mmol), DMAP (339 mg, 2.77 mmol) and 4-methylbenzenesulfonyl chloride (6.35 g, 33.3 mmol) at 0 °C. The yellow reaction mixture was stirred for 3 hs at room temperature. Then the reaction mixture was poured on aqueous HCl (30 mL) and DCM (30 mL) and the layers were separated. The aqueous layer was extracted with DCM. The organic layer was concentrated and the residue was purified by flash column chromatography to give the title compound as an oil (4.7 g, 56.8 % yield).

Step 2:

ethyl 2-[(4-bromo-2,3-difluoro-phenoxy)methyl]cyclopropanecarboxylate

25 4-bromo-2,3-difluorophenol (9 g, 43.1 mmol), ethyl 2-((tosyloxy)methyl)cyclopropane-1-carboxylate (12.8 g, 43.1 mmol) and Cs₂CO₃ (14 g, 43.1 mmol) was suspended in DMF (40 mL). The resulting mixture was heated at 65 °C overnight. Then the mixture was allowed to cool,

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diluted with water and extracted with ethyl ether. The combined organic phases were washed with Na₂CO₃ aqueous solution and concentrated. The residue was purified by flash column chromatography to give the title compound as an oil (8.5 g, 58.9% yield).

Step 3:

5 **2-[[2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]methyl]cyclopropanecarbonitrile**

The title compound was prepared in similar procedures to the step2, step 3, step 4 and step 5 of Reference Example 193 using ethyl 2-[(4-bromo-2,3-difluorophenoxy)methyl]cyclopropanecarboxylate as the starting materials.

10 **Intermediate 101**

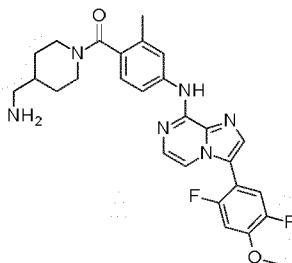
2-(3-fluoro-4-methylsulfanyl-phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

A mixture of 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (2.54 g, 10 mmol), 4-bromo-2-fluoro-1-methylsulfanyl-benzene (2.2 g, 10 mmol), 1,1'-

bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (653 mg, 0.8 mmol) and potassium acetate (1.96 g, 20 mmol) in 1,4-dioxane (20 mL) was stirred at 80 °C overnight. Then the mixture was poured into water and extracted with ethyl acetate. The organic layer was dried and concentrated. The residue was purified by flash column chromatography to afford the title compound as an oil (1.6 g, 61 % yield).

20 **Reference Example 194**

(4-(aminomethyl)piperidin-1-yl)(4-((3-(2,5-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone



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Step1:

tert-butyl N-[[1-[4-[[3-(2,5-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate

To a solution of tert-butyl N-[[1-[4-[[3-iodoimidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate (intermediate 73, 200 mg, 339 μ mol) in water (2.5mL) and THF (5 mL) was added (2,5-difluoro-4-methoxyphenyl)boronic acid (82.8 mg, 440 μ mol), 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (55.3 mg, 67.7 μ mol) and potassium phosphate tribasic (216 mg, 1.02 mmol). Then the mixture was degassed for 5 min with nitrogen and then stirred overnight at 80 °C. After cooling to room temperature, the mixture was concentrated and DCM was added. The organic layer was dried over Na₂SO₄ and concentrated *in vacuo*. The residue was used into next step reaction directly. MS (ESI, m/z): 607 [M+H]⁺

Step2:

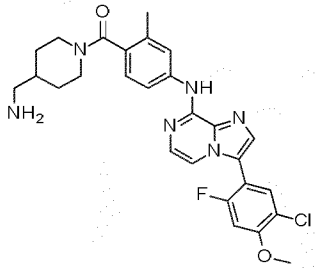
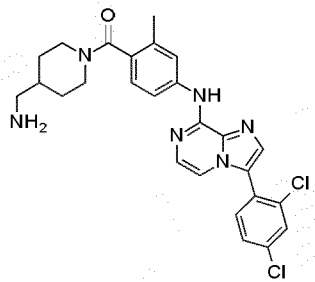
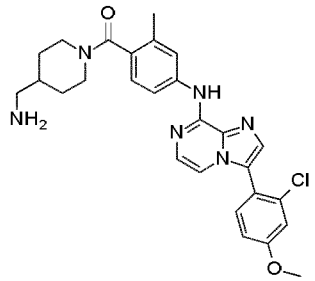
(4-(aminomethyl)piperidin-1-yl)(4-((3-(2,5-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone

To a solution of tert-butyl N-[[1-[4-[[3-(2,5-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate from step 1 in DCM (5 mL) was added CF₃COOH (5 mL). The mixture was stirred for 2h at room temperature. Then the mixture was concentrated and NaHCO₃ aqueous solution was added to neutralize the solution to pH 8-9. The water phase was extracted with DCM. The organic phase was concentrated *in vacuo* and the residue was purified by prep-HPLC to afford the title compound (37 mg) as a solid. MS (ESI, m/z): 507.1 [M+H]⁺

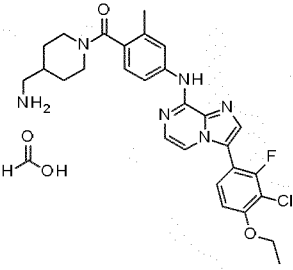
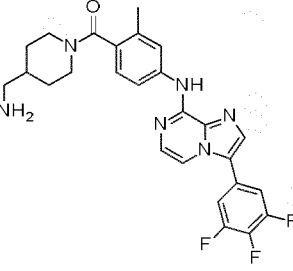
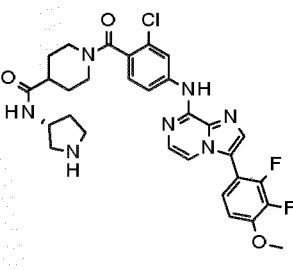
The following examples were prepared in analogy to Reference Example 194:

Ex.	Name	Structure	MS ESI [M+H] ⁺	Starting Material

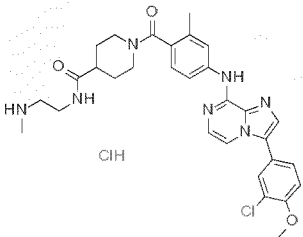
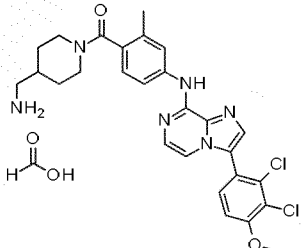
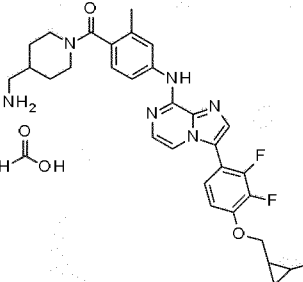
-248-

REF 195	(4-(aminomethyl)piperidin-1-yl)(4-((3-(5-chloro-2-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone		523.1	Intermediate 73 and (5-chloro-2-fluoro-4-methoxyphenyl)boronic acid
REF 196	(4-(aminomethyl)piperidin-1-yl)(4-((3-(2,4-dichlorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone		509.1	Intermediate 73 and (2,4-dichlorophenyl)boronic acid
REF 197	(4-(aminomethyl)piperidin-1-yl)(4-((3-(2-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone		505.1	Intermediate 73 and (2-chloro-4-methoxyphenyl)boronic acid

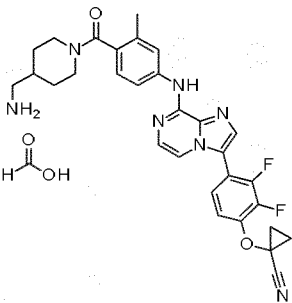
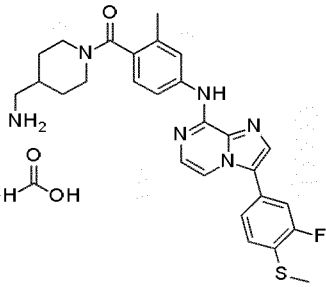
-249-

REF 198	(4-(aminomethyl)piperidin-1-yl)(4-((3-(3-chloro-4-ethoxy-2-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone formate		537.2	Intermediate 73 and (3-chloro-4-ethoxy-2-fluorophenyl)boronic acid
REF 199	(4-(aminomethyl)piperidin-1-yl)(2-methyl-4-((3-(3,4,5-trifluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)methanone		495.3	Intermediate 73 and (3,4,5-trifluorophenyl)boronic acid
REF 200	(R)-1-(2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)-N-(pyrrolidin-3-yl)piperidine-4-carboxamide hydrochloride		611.5	Intermediate 74 and (2,3-difluoro-4-methoxyphenyl)boronic acid

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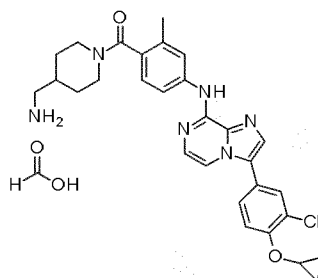
REF 201	1-(4-((3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-(2-(methylamino)ethyl)piperidine-4-carboxamide hydrochloride		576.2	Intermediate 102 and (3-chloro-4-methoxyphenyl)boronic acid
REF 202	[4-(aminomethyl)-1-piperidyl]-[4-[[3-(2,3-dichloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]methanone formate		539.2	Intermediate 73 and (2,3-dichloro-4-methoxyphenyl)boronic acid
REF 203	2-[[4-[8-[4-[4-(aminomethyl)piperidine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]methyl]cyclopropanecarbonitrile formate		572.6	Intermediate 73 and intermediate 100

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REF 204	1-[4-[8-[4-[4-(aminomethyl)piperidine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]cyclopropa ncarbonitrile formate		558.3	Intermediate 73 and intermediate 99
REF 205	[4-(aminomethyl)-1-piperidyl]-[4-[[3-(3-fluoro-4-methylsulfanyl-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone formate		505.2	Intermediate 73 and intermediate 101

Reference Example 206

[4-(aminomethyl)-1-piperidyl]-[4-[[3-[3-chloro-4-(cyclopropoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone formate

**Step 1:**

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4-bromo-2-chloro-1-(cyclopropoxy)benzene

Bromocyclopropane (8.75 g, 72.3 mmol) was added dropwise over 10 mins to a stirred solution of 4-bromo-2-chlorophenol (3 g, 14.5 mmol) and Cs_2CO_3 (11.8 g, 36.2 mmol) in dimethylacetamide (45 mL). The mixture was heated to 150 °C and stirred at this temperature for 16 h. Then the mixture was poured into water. The water layer was extracted with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulphate and concentrated *in vacuo*. The residue was purified by flash column chromatography to give the title compound (3 g). MS (ESI, m/z): 247 $[\text{M}+\text{H}]^+$

Step 2:**2-[3-chloro-4-(cyclopropoxy)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane**

Under N_2 atmosphere, a mixture of 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (3.69 g, 14.5 mmol), 4-bromo-2-chloro-1-cyclopropoxybenzene (3g, 12.1 mmol), potassium acetate (2.38 g, 24.2 mmol) and 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (990 mg, 1.21 mmol) in 1,4-dioxane (50 mL) was stirred at 80 °C overnight. After cooling to room temperature, the mixture was concentrated and the residue was dissolved in DCM. The organic phase was washed with water, dried and concentrated. The residue was purified by flash column to give the title compound (2.6 g) as a solid.

Step 3:**tert-butyl N-[[1-[4-[[3-[3-chloro-4-(cyclopropoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate**

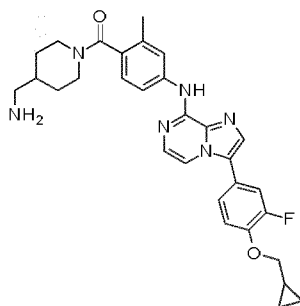
To a solution of tert-butyl N-[[1-[4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate (300 mg, 508 μmol) in water (2.5 mL) and THF (5 mL) was added 2-(3-chloro-4-cyclopropoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (195 mg, 660 μmol), 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (41.5 mg, 50.8 μmol) and potassium phosphate tribasic (324 mg, 308 μl , 1.52 mmol). Then the mixture was degassed for 5 min with nitrogen and then stirred overnight at 70 °C. After cooling to room temperature, the mixture was concentrated. The water phase was extracted with DCM. The organic phase was dried and concentrated to give the crude product (300 mg). The

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crude product was used into next step reaction directly without further purification. MS (ESI, m/z): 631 [M+H]⁺

Step 4:**(4-(aminomethyl)piperidin-1-yl)(4-((3-(3-chloro-4-cyclopropoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone formate**

A solution of tert-butyl N-[[1-[4-[[3-[3-chloro-4-(cyclopropoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate (300 mg, 475 μ mol) in TFA (5 mL) and DCM (5 mL) was stirred at room temperature for 2 h. Then the solution was concentrated and the residue was diluted with water and DCM. The mixture solution was basified to pH 8-9 with K₂CO₃ aqueous solution. The water layer was extracted with DCM. The combined organic phases were dried and concentraed. The residue was purified by prep-HPLC to give the title compound (14 mg) as a solid. MS (ESI, m/z): 531.2 [M+H]⁺

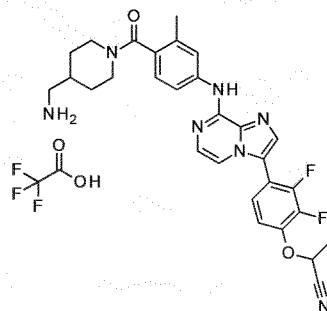
Reference Example 207**(4-(aminomethyl)piperidin-1-yl)(4-((3-(4-(cyclopropylmethoxy)-3-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)methanone**

The title compound was obtained in analogy to Reference Example 206

using (bromomethyl)cyclopropane instead of bromocyclopropane and 4-bromo-2-fluoro-phenol instead of 4-bromo-2-chlorophenol. MS (ESI, m/z): 529.3 [M+H]⁺

Reference Example 208**2-[4-[8-[4-[4-(aminomethyl)piperidine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]propanenitrile; 2,2,2-trifluoroacetic acid**

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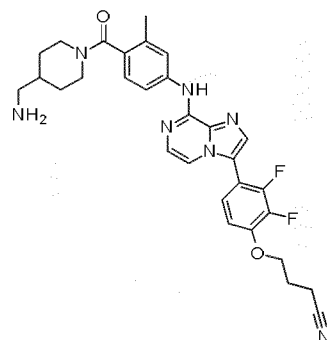


The title compound was obtained in analogy to Reference Example 206

using 2-bromopropanenitrile instead of bromocyclopropane and 4-bromo-2,3-difluoro-phenol instead of 4-bromo-2-chlorophenol. MS (ESI, m/z): 546.5 [M+H]⁺

5 *Reference Example 209*

4-(4-(8-((4-(4-(aminomethyl)piperidine-1-carbonyl)-3-methylphenyl)amino)imidazo[1,2-a]pyrazin-3-yl)-2,3-difluorophenoxy)butanenitrile



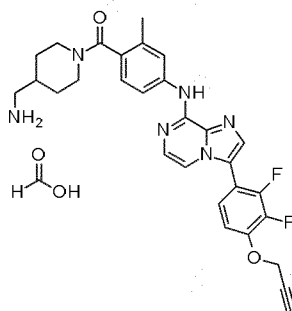
The title compound was obtained in analogy to Reference Example 206

10 using 4-bromobutanenitrile instead of bromocyclopropane and 4-bromo-2,3-difluoro-phenol instead of 4-bromo-2-chlorophenol. MS (ESI, m/z): 560.4 [M+H]⁺

Reference Example 210

[4-(aminomethyl)-1-piperidyl]-[4-[[3-(2,3-difluoro-4-prop-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone;formic acid

-255-

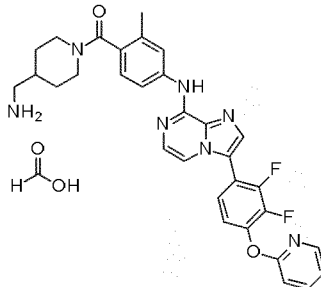


The title compound was obtained in analogy to Reference Example 206

using 3-bromoprop-1-yne instead of bromocyclopropane and 4-bromo-2,3-difluoro-phenol instead of 4-bromo-2-chlorophenol. MS (ESI, m/z): 531.1 $[M+H]^+$

5 **Reference Example 211**

[4-(aminomethyl)-1-piperidyl]-[4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone formate



Step 1:

10 **2-(4-bromo-2,3-difluoro-phenoxy)pyridine**

A mixture of 4-bromo-2,3-difluorophenol (3.5 g, 16.7 mmol), 2-fluoropyridine (2.44 g, 25.1 mmol) and K_2CO_3 (5.79 g, 41.9 mmol) in DMSO (20 mL) was heated at 120 °C for 3 days. Then the mixture was poured into water and extracted with DCM. The organic layer was dried and concentrated. The residue was purified by flash column chromatography to give the title compound as an oil (700 mg, 14.6 % yield).

Step 2:

2-[2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]pyridine

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Under N₂, a mixture of 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (746 mg, 2.94 mmol), 2-(4-bromo-2,3-difluorophenoxy)pyridine (0.7 g, 2.45 mmol), potassium acetate (480 mg, 4.89 mmol) and 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (200 mg, 245 μmol) in 1,4-dioxane (10 mL) was stirred at 80 °C overnight. The reaction solution was filtered and concentrated. The residue was used into next step reaction directly without further purification.

Step 3:

tert-butyl N-[[1-[4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate

A mixture of 2-(2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)pyridine (the crude product from step 2), tert-butyl ((1-(4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)methyl)carbamate (intermediate 73, 400 mg, 677 μmol), potassium phosphate (288 mg, 1.35 mmol) and 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (55.3 mg, 67.7 μmol) in 1,4-dioxane (10 mL) and water (5 mL) was heated at 95 °C for 1 h in a microwave tube. Then the mixture was concentrated and the water layer was extracted with DCM. The organic layer was dried and concentrated. The residue was used into next step reaction directly without further purification.

Step 4:

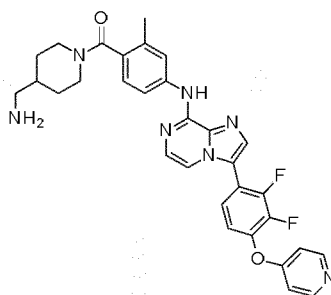
[4-(aminomethyl)-1-piperidyl]-[4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone;formic acid

tert-butyl ((1-(4-((3-(2,3-difluoro-4-(pyridin-2-yloxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidin-4-yl)methyl)carbamate (the crude product from step 3) was dissolved in DCM (5 mL) and TFA (5 mL). The solution was stirred for 1 h. Then the solution was concentrated and the residue was dissolved in DCM. Water (10 mL) was added. The solution was alkalinized by addition of K₂CO₃ to pH 8-9. The water phase was extracted with DCM. The organic phase was concentrated and the residue was purified by prep-HPLC to give the title compound. MS (ESI, m/z):570.2 [M+H]⁺

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Reference Example 212

[4-(aminomethyl)-1-piperidyl]-[4-[[3-[2,3-difluoro-4-(4-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone

**Step 1:****4-(4-bromo-2,3-difluoro-phenoxy)pyridine**

4-bromo-2,3-difluorophenol (3.0 g, 14.4 mmol) in DMA (20 mL) was added potassium tert-butoxide (3.22 g, 28.7 mmol) at 0 °C. The colorless solution was stirred for 1 h at room temperature. Then 4-fluoropyridine hydrochloride (1.92 g, 14.4 mmol) was added. The organic solution was heated at 100 °C overnight. The mixture was poured into water. The water layer was extracted with ethyl acetate. The combined organic layers were washed with saturated NaCl aqueous solution and concentrated. The residue was purified by flash column to give the title compound as an oil (3.3 g, 80% yield).

Step 2:

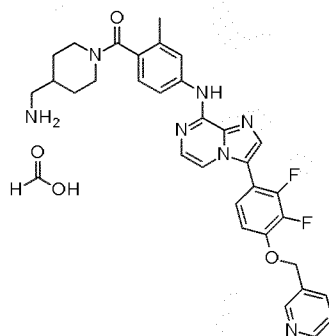
[4-(aminomethyl)-1-piperidyl]-[4-[[3-[2,3-difluoro-4-(4-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone

The title compound was obtained in similar procedures to step 2, step 3 and step 4 of Reference Example 211 using 4-(4-bromo-2,3-difluoro-phenoxy)pyridine as the starting material. MS (ESI, m/z): 570.2 [M+H]⁺

Reference Example 213

[4-(aminomethyl)-1-piperidyl]-[4-[[3-[2,3-difluoro-4-(3-pyridylmethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone formate

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Step 1: 3-[(4-bromo-2,3-difluoro-phenoxy)methyl]pyridine

4-bromo-2,3-difluorophenol (2.09 g, 10 mmol), 3-(chloromethyl)pyridine (1.64 g, 10 mmol), Cs_2CO_3 (3.25 g, 10 mmol) and tetrabutylammoniumiodide (185 mg, 0.5 mmol) was suspended in DMF (15 mL). The resulting mixture was heated to 60 °C overnight. Then the mixture was cooled, diluted with water and extracted with ethyl ether. The combined organic phases were dried and concentrated. The residue was purified by flash column chromatography to give the title compound as a yellow solid (1.6 g, 53% yield).

Step 2:

3-[[2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]methyl]pyridine

Under N_2 , a mixture of 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (1.36 g, 5.3 mmol), 3-[(4-bromo-2,3-difluoro-phenoxy)methyl]pyridine (1.6 g, 5.3 mmol), potassium acetate (1.04 g, 10.6 mmol) and 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (346 mg, 0.424 mmol) in 1,4-dioxane (10 mL) was stirred at 80 °C overnight. The reaction solution was cooled and poured into water. The water phase was extracted with ethyl acetate. The organic phase was concentrated and purified by flash column chromatography to give the title compound as a solid (0.86 g).

Step 3:

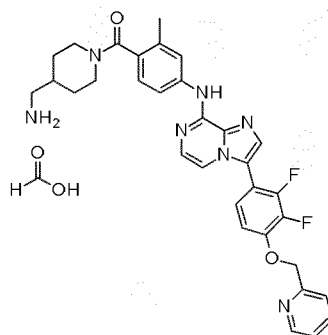
[4-(aminomethyl)-1-piperidyl]-[4-[[3-[2,3-difluoro-4-(3-pyridylmethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone formate

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The title compound was prepared in analogy to Reference Example 194 using intermediate 73 and 3-[[2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]methyl]pyridine as the starting materials. MS (ESI, m/z): 584.2 [M+H]⁺

Reference Example 214

- 5 **[4-(aminomethyl)-1-piperidyl]-[4-[[3-[2,3-difluoro-4-(2-pyridylmethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone;formic acid**

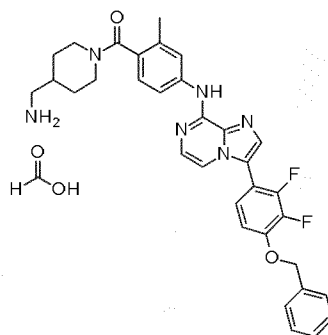


The title compound was obtained in analogy to Reference Example 213

- 10 using 2-(chloromethyl)pyridine instead of 3-(chloromethyl)pyridine. MS (ESI, m/z): 584.3 [M+H]⁺

Reference Example 215

[4-(aminomethyl)-1-piperidyl]-[4-[[3-(4-benzyloxy-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone formate



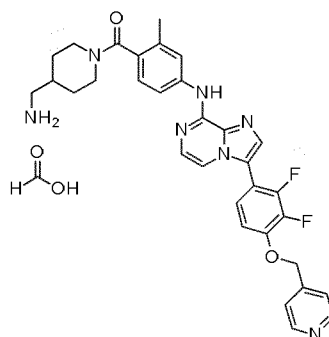
The title compound was obtained in analogy to Reference Example 213

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using chloromethylbenzene instead of 3-(chloromethyl)pyridine. MS (ESI, m/z): 583.2 [M+H]⁺

Reference Example 216

[4-(aminomethyl)-1-piperidyl]-[4-[[3-[2,3-difluoro-4-(4-pyridylmethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone formate

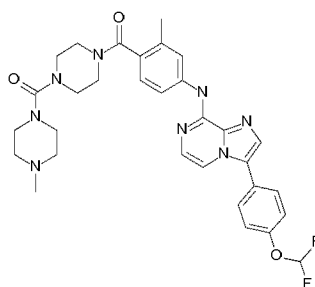


The title compound was obtained in analogy to Reference Example 213

using 4-(chloromethyl)pyridine instead of 3-(chloromethyl)pyridine. MS (ESI, m/z): 584.3 [M+H]⁺

Reference Example 217

[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-(4-methylpiperazine-1-carbonyl)piperazin-1-yl]methanone formate



To a solution of [4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]

-2-methyl-phenyl]-piperazin-1-yl-methanone (Reference Example 218) (100.0 mg, 0.210 mmol, 1 eq.) in ACN (3 mL) was added N,N-diisopropylethylamine (0.11 mL, 0.630 mmol, 3 eq.) and N,N'-carbonyldiimidazole (37.28 mg, 0.230 mmol, 1.1 eq.), then the reaction was stirred at 20 °C

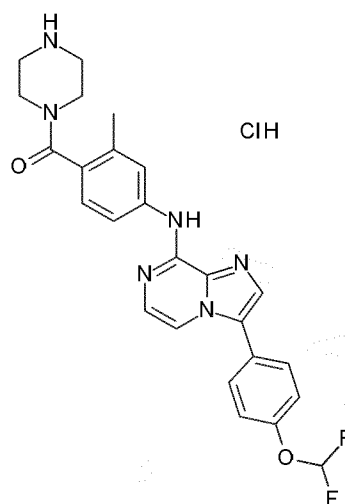
-261-

for 3 h. 1-methylpiperazine (41.87 mg, 0.420 mmol, 2 eq) was added and then stirred at 80 °C for 12 h. After concentration, NMP (3 mL) was added and then stirred at 120 °C for 12 h. The reaction mixture was purified by prep-HPLC to give product 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-(4-methylpiperazine-1-carbonyl)piperazin-1-yl] methanone formate (25.1 mg, 0.040 mmol, 18% yield) as yellow solid.

LC-MS: $[M+H]^+$: 605.2

Reference Example 218

4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-piperazin-1-yl-methanone hydrochloride



Step 1: tert-butyl 4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carboxylate

To a solution of 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoic acid (Intermediate 7) (2.4 g, 5.84 mmol, 1 eq.) in DMF (20 mL) was added 1-BOC-piperazine (1.64 g, 8.78 mmol, 1.5 eq.), N,N-diisopropylethylamine (3.06 mL, 17.54 mmol, 3 eq.) and HATU (4.44 g, 11.7 mmol, 2 eq.), then the reaction was stirred at 25 °C for 12 h. 80 mL of water were added and extracted with ethyl acetate (3x100 mL). The combined organic layers were washed with brine (3x80 mL), dried over Na₂SO₄, filtered and concentrated. 40 mL of MTBE was added to the residue and stirred for 1 h. The suspension was filtered and

dried to give tert-butyl 4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carboxylate (3.4 g, 5.88 mmol, 90 % yield) as yellow solid.

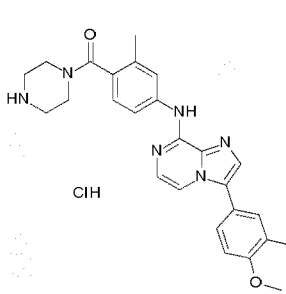
LC-MS: $[M+H]^+$: 579.3

Step 2) Reference Example 218

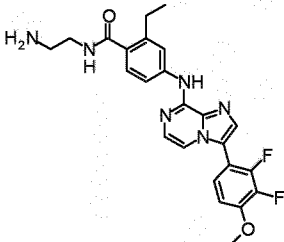
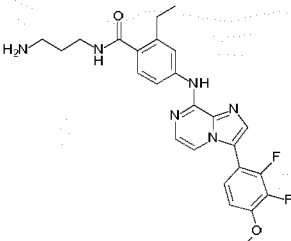
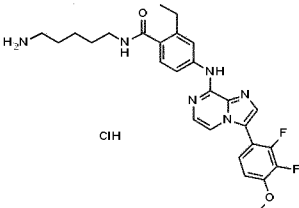
5 [4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-piperazin-1-yl-methanone;hydrochloride

In a 150 mL round-bottomed flask, tert-butyl 4-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carboxylate (Step 1) (3.087 g, 5.18 mmol, Eq: 1) was combined with dioxane (25 mL) to give a light brown suspension. Heating, sonicating
 10 and addition of 1.0 mL MeOH were necessary to get a proper solution. Then hydrogen chloride (4M solution in dioxane) (12.9 mL, 51.8 mmol, Eq: 10) was added slowly. Again 5 mL dioxane were added and the reaction mixture was stirred overnight. Diethylether was added, the suspension sonicated in an ultra sonic bath, filtered and washed with diethylether and dried in high vacuum, leading to the target compound as an off-white solid (2.7 g, yield: 100%). LC-MS:
 15 $[M+H]^+$: 479.3

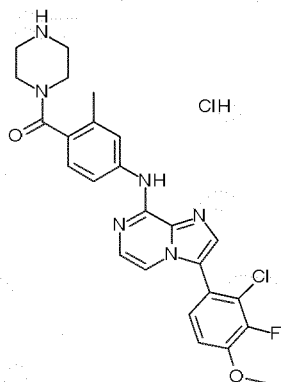
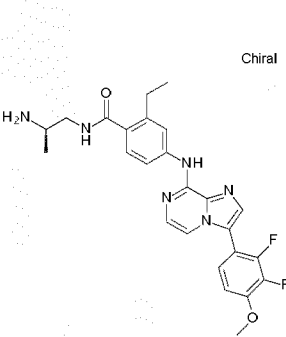
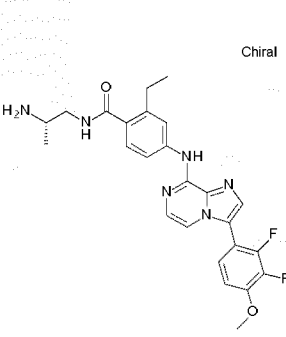
The following Examples and Intermediates were prepared in analogy to Reference Example 218:

Ex.	Name	Structure	MS ESI $[M+H]^+$	Starting Material
REF 219	[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-piperazin-1-yl-methanone hydrochloride		461.1	Intermediate 6. After Step 1, purification by flash chromatography (silica gel, 50g, 0% to 100% DCM/MeOH/NH4OH (95/5/1))

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117	N-(2-aminoethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide; 2,2,2-trifluoroacetic acid		467.3	Intermediate 86 and tert-butyl (2-aminoethyl)carbamate
118	N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide; 2,2,2-trifluoroacetic acid		481.4	Intermediate 86 and tert-butyl (3-aminopropyl)carbamate
REF 220	N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide hydrochloride		507.5	Intermediate 86 and tert-butyl (5-aminopentyl)carbamate

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103	4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-piperazin-1-yl-methanone hydrochloride		495.1	Intermediate 34
104	4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(2R)-2-aminopropyl]benzamide		481.3	Intermediate 86 and tert-butyl N-[(1R)-2-amino-1-methylethyl]carbamate
105	4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(2S)-2-aminopropyl]benzamide		481.3	Intermediate 86 and tert-butyl N-[(1S)-2-amino-1-methylethyl]carbamate

Intermediate 86

4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoic acid

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Step 1) Methyl 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzoate

Under Ar, methyl 2-ethyl-4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)benzoate (Intermediate 42) (2 g, 4.36 mmol, Eq: 1) and (2,3-difluoro-4-methoxyphenyl)boronic acid [CAS#170981-41-6] (860 mg, 4.58 mmol, Eq: 1.05) were combined in dioxane (30 mL). A solution containing Na₂CO₃ [CAS#497-19-8] (1.02 g, 9.59 mmol, Eq: 2.2) in water (3 mL) was added and the off white suspension was degased with Ar. [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane [CAS#95464-05-4] (53.4 mg, 65.4 μ mol, Eq: 0.015) was added and the orange suspension was stirred at 110 °C overnight. At RT, the suspension was filtered. The vessel and the filter cake were washed with ethyl acetate. Isolute was charged into the black suspension. The solvent was evaporated and the crude material was purified by flash chromatography (silica gel, 100 g, 0% to 50% ethyl acetate then 0% to 50% DCM/MeOH/25% aq.NH₃ (95:5:1) in DCM). The target compound was obtained as a light yellow solid (1.53 g, yield:80%). LC-MS (ESP): m/z=439.3 [M+H]⁺.

Step 2) Intermediate 86**4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoic acid**

Under Ar, methyl 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzoate (Step 1) (0.765 g, 1.74 mmol, Eq: 1) was suspended in ethanol (9.79 mL). 1M LiOH solution (3.59 mL, 3.59 mmol, Eq: 2.06) was added and the reaction mixture was stirred at 80°C overnight. The solvent was evaporated and the residue was partitioned between water (pH=12 with 1M NaOH) and ethyl acetate. The aqueous phase was acidified with 1M HCl to pH = 1. The resulting off-white suspension was filtered and the cake was washed with water, leading to the target compound as an off-white solid (574 mg, yield:78%). LC-MS (ESP): m/z=525.3 [M+H]⁺.

The following intermediates were prepared in analogy to Intermediate 86:

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Int.	Name	MS ESI [M+H] ⁺	Starting Material
106	2-ethyl-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid	407.3	Intermediate 42 and (3-fluoro-4-methoxyphenyl)boronic acid
85	4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzoic acid	461.3	Intermediate 42 and 107
108	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid	411.3	Intermediate 49 and (2,3-difluoro-4-methoxyphenyl)boronic acid

Intermediate 109

2-[2,3-difluoro-4-[8-[3-methyl-4-(piperazine-1-carbonyl)anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile

5

Step 1) tert-butyl 4-(4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carboxylate:

In a 50 mL round-bottomed flask, 4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid (Intermediate 1) (1.880 g, 4.15 mmol, Eq: 1), tert-butyl piperazine-1-carboxylate [CAS#57260-71-6] (1.16 g, 6.22 mmol, Eq: 1.5) and HATU (3.15 g, 8.29 mmol, Eq: 2.0) were combined with DMF (20 mL) (fresh bottle) to give a skin colored emulsion. The reaction mixture was sonicated to break some of the remaining solids. The reaction mixture was stirred at room temperature and DIPEA (2.68 g, 3.62 mL, 20.7 mmol, Eq: 5.0) was added.

10

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Vigorous stirring at room temperature was continued for 2 h and then DMF was mostly evaporated in high vacuum at 50 °C. The dark brown oil was diluted with DCM/MeOH (9:1) and charged with Isolute. Volatile solvents were evaporated in vacuum, remaining DMF was distilled off in HV at 50 °C. The crude material was purified by flash chromatography (silica gel, 120 g, 0% to 100% DCM/MeOH/25% aq. NH₃ (95/5/1), solid loading), leading to tert-butyl 4-(4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carboxylate (2.449 g, 4.14 mmol, 99.7 % yield) as a white solid. LC-MS (ESP): m/z=563.1 [M+H]⁺.

Step 2) tert-butyl 4-(4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carboxylate:

In a 100 mL four-necked flask, tert-butyl 4-(4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carboxylate (obtained in Step 1) (1 g, 1.69 mmol, Eq: 1) was combined with 2-(2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)acetonitrile (523 mg, 1.77 mmol, Eq: 1.05), sodium carbonate (394 mg, 3.72 mmol, Eq: 2.2) and dioxane (15 mL). The resulting suspension was stirred and sparged with argon for two minutes. Water (1.5 mL) was added and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane [CAS#95464-05-4] (20.7 mg, 25.3 μmol, Eq: 0.015) was added thereafter. The reaction mixture was refluxed for 48 hrs under argon atmosphere. The reaction mixture was diluted with ethyl acetate, filtered and the vessel as well as the filter cake were washed with plenty ethyl acetate and the obtained black solution was concentrated in vacuum. The crude material was purified by flash chromatography (silica gel, 40 g, 40% ethyl acetate in heptane isocratic directly followed by 0%-50% DCM/MeOH/NH₃ (95/5/1), solid loading). The title compound tert-butyl 4-(4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carboxylate (716 mg, 1.16 mmol, 68.8 % yield) was obtained as a brown waxy solid. LC-MS (ESP): m/z=604.3 [M+H]⁺.

Step 3) 2-[2,3-difluoro-4-[8-[3-methyl-4-(piperazine-1-carbonyl)anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile:

In a 50 mL round-bottomed flask, tert-butyl 4-(4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carboxylate (obtained in Step 2) (716 mg, 1.19 mmol, Eq: 1) was combined with DCM (10 mL) to give a brown solution. TFA (1.48 g, 1 mL, 13 mmol, Eq: 10.9) was added and the reaction mixture was

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stirred at RT for 6 h and quenched with 5 mL of saturated aqueous sodium bicarbonate solution and 5 mL of water. Phases were separated and the separation funnel was washed with DCM/MeOH (9:1) to dissolve the precipitate. The organic phases were combined, dried with MgSO₄ monohydrate and filtered. The resulting light brown solution was evaporated *in vacuo*.

- 5 The crude material was purified by flash chromatography (silica gel, 40 g, 0% to 100% DCM/MeOH/25% aq. NH₃ (90/10/1), solid loading) leading to 2-(2,3-difluoro-4-(8-((3-methyl-4-(piperazine-1-carbonyl)phenyl)amino)imidazo[1,2-a]pyrazin-3-yl)phenoxy)acetonitrile (417 mg, 812 μ mol, 68.4 % yield) as an off-white solid. LC-MS (ESP) m/z =504.2 [M+H]⁺.

- 10 The following intermediates were prepared in analogy to Intermediate 109:

Int.	Name	MS ESI [M+H]] ⁺	Starting Material
110	[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-phenyl]-piperazin-1-yl-methanone	493.1	Intermediate 63 and (2,3-difluoro-4-methoxyphenyl)boronic acid (Step 2)
111	2-[3-chloro-2-fluoro-4-[8-[3-methyl-4-(piperazine-1-carbonyl)anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile	520.2	Intermediate 1 and 2-[3-chloro-2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]acetonitrile
112	2-[4-[8-[3-ethyl-4-(piperazine-1-carbonyl)anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]acetonitrile	518.3	Intermediate 63 and 2-[2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetonitrile (Step 2)

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Intermediate 113**tert-butyl N-[2-[[2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoyl]amino]ethyl]carbamate**

- 5 A mixture of 2-ethyl-4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid hydrochloride (Intermediate 63) (4.45 g, 0.01 mol, Eq: 1), HATU (5.7 g, 15 mmol, Eq: 1.5) and DIPEA (6.46 g, 8.73 mL, 50 mmol, Eq: 5) in DMF (40 mL) was stirred for 15 min. at rt. Then tert-butyl (2-aminoethyl)carbamate (2.45 g, 2.41 mL, 15 mmol, Eq: 1.5) was added and the resulting solution was stirred at RT for 1 1/2h. The reaction mixture was concentrated to dryness. To the liquid was
- 10 added 100mL H₂O and extracted with ethyl acetate. The organic layer was washed with brine, dried over MgSO₄ and evaporated to dryness. The crude product (7.48g) was purified over 100g SiO₂ 60 in DCM/DCM:MeOH 9:1 (0-100%) by flash chromatography. The obtained material (4.5 g) was triturated with 10 mL Et₂O. The mixture was stirred for 1/2 h, filtered, the solid washed with Et₂O and dried, yielding 3.57 g of the title compound as off-white solid (yield:
- 15 65 %). MS (ESP) m/z=551.2 [M+H]⁺.

Intermediate 102**tert-butyl (2-(1-(4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamido)ethyl)(methyl)carbamate**

The title compound was prepared in analogy to Intermediate 113 from Intermediate 68. LC/MS:

- 20 [M+H]⁺= 662.3

The following intermediate was prepared in analogy to Intermediate 113:

Int.	Name	MS ESI [M+H] ⁺	Starting Material

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114	tert-butyl N-[2-[[4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]-2-methylbenzoyl]amino]ethyl]carbamate	479.4	Intermediate 1 and N-BOC-ethylenediamine
115	tert-butyl N-[3-[[4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]-2-methylbenzoyl]amino]propyl]carbamate	551.0	Intermediate 1 and N-BOC-1,3-diaminopropane

Intermediate 116

N-(2-aminoethyl)-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide

5

Step 1)

tert-butyl N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethyl]carbamate

To a solution of tert-butyl N-[2-[[2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoyl]amino]ethyl]carbamate (Intermediate 113) (0.5 g, 0.910 mmol, 1 eq) in water (2 mL)/1,4-dioxane (20 mL) was added 2-[2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetonitrile (0.8 g, 2.73 mmol, 3 eq), 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (0.04 g, 0.050 mmol, 0.050 eq) and sodium carbonate (0.19 g, 1.82 mmol, 2 eq) at 25 °C, the mixture was stirred at 80 °C for 12 h. The mixture was poured into water (50 mL), and extracted with DCM (50 mL x3), the combined organic phases were washed with brine (50 mL x 3), dried over anhydrous Na₂SO₄, and concentrated, the crude product was purified by flash column (PE:EA:DCM=1:1:1) to give tert-butyl N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethyl]carbamate (400 mg, 0.680 mmol, 74.43 % yield) (PE:Ethyl acetate=1:1, R_f=0.1) as yellow solid. LC/MS: [M+H]⁺=592.3

Step 2) Intermediate 116:

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N-(2-aminoethyl)-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide

To a solution of tert-butyl N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethyl]carbamate obtained in step 1 (200.0 mg, 0.340 mmol, 1 eq) in DCM (20 mL) was added trifluoroacetic acid (2.0 mL, 25.96 mmol, 76.79 eq) at 0 °C, the mixture was stirred at 20 °C for 2 h. The mixture was concentrated to give N-(2-aminoethyl)-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide (160 mg, 0.330 mmol, 96.3 % yield) as a brown gum. LC/MS: $[M+H]^+ = 492.3$

The following intermediates were prepared in analogy to Intermediate 116:

Int.	Name	MS ESI $[M+H]^+$	Starting Material
117	N-(2-aminoethyl)-4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide	483.2	Intermediate 113 and 2-(2-chloro-3-fluoro-4-methoxy-phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane
118	N-(2-aminoethyl)-4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide	508.2	Intermediate 113 and Intermediate 55: 2-[3-chloro-2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetonitrile

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119	N-(2-aminoethyl)-4- [[3-(4-chloro-2,3- difluoro- phenyl)imidazo[1,2- a]pyrazin-8- yl]amino]-2-ethyl- benzamide	471.2	Intermediate 113 and 2-(4-chloro-2,3- difluoro-phenyl)- 4,4,5,5-tetramethyl- 1,3,2-dioxaborolane
120	N-(2-aminoethyl)-4- [[3-[4- (difluoromethoxy)- 2,3-difluoro- phenyl]imidazo[1,2- a]pyrazin-8- yl]amino]-2-ethyl- benzamide	503.2	Intermediate 113 and Intermediate 107
121	N-(2-aminoethyl)-4- [[3-[4- (cyanomethoxy)-2,3- difluoro- phenyl]imidazo[1,2- a]pyrazin-8- yl]amino]-2-methyl- benzamide	478.2	Intermediate 114 and 2-[2,3-difluoro-4- (4,4,5,5-tetramethyl- 1,3,2-dioxaborolan-2- yl)phenoxy]acetonitril e
122	N-(3-aminopropyl)- 4-[[3-[4- (cyanomethoxy)-2,3- difluoro- phenyl]imidazo[1,2- a]pyrazin-8-	492.2	Intermediate 115 and 2-[2,3-difluoro-4- (4,4,5,5-tetramethyl- 1,3,2-dioxaborolan-2- yl)phenoxy]acetonitril e

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	yl]amino]-2-methyl- benzamide		
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Intermediate 123

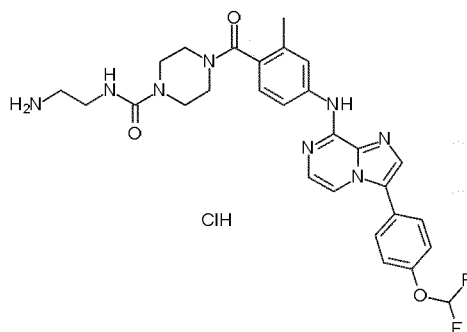
(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)(piperazin-1-yl)methanone hydrochloride

- 5 The title compound was prepared in analogy to Intermediate REF 8 from Intermediate 2 and tert-butyl piperazine-1-carboxylate.

MS obsd. (ESI⁺) [(M-H)⁺]: 479.4

Reference Example 221

- N-(2-aminoethyl)-4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carboxamide hydrochloride**

**Step 1)**

- To a solution of [4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-piperazin-1-yl-methanone (Reference Example 218) (100.0 mg, 0.210 mmol, 1 eq) in DCM (5 mL) was added N,N-diisopropylethylamine (0.18 mL, 1.04 mmol, 5 eq) and bis(trichloromethyl)carbonate (24.81 mg, 0.080 mmol, 0.400 eq) at 0 °C, the mixture was stirred at 0 °C for 1 h, then N-BOC-ethylenediamine (100.45 mg, 0.630 mmol, 3 eq) was added, the mixture was stirred at 25 °C for 12 h, LC-MS showed the reaction was completed.

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The mixture was concentrated and purified by prep-HPLC (TFA) to give tert-butyl N-[2-[[4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carbonyl]amino]ethyl]carbamate (80 mg, 0.120 mmol, 57.59 % yield) as a yellow solid.

5 LC-MS: $[M+H]^+$: 665.3

Step 2)

To a solution of tert-butyl N-[2-[[4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carbonyl]amino]ethyl]carbamate (obtained in step 1) (80.0 mg, 0.120 mmol, 1 eq) in methanol (20 mL) was added

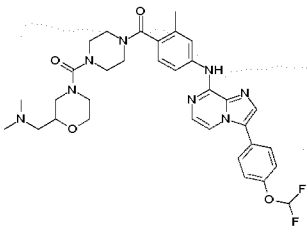
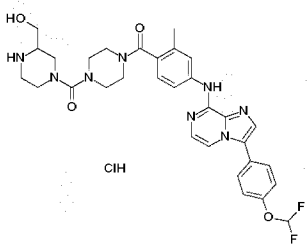
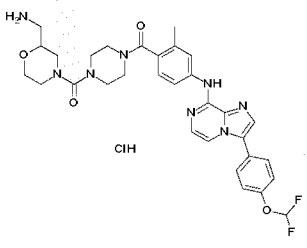
10 hydrochloric acid in MeOH (0.77 mL, 3.1 mmol, 25.72 eq) and then stirred at 25 °C for 2 h. LC-MS showed the reaction was complete. After concentration, 100 mL of saturated NaHCO_3 aqueous were added and extracted with DCM (100 mL x 3). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4 , filtered and concentrated. The residue was purified by prep-HPLC (HCl) to give N-(2-aminoethyl)-4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-
 15 carboxamide hydrochloride (28 mg, 0.040 mmol, 36.24 % yield) as yellow solid.

LC-MS: $[M+H]^+$: 565.1

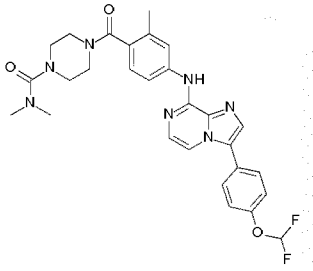
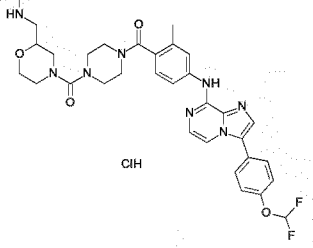
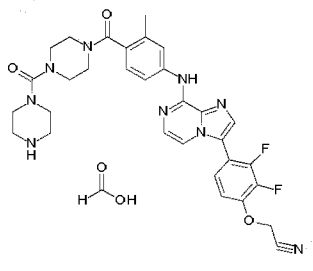
The following examples were prepared in analogy to Reference Example 221 (Step 2 only
 20 required if protecting group needs removal):

Ex.	Name	Structure	MS ESI $[M+H]^+$	Starting Material

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REF 222	[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[2-[(dimethylamino)methyl]morpholine-4-carbonyl]piperazin-1-yl]methanone		649.3	Reference Example 218 and N,N-dimethyl-2-morpholinmethanamine
REF 223	[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[3-(hydroxymethyl)piperazine-1-carbonyl]piperazin-1-yl]methanone hydrochloride		621.3	Reference Example 218 and tert-butyl 2-(hydroxymethyl)piperazine-1-carboxylate
REF 224	[4-[2-(aminomethyl)morpholine-4-carbonyl]piperazin-1-yl]-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-		621.2	Reference Example 218 and tert-butyl N-(morpholin-2-ylmethyl)carbamate

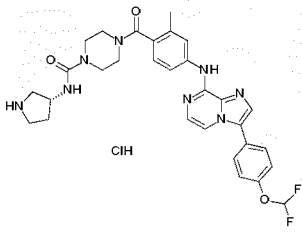
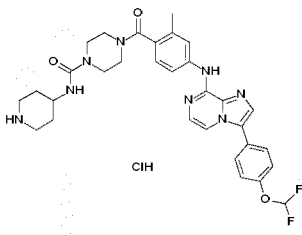
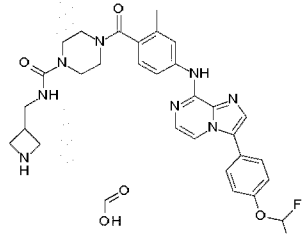
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	phenyl]methanone hydrochloride			
REF 225	4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]-N,N-dimethyl-piperazine-1-carboxamide		550.2	Reference Example 218 and dimethylamine
REF 226	[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[2-(methylaminomethyl)morpholine-4-carbonyl]piperazin-1-yl]methanone hydrochloride		635.1	Reference Example 218 and Carbamic acid, methyl(2-morpholinylmethyl)-, 1, 1-dimethylethyl ester [CAS# 185692-04-0]
REF 227	2-[2,3-difluoro-4-[8-[3-methyl-4-[4-(piperazine-1-carbonyl)piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-		616.2	Intermediate 109 and tert-butyl piperazine-1-carboxylate [CAS#57260-71-6]. Purification: prep HPLC with formic acid

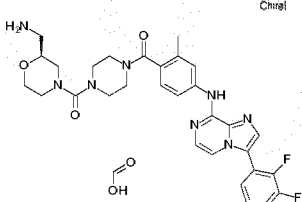
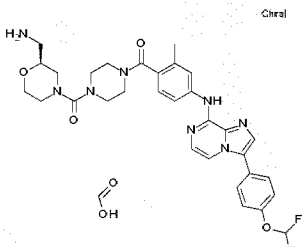
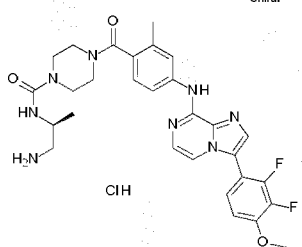
-277-

	yl]phenoxy]acetonitrile formate			
REF 228	4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]-N-[(3S)-pyrrolidin-3-yl]piperazine-1-carboxamide hydrochloride		591.1	Reference Example 218 and (S)-3-amino-1-N-BOC-pyrrolidine
REF 229	N-(2-aminoethyl)-4-[4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazine-1-carboxamide formate		590.2	Intermediate 109 and N-BOC-ethylenediamine Purification: prep HPLC with formic acid
REF 230	[4-[(2R)-2-(aminomethyl)morpholine-4-carbonyl]piperazine-1-yl]-[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-		621.2	Reference Example 134 and tert-butyl N-[(2S)-morpholin-2-yl]methyl]carbamate Purification: prep HPLC with formic acid

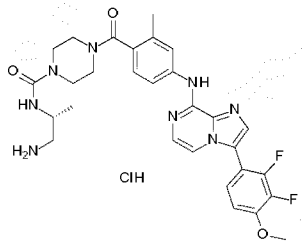
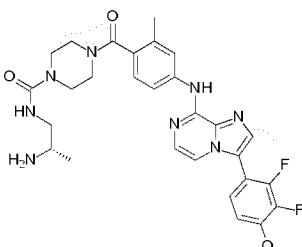
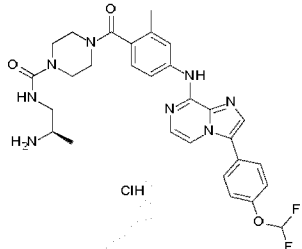
-278-

	phenyl]methanone formate			
REF 231	4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]-N-[(3R)-pyrrolidin-3-yl]piperazine-1-carboxamide hydrochloride		591.3	Reference Example 218 and (R)-(+)-1-BOC-3-aminopyrrolidine
REF 232	4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]-N-(4-piperidyl)piperazine-1-carboxamide hydrochloride		605.3	Reference Example 218 and 4-amino-1-boc-piperidine
REF 233	N-(azetidin-3-ylmethyl)-4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazine-		591.1	Reference Example 218 and 1-BOC-3-(aminomethyl)azetidine. Purification: prep HPLC with formic acid

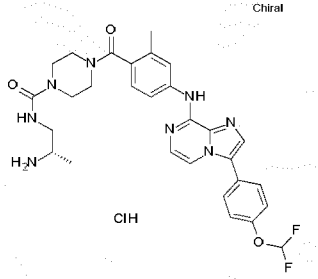
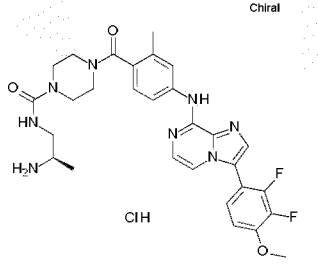
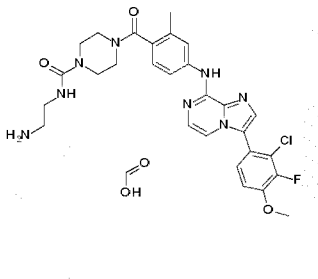
-279-

	1-carboxamide formate			
REF 234	[4-[(2S)-2-(aminomethyl)morpholine-4-carbonyl]piperazin-1-yl]-[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]methanone formate		621.3	Reference Example 134 and 1,1-Dimethylethyl [(2R)-2-morpholinylmethyl]carbamate [CAS# 186202-57-3]. Purification: prep HPLC with formic acid
REF 235	[4-[(2S)-2-(aminomethyl)morpholine-4-carbonyl]piperazin-1-yl]-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]methanone formate		621.3	Reference Example 218 and 1,1-Dimethylethyl [(2R)-2-morpholinylmethyl]carbamate [CAS# 186202-57-3]. Purification: prep HPLC with formic acid
REF 236	N-[(1S)-2-amino-1-methyl-ethyl]-4-[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-		[M- H] ⁻ : 577.6	Reference Example 134 and tert-butyl (S)-(2-aminopropyl)carbamate [CAS#121103-15-9]. Deprotection with 4M HCl in dioxane.

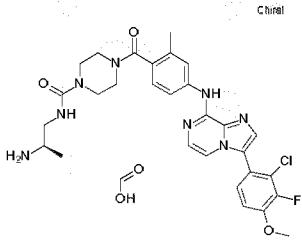
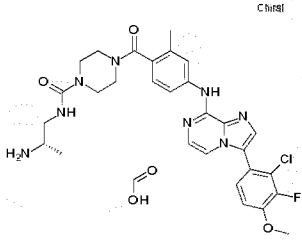
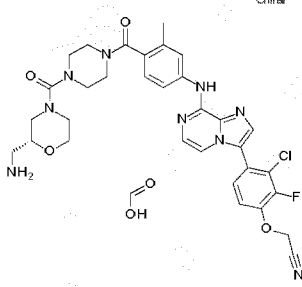
-280-

	benzoyl]piperazine-1-carboxamide hydrochloride			
REF 237	N-[(1R)-2-amino-1-methyl-ethyl]-4-[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carboxamide hydrochloride		579.3	Reference Example 134 and tert-butyl (R)-(2-aminopropyl)carbamate [CAS#333743-54-7]. Deprotection with 4M HCl in dioxane.
REF 238	N-[(2S)-2-aminopropyl]-4-[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carboxamide		579.3	Reference Example 134 and tert-butyl (S)-(1-aminopropan-2-yl)carbamate [CAS#146552-71-8]. Deprotection with 4M HCl in dioxane.
REF 239	N-[(2R)-2-aminopropyl]-4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-		[M-H] ⁻ : 577.3	Reference Example 218 and tert-butyl (R)-(1-aminopropan-2-yl)carbamate hydrochloride [CAS#100927-10-4]. Deprotection with 4M HCl in dioxane.

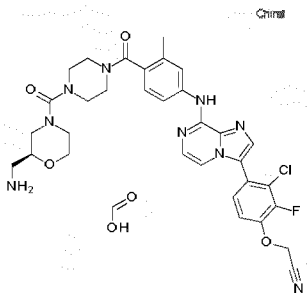
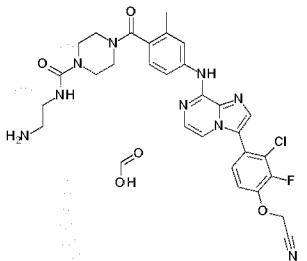
-281-

	1-carboxamide hydrochloride			
REF 240	N-[(2S)-2-aminopropyl]-4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazine-1-carboxamide hydrochloride		579.3	Reference Example 218 and tert-butyl (S)-(1-aminopropan-2-yl)carbamate hydrochloride [CAS#146552-71-8]
REF 241	N-[(2R)-2-aminopropyl]-4-[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazine-1-carboxamide hydrochloride		579.3	Reference Example 134 and tert-butyl (R)-(1-aminopropan-2-yl)carbamate hydrochloride [CAS#100927-10-4].
REF 242	N-(2-aminoethyl)-4-[4-[[3-(2-chloro-3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazine-		581.2	Intermediate 103 ([4-[[3-(2-chloro-3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-piperazin-1-yl-

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	1-carboxamide formate			methanone) and N-BOC-ethylenediamine. Purification: prep HPLC with formic acid
REF 243	N-[(2R)-2-aminopropyl]-4-[4-[[3-(2-chloro-3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazine-1-carboxamide formate		595.2	Intermediate 103 and tert-butyl (R)-(1-aminopropan-2-yl)carbamate hydrochloride [CAS#100927-10-4]. Purification: prep HPLC with formic acid
REF 244	N-[(2S)-2-aminopropyl]-4-[4-[[3-(2-chloro-3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazine-1-carboxamide formate		595.2	Intermediate 103 and tert-butyl (S)-(1-aminopropan-2-yl)carbamate hydrochloride [CAS#146552-71-8]. Purification: prep HPLC with formic acid
REF 245	2-[4-[8-[4-[4-[(2R)-2-(aminomethyl)morpholine-4-carbonyl]piperazine-1-carbonyl]-3-methyl-		662.4	Intermediate 111 and tert-butyl N-[(2S)-morpholin-2-yl]methyl]carbamate. Deprotection in DCM:TFA 10:2, 20°C.

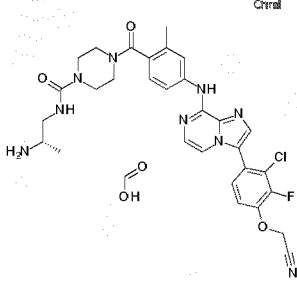
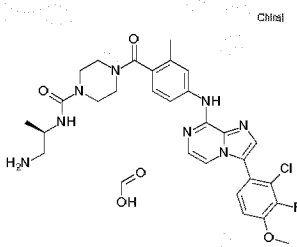
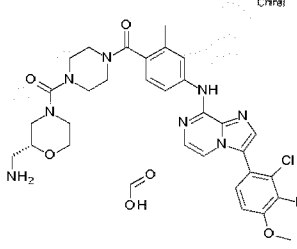
-283-

	anilino]imidazo[1,2-a]pyrazin-3-yl]-3-chloro-2-fluorophenoxy]acetonitrile formate			Purification: prep HPLC with formic acid
REF 246	2-[4-[8-[4-[4-[(2S)-2-(aminomethyl)morpholine-4-carbonyl]piperazine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]-3-chloro-2-fluorophenoxy]acetonitrile formate		662.4	Intermediate 111 and tert-butyl N-[(2R)-morpholin-2-yl]methyl]carbamate. Deprotection in DCM:TFA 10:2, 20°C. Purification: prep HPLC with formic acid
REF 247	N-(2-aminoethyl)-4-[4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazine-1-carboxamide formate		606.2	Intermediate 111 and N-BOC-ethylenediamine. Deprotection in DCM:TFA 10:2, 20°C. Purification: prep HPLC with formic acid

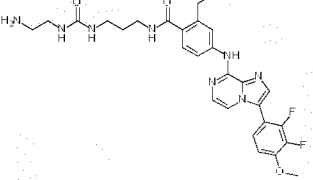
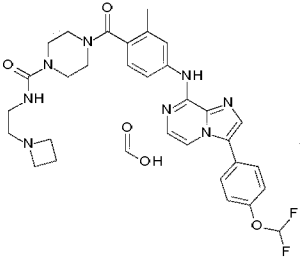
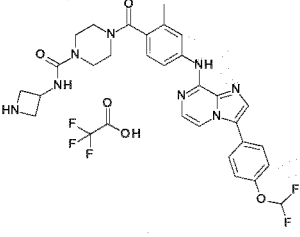
-284-

REF 248	N-[(1R)-2-amino-1-methyl-ethyl]-4-[4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carboxamide formate		620.3	Intermediate 111 and tert-butyl (R)-(2-aminopropyl)carbamate [CAS#333743-54-7]. Deprotection in DCM:TFA 10:2, 20°C. Purification: prep HPLC with formic acid
REF 249	N-[(1S)-2-amino-1-methyl-ethyl]-4-[4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carboxamide formate		620.3	Intermediate 111 and tert-butyl (R)-(2-aminopropyl)carbamate [CAS#333743-54-7]. Deprotection in DCM:TFA 10:2, 20°C. Purification: prep HPLC with formic acid
REF 250	N-[(2R)-2-aminopropyl]-4-[4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-		620.3	Intermediate 111 and tert-butyl (R)-(1-aminopropan-2-yl)carbamate hydrochloride [CAS#100927-10-4]. Deprotection in DCM:TFA 10:2, 20°C.

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	1-carboxamide formate			Purification: prep HPLC with formic acid
REF 251	N-[(2S)-2-aminopropyl]-4-[4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazine-1-carboxamide formate		620.4	Intermediate 111 and tert-butyl (S)-(1-aminopropan-2-yl)carbamate hydrochloride [CAS#146552-71-8]. Deprotection in DCM:TFA 10:2, 20°C. Purification: prep HPLC with formic acid
REF 252	N-[(1R)-2-amino-1-methyl-ethyl]-4-[4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazine-1-carboxamide formate		595.1	Intermediate 103 and tert-butyl (R)-(2-aminopropyl)carbamate [CAS#333743-54-7]. Purification: prep HPLC with formic acid
REF 253	[4-[(2R)-2-(aminomethyl)morpholine-4-carbonyl]piperazine-1-yl]-4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-		637.2	Intermediate 103 and tert-butyl N-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]methyl]carbamate. Deprotection in DCM:TFA 2:1, rt.

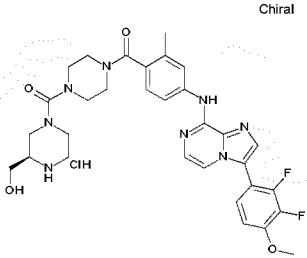
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	a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone formate			Purification: prep HPLC with formic acid
119	N-[3-(2-aminoethylcarbamoylamino)propyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		567.3	Example 118 and N-BOC-ethylenediamine
REF 254	N-[2-(azetidin-1-yl)ethyl]-4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazine-1-carboxamide formate		605.3	Reference Example 218 and 1-Azetidineethanamine
REF 255	N-(azetidin-3-yl)-4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazine-		577.3	Reference Example 218 and 1-BOC-3-(amino)azetidine Deprotection: 2h at rt in a 10/1 DCM/TFA mixture.

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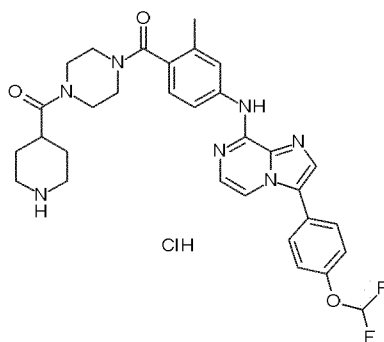
	1-carboxamide trifluoroacetate			
REF 256	4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]-N-[rac-(3R,4R)-4-hydroxypyrrolidin-3-yl]piperazine-1-carboxamide hydrochloride		607.3	Reference Example 218 and rac-tert-butyl (3R,4R)-3-amino-4-hydroxypyrrolidine-1-carboxylate hydrochloride [CAS#148214-90-8]
REF 257	4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]-N-[rac-(3R,4R)-4-methoxypyrrolidin-3-yl]piperazine-1-carboxamide hydrochloride		621.3	Reference Example 218 and rac-tert-butyl (3R,4R)-3-amino-4-methoxypyrrolidine-1-carboxylate [CAS#429673-79-0]
120	N-[3-(3-aminopropylcarbamoylamino)propyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-		581.2	Example 118 and N-BOC-1,3-diaminopropane

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	yl]amino]-2-ethyl-benzamide			
REF 258	(R)-(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)(3-(hydroxymethyl)piperazin-1-yl)methanone hydrochloride		621.4	From Reference Example 134 and tert-butyl (R)-2-(hydroxymethyl)piperazine-1-carboxylate

Example REF 259:

[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-(piperidine-4-carbonyl)piperazin-1-yl]methanone hydrochloride



5

Step 1) tert-butyl 4-[4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carbonyl]piperidine-1-carboxylate

In a 25 mL vial, (4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylphenyl)(piperazin-1-yl)methanone hydrochloride; Reference Example 218 (250 mg, 243 μmol, Eq: 1) and DIPEA (157 mg, 212 μL, 1.21 mmol, Eq: 5.0) were combined with DMF (5

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mL) to give a light yellow suspension, that was stirred until most solids were dissolved. Then 1-(tert-butoxycarbonyl)piperidine-4-carboxylic acid (83.5 mg, 364 μ mol, Eq: 1.5) and HATU (185 mg, 485 μ mol, Eq: 2.0) were added. The walls of the tube were washed down with some DMF and the reaction mixture was stirred at RT for 2 h. The reaction mixture was poured into 10 mL ethyl acetate and extracted once with 0.1 M aq. NaOH. The organic phase was washed with brine, dried with magnesium sulfate monohydrate, filtered and the resulting solution was concentrated *in vacuo*. The crude material was purified by flash chromatography (silica gel, 25g, 0% to 75% DCM/MeOH/aq. 25% NH₄OH (95/5/1)) leading to 101 mg off-white solid. MS: [M+H]⁺; 690.4

10 Step 2) Reference Example 259

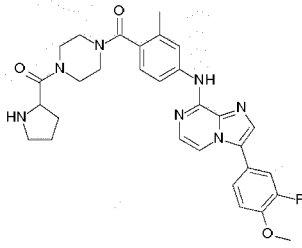
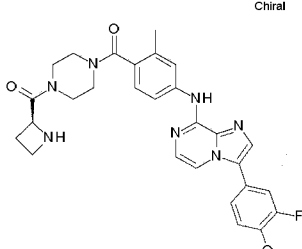
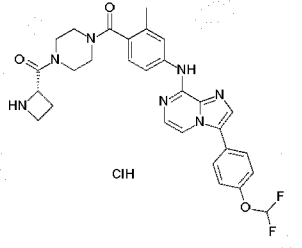
[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-(piperidine-4-carbonyl)piperazin-1-yl]methanone hydrochloride

In a 50 mL round-bottomed flask, tert-butyl 4-(4-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carbonyl)piperidine-1-carboxylate (Step 1) (100 mg, 145 μ mol, Eq: 1) was combined with dioxane (1 mL) to give a colorless solution. Hydrogen chloride (4M in dioxane) (181 μ l, 725 μ mol, Eq: 5) was added. Stirring was continued and hydrogen chloride (4M in dioxane) (181 μ l, 725 μ mol, Eq: 5) was added again. The reaction mixture was stirred overnight. The reaction mixture was diluted with anhydrous ether, stirred and then filtered. The filter cake was washed with ether several times and dried in HV leading to the target compound as an off-white solid (93 mg, yield: 93 %). MS (ISN): [M-H]⁻; 588.5

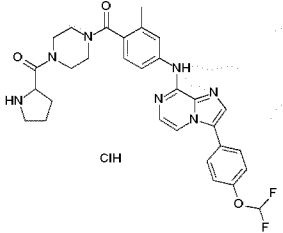
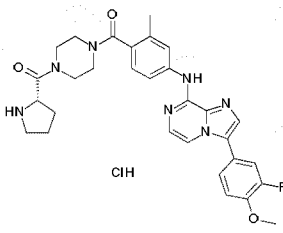
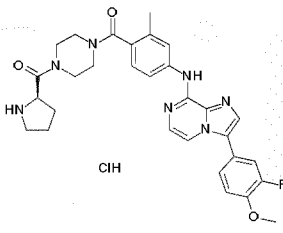
The following examples were prepared in analogy to Reference Example 259 (Step 2 only required if protecting group needs removal):

Ex.	Name	Structure	MS ESI [M+H] ⁺	Starting Material
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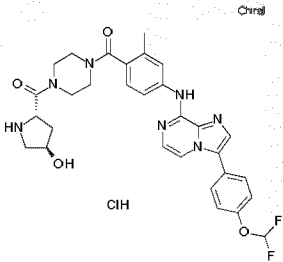
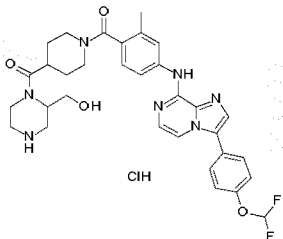
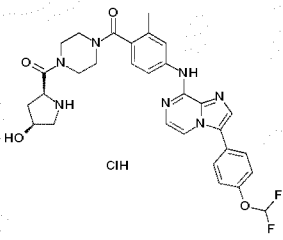
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REF 260	[4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-(pyrrolidine-2-carbonyl)piperazin-1-yl]methanone		[M-H] ⁻ ; 556.6	Reference Example 219 and 1-(tert-butoxycarbonyl)pyrrolidine-2-carboxylic acid. Deprotection: 45 min at rt. Purified by flash chromatography (silica gel, 0% to 100% DCM/MeOH/NH ₄ OH (90/10/1))
REF 261	[4-[(2S)-azetidine-2-carbonyl]piperazin-1-yl]-[4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]methanone		[M-H] ⁻ ; 542.6	Reference Example 219 and (S)-1-(tert-butoxycarbonyl)azetidine-2-carboxylic acid. Deprotection: 45 min at rt. Purified by flash chromatography (silica gel, 0% to 100% DCM/MeOH/NH ₄ OH (90/10/1))
REF 262	[4-[(2S)-azetidine-2-carbonyl]piperazin-1-yl]-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]methanone hydrochloride		[M-H] ⁻ ; 560.2	Reference Example 218 and (S)-1-(tert-butoxycarbonyl)azetidine-2-carboxylic acid.

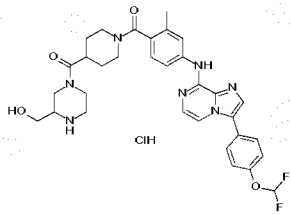
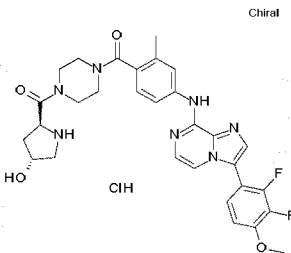
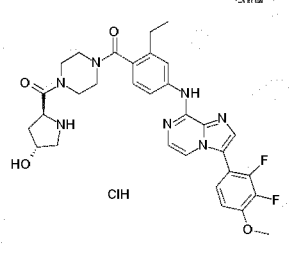
-291-

REF 263	[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-(pyrrolidine-2-carbonyl)piperazin-1-yl]methanone hydrochloride		[M-H] ⁻ ; 556.6	Reference Example 218 and 1-(tert-butoxycarbonyl)pyrrolidine-2-carboxylic acid.
REF 264	[4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[(2S)-pyrrolidine-2-carbonyl]piperazin-1-yl]methanone hydrochloride		[M-H] ⁻ ; 556.4	Reference Example 219 and (S)-1-(tert-butoxycarbonyl)pyrrolidine-2-carboxylic acid.
REF 265	[4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[(2R)-pyrrolidine-2-carbonyl]piperazin-1-yl]methanone hydrochloride		[M-H] ⁻ ; 556.4	Reference Example 219 and (R)-1-(tert-butoxycarbonyl)pyrrolidine-2-carboxylic acid.

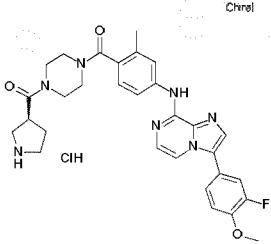
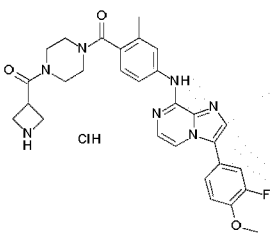
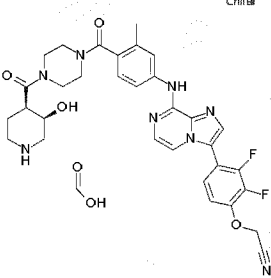
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REF 266	[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[(2S,4R)-4-hydroxypyrrolidine-2-carbonyl]piperazin-1-yl]methanone hydrochloride		[M-H] ⁻ ; 590.4	Reference Example 218 and (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid.
REF 267	[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[2-(hydroxymethyl)piperazine-1-carbonyl]-1-piperidyl]methanone hydrochloride		[M+H] ⁺ ; 620.2	Reference Example 218 and tert-butyl 3-(hydroxymethyl)piperazine-1-carboxylate
REF 268	[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[(2S,4S)-4-hydroxypyrrolidine-2-carbonyl]piperazin-1-yl]methanone hydrochloride		[M-H] ⁻ ; 590.5	Reference Example 218 and (2S,4S)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid. Deprotection: 5eq HCl in dioxane (4M) in diethylether/MeOH 5/2 at rt overnight.

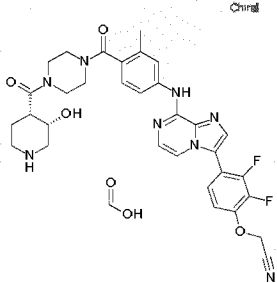
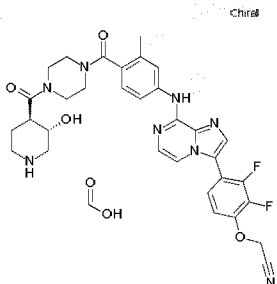
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REF 269	[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[3-(hydroxymethyl)piperazine-1-carbonyl]-1-piperidyl]methanone hydrochloride		620.5(M+H)	Reference Example 1 and tert-butyl 2-(hydroxymethyl)piperazine-1-carboxylate. Deprotection with 10 eq HCl 4M in dioxane, 45 min at rt.
REF 270	[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[(2S,4R)-4-hydroxypyrrolidine-2-carbonyl]piperazin-1-yl]methanone hydrochloride		[M-H] ⁻ ; 590.5	Reference Example 134 and (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid [CAS#13726-69-7]
REF 271	[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylphenyl]-[4-[(2S,4R)-4-hydroxypyrrolidine-2-carbonyl]piperazin-1-yl]methanone hydrochloride		606.4	Intermediate 110 and (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid [CAS#13726-69-7]. Purification: prep HPLC with HCl

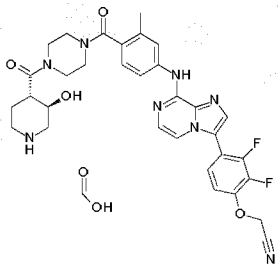
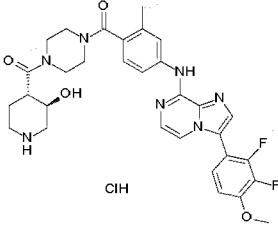
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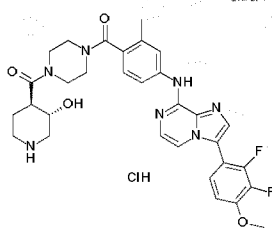
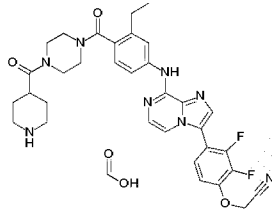
REF 272	[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-[(3S)-pyrrolidine-3-carbonyl]piperazin-1-yl]methanone hydrochloride		558.5	Reference Example 219 and (3S)-1-(tert-Butoxycarbonyl)-3-pyrrolidinecarboxylic acid
REF 273	[4-(azetidine-3-carbonyl)piperazin-1-yl]-[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone hydrochloride		544.5	Reference Example 219 and 1-Boc-Azetidine-3-carboxylic acid
REF 274	2-[2,3-difluoro-4-[8-[4-[4-[(3R,4R)-3-hydroxypiperidine-4-carbonyl]piperazine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		631.1	Intermediate 109 and (3R,4R)-1-tert-butoxycarbonyl-3-hydroxy-piperidine-4-carboxylic acid [CAS# 1932301-36-4]. Deprotection: 2h at rt in a 80/20 DCM/TFA mixture (95 eq TFA), then neutralized with sat. Na ₂ CO ₃ to pH8.

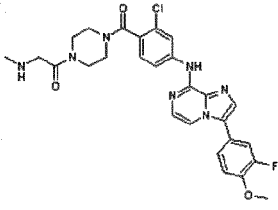
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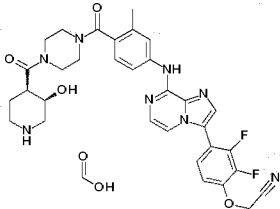
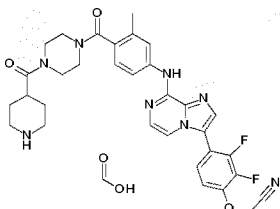
				Purification: prep HPLC with formic acid
REF 275	2-[2,3-difluoro-4-[8-[4-[4-[(3S,4S)-3-hydroxypiperidine-4-carbonyl]piperazine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		631.1	Intermediate 109 and (3S,4S)-1-tert-butoxycarbonyl-3-hydroxy-piperidine-4-carboxylic acid, obtained by saponification of 1,4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) 4-methyl ester, (3S,4S)- [CAS# 2166250-53-7] Deprotection: 2h at rt in a 80/20 DCM/TFA mixture (95 eq TFA), then neutralized with sat. Na ₂ CO ₃ to pH 8. Purification: prep. HPLC in presence of formic acid
REF 276	2-[2,3-difluoro-4-[8-[4-[4-[(3S,4R)-3-hydroxypiperidine-4-carbonyl]piperazine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		631.1	Intermediate 109 and (3S,4R)-1-tert-butoxycarbonyl-3-hydroxy-piperidine-4-carboxylic acid obtained by saponification of 1,4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,

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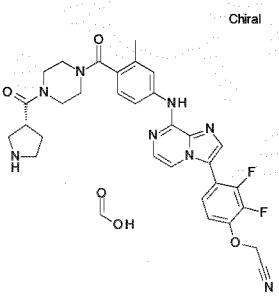
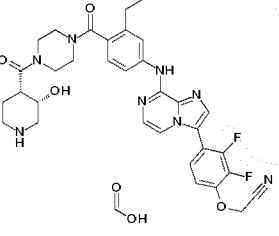
				1-dimethylethyl) 4-ethyl ester, (3S,4R)- [CAS# 1805790-50-4]. Deprotection: 2h at rt in a 80/20 DCM/TFA mixture (95 eq TFA), then neutralized with sat. Na₂CO₃ to pH8. Purification: prep HPLC with formic acid as additive
REF 277	2-[2,3-difluoro-4-[8-[4-[4-[(3R,4S)-3-hydroxypiperidine-4-carbonyl]piperazine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		631.1	Intermediate 109 and 1, 4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) ester, (3R,4S)- [CAS# 1821775-81-8]. Deprotection: 2h at rt in a 80/20 DCM/TFA mixture (95 eq TFA), then neutralized with sat. Na₂CO₃ to pH8. Purification: prep HPLC with formic acid as additive
REF 278	[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[(3R,4S)-		606.3	Reference Example 134 and 1,4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl)

	3-hydroxypiperidine-4-carbonyl]piperazin-1-yl]methanone hydrochloride			ester, (3R,4S)- [CAS# 1821775-81-8].
REF 279	[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[(3S,4R)-3-hydroxypiperidine-4-carbonyl]piperazin-1-yl]methanone hydrochloride		606.3	Reference Example 134 and (3S,4R)-1-tert-butoxycarbonyl-3-hydroxy-piperidine-4-carboxylic acid obtained by saponification of 1,4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) 4-ethyl ester, (3S,4R)- [CAS# 1805790-50-4].
REF 280	2-[4-[8-[3-ethyl-4-[4-(piperidine-4-carbonyl)piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile formate		629.1	Intermediate 112 and 1-(tert-butoxycarbonyl)piperidine-4-carboxylic acid. Deprotection: 0.5h at rt in a 80/20 DCM/TFA mixture (13 eq TFA), then neutralized with sat. Na ₂ CO ₃ to pH8. Purification: prep HPLC with formic acid as additive

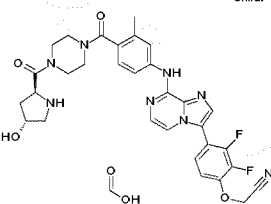
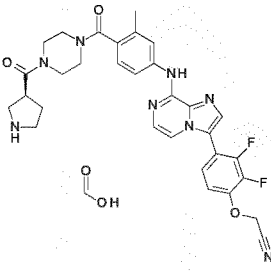
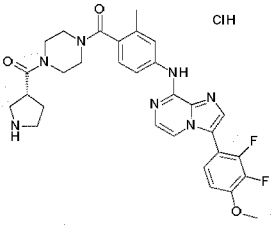
REF 281	[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-[rac-(3S,4S)-3-hydroxypiperidine-4-carbonyl]piperazin-1-yl]methanone		606.3	Reference Example 134 and (3S,4S)-1-tert-butoxycarbonyl-3-hydroxy-piperidine-4-carboxylic acid, obtained by saponification of 1,4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) 4-methyl ester, (3S,4S)- [CAS# 2166250-53-7] Purification: prep HPLC
121	N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide trifluoroacetate		623.3	Example 117 and FMOC-ARG-OH. Deprotection using 22 eq piperidine at 0-20°C for 12h. Purification by prep HPLC (TFA as additive).
REF 282	1-(4-(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperazin-1-yl)-2-		552.2	Intermediate 123 and 2-((tert-butoxycarbonyl)(methyl)amino)acetic acid

	(methylamino)ethanone			
REF 283	2-[2,3-difluoro-4-[8-[3-methyl-4-[4-[rac-(3R,4R)-3-hydroxypiperidine-4-carbonyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		631.3	Intermediate 109 and 1,4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) ester, (3R,4R)-rel- [CAS# 1932301-36-4]. Deprotection: 1h at rt in a 80/20 DCM/TFA mixture (13 eq TFA), then neutralized with sat. Na₂CO₃ to pH8. Purification: prep HPLC with formic acid as additive
REF 284	2-[2,3-difluoro-4-[8-[3-methyl-4-[4-(piperidine-4-carbonyl)piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		615.3	Intermediate 109 and N-BOC-isonipecotic acid. Deprotection: 1h at rt in a 80/20 DCM/TFA mixture (13 eq TFA), then neutralized with sat. Na₂CO₃ to pH8. Purification: prep. HPLC with formic acid as additive

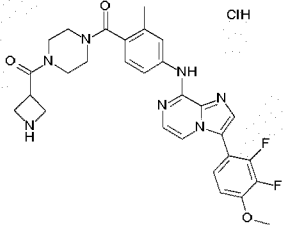
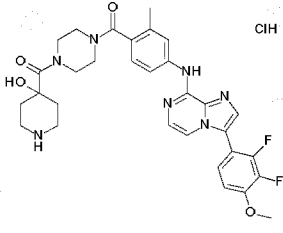
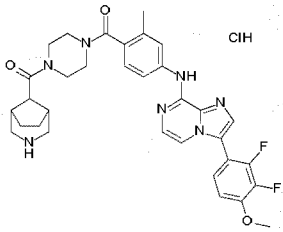
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REF 285	2-[2,3-difluoro-4-[8-[3-methyl-4-[4-[(3R)-pyrrolidine-3-carbonyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate	 Chiral	601.3	Intermediate 109 and (R)-1-BOC-pyrrolidine-3-carboxylic acid. Deprotection: 1h at rt in a 80/20 DCM/TFA mixture (60 eq TFA), then neutralized with sat. Na₂CO₃ to pH8. Purification: prep. HPLC with formic acid as additive
REF 286	2-[4-[8-[3-ethyl-4-[4-[rac-(3S,4S)-3-hydroxypiperidine-4-carbonyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile formate		645.3	Intermediate 112 and (3S,4S)-1-tert-butoxycarbonyl-3-hydroxy-piperidine-4-carboxylic acid, obtained by saponification of 1,4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) 4-methyl ester, (3S,4S)-[CAS# 2166250-53-7] Deprotection: 1h at rt in a 80/20 DCM/TFA mixture (95 eq TFA), then neutralized with sat. Na₂CO₃ to pH8. Purification: prep HPLC

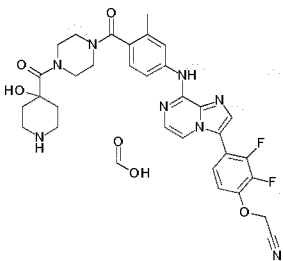
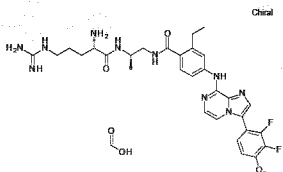
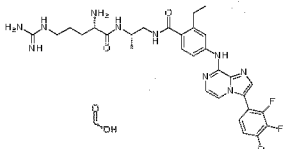
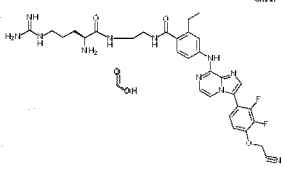
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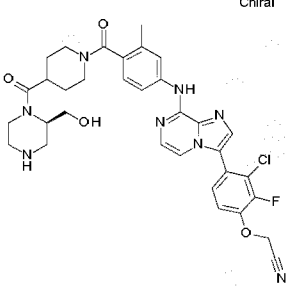
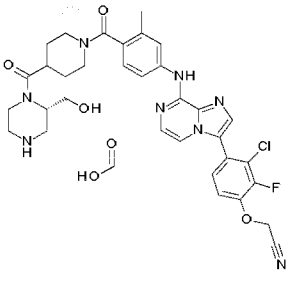
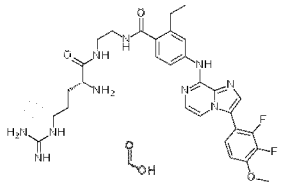
REF 287	2-[2,3-difluoro-4-[8-[4-[4-[(2S,4R)-4-hydroxypyrrolidine-2-carbonyl]piperazine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate	 Chiral	617.3	Intermediate 109 and (2R,4S)-1-tert-butoxycarbonyl-4-hydroxy-pyrrolidine-2-carboxylic acid. Deprotection: 1h at rt in a 80/20 DCM/TFA mixture (62 eq TFA), then neutralized with sat. Na ₂ CO ₃ to pH8. Purification: prep HPLC
REF 288	2-[2,3-difluoro-4-[8-[3-methyl-4-[4-[(3S)-pyrrolidine-3-carbonyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile; formic acid	 Chiral	601.1	Intermediate 109 and (S)-1-BOC-pyrrolidine-3-carboxylic acid. Deprotection: 1h at rt in a 100/10 DCM/TFA mixture (160 eq TFA), Purification: prep HPLC
REF 289	(R)-(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)(pyrrolidin-3-yl)methanone hydrochloride	 Chiral ClH	576.5	Reference Example 134 and (R)-1-BOC-pyrrolidine-3-carboxylic acid

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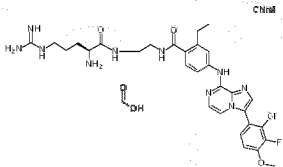
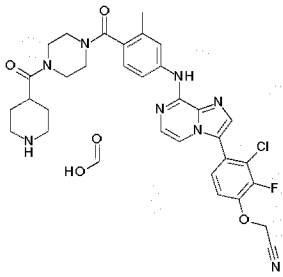
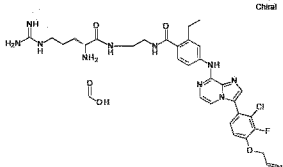
REF 290	[4-(azetidine-3-carbonyl)piperazin-1-yl]-[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]methanone;hydrochloride		562.7	Reference Example 134 and 1-(tert-butoxycarbonyl)azetidine-3-carboxylic acid
REF 291	[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-(4-hydroxypiperidine-4-carbonyl)piperazin-1-yl]methanone hydrochloride		606.5	Reference Example 134 and 1-(tert-butoxycarbonyl)-4-hydroxypiperidine-4-carboxylic acid
REF 292	[4-(3-azabicyclo[3.2.1]octane-8-carbonyl)piperazin-1-yl]-[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]methanone hydrochloride		616.4	Reference Example 134 and 3-(tert-butoxycarbonyl)bicyclo[3.2.1]octane-8-carboxylic acid

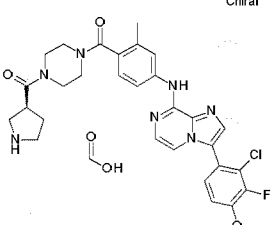
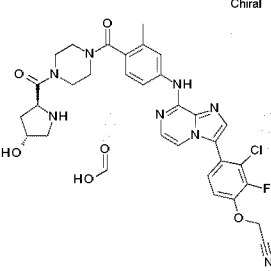
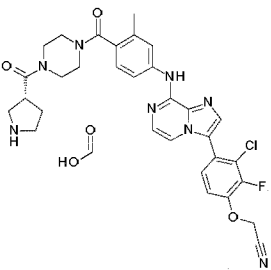
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REF 293	2-[2,3-difluoro-4-[8-[4-[4-(4-hydroxypiperidine-4-carbonyl)piperazine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		631.3	Intermediate 109 and 1-(tert-butoxycarbonyl)-4-hydroxypiperidine-4-carboxylic acid
122	N-[(2R)-2-[[[(2S)-2-amino-5-guanidinopentanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide formate		637.1	Intermediate 104 and FMOC-ARG-OH. Deprotection using 22 eq piperidine at 0-20°C for 12h. Purification by prep HPLC (formic acid as additive).
123	N-[(2S)-2-[[[(2S)-2-amino-5-guanidinopentanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide formate		637.1	Intermediate 105 and FMOC-ARG-OH. Deprotection using 22 eq piperidine at 0-20°C for 12h. Purification by prep HPLC (formic acid as additive).
124	N-[2-[[[(2S)-2-amino-5-guanidinopentanoyl]amino]ethyl]-4-[[3-[4-		648.2	Intermediate 116 and BOC-ARG-OH. Deprotection: 2h at rt in a 100/20 DCM/TFA

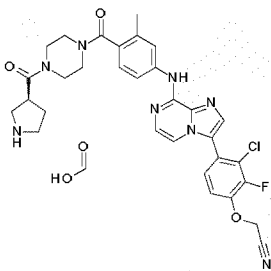
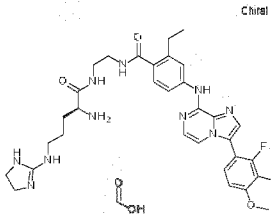
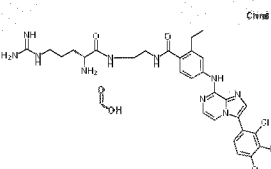
	(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide formate			mixture (200 eq TFA), then neutralized with sat. Na ₂ CO ₃ to pH8. Purification: prep HPLC
REF 294	2-[3-chloro-2-fluoro-4-[8-[4-[4-[(2R)-2-(hydroxymethyl)piperazine-1-carbonyl]piperidine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile	 Chiral	661.3	Intermediate 111 and 124. Deprotection: 1h at rt in a 100/10 DCM/TFA mixture (160 eq TFA), Purification: prep HPLC
REF 295	2-[3-chloro-2-fluoro-4-[8-[4-[4-[(2S)-2-(hydroxymethyl)piperazine-1-carbonyl]piperidine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate	 Chiral	661.2	Intermediate 111 and Intermediate 125. Deprotection: 1 h at rt in a 100/10 DCM/TFA mixture (160 eq TFA), Purification: prep HPLC
125	N-[2-[[[(2R)-2-amino-5-guanidinopentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-	 Chiral	623.1	Example 117 and FMOC-D-ARG-OH. Deprotection using 22 eq piperidine at 0-20 °C for 12h.

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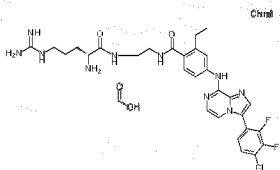
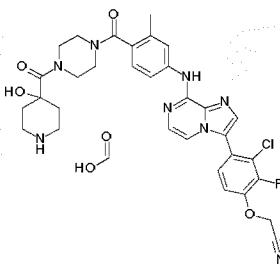
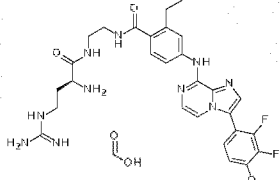
	phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide formate			Purification by prep HPLC.
126	N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2-chloro-3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide formate		639.3	Intermediate 117 and BOC-ARG-OH. Deprotection: 2h at rt in a 100/10 DCM/TFA mixture (38 eq TFA). Purification: prep HPLC
REF 296	2-[3-chloro-2-fluoro-4-[8-[3-methyl-4-[4-(piperidine-4-carbonyl)piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		631.3	Intermediate 111 and N-BOC-isonipecotic acid. Deprotection: 1h at rt in a 100/10 DCM/TFA mixture. Purification: prep HPLC.
127	N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-		664.1	Intermediate 118 and FMOC-D-ARG-OH. Deprotection using 22 eq piperidine at 0-20°C for 12h. Purification by prep HPLC.

	yl]amino]-2-ethylbenzamide formate			
REF 297	[4-[[3-(2-chloro-3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[(3S)-pyrrolidine-3-carbonyl]piperazin-1-yl]methanone formate		592.1	Intermediate 103 and (S)-1-BOC-pyrrolidine-3-carboxylic acid. Deprotection: 1h at rt in a 100/10 DCM/TFA mixture. Purification: prep HPLC
REF 298	2-[3-chloro-2-fluoro-4-[8-[4-[4-[(2S,4R)-4-hydroxypyrrolidine-2-carbonyl]piperazine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		633.3	Intermediate 111 and (2R,4S)-1-tert-butoxycarbonyl-4-hydroxy-pyrrolidine-2-carboxylic acid. Deprotection: 1h at rt in a 10/1 DCM/TFA mixture (95 eq TFA). Purification: prep. HPLC
REF 299	2-[3-chloro-2-fluoro-4-[8-[3-methyl-4-[4-[(3R)-pyrrolidine-3-carbonyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		617.3	Intermediate 111 and (R)-1-BOC-pyrrolidine-3-carboxylic acid. Deprotection: 1h at rt in a 10/1 DCM/TFA mixture Purification: prep. HPLC

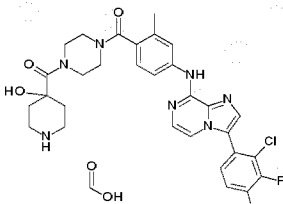
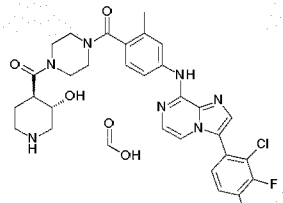
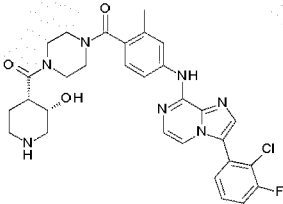
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REF 300	2-[3-chloro-2-fluoro-4-[8-[3-methyl-4-[4-[(3S)-pyrrolidine-3-carbonyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		617.3	Intermediate 111 and (S)-1-BOC-pyrrolidine-3-carboxylic acid. Deprotection: 1h at rt in a 10/1 DCM/TFA mixture Purification: prep. HPLC
128	N-[2-[[[(2S)-2-amino-5-(4,5-dihydro-1H-imidazol-2-ylamino)pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide formate		649.4	Example 117 and (2S)-2-(tert-butoxycarbonylamino)-5-(4,5-dihydro-1H-imidazol-2-ylamino)pentanoic acid. Purification: prep. HPLC
129	N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2-chloro-3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide formate		639.4	Intermediate 117 and FMOC-D-ARG-OH. Deprotection using 22 eq piperidine at 20°C for 12h. Purification by prep HPLC.

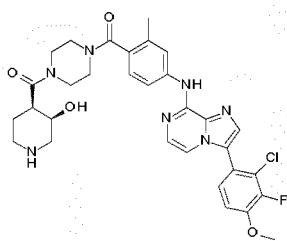
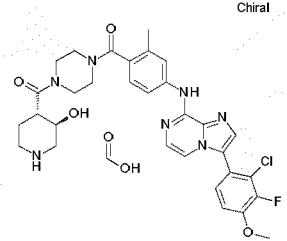
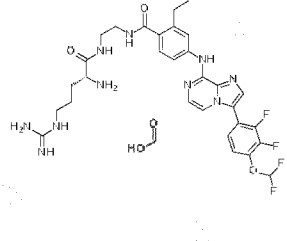
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130	N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide formate		627.3	Intermediate 119 and Fmoc-D-ARG-OH. Deprotection using 22 eq piperidine at 20°C for 12h. Purification by prep HPLC.
REF 301	2-[3-chloro-2-fluoro-4-[8-[4-[4-(4-hydroxypiperidine-4-carbonyl)piperazine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		647.3	Intermediate 111 and 1-(tert-butoxycarbonyl)-4-hydroxypiperidine-4-carboxylic acid. Deprotection: 1h at rt in a 10/1 DCM/TFA mixture Purification: prep. HPLC.
131	N-[2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide formate		609.2	Example 117 and (2S)-2-(tert-butoxycarbonylamino)-4-guanidino-butanoic acid. Purification: prep. HPLC

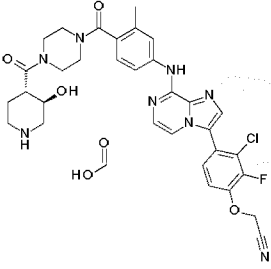
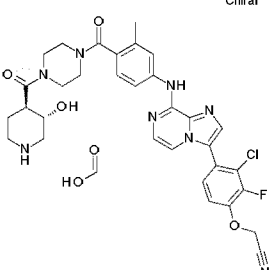
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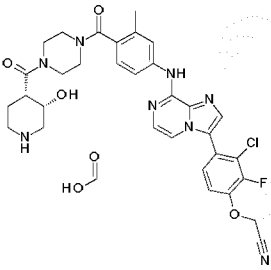
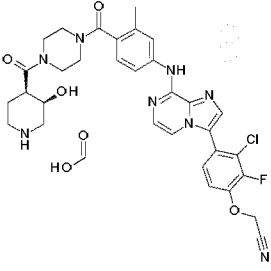
REF 302	[4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-(4-hydroxypiperidine-4-carbonyl)piperazin-1-yl]methanone formate		622.1	Intermediate 103 and 1-(tert-butoxycarbonyl)-4-hydroxypiperidine-4-carboxylic acid. Purification: prep. HPLC
REF 303	[4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-[(3S,4R)-3-hydroxypiperidine-4-carbonyl]piperazin-1-yl]methanone formate		622.2	Intermediate 103 and (3S,4R)-1-tert-butoxycarbonyl-3-hydroxy-piperidine-4-carboxylic acid obtained by saponification of 1,4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) 4-ethyl ester, (3S,4R)- [CAS# 1805790-50-4].
REF 304	[4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-[(3S,4S)-3-hydroxypiperidine-4-carbonyl]piperazin-1-yl]methanone		622.2	Intermediate 103 and (3S,4S)-1-tert-butoxycarbonyl-3-hydroxy-piperidine-4-carboxylic acid, obtained by saponification of 1,4-piperidinedicarboxylic acid, 3-hydroxy-, 1-

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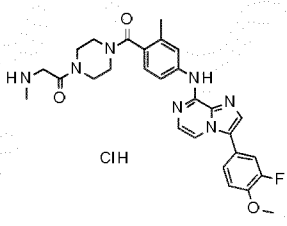
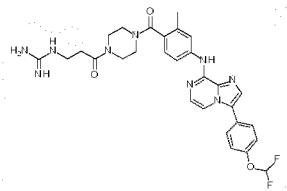
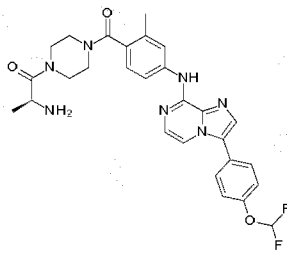
				(1,1-dimethylethyl) 4-methyl ester, (3S,4S)- [CAS# 2166250-53-7]
REF 305	[4-[[3-(2-chloro-3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[(3R,4R)-3-hydroxypiperidine-4-carbonyl]piperazin-1-yl]methanone		622.2	Intermediate 103 and 1,4-piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) ester, (3R,4R)-rel- [CAS# 206111-42-4].
REF 306	[4-[[3-(2-chloro-3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[(3R,4S)-3-hydroxypiperidine-4-carbonyl]piperazin-1-yl]methanone formate		622.2	Intermediate 103 and 1,4-piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) ester, (3R,4S)- [CAS# 1821775-81-8]. Purification: prep. HPLC
132	N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-		659.2	Intermediate 120 and (2R)-2-(tert-butoxycarbonylamino)-5-guanidino-pentanoic acid hydrate hydrochloride

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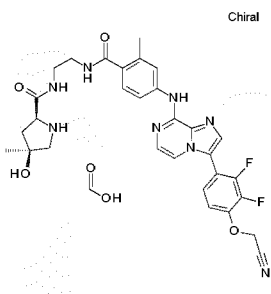
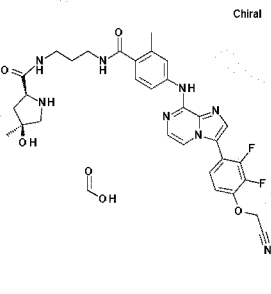
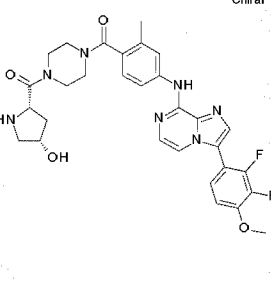
	yl]amino]-2-ethyl-benzamide formate			
REF 307	2-[3-chloro-2-fluoro-4-[8-[4-[4-[(3R,4S)-3-hydroxypiperidine-4-carbonyl]piperazine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		647.2	Intermediate 111 and 1,4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) ester, (3R,4S)- [CAS# 1821775-81-8]. Deprotection: 1h at rt in a 10/1 DCM/TFA mixture Purification: prep. HPLC
REF 308	2-[3-chloro-2-fluoro-4-[8-[4-[4-[(3S,4R)-3-hydroxypiperidine-4-carbonyl]piperazine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		647.2	Intermediate 111 and (3S,4R)-1-tert-butoxycarbonyl-3-hydroxy-piperidine-4-carboxylic acid obtained by saponification of 1,4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) 4-ethyl ester, (3S,4R)- [CAS# 1805790-50-4]. Deprotection: 1h at rt in a 10/1 DCM/TFA mixture Purification: prep HPLC (FA as additive)

REF 309	2-[3-chloro-2-fluoro-4-[8-[4-[4-[(3S,4S)-3-hydroxypiperidine-4-carbonyl]piperazine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		647.2	Intermediate 111 and (3S,4S)-1-tert-butoxycarbonyl-3-hydroxy-piperidine-4-carboxylic acid, obtained by saponification of 1,4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) 4-methyl ester, (3S,4S)-[CAS# 2166250-53-7]. Deprotection: 1h at rt in a 10/1 DCM/TFA mixture Purification: prep HPLC (FA as additive)
REF 310	2-[3-chloro-2-fluoro-4-[8-[4-[4-[(3R,4R)-3-hydroxypiperidine-4-carbonyl]piperazine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		647.2	Intermediate 111 and 1,4-Piperidinedicarboxylic acid, 3-hydroxy-, 1-(1,1-dimethylethyl) ester, (3R,4R)-rel-[CAS# 206111-42-4]. Deprotection: 1h at rt in a 10/1 DCM/TFA mixture Purification: prep HPLC (FA as additive)

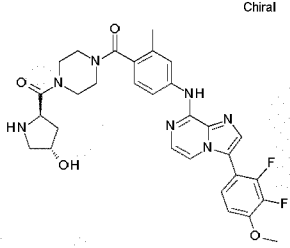
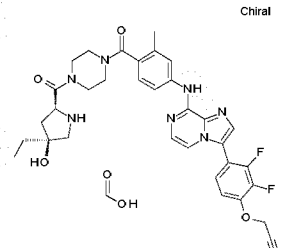
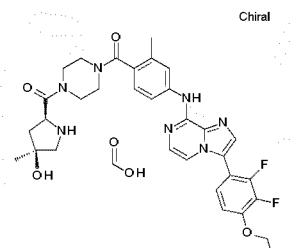
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REF 311	1-(4-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)-2-(methylamino)ethanone hydrochloride	 ClH	532.2	Reference Example 219 and 2-((tert-butoxycarbonyl)(methyl)amino)acetic acid
REF 312	1-(3-(4-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)-3-oxopropyl)guanidine		592.3	Reference Example 218 and 3-guanidinopropanoic acid
REF 313	(2S)-2-amino-1-[4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]piperazin-1-yl]propan-1-one hydrochloride	 Chiral	[M-H] ⁻ ; 584.4	Reference Example 218 and N-Boc-L-Alanine

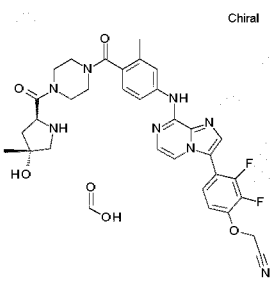
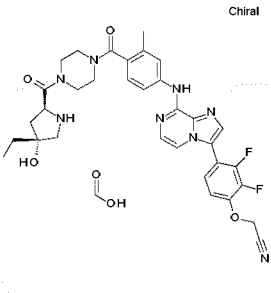
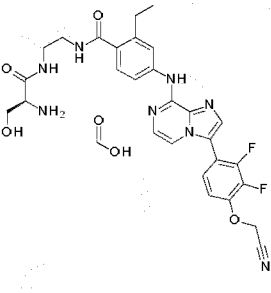
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133	(2S,4S)-N-[2-[[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]ethyl]-4-hydroxy-4-methylpyrrolidine-2-carboxamide formate		605.2	Intermediate 121 and 1,2-Pyrrolidinedicarboxylic acid, 4-hydroxy-4-methyl-, 1-(1,1-dimethylethyl) ester, (2S,4S)- [CAS#1199793-52-6]
134	(2S,4S)-N-[3-[[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]propyl]-4-hydroxy-4-methylpyrrolidine-2-carboxamide formate		619.1	Intermediate 122 and 1,2-Pyrrolidinedicarboxylic acid, 4-hydroxy-4-methyl-, 1-(1,1-dimethylethyl) ester, (2S,4S)- [CAS#1199793-52-6]
REF 314	[4-[[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-4-[(2S,4S)-4-hydroxypyrrolidine-2-carbonyl]piperazin-1-yl]methanone		[M-H] ⁻ ; 590.0	Reference Example 134 and (2S,4S)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid [CAS#87691-27-8]

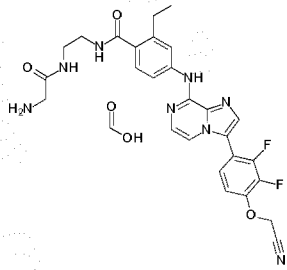
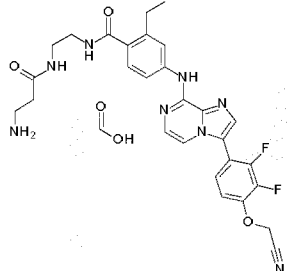
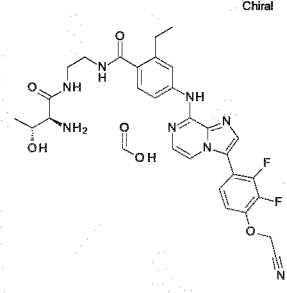
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REF 315	[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[rac-(2R,4S)-4-hydroxypyrrolidine-2-carbonyl]piperazin-1-yl]methanone		[M-H] ⁻ ; 590.4	Reference Example 134 and (2R,4S)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid [CAS#147266-92-0]
REF 316	2-[4-[8-[4-[4-[(2S,4S)-4-ethyl-4-hydroxy-pyrrolidine-2-carbonyl]piperazine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]acetonitrile formate		645.5	Intermediate 109 and Intermediate 126
REF 317	2-[2,3-difluoro-4-[8-[4-[4-[(2S,4S)-4-hydroxy-4-methylpyrrolidine-2-carbonyl]piperazine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate		631.2	Intermediate 109 and 1,2-pyrrolidinedicarboxylic acid, 4-hydroxy-4-methyl-, 1-(1,1-dimethylethyl) ester, (2S,4S)- [CAS#1199793-52-6]

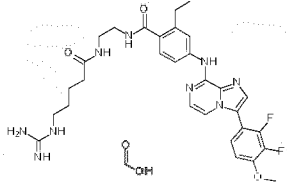
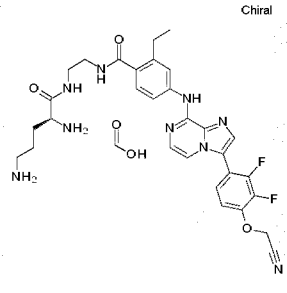
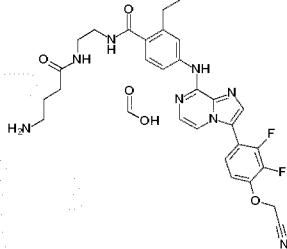
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REF 318	2-[2,3-difluoro-4-[8-[4-[4-[(2S,4R)-4-hydroxy-4-methyl-pyrrolidine-2-carbonyl]piperazine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]phenoxy]acetonitrile formate	 Chiral	631.4	Intermediate 109 and 1, 2-Pyrrolidinedicarboxylic acid, 4-hydroxy-4-methyl-, 1-(1,1-dimethylethyl) ester, (2S,4R)- [CAS#1365970-67-7]
REF 319	2-[4-[8-[4-[4-[(2S,4R)-4-ethyl-4-hydroxy-pyrrolidine-2-carbonyl]piperazine-1-carbonyl]-3-methyl-anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]acetonitrile formate	 Chiral	645.4	Intermediate 109 and Intermediate 127
135	N-[2-[[[(2S)-2-amino-3-hydroxy-propanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide formate	 Chiral	579.4	Intermediate 116 and BOC-SER-OH

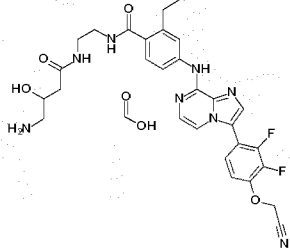
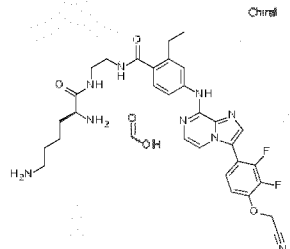
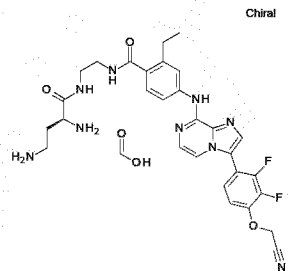
-317-

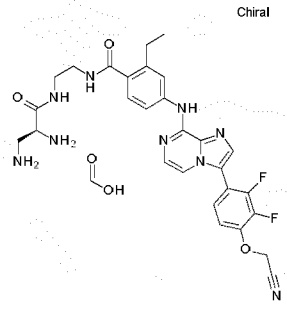
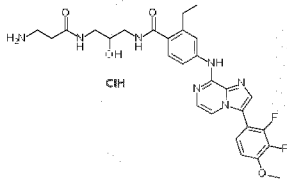
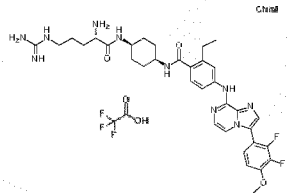
136	N-[2-[(2-aminoacetyl)amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide formate		549.4	Intermediate 116 and BOC-glycine
137	N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide formate		563.3	Intermediate 116 and BOC-BETA-ALA-OH
138	N-[2-[[[(2S,3R)-2-amino-3-hydroxybutanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide formate		593.3	Intermediate 116 and BOC-THR-OH

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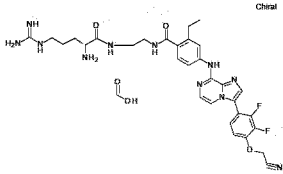
139	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-(5-guanidinopentanoylamino)ethyl]benzamide formate		608.1	Example 117 and 5-guanidinopentanoic acid
140	4-[[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,5-diaminopentanoyl]amino]ethyl]-2-ethylbenzamide formate		606.2	Intermediate 116 and BOC-ORN(BOC)-OH
141	N-[2-(4-aminobutanoylamino)ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide formate		577.5	Intermediate 116 and BOC-gamma-abu-OH

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142	N-[2-[(4-amino-3-hydroxy-butanoyl)amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide formate		593.4	Intermediate 116 and 4-(tert-butoxycarbonylamino)-3-hydroxy-butanoic acid
143	4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,6-diaminohexanoyl]amino]ethyl]-2-ethyl-benzamide formate		620.4	Intermediate 116 and BOC-LYS(BOC)-OH
144	4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,4-diaminobutanoyl]amino]ethyl]-2-ethyl-benzamide formate		592.4	Intermediate 116 and (2S)-2,4-bis(tert-butoxycarbonylamino)butanoic acid

145	4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,3-diaminopropanoyl]amino]ethyl]-2-ethyl-benzamide formate		578.4	Intermediate 116 and (2S)-2,3-bis(tert-butoxycarbonylamino) propanoic acid
146	N-[3-(3-aminopropanoylamino)-2-hydroxy-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide hydrochloride		568.3	Intermediate 147 and 3-((tert-butoxycarbonyl)amino) propanoic acid [CAS#3303-84-2]
REF 320	N-[4-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]cyclohexyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide trifluoroacetate		677.4	Reference Example 321 and L-arginine. Deprotection with TFA/DCM 2/1 at rt for 2 h, then precipitated from the reaction mixture by the addition of diethylether.

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148	N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide formate		648.1	Intermediate 116 and Fmoc-D-ARG-OH. Deprotection with 10 eq piperidine in DCM at rt for 12h. Purification with prep HPLC (FA)
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Intermediate 126**(2S,4S)-1-tert-butoxycarbonyl-4-ethyl-4-hydroxy-pyrrolidine-2-carboxylic acid****And Intermediate 127****5 (2S,4R)-1-tert-butoxycarbonyl-4-ethyl-4-hydroxy-pyrrolidine-2-carboxylic acid**

Ethylmagnesium bromide (7.27 mL, 21.81 mmol, 2.5 eq) was added dropwise to a THF (50 mL) solution of (2S)-1-tert-butoxycarbonyl-4-oxo-pyrrolidine-2-carboxylic acid [CAS#84348-37-8] (2.0 g, 8.72 mmol, 1 eq) at - 20°C under nitrogen atmosphere. The resulting mixture was stirred at the same temperature for 1 h and then further stirred at 0 °C for 10 h. The reaction mixture

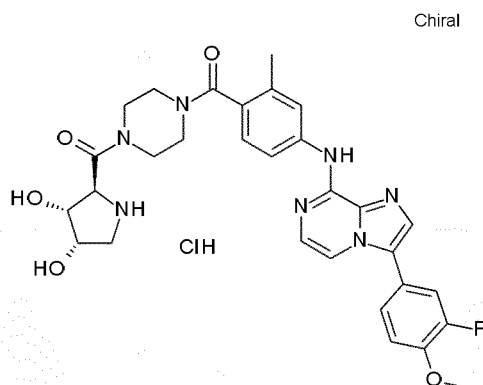
10 was poured into 1 N aqueous hydrochloric acid solution (100 mL) under ice cooling, followed by extraction with ethyl acetate. The organic layer was washed with brine and dried over anhydrous Na₂SO₄. The solvent was evaporated under reduced pressure and the crude product was purified by prep. HPLC(FA as additive) to deliver (2S,4S)-1-tert-butoxycarbonyl-4-ethyl-4-hydroxy-pyrrolidine-2-carboxylic acid (Intermediate 126) (0.800 g, 3.09 mmol, 35.36% yield) as off

15 white solid and (2S,4R)-1-tert-butoxycarbonyl-4-ethyl-4-hydroxy-pyrrolidine-2-carboxylic acid (Intermediate 127) (0.200 g, 0.770 mmol, 8.84 % yield) as off white solid.

Reference Example 322

((2S,3R,4S)-3,4-dihydroxypyrrolidin-2-yl)(4-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)methanone hydrochloride

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Step 1: tert-butyl (S)-2-(4-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carbonyl)-2,5-dihydro-1H-pyrrole-1-carboxylate

- 5 The title compound was prepared in analogy to Reference Example 259 from Reference Example 219 and (S)-1-(tert-butoxycarbonyl)-2,5-dihydro-1H-pyrrole-2-carboxylic acid without cleavage of the Boc-protective group.

MS (ESI) $[M+H]^+$: 656.5

Step 2: tert-butyl (2S,3R,4S)-2-(4-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carbonyl)-3,4-dihydroxypyrrolidine-1-carboxylate

- tert-butyl (S)-2-(4-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carbonyl)-2,5-dihydro-1H-pyrrole-1-carboxylate (50 mg, 76.3 μ mol, Eq: 1) was dissolved in a mixture of tert-BuOH (750 μ l), tetrahydrofuran (200 μ l) and
- 15 water (50 μ l). Osmium tetroxide in water (4%) (48.5 mg, 59.8 μ L, 7.63 μ mol, Eq: 0.1) was added, followed by 4-methylmorpholine N-oxide (13.4 mg, 114 μ mol, Eq: 1.5). The mixture was stirred overnight. Then additional osmium tetroxide in water (4 %) (48.5 mg, 59.8 μ l, 7.63 μ mol, Eq: 0.1) and 4-methylmorpholine N-oxide (13.4 mg, 114 μ mol, Eq: 1.5) were added and the mixture was stirred over 72 h. The reaction was quenched by addition of sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$ and
- 20 then extracted with 2-MeTHF. The combined organic layers were washed with sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$ and brine and then concentrated *in vacuo*. The residue was purified by prep. HPLC to obtain the title compound (52.6 mg) as a light brown solid.

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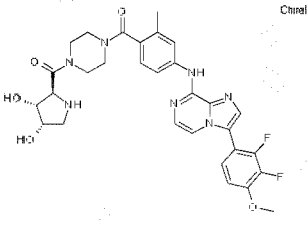
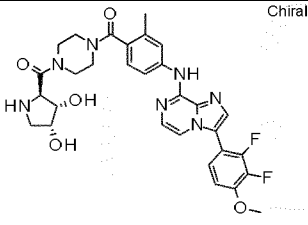
MS (ESI) $[M+H]^+$: 690.4

Step 3: ((2S,3R,4S)-3,4-dihydroxypyrrolidin-2-yl)(4-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)methanone hydrochloride

- 5 4M HCl in dioxane (50 μ l) was added to tert-butyl ((2S,3R,4S)-2-(4-(4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carbonyl)-3,4-dihydroxypyrrolidine-1-carboxylate (8.3 mg, 12 μ mol, Eq: 1) in DCM (200 μ L). The reaction mixture was stirred overnight and then concentrated *in vacuo* to give the title compound (8.9 mg) as a white solid. MS (ESI) $[M+H]^+$: 590.3

10

The following examples were prepared in analogy to Reference Example 322

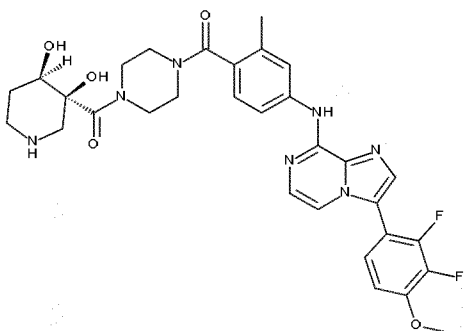
Ex.	Name	Structure	MS ESI $[M+H]^+$	Starting Material
REF 323	(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)((2S,3R,4S)-3,4-dihydroxypyrrolidin-2-yl)methanone		608.2	from Reference Example 134 and (S)-1-(tert-butoxycarbonyl)-2,5-dihydro-1H-pyrrole-2-carboxylic acid
REF 324	(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-		608.3	from Reference Example 134 and (R)-1-(tert-butoxycarbonyl)-2,5-

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	methylbenzoyl)piperazin-1-yl)((2R,3S,4R)-3,4-dihydroxypyrrolidin-2-yl)methanone			dihydro-1H-pyrrole-2-carboxylic acid
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Reference Example 325

rel-(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)((3R,4S)-3,4-dihydropiperidin-3-yl)methanone



5

Step 1: 1-(tert-butoxycarbonyl)-1,2,5,6-tetrahydropyridine-3-carboxylic acid

1,2,5,6-tetrahydropyridine-3-carboxylic acid hydrochloride (1 g, 6.11 mmol, Eq: 1) was combined with dioxane (7.8mL) and water (7.8 mL) to give a orange solution. Then di-tert-butyl dicarbonate (1.47 g, 6.72 mmol, Eq: 1.1) was slowly added as, a solution in dioxane (7.8 mL).

- 10 After 15min, NaOH (8mL, 8 mmol, Eq: 1.31) was added and the RM stirred at RT overnight. The volatiles were removed, the reaction mixture was poured into 50 mL tBuOMe and extracted with 1 M HCl (2 x 25 mL). The aqueous layer was back-extracted with tBuOMe (2 x 25 mL). The organic layers were combined, washed with sat NaCl (2 x 25 mL), then dried over MgSO₄, filtered and concentrated in vacuo, the crude intermediate was used in the next step without
- 15 further purification. MS (ESI) [M+H]⁺: 228.0

Step 2: 1-tert-butyl 5-O-methyl 3,6-dihydro-2H-pyridine-1,5-dicarboxylate

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1-(tert-Butoxycarbonyl)-1,2,5,6-tetrahydropyridine-3-carboxylic acid (409 mg, 1.8 mmol, Eq: 1) was dissolved in DMF (9 mL). potassium carbonate (298 mg, 2.16 mmol, Eq: 1.2) and MeI (511 mg, 225 μ L, 3.6 mmol, Eq: 2) were successively added and RM was stirred at RT overnight. The RM was concentrated under HV. Residue was dissolved in ethyl acetate, filtered and
5 concentrated under vacuum. MS (ESI) $[M+H]^+$: 186.1 (carbamic acid, M-55)

Step 3: 1-tert-butyl 3-O-methyl (3R,4S)-3,4-dihydroxypiperidine-1,3-dicarboxylate

1-(tert-butyl) 3-methyl 5,6-dihydropyridine-1,3(2H)-dicarboxylate (434 mg, 1.8 mmol, Eq: 1) was dissolved in tBuOH (20 mL). NMO (211 mg, 1.8 mmol, Eq: 1) and 4% osmium tetroxide in water (1.14 g, 1.41 mL, 180 μ mol, Eq: 0.1) were successively added. Sodium thiosulfate (1.42 g,
10 8.99 mmol, Eq: 5) was added to quench the reaction but insoluble in tBuOH. The minimum amount of saturated $Na_2S_2O_3$ solution was added to solubilize the salt and RM was stirred for 1 h. RM was filtered through a pad of celite and concentrated under vacuum. Purification by combiflash. MS (ESI) $[M+H]^+$: 176.1 (M-Boc)

**Step 4: 5-(tert-butyl) 3a-methyl (3aR,7aS)-2,2-dimethyldihydro-[1,3]dioxolo[4,5-c]pyridine-
15 3a,5(4H,6H)-dicarboxylate**

To a solution of rac-1-(tert-butyl) 3-methyl (3R,4S)-3,4-dihydroxypiperidine-1,3-dicarboxylate (320 mg, 1.16 mmol, Eq: 1) in DMF (1.16 mL) was added successively 2,2-dimethoxypropane (484 mg, 570 μ L, 4.65 mmol, Eq: 4) and pTsOH (22.1 mg, 116 μ mol, Eq: 0.1). RM was stirred and heated at 40 °C for 8 h and at 30 °C for 48 h. Purification by column chromatography, solid
20 loaded with 1.2 g of silica, 12 g, heptane/ethyl acetate. Enantiomers were separated by SFC.

MS (ESI) $[M+H]^+$: 260.2 (M-tBu)

Step 5: (3aS,7aR)-5-(tert-butoxycarbonyl)-2,2-dimethyltetrahydro-[1,3]dioxolo[4,5-c]pyridine-3a(4H)-carboxylic acid

To a solution of 5-(tert-butyl) 3a-methyl (3aS,7aR)-2,2-dimethyldihydro-[1,3]dioxolo[4,5-
25 c]pyridine-3a,5(4H,6H)-dicarboxylate (100 mg, 317 μ mol, Eq: 1) in THF (1 mL)/MeOH (500 μ L) was added LiOH (1 mL, 2 mmol, Eq: 6.31). The RM was stirred at RT for 2 h. Volatiles were removed under vacuum and mixture was put in the freezer overnight. DCM was added and mixture was stirred. Aqueous phase was acidified with ammonium chloride and then with HCl 1M until pH 4. Phases were separated and extraction with 2x 10 mL of DCM. Organic layers

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were combined, filtered through a pad of MgSO₄, concentrated *in vacuo* to provide an oil. MS (ESI) [M-H]⁻: 300.3

Step 6: rel-(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazin-1-yl)((3R,4S)-3,4-dihydroxypiperidin-3-yl)methanone

- 5 The title compound was prepared in analogy to Reference Example 259 from Reference Example 134 and rel-(3aR,7aS)-5-(tert-butoxycarbonyl)-2,2-dimethyltetrahydro-[1,3]dioxolo[4,5-c]pyridine-3a(4H)-carboxylic acid. MS (ESI) [M+H]⁺: 622.4

Intermediate 124:

tert-butyl (3R)-3-[[tert-butyl(dimethyl)silyl]oxymethyl]piperazine-1-carboxylate

- 10 To a solution of tert-butyl (3R)-3-(hydroxymethyl)piperazine-1-carboxylate [CAS# 278788-66-2] (200.0 mg, 0.920 mmol, 1 eq) and imidazole (75.54 mg, 1.11 mmol, 1.2 eq) in DCM (2 mL) was added tert-butyldimethylchlorosilane (153.31 mg, 1.02 mmol, 1.1 eq). The reaction was stirred at 20 °C for 12 h. The reaction was concentrated. The residue was purified by prep-TLC(PE:EtOAc=0:1) to give tert-butyl (3R)-3-[[tert-butyl(dimethyl)silyl]oxymethyl]piperazine-1-carboxylate (180 mg, 0.540 mmol, 58.89 % yield) as colorless oil.

The following Intermediate was prepared in analogy to Intermediate 124

Int.	Name	MS ESI [M+H] ⁺	Starting Material
12 5	tert-butyl (3S)-3-[[tert-butyl(dimethyl)silyl]oxymethyl]piperazine-1-carboxylate		tert-butyl (3S)-3-(hydroxymethyl)piperazine-1-carboxylate

Intermediate 129

- 20 **2-(4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2,3-difluorophenoxy)propanenitrile**

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To a solution of Intermediate 54 (500mg, 1.78 mmol) in MeCN (30 mL) was added potassium carbonate (491 mg, 3.55 mmol) and 3-bromobutanenitrile (263 mg, 1.78 mmol), the reaction was stirred for 16 h at 60 °C. The reaction mixture was filtered and the filtrate was concentrated in vacuum. The residue was washed with brine and extracted in DCM. The organic layer was dried
5 over anhydrous Na₂SO₄ and concentrated under reduced pressure to give 2-(4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2,3-difluorophenoxy)propanenitrile (530 mg, 1.58 mmol, 89.2 % yield) which was directly used for the next step without further purification.

Intermediate 130

4-((3-(4-(1-Cyanoethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-
10 methylbenzoic acid

To a solution of Intermediate 129 (520mg, 1.55 mmol) in the mixture solvent of MeCN (20mL) and acetic acid (4 mL) was added 4-amino-2-methylbenzoic acid (235 mg, 1.55 mmol), the reaction was stirred for 15 hours at 90 °C. The reaction mixture was cooled to room temperature and filtered. The filter cake was dried in vacuum to give 4-((3-(4-(1-cyanoethoxy)-2,3-
15 difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid (560 mg, 1.25 mmol, 80.2 % yield). MS (ESI) [M+H]⁺: 450.1

Intermediate 131

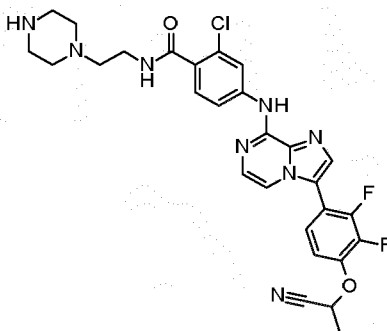
2-chloro-4-((3-(4-(1-cyanoethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid

20 To a solution of Intermediate 129 (500mg, 1.49 mmol) in the mixture solvent of MeCN (20mL) and acetic acid (4 mL) was added 4-amino-2-chlorobenzoic acid (256 mg, 1.49 mmol), the reaction was stirred for 15 hours at 90 °C. The reaction mixture was cooled to room temperature and filtered. The filter cake was dried in vacuum to give 2-chloro-4-((3-(4-(1-cyanoethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid (530mg, 1.13 mmol, 75.5 %
25 yield). MS (ESI) [M+H]⁺: 470.3

Example 149

2-Chloro-4-[[3-[4-(1-cyanoethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)benzamide formate

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Step 1: tert-butyl 4-[2-[[2-chloro-4-[[3-[4-(1-cyanoethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]ethyl]piperazine-1-carboxylate

To a solution of Intermediate 131 (100mg, 213 μ mol) in DMF (3 mL) was added tert-butyl 4-(2-aminoethyl)piperazine-1-carboxylate (48.8 mg, 213 μ mol), triethylamine (43.1 mg, 426 μ mol) and 2,4,6-tripropyl-1,3,5,2,4,6-trioxatriphosphinane 2,4,6-trioxide (102 mg, 319 μ mol). The reaction was stirred for 30 minutes at room temperature. The mixture was poured into water and filtered. The filter cake was dried in vacuum to give tert-butyl 4-[2-[[2-chloro-4-[[3-[4-(1-cyanoethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]ethyl]piperazine-1-carboxylate (135 mg).

Step 2: 2-chloro-4-[[3-[4-(1-cyanoethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)benzamide formate

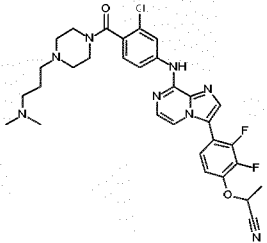
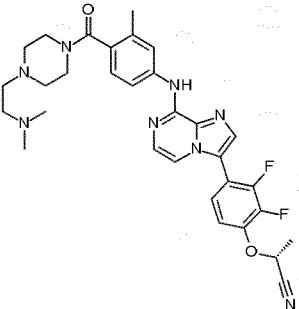
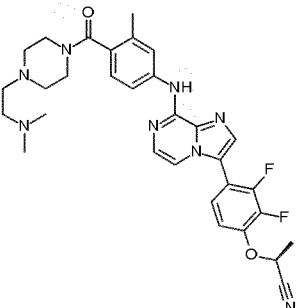
To a solution of tert-butyl 4-(2-((2-chloro-4-((3-(4-(1-cyanoethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamido)ethyl)piperazine-1-carboxylate (135mg) in THF (10 mL) was added concentrated HCl (2 mL), the reaction was stirred for two hours at room temperature. The reaction mixture was cooled to 0 °C and basified with ammonia. The mixture was extracted in ethyl acetate and the organic layer was concentrated in vacuum. The residue was purified by preparative HPLC to give 2-chloro-4-[[3-[4-(1-cyanoethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)benzamide (45 mg). MS obsd. (ESI⁺) [(M+H)⁺]: 581

The following examples were prepared in analogy to Example 149, the deprotection step 2 was only applied for intermediates derived from Boc-protected amines.

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Ex [#]	Name	Structure	ESI [M+H] ⁺	Starting Material
REF 326	2-[4-[8-[4-[4-[3-(dimethylamino)propyl]piperazine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]propanenitrile formate		603.4	Intermediate 130 and N,N-dimethyl-3-(piperazin-1-yl)propan-1-amine
REF 327	2-[4-[8-[4-[4-[2-(dimethylamino)ethyl]piperazine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]propanenitrile; 2,2,2-trifluoroacetic acid		589.4	Intermediate 130 and N,N-dimethyl-2-(piperazin-1-yl)ethan-1-amine
REF 328	2-[4-[8-[3-chloro-4-[4-[2-(dimethylamino)ethyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-		609.5	Intermediate 131 and N,N-dimethyl-2-(piperazin-1-yl)ethan-1-amine

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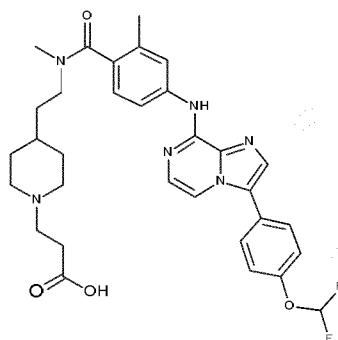
	phenoxy]propanenitrile formate			
REF 329	2-[4-[8-[3-chloro-4-[4-[3-(dimethylamino)propyl]piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]propanenitrile		623.5	Intermediate 131 and N,N-dimethyl-3-(piperazin-1-yl)propan-1-amine
REF 330	(2R)-2-[4-[8-[4-[4-[2-(dimethylamino)ethyl]piperazine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]propanenitrile formate		589.4	The compound obtained by chiral separation of Reference Example 327
REF 331	((2S)-2-[4-[8-[4-[4-[2-(dimethylamino)ethyl]piperazine-1-carbonyl]-3-methylanilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-		589.4	The compound was obtained by chiral separation of Reference Example 327

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	phenoxy]propanenitrile formate			
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Example 150

3-(4-(2-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamido)ethyl)piperidin-1-yl)propanoic acid



5

Step 1)

N-[2-[1-(2-cyanoethyl)-4-piperidyl]ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide

4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethyl-N-(2-(piperidin-4-yl)ethyl)benzamide (Example 81, 96 mg, 180 μ mol, Eq: 1), acrylonitrile (95.3 mg, 1.8 mmol, Eq: 10) and DIPEA (116 mg, 157 μ L, 898 μ mol, Eq: 5) were combined with dioxane (3mL) and stirred at 100 °C overnight. The reaction mixture was concentrated to dryness and purified by flash chromatography to give a brown viscous oil (53 mg, yield: 54 %). MS (ESI): $[M+H]^+$: 588.5

Step 2)

3-[4-[2-[1-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]-methyl-amino]ethyl]-1-piperidyl]propanoic acid

N-(2-(1-(2-cyanoethyl)piperidin-4-yl)ethyl)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamide (25 mg, 42.5 μ mol, Eq: 1) was combined with

15

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dioxane (0.25 mL). 2M aq NaOH (425 μ L, 851 μ mol, Eq: 20) was added, and the reaction mixture was stirred at 100 °C overnight. After cooling down to RT, the reaction mixture was directly acidified with 2M aq HCl solution. The crude product obtained was purified by preparative HPLC. Finally the product was lyophilized to give the target compound as a light brown solid (3.7 mg, yield: 14%). MS (ESI): [M-H]⁻: 605.8

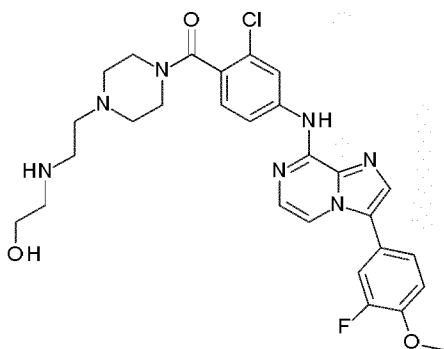
Intermediate 132

[4-(2-chloroethyl)piperazin-1-yl]-[2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]methanone

2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid (Intermediate 2) (200 mg, 484 μ mol, Eq: 1) was combined with DMF (6mL). DIPEA (188 mg, 254 μ l, 1.45 mmol, Eq: 3) and HATU (368 mg, 969 μ mol, Eq: 2.00) were added, followed, after stirring at RT for 15 minutes, by addition of 1-(2-chloroethyl)piperazine [CAS 61308-25-6] (108 mg, 727 μ mol, Eq: 1.5). After stirring for 3 h at RT, the reaction mixture was poured into 25 mL H₂O and extracted with ethyl acetate. The crude product was used without further purification. MS (ESI): [M+H]⁺: 544.3

Reference Example 332

(2-Chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)(4-(2-chloroethyl)piperazin-1-yl)methanone



(2-chloro-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)(4-(2-chloroethyl)piperazin-1-yl)methanone (Intermediate 132) (40 mg, 73.6 μ mol, Eq: 1), 2-aminoethan-1-ol (6.72 mg, 110 μ mol, Eq: 1.50), sodium carbonate (11.7 mg, 110 μ mol, Eq: 1.50), potassium iodide (611 μ g, 3.68 μ mol, Eq: 0.05) were combined with BuOH (800 μ l) and

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stirred at 105 °C for 24 h. After extraction with DCM/water, the crude material was purified via prep HPLC to give the target compound (6.9 mg, yield: 16 %). MS (ESI): $[M+H]^+$: 568.2

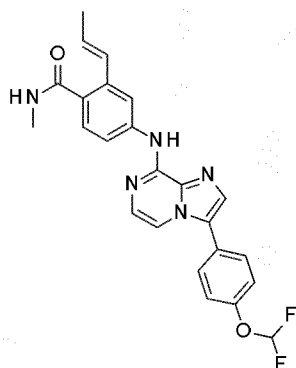
Intermediate 48

Methyl 4-amino-2-vinylbenzoate

- 5 A mixture of methyl 4-amino-2-bromobenzoate (500 mg, 2.17 mmol, Eq: 1), 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (502 mg, 553 μ L, 3.26 mmol, Eq: 1.5), Na_2CO_3 (461 mg, 4.35 mmol, Eq: 2) and 1,1'-bis(diphenylphosphino)ferrocenedichloro palladium(II) dichloromethane complex (159 mg, 217 μ mol, Eq: 0.1) in dioxane (6 mL) and water (600 μ L) was heated in a microwave at 100 °C for 30 min. The reaction mixture was then poured into 30 mL H_2O and extracted with ethyl acetate (3 x 50 mL). The organic layers were dried over MgSO_4 and concentrated in vacuo. The crude material was purified by flash chromatography. MS (ESI): $[M+H]^+$: 178.2

Example 151

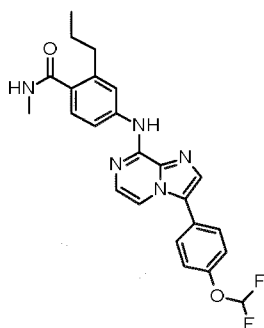
- (E)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methyl-2-(prop-1-en-1-yl)benzamide



- 2-Bromo-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methylbenzamide (Intermediate 93) (50 mg, 102 μ mol, Eq: 1), (E)-prop-1-en-1-ylboronic acid (13.2 mg, 154 μ mol, Eq: 1.5), Na_2CO_3 (21.7 mg, 205 μ mol, Eq: 2) and 1,1'-bis(diphenylphosphino)ferrocenedichloro palladium(II) dichloromethane complex (7.49 mg, 10.2 μ mol, Eq: 0.1) were combined in dioxane (1.5 mL) and water (150 μ L) and heated in the microwave at 90 °C for 30 min. The reaction mixture was poured into 50 mL H_2O and extracted with ethyl acetate (3 x 75 mL). The organic layers were dried over MgSO_4 and concentrated in

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vacuo. The crude material was purified by prep HPLC to give the target compound (68 %). MS (ESI): $[M+H]^+$: 450.2

Example 152**4-((3-(4-(Difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methyl-2-propylbenzamide**

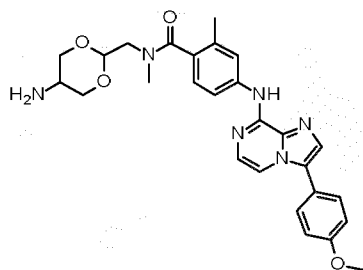
4-((3-(4-(Difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methyl-2-propylbenzamide (Example 151) (20.8 mg, 46.1 μ mol, 76.7 % yield) was dissolved in MeOH and palladium on carbon was added. The reaction was stirred under hydrogen. The reaction mixture was carefully filtered under argon through Celite. MS (ESI): $[M+H]^+$: 452.1

Intermediate 133**N-(2,2-Diethoxyethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamide**

4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid (Intermediate 4) (150 mg, 401 μ mol, Eq: 1) and 2,2-diethoxy-N-methylethanamine (70.8 mg, 481 μ mol, Eq: 1.20) were combined with DMF (4.5 mL). HATU (305 mg, 801 μ mol, Eq: 2.00) and DIPEA (155 mg, 210 μ l, 1.2 mmol, Eq: 3.00) were added, and the reaction mixture was stirred at RT. The reaction mixture was directly purified by flash chromatography (reverse phase, 20 g, 0% to 100% acetonitrile in water). MS (ESI): $[M+H]^+$: 504.3

Example 153**N-((5-Amino-1,3-dioxan-2-yl)methyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamide**

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N-(2,2-Diethoxyethyl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamide (Intermediate 133) (100 mg, 199 μmol , Eq: 1) and benzyl (1,3-dihydroxypropan-2-yl)carbamate (47 mg, 209 μmol , Eq: 1.05) were combined with toluene (1.5 mL), pTsOH (1.89 mg, 9.93 μmol , Eq: 0.05) was added, and the reaction mixture was stirred at reflux overnight. After cooling down to RT, the reaction mixture was concentrated to dryness, and purified by flash chromatography. MS (ESI): $[\text{M}+\text{H}]^+$: 637.4.

The product obtained was dissolved in MeOH, palladium on carbon 10% was added and the reaction mixture obtained was stirred under hydrogen. The crude was purified by flash chromatography. MS (ESI): $[\text{M}+\text{H}]^+$: 503.3

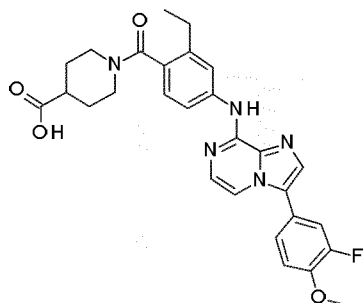
The following examples were prepared in analogy to Example 153

Example	Name	Structure	MS ESI $[\text{M}+\text{H}]^+$	Starting Material
REF 333	N-(2-(aminomethyl)-1,3-dioxan-5-yl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide		489.2	Intermediate 154 and benzyl (2,2-diethoxyethyl)carbamate

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Intermediate 154**N-(1,3-Dihydroxypropan-2-yl)-4-((3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide**

5 4-((3-(4-Methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoic acid (Intermediate 4) (150 mg, 401 μ mol, Eq: 1) and 2-aminopropane-1,3-diol (36.5 mg, 401 μ mol, Eq: 1.50) were combined with DMF (3 mL) to give a light yellow suspension. HATU (152 mg, 401 μ mol, Eq: 1.50) and DIPEA (104 mg, 140 μ l, 801 μ mol, Eq: 3.00) were added, and the reaction mixture was stirred at RT. The reaction mixture was directly purified by flash chromatography (reverse
10 phase, 20g, 0% to 100% acetonitrile in water). MS (ESI): $[M+H]^+$: 448.2.

Reference Example 334**1-(2-Ethyl-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperidine-4-carboxylic acid**

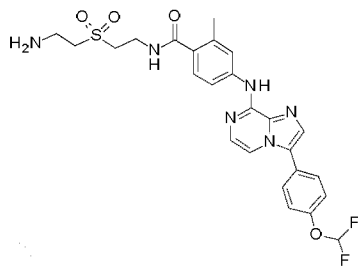
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This example was prepared in analogy to Reference Example 1 from Intermediate 106. MS (ESI): $[M+H]^+$: 518.3

Reference Example 335

20 **N-(2-((2-Aminoethyl)sulfonyl)ethyl)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide**

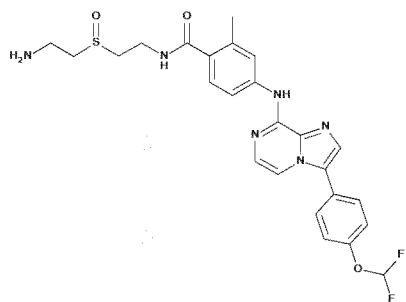
-337-



A solution of 3-chloroperoxybenzoic acid (19.9 mg, 80.7 μmol , Eq: 2.2) in DCM (2 mL) was added slowly to a solution of N-(2-((2-aminoethyl)thio)ethyl)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide (Intermediate 84) (18.8 mg, 36.7 μmol , Eq: 1) in DCM (2 mL) at -78°C under Ar. The mixture was stirred at -78°C for 1h and then warmed to RT. The reaction mixture was poured into 5 mL 1 M NaOH and extracted with DCM (5 x 20 mL). The organic layers were dried over sodium sulphate and concentrated in vacuo. MS (ESI): $[M+H]^+$: 545.2

Reference Example 336

10 N-(2-((2-Aminoethyl)sulfinyl)ethyl)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide



A solution of 3-chloroperoxybenzoic acid (7.4 mg, 33 μmol , Eq: 0.9) in DCM (2 mL) was added slowly to a solution of N-(2-((2-aminoethyl)thio)ethyl)-4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide (84-001) (18.8 mg, 36.7 μmol , Eq: 1) in DCM (2 mL) at -78°C under Ar. The mixture was stirred at -78°C for 1h. The RM was quenched at -78°C with NaOH. The reaction mixture was poured into 5 mL 1 M NaOH and extracted with DCM (3 x 20 mL). The organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. MS (ESI): $[M+H]^+$: 529.2

Intermediate 107**2-(4-(Difluoromethoxy)-2,3-difluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane****Step1: 1-bromo-4-(difluoromethoxy)-2,3-difluorobenzene**

5 4-bromo-2,3-difluorophenol (500 mg, 2.39 mmol, Eq: 1), sodium 2-chloro-2,2-difluoroacetate (730 mg, 4.78 mmol, Eq: 2) and potassium carbonate (397 mg, 2.87 mmol, Eq: 1.2) were dissolved in DMF (6 mL) and water (1.5 mL). The reaction mixture was heated to 100 °C and stirred for 3 h. The reaction mixture was poured into 20 mL sat NaHCO₃ and extracted with DCM (5 x 40 mL). The organic layers were dried over Na₂SO₄ and concentrated in vacuo. The
10 crude material was purified by flash chromatography.

Step2: 2-(4-(difluoromethoxy)-2,3-difluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

1-bromo-4-(difluoromethoxy)-2,3-difluorobenzene (240 mg, 927 µmol, Eq: 1), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (282 mg, 1.11 mmol, Eq: 1.2), potassium acetate (182 mg, 1.85 mmol, Eq: 2) and dichlorobis(triphenylphosphine)palladium(II) (32.5 mg, 46.3 µmol, Eq: 0.05) were dissolved in dioxane (1 mL). The reaction mixture was heated to 100 °C and
15 stirred for O/N. The crude material was purified by flash chromatography (silica gel, 40 g, 0% to 35% ethyl acetate in heptane). MS (ESI): [M+H]⁺: 306.1

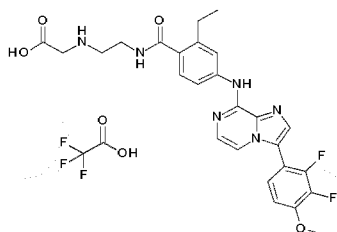
Intermediate 88**2-(2-chloro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)acetonitrile**

20 2-(4-bromo-2-chlorophenoxy)acetonitrile (500 mg, 2.03 mmol, Eq: 1), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (567 mg, 2.23 mmol, Eq: 1.10), potassium acetate (398 mg, 4.06 mmol, Eq: 2.00) and bis(triphenylphosphine)palladium(II)chloride (71.2 mg, 101 µmol, Eq: 0.05) were combined with dioxane (7.5 mL). After degassing with N₂, the reaction mixture was heated to 100 °C and stirred overnight. The reaction mixture was cooled to RT, adsorbed on
25 Isolute HM-N and after evaporation to dryness, the crude material was purified by flash chromatography (silica gel, 40 g, 0% to 80% ethyl acetate in heptane). MS (ESI): [M+H]⁺: 293.9

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Reference Example 337

(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethyl)glycine compound with 2,2,2-trifluoroacetic acid



5 Step1: tert-butyl (2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethyl)glycinate

N-(2-aminoethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride (Intermediate 117) (40 mg, 79.5 μ mol, Eq: 1) was combined with DMF (600 μ l). TEA (32.2 mg, 44.3 μ l, 318 μ mol, Eq: 4.00) was added dropwise, followed by
10 addition of tert-butyl 2-chloroacetate (13.2 mg, 12.5 μ L, 87.5 μ mol, Eq: 1.10). The reaction mixture was stirred at RT for 24h. The crude material was purified by prep HPLC. MS (ESI): [M+H]⁺: 581.4

Step2: 2 (2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethyl)glycine compound trifluoroacetate

15 tert-Butyl (2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethyl)glycinate (15 mg, 25.8 μ mol, Eq: 1) was combined with DCM (200 μ L). TFA (29.5 mg, 19.9 μ L, 258 μ mol, Eq: 10.0) was added, and the reaction mixture was stirred at RT. The reaction mixture was concentrated to dryness, and lyophilized.

MS (ESI): [M+H]⁺: 525.2

20

The following examples were prepared in analogy to Reference Example 337

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Ex#	Name	Structure	MS ESI [M+H] ⁺	Starting Material
REF 338	(3-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)glycine compound trifluoroacetate		539.2	From Intermediate 87 and tert-butyl 2-chloroacetate
REF 339	(5-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)pentyl)glycine hydrochloride		567.2	From Intermediate REF 220 and tert-butyl 2-chloroacetate

Intermediate 135**N-(2-(2-chloroethoxy)ethyl)-4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide**

- 5 To a solution of 4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzoic acid (75 mg, 163 μ mol, Eq: 1) in DMF (815 μ l) was added DIPEA (84.2 mg, 114 μ l, 652 μ mol, Eq: 4) and HATU (124 mg, 326 μ mol, Eq: 2). RM was stirred for

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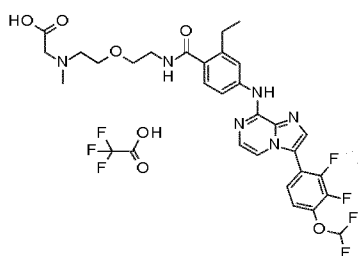
15 min. Then 2-(2-chloroethoxy)ethan-1-amine hydrochloride (26.1 mg, 163 μmol , Eq: 1) was added and the RM was stirred overnight. The RM was purified via prep HPLC. MS (ESI): $[\text{M}+\text{H}]^+$: 566.3

5 The following intermediates were prepared in analogy to Intermediate 135

Int.	Name	MS ESI $[\text{M}+\text{H}]^+$	Starting Material
136	N-(2-(2-chloroethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide	530.2	From 86 and 2-(2-chloroethoxy)ethan-1-amine hydrochloride

Reference Example 340

N-(2-(2-(4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)-N-methylglycine trifluoroacetate



10

Step1: tert-Butyl N-(2-(2-(4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)-N-methylglycinate

A mixture of N-(2-(2-chloroethoxy)ethyl)-4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide (Intermediate 135) (50 mg, 88.3 μmol , Eq: 1), tert-butyl methylglycinate (25.7 mg, 177 μmol , Eq: 2), K_2CO_3 (24.4 mg, 177 μmol , Eq: 2) and KI (14.7 mg, 88.3 μmol , Eq: 1) in MeCN/dioxane was heated at 90 $^\circ\text{C}$ for 2 days. Purification by flash chromatography. MS (ESI): $[\text{M}+\text{H}]^+$: 675.4

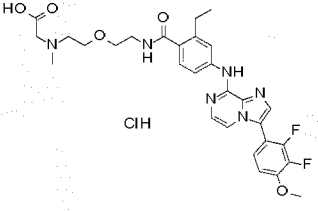
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Step2: N-(2-(2-(4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)-N-methylglycine compound trifluoroacetate

2,2,2-Trifluoroacetic acid (298 mg, 200 μ L, 2.61 mmol, Eq: 36.7) was added to a solution of tert-butyl N-(2-(2-(4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)-N-methylglycinate (48 mg, 71.1 μ mol, Eq: 1) in DCM (200 μ L). RM was stirred for 24 h. The reaction mixture was concentrated to dryness, and lyophilized. MS (ESI): $[M+H]^+$: 619.4

The following examples were prepared in analogy to Reference Example 340

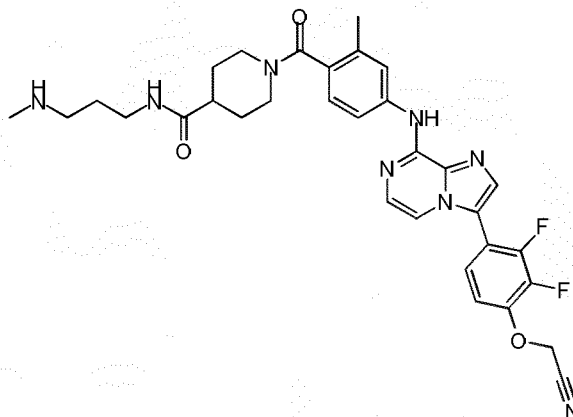
Ex#	Name	Structure	MS ESI $[M+H]^+$	Starting Material
REF 341	N-(2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)-N-methylglycine hydrochloride		583.3	From Intermediate 136 and tert-butyl methylglycinate. Deprotection with HCl

10

Reference Example 342

1-(4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-(3-(methylamino)propyl)piperidine-4-carboxamide

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Step 1: benzyl 4-((3-((tert-butoxycarbonyl)(methyl)amino)propyl)carbamoyl)piperidine-1-carboxylate

To a stirred solution of 1-[(benzyloxy)carbonyl]piperidine-4-carboxylic acid (500.0 mg, 1.9 mmol, 1 eq) and N-(3-aminopropyl)-N-methylcarbamic acid tert-butyl ester (357.53 mg, 1.9 mmol, 1 eq) in DMF (5 mL) was added O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU) (1444.15 mg, 3.8 mmol, 2 eq) and N,N-diisopropylethylamine (1.32 mL, 7.6 mmol, 4 eq) in 20 °C and the mixture stirred at 20 °C for 4 h. The reaction was quenched by water and extracted with EA (20 mLx2), and the combined organic layers were concentrated under reduce pressure. The residue was purified by flash chromatography to get the product benzyl 4-[3-[tert-butoxycarbonyl(methyl)amino]propylcarbamoyl]piperidine-1-carboxylate (640 mg, 1.48 mmol, 77.73% yield) as a yellow oil. (ESI⁺) [(M+23)⁺]: 456.3

Step 2: tert-butyl methyl(3-(piperidine-4-carboxamido)propyl)carbamate

To a solution of benzyl 4-[3-[tert-butoxycarbonyl(methyl)amino]propylcarbamoyl]piperidine-1-carboxylate (500.0 mg, 1.15 mmol, 1 eq) in methanol (10 mL) was added Pd/C (50.0 mg, 1.15 mmol, 1 eq) slowly at 20 °C, the mixture was stirred at 20 °C for 16 h under H₂ atmosphere, the mixture was filtered and concentrated to get the product tert-butyl N-methyl-N-[3-(piperidine-4-carboxylamino)propyl]carbamate (360 mg, 1.2 mmol, 88.62 % yield) as a yellow oil in crude form. (ESI⁺) [(M+1)⁺]: 300.2

Step 3: tert-butyl methyl(3-(1-(2-methyl-4-nitrobenzoyl)piperidine-4-carboxamido)propyl)carbamate

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To a solution of 2-methyl-4-nitro-benzoic acid (254.11 mg, 1.4 mmol, 1.2 eq) and 2-methyl-4-nitro-benzoic acid (254.11 mg, 1.4 mmol, 1.2 eq) in DMF (5 mL), was added N,N-diisopropylethylamine (0.2 mL, 1.17 mmol, 1 eq) and O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (444.48 mg, 1.17 mmol, 1 eq) at 20 °C, the mixture
5 was stirred at 20 °C for 4 h, the mixture was concentrated to get a residue, which was purified by flash chromatography to get the title compound (300 mg, 0.650 mmol, 47.16% yield) as a white solid. (ESI⁺) [(M+23)⁺] : 485.2

Step 4: tert-butyl (3-(1-(4-amino-2-methylbenzoyl)piperidine-4-carboxamido)propyl)(methyl)carbamate

10 To a solution of tert-butyl N-methyl-N-[3-[[1-(2-methyl-4-nitro-benzoyl)piperidine-4-carbonyl]amino]propyl]carbamate (50.0 mg, 0.110 mmol, 1 eq) in methanol (10 mL) was added Pd/C (5.0 mg, 0.110 mmol, 1 eq) at 20 °C, the mixture was stirred at 20 °C for 16 h under H₂. The mixture was filtered and concentrated and the residue was purified by prep-TLC (DCM:MeOH = 10:1) to give the title compound (25 mg, 0.060 mmol, 53.47% yield) as a
15 colorless oil. (ESI⁺) [(M+23)⁺] : 455.2

Step 5: 2-(4-bromo-2,3-difluorophenoxy)acetonitrile

To a mixture of bromoacetonitrile (2.3 g, 19.14 mmol, 2 eq) and potassium carbonate (2.65 g, 19.14 mmol, 2 eq) in DMF (25 mL) was added bromoacetonitrile (2.3 g, 19.14 mmol, 2 eq) and the mixture was stirred for 12 h at 25 °C. The reaction was diluted with water (100 mL) and
20 extracted with ethyl acetate (75 mLx2). The combined organic layers were washed with 50 mL water and 50mL saturated brine sequentially, dried by MgSO₄ and concentrated to dryness. The crude product was then purified by flash column chromatography eluting 20% ethyl acetate in petroleum ether to give the desired product as light yellow oil. ¹H NMR (400 MHz, CHLOROFORM-d) δ = 7.39 - 7.31 (m, 1H), 6.91 - 6.81 (m, 1H), 4.87 (d, J=1.3 Hz, 2H) ppm.

25 **Step 6: 2-(2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)acetonitrile**

The title compound was obtained in analogy to **step 4** in the preparation of Intermediate 27 using 2-(4-bromo-2,3-difluorophenoxy)acetonitrile, used in crude form.

Step 7: 2-(4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2,3-difluorophenoxy)acetonitrile

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The title compound was obtained in analogy to **step 5** in the preparation of Intermediate 27 using 2-(2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)acetonitrile. (ESI⁺) [(M+1)⁺] : 321.0

Step 8: tert-butyl (3-(1-(4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamido)propyl)(methyl)carbamate

To a solution of 2-[4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2,3-difluoro-phenoxy]acetonitrile (18.53 mg, 0.060 mmol, 1 eq) and tert-butyl N-[3-[[1-(4-amino-2-methyl-benzoyl)piperidine-4-carbonyl]amino]propyl]-N-methyl-carbamate (25.0 mg, 0.060 mmol, 1 eq) in tert-butanol (2 mL) was added potassium carbonate (15.98 mg, 0.120 mmol, 2 eq) and Brettphos Pd G3 (2.62 mg, 0.060 mmol, 0.050 eq) at 20 °C, the mixture was stirred at 80 °C for 4 h, the mixture was filtered and concentrated to give the title compound (20 mg, 0.030 mmol, 44.42 % yield) as a yellow oil. (ESI⁺) [(M+1)⁺] : 717.3

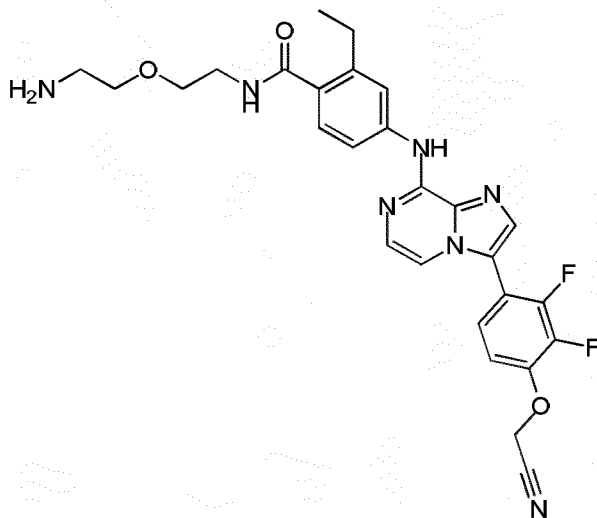
Step 9: 1-(4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)-N-(3-(methylamino)propyl)piperidine-4-carboxamide

The title compound was obtained in analogy to step 2, Example 5 using tert-butyl (3-(1-(4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperidine-4-carboxamido)propyl)(methyl)carbamate. (ESI⁺) [(M+1)⁺] : 617.2

Reference Example 343

N-(2-(2-aminoethoxy)ethyl)-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide

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Step 1: methyl 4-nitro-2-vinylbenzoate

A solution of methyl 2-bromo-4-nitro-benzoate (15.0 g, 57.68 mmol, 1 eq), vinylboronic acid pinacol ester (13.33 g, 86.53 mmol, 1.5 eq), potassium phosphate (14.33 mL, 173.05 mmol, 3 eq) and 1,1'-bis(di-tert-butylphosphino)ferrocene palladium dichloride (3.76 g, 5.77 mmol, 0.100 eq) in toluene (150 mL) and water (5 mL) was heated to 100 °C for 15 h under nitrogen atmosphere. The reaction mixture was concentrated and the residue was purified by silica gel chromatography eluting with petroleum ether/ethyl acetate = 50:1 to afford product methyl 4-nitro-2-vinylbenzoate (6.2 g, 29.93 mmol, 51.88% yield) as a light yellow solid.

Step 2: 4-nitro-2-vinylbenzoic acid

To a solution of methyl 4-nitro-2-vinyl-benzoate (2.0 g, 9.65 mmol, 1 eq) in THF (25 mL) and water (5 mL) was added lithium hydroxide hydrate (0.81 g, 19.31 mmol, 2 eq). The resulting mixture was stirred at 20 °C for 15 h. Then most solvent was removed, the mixture was neutralized with 3 N HCl and extracted with DCM, the obtained organic layer was dried over Na₂SO₄ and concentrated to afford 4-nitro-2-vinyl-benzoic acid (1.68 g, 8.7 mmol, 90.1 % yield) as a yellow solid, which was used directly in next step without further purification.

Step 3: tert-butyl (2-(2-(4-nitro-2-vinylbenzamido)ethoxy)ethyl)carbamate

The title compound was obtained in analogy to step 3, Reference Example 342 using tert-butyl (2-(2-aminoethoxy)ethyl)carbamate and 4-nitro-2-vinylbenzoic acid. (ESI⁺) [(M+23)⁺] : 402.3

Step 4: tert-butyl (2-(2-(4-amino-2-ethylbenzamido)ethoxy)ethyl)carbamate

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The title compound was obtained in analogy to step 4 in Reference Example 342 using tert-butyl (2-(2-(4-nitro-2-vinylbenzamido)ethoxy)ethyl)carbamate. (ESI⁺) [(M+23)]⁺: 374.1

Step 5: tert-butyl (2-(2-(4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)carbamate

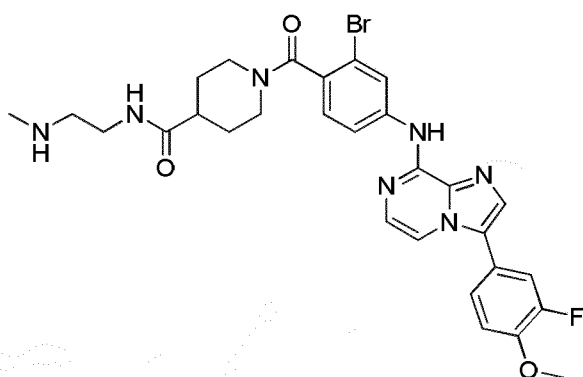
- 5 The title compound was obtained in analogy to step 8 in Reference Example 342 using 2-(4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2,3-difluorophenoxy)acetonitrile and tert-butyl (2-(2-(4-amino-2-ethylbenzamido)ethoxy)ethyl)carbamate. (ESI⁺) [(M+1)]⁺: 636.1

Step 6: N-(2-(2-aminoethoxy)ethyl)-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide

- 10 The title compound was obtained in analogy to step 2, Example 5 using tert-butyl (2-(2-(4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)carbamate. (ESI⁺) [(M+1)]⁺: 536.4

Reference Example 344

- 15 **1-(2-bromo-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)-N-(2-(methylamino)ethyl)piperidine-4-carboxamide; formic acid**



Step 1: benzyl 4-((2-((tert-butoxycarbonyl)(methylamino)ethyl)carbamoyl)piperidine-1-carboxylate; formic acid

- 20 To a solution of 1-[(benzyloxy)carbonyl]piperidine-4-carboxylic acid (1.0 g, 3.8 mmol, 1 eq) in DCM (30 mL) was added N-(2-aminoethyl)-N-methyl carbamic acid tert-butyl ester (727.96 mg, 4.18 mmol, 1.1 eq), triethylamine (1.59 mL, 11.39 mmol, 3 eq) and 1-propanephosphonic anhydride (3625.43 mg, 5.7 mmol, 1.5 eq). The mixture was stirred at 25 °C for 6 h. The reaction

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mixture was washed with aqueous hydrochloric acid, dried over magnesium sulfate, filtered and the filtrate concentrated in vacuo. The residue was purified by prep-HPLC (FA as modifier) to give benzyl 4-[2-[tert-butoxycarbonyl(methyl)amino]ethylcarbamoyl]piperidine-1-carboxylate (1.3 g, 3.1 mmol, 81.59 % yield) as colorless oil. MS (ESI⁺) [M-Boc+H]⁺ : 320

5 **Step 2: tert-butyl methyl(2-(piperidine-4-carboxamido)ethyl)carbamate**

To a solution of benzyl 4-[2-[tert-butoxycarbonyl(methyl)amino]ethylcarbamoyl]piperidine-1-carboxylate (1200.0 mg, 2.86 mmol, 1 eq) in ethyl acetate (30 mL) was added Pd/C (302.92 mg, 0.290 mmol, 0.100 eq). The mixture was stirred at 25 °C for 14 h under H₂ balloon. The mixture was filtered through a Celite pad, and the filtrate was concentrated to give tert-butyl N-methyl-N-[2-(piperidine-4-carboxylamino)ethyl]carbamate (750 mg, 2.63 mmol, 91.88 % yield) as black oil. MS (ESI⁺) [M+H]⁺ : 286

Step 3: methyl 2-bromo-4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)benzoate

To a solution of 8-chloro-3-iodo-imidazo[1,2-a]pyrazine (2.0 g, 7.16 mmol, 1 eq) in MeCN (18 mL)/acetic acid (2 mL) was added methyl 4-amino-2-bromo-benzoate (1646.4 mg, 7.16 mmol, 1 eq). The mixture was stirred at 90 °C for 14 h. The mixture was filtered and the solid was washed by acetonitrile to give methyl 2-bromo-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoate (2.8 g, 5.92 mmol, 73% yield) as white solid. MS (ESI⁺) [M+H]⁺ : 474.7

Step 4: methyl 2-bromo-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoate

20 The title compound was obtained in analogy to step 5 in the preparation of Intermediate 27 using methyl 2-bromo-4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)benzoate and 2-(3-fluoro-4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI⁺) [M+H]⁺ : 472.8

Step 5: 2-bromo-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid

25 A solution of methyl 2-bromo-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoate (200.0 mg, 0.420 mmol, 1 eq) in methanol (10 mL) was stirred at 80 °C for 10 min. Then 4M aq. sodium hydroxide (5.0 mL, 20 mmol, 47.13 eq) was added. The mixture was stirred at 80 °C for 4 h. The reaction mixture was concentrated *in vacuo*, diluted with water, and acidified with 2 N HCl. The solid was collected and thoroughly dried to give 2-bromo-4-[[3-

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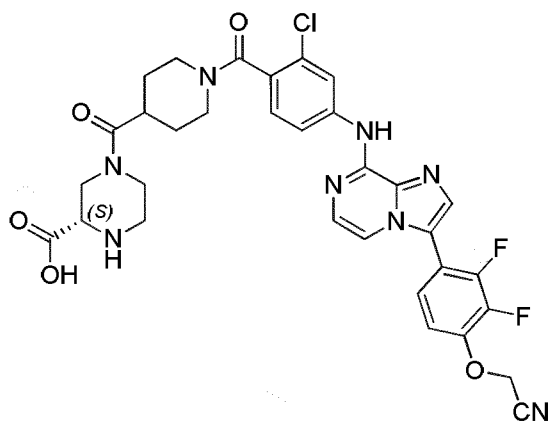
(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid (180 mg, 0.390 mmol, 64.93 % yield) as off white solid. (ESI⁺) [M+H]⁺ : 458.9

Step 6: 1-(2-bromo-4-((3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)-N-(2-(methylamino)ethyl)piperidine-4-carboxamide; formic acid

- 5 To a mixture of O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (99.79 mg, 0.260 mmol, 1.2 eq) and triethylamine (0.06 mL, 0.440 mmol, 2 eq) in DMF (4 mL) was added 2-bromo-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid (100.0 mg, 0.220 mmol, 1 eq) and tert-butyl N-methyl-N-[2-(piperidine-4-carbonylamino)ethyl]carbamate (93.62 mg, 0.330 mmol, 1.5 eq) slowly at 25 °C. Then the
- 10 mixture was stirred at 25 °C for 12 h. Then to the mixture was added HCl indioxane (3 mL). The mixture was stirred at 25°C for 4 h. The mixture was filtered and the filtrate was purified by prep-HPLC (FA as additive) to give 1-[2-bromo-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide (40 mg, 0.060 mmol, 26.73 % yield) as light yellow solid. MS (ESI⁺) [M+H]⁺ : 626

15 **Reference Example 345**

(2S)-4-[1-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperidine-4-carbonyl]piperazine-2-carboxylic acid; formic acid



Step 1: (S)-1-tert-butyl 2-methyl 4-(piperidine-4-carbonyl)piperazine-1,2-dicarboxylate

- 20 To a mixture of 1-benzylpiperidine-4-carboxylic acid (300 mg, 1.37 mmol), (S)-1-tert-butyl 2-methyl piperazine-1,2-dicarboxylate (501 mg, 2.05 mmol) and triethylamine (0.57 mL, 4.1 mmol) in DMF (10 mL) was added dropwise 1-propanephosphonic anhydride (1295 mg, 2.05

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mmol) at 25 °C under N₂. The mixture was stirred at 25 °C for 2 hours. The reaction mixture was poured into water (50 mL), it was extracted by ethyl acetate (50 mLx3), the combined organic layers were washed by brine (50 mL), dried by Na₂SO₄, filtered and concentrated to give the crude intermediate. A mixture of above residue (400 mg, 0.900 mmol) and palladium hydroxide
5 on carbon (40 mg, 0.900 mmol) in methanol (10 mL) was stirred at 25 °C under a hydrogen balloon for 16 hours. The reaction mixture was filtered and concentrated to afford (S)-1-tert-butyl 2-methyl 4-(piperidine-4-carbonyl)piperazine-1,2-dicarboxylate (220 mg, 0.620 mmol, 69% yield) as a colorless oil. MS (ESI⁺) [M+H]⁺ : 356.1

Step 2: 2-chloro-4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid

10 The title compound was obtained in analogy to step 3 of Reference Example 344 using 8-chloro-3-iodoimidazo[1,2-a]pyrazine and 4-amino-2-chlorobenzoic acid. MS (ESI⁺) [M+H]⁺ : 415.0

Step 3: (S)-1-tert-butyl 2-methyl 4-(1-(2-chloro-4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperidine-4-carbonyl)piperazine-1,2-dicarboxylate

To a mixture of 2-chloro-4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)benzoic acid (2.0 g, 4.82
15 mmol), N-hydroxysuccinimide (0.72 g, 6.27 mmol) in DMF (10 mL) and THF (30 mL) was added 1-ethyl-(3-(3-dimethylamino)propyl)-carbodiimide hydrochloride (1.4 mL, 5.31 mmol) at 25 °C under N₂. The mixture was stirred at 25 °C for 16 hours. LC-MS indicated the reaction was completed. The reaction mixture was concentrated and the residue was poured into water (50 mL). The mixture was filtered and the filtrate was concentrated to afford a residue (1.1 g,
20 2.15 mmol) as a white solid. A mixture of the above residue (303 mg, 0.590 mmol), (S)-1-tert-butyl 2-methyl 4-(piperidine-4-carbonyl)piperazine-1,2-dicarboxylate (220 mg, 0.590 mmol) and triethylamine (0.12 mL, 0.890 mmol) in THF (5 mL) was stirred at 25 °C for 2 h. The reaction mixture was concentrated to afford (S)-1-tert-butyl 2-methyl 4-(1-(2-chloro-4-((3-iodoimidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperidine-4-carbonyl)piperazine-1,2-
25 dicarboxylate (350 mg, 0.470 mmol) as a white solid. MS (ESI⁺) [M+H]⁺ : 752.1

Step 4: (S)-1-tert-butyl 2-methyl 4-(1-(2-chloro-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperidine-4-carbonyl)piperazine-1,2-dicarboxylate

The title compound was obtained in analogy to step 5 in the preparation of Intermediate 27 using
30 (S)-1-tert-butyl 2-methyl 4-(1-(2-chloro-4-((3-iodoimidazo[1,2-a]pyrazin-8-

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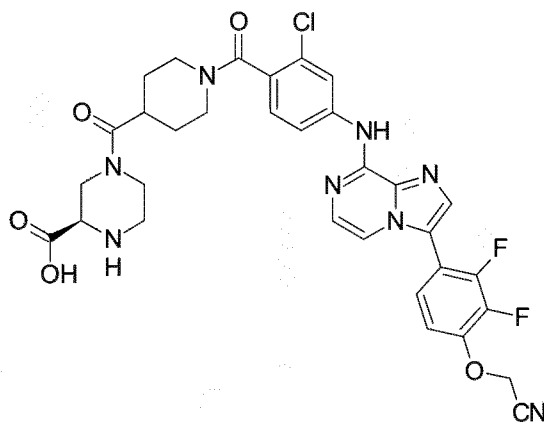
yl)amino)benzoyl)piperidine-4-carbonyl)piperazine-1,2-dicarboxylate and 2-(2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)acetonitrile. (ESI⁺) [(M+H)⁺] : 793.0

Step 5: (2S)-4-[1-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperidine-4-carbonyl]piperazine-2-carboxylic acid; formic acid

A mixture of (S)-1-tert-butyl 2-methyl 4-(1-(2-chloro-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperidine-4-carbonyl)piperazine-1,2-dicarboxylate (100 mg, 0.130 mmol) and lithium chloride (107 mg, 2.52 mmol) in triethylamine (0.1 mL, 0.720 mmol) and DMF (0.5 mL) was stirred at 100 °C under N₂ for 16 hours. To the mixture was added dropwise trifluoroacetic acid (0.2 mL, 2.6 mmol) at 25 °C. The mixture was stirred at 25 °C under N₂ for 16 hours. The reaction mixture was purified directly via prep-HPLC and then lyophilized to afford the title compound (7.5 mg, 0.010 mmol) as a white solid. (ESI⁺) [M+H]⁺: 679.0

Reference Example 346

(R)-4-(1-(2-chloro-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzoyl)piperidine-4-carbonyl)piperazine-2-carboxylic acid; formic acid



The title compound was obtained in analogy to Reference Example 345 via a 5-step sequence using (R)-1-tert-butyl 2-methyl piperazine-1,2-dicarboxylate instead of (S)-1-tert-butyl 2-methyl piperazine-1,2-dicarboxylate.

(ESI⁺) [M+H]⁺ : 679.0

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Intermediate 137

2-[4-[8-[3-chloro-4-[4-(2-chloroethyl)piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]acetonitrile

5 **Step 1: 1-(2-chloroethyl)piperazine bis(2,2,2-trifluoroacetate)**

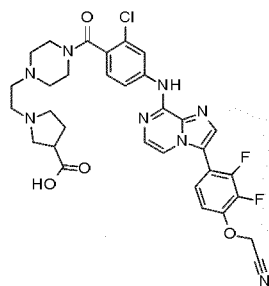
To a solution of tert-butyl 4-(2-chloroethyl)piperazine-1-carboxylate (1 g, 4.02 mmol) in DCM (10mL) / TFA (10 mL), the reaction was stirred for two hours at room temperature. The reaction mixture was concentrated in vacuum to give 1-(2-chloroethyl)piperazine bis(2,2,2-trifluoroacetate) (1.48 g).

10 **Step 2: 2-[4-[8-[3-chloro-4-[4-(2-chloroethyl)piperazine-1-carbonyl]anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]acetonitrile**

To a solution of Intermediate 29 (200mg, 439 μ mol) in DMF (5 mL) was added 1-(2-chloroethyl)piperazine bis(2,2,2-trifluoroacetate) (165 mg, 439 μ mol), triethylamine (178 mg, 245 μ L, 1.76 mmol) and 2,4,6-tripropyl-1,3,5,2,4,6-trioxatriphosphinane 2,4,6-trioxide (411 μ L, 658 μ mol), the reaction was stirred for two hours at room temperature. The mixture was washed with brine and extracted in DCM. The organic layer was concentrated *in vacuo* to give crude 2-(4-(8-((3-chloro-4-(4-(2-chloroethyl)piperazine-1-carbonyl)phenyl)amino)imidazo[1,2-a]pyrazin-3-yl)-2,3-difluorophenoxy)acetonitrile (270mg, 428 μ mol, 97.6 % yield). MS (ESI) [M+H]⁺ : 586.1

20 **Reference Example 347**

1-[2-[4-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperazin-1-yl]ethyl]pyrrolidine-3-carboxylic acid trifluoroacetate



Step 1: tert-butyl 1-[2-[4-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperazin-1-yl]ethyl]pyrrolidine-3-carboxylate

To a solution of Intermediate 137 (80mg, 136 μ mol) in DMSO (3mL) was added sodium carbonate (28.9 mg, 273 μ mol) and tert-butyl pyrrolidine-3-carboxylate (46.7 mg, 273 μ mol), the reaction was stirred for 15 hours at 60 °C. The reaction mixture was cooled to room temperature and filtered. The filtrate was poured into water and the mixture was filtered. The filter cake was dried in vacuum to give tert-butyl 1-[2-[4-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperazin-1-yl]ethyl]pyrrolidine-3-carboxylate (100 mg, 128 μ mol, 93.5 % yield).

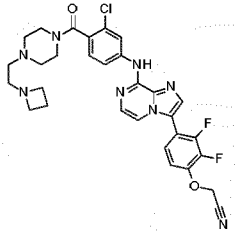
Step2: 1-[2-[4-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperazin-1-yl]ethyl]pyrrolidine-3-carboxylic acid trifluoroacetate

To a solution of tert-butyl 1-[2-[4-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperazin-1-yl]ethyl]pyrrolidine-3-carboxylate (100mg, 128 μ mol) in THF (5mL) was added 6N HCl (2 mL), the reaction mixture was stirred for two hours at room temperature. The mixture was neutralized with ammonium hydroxide. The mixture was extracted in ethyl acetate and the organic layer was concentrated in vacuum. The residue was purified by preparative HPLC to give 1-[2-[4-[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]piperazin-1-yl]ethyl]pyrrolidine-3-carboxylic acid (16 mg). MS (ESI) [M+H]⁺ : 665.1

The following examples were prepared in analogy to Reference Example 347, the hydrolysis of tert butyl ester step 2 was only applied for intermediates containing a tert butyl ester group.

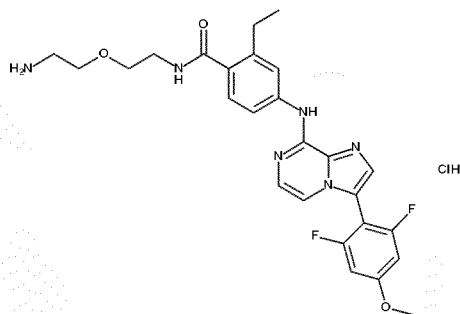
Ex.	Name	Structure	ESI [M+H] ⁺	Starting Material

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REF 348	2-[4-[8-[4-[4-[2-(azetidin-1-yl)ethyl]piperazine-1-carbonyl]-3-chloro-anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]acetonitrile trifluoroacetate		607.1	Intermediate 137 and azetidine hydrochloride
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Reference Example 349

N-[2-(2-aminoethoxy)ethyl]-4-[[3-(2,6-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide hydrochloride



5

Step 1:

tert-butyl N-[2-[2-[[2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]ethoxy]ethyl]carbamate (Intermediate 138)

- A mixture Intermediate 63 (1.421 g, 3.2 mmol), triethylamine (1.62 g, 2.23 mL, 16 mmol),
- 10 TBTU (1.22 g, 3.68 mmol) and tert-butyl (2-(2-aminoethoxy)ethyl)carbamate (816 mg, 3.99 mmol) in DMF (20 mL) was stirred at room temperature overnight. The reaction mixture was poured into 150 mL water and extracted with ethyl acetate (2 x 100 mL). The crude material was adsorbed on Isolute and purified by flash chromatography (silica gel, 80 g, 0% to 100% ethyl acetate in heptane) to yield tert-butyl (2-(2-(2-ethyl-4-((3-iodoimidazo[1,2-a]pyrazin-8-

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yl)amino)benzamido)ethoxy)ethyl)carbamate (1.561 g, 2.63 mmol, 82.2 %). MS (ESI, m/z): 595.4 [M+H]⁺.

Step 2:**tert-butyl N-[2-[2-[[4-[[3-(2,6-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethoxy]ethyl]carbamate**

A mixture of tert-butyl N-[2-[2-[[2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoyl]amino]ethoxy]ethyl]carbamate (Intermediate 138) (89.2 mg, 150 μmol), (2,6-difluoro-4-methoxyphenyl)boronic acid (19.7 mg, 225 μmol), 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (12.2 mg, 15 μmol) and Na₂CO₃ (31.8 mg, 300 μmol) in dioxane (1 mL) / water (0.1 mL) was stirred at 110 °C overnight. The mixtures were concentrated in vacuo, pre-purified by passing through a 4 g silica column eluting with 30 mL of a ethyl acetate / MeOH 9/1 solution and concentrated. Purification with preparative HPLC on reversed phase (Gemini 5um C18 75x30) eluting with a gradient formed from water (+0.1% NEt₃) / acetonitrile yielded after evaporation of the product containing fractions tert-butyl N-[2-[2-[[4-[[3-(2,6-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethoxy]ethyl]carbamate (7.8 mg, 12.8 μmol, 8.5 %). MS (ESI, m/z): 611.4 [M+H]⁺.

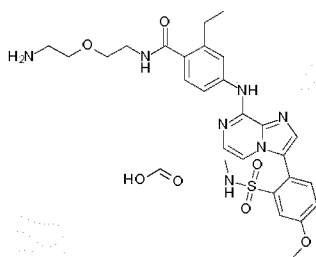
Step 3:**Reference Example 349****N-[2-(2-aminoethoxy)ethyl]-4-[[3-(2,6-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride**

A mixture of tert-butyl N-[2-[2-[[4-[[3-(2,6-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethoxy]ethyl]carbamate and excess 4N HCl (dioxane) in DCM (2 mL) was stirred at room temperature for 2 h and evaporated to dryness. The residue was triturated with 2 mL of Et₂O and the product was filtered off to yield after drying N-(2-(2-aminoethoxy)ethyl)-4-((3-(2,6-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride (4.8 mg, 9.4 μmol, 73.5 %). MS (ESI, m/z): 509.4 [M+H]⁺.

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Reference Example 350

N-[2-(2-aminoethoxy)ethyl]-2-ethyl-4-[[3-[4-methoxy-2-(methylsulfamoyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzamide; formic acid

**5 Step 1:**

tert-butyl N-[2-[2-[[2-ethyl-4-[[3-[4-methoxy-2-(methylsulfamoyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]ethoxy]ethyl]carbamate

In analogy to the procedure described for the synthesis of Reference Example 349

10 N-[2-(2-aminoethoxy)ethyl]-4-[[3-(2,6-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide hydrochloride the title compound was prepared from tert-butyl N-[2-[2-[[2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoyl]amino]ethoxy]ethyl]carbamate (Intermediate 138) and 5-methoxy-N-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenesulfonamide. MS (ESI, m/z): 668.4 [M+H]⁺.

15 Step 2:

N-[2-(2-aminoethoxy)ethyl]-2-ethyl-4-[[3-[4-methoxy-2-(methylsulfamoyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzamide formate

In analogy the procedure described for the synthesis of Reference Example 349

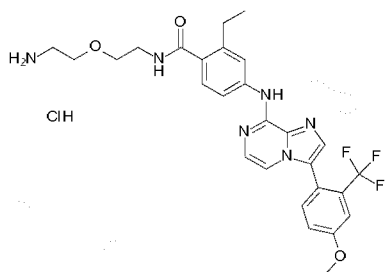
20 N-[2-(2-aminoethoxy)ethyl]-4-[[3-(2,6-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide hydrochloride the title compound was prepared from tert-butyl N-[2-[2-[[2-ethyl-4-[[3-[4-methoxy-2-(methylsulfamoyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]ethoxy]ethyl]carbamate through acidic cleavage of the protecting group followed by reversed phase column chromatography eluting with a gradient formed from water

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(+0.1% formic acid) / acetonitrile. Evaporation of the product containing fractions yielded the title compound. MS (ESI, m/z): 568.3 [M+H]⁺.

Reference Example 351

N-(2-(2-aminoethoxy)ethyl)-2-ethyl-4-((3-(4-methoxy-2-(trifluoromethyl)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide hydrochloride



Step 1:

tert-butyl (2-(2-(2-ethyl-4-((3-(4-methoxy-2-(trifluoromethyl)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamido)ethoxy)ethyl)carbamate

In analogy to the procedure described for the synthesis of Reference Example 349

N-[2-(2-aminoethoxy)ethyl]-4-[[3-(2,6-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide hydrochloride the title compound was prepared from tert-butyl N-[2-[2-[[2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoyl]amino]ethoxy]ethyl]carbamate (Intermediate 138) and 2-(4-methoxy-2-(trifluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI, m/z): 643.3 [M+H]⁺.

Step 2:

N-(2-(2-aminoethoxy)ethyl)-2-ethyl-4-((3-(4-methoxy-2-(trifluoromethyl)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide hydrochloride

In analogy the procedure described for the synthesis of Reference Example 349

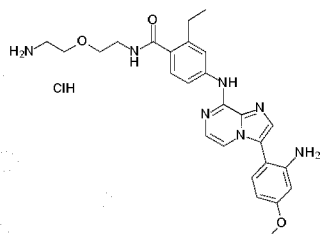
N-[2-(2-aminoethoxy)ethyl]-4-[[3-(2,6-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide hydrochloride the title compound was prepared from tert-butyl (2-(2-(2-ethyl-4-((3-(4-methoxy-2-(trifluoromethyl)phenyl)imidazo[1,2-a]pyrazin-8-

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yl)amino)benzamido)ethoxy)ethyl)carbamate through acidic cleavage of the protecting group.
MS (ESI, m/z): 543.3 [M+H]⁺.

Reference Example 352

4-((3-(2-amino-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(2-(2-aminoethoxy)ethyl)-2-ethylbenzamide hydrochloride



Step 1:

tert-butyl (2-(2-(4-((3-(2-((tert-butoxycarbonyl)amino)-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)carbamate

10 In analogy to the procedure described for the synthesis of Reference Example 349

N-[2-(2-aminoethoxy)ethyl]-4-[[3-(2,6-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide hydrochloride the title compound was prepared from tert-butyl N-[2-[2-[[2-ethyl-4-[(3-iodoimidazo[1,2-a]pyrazin-8-yl)amino]benzoyl]amino]ethoxy]ethyl]carbamate (Intermediate 138) and tert-butyl (5-methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)carbamate. MS (ESI, m/z): 690.5 [M+H]⁺.

Step 2:

4-((3-(2-amino-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(2-(2-aminoethoxy)ethyl)-2-ethylbenzamide hydrochloride

20 In analogy the procedure described for the synthesis of Reference Example 349

N-[2-(2-aminoethoxy)ethyl]-4-[[3-(2,6-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide hydrochloride the title compound was prepared from tert-butyl (2-(2-(4-((3-(2-((tert-butoxycarbonyl)amino)-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-

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2-ethylbenzamido)ethoxy)ethyl)carbamate through acidic cleavage of the protecting group. MS (ESI, m/z): 490.4 [M+H]⁺.

Intermediate 139**3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-amine**

- 5 In a sealed pressure tube a suspension of 8-chloro-3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazine (Intermediate 21, 0.062 g, 210 μ mol, Eq: 1) in isopropanol (839 μ l) and 25% aq ammonia (1.31 g, 1.46 mL, 19.3 mmol, Eq: 92) was heated to 115 °C for 19 h. The reaction mixture was diluted with water, the suspension filtered and washed with water. The solid was collected and dried *in vacuo*. The compound 3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-amine (0.046 g, 167 μ mol, 79.4 % yield) was obtained
10 as light brown solid. MS ESI (m/z): 277.2 [M+H]⁺

Intermediate 140**tert-butyl (2S,4R)-4-hydroxy-2-(piperazine-1-carbonyl)pyrrolidine-1-carboxylate****Step 1: benzyl 4-[(2S,4R)-1-tert-butoxycarbonyl-4-hydroxy-pyrrolidine-2-carbonyl]piperazine-1-carboxylate**
15

- To a clear solution of (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid (1.5 g, 6.29 mmol, Eq: 1) and DIPEA (1.63 g, 2.2 mL, 12.6 mmol, Eq: 2) in dry DMF (15.7 mL) was added HATU (2.39 g, 6.29 mmol, Eq: 1) and the mixture stirred 10 minutes at room temperature. Then a solution of benzyl piperazine-1-carboxylate (1.41 g, 6.29 mmol, Eq: 1) in
20 dry DMF (15.7 mL) was added and stirring at room temperature was continued for 2 h. Then the reaction mixture was concentrated *in vacuo*. The crude material was purified by silica gel chromatography using heptane/ (ethyl acetate/EtOH/NH₄OH 75:25:2) as eluent. The compound benzyl 4-((2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carbonyl)piperazine-1-carboxylate (3.177 g, 5.79 mmol, 92 % yield) was obtained as yellow oil with an purity of 79 %
25 (contains 21% DMF acc to NMR) and was used without further purification. MS ESI (m/z): 478.2184 [M+HCOO]⁻

Step 2: tert-butyl (2S,4R)-4-hydroxy-2-(piperazine-1-carbonyl)pyrrolidine-1-carboxylate

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A flask containing a solution of benzyl 4-((2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carbonyl)piperazine-1-carboxylate (3.17 g, 5.78 mmol, Eq: 1) in methanol (38.5 mL) was evacuated 3 x (frothing) and flushed with argon. Then 10% palladium on carbon (123 mg, 116 μ mol, Eq: 0.02) was added and degassing repeated. Then the apparatus was again
5 4 x evacuated (frothing) and flushed with hydrogen. The reaction was stirred 5 hours at room temperature under hydrogen. Then the reaction was filtered through a glass fibre filter, washed with MeOH and the obtained solution concentrated *in vacuo*. The obtained material was triturated with heptane/diisopropyl ether, filtered washed and dried *in vacuo*. The compound tert-butyl (2S,4R)-4-hydroxy-2-(piperazine-1-carbonyl)pyrrolidine-1-carboxylate (1.660 g, 5.38
10 mmol, 93.1 % yield) was obtained as light yellow solid. MS ESI (m/z): 300.2 [M+H]⁺

Intermediate 141**tert-butyl (E)-4-(N,N'-bis(tert-butoxycarbonyl)-1H-pyrazole-1-carboximidamido)butanoate**

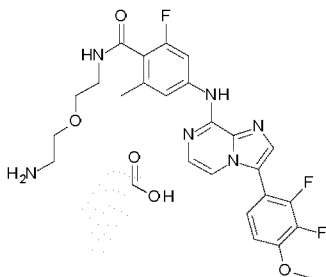
Biorg and Med Chem Lett 2014, vol 24 #23 p5525-5529

A solution of tert-butyl (E)-(((tert-butoxycarbonyl)imino)(1H-pyrazol-1-yl)methyl)carbamate
15 (0.155g, 484 μ mol, Eq: 1), triphenylphosphine (201 mg, 727 μ mol, Eq: 1.5) and tert-butyl 4-hydroxybutanoate (101 mg, 630 μ mol, Eq: 1.3) in dry THF (1.86 mL) was cooled to 0 °C. Then DIAD (156 mg, 150 μ L, 727 μ mol, Eq: 1.5) was added dropwise. Then the cooling bath was removed and the reaction heated to reflux for 16 hours. Then the reaction was quenched with water and diluted with dichloromethane. The mixture was extracted 2 x with dichloromethane
20 and the organic layers were washed 1 x with water. The combined organic layers were dried with sodium sulfate, filtered and concentrated *in vacuo*. The crude material was purified by silica gel chromatography using heptane/ ethyl acetate as eluent. The compound tert-butyl (E)-4-(N,N'-bis(tert-butoxycarbonyl)-1H-pyrazole-1-carboximidamido)butanoate (52 mg, 107 μ mol, 22.1 % yield) was obtained as colorless oil with a purity of 93 % (UV, 220 nm). MS ESI (m/z): 453.4
25 [M+H]⁺, ¹H NMR (300MHz, chloroform-d) δ = 7.94 (br s, 1H), 7.68 (dd, J=0.6, 1.6 Hz, 1H), 6.41 (dd, J=1.6, 2.8 Hz, 1H), 3.72 (br t, J=7.4 Hz, 2H), 2.32 (t, J=7.5 Hz, 2H), 2.01 (quin, J=7.4 Hz, 2H), 1.50 (s, 9H), 1.43 (s, 9H), 1.27 (s, 9H)

Reference Example 353

N-(2-(2-Aminoethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzamide formate
30

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Step 1: tert-Butyl 4-bromo-2-fluoro-6-methylbenzoate

In a pressure tube to a white suspension of 4-bromo-2-fluoro-6-methylbenzoic acid (700 mg, 3 mmol, Eq: 1) in dry toluene (1.88 mL) was added N,N-dimethylformamide di-tert-butyl acetal (4.41 g, 5.19 mL, 19.5 mmol, Eq: 6.5). The tube was sealed and the mixture heated to 80°C for 3 hours. The reaction mixture was diluted with water, ethyl acetate and sat. aqueous NaHCO₃ solution. The mixture was extracted 2 x with ethyl acetate and the organic layers washed 1 x with sat. aqueous NaHCO₃ solution and 2 x with brine. The combined organic layers were dried with sodium sulfate, filtered and concentrated in vacuo. The crude material (drypack on silica gel) was purified by silica gel chromatography using heptane/ ethyl acetate as eluent. The compound tert-butyl 4-bromo-2-fluoro-6-methylbenzoate (794.9 mg, 2.69 mmol, 89.7 % yield) was obtained as colorless oil and was used without further purification. MS EI (m/z): 290.0 [M]⁺

Step 2: tert-Butyl 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzoate

A brown suspension of 3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-amine (Intermediate 139, 300 mg, 1.09 mmol, Eq: 1), tert-butyl 4-bromo-2-fluoro-6-methylbenzoate (628 mg, 2.17 mmol, Eq: 2) and sodium tert-butoxide (157 mg, 1.63 mmol, Eq: 1.5) in THF (10.9 mL) in a pressure tube was sparged with argon for 5 minutes while sonicating the vessel in an ultra-sonic bath. Then 1,1'-bis(diphenylphosphino)ferrocene (72.2 mg, 130 μmol, Eq: 0.12) and tris(dibenzylideneacetone)dipalladium (0) (39.8 mg, 43.4 μmol, Eq: 0.04) were added and degassing continued for 1 minute. The tube was sealed and heated to 130 °C for 3 hours. Then the mixture was concentrated *in vacuo*. The crude material (drypack on silica gel) was purified by silica gel chromatography using heptane/ ethyl acetate as eluent. The compound tert-butyl 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzoate (367 mg, 758 μmol, 69.8 % yield) was obtained as yellow solid and was used without further purification. MS ESI (m/z): 485.2 [M+H]⁺

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Step 3: 4-((3-(2,3-Difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzoic acid hydrochloride

To a solution of tert-butyl 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzoate (367 mg, 758 μ mol, Eq: 1) in dioxane (1.52 mL) was added 4 M HCl in dioxane (11.4 mL, 45.5 mmol, Eq: 60) and the reaction was heated to 70 °C for 3 hours. Then again 4 M HCl in dioxane (5.68 mL, 22.7 mmol, Eq: 30) was added and the reaction stirred at 70 °C for 1 hour. The mixture was further diluted with dioxane and concentrated in vacuo. The compound 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzoic acid hydrochloride (410 mg, 750 μ mol, 99 % yield) was obtained as light brown solid and was used without further purification. MS ESI (m/z): 429.2 [M+H]⁺

Step 4: tert-Butyl N-[2-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-fluoro-6-methyl-benzoyl]amino]ethoxy]ethyl]carbamate

To a solution of 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzoic acid hydrochloride (20 mg, 40.4 μ mol, Eq: 1) and DIPEA (20.9 mg, 28.3 μ l, 162 μ mol, Eq: 4) in dry DMF (207 μ l) was added HATU (15.4 mg, 40.4 μ mol, Eq: 1) and the mixture stirred 10 minutes at room temperature (thick suspension). Then tert-butyl (2-(2-aminoethoxy)ethyl)carbamate hydrochloride (14.6 mg, 60.7 μ mol, Eq: 1.5) was added, the reaction diluted with dry DMF (104 μ l) and the mixture stirred at room temperature for 1 hour. Then the reaction was concentrated in vacuo. The crude material was purified by silica gel chromatography using dichloromethane/ methanol as eluent. The compound tert-butyl (2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzamido)ethoxy)ethyl)carbamate (0.031 g, 40.3 μ mol, 99.8 % yield) was obtained as colorless amorphous solid and was used without further purification. MS ESI (m/z): 615.4 [M+H]⁺

Step 5: N-(2-(2-Aminoethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzamide formate

To a solution of tert-butyl (2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzamido)ethoxy)ethyl)carbamate (31 mg, 40.3 μ mol, Eq: 1) in dioxane (202 μ l) was added 4 M HCl in dioxane (403 μ l, 1.61 mmol, Eq: 40) and the resulting

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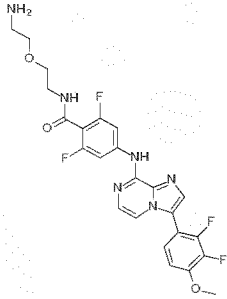
mixture stirred at room temperature (suspension). The reaction was diluted with dichloromethane and basified with 0.5 mL 7 M ammonia in MeOH. Then 1 spoon amine-silica gel was added and the mixture concentrated in vacuo. The crude material (drypack on amine silica gel) was purified by amine silica gel chromatography using dichloromethane/ methanol as eluent. The obtained

5 material was further purified by preparative reversed phase HPLC (Column: Phenomenex Gemini-NX 5u 110A, l: 100 mm, dia: 30 mm) using water containing 0.1% formic acid / acetonitrile as eluent. The compound N-(2-(2-aminoethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzamide formate (9 mg, 16.1 μ mol, 39.8 % yield) was obtained as white solid. MS ESI (m/z): 515.3 $[M+H]^+$, 258.2

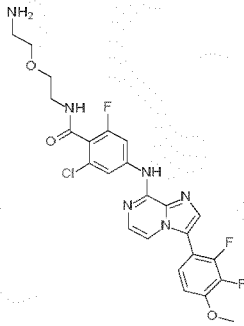
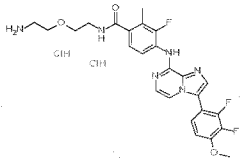
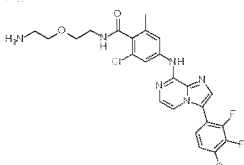
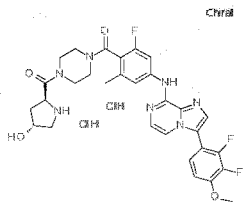
10 $[M+2H]^{2+}$

The following examples were prepared in analogy to Reference Example 353. HCl-salts were isolated in case the compounds were clean after the last step without further purification. The free base was isolated, if the compounds were clean after silica gel chromatography or when a

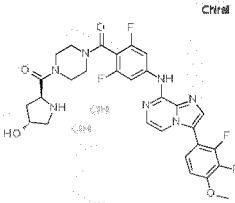
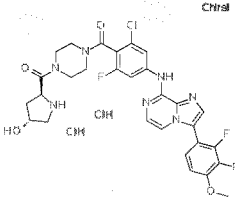
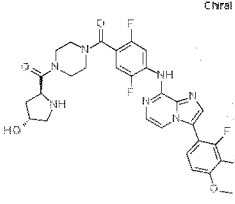
15 basic eluent was used during preparative HPLC.

Ex.	Name	Structure	Color and form, analytics	Starting Materials
REF 354	N-(2-(2-aminoethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2,6-difluorobenzamide		White lyoph powder, MS ESI (m/z): 519.2 $[M+H]^+$, 260.2 $[M+2H]^{2+}$	4-bromo-2,6-difluorobenzoic acid

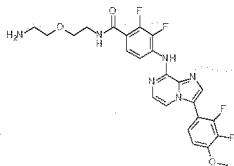
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REF 355	N-(2-(2-aminoethoxy)ethyl)-2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-6-fluorobenzamide		White lyoph powder, MS ESI (m/z): 535.2, 537.2 [M+H] ⁺ , 268.2, 269.1 [M+2H] ²⁺	4-bromo-2-chloro-6-fluorobenzic acid
REF 356	N-(2-(2-aminoethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-3-fluoro-2-methylbenzamide dihydrochloride		Off-white solid, MS ESI (m/z): 513.3 [M-H] ⁻	4-bromo-3-fluoro-2-methylbenzoic acid
REF 357	N-(2-(2-aminoethoxy)ethyl)-2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-6-methylbenzamide		Off-white solid, MS ESI (m/z): 531.2 [M+H] ⁺	4-bromo-2-chloro-6-methylbenzoic acid
REF 358	(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzoyl)piperazine-1-yl)((2S,4R)-4-		MS ESI (m/z): 610.2391 [M+H] ⁺	Intermediate 139

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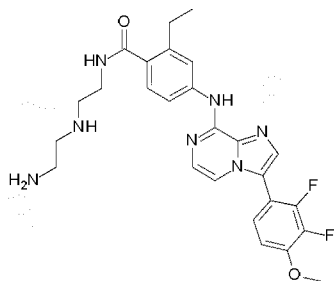
	hydroxypyrrolidin-2-yl)methanone dihydrochloride			
REF 359	(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2,6-difluorobenzoyl)piperazin-1-yl)((2S,4R)-4-hydroxypyrrolidin-2-yl)methanone dihydrochloride		MS ESI (m/z): 614.3 [M+H] ⁺ , 307.7 [M+2H] ²⁺	4-bromo-2,6-difluorobenzoic acid, Intermediate 139
REF 360	(4-(2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-6-fluorobenzoyl)piperazin-1-yl)((2S,4R)-4-hydroxypyrrolidin-2-yl)methanone dihydrochloride		MS ESI (m/z): 630.3, 632.4 [M+H] ⁺ , 315.7, 316.5 [M+2H] ²⁺	4-bromo-2-chloro-6-fluorobenzoic acid, Intermediate 139
REF 361	(4-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2,5-difluorobenzoyl)piperazin-1-yl)((2S,4R)-4-hydroxypyrrolidin-2-yl)methanone dihydrochloride		MS ESI (m/z): 614.3 [M+H] ⁺ , 307.7 [M+2H] ²⁺	4-bromo-2,5-difluorobenzoic acid, Intermediate 139

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	hydroxypyrrolidin-2-yl)methanone			
REF 362	N-(2-(2-aminoethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2,3-difluorobenzamide		MS ESI (m/z): 519.3 [M+H] ⁺ , 260.2 [M+2H] ²⁺	4-bromo-2,3-difluorobenzoic acid

Reference Example 363

N-(2-((2-Aminoethyl)amino)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide



5

To a solution of 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzoic acid hydrochloride (Example 86, 100 mg, 217 μ mol, Eq: 1) and DIPEA (112 mg, 152 μ l, 868 μ mol, Eq: 4) in dry DMF (1.08 mL) was added HATU (107 mg, 282 μ mol, Eq: 1.3) and the mixture was shaken for 15 minutes at room temperature. Then N1-(2-aminoethyl)ethane-1,2-diamine (89.5 mg, 93.8 μ l, 868 μ mol, Eq: 4) was added and shaking continued at room temperature for 3 hours. Then the reaction mixture was concentrated in vacuo. The material was purified by preparative reversed phase HPLC (Column: YMC Actus Triart C18 5 μ m, l:100mm, dia:30mm) using water containing 0.1% triethylamine / acetonitrile as eluent. The compound N-(2-((2-aminoethyl)amino)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide (39 mg, 74.2 μ mol, 34.2 % yield) was obtained as white solid. MS ESI (m/z): 510.2433 [M+H]⁺

15

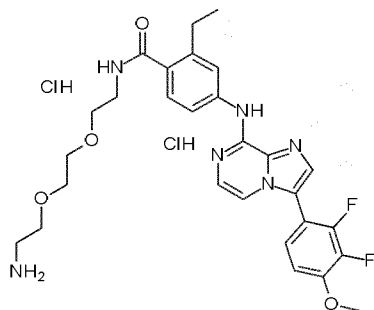
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The following examples were prepared in analogy to Reference Example 363.

Ex.	Name	Structure	Color and form, MS	Starting Materials
REF 364	rac-N-((1R,2S)-2-aminocyclohexyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide		Brown solid, MS ESI (m/z): 521.2 [M+H] ⁺	rac-(1R,2S)-cyclohexane-1,2-diamine
REF 365	N-((1S,2S)-2-aminocyclopentyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide		White solid, MS ESI (m/z): 507.3 [M+H] ⁺	(1S,2S)-cyclopentane-1,2-diamine dihydrochloride

Reference Example 366

- 5 N-(2-(2-(2-Aminoethoxy)ethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide dihydrochloride



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Step 1: tert-Butyl (2-(2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethoxy)ethyl)carbamate

To a solution of 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzoic acid hydrochloride (Example 86, 40 mg, 86.8 μ mol, Eq: 1) and DIPEA (44.9 mg, 60.6 μ l, 347 μ mol, Eq: 4) in dry DMF (434 μ l) was added HATU (36.3 mg, 95.5 μ mol, Eq: 1.1) and the mixture was shaken for 10 minutes at room temperature.

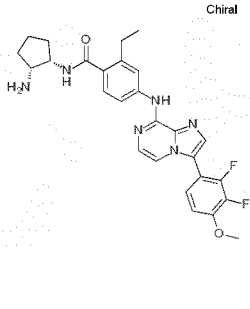
Then tert-butyl (2-(2-(2-aminoethoxy)ethoxy)ethyl)carbamate (28 mg, 113 μ mol, Eq: 1.3) was added and shaking continued at room temperature for 4 hours. The reaction mixture was diluted with ethyl acetate, sat. aqueous NaHCO_3 solution and brine. The mixture was extracted 2x with ethyl acetate and the organic layers were washed 2x with brine. The combined organic layers were dried with sodium sulfate, filtered and concentrated in vacuo. The crude material was purified by silica gel chromatography using dichloromethane/ methanol as eluent. The compound tert-butyl (2-(2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethoxy)ethyl)carbamate (41.1 mg, 62.8 μ mol, 72.3 % yield) was obtained as off-white solid . MS ESI (m/z): 655.4 $[\text{M}+\text{H}]^+$

Step 2: N-(2-(2-(2-aminoethoxy)ethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide dihydrochloride

In a 5 mL round-bottomed flask, tert-butyl (2-(2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethoxy)ethyl)carbamate (41.4 mg, 63.2 μ mol, Eq: 1) and 4 M HCl in dioxane (632 μ l, 2.53 mmol, Eq: 40) were combined to give a light yellow solution. The reaction mixture was stirred at room temperature for 3 hours. The reaction was diluted with water and directly lyophilized. The compound N-(2-(2-(2-aminoethoxy)ethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide dihydrochloride (37.3 mg, 59.4 μ mol, 94 % yield) was obtained as yellow solid. MS ESI (m/z): 278.3 $[\text{M}+2\text{H}]^{2+}$

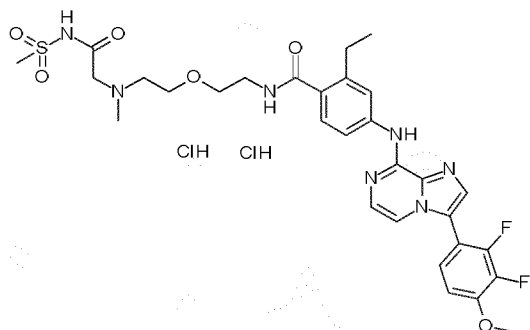
The following examples were prepared in analogy to Reference Example 366. In case the free base was isolated, the obtained material was further purified by silica gel chromatography and/or preparative HPLC.

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Ex.	Name	Structure	Color and form, MS	Starting Materials
REF 367	N-((1S,2R)-2-aminocyclopentyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide		Light brown solid, MS ESI (m/z): 507.3 [M+H] ⁺ , 254.3 [M+2H] ²⁺	tert-butyl ((1R,2S)-2-aminocyclopentyl)carbamate

Reference Example 368

4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(2-(2-(methyl(2-(methylsulfonamido)-2-oxoethyl)amino)ethoxy)ethyl)benzamide dihydrochloride



5

To a solution of N-(2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)-N-methylglycine hydrochloride (Reference Example 341, 20 mg, 32.3 μ mol, Eq: 1), methanesulfonamide (3.99 mg, 42 μ mol, Eq: 1.3) and DMAP (5.13 mg, 42 μ mol, Eq: 1.3) in dry dichloromethane (215 μ l) was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (6.52 mg, 7.43 μ L, 42 μ mol, Eq: 1.3) and the mixture stirred at room temperature for 18 hours. Then the reaction was concentrated in vacuo.

The crude material was purified by preparative reversed phase HPLC (Column: YMC Actus Triart C18, 12 nm, 5 μ m, 1:100mm, dia:30mm) using acetonitrile / water containing 0.1% formic

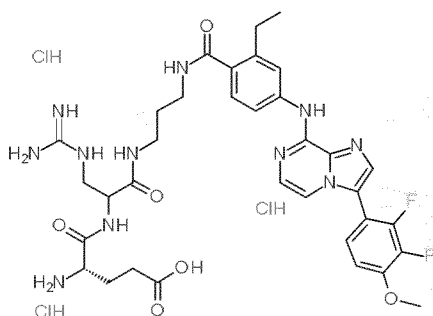
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acid as eluent. The obtained solution was lyophilized. The residue was redissolved in 0.1M aq. HCl and again lyophilized.

The compound 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(2-(2-(methyl(2-(methylsulfonamido)-2-oxoethyl)amino)ethoxy)ethyl)benzamide dihydrochloride (16.5 mg, 22.5 μ mol, 69.7 % yield) was obtained as light yellow solid. MS ESI (m/z): 660.2417 [M+H]⁺

Example 155

(4S)-4-Amino-5-((1-((3-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)amino)-3-guanidino-1-oxopropan-2-yl)amino)-5-oxopentanoic acid trihydrochloride (Epimers 1:1)



Step 1: Boc-Glu(OtBu)-Agp(Boc)₂-OH

A solution of Fmoc-Agp(Boc)₂-OH (426 mg, 750 μ mol, Eq: 0.625) and DIPEA biotech grade (775 mg, 1.05 mL, 6 mmol, Eq: 5) in dry dichloromethane (6.5 mL) was added to 2-chlorotrityl chloride-resin (Bachem, 1.6 mmol/g, 0.75 g, 1.2 mmol, Eq: 1) in a dried glass bottle and put under argon. The reaction mixture was shaken under argon atmosphere for 16 hours at room temperature. To the mixture was added methanol (596 μ l) (0.8 mL per gram resin) and the reaction mixture was shaken for 4 hours at room temperature to cap the remaining chloride. The mixture was filtered and then washed 3 x with 5 mL dichloromethane, followed by 3 x 5 mL DMF. 4-methylpiperidine/DMF/DCM 2:1:1 (4.65 mL) was added to the resin. The reaction mixture was shaken for 30 minutes at room temperature. The resin was filtered and washed 2 x with 5 mL DCM and 2 x with 5 mL DMF. Again 4-methylpiperidine/DMF/DCM 2:1:1 (4.65 mL) was added to the resin and the mixture shaken for 30 minutes at room temperature. The resin was filtered and washed 2 x with 5 mL DCM and 2 x with 2 mL DMF. On the side a

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solution of Boc-Glu(OtBu)-OH (455 mg, 1.5 mmol, Eq: 1.25) and DIPEA (388 mg, 524 μ l, 3 mmol, Eq: 2.5) in DMF/DCM 1:1 (4.65 mL) was treated with HATU (570 mg, 1.5 mmol, Eq: 1.25) and stirred for 10 minutes. The resulting mixture was added to the resin and shaken for 18 hours. The resin was filtered and washed 3 x with 5 mL DMF and 3 x with 5 mL DCM. Then the resin was treated with 5 mL DCM/HFIP 4:1 and shaken 1 hour. The mixture was filtered and washed 3x with DCM. This cleavage procedure was repeated 1 more time. The obtained filtrates were combined and concentrated in vacuo. The obtained oil was redissolved in acetonitrile/water and was lyophilized. The compound Boc-Glu(OtBu)-Agp(Boc)₂-OH (156 mg, 247 μ mol, 32.9 % yield) was obtained as light brown lyoph powder and was used without further purification. MS ESI (m/z): 632.5 [M+H]⁺

Step 2: tert-butyl (12S,E)-6,12-bis((tert-butoxycarbonyl)amino)-9-((3-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)carbamoyl)-2,2-dimethyl-4,11-dioxo-3-oxa-5,7,10-triazapentadec-5-en-15-oate (Epimers 1:1)

To a solution of Boc-Glu(OtBu)-Agp(Boc)₂-OH (74.2 mg, 117 μ mol, Eq: 1.3) and DIPEA (46.7 mg, 63.1 μ l, 361 μ mol, Eq: 4) in dry DMF (452 μ l) was added HATU (44.7 mg, 117 μ mol, Eq: 1.3) and the mixture stirred 10 minutes at room temperature. Then N-(3-aminopropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide dihydrochloride (Example 118, 50 mg, 90.3 μ mol, Eq: 1) was added and stirring at room temperature continued for 1.5 hours, then stored in the fridge for 16 hours. The reaction was concentrated in vacuo at 45 °C. The crude material was purified by silica gel chromatography using dichloromethane/ methanol as eluent. The obtained material was further purified by preparative reversed phase HPLC (Column: Phenomenex Gemini-NX 5u 110A, 1: 100 mm, dia: 30 mm) using acetonitrile / water containing 0.1% triethylamine as eluent.

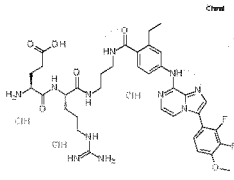
The compound tert-butyl (12S,E)-6,12-bis((tert-butoxycarbonyl)amino)-9-((3-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)carbamoyl)-2,2-dimethyl-4,11-dioxo-3-oxa-5,7,10-triazapentadec-5-en-15-oate (Epimers 1:1, 0.035 g, 30.7 μ mol, 34 % yield) was obtained as off-white amorphous with a purity of 96 % (total UV, 210-400 nm). MS ESI (m/z): 1080.5 [M+H]⁺

Step 3: (4S)-4-amino-5-((1-((3-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)amino)-3-guanidino-1-oxopropan-2-yl)amino)-5-oxopentanoic acid trihydrochloride (Epimers 1:1)

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To a solution of tert-butyl (12S,E)-6,12-bis((tert-butoxycarbonyl)amino)-9-((3-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)carbamoyl)-2,2-dimethyl-4,11-dioxo-3-oxa-5,7,10-triazapentadec-5-en-15-oate (0.035 g, 32 μ mol, Eq: 1) in dioxane (107 μ L) was added 4M HCl in dioxane (480 μ L, 1.92 mmol, Eq: 60) and the mixture stirred 16 hours at room temperature. Then the reaction was diluted with more dioxane and directly lyophilized. The compound (4S)-4-amino-5-(((1-((3-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)amino)-3-guanidino-1-oxopropan-2-yl)amino)-5-oxopentanoic acid trihydrochloride (30 mg, 29.7 μ mol, 93 % yield) was obtained as white lyoph powder with a purity of 84 % (96% by total UV (210-400nm), 13% dioxane acc to NMR). MS ESI (m/z): 738.4 [M+H]⁺

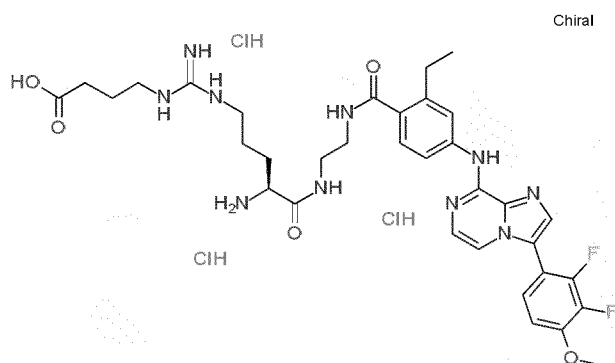
The following examples were prepared in analogy to example 155.

Ex.	Name	Structure	Color and form, analytics	Starting Materials
156	(S)-4-amino-5-(((S)-1-((3-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)amino)-5-guanidino-1-oxopentan-2-yl)amino)-5-oxopentanoic acid trihydrochloride		Off-white lyophilized powder, MS ESI (m/z): 766.4 [M+H] ⁺	Fmoc-Arg(Boc) ₂ -OH, Boc-Glu-OtBu

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Example 157

(S)-7-amino-1-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylphenyl)-12-imino-1,6-dioxo-2,5,11,13-tetraazaheptadecan-17-oic acid trihydrochloride



5 Step 1: benzyl tert-butyl (5-((2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethyl)amino)-5-oxopentane-1,4-diyl)(S)-dicarbamate

To a solution of Boc-Orn(Z)-OH (112 mg, 306 μ mol, Eq: 1.1) in dry DMF (1.39 mL) and DIPEA (180 mg, 243 μ L, 1.39 mmol, Eq: 5) was added HATU (116 mg, 306 μ mol, Eq: 1.1) and the mixture stirred 10 minutes at room temperature. Then N-(2-aminoethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide dihydrochloride (Example 117, 0.15 g, 278 μ mol, Eq: 1) was added and stirring at room temperature continued for 2 hours. Then the reaction mixture was diluted with ethyl acetate, water and sat. aqueous NaHCO₃ solution. The mixture was extracted 2 x with ethyl acetate and the organic layers were washed 2 x with brine. The combined organic layers were dried with sodium sulfate, filtered and concentrated in vacuo. The crude material was purified by silica gel chromatography using dichloromethane/ methanol as eluent. The compound benzyl tert-butyl (5-((2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethyl)amino)-5-oxopentane-1,4-diyl)(S)-dicarbamate (0.207 g, 254 μ mol, 91.3 % yield) was obtained as light brown amorphous solid. MS ESI (m/z): 815.6 [M+H]⁺

Step 2: tert-butyl (S)-(5-amino-1-((2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethyl)amino)-1-oxopentan-2-yl)

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A suspension of benzyl tert-butyl (5-((2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethyl)amino)-5-oxopentane-1,4-diyl)(S)-dicarbamate (0.207 g, 254 μ mol, Eq: 1) in methanol (2.54 mL) was evacuated 3 x (frothing) and flushed with argon. Then 10% palladium on charcoal (27 mg, 25.4 μ mol, Eq: 0.1) was added and degassing
5 repeated. Then again the mixture was evacuated 3 x (frothing) and flushed with hydrogen. The reaction was stirred 3 hours at room temperature under hydrogen. Then the reaction was diluted with ethanol (2.54 mL) and stirring under hydrogen continued for another 20 hours. The reaction mixture was filtered and washed with EtOH and dichloromethane/MeOH 9:1. The obtained solution was concentrated in vacuo. The compound tert-butyl (S)-(5-amino-1-((2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethyl)amino)-
10 1-oxopentan-2-yl)carbamate (162 mg, 238 μ mol, 93.7 % yield) was obtained as light brown amorphous solid and was used without further purification. MS ESI (m/z): 681.5 [M+H]⁺

Step 3: tert-butyl (S,Z)-13-(tert-butoxycarbonyl)-7-((tert-butoxycarbonyl)amino)-12-((tert-butoxycarbonyl)imino)-1-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylphenyl)-1,6-dioxo-2,5,11,13-tetraazaheptadecan-17-oate
15

A solution of tert-butyl (E)-4-(N,N'-bis(tert-butoxycarbonyl)-1H-pyrazole-1-carboximidamido)butanoate (Intermediate 141, 21.4 mg, 44.1 μ mol, Eq: 1) in acetonitrile (294 μ l) was added to tert-butyl (S)-(5-amino-1-((2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethyl)amino)-1-oxopentan-2-yl)carbamate (30 mg, 44.1 μ mol, Eq: 1). To the resulting suspension DIPEA (12.5 mg, 16.9 μ L, 97 μ mol, Eq: 2.2) was added and the reaction stirred 16 hours at room temperature. Again tert-butyl (E)-4-(N,N'-bis(tert-butoxycarbonyl)-1H-pyrazole-1-carboximidamido)butanoate (Intermediate 141, 9.97 mg, 22 μ mol, Eq: 0.5) in acetonitrile (147 μ l) was added and stirring at room temperature continued. Then the reaction was concentrated in
25 vacuo. The crude material was purified by silica gel chromatography using heptane/ (ethyl acetate/EtOH/NH₄OH 75:25:2) as eluent. The compound tert-butyl (S,Z)-13-(tert-butoxycarbonyl)-7-((tert-butoxycarbonyl)amino)-12-((tert-butoxycarbonyl)imino)-1-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylphenyl)-1,6-dioxo-2,5,11,13-tetraazaheptadecan-17-oate (0.014 g, 13.1 μ mol, 29.8 % yield) was obtained as
30 colorless amorphous solid and was used without further purification. MS ESI (m/z): 1065.6 [M+H]⁺

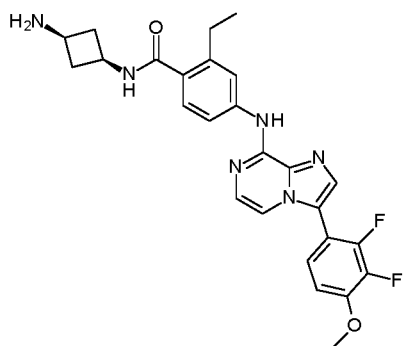
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Step 4: (S)-7-amino-1-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylphenyl)-12-imino-1,6-dioxo-2,5,11,13-tetraazaheptadecan-17-oic acid trihydrochloride

To a suspension of tert-butyl (S,Z)-13-(tert-butoxycarbonyl)-7-((tert-butoxycarbonyl)amino)-12-
 5 ((tert-butoxycarbonyl)imino)-1-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylphenyl)-1,6-dioxo-2,5,11,13-tetraazaheptadecan-17-oate (13 mg, 12.2 μ mol, Eq: 1) in dioxane (40.7 μ L) was added 4M HCl in dioxane (305 μ L, 1.22 mmol, Eq: 100) and the resulting solution stirred at room temperature for 4 hours. The reaction was diluted with dioxane and directly lyophilized. The compound (S)-7-amino-1-(4-((3-(2,3-difluoro-4-
 10 methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylphenyl)-12-imino-1,6-dioxo-2,5,11,13-tetraazaheptadecan-17-oic acid trihydrochloride (7 mg, 8.13 μ mol, 66.6 % yield) was obtained as white lyoph powder with a purity of 95 % (UV, 265 nm). MS ESI (m/z): 709.3379 [M+H]⁺

Reference Example 369

15 **Cis N-(3-aminocyclobutyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide**



Step 1:

20 **Cis-tert-butyl N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]cyclobutyl]carbamate**

Under Ar, 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzoic acid, Intermediate 86 (100 mg, 236 μ mol, Eq: 1) was suspended in DMF (1 mL). tert-Butyl cis-N-(3-aminocyclobutyl)carbamate [CAS#1212395-34-0] (1.18 mmol, Eq: 5) was

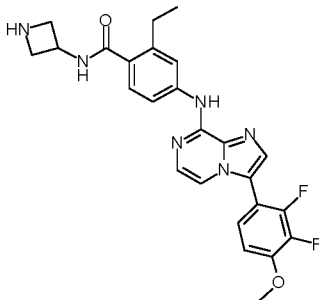
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added. Additional tert-Butyl cis-N-(3-aminocyclobutyl)carbamate [CAS#1212395-34-0] (283 μ mol, Eq: 1.2) and 2-(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yl)-1,1,3,3-tetramethylisouronium hexafluorophosphate(V) (HATU) (179 mg, 471 μ mol, Eq: 2) were added and the yellow solution was stirred at RT over 2 h. The solvent was evaporated and the crude material was purified by
 5 flash chromatography (silica gel, 20g, 0% to 100% DCM/MeOH/NH₄OH (95/5/1)) leading to the target compound (orange foam, 140 mg). MS (ESI, m/z): 593.3 [M+H]⁺.

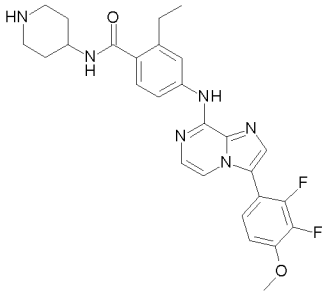
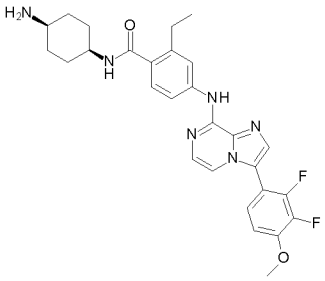
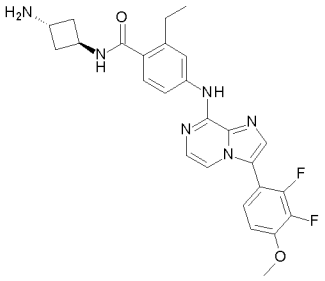
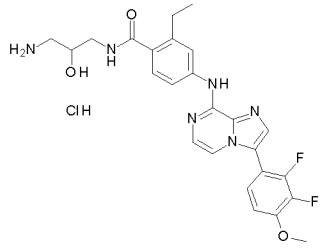
Step 2:**Cis N-(3-aminocyclobutyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide**

10 Under Ar, cis-tert-butyl N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]cyclobutyl]carbamate obtained in step 1 (140 mg) was dissolved in MeOH (1 mL). 4M HCl in dioxane (1.07 mL, 4.27 mmol, Eq: 10) was added and the RM was stirred at RT over 3 h. DCM/MeOH/aq. NH₃ was added till the HCl was neutralized and the RM was evaporated. The crude product was purified by flash chromatography (silica gel,
 15 20g, 0% to 100% DCM/MeOH/aq. 25% NH₄OH (90/10/1)) leading to the title compound (white solid, 103 mg). MS (ESI, m/z): 493.2 [M+H]⁺.

The following examples were prepared in analogy to Reference Example 369.

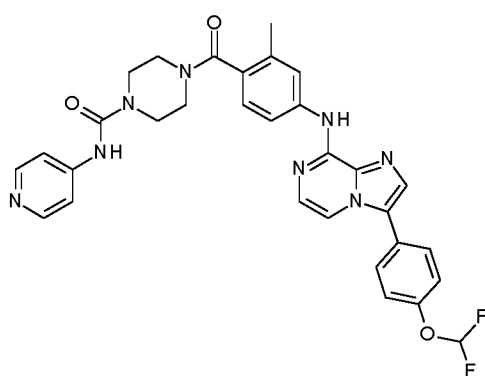
Ex.	Name	Structure	ESI MS [M+H]] ⁺	Starting Materials
REF 370	N-(azetidin-3-yl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide		479.3	Intermediate 86 and tert-butyl 3-aminoazetidine-1-carboxylate. Deprotection with

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				TFA/DCM 1:2 at rt for 1 h.
REF 371	4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(4-piperidyl)benzamide		507.3	Intermediate 86 and tert-butyl 4-aminopiperidine-1-carboxylate
REF 321	Cis-N-(4-aminocyclohexyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide		521.3	Intermediate 86 and cis-tert-butyl (-4-aminocyclohexyl)carbamate
REF 372	N-(3-aminocyclobutyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide		493.3	Intermediate 86 and trans-tert-butyl (3-aminocyclobutyl)carbamate
147	N-(3-amino-2-hydroxypropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;hydrochloride		495.4	86 and tert-butyl (3-amino-2-hydroxypropyl)carbamate [CAS#144912-84-5]. Product isolated by filtration of reaction mixture

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				following deprotection step.
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Reference Example 373**4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-N-(4-pyridyl)piperazine-1-carboxamide**

5

To a solution of [4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-piperazin-1-yl-methanone hydrochloride (Reference Example 218) (100.0 mg, 0.210 mmol, 1 eq) in DMF (5 mL) was added phenyl N-(4-pyridyl)carbamate (67.16 mg, 0.310 mmol, 1.5 eq) and N,N-diisopropylethylamine (0.11 mL, 0.630 mmol, 3 eq), then the reaction was stirred at 25 °C for 12 h. The reaction mixture was purified by prep-HPLC (basic) to give product 4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-N-(4-pyridyl)piperazine-1-carboxamide (30.5 mg, 0.050 mmol, 24% yield) as a yellow solid. MS (ESI, m/z): 599.1 [M+H]⁺.

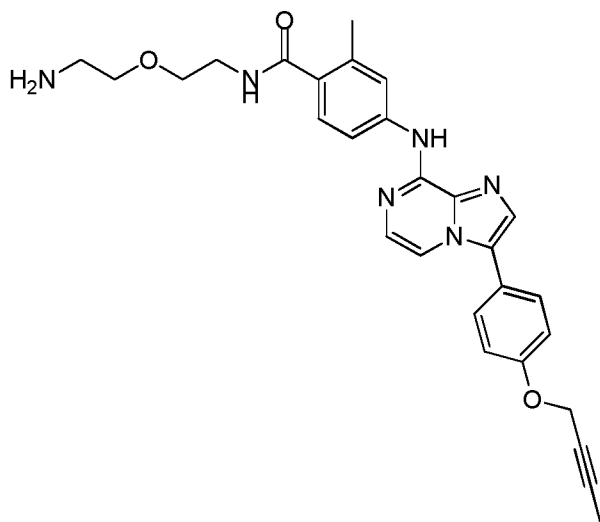
10

Reference Example 374

N-[2-(2-aminoethoxy)ethyl]-4-[[3-(4-but-2-ynoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide; 2,2,2-trifluoroacetic acid

15

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Step 1: tert-butyl N-[2-[2-[(2-methyl-4-nitro-benzoyl)amino]ethoxy]ethyl]carbamate

The title compound was obtained in analogy to step 1 in the preparation of Example 5 using tert-butyl N-[2-(2-aminoethoxy)ethyl]carbamate and 2-methyl-4-nitro-benzoic acid for condensation.

5 MS (ESI) m/z: 390.1 [M+Na]⁺

Step 2: tert-butyl N-[2-[2-[(4-amino-2-methyl-benzoyl)amino]ethoxy]ethyl]carbamate

The title compound was obtained in analogy to step 4 in the preparation of Reference Example 342 using tert-butyl N-[2-[2-[(2-methyl-4-nitro-benzoyl)amino]ethoxy]ethyl]carbamate as starting material in hydrogenation. MS (ESI) m/z: 360.2 [M+Na]⁺

10 **Step 3: 4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)phenol**

The title compound was obtained in analogy to step 1 in the preparation of Example 158 using 8-chloro-3-iodo-imidazo[1,2-a]pyrazine and (4-hydroxyphenyl)boronic acid as reaction partners. MS (ESI) m/z: 245.9 [M+H]⁺

Step 4: 3-(4-but-2-ynoxyphenyl)-8-chloro-imidazo[1,2-a]pyrazine

15 A mixture of 4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)phenol (100.0 mg, 0.410 mmol, 1 eq), 1-bromo-2-butyne (81.2 mg, 0.610 mmol, 1.5 eq) and potassium carbonate (112.52 mg, 0.810 mmol, 2 eq) in DMF (3 mL) was stirred at 25 °C for 16 h. The mixture was filtered and the obtained crude product was purified by flash column to afford 78 mg of 3-(4-but-2-ynoxyphenyl)-8-chloro-imidazo[1,2-a]pyrazine as yellow solid. MS (ESI) m/z: 298.0 [M+H]⁺

Step 5: tert-butyl N-[2-[2-[[4-[[3-(4-but-2-ynoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino] - 2-methyl-benzoyl]amino]ethoxy]ethyl]carbamate

A mixture of tert-butyl N-[2-[2-[(4-amino-2-methyl-benzoyl)amino]ethoxy]ethyl]carbamate (80.0 mg, 0.240 mmol, 1 eq), 3-(4-but-2-ynoxyphenyl)-8-chloro-imidazo[1,2-a]pyrazine (70.59 mg, 0.240 mmol, 1 eq), cesium carbonate (231.76 mg, 0.710 mmol, 3 eq), tris(dibenzylideneacetone)dipalladium (0) (21.71 mg, 0.020 mmol, 0.100 eq) and 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (13.72 mg, 0.020 mmol, 0.100 eq) in 1,4-dioxane (5 mL) was stirred under N₂ at 115 °C under microwave irradiation for 2 h. The mixture was filtered and concentrated to give the crude product, which was purified by prep-TLC (DCM/MeOH/MeCN = 10:1:1) to afford 65 mg of the title compound as light yellow solid. MS (ESI) m/z: 599.3. [M+H]⁺

Step 6: N-[2-(2-aminoethoxy)ethyl]-4-[[3-(4-but-2-ynoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide; 2,2,2-trifluoroacetic acid

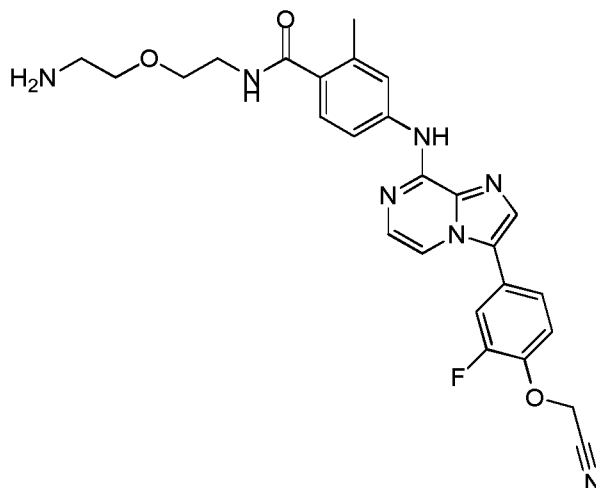
A solution of tert-butyl N-[2-[2-[[4-[[3-(4-but-2-ynoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino] -2-methyl-benzoyl]amino]ethoxy]ethyl]carbamate (65.0 mg, 0.110 mmol, 1 eq) in DCM (4 mL) was added trifluoroacetic acid (0.5 mL, 6.49 mmol, 59.78 eq) and stirred at 20 °C for 16 h. The mixture was concentrated and the obtained residue was purified by prep-HPLC (TFA) to afford 20.6 mg of the title compound as white solid. MS (ESI) m/z: 499.2. [M+H]⁺

Reference Example 375

N-[2-(2-aminoethoxy)ethyl]-4-[[3-[4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide; formic acid

Step 1: 4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenol

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The title compound was obtained in analogy to step 1 in the preparation of Example 158 using 8-chloro-3-iodo-imidazo[1,2-a]pyrazine and 3-fluoro-4-hydroxyphenylboronic acid as starting compounds. MS (ESI) m/z : 264.0 $[M+H]^+$

5 **Step 2: 2-[4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenoxy]acetonitrile**

The title compound was obtained in analogy to step 4 in the preparation of Reference Example 374 using 4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenol and bromoacetonitrile as reactants. MS (ESI) m/z : 303.0. $[M+H]^+$

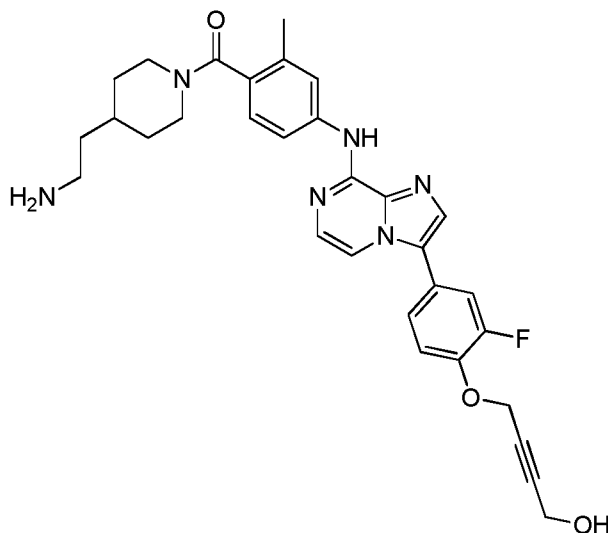
10 **Step 3: tert-butyl N-[2-[2-[[4-[[3-[4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethoxy]ethyl]carbamate**

The title compound was obtained in analogy to step 5 in the preparation of Reference Example 374 using tert-butyl N-[2-[2-[(4-amino-2-methyl-benzoyl)amino]ethoxy]ethyl]carbamate and 2-[4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenoxy]acetonitrile as coupling reactants. MS (ESI) m/z : 604.5 $[M+H]^+$

15 **Step 4: N-(2-(2-aminoethoxy)ethyl)-4-((3-(4-(cyanomethoxy)-3-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide; formic acid**

The title compound was obtained in analogy to step 6 in the preparation of Reference Example 374 using tert-butyl N-[2-[2-[[4-[[3-[4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethoxy]ethyl]carbamate as starting material. MS (ESI) m/z : 504.2 $[M+H]^+$

20

Reference Example 376**Step 1: 4-hydroxybut-2-yn-1-yl methanesulfonate**

The title compound was obtained in analogy to step 4 in the preparation of 159 using but-2-yne-
 5 1,4-diol as starting material. The product was directly used in crude form.

Step 2: 4-[4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenoxy]but-2-yn-1-ol

The title compound was obtained in analogy to step 7 in the preparation of Example 159 using 4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenol and 4-hydroxybut-2-ynyl methanesulfonate as starting material. MS (ESI) m/z: 332.0 [M+H]⁺

Step 3: tert-butyl N-[2-[1-(4-amino-2-methyl-benzoyl)-4-piperidyl]ethyl]carbamate

The title compound was obtained in analogy to step 1 in the preparation of Example 159 using 4-amino-2-methyl benzoic acid and 4-(2-BOC-aminoethyl)piperidine for. MS (ESI) m/z: 362.2 [M+H]⁺

Step 4: tert-butyl N-[2-[1-[4-[[3-[3-fluoro-4-(4-hydroxybut-2-ynoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]ethyl]carbamate

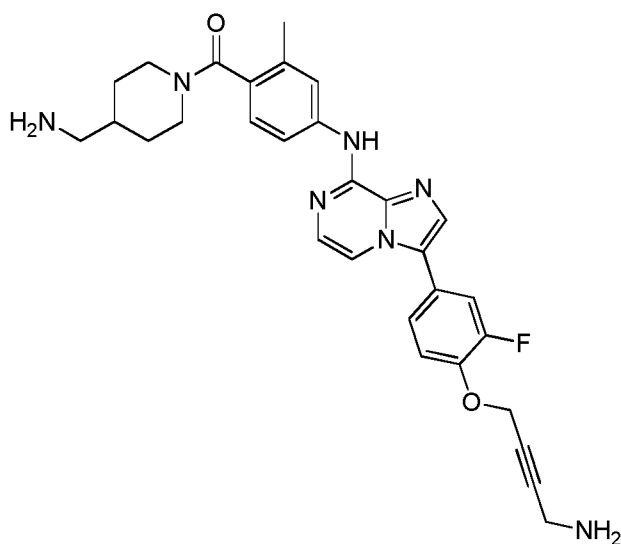
The title compound was obtained in analogy to step 2 in the preparation of Example 158 using tert-butyl N-[2-[1-(4-amino-2-methyl-benzoyl)-4-piperidyl]ethyl]carbamate and 4-[4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenoxy]but-2-yn-1-ol. MS (ESI) m/z: 657.4 [M+H]⁺

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Step 5: [4-(2-aminoethyl)-1-piperidyl]-[4-[[3-[3-fluoro-4-(4-hydroxybut-2-ynoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone

The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-butyl N-[2-[1-[4-[[3-[3-fluoro-4-(4-hydroxybut-2-ynoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]ethyl]carbamate as substrate. MS (ESI) m/z: 557.4 [M+H]⁺

Reference Example 377



[4-[[3-[4-(4-aminobut-2-ynoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-(aminomethyl)-1-piperidyl]methanone; formic acid

Step 1: 4-((tert-butoxycarbonyl)amino)but-2-yn-1-yl methanesulfonate

The title compound was obtained in analogy to step 4 in the preparation of Example 159 using tert-butyl (4-hydroxybut-2-yn-1-yl)carbamate as starting material. The product was directly used in crude form.

Step 2: tert-butyl N-[4-[4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenoxy]but-2-ynyl]carbamate

The title compound was obtained in analogy to step 7 in the preparation of Example 159 using 4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenol and 4-(tert-butoxycarbonylamino)but-2-ynyl methanesulfonate as starting materials. MS (ESI) m/z: 431.0 [M+H]⁺

Step 3: tert-butyl ((1-(2-methyl-4-nitrobenzoyl)piperidin-4-yl)methyl)carbamate

The title compound was obtained in analogy to step 1 in the preparation of Example 5 using 4-amino-2-methyl benzoic acid and 4-(tert-butoxycarbonylaminomethyl)piperidine. MS (ESI) m/z: 400.1 [M+Na]⁺

5 Step 4: tert-butyl N-[[1-(4-amino-2-methyl-benzoyl)-4-piperidyl]methyl]carbamate

To a stirred suspension mixture of NiCl₂·6H₂O (503.81 mg, 2.12 mmol, 0.500 eq) and sodium borohydride (80.19 mg, 2.12 mmol, 0.500 eq) in methanol (20 mL) was dropwise added a solution of tert-butyl N-[[1-(2-methyl-4-nitro-benzoyl)-4-piperidyl]methyl]carbamate (1.6 g, 4.24 mmol, 1 eq) in THF (6 mL) at 0 °C. Then another batch of sodium borohydride (481.14 mg, 12.72 mmol, 3 eq) was added at 0 °C and the reaction mixture was stirred for 1 h at 10 °C. The solid was filtered and the solvent was removed in vacuum. The residue was treated with a mixture of EA/H₂O (1/1, 200 mL), the organic layer was washed with sat. NH₄Cl (50 mL) and brine (50 mL), dried over sodium sulfate and filtered, concentrated in vacuum to give tert-butyl N-[[1-(4-amino-2-methyl-benzoyl)-4-piperidyl]methyl]carbamate (1.44 g, 4.14 mmol, 97.77 %
15 yield) as white solid. MS (ESI) m/z: 348.1 [M+H]⁺

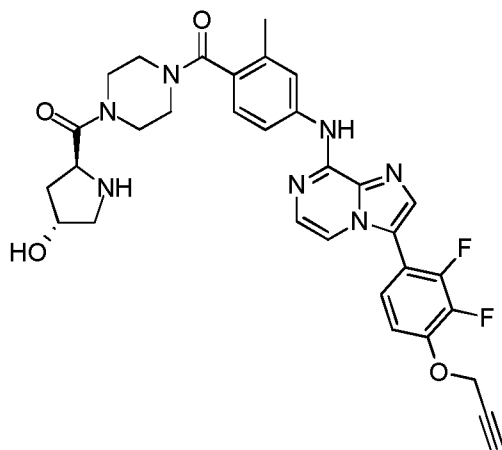
Step 5: tert-butylN-[[1-[4-[[3-[4-[4-(tert-butoxycarbonylamino)but-2-ynoxy]-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate

The title compound was obtained in analogy to step 2 in the preparation of Example 158 using
20 tert-butyl N-[[1-(4-amino-2-methyl-benzoyl)-4-piperidyl]methyl]carbamate and tert-butyl N-[4-[4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2-fluoro-phenoxy]but-2-ynyl]carbamate. MS (ESI) m/z: 742.5 [M+H]⁺

Step 6: [4-[[3-[4-(4-aminobut-2-ynoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-(aminomethyl)-1-piperidyl]methanone; formic acid

25 The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-butyl N-[[1-[4-[[3-[4-[4-(tert-butoxycarbonylamino)but-2-ynoxy]-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-4-piperidyl]methyl]carbamate. MS (ESI) m/z: 542.3 [M+H]⁺

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Reference Example 378**Step 1: tert-butyl 4-(2-methyl-4-nitrobenzoyl)piperazine-1-carboxylate**

The title compound was obtained in analogy to step 3 in the preparation of Example 158 using 2-methyl-4-nitrobenzoic acid and tert-butyl piperazine-1-carboxylate. MS (ESI) m/z: 350.2. [M+H]⁺

Step 2: tert-butyl 4-(4-amino-2-methylbenzoyl)piperazine-1-carboxylate

The title compound was obtained in analogy to step 4 in the preparation of Reference Example 342 using tert-butyl 4-(2-methyl-4-nitrobenzoyl)piperazine-1-carboxylate as substrate. MS (ESI) m/z: 320.2. [M+H]⁺

Step 3: tert-butyl 4-[4-[[3-(2,3-difluoro-4-prop-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carboxylate

The title compound was obtained in analogy to step 2 in the preparation of Example 158 using tert-butyl 4-(4-amino-2-methyl-benzoyl)piperazine-1-carboxylate and 8-chloro-3-(2,3-difluoro-4-prop-2-yloxy-phenyl)imidazo[1,2-a]pyrazine. MS (ESI) m/z: 603.1 [M+H]⁺

Step 4: [4-[[3-(2,3-difluoro-4-prop-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-piperazin-1-yl-methanone

The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-butyl 4-[4-[[3-(2,3-difluoro-4-prop-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carboxylate as substrate. MS (ESI) m/z: 503.3. [M+H]⁺

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Step 5: tert-butyl (2S,4R)-2-[4-[4-[[3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carbonyl]-4-hydroxy-pyrrolidine-1-carboxylate

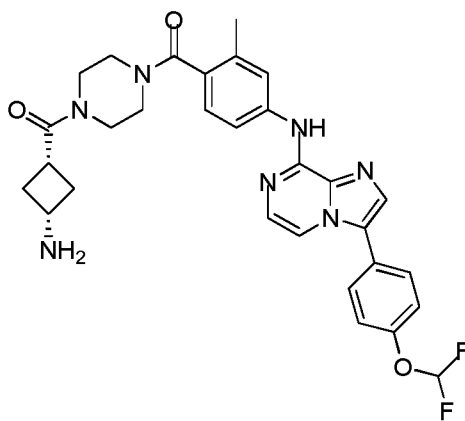
The title compound was obtained in analogy to step 3 in the preparation of Example 158 using
 5 [4-[[3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-piperazin-1-yl-methanone and (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid. MS (ESI) m/z: 716.3. $[M+H]^+$

Step 6: [4-[[3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-[(2S,4R)-4-hydroxypyrrolidine-2-carbonyl]piperazin-1-yl]methanone

10 The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-butyl (2S,4R)-2-[4-[4-[[3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carbonyl]-4-hydroxy-pyrrolidine-1-carboxylate as substrate. MS (ESI) m/z: 616.3. $[M+H]^+$

Reference Example 379

15 **[4-(3-aminocyclobutanecarbonyl)piperazin-1-yl]-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone hydrochloride**

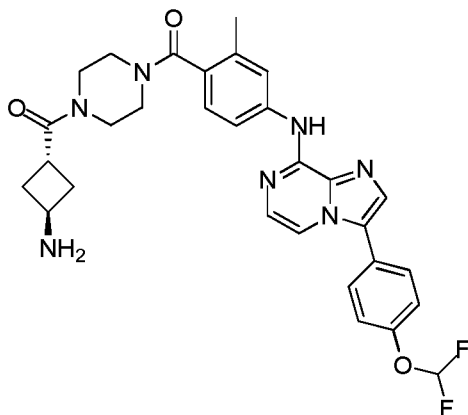


The title compound was obtained in analogy to Reference Example 380 using (1S,3S)-3-((tert-butoxycarbonyl)amino)cyclobutanecarboxylic acid instead of (1R,3R)-3-((tert-butoxycarbonyl)amino)cyclobutanecarboxylic acid. MS (ESI, m/z): 576.2 $[M+H]^+$
 20

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Reference Example 380

[4-(3-aminocyclobutanecarbonyl)piperazin-1-yl]-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone hydrochloride



5

Step 1: tert-butyl 4-(4-((3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzoyl)piperazine-1-carboxylate

The title compound was obtained in analogy to step 2 in the preparation of Example 158 using 8-chloro-3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazine and tert-butyl 4-(4-amino-2-methyl-benzoyl)piperazine-1-carboxylate. MS (ESI) m/z: 579.1 [M+H]⁺

10

Step 2: [4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-piperazin-1-yl-methanone

The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-butyl 4-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]piperazine-1-carboxylate. MS (ESI) m/z: 479.2 [M+H]⁺

15

Step 3: [4-(3-aminocyclobutanecarbonyl)piperazin-1-yl]-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone hydrochloride

To a mixture of (1r,3r)-3-((tert-butoxycarbonyl)amino)cyclobutanecarboxylic acid (53.98 mg, 0.250 mmol, 1.5 eq) and [4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-piperazin-1-yl-methanone (80.0 mg, 0.170 mmol, 1 eq) in DMF (1 mL) was

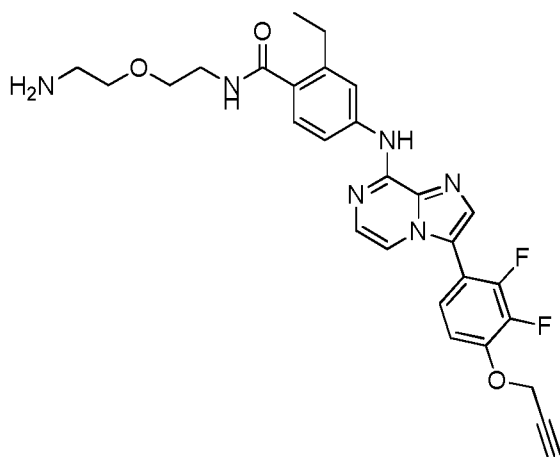
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added triethylamine (0.07 mL, 0.500 mmol, 3 eq) and 1-propanephosphonic anhydride (159.59 mg, 0.250 mmol, 1.5 eq) (50% in DMF solution) slowly at 25 °C. Then the mixture was stirred at 25 °C for 16 h, and conc. HCl (0.5 mL, 6 mmol, 35.89 eq) was added to the mixture and the mixture was stirred at 25 °C for another 48 h. After that the mixture was filtered and purified by prep-HPLC to give [4-(3-aminocyclobutanecarbonyl)piperazin-1-yl]-[4-[[3-[4-

5 (difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]methanone hydrochloride (31.08 mg, 0.050 mmol, 28.62 % yield) as white solid. MS (ESI) m/z: 576.3 [M+H]⁺

Reference Example 381



10

Step 1: tert-butyl (2-(2-(4-((3-(2,3-difluoro-4-(prop-2-yn-1-yloxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)carbamate

The title compound was obtained in analogy to step 3 in the preparation of Example 158 using 4-((3-(2,3-difluoro-4-(prop-2-yn-1-yloxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-

15 ethylbenzoic acid and tert-butyl (2-(2-aminoethoxy)ethyl)carbamate as coupling partners. MS (ESI) m/z: 635.5 [M+H]⁺

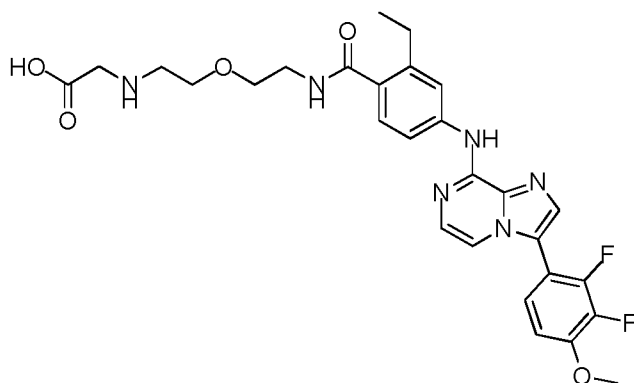
Step 2: N-(2-(2-(2-aminoethoxy)ethyl)-4-((3-(2,3-difluoro-4-(prop-2-yn-1-yloxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide

The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-

20 butyl (2-(2-(4-((3-(2,3-difluoro-4-(prop-2-yn-1-yloxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)carbamate as substrate. MS (ESI) m/z: 535.3 [M+H]⁺

Reference Example 382

2-[2-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethoxy]ethylamino]acetic acid; formic acid



5 Step 1: 2,5-dioxopyrrolidin-1-yl 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzoate

To a solution of 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzoic acid (2.0 g, 4.71 mmol, 1 eq) in THF (30 mL)/DMF (10 mL) was added N-hydroxysuccinimide (813.55 mg, 7.07 mmol, 1.5 eq) and 1-ethyl-(3-(3-dimethylamino)propyl)-carbodiimide hydrochloride (1084.07 mg, 5.66 mmol, 1.2 eq). The mixture was stirred at 25 °C
 10 for 3 h. The solvent was evaporated and water was added. The resulting suspension was filtered and the solid was dried in vacuo to give the title compound (1.8 g, 3.45 mmol, 73 % yield) as light yellow solid. MS (ESI) m/z: 522 [M+H]⁺

15 Step 2: N-(2-(2-aminoethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide

To a solution of 2,5-dioxopyrrolidin-1-yl 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzoate (1100 mg, 2.11 mmol, 1 eq) in THF (20 mL) was added triethylamine (0.44 mL, 3.16 mmol, 1.5 eq) and 1,5-diamino-3-oxapentane (329 mg, 3.16 mmol, 1.5 eq). The mixture was stirred at 25 °C for 3 h. The solvent was evaporated. The solid was
 20 triturated with water and filtered to afford the title compound (912 mg, 1.79 mmol) as off-white solid. MS (ESI) m/z: 511 [M+H]⁺

Step 3: methyl 2-((2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)amino)acetate

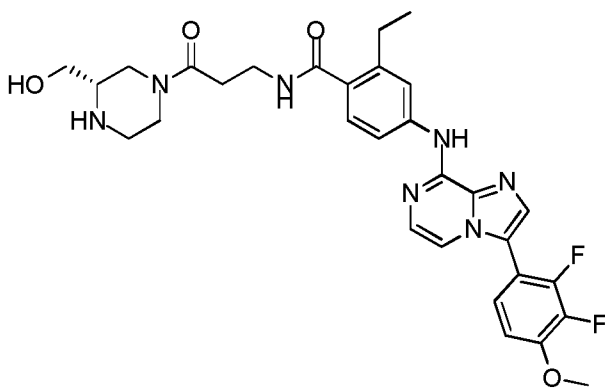
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To a solution of N-(2-(2-aminoethoxy)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide (500 mg, 0.980 mmol, 1 eq) in DMF (5 mL) was added triethylamine (0.2 mL, 1.47 mmol, 1.5 eq) and methyl chloroacetate (138 mg, 1.27 mmol, 1.3 eq). The mixture was stirred at 25 °C for 4 h. To the mixture was added water and the pH of
5 mixture was adjusted to around 4 by 1 M aq. HCl. The mixture was extracted with ethyl acetate (50 mLx3). The pH of aqueous solution was adjusted to around 8. The resulting suspension was filtered and the residue was dried to give the title compound (500 mg, 0.980 mmol, 1 eq) as a yellow solid. MS (ESI) m/z: 583 [M+H]⁺

Step 4: 2-((2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)amino)acetic acid; formic acid

To a solution of methyl 2-((2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethoxy)ethyl)amino)acetate (50 mg, 0.09 mmol, 1 eq) in methanol (2 mL) was added aq. sodium hydroxide solution (0.5 mL, 2 mmol, 23.3 eq, 4 N). The mixture was stirred at 25 °C for 4 h. The pH was adjusted to around 6 by addition of 2 M aq. HCl. The
15 solvent was evaporated and the residue was purified by prep. HPLC to give the title compound (18 mg, 0.030 mmol) as a white solid. MS (ESI) m/z: 569 [M+H]⁺

Example 160



Step 1: 3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propanoic acid

The title compound was obtained in analogy to step 3 in the preparation of Example 158 using 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoic acid and beta-alanine. MS (ESI) m/z: 496.3. [M+H]⁺

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Step 2: tert-butyl (2S)-4-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propanoyl]-2-(hydroxymethyl)piperazine-1-carboxylate

The title compound was obtained in analogy to step 3 in the preparation of Example 158 using 3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-

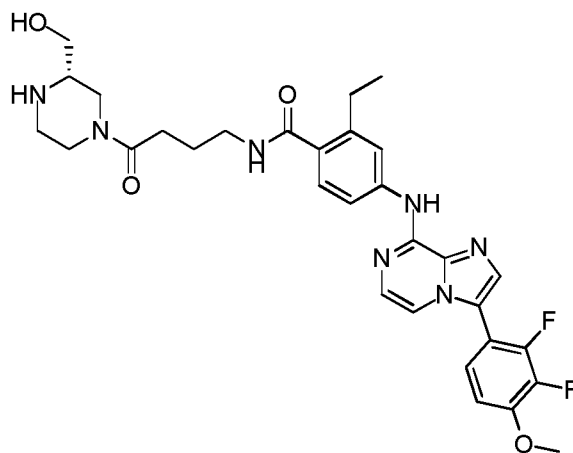
5 benzoyl]amino]propanoic acid and tert-butyl (2S)-2-(hydroxymethyl)piperazine-1-carboxylate as reactants. MS (ESI) m/z: 694.2 [M+H]⁺

Step 3: 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[3-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-3-oxo-propyl]benzamide

The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-
10 butyl (2S)-4-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propanoyl]-2-(hydroxymethyl)piperazine-1-carboxylate as starting material. MS (ESI) m/z: 594.3. [M+H]⁺

Example 161

**4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[4-
15 [(3S)-3-(hydroxymethyl)piperazin-1-yl]-4-oxo-butyl]benzamide**

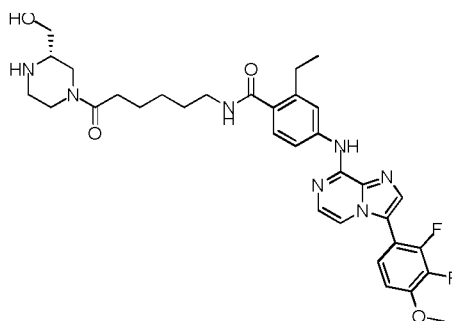


The title compound was obtained in analogy to Example 160 by using 4-aminobutyric acid as starting material instead of beta-alanine. MS (ESI) m/z: 608.4. [M+H]⁺

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Example 162

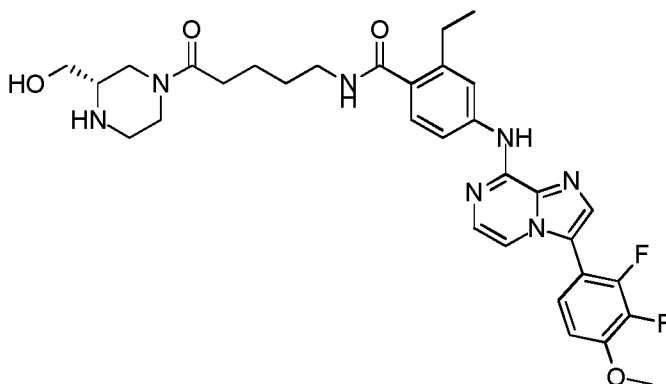
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[6-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-6-oxo-hexyl]benzamide



- 5 The title compound was obtained in analogy to Example 160 by using 6-aminohexanoic acid as starting material instead of beta-alanine. MS (ESI) m/z : 636.4 $[M+H]^+$

Example 163

4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[5-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-5-oxo-pentyl]benzamide



10

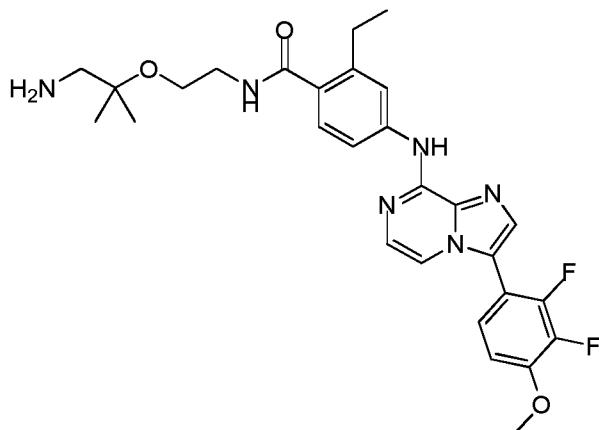
The title compound was obtained in analogy to Example 160 by using 5-aminovaleric acid as starting material instead of beta-alanine. MS (ESI) m/z : 622.4. $[M+H]^+$

Reference Example 383

N-[2-(2-amino-1,1-dimethyl-ethoxy)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid

15

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**Step 1: tert-butyl N-(2-allyloxy-2-methyl-propyl)carbamate**

The title compound was obtained in analogy to step 2 in the preparation of Reference Example 384 using tert-butyl 2-hydroxy-2-methylpropylcarbamate and allyl tert-butyl carbonate for
5 coupling reaction.

^1H NMR (400 MHz, CHLOROFORM- d) δ = 6.01 - 5.83 (m, 1 H), 5.37 - 5.10 (m, 2 H), 4.86 (br s, 1 H), 3.90 (d, J = 5.4 Hz, 2 H), 3.18 (d, J = 5.9 Hz, 2 H), 1.46 (s, 9 H), 1.20 (s, 6 H) ppm.

Step 2: tert-butyl N-[2-(2-hydroxyethoxy)-2-methyl-propyl]carbamate

The title compound was obtained in analogy to step 3 in the preparation of Reference Example
10 384 using tert-butyl N-(2-allyloxy-2-methyl-propyl)carbamate for ozonolysis.

^1H NMR (400 MHz, CHLOROFORM- d) δ = 4.85 (br s, 1 H), 3.64 (t, J = 4.3 Hz, 2 H), 3.43 - 3.36 (m, 2 H), 3.10 (d, J = 6.0 Hz, 2 H), 2.10 (br s, 1 H), 1.38 (s, 9 H), 1.11 (s, 6 H) ppm.

Step 3: 2-[2-(tert-butoxycarbonylamino)-1,1-dimethyl-ethoxy]ethyl methanesulfonate

The title compound was obtained in analogy to step 4 in the preparation of Example 159 using
15 tert-butyl N-[2-(2-hydroxyethoxy)-2-methyl-propyl]carbamate as starting material. The product was directly used in crude form.

Step 4: tert-butyl N-[2-(2-azidoethoxy)-2-methyl-propyl]carbamate

The title compound was obtained in analogy to step 5 in the preparation of Reference Example 384 using 2-[2-(tert-butoxycarbonylamino)-1,1-dimethyl-ethoxy]ethyl methanesulfonate and
20 sodium azide.

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¹H NMR (400 MHz, CHLOROFORM-d) δ = 4.94 (br s, 1 H), 3.60 - 3.53 (m, 1 H), 3.60 - 3.53 (m, 1 H), 3.35 (t, J = 4.9 Hz, 2 H), 3.19 (d, J = 6.0 Hz, 2 H), 1.47 (s, 9 H), 1.21 (s, 6 H) ppm.

Step 5: tert-butyl N-[2-(2-aminoethoxy)-2-methyl-propyl]carbamate

The title compound was obtained in analogy to step 6 in the preparation of Reference Example 384 using tert-butyl N-[2-(2-azidoethoxy)-2-methyl-propyl]carbamate for reduction, used directly in crude form.

Step 6: tert-butyl N-[2-methyl-2-[2-[(4-nitro-2-vinyl-benzoyl)amino]ethoxy]propyl]carbamate

The title compound was obtained in analogy to step 3 in the preparation of Example 158 using 4-nitro-2-vinyl-benzoic acid and tert-butyl N-[2-(2-aminoethoxy)-2-methyl-propyl]carbamate. MS (ESI) m/z : 420.2 $[M+Na]^+$

Step 7: tert-butyl N-[2-[2-[(4-amino-2-ethyl-benzoyl)amino]ethoxy]-2-methyl-propyl]carbamate

The title compound was obtained in analogy to step 4 of the preparation of Example 164 using tert-butyl N-[2-methyl-2-[2-[(4-nitro-2-vinyl-benzoyl)amino]ethoxy]propyl]carbamate as substrate for this hydrogenation. MS (ESI) m/z : 380.1 $[M+H]^+$

Step 8: tert-butyl N-[2-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethoxy]-2-methyl-propyl]carbamate

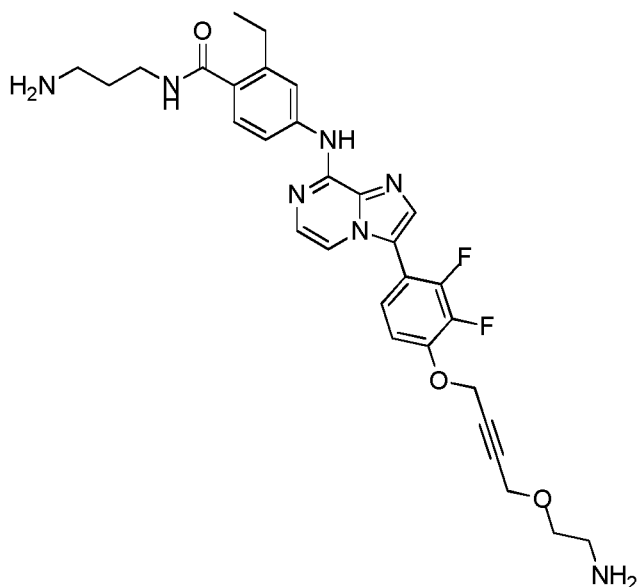
The title compound was obtained in analogy to step 2 in the preparation of Example 158 using tert-butyl N-[2-[2-[(4-amino-2-ethyl-benzoyl)amino]ethoxy]-2-methyl-propyl]carbamate and 8-chloro-3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazine. MS (ESI) m/z : 639.2 $[M+H]^+$

Step 9: N-[2-(2-amino-1,1-dimethyl-ethoxy)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide

The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-butyl N-[2-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethoxy]-2-methyl-propyl]carbamate as substrate. MS (ESI) m/z : 539.3 $[M+H]^+$

Example 159

4-[[[3-[4-[4-(2-aminoethoxy)but-2-ynoxy]-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(3-aminopropyl)-2-ethyl-benzamide



5 Step 1: tert-butyl (3-(2-ethyl-4-nitrobenzamido)propyl)carbamate

The title compound was obtained in analogy to step 3 in the preparation of Example 158 using tert-butyl (3-aminopropyl)carbamate and 2-ethyl-4-nitrobenzoic acid. MS (ESI) m/z: 352.2 [M+H]⁺

Step 2: tert-butyl (3-(4-amino-2-ethylbenzamido)propyl)carbamate

- 10 The title compound was obtained in analogy to step 4 in the preparation of Example 164 using tert-butyl (3-(2-ethyl-4-nitrobenzamido)propyl)carbamate as starting material. MS (ESI) m/z: 332.2 [M+H]⁺

Step 3: tert-butyl N-[3-[[4-[[3-(2,3-difluoro-4-hydroxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propyl]carbamate

- 15 The title compound was obtained in analogy to step 2 in the preparation of Example 158 using 4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2,3-difluoro-phenol and tert-butyl N-[3-[(4-amino-2-ethyl-benzoyl)amino]propyl]carbamate as reactants. MS (ESI) m/z: 567.2 [M+H]⁺

Step 4: 2-(tert-butoxycarbonylamino)ethyl methanesulfonate

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To a solution of N-BOC-ethanolamine (2.0 g, 12.41 mmol, 1 eq) and triethylamine (3.46 mL, 24.81 mmol, 2 eq) in DCM (5 mL) was added methanesulfonyl chloride (1.44 mL, 18.61 mmol, 1.5 eq) at 20 °C, the mixture was stirred at 20 °C for 2 h. The mixture was quenched with 1 N aq. HCl, and then the mixture was extracted with ethyl acetate (30 mLx2), and dried over Na₂SO₄,
5 filtered and concentrated to get the title compound (2.5 g, 10.45 mmol, 84.21 % yield) as a yellow oil, which was used without further purification.

Step 5: tert-butyl N-[2-(4-hydroxybut-2-ynoxy)ethyl]carbamate

A mixture of 2-butyne-1,4-diol (1.44 g, 16.72 mmol, 2 eq) and sodium hydroxide in water (8.36 mL, 16.72 mmol, 2 eq) was stirred at 90 °C for 0.5 h, then 2-(tert-butoxycarbonylamino)ethyl
10 methanesulfonate (2.0 g, 8.36 mmol, 1 eq) was added to the mixture at 90 °C and stirred for 5 h. The solution was poured into water and extracted with ethyl acetate (30 mLx2), the combined organic layers were concentrated and the obtained residue was purified by silica gel chromatography (PE/EA = 4:1) to afford tert-butyl N-[2-(4-hydroxybut-2-ynoxy)ethyl]carbamate (500 mg, 2.18 mmol) as colorless oil.

Step 6: 4-[2-(tert-butoxycarbonylamino)ethoxy]but-2-ynyl methanesulfonate

The title compound was obtained in analogy to step 4 in the preparation of Example 159 using tert-butyl N-[2-(4-hydroxybut-2-ynoxy)ethyl]carbamate as starting material. The product was directly used in crude form.

Step 7: tert-butyl N-[3-[[4-[[3-[4-[4-[2-(tert-butoxycarbonylamino)ethoxy]but-2-ynoxy]-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propyl]carbamate

To a solution of tert-butyl N-[3-[[4-[[3-(2,3-difluoro-4-hydroxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propyl]carbamate (50.0 mg, 0.090 mmol, 1 eq) and potassium carbonate (24.39 mg, 0.180 mmol, 2 eq) in acetonitrile (1 mL) was added 4-[2-(tert-
25 butoxycarbonylamino)ethoxy]but-2-ynyl methanesulfonate (40.68 mg, 0.130 mmol, 1.5 eq) at 20 °C, the mixture was stirred at 60 °C for 16 h. The mixture was concentrated and purified by prep-HPLC to get the title compound (30 mg, 0.040 mmol, 43.7% yield) as a white solid. MS (ESI) m/z: 778.2 [M+H]⁺

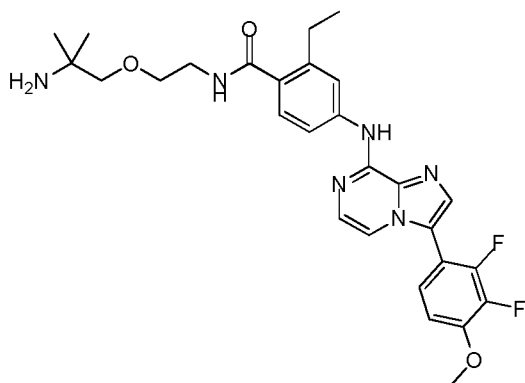
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Step 8: 4-[[3-[4-[4-(2-aminoethoxy)but-2-ynoxy]-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(3-aminopropyl)-2-ethyl-benzamide

The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-butyl N-[3-[[4-[4-[4-(2-tert-butoxycarbonylamino)ethoxy]but-2-ynoxy]-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propyl]carbamate as reactant.
 MS (ESI) m/z: 578.4 [M+H]⁺

Reference Example 384

N-[2-(2-amino-2-methyl-propoxy)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid



Step 1: allyl tert-butyl carbonate

To a solution of allyl alcohol (19.96 g, 343.64 mmol, 3 eq) and di-tert-butyl dicarbonate (25.0 g, 114.55 mmol, 1 eq) was slowly added 4-dimethylaminopyridine (2.8 g, 22.91 mmol, 0.200 eq). The mixture was stirred at 15 °C for 1 h. The mixture was diluted with MTBE, washed with brine, dried over Na₂SO₄ and concentrated. The residue was purified by silica gel chromatography eluting with PE:EA = 50:1 to afford allyl tert-butyl carbonate (12 g, 75.86 mmol) as colorless oil.

¹H NMR (400 MHz, CHLOROFORM-d) δ = 5.99 - 5.87 (m, 1 H), 5.33 (dd, J = 1.4, 17.2 Hz, 1 H), 5.24 (dd, J = 1.2, 10.4 Hz, 1 H), 4.55 (td, J = 1.2, 5.8 Hz, 2 H), 1.48 (s, 9 H) ppm.

Step 2: tert-butyl N-(2-allyloxy-1,1-dimethyl-ethyl)carbamate

To a mixture of tert-butyl (1-hydroxy-2-methylpropan-2-yl)carbamate (500.0 mg, 2.64 mmol, 1 eq), allyl tert-butyl carbonate (835 mg, 5.28 mmol, 2 eq) in THF (10 mL) was added

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tetrakis(triphenylphosphine)palladium(0) (610.6 mg, 0.530 mmol, 0.200 eq). The resulting mixture was stirred at 80 °C for 12 h under nitrogen. The mixture was concentrated and the residue was purified by silica gel chromatography eluting with PE:EA = 50:1 to afford tert-butyl N-(2-allyloxy-1,1-dimethyl-ethyl)carbamate (250 mg, 1.09 mmol, 41.26 % yield) as colorless oil.

¹H NMR (400 MHz, CHLOROFORM-d) δ = 5.90 - 5.75 (m, 1 H), 5.26 - 5.05 (m, 2 H), 4.69 (br s, 1 H), 3.93 (d, J = 5.5 Hz, 2 H), 3.30 (s, 2 H), 1.36 (s, 9 H), 1.23 (s, 6 H) ppm.

Step 3: tert-butyl N-[2-(2-hydroxyethoxy)-1,1-dimethyl-ethyl]carbamate

Through a solution of tert-butyl N-(2-allyloxy-1,1-dimethyl-ethyl)carbamate (250.0 mg, 1.09 mmol, 1 eq) in DCM (20 mL) cooled to -78 °C was bubbled ozone until the mixture turned blue. The mixture was warmed to 0 °C and then sodium borohydride (82.49 mg, 2.18 mmol, 2 eq) was added. The mixture was stirred for 3 h, quenched with saturated NH₄Cl solution and then the organic phase was separated. The mixture was dried over sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with PE:EA from 10:1 to 3:1 to afford tert-butyl N-[2-(2-hydroxyethoxy)-1,1-dimethyl-ethyl]carbamate (80 mg, 0.340 mmol, 31.45 % yield) as colorless oil.

¹H NMR (400 MHz, CHLOROFORM-d) δ = 4.61 (br s, 1 H), 3.69 - 3.65 (m, 2 H), 3.55 - 3.49 (m, 2 H), 3.41 (s, 2 H), 1.37 (s, 9 H), 1.22 (s, 6 H) ppm.

Step 4: 2-[2-(tert-butoxycarbonylamino)-2-methyl-propoxy]ethyl methanesulfonate

The title compound was obtained in analogy to step 4 in the preparation of Example 159 using tert-butyl N-[2-(2-hydroxyethoxy)-1,1-dimethyl-ethyl]carbamate as starting material. The product was directly used in crude form.

Step 5: tert-butyl N-[2-(2-azidoethoxy)-1,1-dimethyl-ethyl]carbamate

To a solution of 2-[2-(tert-butoxycarbonylamino)-2-methyl-propoxy]ethyl methanesulfonate (550.0 mg, 1.77 mmol, 1 eq) in DMF (5 mL) was added sodium azide (0.31 mL, 8.83 mmol, 5 eq). The resulting mixture was stirred at 50 °C for 2 h. The mixture was diluted with water, extracted with ethyl acetate, washed with brine, dried over sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with PE:EA = 10:1 to afford tert-butyl

N-[2-(2-azidoethoxy)-1,1-dimethyl-ethyl]carbamate (380 mg, 1.47 mmol, 83.29 % yield) as colorless oil.

¹H NMR (400 MHz, chloroform-d) δ = 4.63 (br s, 1 H), 3.62 - 3.57 (m, 2 H), 3.40 (s, 2 H), 3.29 (t, J = 4.9 Hz, 2 H), 1.36 (s, 9 H), 1.23 (s, 6 H) ppm.

5 **Step 6: tert-butyl N-[2-(2-aminoethoxy)-1,1-dimethyl-ethyl]carbamate**

To a solution of tert-butyl N-[2-(2-azidoethoxy)-1,1-dimethyl-ethyl]carbamate (380.0 mg, 1.47 mmol, 1 eq) in ethyl acetate (5 mL) was added palladium on carbon (38.0 mg, 0.040 mmol, 0.020 eq). The resulting mixture was hydrogenated at 760 mmHg at 15 °C for 2 h and the catalyst was removed by filtration. The filtrate was concentrated to afford tert-butyl N-[2-(2-
10 aminoethoxy)-1,1-dimethyl-ethyl]carbamate (360 mg, 1.55 mmol, crude) as colorless oil, which was used without further purification.

Step 7: tert-butyl N-[1,1-dimethyl-2-[2-[(4-nitro-2-vinyl-benzoyl)amino]ethoxy]ethyl]carbamate

The title compound was obtained in analogy to step 3 in the preparation of Example 158 using 4-
15 nitro-2-vinyl-benzoic acid and tert-butyl N-[2-(2-aminoethoxy)-1,1-dimethyl-ethyl]carbamate for condensation. MS (ESI) m/z : 430.3. $[M+Na]^+$

Step 8: tert-butyl N-[2-[2-[(4-amino-2-ethyl-benzoyl)amino]ethoxy]-1,1-dimethyl-ethyl]carbamate

The title compound was obtained in analogy to step 4 in the preparation of Reference Example
20 342 using tert-butyl N-[1,1-dimethyl-2-[2-[(4-nitro-2-vinyl-benzoyl)amino]ethoxy]ethyl]carbamate as substrate. MS (ESI) m/z : 402.3. $[M+Na]^+$

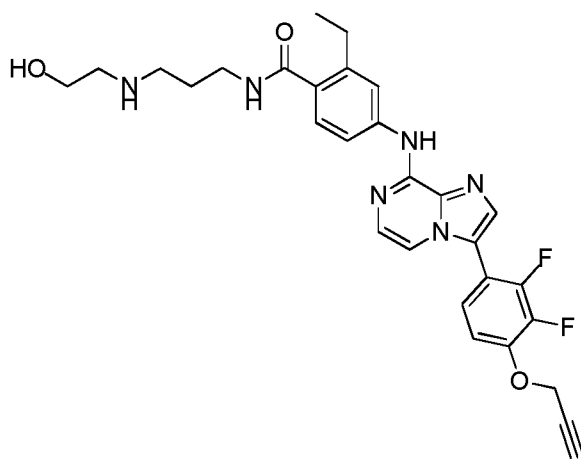
Step 9: tert-butyl N-[2-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethoxy]-1,1-dimethyl-ethyl]carbamate

The title compound was obtained in analogy to **step 2** in the preparation of Example 158 using
25 tert-butyl N-[2-[2-[(4-amino-2-ethyl-benzoyl)amino]ethoxy]-1,1-dimethyl-ethyl]carbamate and 8-chloro-3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazine. MS (ESI) m/z : 639.4. $[M+H]^+$

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Step 10: N-[2-(2-amino-2-methyl-propoxy)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid

The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-butyl N-[2-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethoxy]-1,1-dimethyl-ethyl]carbamate as substrate. MS (ESI) m/z: 539.2 [M+H]⁺

Reference Example 385**4-[[3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[3-(2-hydroxyethylamino)propyl]benzamide****Step 1: 4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2,3-difluoro-phenol**

The title compound was obtained in analogy to step 5 in the preparation of Intermediate 27 using 8-chloro-3-iodo-imidazo[1,2-a]pyrazine and 2,3-difluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenol. MS (ESI) m/z: 282.0 [M+H]⁺

Step 2: 8-chloro-3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazine

The title compound was obtained in analogy to step 4 in the preparation of Reference Example 374 using 4-(8-chloroimidazo[1,2-a]pyrazin-3-yl)-2,3-difluoro-phenol and propargyl bromide as reactants. MS (ESI) m/z: 320.1. [M+H]⁺

Step 3: tert-butyl N-[3-(benzyloxycarbonylamino)propyl]-N-(2-hydroxyethyl)carbamate

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To a solution of benzyl N-[3-(2-hydroxyethylamino)propyl]carbamate (120.0 mg, 0.480 mmol, 1 eq) and triethylamine (0.07 mL, 0.480 mmol, 1 eq) in DCM (5 mL) was added di-
t-butylidicarbonate (103.8 mg, 0.480 mmol, 1 eq), the mixture was stirred at 20 °C for 16 h. The
mixture was concentrated and the obtained residue purified by reverse phase flash column
5 chromatography to get the product tert-butyl N-[3-(benzyloxycarbonylamino)propyl]-N-(2-
hydroxyethyl)carbamate (80 mg, 0.230 mmol, 47.73 % yield) as a colorless oil. MS (ESI) m/z:
353.2 [M+H]⁺

Step 4: tert-butyl N-(3-aminopropyl)-N-(2-hydroxyethyl)carbamate

To a solution of tert-butyl N-[3-(benzyloxycarbonylamino)propyl]-N-(2-hydroxyethyl)carbamate
10 (80.0 mg, 0.230 mmol, 1 eq) in methanol (2 mL) was added Pd/C (0.230 mmol, 1 eq) at 20 °C,
the mixture was stirred at 20 °C for 24 h, filtered and concentrated to get the product tert-butyl
N-(3-aminopropyl)-N-(2-hydroxyethyl)carbamate (30 mg, 0.140 mmol, 40.36 % yield) as a
colorless oil, which was used without further purification in the next step.

**Step 5: 4-((3-(2,3-difluoro-4-(prop-2-yn-1-yloxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-
15 2-ethylbenzoic acid**

The title compound was obtained in analogy to step 2 in the preparation of Example 158 using 8-
chloro-3-(2,3-difluoro-4-prop-2-yloxy-phenyl)imidazo[1,2-a]pyrazine and 4-amino-2-
ethylbenzoic acid as reactants. MS (ESI) m/z: 449.1 [M+H]⁺

**Step 6: tert-butyl N-[3-[[4-[[3-(2,3-difluoro-4-prop-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-
20 8-yl]amino]-2-ethyl-benzoyl]amino]propyl]-N-(2-hydroxyethyl)carbamate**

The title compound was obtained in analogy to step 3 in the preparation of Example 158 using 4-
((3-(2,3-difluoro-4-(prop-2-yn-1-yloxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-
ethylbenzoic acid and tert-butyl N-(3-aminopropyl)-N-(2-hydroxyethyl)carbamate as coupling
partners. MS (ESI) m/z: 649.3 [M+H]⁺

**Step 7: 4-[[3-(2,3-difluoro-4-prop-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-
25 ethyl-N-[3-(2-hydroxyethylamino)propyl]benzamide**

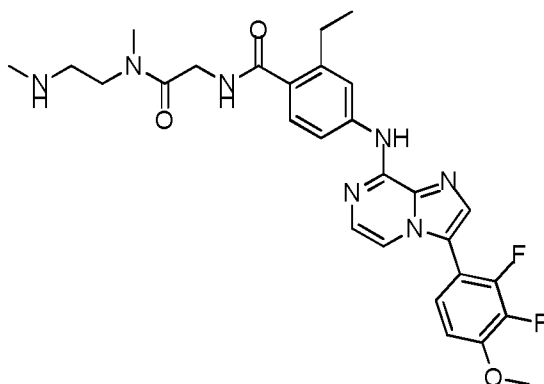
The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-
butyl N-[3-[[4-[[3-(2,3-difluoro-4-prop-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-

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ethyl-benzoyl]amino]propyl]-N-(2-hydroxyethyl)carbamate as starting material. MS (ESI) m/z: 549.4 [M+H]⁺

Example 158

4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(2-(methyl(2-(methylamino)ethyl)amino)-2-oxoethyl)benzamide; formic acid



Step 1: 8-chloro-3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazine

A mixture of 8-chloro-3-iodo-imidazo[1,2-a]pyrazine (10.0 g, 35.78 mmol, 1 eq), 2,3-difluoro-4-methoxyphenylboronic acid (8.07 g, 42.94 mmol, 1.2 eq), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (2.62 g, 3.58 mmol, 0.100 eq) and sodium carbonate (7.58 g, 71.56 mmol, 2 eq) in 1,4-dioxane (72 mL) and water (8 mL) was stirred for 15 h at 80 °C under N₂. The mixture was filtered and the filtrate was concentrated in vacuo to give a crude product, which was purified by silica gel chromatography eluting with petroleum ether/ethyl acetate = 2:1 to give product 8-chloro-3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazine (6 g, 20.29 mmol, 50.81 % yield) as a light yellow solid. MS (ESI) m/z: 296.0 [M+H]⁺

Step 2: 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzoic acid

A mixture of 4-amino-2-ethyl-benzoic acid (216.91 mg, 1.12 mmol, 1.1 eq) and 8-chloro-3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazine (300.0 mg, 1.01 mmol, 1 eq) in acetonitrile (6.3 mL) and acetic acid (0.700 mL) was stirred for 12 h at 65 °C. The solvent was removed in vacuo to give 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-

benzoic acid (400 mg, 0.940 mmol, 72.64 % yield) as an off-white solid, which was used without further purification in the next step. MS (ESI) m/z : 425.0 $[M+H]^+$

Step 3: tert-butyl 2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)acetate

- 5 To a solution of 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoic acid (400.0 mg, 0.940 mmol, 1 eq) in DMF (8 mL) was added O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (430 mg, 1.13 mmol, 1.2 eq) and N,N-diisopropylethylamine (0.33 mL, 1.89 mmol, 2 eq), then the mixture was stirred for 0.2 h at 10 °C, tert-butyl glycinate (135.99 mg, 1.04 mmol, 1.1 eq) was added and the
- 10 mixture was stirred for 15 h at 10 °C. The mixture was diluted with water, filtered and dried to give tert-butyl 2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]acetate (536 mg, 1 mmol, 88 % yield) as a light yellow solid. MS (ESI) m/z : 538.1 $[M+H]^+$

Step 4: 2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)acetic acid

- To a solution of tert-butyl 2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]acetate (536.0 mg, 0.830 mmol, 1 eq) in 1,4-dioxane (6 mL) was added 4 M HCl in dioxane (6.22 mL, 24.89 mmol, 30 eq), and the mixture was stirred for 15 h at 30 °C. The solvent was evaporated to give crude 2-[[4-[[3-(2,3-difluoro-4-methoxy-
- 20 phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]acetic acid (455 mg, 0.950 mmol, 91.14 % yield) as an off-white solid, which was used in the next step without further purification. MS (ESI) m/z : 482.2 $[M+H]^+$

Step 5: tert-butyl (2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)-N-methylacetamido)ethyl)(methyl)carbamate

- 25 The title compound was obtained in analogy to step 1 in the preparation of Example 5 using 2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)acetic acid and tert-butyl N-methyl-N-[2-(methylamino)ethyl]carbamate as reactants. MS (ESI) m/z : 652.3 $[M+H]^+$

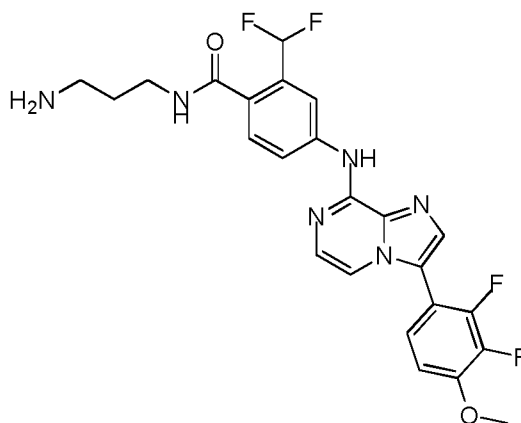
-404-

Step 6: 4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(2-(methyl(2-(methylamino)ethyl)amino)-2-oxoethyl)benzamide

The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-butyl (2-(2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)-N-methylacetamido)ethyl)(methyl)carbamate as reactant. MS (ESI) m/z: 552.1 [M+H]⁺

Example 165

N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(difluoromethyl)benzamide; formic acid



10

Step 1: methyl 2-(difluoromethyl)-4-nitrobenzoate

A solution of methyl 2-formyl-4-nitro-benzoate (500.0 mg, 2.39 mmol, 1 eq) in DCM (20 mL) was cooled to -15 °C and diethylaminosulfur trifluoride (1926.64 mg, 11.95 mmol, 5 eq) was added. The resulting mixture was stirred at 10 °C for 15 h. The mixture was quenched with sat. NaHCO₃. The organic separated layer was dried over sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with PE:EA = 100:1 to afford methyl 2-(difluoromethyl)-4-nitro-benzoate (380 mg, 1.64 mmol, 68.77 % yield) as yellow oil.

¹H NMR (400 MHz, CHLOROFORM-d) δ = 8.68 (d, *J* = 2.0 Hz, 1 H), 8.41 (dd, *J* = 2.3, 8.5 Hz, 1 H), 8.24 (d, *J* = 8.5 Hz, 1 H), 7.70 - 7.41 (m, 1 H), 4.03 (s, 3 H) ppm.

Step 2: 2-(difluoromethyl)-4-nitrobenzoic acid

20

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To a solution of methyl 2-(difluoromethyl)-4-nitro-benzoate (380.0 mg, 1.64 mmol, 1 eq) in THF (10 mL) and water (1 mL) was added LiOH.H₂O (137.7 mg, 3.28 mmol, 2 eq). The resulting mixture was stirred at 10 °C for 2 h. The mixture was acidified with 1N HCl to pH = 3 and extracted with ethyl acetate (50 mLx2), washed with brine, dried over Na₂SO₄ and concentrated to afford 2-(difluoromethyl)-4-nitro-benzoic acid (350 mg, 1.61 mmol, 98.05% yield) as yellow solid, which was used directly in next step.

Step 3: tert-butyl N-[3-[[2-(difluoromethyl)-4-nitro-benzoyl]amino]propyl]carbamate

The title compound was obtained in analogy to step 3 in the preparation of Example 158 using 2-(difluoromethyl)-4-nitro-benzoic acid and N-BOC-1,3-diaminopropane. MS (ESI) m/z: 396.3. [M+Na]⁺

Step 4: tert-butyl N-[3-[[4-amino-2-(difluoromethyl)benzoyl]amino]propyl]carbamate

The title compound was obtained in analogy to step 4 in the preparation of Reference Example 342 using tert-butyl N-[3-[[2-(difluoromethyl)-4-nitro-benzoyl]amino]propyl] carbamate as substrate for hydrogenation. MS (ESI) m/z: 366.1 [M+Na]⁺

Step 5: tert-butyl N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(difluoromethyl)benzoyl]amino]propyl]carbamate

A mixture of 8-chloro-3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazine (70.0 mg, 0.240 mmol, 1 eq), tert-butyl N-[3-[[4-amino-2-(difluoromethyl)benzoyl]amino]propyl]carbamate (97.55 mg, 0.280 mmol, 1.2 eq), Brettphos Pd G3 (21.46 mg, 0.020 mmol, 0.100 eq), potassium carbonate (98.16 mg, 0.710 mmol, 3 eq) in tert-butanol (5 mL) were stirred for 15 h at 110 °C under nitrogen protection. The mixture was filtered and the solvent was removed in vacuum to give crude product, which was purified by prep-TLC (DCM/MeOH = 10/1) to give product tert-butyl N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(difluoromethyl)benzoyl]amino]propyl]carbamate (110 mg, 0.180 mmol, 77 % yield). MS (ESI) m/z: 603.2 [M+H]⁺

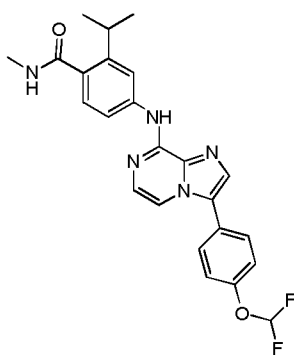
Step 6: N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(difluoromethyl)benzamide

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The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-butyl N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(difluoromethyl)benzoyl]amino]propyl]carbamate as substrate. MS (ESI) m/z: 503.3 [M+H]⁺

Example 166

5 **4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-isopropyl-N-methyl-benzamide**

**Step 1: methyl 2-isopropenyl-4-nitro-benzoate**

The title compound was obtained in analogy to step 1 in the preparation of Example 167 using 2-bromo-4-nitro-benzoate and 4,4,5,5-tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane.

¹H NMR (400 MHz, chloroform-d) δ = 8.20 - 8.12 (m, 2 H), 7.94 - 7.90 (m, 1 H), 5.25 (quin, J = 1.4 Hz, 1 H), 4.99 - 4.94 (m, 1 H), 3.92 (s, 3 H), 2.14 (dd, J = 0.9, 1.5 Hz, 3 H) ppm.

Step 2: 2-isopropenyl-N-methyl-4-nitro-benzamide

The title compound was obtained in analogy to step 4 in the preparation of Reference Example 15 342 using methyl 2-isopropenyl-4-nitro-benzoate.

Step 3: 4-amino-2-isopropyl-N-methyl-benzamide

The title compound was obtained in analogy to step 3 in the preparation of Example 167 using 2-isopropenyl-N-methyl-4-nitro-benzamide as substrate. MS (ESI) m/z: 193.2 [M+H]⁺

20 **Step 4: 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-isopropyl-N-methyl-benzamide**

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The title compound was obtained in analogy to step 2 in the preparation of Example 158 using 8-chloro-3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazine and 4-amino-2-isopropyl-N-methyl-benzamide for this substitution reaction. MS (ESI) m/z: 452.2 [M+H]⁺

Reference Example 386

5 **N-[2-(2-aminoethoxy)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-fluoroethyl)benzamide**

Step 1: tert-butyl 2-formyl-4-nitrobenzoate

To a solution of tert-butyl 4-nitro-2-vinyl-benzoate (3.2 g, 12.84 mmol, 1 eq) in DCM (50 mL) cooled to -78 was bubbled ozone (6162.24 mg, 128.38 mmol, 10 eq) until the reaction mixture
10 turn blue, and the nitrogen was bubbled for 5 min. Dimethylsulfide (10.0 mL, 12.84 mmol, 1 eq) was added, the resulting mixture was stirred at 25 °C for 15 h. The mixture was concentrated and the residue was purified by silica gel chromatography eluting with PE:EA=10:1 to afford tert-butyl 2-formyl-4-nitro-benzoate (1.9 g, 7.56 mmol, 58.91% yield) as white solid. MS (ESI) m/z: 252.1 [M+H]⁺

15 **Step 2: tert-butyl 2-[(E)-2-bromo-2-fluoro-vinyl]-4-nitro-benzoate**

To a solution of tert-butyl 2-formyl-4-nitro-benzoate (0.6 g, 2.39 mmol, 1 eq) and triphenylphosphine (2505.51 mg, 9.55 mmol, 4 eq) in THF (20 mL) was added tribromo(fluoro)methane (1616.3 mg, 5.97 mmol, 2.5 eq). The resulting mixture was stirred at 70 °C under nitrogen for 15 h. The mixture was concentrated and then purified by silica
20 gel chromatography eluting with PE:EA = 20:1 to afford tert-butyl 2-[(E)-2-bromo-2-fluoro-vinyl]-4-nitro-benzoate (600 mg, 1.73 mmol, 73% yield) as white solid.

Step 3: tert-butyl 4-amino-2-(2-fluoroethyl)benzoate

The title compound was obtained in analogy to step 4 in the preparation of Reference Example 342 using tert-butyl 2-[(E)-2-bromo-2-fluoro-vinyl]-4-nitro-benzoate. MS (ESI) m/z: 240.1
25 [M+H]⁺

Step 4: 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-fluoroethyl)benzoic acid

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A solution of tert-butyl 4-amino-2-(2-fluoroethyl)benzoate (194.24 mg, 0.810 mmol, 1.2 eq) and 8-chloro-3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazine (200.0 mg, 0.680 mmol, 1 eq) in ACN (4.5 mL) and acetic acid (0.500 mL) was heated to 80 °C for 15 h. The mixture was purified by prep-HPLC to afford 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-fluoroethyl)benzoic acid (160 mg, 0.360 mmol, 53 % yield) as off-white solid.
 MS (ESI) m/z: 443.2 [M+H]⁺

Step 5: tert-butyl N-[2-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-fluoroethyl)benzoyl]amino]ethoxy]ethyl]carbamate

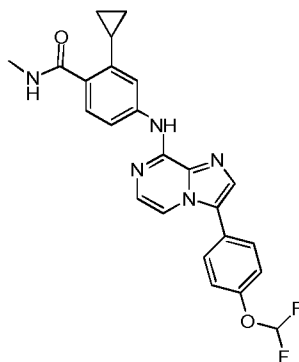
The title compound was obtained in analogy to step 3 in the preparation of Example 158 using 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-fluoroethyl)benzoic acid and tert-butyl (2-(2-aminoethoxy)ethyl)carbamate. MS (ESI) m/z: 629.1 [M+H]⁺

Step 6: N-[2-(2-aminoethoxy)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-fluoroethyl)benzamide

The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-butyl N-[2-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-fluoroethyl)benzoyl]amino]ethoxy]ethyl]carbamate as. MS (ESI) m/z: 529.3 [M+H]⁺

Example 167

2-cyclopropyl-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide



Step 1: 2-cyclopropyl-4-nitro-benzoate

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A solution of methyl 2-bromo-4-nitro-benzoate (600.0 mg, 2.31 mmol, 1 eq), cyclopropylboronic acid (594.49 mg, 6.92 mmol, 3 eq), potassium phosphate (0.96 mL, 11.54 mmol, 5 eq) and 1,1'-bis(di-tert-butylphosphino)ferrocene palladium dichloride (150 mg, 0.230 mmol, 0.100 eq) in toluene (10 mL) and water (0.4 mL) was heated to 100 °C for 15 h under
5 nitrogen. The reaction mixture was concentrated and the residue was purified by silica gel chromatography eluting with PE:EA from 10:1 to 5:1 to afford methyl 2-cyclopropyl-4-nitro-benzoate (450 mg, 2.03 mmol, 88 % yield).

¹H NMR (400 MHz, chloroform-d) δ = 8.04 (dd, J = 2.3, 8.5 Hz, 1 H), 7.92 (d, J = 8.5 Hz, 1 H), 7.86 (d, J = 2.3 Hz, 1 H), 3.99 (s, 3 H), 2.69 (tt, J = 5.4, 8.5 Hz, 1 H), 1.19 - 1.11 (m, 2 H), 0.86
10 - 0.79 (m, 2 H) ppm.

Step 2: 2-cyclopropyl-N-methyl-4-nitro-benzamide

To a solution of methyl 2-cyclopropyl-4-nitro-benzoate (350.0 mg, 1.58 mmol, 1 eq) in methanol (10 mL) was added methylamine in methanol (10.0 mL). The resulting mixture was heated to 80 °C for 15 h. The mixture was concentrated and the obtained residue was triturated with
15 MTBE (10 mL) to give 2-cyclopropyl-N-methyl-4-nitro-benzamide (220 mg, 1 mmol, 63.14 % yield). MS (ESI) m/z : 222.2 [M+H]⁺

Step 3: 4-amino-2-cyclopropyl-N-methyl-benzamide

The title compound was obtained in analogy to step 4 in the preparation of Reference Example 342 using 2-cyclopropyl-N-methyl-4-nitro-benzamide. MS (ESI) m/z : 191.2. [M+H]⁺

20 Step 4: 8-chloro-3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazine

The title compound was obtained in analogy to step 1 in the preparation of Example 158 using 8-chloro-3-iodoimidazo[1,2-a]pyrazine and (4-(difluoromethoxy)phenyl)boronic acid. MS (ESI) m/z : 296.1 [M+H]⁺

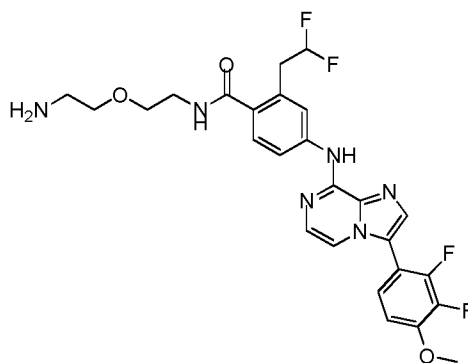
25 Step 5: 2-cyclopropyl-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide

The title compound was obtained in analogy to step 2 in the preparation of Example 158 using 8-chloro-3-(4-(difluoromethoxy)phenyl)imidazo[1,2-a]pyrazine and 4-amino-2-cyclopropyl-N-methyl-benzamide as substrates. MS (ESI) m/z : 450.1. [M+H]⁺

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Reference Example 387

N-[2-(2-aminoethoxy)ethyl]-2-(2,2-difluoroethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide; formic acid



5 **Step 1: methyl 2-formyl-4-nitrobenzoate**

A solution of methyl 4-nitro-2-vinyl-benzoate (3.5 g, 17 mmol, 1 eq) in DCM (20 mL) was stirred under ozone (100 mL, 16.9 mmol, 1 eq) at -40 °C for 0.5 h, the mixture was quenched with dimethylsulfide (10.0 mL, 16.9 mmol, 1 eq) and then concentrated to give the desired product methyl 2-formyl-4-nitro-benzoate (2.8 g, 13 mmol, 79% yield), which was used in the
 10 next step without further purification. MS (ESI) m/z: 210.1 [M+H]⁺

Step 2: methyl 2-(2,2-difluorovinyl)-4-nitro-benzoate

To a solution of methyl 2-formyl-4-nitro-benzoate (647.0 mg, 3.09 mmol, 1 eq) in DMF (5 mL) was added triphenylphosphine (973.6 mg, 3.71 mmol, 1.2 eq) and (2-chloro-2,2-difluoro-acetyl)oxysodium (707.41 mg, 4.64 mmol, 1.5 eq). The resulting suspension was stirred at 100
 15 °C for 0.5 h under nitrogen. The mixture was diluted with water (100 mL), extracted with ethyl acetate (50 mLx2), washed with brine, dried over sodium sulfate and concentrated. The residue was purified by prep-TLC (PE:EA = 5:1) to afford methyl 2-(2,2-difluorovinyl)-4-nitro-benzoate (130 mg, 0.530 mmol, 17.28 % yield) as white solid.

¹H NMR (400 MHz, CHLOROFORM-d) δ = 8.48 - 8.43 (m, 1 H), 8.17 - 8.11 (m, 2 H), 6.41 -
 20 6.30 (m, 1 H) ppm.

Step 3: methyl 4-amino-2-(2,2-difluoroethyl)benzoate

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The title compound was obtained in analogy to step 4 in the preparation of Reference Example 342 using methyl 2-(2,2-difluorovinyl)-4-nitro-benzoate. MS (ESI) m/z: 216.1 [M+H]⁺

Step 4: methyl 2-(2,2-difluoroethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoate

- 5 The title compound was obtained in analogy to step 2 in the preparation of Example 158 using methyl 4-amino-2-(2,2-difluoroethyl)benzoate and 1-chloro-6-(2,3-difluoro-4-methoxy-phenyl)pyrrolo[1,2-a]pyrazine. MS (ESI) m/z: 475.2 [M+H]⁺

Step 5: 2-(2,2-difluoroethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid

- 10 To a solution of methyl 2-(2,2-difluoroethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoate (60.0 mg, 0.130 mmol, 1 eq) in THF (3 mL) and water (1 mL) was added lithium hydroxide monohydrate (6.37 mg, 0.150 mmol, 1.2 eq). The mixture was acidified with 1N aq. HCl to pH = 3 and extracted with ethyl acetate (50 mL), washed with brine, dried over sodium sulfate and concentrated to afford 2-(2,2-difluoroethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid (50 mg, 0.110 mmol, 85 %
15 yield) as white solid. MS (ESI) m/z: 461.1 [M+H]⁺

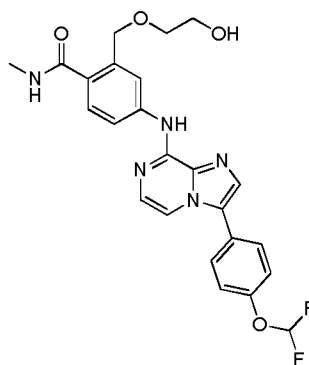
Step 6: tert-butyl N-[2-[2-[[2-(2,2-difluoroethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]ethoxy]ethyl]carbamate

- The title compound was obtained in analogy to step 3 in the preparation of Example 158 using 2-
20 (2,2-difluoroethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid and N-BOC-2-(2-amino-ethoxy)-ethylamine for this condensation. MS (ESI) m/z: 647.4 [M+H]⁺

Step 7: N-[2-(2-aminoethoxy)ethyl]-2-(2,2-difluoroethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide

- 25 The title compound was obtained in analogy to step 2 in the preparation of Example 5 using tert-butyl N-[2-[2-[[2-(2,2-difluoroethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]ethoxy]ethyl]carbamate as substrate. MS (ESI) m/z: 547.2 [M+H]⁺

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Example 168**4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-hydroxyethoxymethyl)-N-methyl-benzamide****5 Step 1: 1-bromo-2-(chloromethyl)-4-nitro-benzene**

A mixture of (2-bromo-5-nitro-phenyl)methanol (2.0 g, 8.62 mmol, 1 eq) and SOCl_2 (1.03 g, 8.62 mmol, 1 eq) in 1,4-dioxane (20 mL) was heated to 60 °C for 1 h. The mixture was concentrated and the residue was purified by silica gel chromatography eluting with PE:EA = 20:1 to afford 1-bromo-2-(chloromethyl)-4-nitro-benzene (1.8 g, 7.19 mmol, 83 % yield).

- 10 ^1H NMR (400 MHz, CHLOROFORM- d) δ = 8.31 (d, J = 2.7 Hz, 1 H), 7.99 (dd, J = 2.7, 8.8 Hz, 1 H), 7.72 (d, J = 8.7 Hz, 1 H), 4.73 - 4.64 (m, 2H) ppm.

Step 2: 2-[(2-bromo-5-nitro-phenyl)methoxy]ethanol

- To an ice-cooled solution of ethylene glycol (1.67 mL, 29.94 mmol, 5 eq) in THF (20 mL) and DMF (20 mL) was added sodium hydride, 60 % in oil (0.36 g, 8.98 mmol, 1.5 eq). The resulting mixture was stirred for 5 min, and then 1-bromo-2-(chloromethyl)-4-nitro-benzene (1.5 g, 5.99 mmol, 1 eq) in THF (5mL) was added. The resulting suspension was stirred at 10 °C for 15 h. The mixture was poured into saturated aq. NH_4Cl (200 mL) solution, extracted with EA (50 mLx2), washed with brine, dried over sodium sulfate and concentrated. The crude material was purified by silica gel chromatography eluting with PE:EA from 5:1 to 3:1 to afford 2-[(2-bromo-5-nitro-phenyl)methoxy]ethanol (1 g, 3.62 mmol, 60 % yield).
- 15
20

^1H NMR (400 MHz, CHLOROFORM- d) δ = 8.39 (d, J = 2.8 Hz, 1 H), 8.04 (dd, J = 2.8, 8.7 Hz, 1 H), 7.75 (d, J = 8.7 Hz, 1 H), 4.69 (s, 2 H), 3.93 - 3.88 (m, 2 H), 3.81 - 3.77 (m, 2 H) ppm.

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Step 3: 2-(2-(2-hydroxyethoxymethyl)-4-nitro-benzonitrile

A mixture of 2-[(2-bromo-5-nitro-phenyl)methoxy]ethanol (1.0 g, 3.62 mmol, 1 eq), zinc cyanide (1.28 g, 10.87 mmol, 3 eq) and tetrakis(triphenylphosphine)palladium(0) (418.56 mg, 0.360 mmol, 0.100 eq) in DMF (10 mL) was heated to 110 °C for 15 h under nitrogen protection.

- 5 The mixture was diluted with water (100 mL), extracted with EA (50 mLx2), dried over sodium sulfate and concentrated. The residue was purified by silica gel chromatography eluting with PE:EA from 10:1 to 5:1 to afford 2-(2-(2-hydroxyethoxymethyl)-4-nitro-benzonitrile (600 mg, 2.7 mmol, 74 % yield).

¹H NMR (400 MHz, CHLOROFORM-d) δ = 8.54 - 8.44 (m, 1 H), 8.28 (dd, J = 2.3, 8.5 Hz, 1 H), 7.90 (d, J = 8.4 Hz, 1 H), 4.87 (s, 2 H), 3.92 - 3.86 (m, 2 H), 3.83 - 3.77 (m, 2 H) ppm.

Step 4: 2-(2-(2-hydroxyethoxymethyl)-4-nitro-benzoic acid

A mixture of 2-(2-(2-hydroxyethoxymethyl)-4-nitro-benzonitrile (600 mg, 2.7 mmol, 1 eq) in aq.sodium hydroxide (10.0 mL, 0.270 mmol, 0.100 eq) was heated to 100 °C for 3 h. The mixture was acidified with 2 N HCl aq. to pH = 4 and extracted with EA (100 mLx2), washed
15 with brine, dried over Na₂SO₄ and concentrated. The residue was triturated with DCM to afford 2-(2-(2-hydroxyethoxymethyl)-4-nitro-benzoic acid (450 mg, 1.87 mmol, 69.09 % yield). MS (ESI) m/z: 264.0. [M+Na]⁺

Step 5: 2-(2-(2-hydroxyethoxymethyl)-N-methyl-4-nitro-benzamide

The title compound was obtained in analogy to step 3 in the preparation of Example 158 using 2-
20 (2-(2-hydroxyethoxymethyl)-4-nitro-benzoic acid and methylamine (2 M in THF). MS (ESI) m/z: 277.0 [M+Na]⁺

Step 6: 4-amino-2-(2-(2-hydroxyethoxymethyl)-N-methyl-benzamide

The title compound was obtained in analogy to step 4 in the preparation of Reference Example 342 using 2-(2-(2-hydroxyethoxymethyl)-N-methyl-4-nitro-benzamide. MS (ESI) m/z: 225.3
25 [M+H]⁺

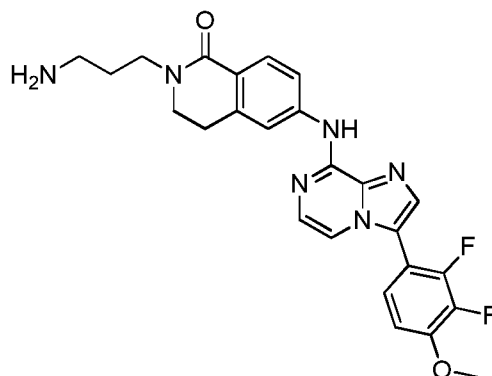
Step 7: 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-hydroxyethoxymethyl)-N-methyl-benzamide

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A mixture of 4-amino-2-(2-hydroxyethoxymethyl)-N-methyl-benzamide (120 mg, 0.540 mmol, 1 eq), 8-chloro-3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazine (158.21 mg, 0.540 mmol, 1 eq), Brettphos Pd G3 (45.88 mg, 0.050 mmol, 0.100 eq) and K₂CO₃ (147.91 mg, 1.07 mmol, 2 eq) was heated to 110 °C for 15 h under nitrogen. The mixture was diluted with water, and
 5 extracted with ethyl acetate (100 mLx2). The combined organic phases were washed with brine, dried over sodium sulfate and concentrated. The residue was purified by prep-TLC (DCM:MeOH = 10:1) to afford 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-hydroxyethoxymethyl)-N-methyl-benzamide (55.5 mg, 0.110 mmol, 21 % yield). MS (ESI) m/z: 484.0 [M+H]⁺

10 **Example 164**

2-(3-aminopropyl)-6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3,4-dihydroisoquinolin-1-one



Step 1: 6-bromo-2-(3-tetrahydropyran-2-yloxypropyl)-3,4-dihydroisoquinolin-1-one

15 To a mixture of 6-bromo-3,4-dihydro-2H-isoquinolin-1-one (400 mg, 1.77 mmol, 1 eq) in DMF (10 mL) was added sodium hydride (141.55 mg, 3.54 mmol, 2 eq) at 0 °C. Then the mixture was stirred at 0 °C for 0.5 h. Then 2-(3-bromopropoxy)tetrahydro-2H-pyran (1184.29 mg, 5.31 mmol, 3 eq) was added to the mixture at 25 °C and the mixture was stirred at 25 °C for another 15.5 h. Then the mixture was poured into water (30.0 mL) and extracted with ethyl acetate (50.0
 20 mL*2). The organic phase was dried and concentrated in vacuo to give the crude product as brown oil. The crude product was purified by silica gel column chromatography eluting with PE/EA from 20:1 to 2:1 to give 6-bromo-2-(3-tetrahydropyran-2-yloxypropyl)-3,4-dihydroisoquinolin-1-one (500 mg, 1.36 mmol, 76.73 % yield) as yellow oil. MS (ESI, m/z): 284.0 [M-84+H]⁺, 286.1 [M-84+2+H]⁺

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Step 2: 3-(2,3-difluoro-4-methoxyphenyl)-N-(4-methoxybenzyl)imidazo[1,2-a]pyrazin-8-amine

The title compound was obtained in analogy to step 2 in the preparation of Example 158 using 8-chloro-3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazine and (4-methoxyphenyl)methanamine. MS (ESI) m/z: 397.2 [M+H]⁺

Step 3: 3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-amine

To a stirred solution of 3-(2,3-difluoro-4-methoxyphenyl)-N-(4-methoxybenzyl)imidazo[1,2-a]pyrazin-8-amine (2 g, 5 mmol, 1 eq) in DCM (10 mL) was added TFA (10 mL). The reaction mixture was stirred at 30 °C for 16 h. The mixture was concentrated under reduced pressure to give 1.5 g of the crude product, used directly in the next step without further purification.

Step 4: 6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(3-tetrahydropyran-2-yloxypropyl)-3,4-dihydroisoquinolin-1-one

To a mixture of 6-bromo-2-(3-tetrahydropyran-2-yloxypropyl)-3,4-dihydroisoquinolin-1-one (440.16 mg, 1.2 mmol, 1.1 eq) and 3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-amine (300.0 mg, 1.09 mmol, 1 eq) in tert-butanol (10 mL) was added potassium carbonate (300 mg, 2.17 mmol, 2 eq) and BrettPhos-Pd-G3 (197.0 mg, 0.220 mmol, 0.200 eq) at 25 °C. Then the mixture was stirred at 110 °C for 16 h. Then the mixture was poured into water (30.0 mL) and extracted with ethyl acetate (50.0 mL*2). The organic phase was dried and concentrated in vacuo to give the crude product as brown solid. The crude product was triturated with ethyl acetate (20.0 mL) to give 6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(3-tetrahydropyran-2-yloxypropyl)-3,4-dihydroisoquinolin-1-one (400 mg, 0.710 mmol, 65.32 % yield) as white solid. MS (ESI) m/z: 564.3 [M+H]⁺

Step 5: 6-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-(3-hydroxypropyl)-3,4-dihydroisoquinolin-1(2H)-one

A mixture of 6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(3-tetrahydropyran-2-yloxypropyl)-3,4-dihydroisoquinolin-1-one (400.0 mg, 0.710 mmol, 1 eq) in HCl/MeOH (10.0 mL, 40 mmol, 56.36 eq) was stirred at 25 °C for 16 h. Then the mixture was

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concentrated in vacuo to give the crude product as grey solid. The crude product was purified by prep-HPLC (FA) to give 250 mg desired product as white solid. MS (ESI) m/z : 480.2 $[M+H]^+$

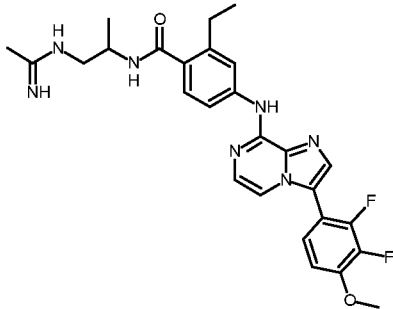
Step 6: 3-[6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-1-oxo-3,4-dihydroisoquinolin-2-yl]propyl methanesulfonate

- 5 The title compound was obtained in analogy to step 4 in the preparation of Example 159 using 6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(3-hydroxypropyl)-3,4-dihydroisoquinolin-1-one as starting material. MS (ESI) m/z : 558.2 $[M+H]^+$

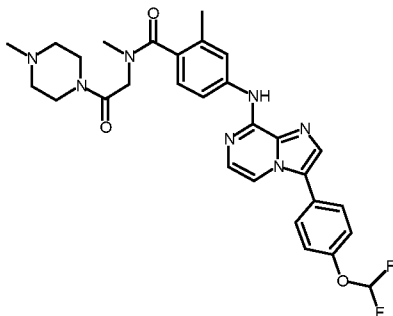
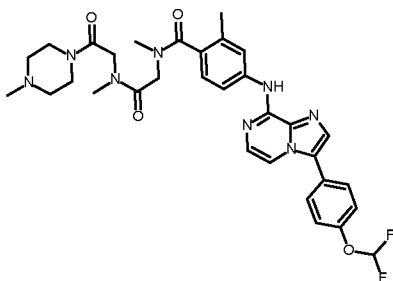
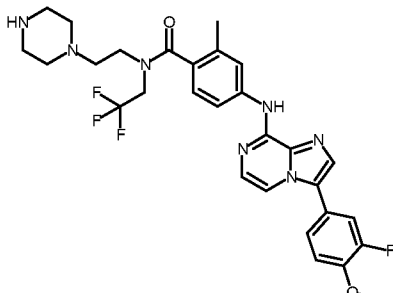
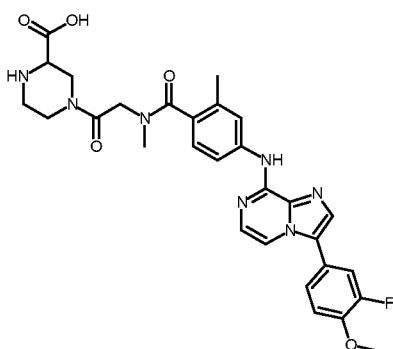
Step 7: 2-(3-aminopropyl)-6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3,4-dihydroisoquinolin-1-one

- 10 To a mixture of NH_3 in THF (2.0 mL, 8 mmol, 111.51 eq) was added 3-[6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-1-oxo-3,4-dihydroisoquinolin-2-yl]propyl methanesulfonate (40.0 mg, 0.070 mmol, 1 eq) at -78 °C. Then the mixture was stirred at -78 °C for 5 h. Then the mixture was concentrated in vacuo and purified by prep-HPLC to give 2-(3-aminopropyl)-6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3,4-dihydroisoquinolin-1-one (14 mg, 0.030 mmol, 40 % yield) as a white solid. MS (ESI) m/z : 479.3 $[M+H]^+$
- 15

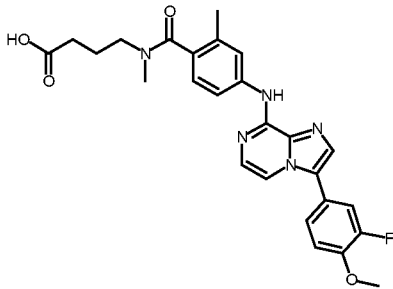
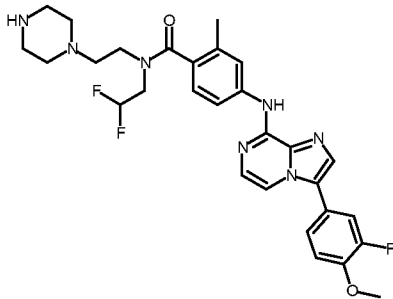
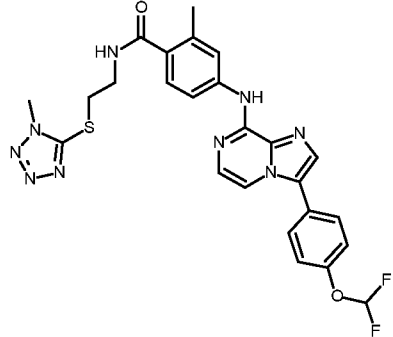
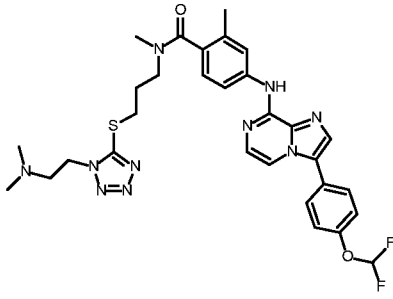
The following additional Examples have also been prepared with the methods described above:

Ex.	Name	Structure	ESI MS $[M+H]^+$
169	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[1-(ethanimidoylamino)propan-2-yl]-2-ethylbenzamide		522.3

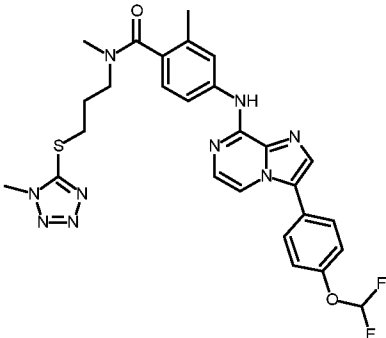
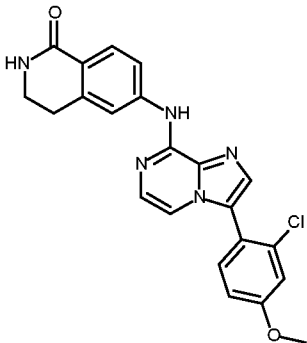
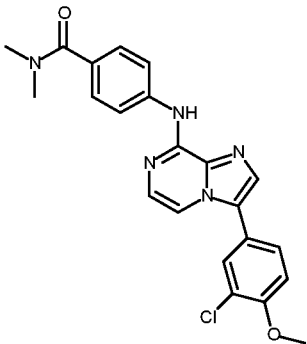
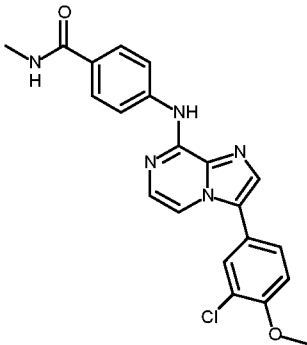
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170	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-methylpiperazin-1-yl)-2-oxoethyl]benzamide		564.41
171	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-[methyl-[2-(4-methylpiperazin-1-yl)-2-oxoethyl]amino]-2-oxoethyl]benzamide		635.47
172	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)-N-(2,2,2-trifluoroethyl)benzamide;hydrochloride		586.3
173	4-[2-[[4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]-methylamino]acetyl]piperazine-2-carboxylic acid;hydrochloride		576.3

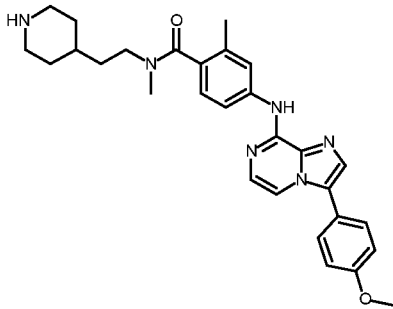
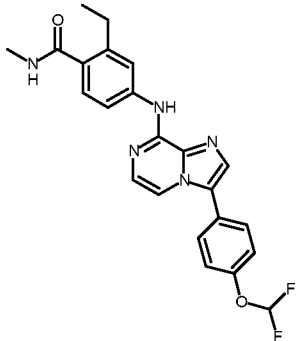
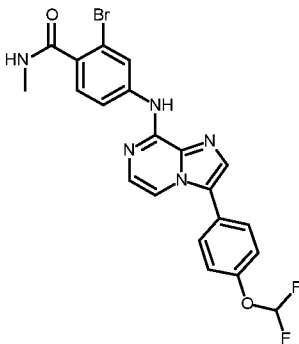
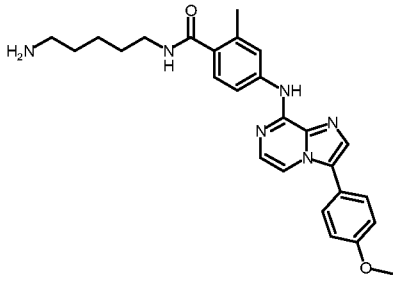
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174	4-[[4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]-methylamino]butanoic acid		492.2
175	N-(2,2-difluoroethyl)-4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;hydrochloride		568.3
176	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(1-methyltetrazol-5-yl)sulfanylethyl]benzamide		552.2
177	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-[1-[2-(dimethylamino)ethyl]tetrazol-5-yl]sulfanylpropyl]-N,2-dimethylbenzamide;2,2,2-trifluoroacetic acid		637.58

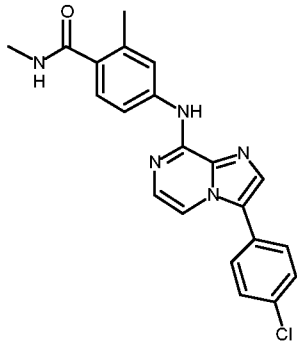
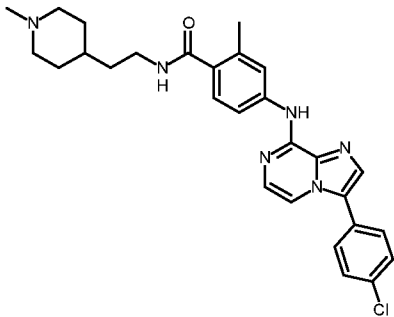
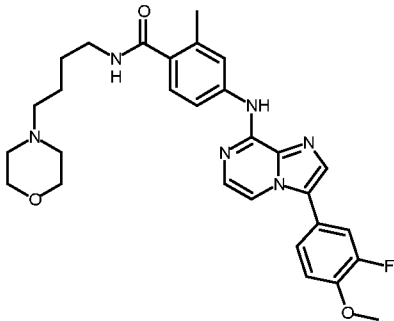
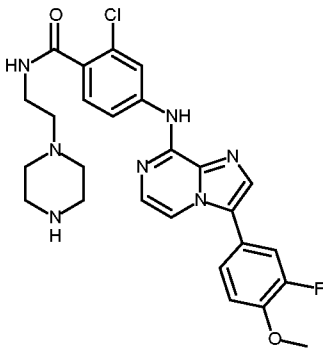
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178	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[3-(1-methyltetrazol-5-yl)sulfanylpropyl]benzamide		580.5
179	6-[[3-(2-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3,4-dihydro-2H-isoquinolin-1-one		420.1
180	4-[[3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethylbenzamide;2,2,2-trifluoroacetic acid		422.3
181	4-[[3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methylbenzamide;2,2,2-trifluoroacetic acid		408.2

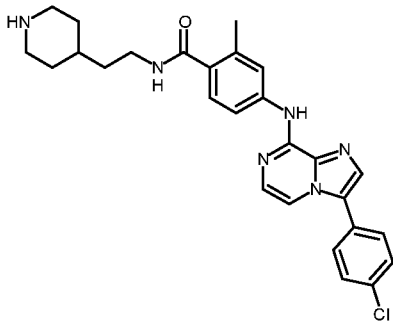
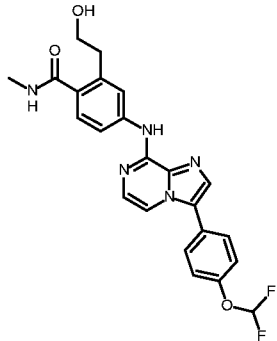
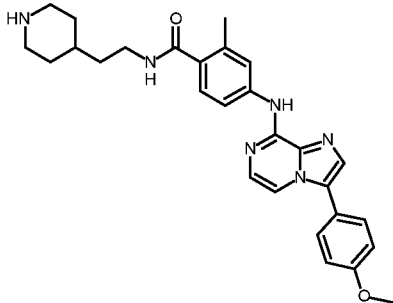
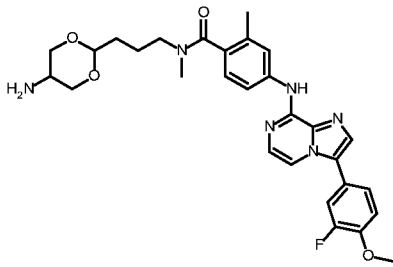
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182	4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-piperidin-4-ylethyl)benzamide;hydrochloride		499.5
183	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methylbenzamide		438.0
93	2-bromo-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methylbenzamide		490
184	N-(5-aminopentyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		459.4

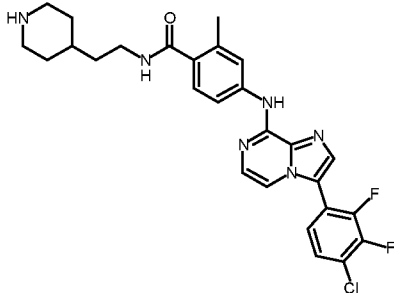
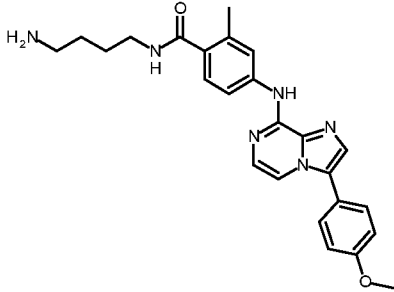
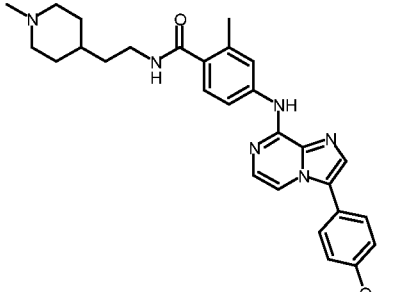
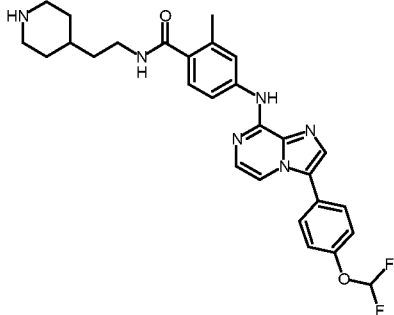
-421-

185	4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide		392.2
186	4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(1-methylpiperidin-4-yl)ethyl]benzamide		504.4
187	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-morpholin-4-ylbutyl)benzamide		533.3
188	2-chloro-4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)benzamide;hydrochloride		525.8

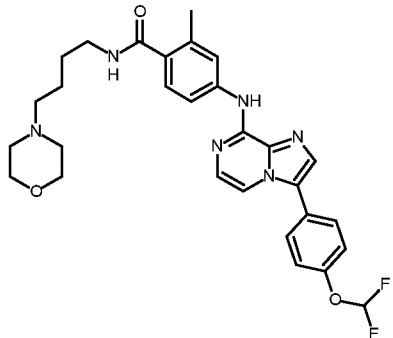
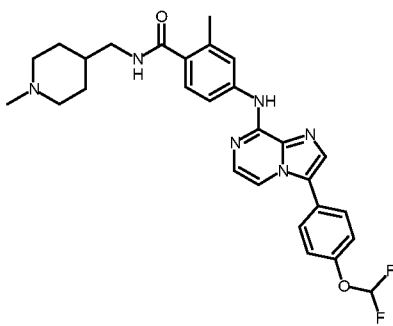
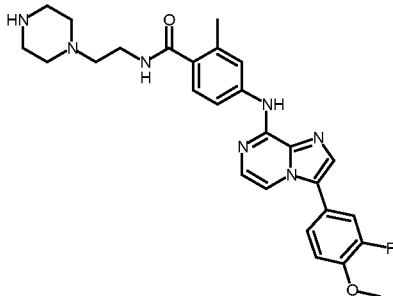
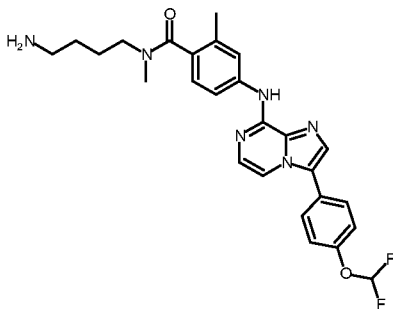
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189	4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperidin-4-ylethyl)benzamide;hydrochloride		489.2
190	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-hydroxyethyl)-N-methylbenzamide		454.3
191	4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperidin-4-ylethyl)benzamide;hydrochloride		485.2
192	N-[3-(5-amino-1,3-dioxan-2-yl)propyl]-4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide		547.4

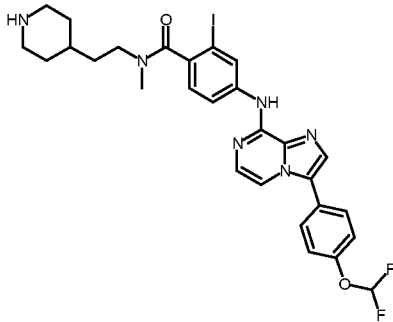
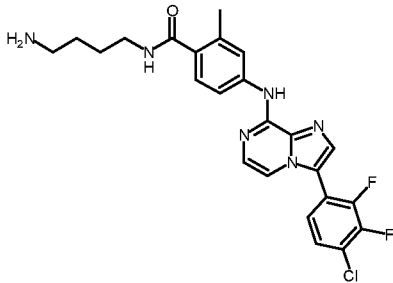
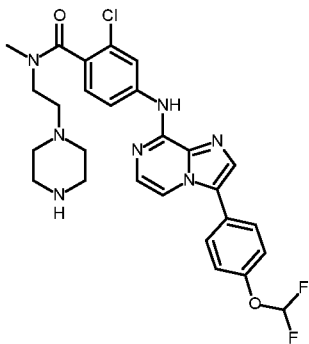
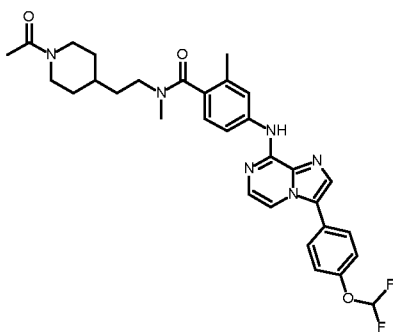
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193	4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperidin-4-ylethyl)benzamide;hydrochloride		525.2
194	N-(4-aminobutyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		445.3
195	4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(1-methylpiperidin-4-yl)ethyl]benzamide;hydrochloride		499.3
196	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperidin-4-ylethyl)benzamide;hydrochloride		521.2

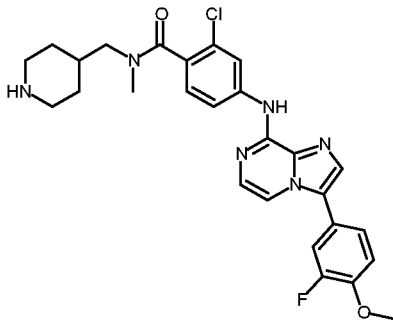
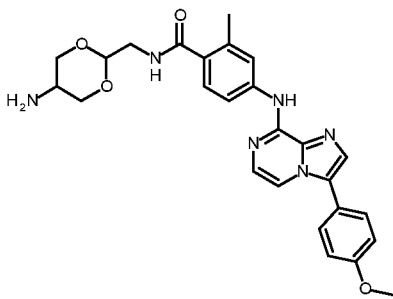
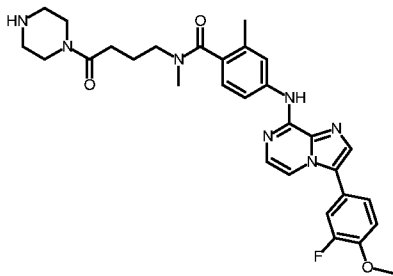
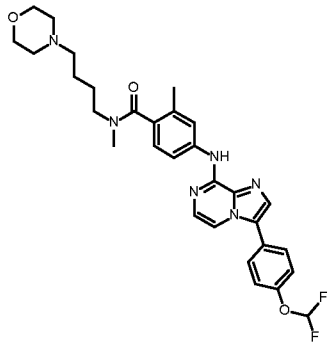
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197	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-morpholin-4-ylbutyl)benzamide		552.2
198	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(1-methylpiperidin-4-yl)methyl]benzamide		521.1
199	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;hydrochloride		504.3
200	N-(4-aminobutyl)-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide;hydrochloride		595.3

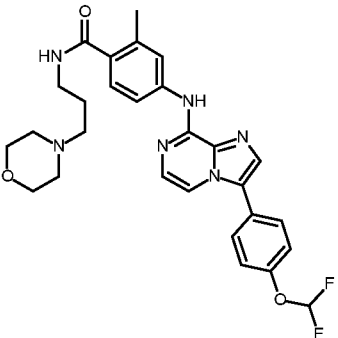
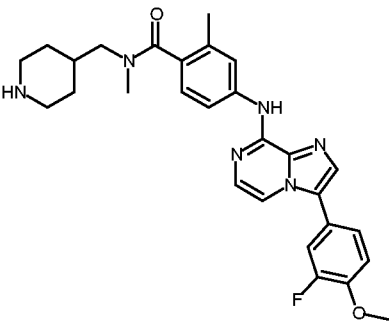
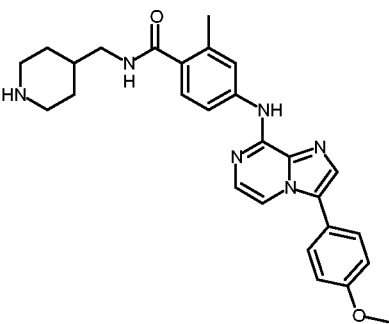
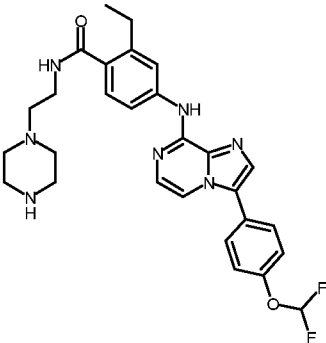
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201	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-iodo-N-methyl-N-(2-piperidin-4-ylethyl)benzamide;hydrochloride		647.2
202	N-(4-aminobutyl)-4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		485.1
203	2-chloro-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;hydrochloride		556.1
204	N-[2-(1-acetylpiperidin-4-yl)ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide		577.3

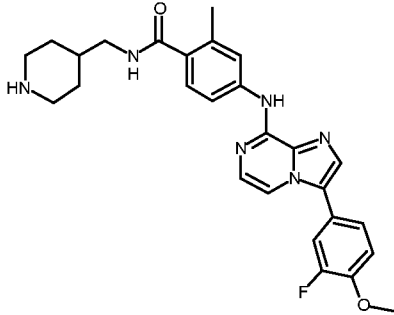
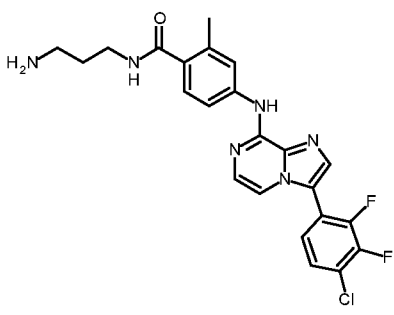
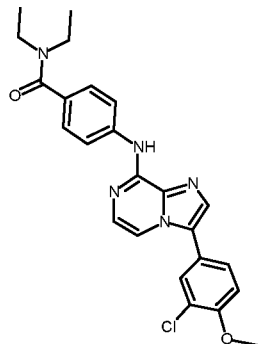
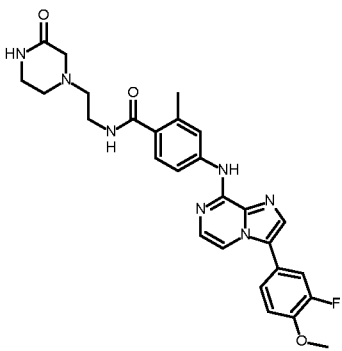
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205	2-chloro-4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(piperidin-4-ylmethyl)benzamide;hydrochloride		523.2
206	N-[(5-amino-1,3-dioxan-2-yl)methyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide		489.2
207	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(4-oxo-4-piperazin-1-ylbutyl)benzamide;hydrochloride		560.3
208	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(4-morpholin-4-ylbutyl)benzamide		565.2

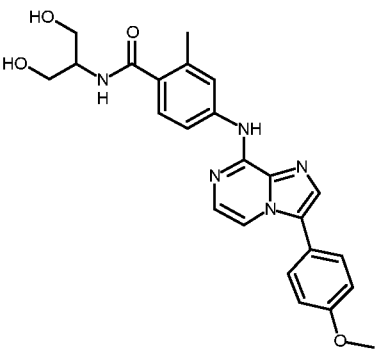
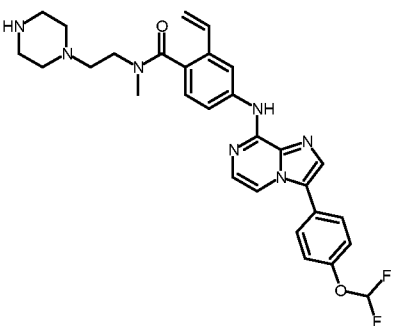
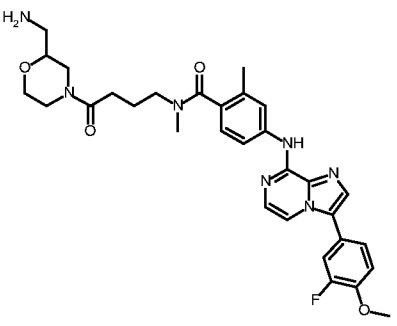
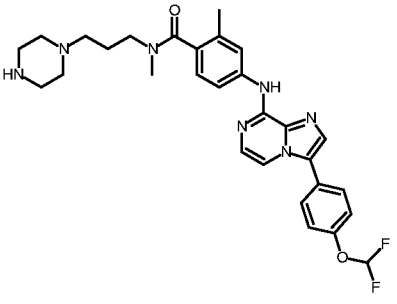
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209	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(3-morpholin-4-ylpropyl)benzamide		537.2
210	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(piperidin-4-ylmethyl)benzamide;hydrochloride		503.2
211	4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(piperidin-4-ylmethyl)benzamide;hydrochloride		471.4
212	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(2-piperazin-1-ylethyl)benzamide;hydrochloride		536.1

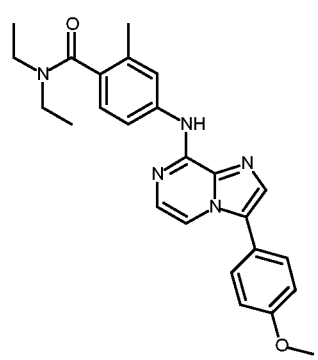
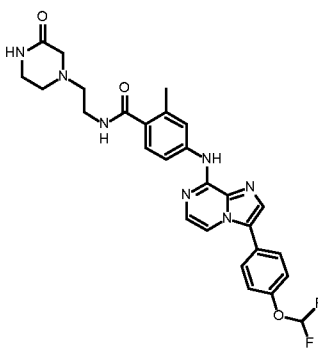
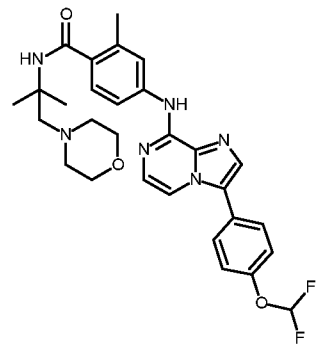
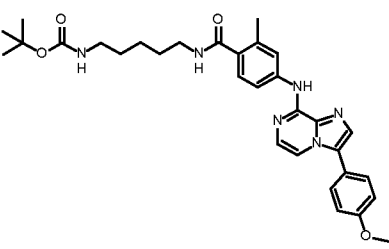
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213	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(piperidin-4-ylmethyl)benzamide;hydrochloride		489.3
214	N-(3-aminopropyl)-4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		471.3
215	4-[[3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-diethylbenzamide		450.2
216	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(3-oxopiperazin-1-yl)ethyl]benzamide		518.2

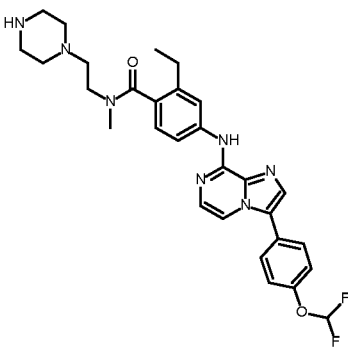
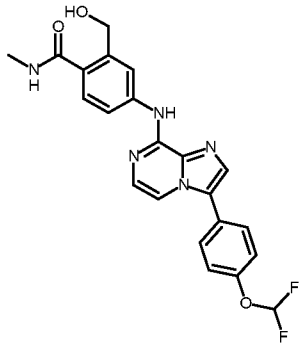
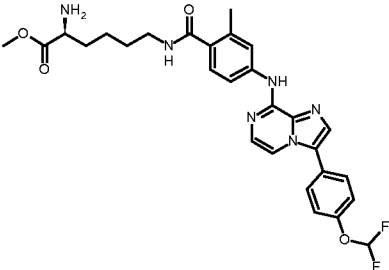
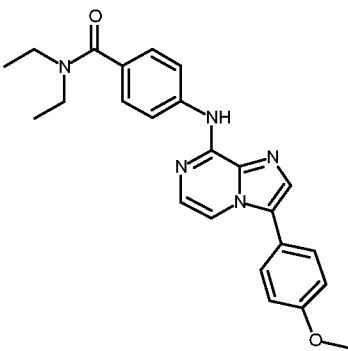
-429-

154	N-(1,3-dihydroxypropan-2-yl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide		448.3
217	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethenyl-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;hydrochloride		548.2
218	N-[4-[2-(aminomethyl)morpholin-4-yl]-4-oxobutyl]-4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide;hydrochloride		590.3
219	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-piperazin-1-ylpropyl)benzamide;hydrochloride		551.1

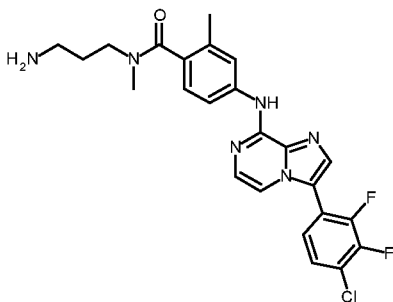
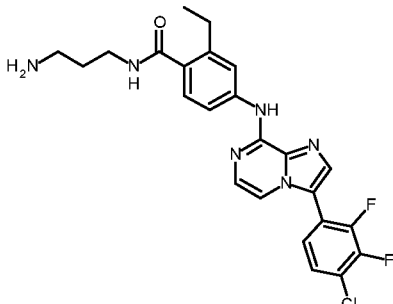
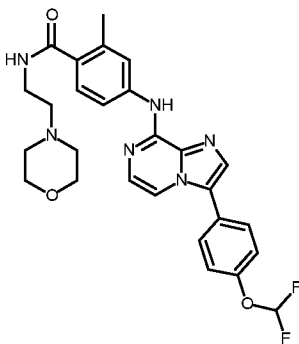
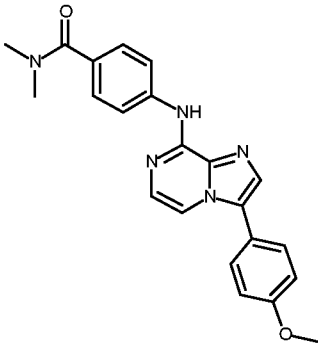
-430-

220	N,N-diethyl-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide		429
221	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(3-oxopiperazin-1-yl)ethyl]benzamide		536.2
222	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-methyl-1-morpholin-4-ylpropan-2-yl)benzamide		551.3
223	tert-butyl N-[5-[[4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]pentyl]carbamate		559.5

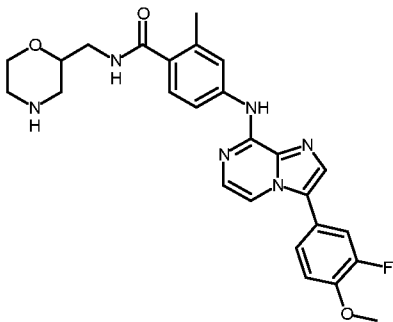
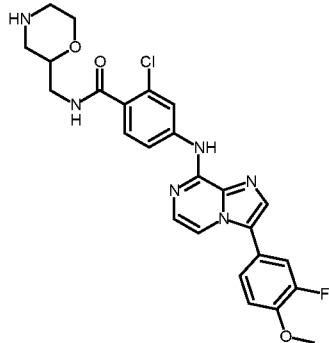
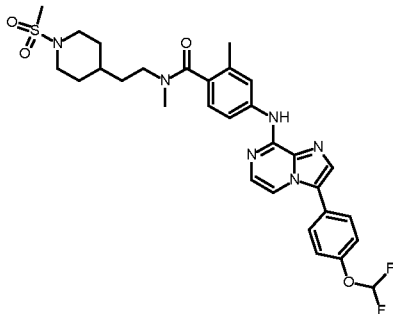
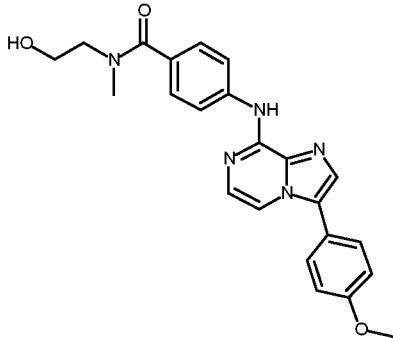
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224	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;hydrochloride		550.3
225	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(hydroxymethyl)-N-methylbenzamide		440.1
226	methyl (2S)-2-amino-6-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]hexanoate;hydrochloride		552.2
227	N,N-diethyl-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide		415

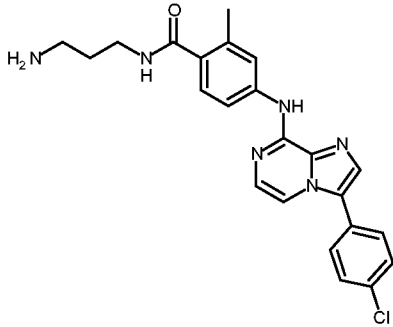
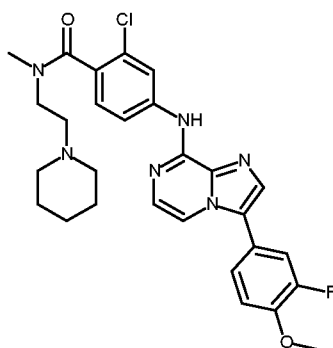
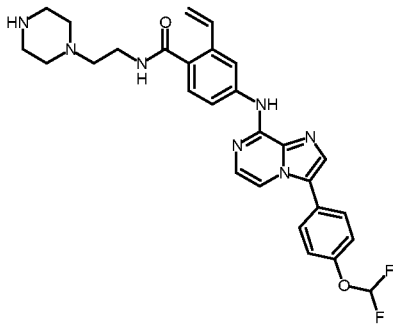
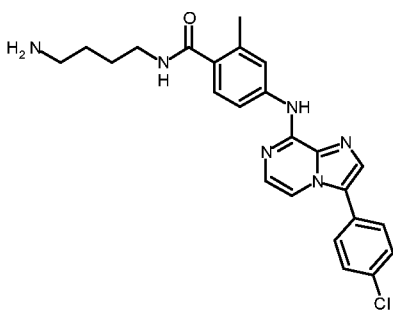
-432-

228	N-(3-aminopropyl)-4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide;hydrochloride		585.1
229	N-(3-aminopropyl)-4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		585.1
230	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-morpholin-4-ylethyl)benzamide		523.2
231	4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethylbenzamide		387 (M-H)-

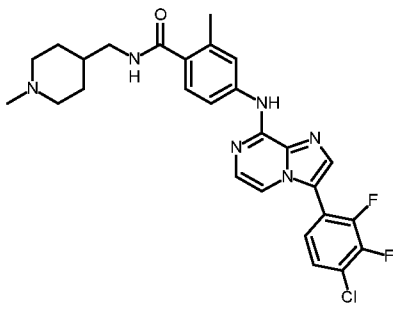
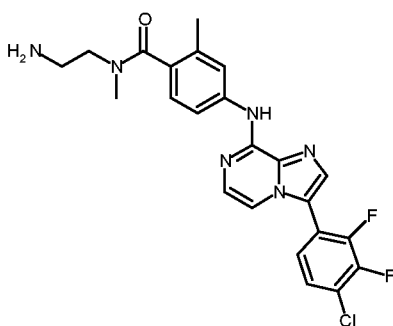
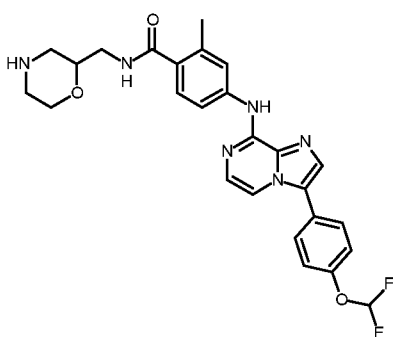
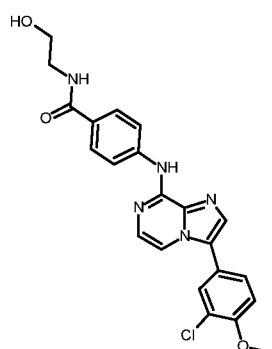
-433-

232	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(morpholin-2-ylmethyl)benzamide;hydrochloride		491.2
233	2-chloro-4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(morpholin-2-ylmethyl)benzamide;hydrochloride		512.5
234	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(1-methylsulfonylpiperidin-4-yl)ethyl]benzamide		613.3
235	N-(2-hydroxyethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methylbenzamide		417

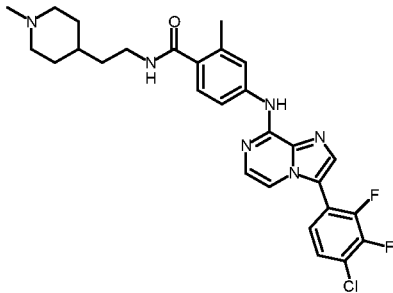
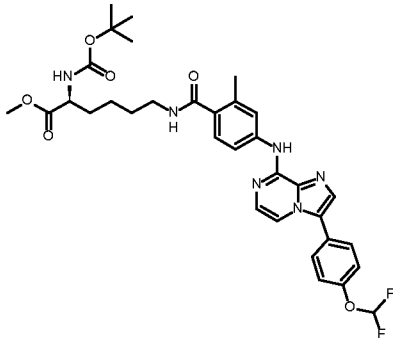
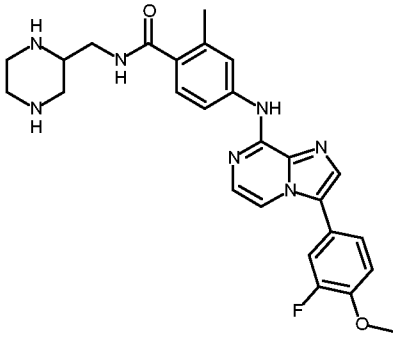
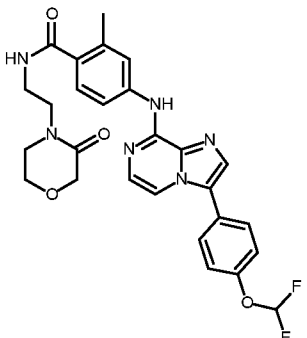
-434-

236	N-(3-aminopropyl)-4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		433.4 (M-H)-
237	2-chloro-4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperidin-1-ylethyl)benzamide		537.6
238	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethenyl-N-(2-piperazin-1-ylethyl)benzamide;hydrochloride		534.2
239	N-(4-aminobutyl)-4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		447.4 (M-H)-

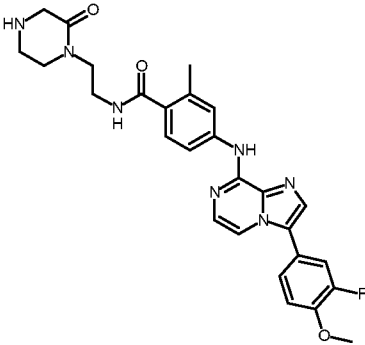
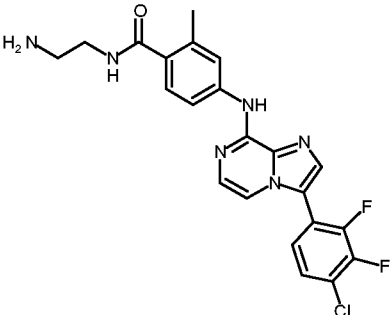
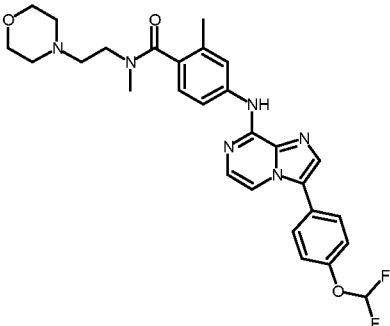
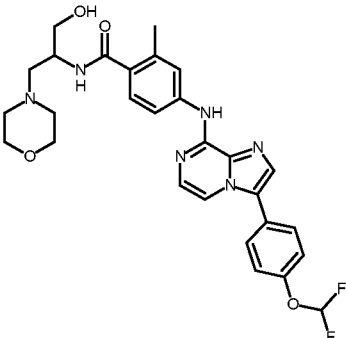
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240	4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(1-methylpiperidin-4-yl)methyl]benzamide		525.3
241	N-(2-aminoethyl)-4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide;hydrochloride		471.1
242	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(morpholin-2-ylmethyl)benzamide;hydrochloride		509.2
243	4-[[3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-hydroxyethyl)benzamide		438.1

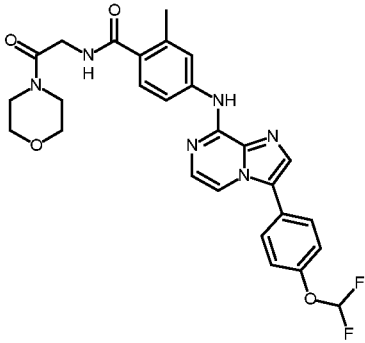
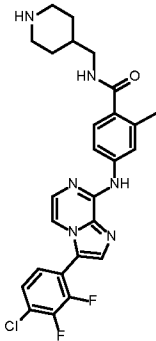
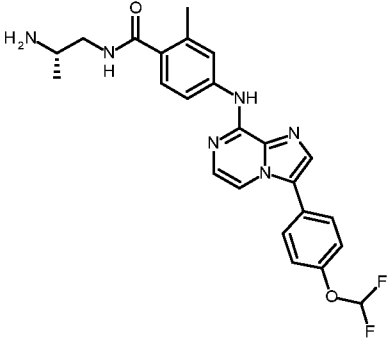
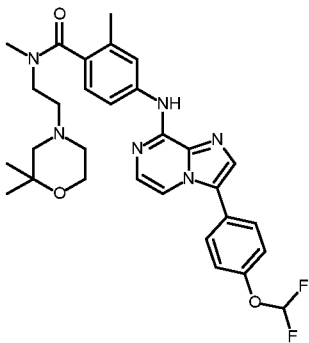
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244	4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(1-methylpiperidin-4-yl)ethyl]benzamide		539.3
245	methyl (2S)-6-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]-2-[(2-methylpropan-2-yl)oxycarbonylamino]hexanoate		653.5
246	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(piperazin-2-ylmethyl)benzamide;hydrochloride		490.2
247	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(3-oxomorpholin-4-yl)ethyl]benzamide		537.2

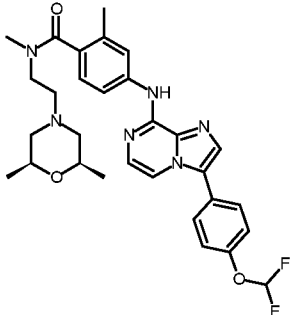
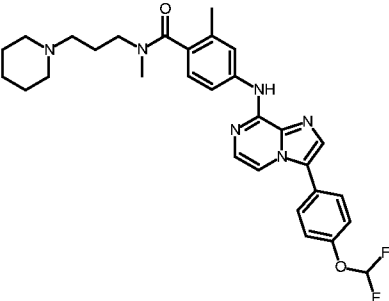
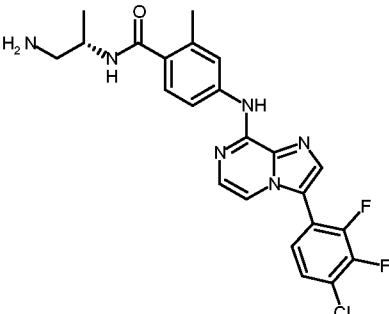
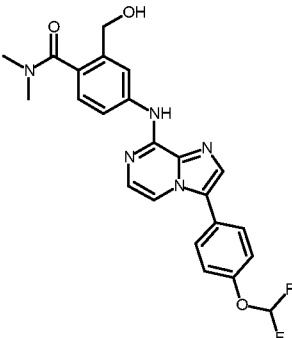
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248	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(2-oxopiperazin-1-yl)ethyl]benzamide;hydrochloride		518.1
249	N-(2-aminoethyl)-4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		457.1
250	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-morpholin-4-ylethyl)benzamide		537.5
251	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(1-hydroxy-3-morpholin-4-ylpropan-2-yl)-2-methylbenzamide		553.3

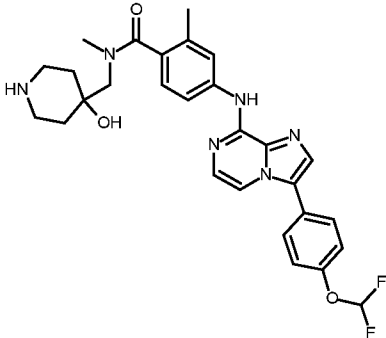
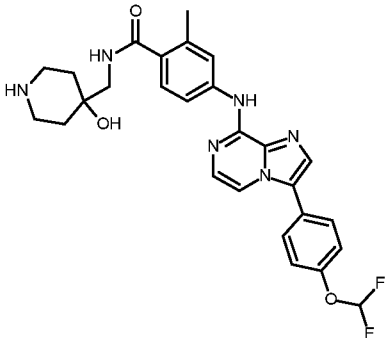
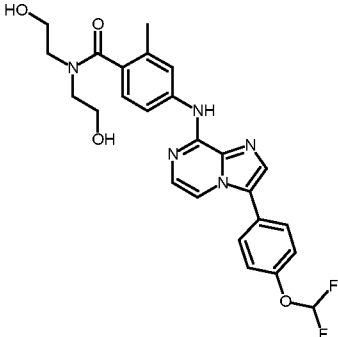
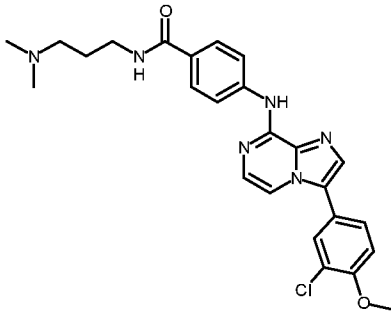
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252	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-morpholin-4-yl-2-oxoethyl)benzamide		537.2
253	4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(piperidin-4-ylmethyl)benzamide;hydrochloride		511.2
254	N-[(2S)-2-aminopropyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		467.2
255	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(2,2-dimethylmorpholin-4-yl)ethyl]-N,2-dimethylbenzamide		565.2

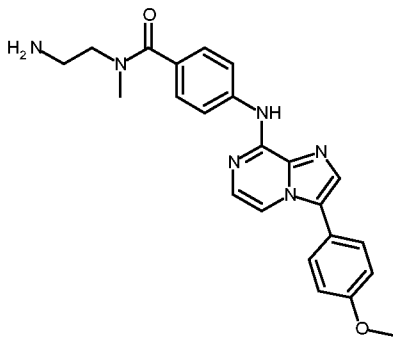
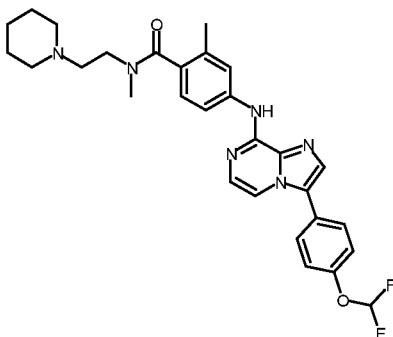
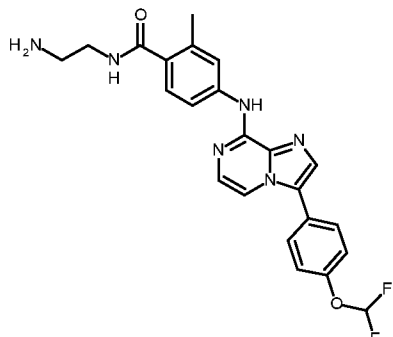
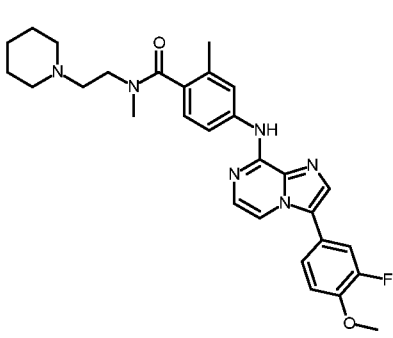
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256	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-[rac-(2R,6S)-2,6-dimethylmorpholin-4-yl]ethyl]benzamide	AND Enantiomer 	565.2
257	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-piperidin-1-ylpropyl)benzamide		549.3
258	N-[(2S)-1-aminopropan-2-yl]-4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		471.3
259	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(hydroxymethyl)-N,N-dimethylbenzamide		454.1

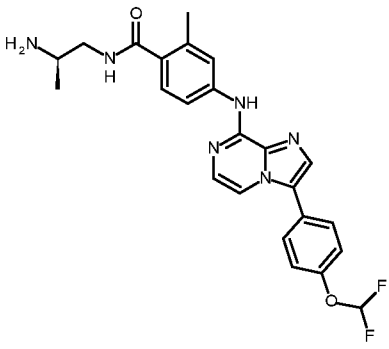
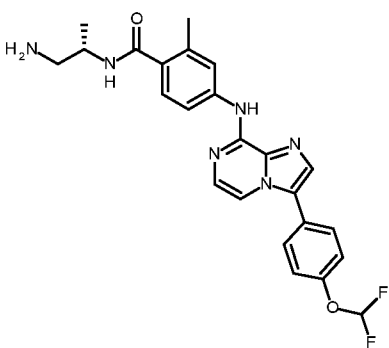
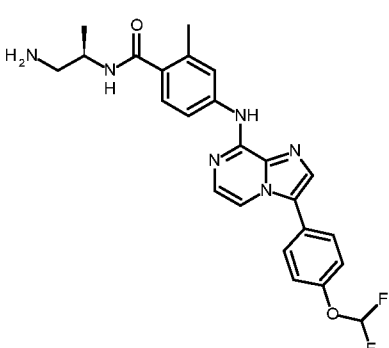
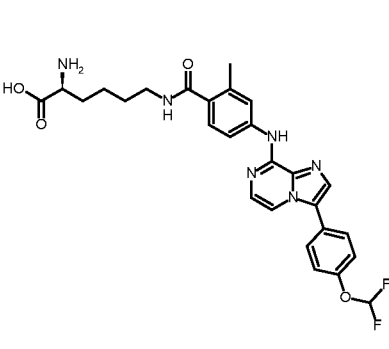
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260	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(4-hydroxypiperidin-4-yl)methyl]-N,2-dimethylbenzamide;hydrochloride		537.3
261	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(4-hydroxypiperidin-4-yl)methyl]-2-methylbenzamide;hydrochloride		523.3
262	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-bis(2-hydroxyethyl)-2-methylbenzamide		498.3
263	4-[[3-(3-chloro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-(dimethylamino)propyl]benzamide		477.4

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264	N-(2-aminoethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methylbenzamide;hydrochloride		417.2
265	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-piperidin-1-ylethyl)benzamide		532.2
266	N-(2-aminoethyl)-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		453.3
267	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-piperidin-1-ylethyl)benzamide		517.3

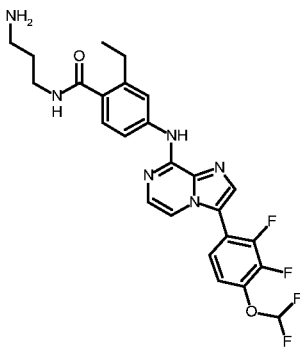
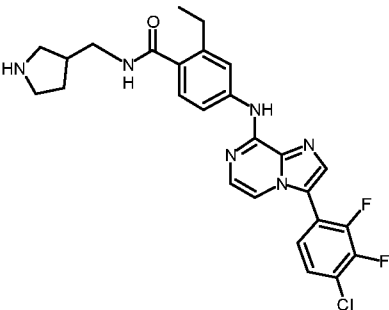
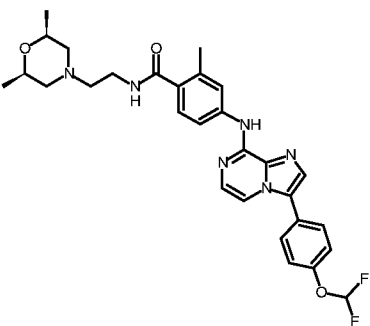
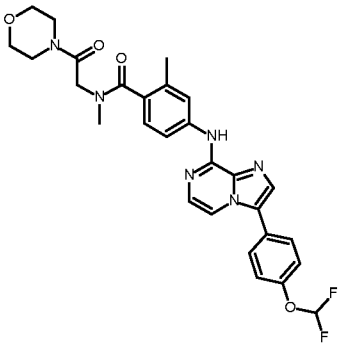
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268	N-[(2R)-2-aminopropyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		467.2
269	N-[(2S)-1-aminopropan-2-yl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		567.26
270	N-[(2R)-1-aminopropan-2-yl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		467.26
271	(2S)-2-amino-6-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]hexanoic acid		537.4(M-H)

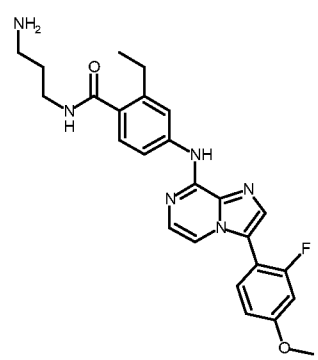
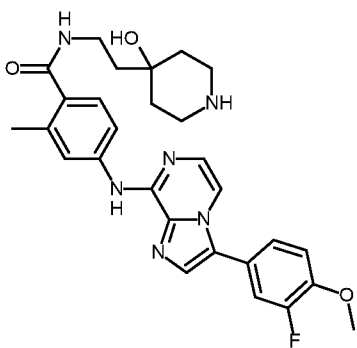
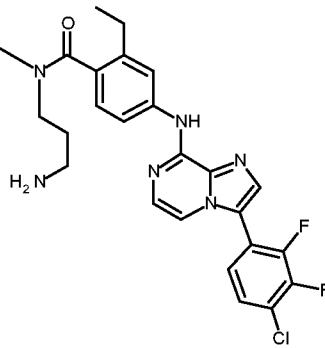
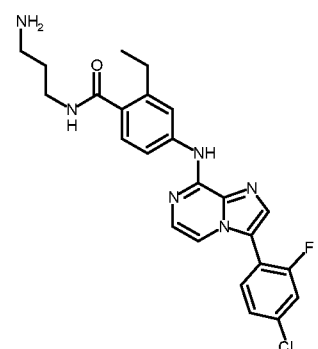
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272	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(5-piperazin-1-ylpentyl)benzamide;hydrochloride		546.3
273	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(5-oxo-5-piperazin-1-ylpentyl)benzamide		572.5(M-H)
274	6-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-3,4-dihydroisoquinolin-1-one		418.3
275	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-piperazin-1-ylpropyl)benzamide		532.2

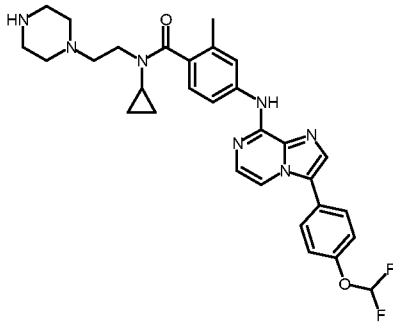
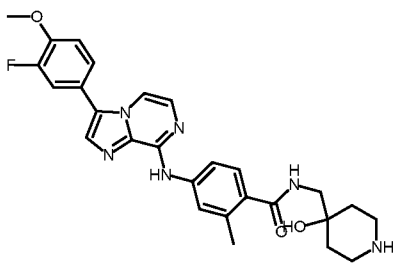
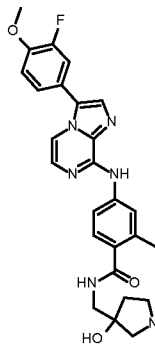
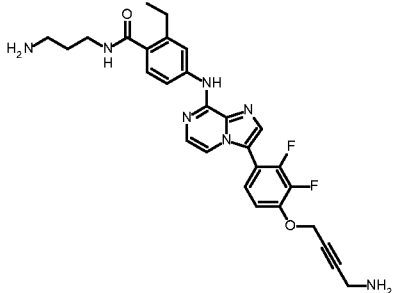
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276	N-(3-aminopropyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		517.2
277	4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(pyrrolidin-3-ylmethyl)benzamide;hydrochloride		511.6
278	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-[rac-(2R,6S)-2,6-dimethylmorpholin-4-yl]ethyl]benzamide	AND Enantiomer 	551.2
279	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-morpholin-4-yl-2-oxoethyl)benzamide		551.3

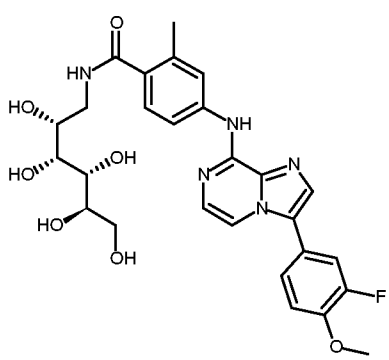
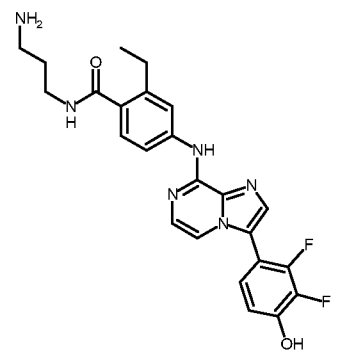
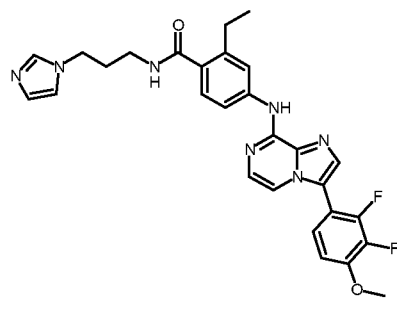
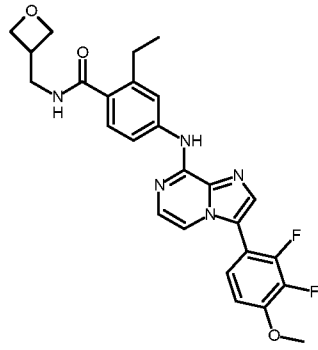
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280	N-(3-aminopropyl)-2-ethyl-4-[[3-(2-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;hydrochloride		463.2
281	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(4-hydroxypiperidin-4-yl)ethyl]-2-methylbenzamide;2,2,2-trifluoroacetic acid		519.3
282	N-(3-aminopropyl)-4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methylbenzamide;hydrochloride		499.1
283	N-(3-aminopropyl)-4-[[3-(4-chloro-2-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		467.1

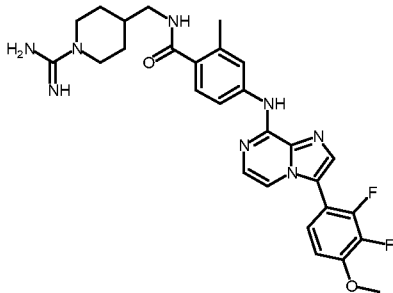
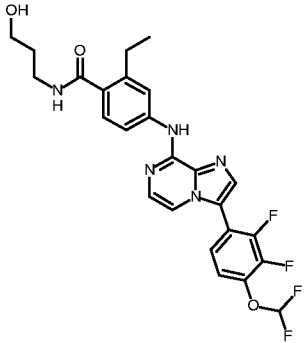
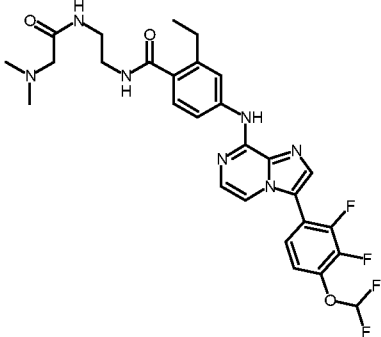
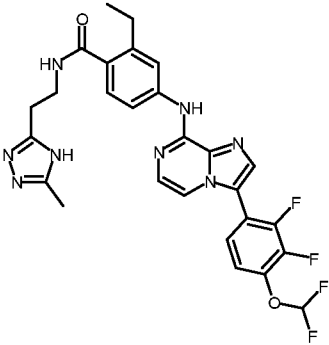
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284	N-cyclopropyl-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;hydrochloride		563.4
285	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(4-hydroxypiperidin-4-yl)methyl]-2-methylbenzamide;2,2,2-trifluoroacetic acid		504.4
286	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(3-hydroxypyrrolidin-3-yl)methyl]-2-methylbenzamide;2,2,2-trifluoroacetic acid		489.3
287	4-[[3-[4-(4-aminobut-2-ynoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(3-aminopropyl)-2-ethylbenzamide		534.1

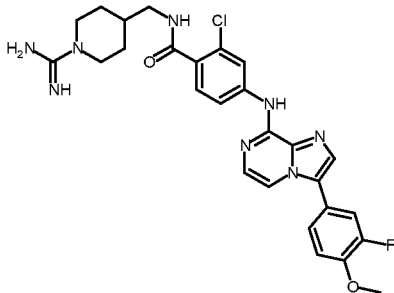
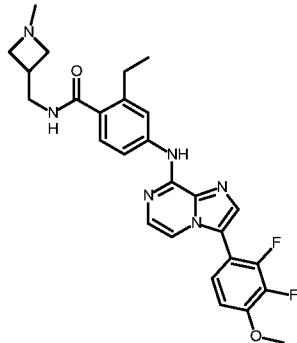
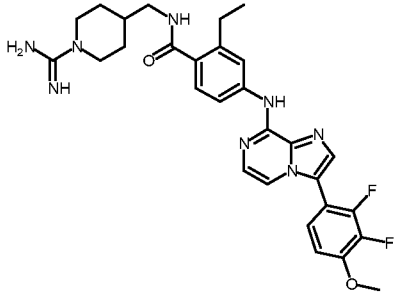
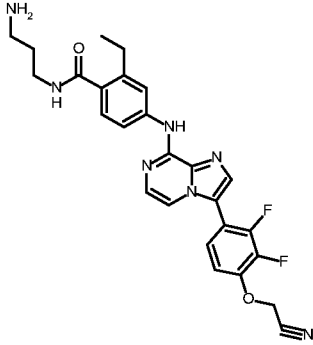
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288	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(2R,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]benzamide		556.3
289	N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-hydroxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		467.2
290	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(3-imidazol-1-ylpropyl)benzamide		532.4
291	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(oxetan-3-ylmethyl)benzamide		494.3

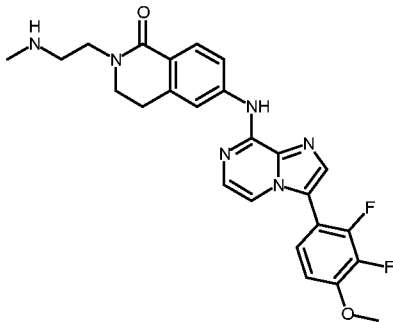
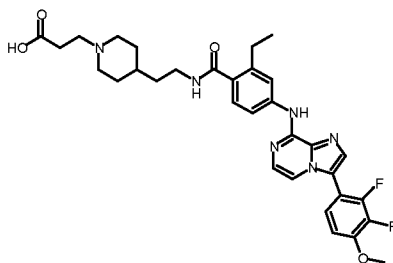
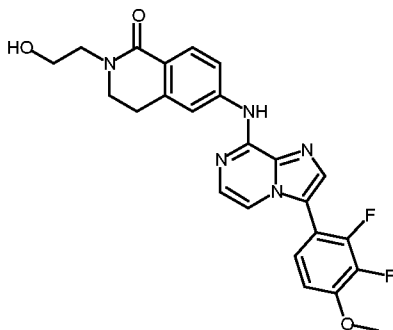
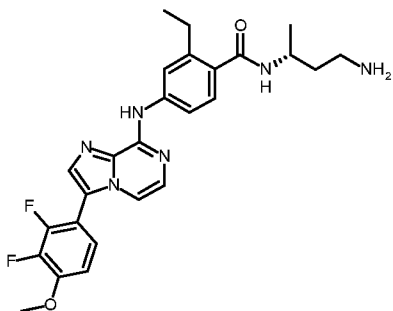
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292	N-[(1-carbamimidoylpiperidin-4-yl)methyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide		549.4
293	4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(3-hydroxypropyl)benzamide		518.4
294	4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[2-(dimethylamino)acetyl]amino]ethyl]-2-ethylbenzamide		588.4
295	4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-(5-methyl-4H-1,2,4-triazol-3-yl)ethyl]benzamide		569.3

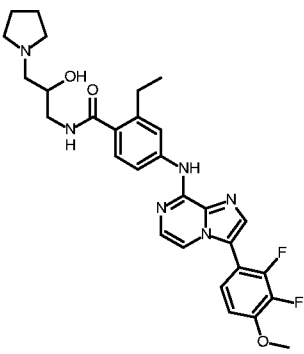
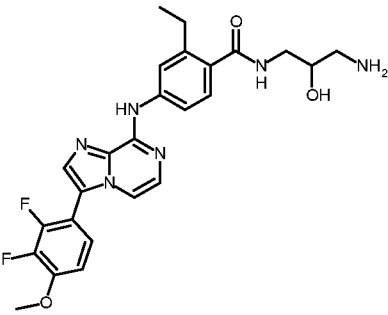
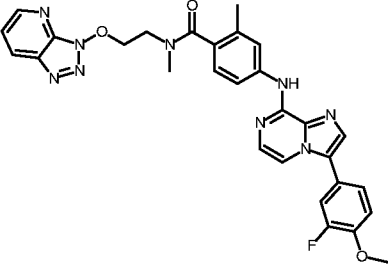
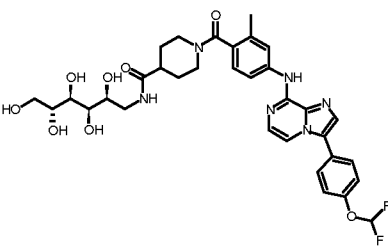
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296	N-[(1-carbamimidoylpiperidin-4-yl)methyl]-2-chloro-4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide		551.4
297	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(1-methylazetidin-3-yl)methyl]benzamide		507.3
298	N-[(1-carbamimidoylpiperidin-4-yl)methyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		561.6(M-H)
299	N-(3-aminopropyl)-4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide; 2,2,2-trifluoroacetic acid		506.4

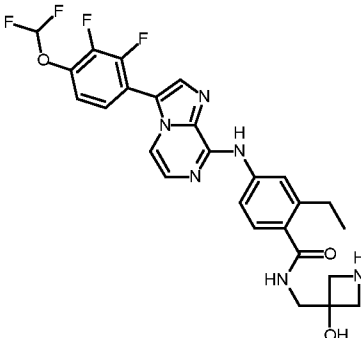
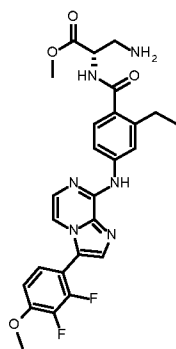
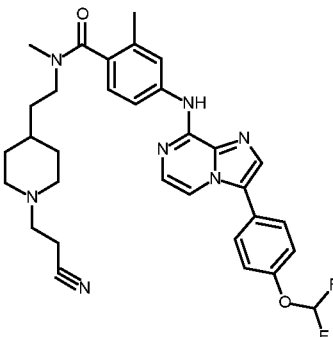
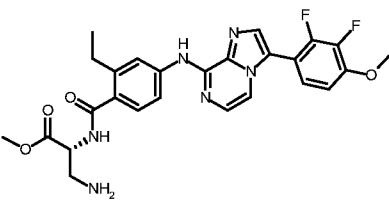
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300	6-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-[2-(methylamino)ethyl]-3,4-dihydroisoquinolin-1-one;hydrochloride		479.3
301	3-[4-[2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzoyl]amino]ethyl]piperidin-1-yl]propanoic acid		607.3
302	6-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-hydroxyethyl)-3,4-dihydroisoquinolin-1-one		466.3
303	N-[(2R)-4-aminobutan-2-yl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		495.4

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304	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(2-hydroxy-3-pyrrolidin-1-ylpropyl)benzamide		551.5
147	N-(3-amino-2-hydroxypropyl)-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide; hydrochloride		497.2
305	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(triazolo[4,5-b]pyridin-3-yl)oxy]ethyl]benzamide		568.2
306	1-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]-N-[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]piperidine-4-carboxamide		685.5

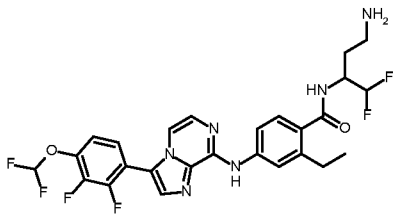
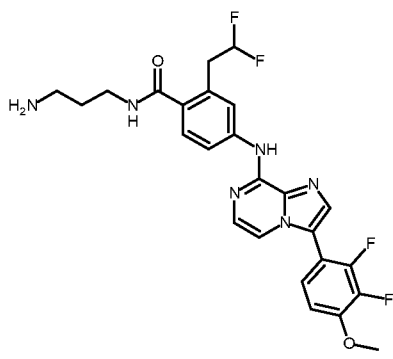
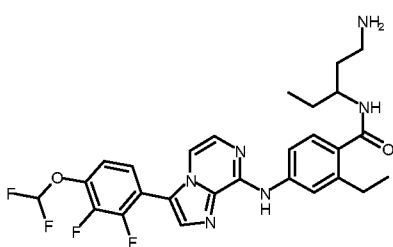
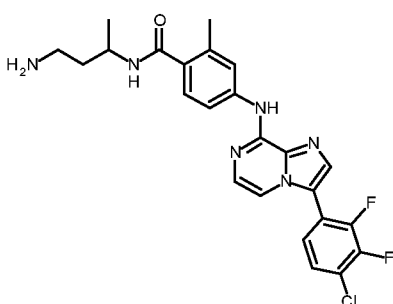
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307	4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(3-hydroxyazetidin-3-yl)methyl]benzamide;hydrochloride		545.3
308	methyl (2S)-3-amino-2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzoyl]amino]propanoate;hydrochloride		525.4
309	N-[2-[1-(2-cyanoethyl)piperidin-4-yl]ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide		588.5
310	methyl (2R)-3-amino-2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzoyl]amino]propanoate;hydrochloride		525.3

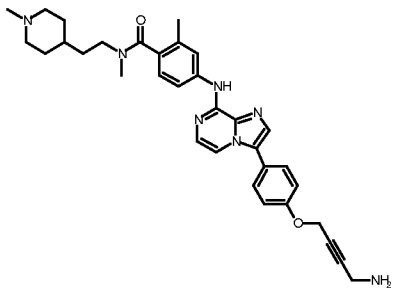
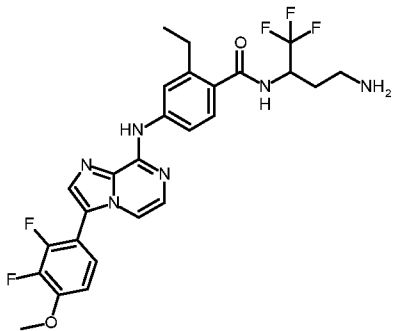
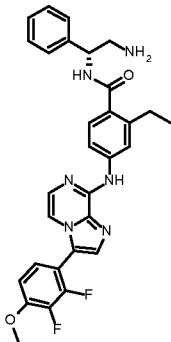
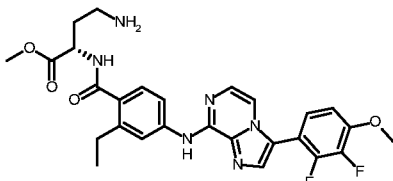
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311	4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(3-hydroxypyrrolidin-3-yl)methyl]benzamide;hydrochloride		559.4
312	N-[(2S)-1-aminopropan-2-yl]-4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		517.4
313	4-[[3-[4-(4-aminobut-2-ynoxy)-3-fluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,N,2-trimethylbenzamide		473.2
314	4-[3-[[2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]propyl]piperazine-2-carboxylic acid;formic acid		600.0

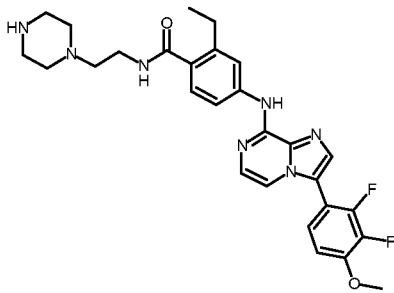
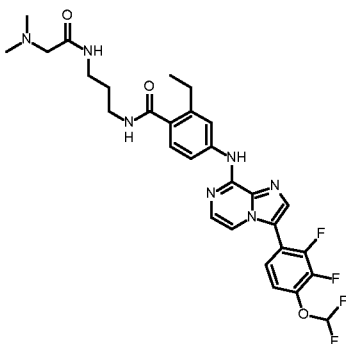
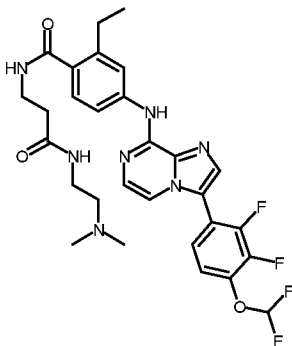
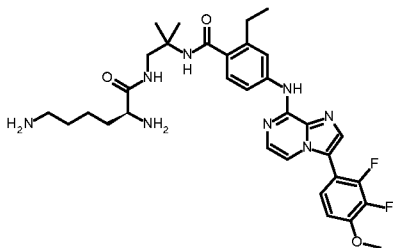
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315	N-(4-amino-1,1-difluorobutan-2-yl)-4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		567.4
316	N-(3-aminopropyl)-2-(2,2-difluoroethyl)-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;formic acid		517.2
317	N-(1-aminopentan-3-yl)-4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		545.4
318	N-(4-aminobutan-2-yl)-4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;hydrochloride		485.2

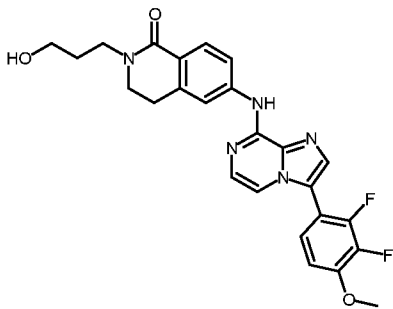
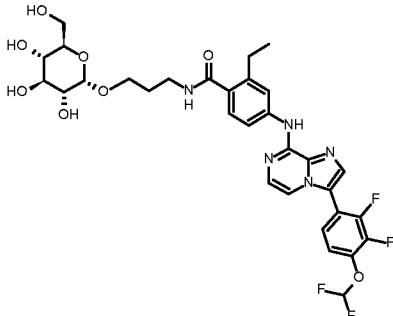
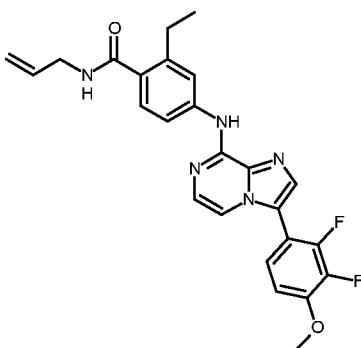
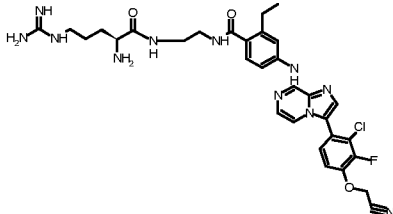
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319	4-[[3-[4-(4-aminobut-2-ynoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(1-methylpiperidin-4-yl)ethyl]benzamide;formic acid		566.3
320	N-(4-amino-1,1,1-trifluorobutan-2-yl)-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		549.4
321	N-[(1R)-2-amino-1-phenylethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		543.2
322	methyl (2S)-4-amino-2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzoyl]amino]butanoate;hydrochloride		539.4

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323	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(2-piperazin-1-ylethyl)benzamide		536.3
324	4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-[[2-(dimethylamino)acetyl]amino]propyl]-2-ethylbenzamide		602.5
325	4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-[2-(dimethylamino)ethylamino]-3-oxopropyl]-2-ethylbenzamide		602.4
326	N-[1-[[[(2S)-2,6-diaminohexanoyl]amino]-2-methylpropan-2-yl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		623.5

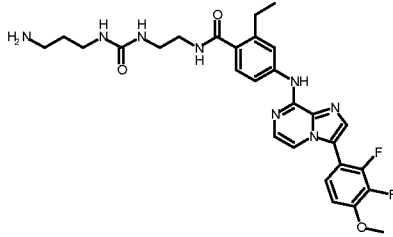
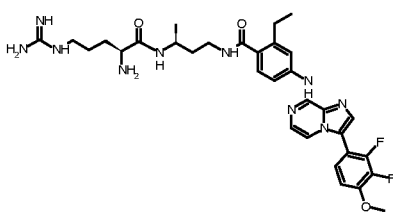
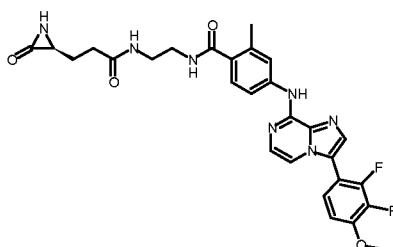
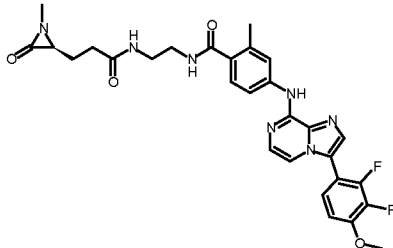
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327	6-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(3-hydroxypropyl)-3,4-dihydroisoquinolin-1-one		480.2
328	4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[3-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxypropyl]benzamide		680.3
329	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-prop-2-enylbenzamide		464.3
330	N-[2-[[[(2S)-2-amino-5-carbamimidamidopentanoyl]amino]ethyl]-4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide; formic acid		664.3

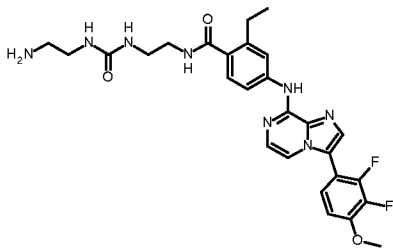
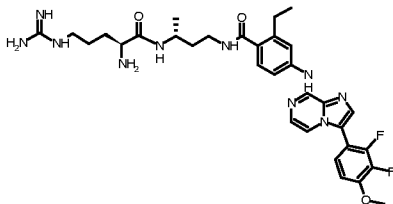
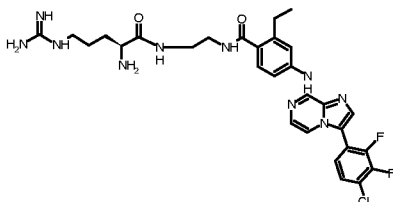
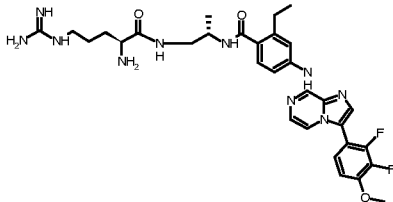
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331	N-[(2R)-1-[(2S)-2-amino-5-carbamimidamidopentanoyl]amino]propan-2-yl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide; formic acid		637.4
332	N-[2-[(2S)-2-amino-5-(carbamoylamino)pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		624.1
333	N-[2-[(2S)-2-amino-5-carbamimidamidopentanoyl]amino]ethyl]-4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide; formic acid		659.2
334	N-(3-amino-2-hydroxypropyl)-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		497.3

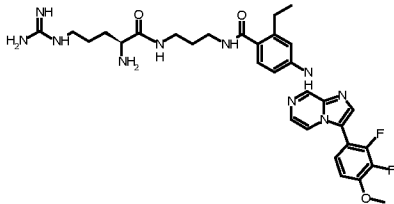
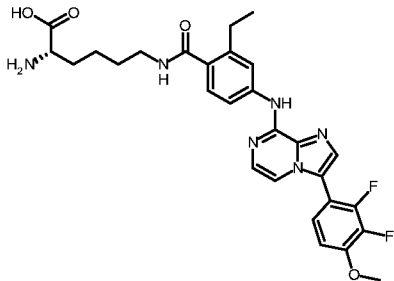
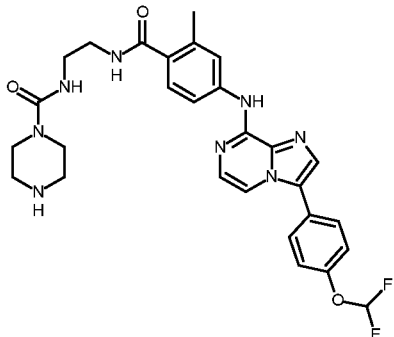
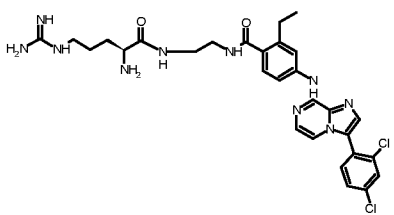
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335	N-[2-(3-aminopropylcarbamoylamino)ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		567.2
336	N-[(3S)-3-[[[(2S)-2-amino-5-carbamimidamidopentanoyl]amino]butyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		651.2
337	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-[3-[(2S)-3-oxoaziridin-2-yl]propanoylamino]ethyl]benzamide		564.3
338	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-[3-[(2S)-1-methyl-3-oxoaziridin-2-yl]propanoylamino]ethyl]benzamide		578.3

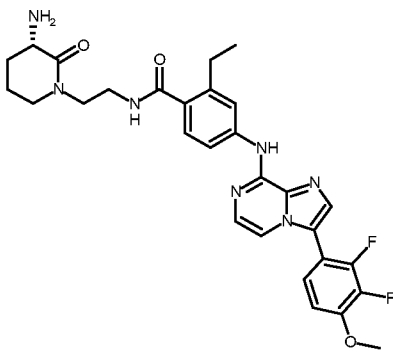
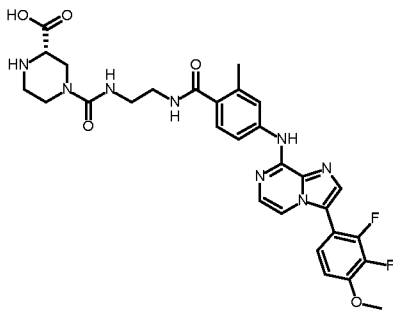
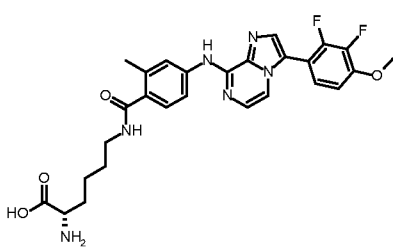
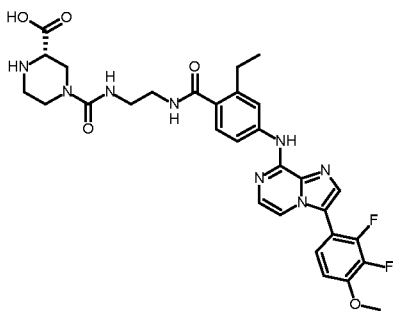
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339	N-[2-(2-aminoethylcarbamoylamino)ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		553.2
340	N-[(3R)-3-[[[(2S)-2-amino-5-carbamimidamidopentanoyl]amino]butyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		651.3
341	N-[2-[[[(2S)-2-amino-5-carbamimidamidopentanoyl]amino]ethyl]-4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;formic acid		627.2
342	N-[(2S)-1-[[[(2S)-2-amino-5-carbamimidamidopentanoyl]amino]propan-2-yl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;formic acid		637.4

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343	N-[3-[[[(2S)-2-amino-5-carbamimidamidopentanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;2,2,2-trifluoroacetic acid		637.2
344	(2S)-2-amino-6-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzoyl]amino]hexanoic acid;2,2,2-trifluoroacetic acid		553.2
345	N-[2-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]ethyl]piperazine-1-carboxamide		565
346	N-[2-[[[(2S)-2-amino-5-carbamimidamidopentanoyl]amino]ethyl]-4-[[3-(2,4-dichlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		625.2

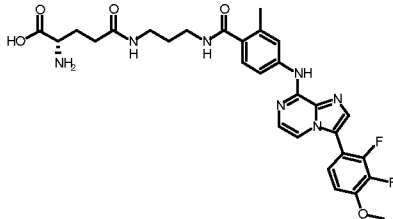
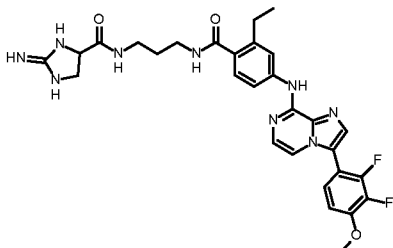
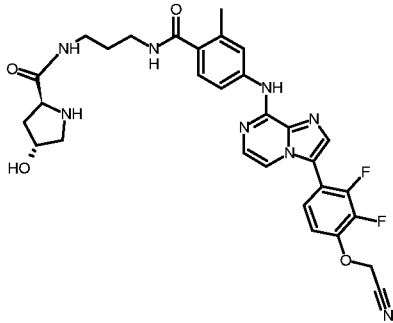
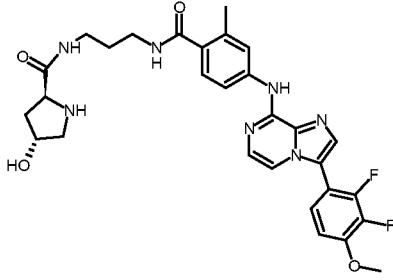
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347	N-[2-[(3S)-3-amino-2-oxopiperidin-1-yl]ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		564.2
348	(2S)-4-[2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]ethylcarbamoyl]piperazine-2-carboxylic acid;formic acid		609.2
349	(2S)-2-amino-6-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]hexanoic acid;2,2,2-trifluoroacetic acid		539.4
350	(2S)-4-[2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzoyl]amino]ethylcarbamoyl]piperazine-2-carboxylic acid;formic acid		623.2

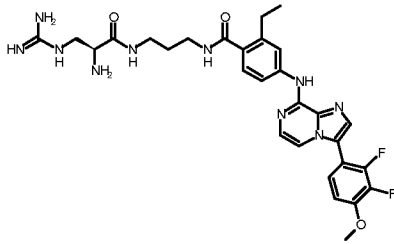
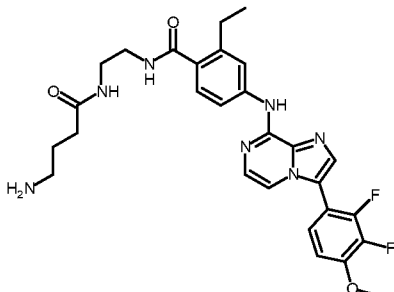
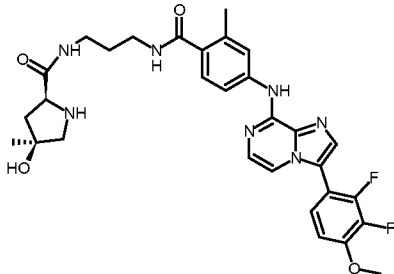
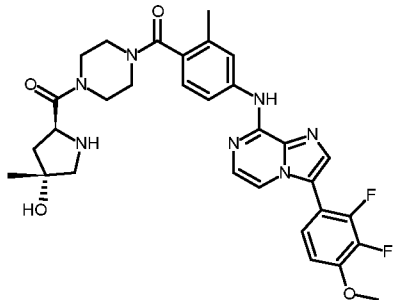
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351	N-[2-[[[(2R)-2-amino-5-carbamimidamidopentanoyl]amino]ethyl]-4-[[3-(2,4-dichlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;formic acid		625.2
352	(2R)-4-[2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]ethyl]carbamoyl]piperazine-2-carboxylic acid;formic acid		609.3
353	(2R)-4-[2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzoyl]amino]ethyl]carbamoyl]piperazine-2-carboxylic acid;formic acid		623.2
354	N-[2-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]ethyl]piperidine-4-carboxamide		564

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355	(2S)-2-amino-5-[3-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]propyl amino]-5-oxopentanoic acid		596.4
356	N-[3-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzoyl]amino]propyl]-2-iminoimidazolidine-4-carboxamide;formic acid		592.3
357	(2S,4R)-N-[3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]propyl]-4-hydroxypyrrolidine-2-carboxamide;formic acid		605.3
358	(2S,4R)-N-[3-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]propyl]-4-hydroxypyrrolidine-2-carboxamide;formic acid		580.4

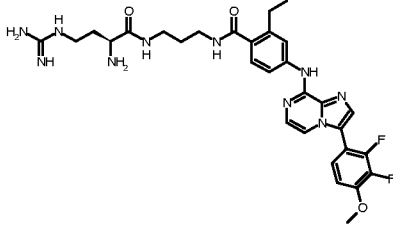
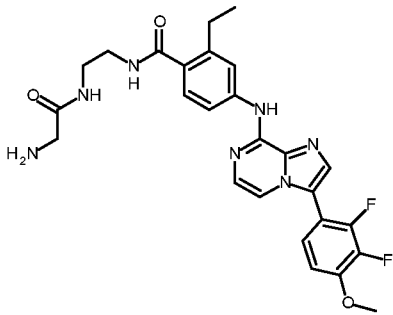
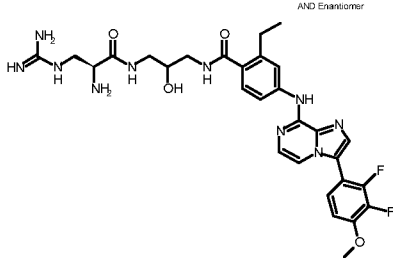
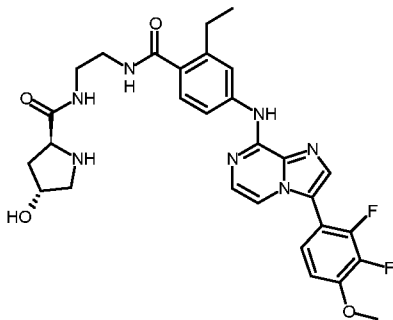
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359	N-[3-[[[(2S)-2-amino-3-carbamimidamidopropanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;formic acid		609.3
360	N-[2-(4-aminobutanoylamino)ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;formic acid		552.1
361	(2S,4S)-N-[3-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]propyl]-4-hydroxy-4-methylpyrrolidine-2-carboxamide;formic acid		594.4
362	[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]-[4-[(2S,4R)-4-hydroxy-4-methylpyrrolidine-2-carbonyl]piperazin-1-yl]methanone;formic acid		606.5

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363	(2S,4R)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]ethyl]-4-hydroxypyrrolidine-2-carboxamide;formic acid		566.3
364	N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;formic acid		538.1
365	(2S,4R)-N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]ethyl]-4-hydroxypyrrolidine-2-carboxamide;formic acid		591.2
366	(2S,4S)-N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]ethyl]-4-ethyl-4-hydroxypyrrolidine-2-carboxamide;formic acid		619.4

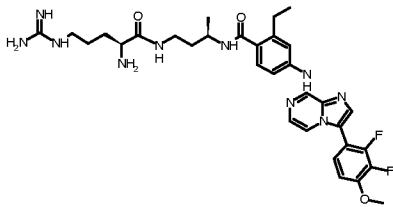
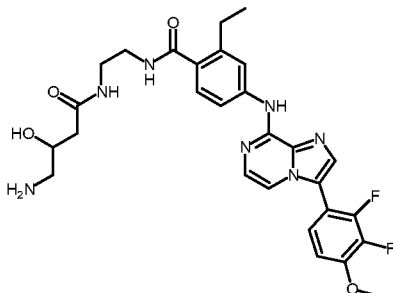
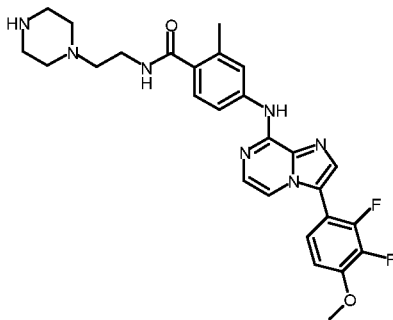
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367	N-[3-[[[(2S)-2-amino-4-carbamimidamidobutanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;formic acid		623.4
368	N-[2-[(2-aminoacetyl)amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;formic acid		524.1
369	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2R)-2-amino-3-carbamimidamidopropanoyl]amino]propyl]benzamide;formic acid		625.4
370	(2S,4R)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzoyl]amino]ethyl]-4-hydroxypyrrolidine-2-carboxamide;formic acid		580.1

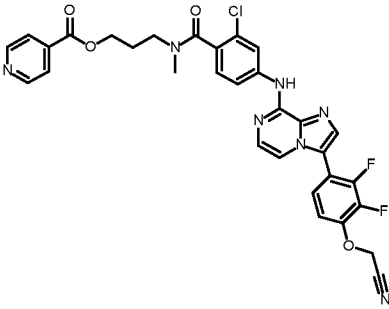
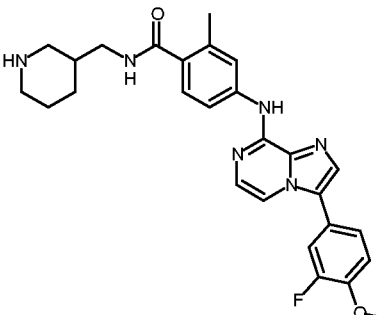
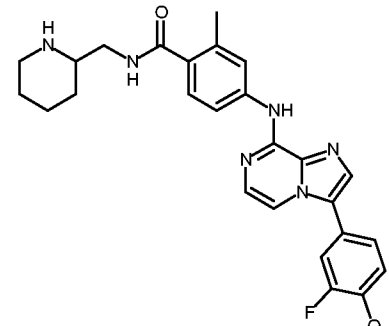
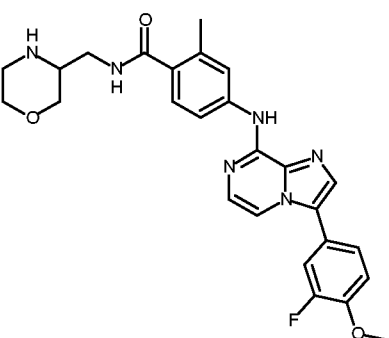
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371	(2S,4S)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]ethyl]-4-ethyl-4-hydroxypyrrolidine-2-carboxamide;formic acid		594.3
372	(2S,4S)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzoyl]amino]ethyl]-4-hydroxy-4-methylpyrrolidine-2-carboxamide;formic acid		580
373	N-[2-[[[(2S)-2-amino-3-hydroxypropanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;formic acid		554.1
374	N-[3-[(2-aminoacetyl)amino]-2-hydroxypropyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-		554.3

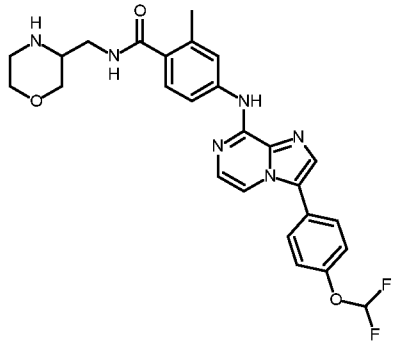
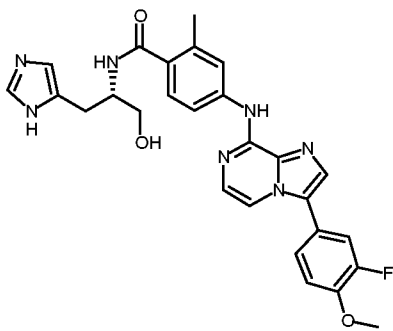
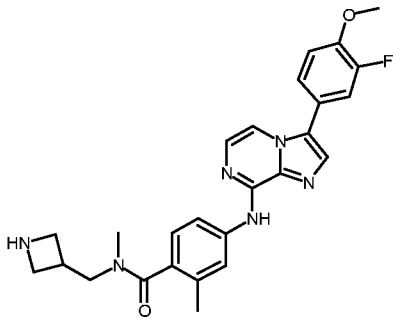
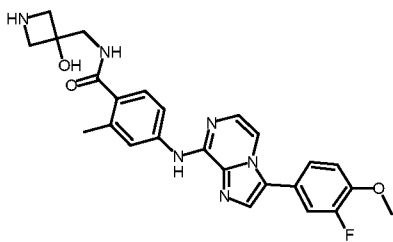
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	ethylbenzamide;hydrochlorid e		
375	N-[(2R)-4-[(2S)-2-amino-5-carbamimidamidopentanoyl]amino]butan-2-yl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;formic acid		651.2
376	N-[2-[(4-amino-3-hydroxybutanoyl)amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;formic acid		568.2
377	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide		522.3

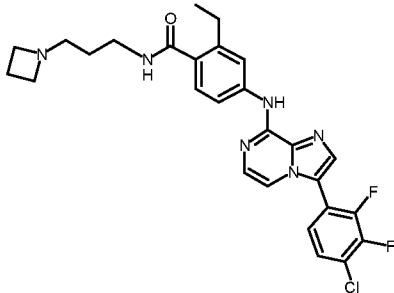
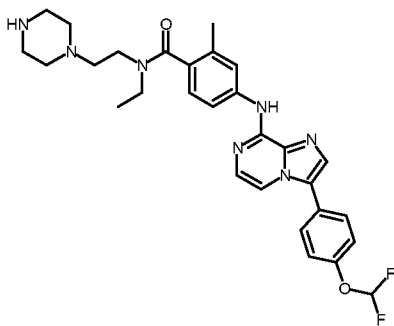
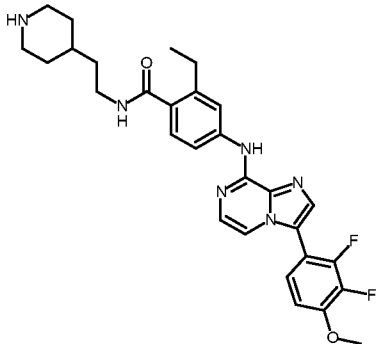
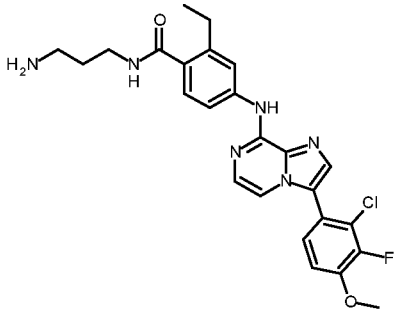
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378	3-[[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]-methylamino]propyl pyridine-4-carboxylate;2,2,2-trifluoroacetic acid		632.3
379	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(piperidin-3-ylmethyl)benzamide;hydrochloride		489.2
380	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(piperidin-2-ylmethyl)benzamide;hydrochloride		489.2
381	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(morpholin-3-ylmethyl)benzamide;hydrochloride		491.2

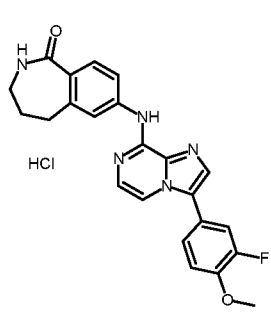
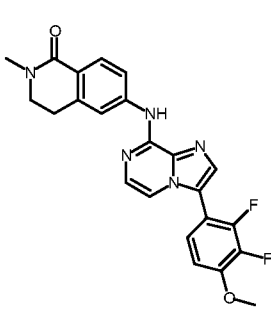
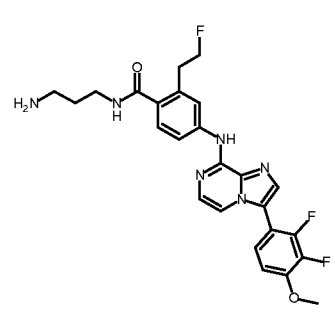
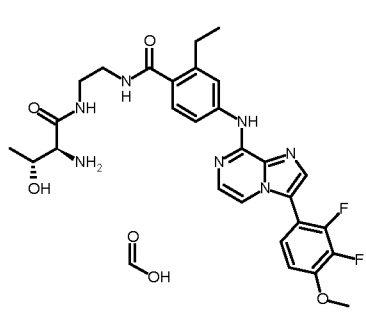
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382	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(morpholin-3-ylmethyl)benzamide;hydrochloride		509.2
383	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(2S)-1-hydroxy-3-(1H-imidazol-5-yl)propan-2-yl]-2-methylbenzamide		516.2
384	N-(azetidin-3-ylmethyl)-4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide;formic acid		475.3
385	4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(3-hydroxyazetidin-3-yl)methyl]-2-methylbenzamide;hydrochloride		477.2

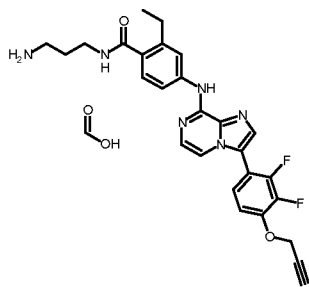
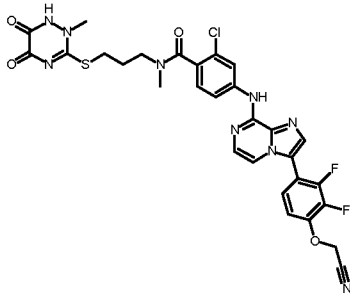
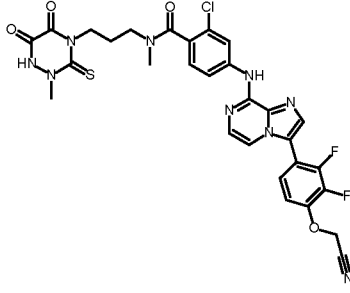
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386	N-[3-(azetidin-1-yl)propyl]-4-[[3-(4-chloro-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		525
387	4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-ethyl-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;hydrochloride		548.3 (M-H)-
388	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(2-piperidin-4-ylethyl)benzamide;hydrochloride		535.3
389	N-(3-aminopropyl)-4-[[3-(2-chloro-3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;hydrochloride		497.4

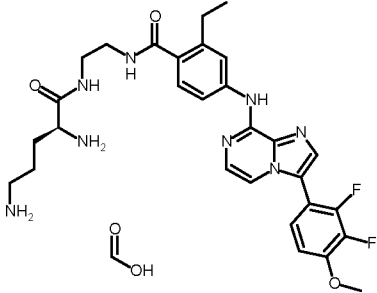
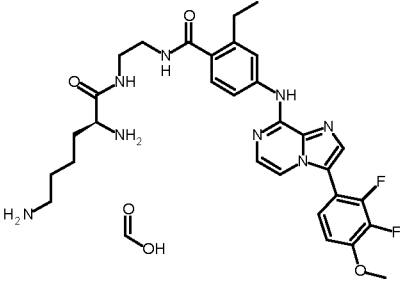
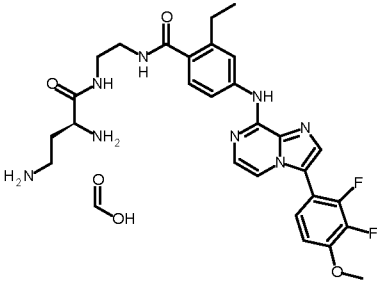
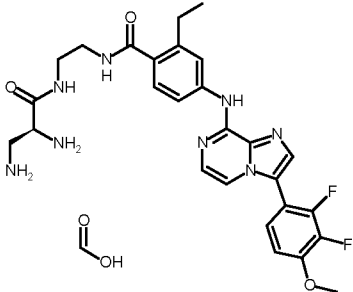
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390	7-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2,3,4,5-tetrahydro-2-benzazepin-1-one hydrochloride		418.5
391	6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-3,4-dihydroisoquinolin-1-one		436.2
392	N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-fluoroethyl)benzamide		499.33
393	N-[2-[[[(2S,3R)-2-amino-3-hydroxy-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		568.1

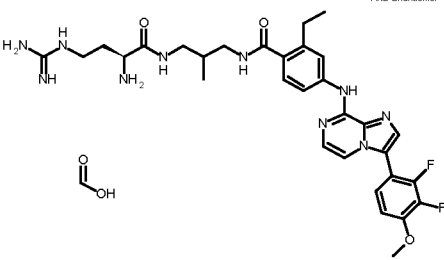
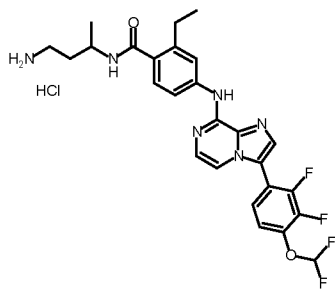
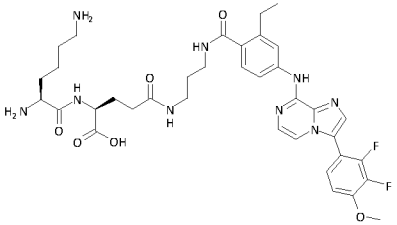
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394	N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		505.2
395	2-chloro-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methyl-N-(3-((2-methyl-5,6-dioxo-1,2,5,6-tetrahydro-1,2,4-triazin-3-yl)thio)propyl)benzamide		668.3
396	2-chloro-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-methyl-N-(3-(2-methyl-5,6-dioxo-3-thioxo-1,2,4-triazinan-4-yl)propyl)benzamide		668.3

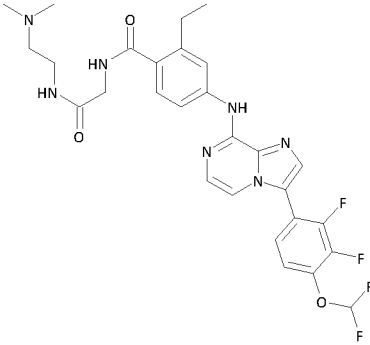
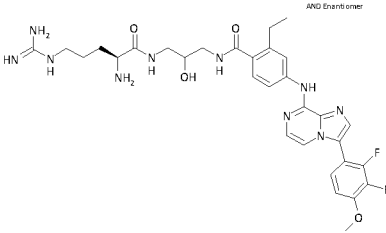
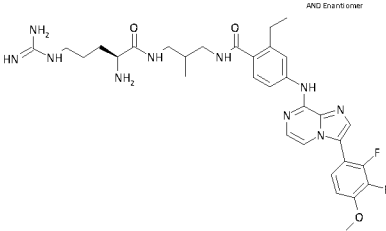
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397	N-[2-[[[(2S)-2,5-diaminopentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		581.2
398	N-[2-[[[(2S)-2,6-diaminohexanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		595.2
399	N-[2-[[[(2S)-2,4-diaminobutanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		567.1
400	N-[2-[[[(2S)-2,3-diaminopropanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		553.3

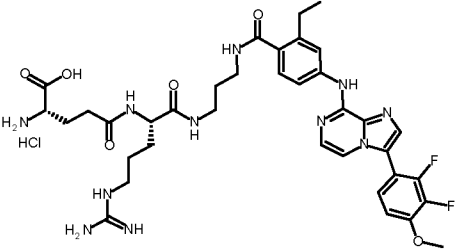
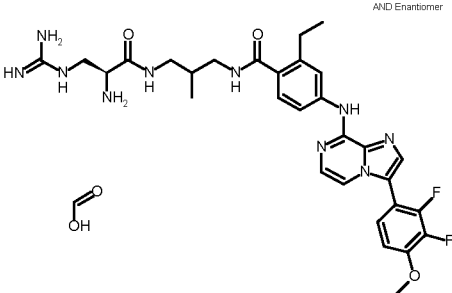
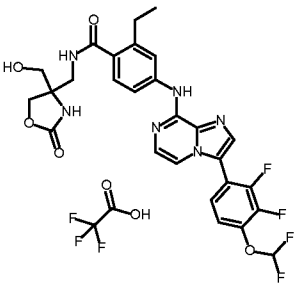
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401	rac-N-(3-((R)-2-amino-4-guanidinobutanamido)-2-methylpropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide diformate		637.4
402	N-(4-aminobutan-2-yl)-4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		531.4
403	N2-(L-lysyl)-N5-(3-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)-L-glutamine trihydrochloride		738.35

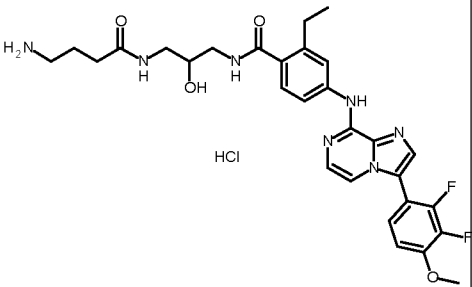
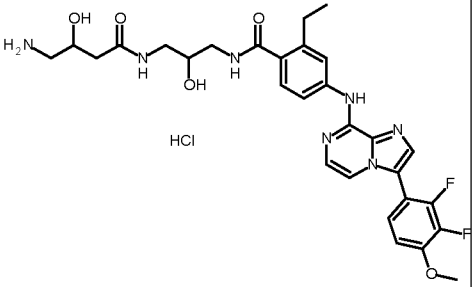
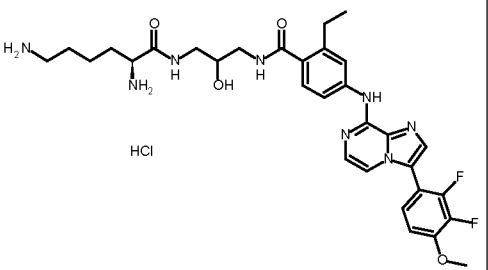
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404	4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(2-((2-(dimethylamino)ethyl)amino)-2-oxoethyl)-2-ethylbenzamide		588.3
405	rac-N-(3-((R)-2-amino-5-guanidinopentanamido)-2-hydroxypropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide diformate		653.4
406	rac-N-(3-((R)-2-amino-5-guanidinopentanamido)-2-methylpropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide diformate		651.4

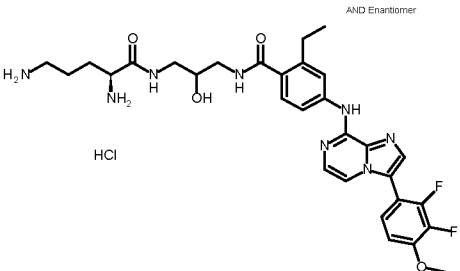
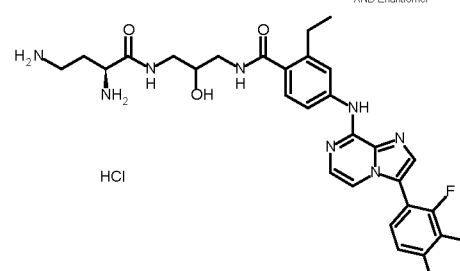
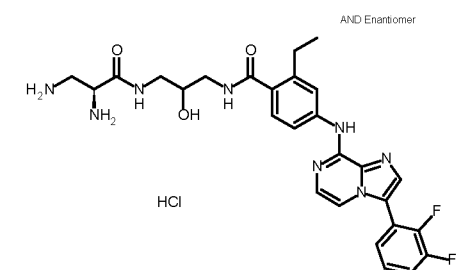
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407	N5-((S)-1-((3-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)amino)-5-guanidino-1-oxopentane-2-yl)-L-glutamine trihydrochloride		766.36
408	rac-N-(3-((R)-2-amino-3-guanidinopropanamido)-2-methylpropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide diformate		623.4
409	4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-((4-(hydroxymethyl)-2-oxooxazolidin-4-yl)methyl)benzamide		589.3

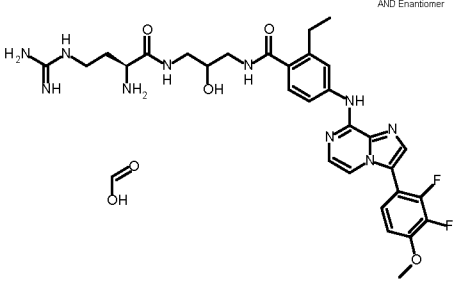
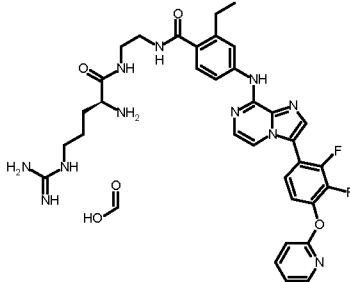
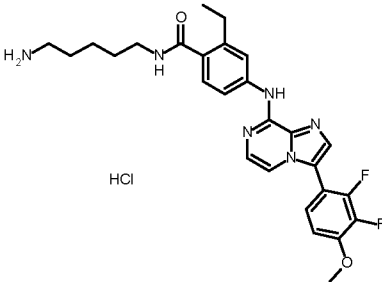
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410	N-(3-(4-aminobutanamido)-2-hydroxypropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		582.3
411	N-(3-(4-amino-3-hydroxybutanamido)-2-hydroxypropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		598.3
412	rac-N-(3-((R)-2,6-diaminohexanamido)-2-hydroxypropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide dihydrochloride		625.4

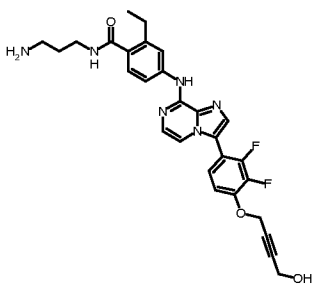
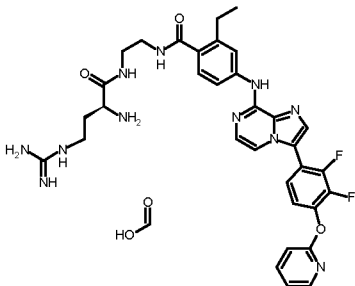
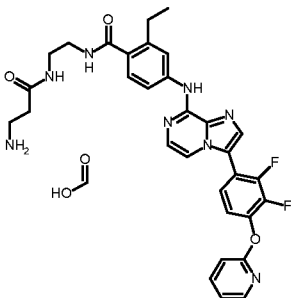
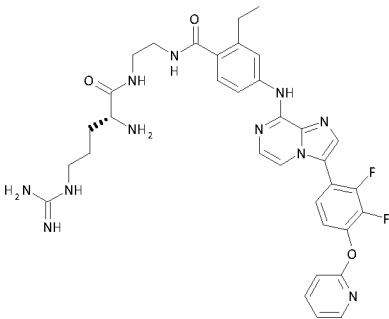
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413	rac-N-(3-((R)-2,5-diaminopentanamido)-2-hydroxypropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide dihydrochloride		611.4
414	rac-N-(3-((R)-2,4-diaminobutanamido)-2-hydroxypropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide dihydrochloride		597.4
415	N-[3-[[2S)-2,3-diaminopropanoyl]amino]-2-hydroxypropyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide; dihydrochloride		583.3

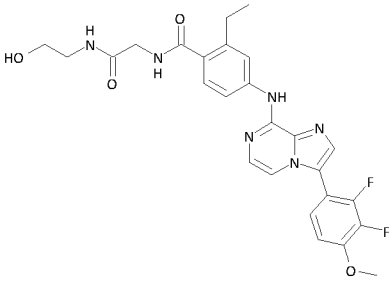
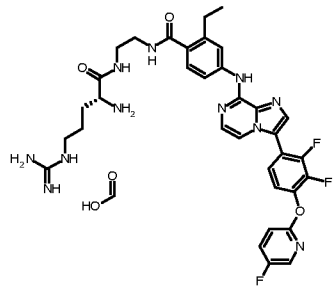
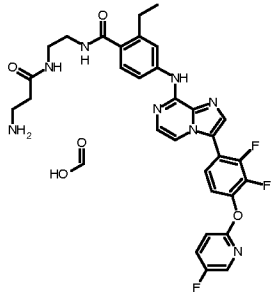
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416	rac-N-(3-((R)-2-amino-4-guanidinobutanamido)-2-hydroxypropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide diformate		639.3
417	N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		686.5
418	N-(5-aminopentyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride N-(5-aminopentyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		507.5 (M-H)-

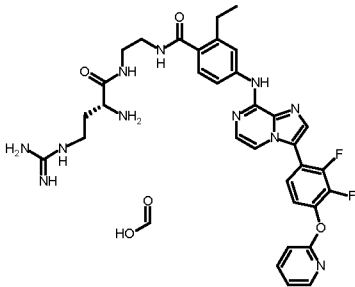
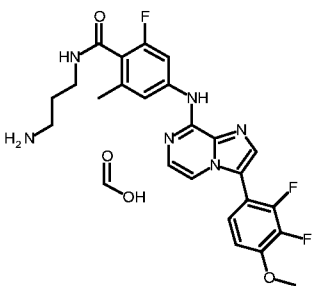
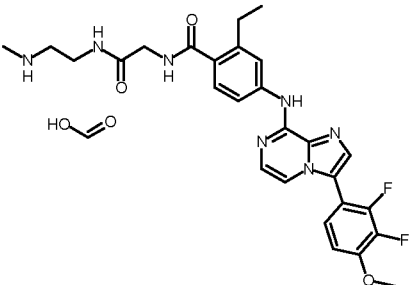
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419	N-(3-aminopropyl)-4-[[3-[2,3-difluoro-4-(4-hydroxybut-2-ynoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide		535.4
420	N-[2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		672.2
421	N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		601.4
422	N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		686.3

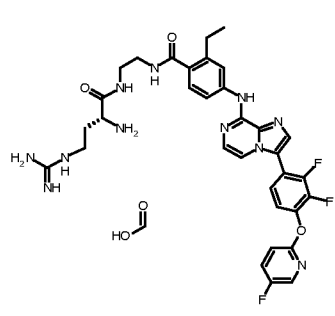
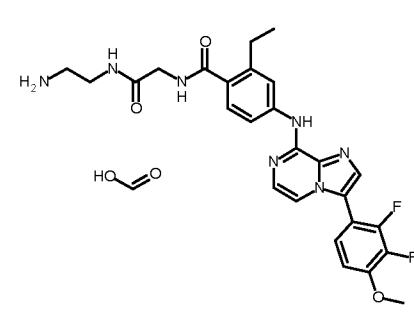
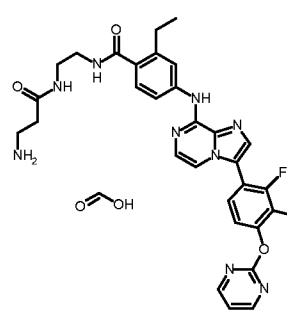
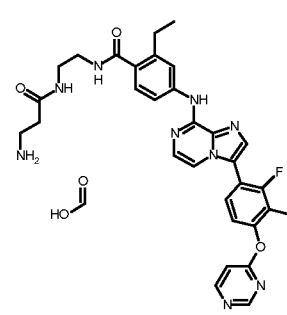
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423	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(2-((2-hydroxyethyl)amino)-2-oxoethyl)benzamide		525.3
424	N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(5-fluoro-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		704.4
425	N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[2,3-difluoro-4-(5-fluoro-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		619.3

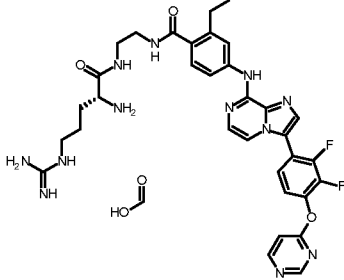
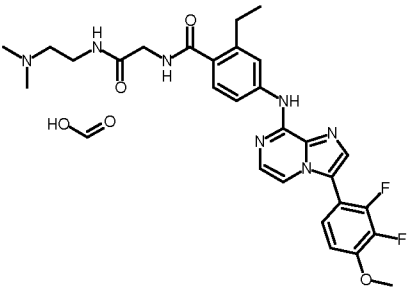
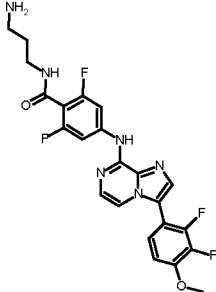
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426	N-[2-[[[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		672.5
427	N-(3-aminopropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzamide formate		485.3
428	4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-[2-(methylamino)ethylamino]-2-oxo-ethyl]benzamide; formic acid		538.2

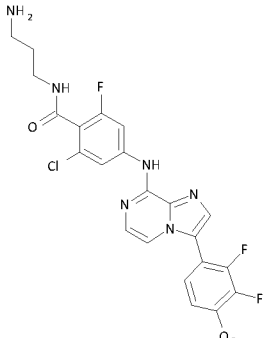
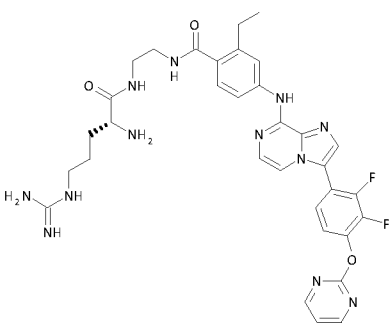
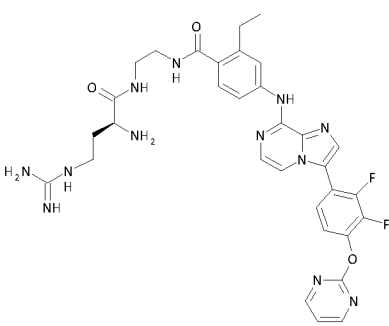
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429	N-[2-[[[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-fluoro-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		690.3
430	N-[2-(2-aminoethylamino)-2-oxo-ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		524.1
431	N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		602.3
432	N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		602.2

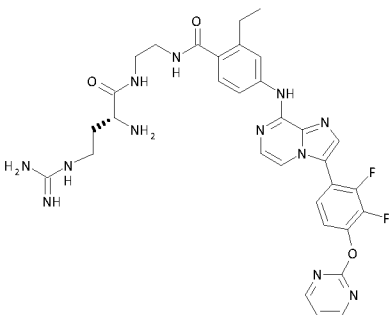
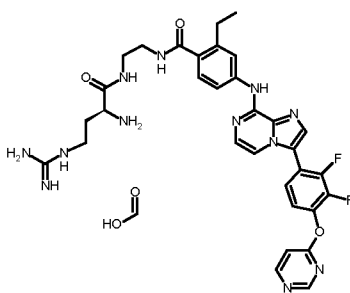
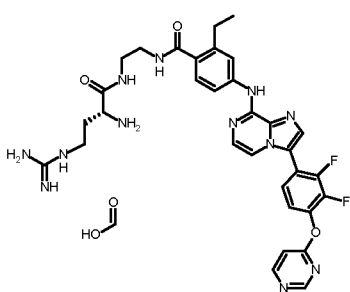
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433	N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		687.3
434	4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(dimethylamino)ethylamino]-2-oxo-ethyl]-2-ethyl-benzamide; formic acid		552.3
435	N-(3-aminopropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2,6-difluorobenzamide		489.3

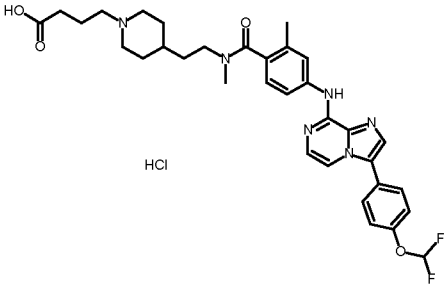
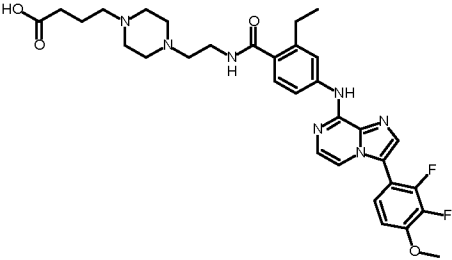
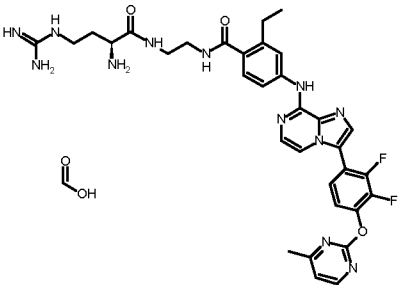
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436	N-(3-aminopropyl)-2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-6-fluorobenzamide		505.2
437	N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		687.3
438	N-[2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		673.3

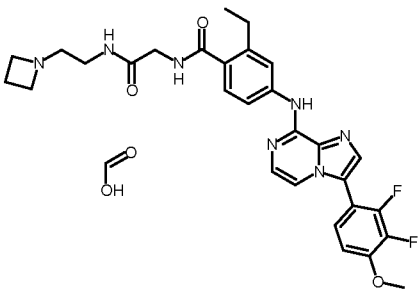
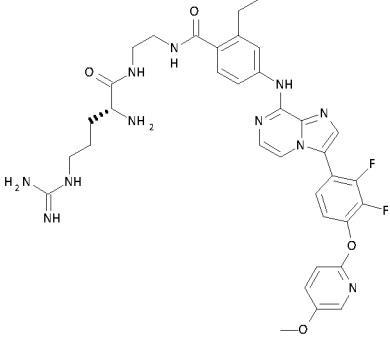
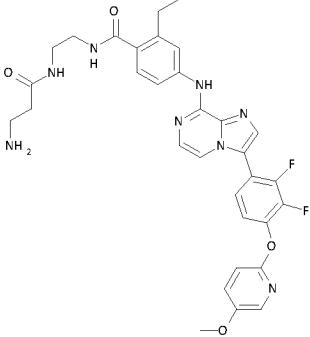
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439	N-[2-[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		673.3
440	N-[2-[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		673.4
441	N-[2-[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		673.4
442	4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(3-(((2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-		680.3

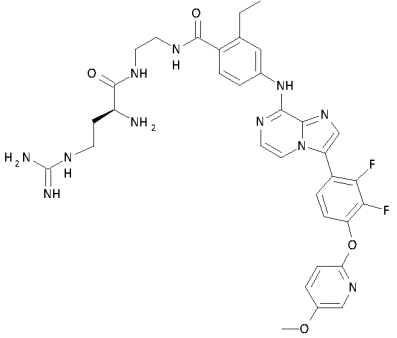
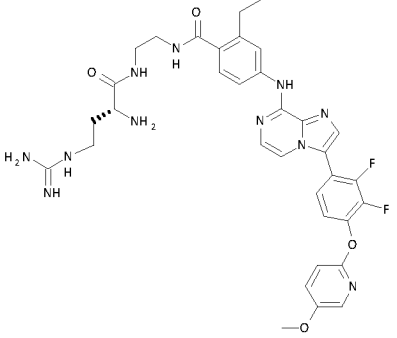
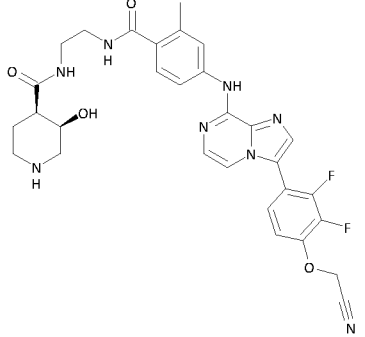
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	2H-pyran-2- l)oxy)propyl)benzamide		
443	4-(4-(2-(4-((3-(4-((difluoromethoxy)phenyl)imi dazo[1,2-a]pyrazin-8- yl)amino)-N,2- dimethylbenzamido)ethyl)pi peridin-1-yl)butanoic acid hydrochloride		622.3
444	4-(4-(2-(4-((3-(2,3-difluoro- 4- methoxyphenyl)imidazo[1,2- a]pyrazin-8-yl)amino)-2- ethylbenzamido)ethyl)pipera zin-1-yl)butanoic acid		622.3
445	(S)-N-(2-(2-amino-4- guanidinobutanamido)ethyl)- 4-((3-(2,3-difluoro-4-((4- methylpyrimidin-2- yl)oxy)phenyl)imidazo[1,2- a]pyrazin-8-yl)amino)-2- ethylbenzamide formiate 1:2		687.3

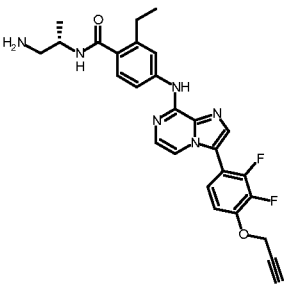
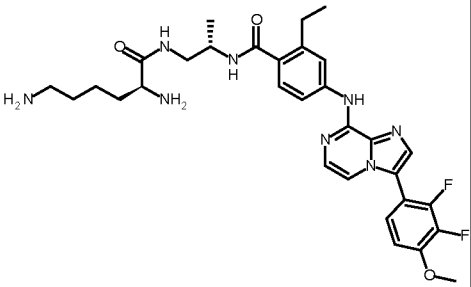
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446	N-[2-[2-(azetidin-1-yl)ethylamino]-2-oxo-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		564.2
447	N-[2-[[2-(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(5-methoxy-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		716.3
448	N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[2,3-difluoro-4-(5-methoxy-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		631.4

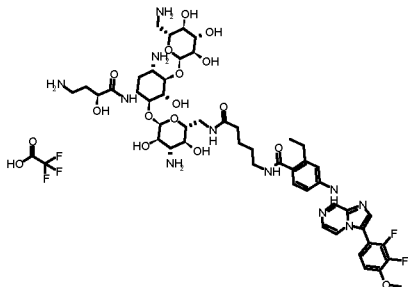
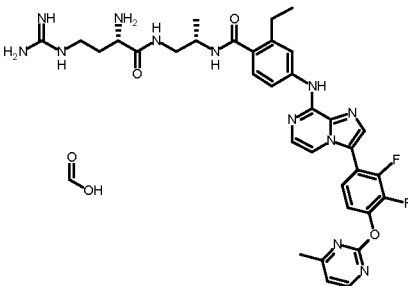
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449	N-[2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-methoxy-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		702.4
450	N-[2-[[[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-methoxy-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide		702.5
451	(3R,4R)-N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-3-hydroxy-piperidine-4-carboxamide; formic acid		596.2

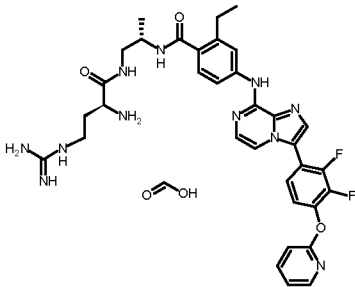
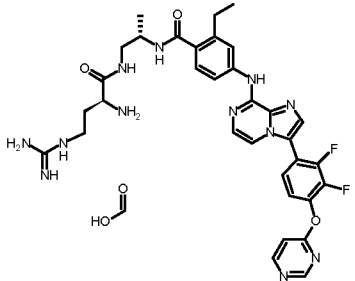
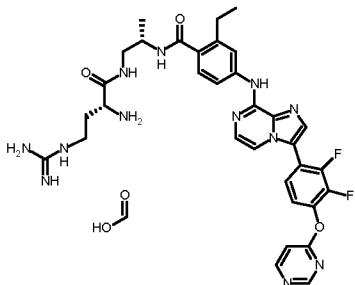
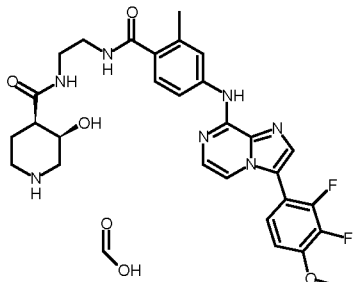
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452	N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide		505.2
453	N-[(1S)-2-[[[(2S)-2,6-diaminohexanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide		609.3

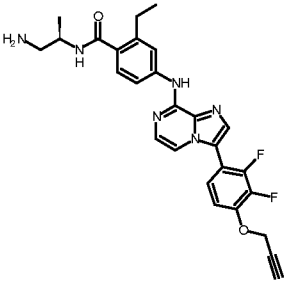
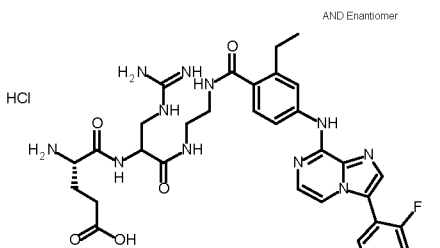
-493-

454	N-(5-((((2R,3S,4S,5R,6R)-4-amino-6-(((1S,2S,3R,4S,6R)-4-amino-6-((S)-4-amino-2-hydroxybutanamido)-3-(((2R,3R,4S,5S,6R)-6-(aminomethyl)-3,4,5-trihydroxytetrahydro-2H-pyran-2-yl)oxy)-2-hydroxycyclohexyl)oxy)-3,5-dihydroxytetrahydro-2H-pyran-2-yl)methyl)amino)-5-oxopentyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide tetrakis(2,2,2-trifluoroacetate)		1090.4
455	N-((S)-1-((S)-2-amino-4-guanidinobutanamido)propan-2-yl)-4-((3-(2,3-difluoro-4-((4-methylpyrimidin-2-yl)oxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide formiate 1:2		701.4

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456	N-[(1S)-2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]-1-methyl-ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		686.4
457	N-[(1S)-2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		687.3
458	N-[(1S)-2-[[[(2R)-2-amino-4-guanidino-butanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		687.3
459	(3R,4R)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-3-		571.3

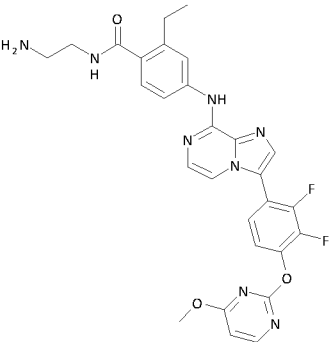
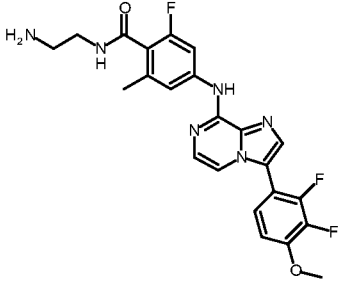
-495-

	hydroxy-piperidine-4-carboxamide; formic acid		
460	N-[(1R)-2-amino-1-methylethyl]-4-[[3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		505.3
461	(4S)-4-amino-5-((1-((2-(4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)ethyl)amino)-3-guanidino-1-oxopropan-2-yl)amino)-5-oxopentanoic acid trihydrochloride	AND Enantiomer 	724.2

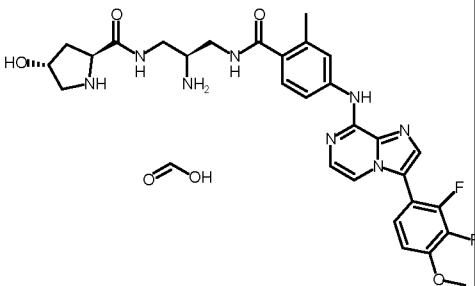
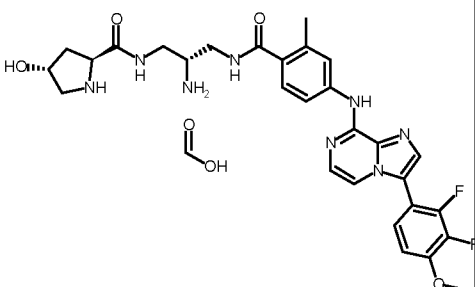
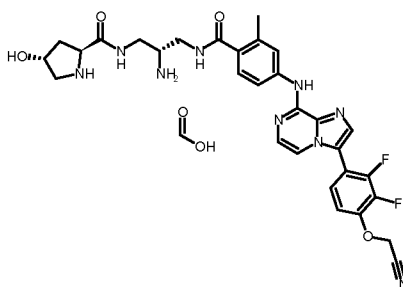
-496-

462	(S)-N-(1-aminopropan-2-yl)-4-((3-(2,3-difluoro-4-((4-methoxypyrimidin-2-yl)oxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide		575.2
463	(S)-N-(1-aminopropan-2-yl)-4-((3-(2,3-difluoro-4-((6-methoxypyrimidin-4-yl)oxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide		575.2
464	4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-2-oxo-ethyl]benzamide		580.3
465	N-[(1R)-2-[[[(2S)-2,6-diaminohexanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide		609.5

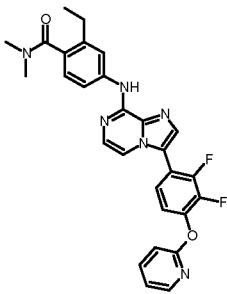
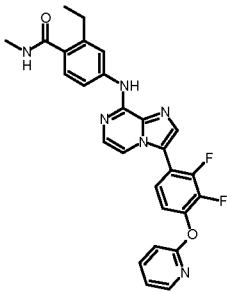
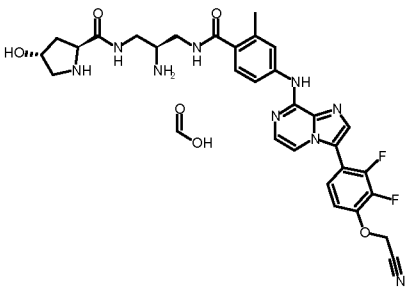
-497-

466	N-(2-aminoethyl)-4-((3-(2,3-difluoro-4-((4-methoxypyrimidin-2-yl)oxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide		561.2
467	N-(2-aminoethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-fluoro-6-methylbenzamide		471.2

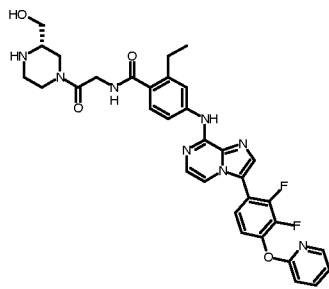
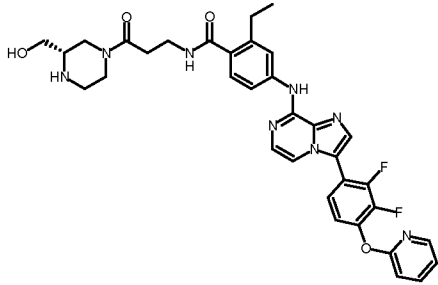
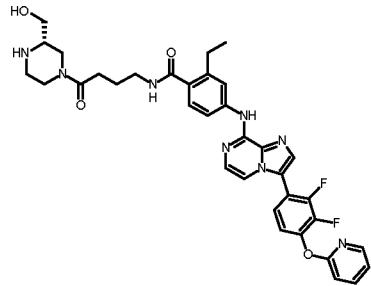
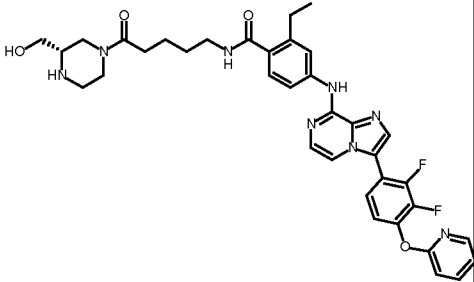
-498-

468	(2S,4R)-N-[(2R)-2-amino-3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide; formic acid		
469	(2S,4R)-N-[(2S)-2-amino-3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide; formic acid		595.3
470	(2S,4R)-N-[(2S)-2-amino-3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide; formic acid		620.2

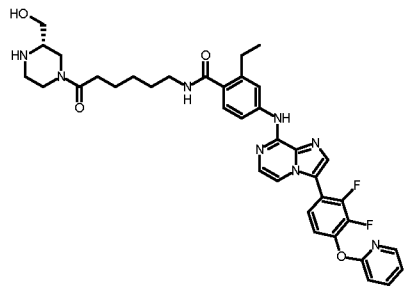
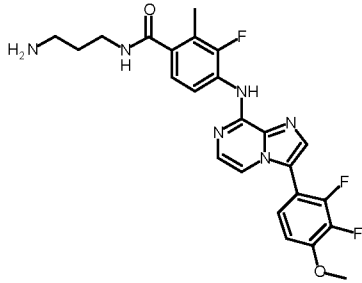
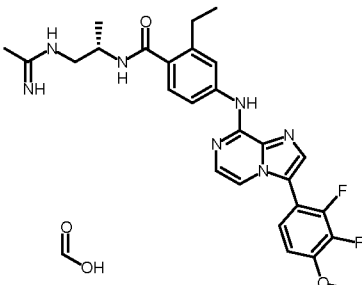
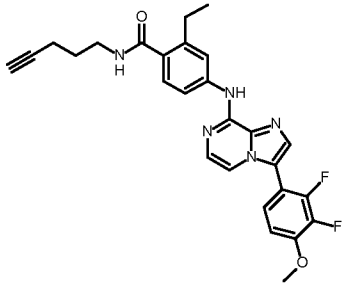
-499-

471	4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N,N-dimethyl-benzamide		515.3
472	4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-benzamide		501.2
473	(2S,4R)-N-[(2R)-2-amino-3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide; formic acid		620.3

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474	4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-2-oxo-ethyl]benzamide		643.4
475	4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[3-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-3-oxo-propyl]benzamide		657.4
476	4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[4-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-4-oxo-butyl]benzamide		671.4
477	4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[5-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-5-oxo-pentyl]benzamide		685.3

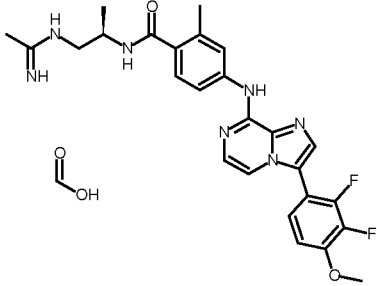
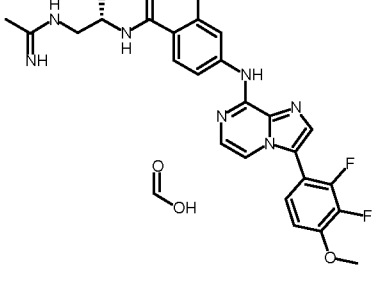
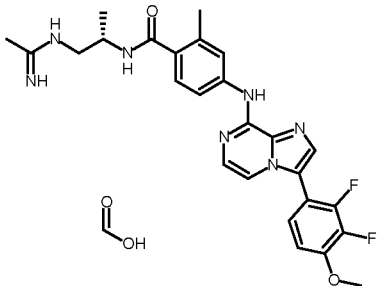
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478	4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[6-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-6-oxo-hexyl]benzamide		699.3
479	N-(3-aminopropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-3-fluoro-2-methylbenzamide		485.2
480	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(2S)-1-(ethanimidoylamino)propan-2-yl]-2-ethylbenzamide; formic acid		522.3
481	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(pent-4-yn-1-yl)benzamide		490.4

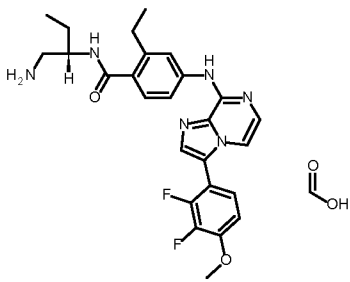
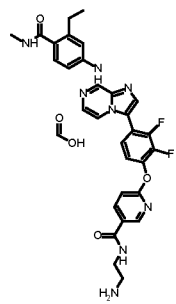
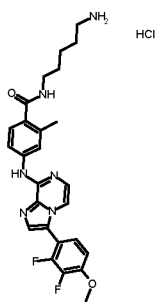
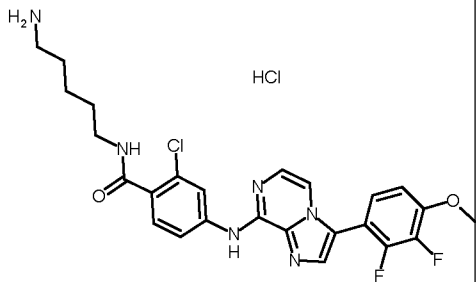
-502-

482	#N!-(3-aminopropyl)-4-[[3-[2,3-difluoro-4-(1,3-thiazol-2-yloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		550.3
483	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(2,3-dihydroxypropyl)-2-ethylbenzamide		498.3
484	N-[1-[[[(2S)-2,6-diaminohexanoyl]amino]methyl]cyclopropyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		621.3
485	rac-(R)-4-((3-(4-((1H-pyrazol-3-yl)methoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(1-aminopropan-2-yl)-2-ethylbenzamide		547.1

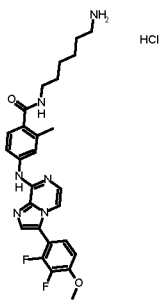
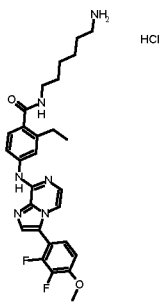
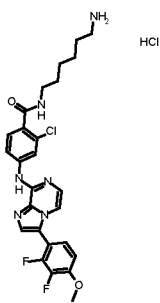
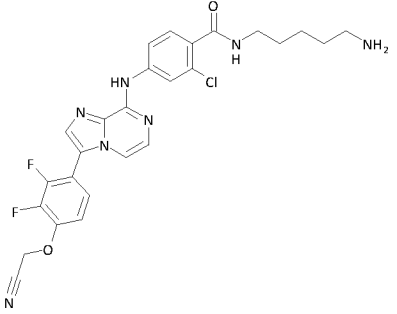
-503-

486	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(2#R!)-1-(ethanimidoylamino)propan-2-yl]-2-methylbenzamide; formic acid		508.4
487	2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(2#S!)-1-(ethanimidoylamino)propan-2-yl]benzamide; formic acid		528.4
488	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(2#S!)-1-(ethanimidoylamino)propan-2-yl]-2-methylbenzamide; formic acid		508.4

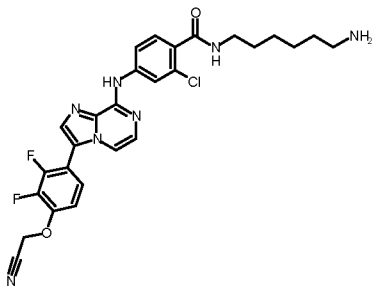
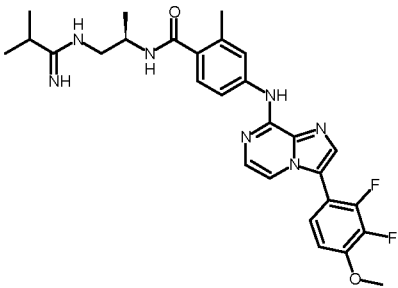
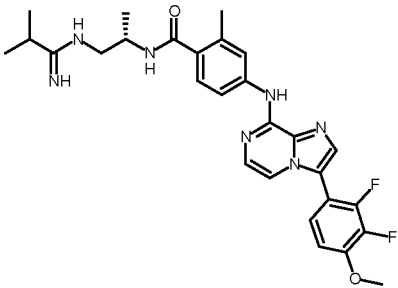
-504-

489	N-[(1S)-1-(aminomethyl)propyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide; formic acid		495.2
490	N-(2-aminoethyl)-6-[4-[8-[3-ethyl-4-(methylcarbamoyl)anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]pyridine-3-carboxamide; formic acid		587.2
491	N-(5-aminopentyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride		495.4
492	N-(5-aminopentyl)-2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide hydrochloride		515.4

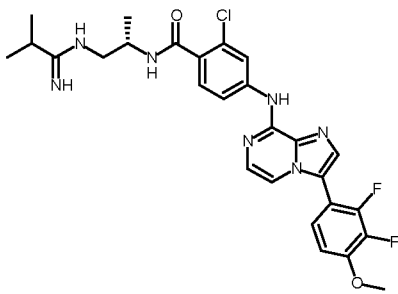
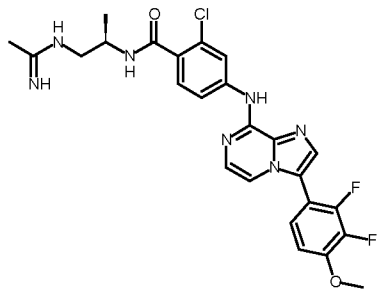
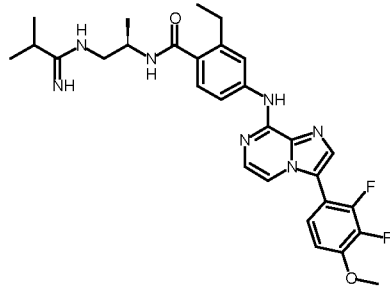
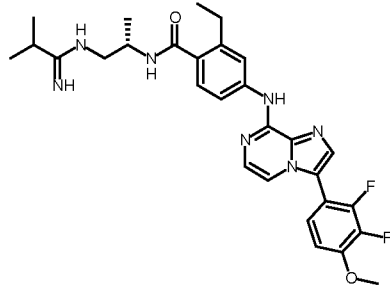
-505-

493	N-(6-aminohexyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride		509.4
494	N-(6-aminohexyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		523.5
495	N-(6-aminohexyl)-2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide hydrochloride		529.4
496	N-(5-aminopentyl)-2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzamide		541.2

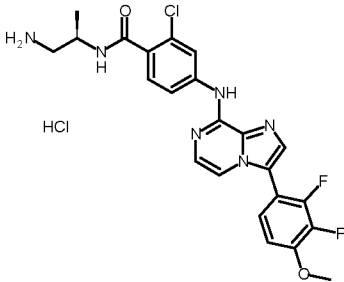
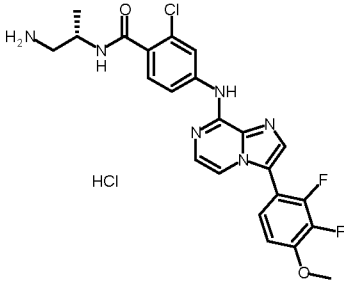
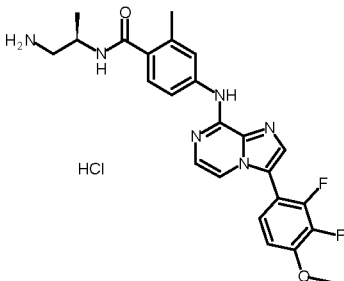
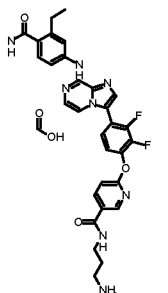
-506-

497	N-(6-aminohexyl)-2-chloro-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide		555.3
498	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(2R)-1-(2-methylpropanimidoylamino)propan-2-yl]benzamide		536.4
499	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(2S)-1-(2-methylpropanimidoylamino)propan-2-yl]benzamide		536.4

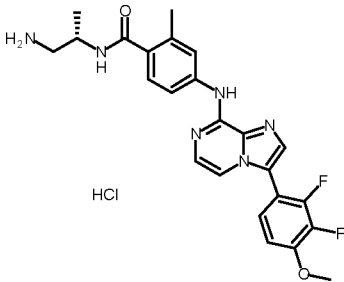
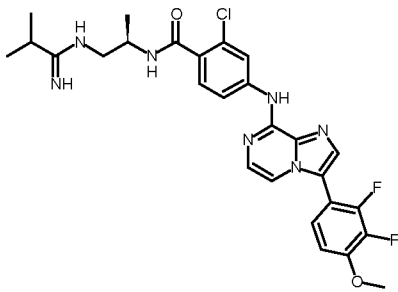
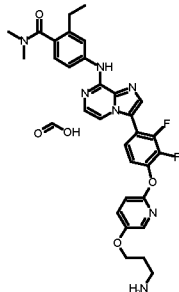
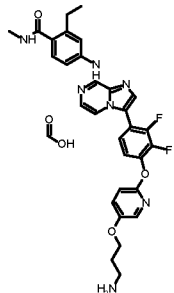
-507-

500	2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-#N!-[(2#S!)-1-(2-methylpropanimidoylamino)propan-2-yl]benzamide		556.4
501	2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-#N!-[(2#R!)-1-(ethanimidoylamino)propan-2-yl]benzamide		528.4
502	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-#N!-[(2#R!)-1-(2-methylpropanimidoylamino)propan-2-yl]benzamide		550.5
503	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-#N!-[(2#S!)-1-(2-methylpropanimidoylamino)propan-2-yl]benzamide		550.5

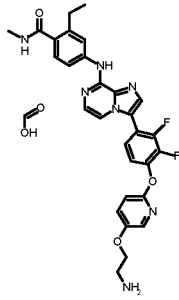
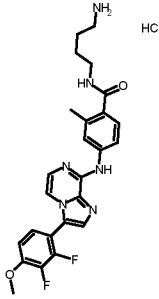
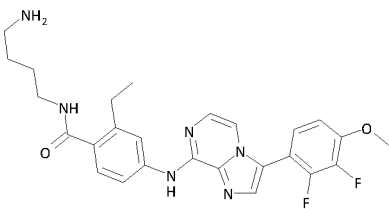
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504	#N!-[(2#R!)-1-aminopropan-2-yl]-2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide; dihydrochloride		487.3
505	#N!-[(2#S!)-1-aminopropan-2-yl]-2-chloro-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide; dihydrochloride		487.4
506	#N!-[(2#R!)-1-aminopropan-2-yl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide; dihydrochloride		467.3
507	N-(3-aminopropyl)-6-[4-[8-[3-ethyl-4-(methylcarbamoyl)anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluorophenoxy]pyridine-3-carboxamide; formic acid		601.2

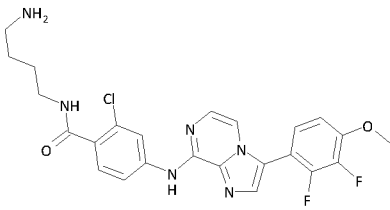
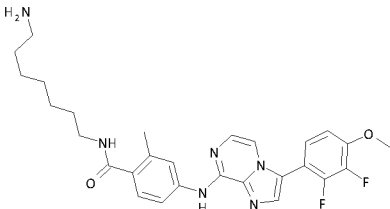
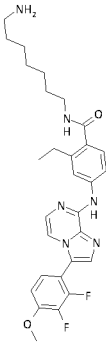
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508	#N!-[(2#S!)-1-aminopropan-2-yl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide; dihydrochloride	 HCl	467.3
509	(R)-2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N-(1-isobutyrimidamidopropan-2-yl)benzamide		556.3
510	4-[[3-[4-[[5-(3-aminopropoxy)-2-pyridyl]oxy]-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N,N-dimethylbenzamide; formic acid		588.3
511	4-[[3-[4-[[5-(3-aminopropoxy)-2-pyridyl]oxy]-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methylbenzamide; formic acid		574.3

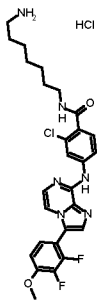
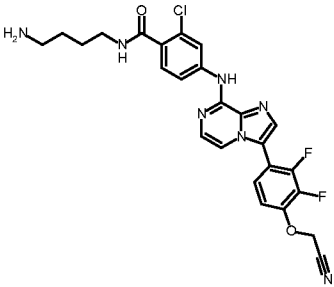
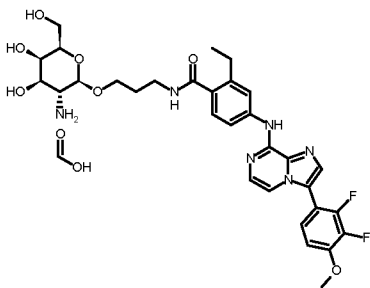
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512	4-[[3-[4-[[5-(2-aminoethoxy)-2-pyridyl]oxy]-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-benzamide; formic acid		560.3
513	N-(4-aminobutyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride		481.4
514	N-(4-aminobutyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		495.4

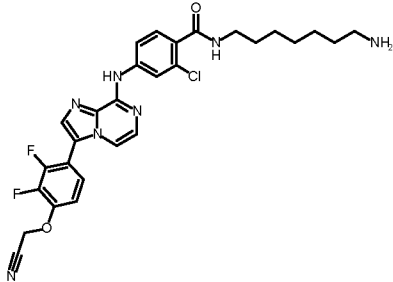
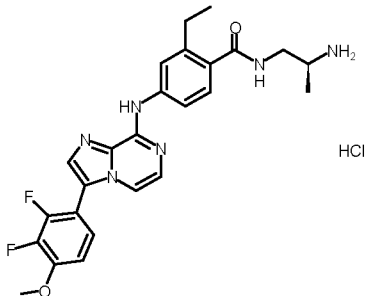
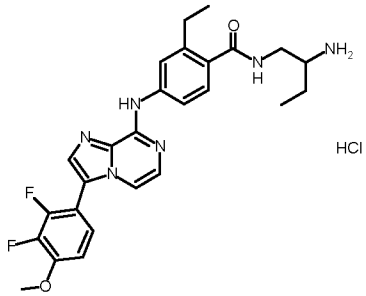
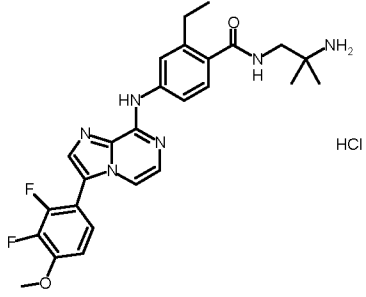
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515	N-(4-aminobutyl)-2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide hydrochloride		502.3
516	N-(7-aminoheptyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-methylbenzamide hydrochloride		524.4
517	N-(7-aminoheptyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		538.4

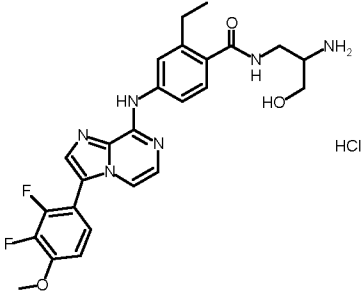
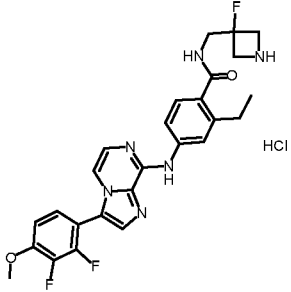
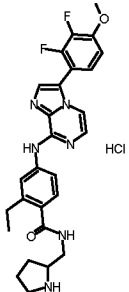
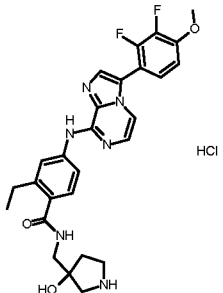
-512-

518	N-(7-aminoheptyl)-2-chloro-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide hydrochloride		544.3
519	N-(4-aminobutyl)-2-chloro-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide		526.2
520	N-[3-[(2R,3R,4R,5R,6R)-3-amino-4,5-dihydroxy-6-(hydroxymethyl)oxan-2-yl]oxypropyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide; formic acid		643.6

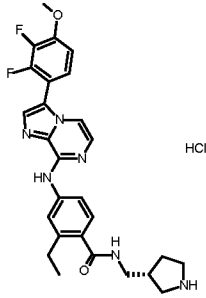
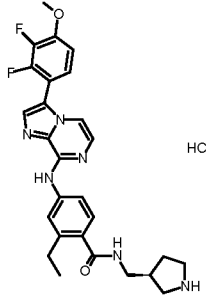
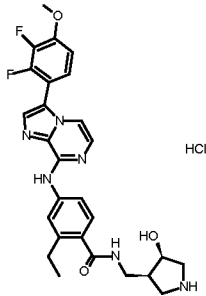
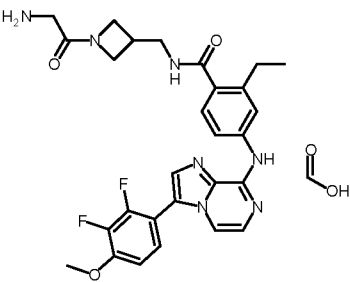
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521	N-(7-aminoheptyl)-2-chloro-4-((3-(4-(cyanomethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)benzamide		526.2
522	(S)-N-(2-aminopropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		479.5 (M-H)-
523	N-(2-aminobutyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		493.5 (M-H)-
524	N-(2-amino-2-methylpropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		493.5 (M-H)-

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525	N-(2-amino-3-hydroxypropyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		495.5 (M-H)-
526	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-((3-fluoroazetidin-3-yl)methyl)benzamide hydrochloride		509.5 (M-H)-
527	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(pyrrolidin-2-ylmethyl)benzamide hydrochloride		505.5 (M-H)-
528	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-((3-hydroxypyrrolidin-3-yl)methyl)benzamide hydrochloride		521.5 (M-H)-

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529	(R)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(pyrrolidin-3-ylmethyl)benzamide hydrochloride		505.5 (M-H)-
530	(S)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(pyrrolidin-3-ylmethyl)benzamide hydrochloride		505.5 (M-H)-
531	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(((3S,4R)-4-hydroxypyrrolidin-3-yl)methyl)benzamide hydrochloride		521.5 (M-H)-
532	N-[[1-(2-aminoacetyl)azetidin-3-yl]methyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		550.2

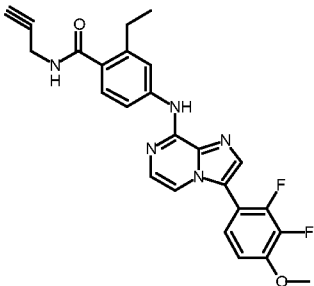
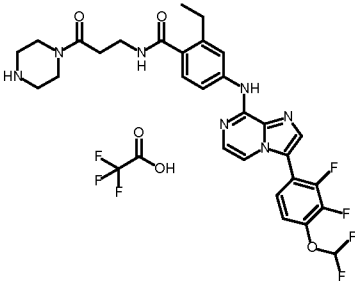
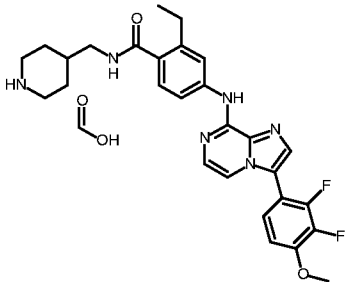
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533	N-(5-([1,2,4]triazolo[4,3-a]pyridin-3-yl)pentyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide		611.5
534	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(6-(piperidin-1-yl)hexyl)benzamide		591.6
535	N-(6-(1H-imidazol-1-yl)hexyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide		574.5
536	N-[(E)-4-aminobut-2-enyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide		493.4

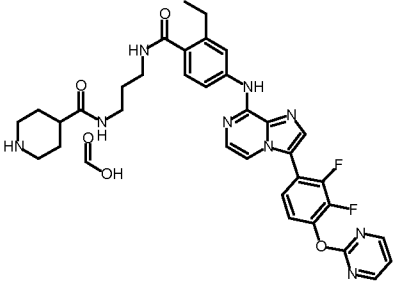
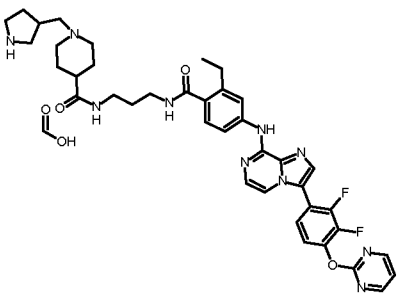
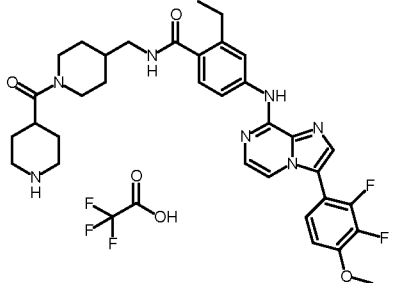
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537	2-ethyl-4-[[3-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methylbenzamide		470.2
538	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-N,2-dimethylbenzamide		424.3
539	N-[(1R)-1-(aminomethyl)-2-hydroxy-ethyl]-4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		497.2
540	N-(8-aminooctyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide hydrochloride		551.5

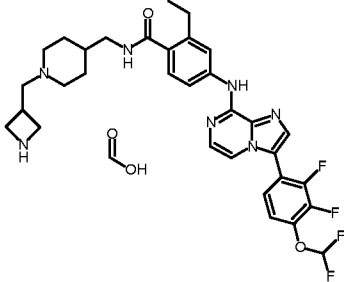
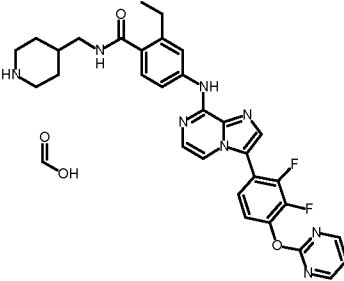
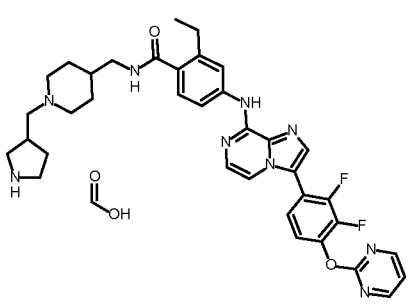
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541	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-prop-2-ynylbenzamide		462.3
542	4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(3-oxo-3-(piperazin-1-yl)propyl)benzamide 2,2,2-trifluoroacetate		600.1
543	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(piperidin-4-ylmethyl)benzamide formate		521.3

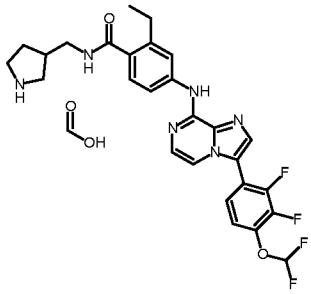
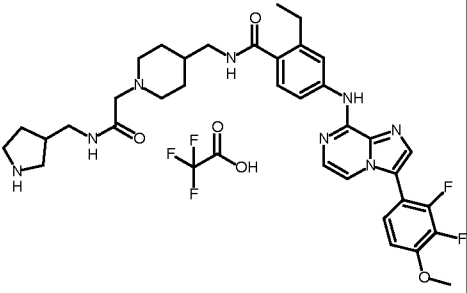
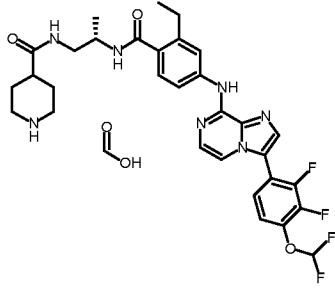
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544	N-(3-(4-((3-(2,3-difluoro-4-(pyrimidin-2-yloxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)piperidine-4-carboxamide formate		656
545	N-(3-(4-((3-(2,3-difluoro-4-(pyrimidin-2-yloxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)-1-(pyrrolidin-3-ylmethyl)piperidine-4-carboxamide formate		739
546	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-((1-(piperidine-4-carbonyl)piperidin-4-yl)methyl)benzamide 2,2,2-trifluoroacetate		632.3

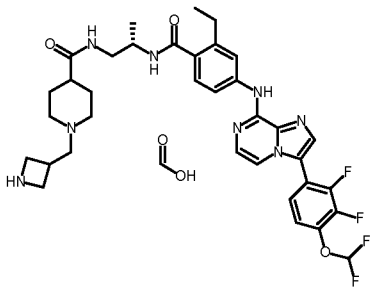
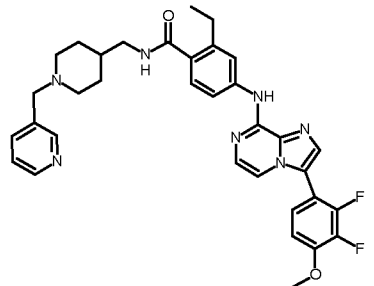
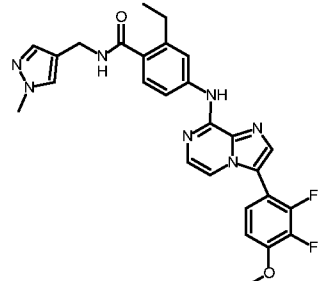
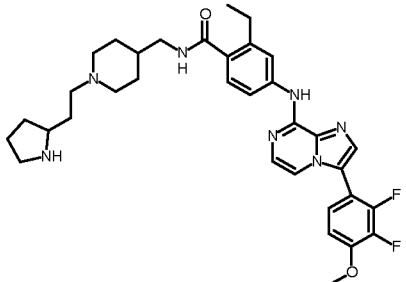
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547	N-((1-(azetidin-3-ylmethyl)piperidin-4-yl)methyl)-4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide formate		626.4
548	4-((3-(2,3-difluoro-4-(pyrimidin-2-yloxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(piperidin-4-ylmethyl)benzamide formate		585
549	4-((3-(2,3-difluoro-4-(pyrimidin-2-yloxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-((1-(pyrrolidin-3-ylmethyl)piperidin-4-yl)methyl)benzamide formate		668

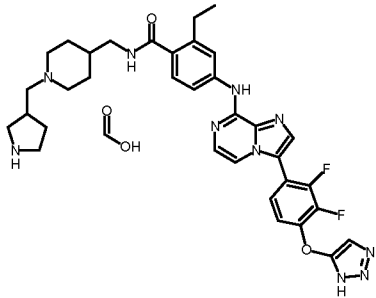
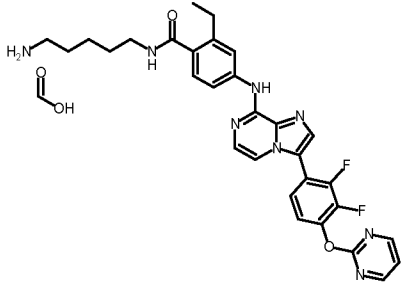
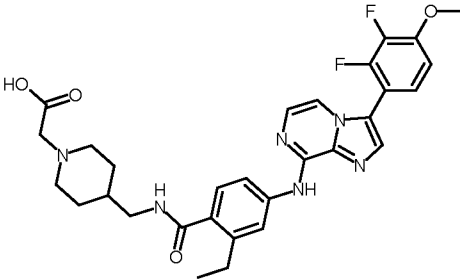
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550	4-[[3-[4-(difluoromethoxy)-2,3-difluorophenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(pyrrolidin-3-ylmethyl)benzamide; formic acid		643.2
551	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-((1-(2-oxo-2-((pyrrolidin-3-ylmethyl)amino)ethyl)piperidin-4-yl)methyl)benzamide bis(2,2,2-trifluoroacetate)		661
552	rac-(R)-N-(2-(4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)piperidine-4-carboxamide formate		628.4

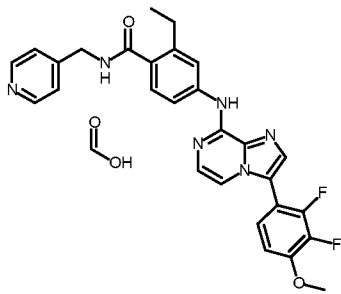
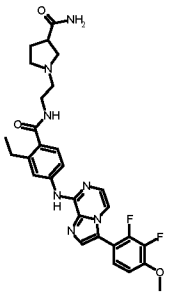
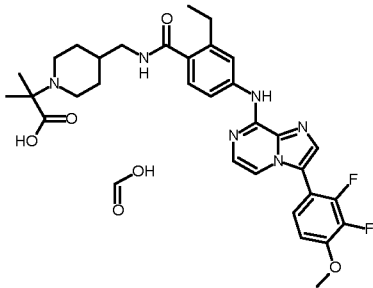
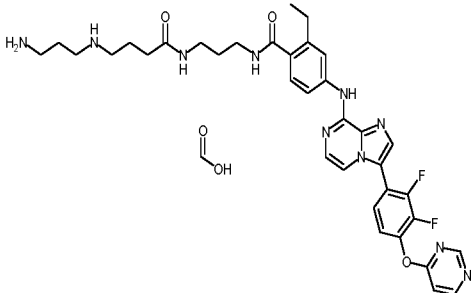
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553	rac-(R)-1-(azetidin-3-ylmethyl)-N-(2-(4-((3-(4-(difluoromethoxy)-2,3-difluorophenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)propyl)piperidine-4-carboxamide formate		697.3
554	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[1-(3-pyridylmethyl)-4-piperidyl]methyl]benzamide		612.1
555	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(1-methylpyrazol-4-yl)methyl]benzamide		518.1
556	4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[1-(2-pyrrolidin-2-ylethyl)-4-piperidyl]methyl]benzamide		618.1

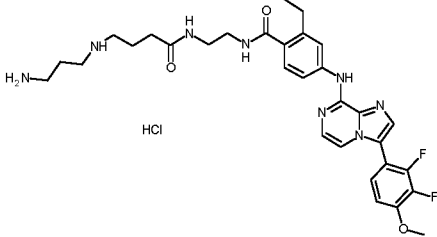
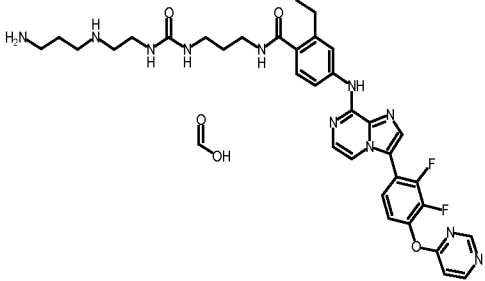
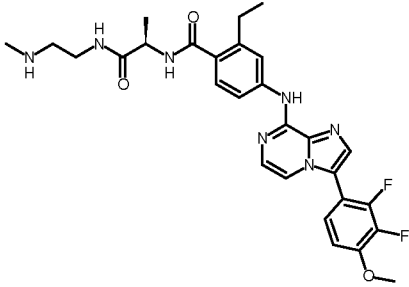
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557	4-[[3-[2,3-difluoro-4-(1H-imidazo[1,2-a]pyrazin-8-yl)amino]-2-ethyl-#N!-[1-(pyrrolidin-3-ylmethyl)piperidin-4-yl]methyl]benzamide;formic acid		657
558	N-(5-aminopentyl)-4-((3-(2,3-difluoro-4-(pyrimidin-2-yloxy)phenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide formate		573
559	2-[4-[[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]methyl]-1-piperidyl]acetic acid		579.2

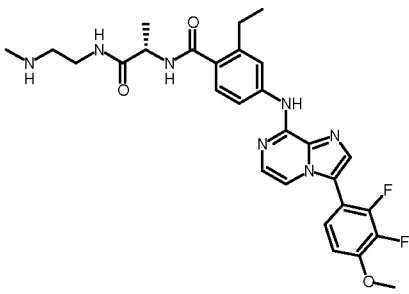
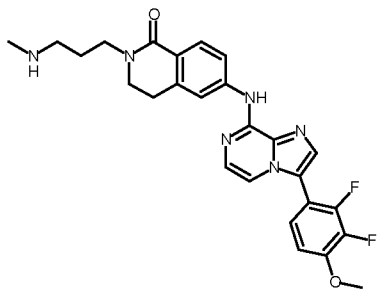
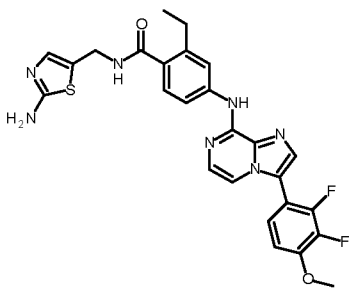
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560	4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethyl-N-(pyridin-4-ylmethyl)benzamide formate		515.2
561	1-[2-[[4-[[3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzoyl]amino]ethyl]pyrrolidine-3-carboxamide		564.3
562	2-(4-(((4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamido)methyl)pyrrolidin-1-yl)-2-methylpropanoic acid compound with formic acid		607.5
563	N-[3-[4-(3-aminopropylamino)butanoyl amino]propyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid		687.4

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564	N-(2-(4-((3-aminopropyl)amino)butanamide)ethyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide trihydrochloride	 HCl	609.4
565	N-[3-[2-(3-aminopropylamino)ethylcarbamoylamino]propyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide; formic acid	 HO-C(=O)-H	688.3
566	4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(1R)-1-methyl-2-[2-(methylamino)ethylamino]-2-oxo-ethyl]benzamide		552.3

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567	4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(1S)-1-methyl-2-[2-(methylamino)ethylamino]-2-oxo-ethyl]benzamide		552.3
568	6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-[3-(methylamino)propyl]-3,4-dihydroisoquinolin-1-one		493.3
569	N-((2-aminothiazol-5-yl)methyl)-4-((3-(2,3-difluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-ethylbenzamide		536.3

*Assay procedures***Antimicrobial susceptibility testing:****90% Growth Inhibitory Concentration (IC90) determination**

- The in vitro antimicrobial activity of the compounds was determined according to the following procedure:

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The assay used a 10-points Iso-Sensitest broth medium to measure quantitatively the *in vitro* activity of the compounds against *Acinetobacter baumannii* ATCC17978 and *Acinetobacter baumannii* ATCC17961.

Stock compounds in DMSO were serially twofold diluted (e.g. range from 50 to 0.097 μM final concentration) in 384 wells microtiter plates and inoculated with 49 μl the bacterial suspension in Iso-Sensitest medium to have a final cell concentration of $\sim 5 \times 10^{(5)}$ CFU/ml in a final volume/well of 50 μl /well. Microtiter plates were incubated at $35 \pm 2^\circ\text{C}$.

Bacterial cell growth was determined with the measurement of optical density at $\lambda=600\text{nm}$ each 20 minutes over a time course of 16h. Growth inhibition was calculated during the logarithmic growth of the bacterial cells with determination of the concentration inhibiting 50% (IC50) and 90% (IC90) of the growth.

Table 1 provides the 90% growth inhibitory concentrations (IC90) in micromoles per liter of the compounds of present invention obtained against the strain *Acinetobacter baumannii* ATCC17978 and *Acinetobacter baumannii* ATCC17961.

Particular compounds of the present invention exhibit an IC90 (*A. baumannii* ATCC17978 and *Acinetobacter baumannii* ATCC17961) $\leq 25 \mu\text{mol/l}$.

More particular compounds of the present invention exhibit an IC90 (*A. baumannii* ATCC17978 and *Acinetobacter baumannii* ATCC17961) $\leq 5 \mu\text{mol/l}$.

Most particular compounds of the present invention exhibit an IC90 (*A. baumannii* ATCC17978 and *Acinetobacter baumannii* ATCC17961) $\leq 1 \mu\text{mol/l}$.

Example	ATCC17978 IC90 [μM]
1	0.12
2	4.60
3	0.21

Example	ATCC17978 IC90 [μM]
4	0.29
5	0.65
6	0.64

Example	ATCC17978 IC90 [μM]
7	1.90
8	2.00
9	0.84

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Example	ATCC17978 IC90 [μ M]
10	0.11
11	0.14
12	0.12
13	0.24
14	0.12
15	1.10
16	0.81
17	0.55
18	2.20
19	0.69
20	0.65
21	0.12
22	0.13
23	0.15
24	0.34
25	0.16
26	0.17
27	0.19
28	3.60

Example	ATCC17978 IC90 [μ M]
29	1.20
30	3.70
31	2.90
32	1.70
33	4.90
34	1.10
35	1.20
36	0.46
37	0.24
38	0.19
39	0.24
40	0.18
41	0.62
42	0.89
43	0.22
44	0.12
45	0.35
46	0.49
47	1.70

Example	ATCC17978 IC90 [μ M]
48	0.22
49	0.47
50	4.30
51	0.96
52	0.75
53	0.24
54	0.82
55	0.26
56	0.25
57	0.29
58	0.17
59	0.13
60	0.22
61	0.19
62	0.25
63	0.09
64	0.23
65	0.12
66	0.31

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Example	ATCC17978 IC90 [μ M]
67	0.12
68	0.17
69	0.27
70	0.70
71	1.10
72	1.00
73	0.14
74	0.06
75	0.09
76	0.17
77	0.10
78	0.13
79	0.09
80	0.27
81	0.20
82	0.27
83	0.25
84	0.14
85	0.07

Example	ATCC17978 IC90 [μ M]
86	0.14
87	0.08
88	0.25
89	0.23
90	0.23
91	0.26
92	0.61
93	0.20
94	0.28
95	0.19
96	0.07
97	1.20
98	0.78
99	0.35
100	0.35
101	0.24
102	0.32
103	0.08
104	1.10

Example	ATCC17978 IC90 [μ M]
105	0.82
106	0.14
107	0.12
108	1.20
109	0.96
110	0.25
111	2.10
112	0.96
113	2.00
114	0.47
115	0.85
116	0.94
117	0.56
118	0.45
119	0.18
120	0.14
121	0.28
122	0.31
123	0.41

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Example	ATCC17978 IC90 [μ M]
124	0.09
125	0.12
126	0.21
127	0.09
128	0.24
129	0.25
130	0.64
131	0.09
132	0.23
133	0.09
134	0.08
135	0.09
136	0.06
137	0.07
138	0.10
139	0.06
140	0.17
141	0.07
142	0.13

Example	ATCC17978 IC90 [μ M]
143	0.16
144	0.09
145	0.15
146	0.19
147	0.45
148	0.10
149	0.45
150	0.65
151	2.00
152	1.10
153	0.53
154	0.82
164	0.29
165	0.53
166	0.98
167	1.10
168	2.00
170	1.90
171	3.60

Example	ATCC17978 IC90 [μ M]
172	6.20
173	8.60
174	8.90
175	2.30
176	0.52
177	0.90
178	1.00
179	1.70
180	0.73
181	1.30
182	0.18
183	0.19
184	0.22
185	0.23
186	0.26
187	0.27
188	0.27
189	0.28
190	0.33

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Example	ATCC17978 IC90 [μ M]
191	0.33
192	0.34
193	0.35
194	0.36
195	0.36
196	0.38
197	0.40
198	0.72
199	0.42
200	0.44
201	0.46
202	0.46
203	0.46
204	0.53
205	0.53
206	0.54
207	0.56
208	0.58
209	0.59

Example	ATCC17978 IC90 [μ M]
210	0.63
211	0.64
212	0.64
213	0.66
214	0.69
215	0.68
216	0.77
217	0.84
218	0.94
219	1.00
220	1.20
221	1.10
222	1.10
223	1.10
224	1.10
225	1.10
226	1.10
227	0.61
228	1.20

Example	ATCC17978 IC90 [μ M]
229	1.20
230	1.20
231	0.40
232	1.30
233	1.30
234	1.30
235	1.00
236	1.40
237	1.50
238	1.80
239	0.54
240	1.10
241	1.90
242	2.00
243	2.10
244	0.44
245	2.20
246	2.20
247	2.40

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Example	ATCC17978 IC90 [μ M]
248	2.40
249	2.50
250	1.20
251	2.70
252	2.80
253	2.90
254	3.30
255	2.20
256	1.90
257	3.60
258	3.60
259	4.10
260	4.30
261	4.90
262	5.00
263	5.00
264	5.10
265	5.10
266	5.10

Example	ATCC17978 IC90 [μ M]
267	5.40
268	5.60
269	7.10
270	7.70
271	9.30
272	0.12
273	0.18
274	0.24
275	0.35
276	0.48
277	0.70
278	1.40
279	3.40
280	0.88
281	0.93
282	1.40
283	2.00
284	2.10
285	2.60

Example	ATCC17978 IC90 [μ M]
286	2.70
287	2.90
288	3.00
289	4.60
290	0.05
291	0.09
292	0.11
293	0.12
294	0.14
295	0.14
296	0.15
297	0.15
298	0.17
299	0.18
300	0.24
301	0.27
302	0.30
303	0.36
304	0.36

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Example	ATCC17978 IC90 [μ M]
305	0.51
306	0.59
307	0.62
308	0.66
309	0.69
310	0.80
311	0.80
312	1.20
313	1.20
314	1.30
315	1.30
316	2.10
317	2.50
318	2.50
319	3.30
320	2.70
321	4.00
322	4.40
323	0.06

Example	ATCC17978 IC90 [μ M]
324	0.11
325	0.15
327	0.29
330	0.11
331	0.30
332	0.32
333	0.34
334	0.35
335	0.43
336	0.48
337	0.52
338	0.54
339	0.56
340	0.59
341	0.65
342	0.73
343	0.75
344	0.80
345	0.90

Example	ATCC17978 IC90 [μ M]
346	0.98
347	1.10
348	1.10
349	1.10
350	1.20
351	1.30
352	1.30
353	1.40
354	1.50
355	2.50
356	0.05
357	0.05
358	0.05
359	0.06
360	0.07
361	0.08
362	0.08
363	0.09
364	0.09

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Example	ATCC17978 IC90 [μ M]
365	0.09
366	0.10
367	0.10
368	0.12
369	0.13
370	0.14
371	0.15
372	0.15
373	0.15
374	0.19
375	0.19
376	0.20
377	0.18
378	0.18
379	1.10
380	2.60
381	1.90
382	3.30
383	0.82

Example	ATCC17978 IC90 [μ M]
384	0.88
385	1.10
386	0.95
387	0.78
388	0.20
389	0.50
390	0.22
392	0.34
393	0.26
394	0.31
395	0.74
396	0.57
397	0.41
398	0.41
399	0.38
400	0.32
401	0.22
402	0.57
403	0.94

Example	ATCC17978 IC90 [μ M]
404	0.36
405	0.36
406	0.24
407	0.94
408	0.41
409	0.45
410	0.21
411	0.32
412	0.77
413	0.47
414	0.39
415	0.52
416	0.24
417	0.85
419	0.67
420	0.72
421	0.44
422	0.87
423	0.21

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Example	ATCC17978 IC90 [μ M]
424	0.90
425	0.60
426	0.82

Example	ATCC17978 IC90 [μ M]
427	0.69
428	0.41
429	0.62

Example	ATCC17978 IC90 [μ M]
435	0.73
436	0.65
568	0.39

Example	ATCC17961 IC90 [μ M]
155	0.34
156	0.34
157	0.32
158	0.16
159	0.23
160	0.15
161	0.08
162	0.08
163	0.08
169	0.07
326	0.19
328	0.3

Example	ATCC17961 IC90 [μ M]
329	0.14
391	0.051
418	0.033
430	0.23
431	0.53
432	0.50
433	0.46
434	0.25
437	0.41
438	0.55
439	0.34
440	0.52

Example	ATCC17961 IC90 [μ M]
441	0.46
442	0.41
443	0.76
444	0.32
445	0.38
446	0.30
447	0.63
448	0.47
449	0.53
450	0.56
451	0.76
452	0.59

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Example	ATCC17961 IC90 [μ M]
453	0.32
454	0.97
455	0.72
456	0.71
457	0.98
458	0.66
459	0.94
460	0.48
461	0.48
462	0.52
463	0.84
464	0.24
465	0.30
466	0.56
467	0.63
468	0.48
469	0.50
470	0.60
471	0.66

Example	ATCC17961 IC90 [μ M]
472	0.21
473	0.21
474	0.91
475	0.41
476	0.36
477	0.33
478	0.38
479	0.49
480	0.27
481	0.26
482	0.88
483	0.21
484	0.28
485	0.80
486	0.068
487	0.12
488	0.29
489	0.50
490	0.45

Example	ATCC17961 IC90 [μ M]
491	0.041
492	0.044
493	0.035
494	0.037
495	0.034
496	0.023
497	0.025
498	0.14
499	0.30
500	0.31
501	0.069
502	0.15
503	0.45
504	0.10
505	0.27
506	0.13
507	0.50
508	0.32
509	0.11

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Example	ATCC17961 IC90 [μ M]
510	0.86
511	0.48
512	0.51
513	0.05
514	0.048
515	0.042
516	0.034
517	0.067
518	0.171
519	0.047
520	0.11
521	0.024
522	0.26
523	0.25
524	0.60
525	0.35
526	0.21
527	0.48
528	0.25

Example	ATCC17961 IC90 [μ M]
529	0.11
530	0.11
531	0.15
532	0.061
533	0.10
534	0.041
535	0.085
536	0.024
537	0.207
538	0.027
539	0.41
540	0.10
541	0.062
542	0.054
543	0.066
544	0.29
545	0.31
546	0.07
547	0.16

Example	ATCC17961 IC90 [μ M]
548	0.47
549	0.49
550	0.15
551	0.077
552	0.21
553	0.26
554	0.17
555	0.15
556	0.31
557	0.48
558	0.19
559	0.27
560	0.08
561	0.19
562	0.32
563	0.19
564	0.50
565	0.30
566	0.95

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Example	ATCC17961 IC90 [μ M]
567	0.65

Example	ATCC17961 IC90 [μ M]
569	0.084

Example 570

A compound of formula (I) can be used in a manner known per se as the active ingredient for the production of tablets of the following composition:

5	<u>Per tablet</u>
	Active ingredient 200 mg
	Microcrystalline cellulose 155 mg
	Corn starch 25 mg
	Talc 25 mg
10	Hydroxypropylmethylcellulose <u>20 mg</u>
	425 mg

Example 571

A compound of formula (I) can be used in a manner known per se as the active ingredient for the production of capsules of the following composition:

15	<u>Per capsule</u>
	Active ingredient 100.0 mg
	Corn starch 20.0 mg
	Lactose 95.0 mg
	Talc 4.5 mg
20	Magnesium stearate <u>0.5 mg</u>
	220.0 mg

Example 572

A compound of formula (I) can be used in a manner known per se as the active ingredient for the production of an infusion solution of the following composition:

- | | | |
|---|--|-----------|
| | Active ingredient | 100 mg |
| 5 | Lactic acid 90% | 100 mg |
| | NaOH q.s. or HCl q.s. for adjustment to pH 4.0 | |
| | Sodium chloride q.s. or glucose q.s. for adjustment of the osmolality to 290 mOsm/kg | |
| | Water for injection (WFI) | ad 100 ml |

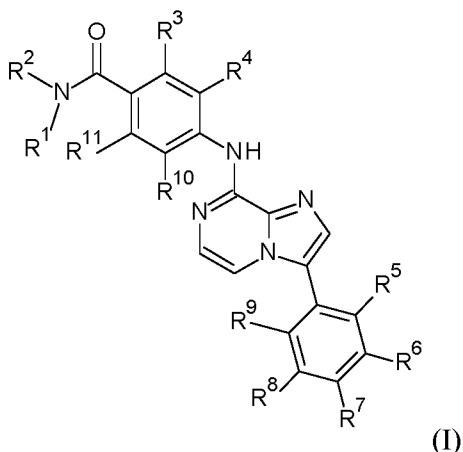
Example 573

- 10 A compound of formula (I) can be used in a manner known per se as the active ingredient for the production of an infusion solution of the following composition:

- | | | |
|----|--|-----------|
| | Active ingredient | 100 mg |
| | Hydroxypropyl-beta-cyclodextrin | 10 g |
| | NaOH q.s. or HCl q.s. for adjustment to pH 7.4 | |
| 15 | Sodium chloride q.s. or glucose q.s. for adjustment of the osmolality to 290 mOsm/kg | |
| | Water for injection (WFI) | ad 100 ml |

CLAIMS

1. A compound of formula (I)

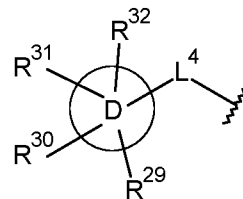


or a pharmaceutically acceptable salt thereof, wherein:

- 5 (i) R¹ is C₁-C₆-alkyl substituted with R¹², R¹³, R¹⁴, R¹⁵ and/or R¹⁶; and
R¹¹ is selected from hydrogen, halogen and C₁-C₆-alkyl; or
- (ii) R¹ and R¹¹, taken together with the atoms to which they are attached, form a
β-, γ-, δ- or ε-lactam;
- R² is selected from hydrogen, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, cyano-C₁-C₆-alkyl,
10 hydroxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-, (C₁-
C₆-alkyl)₂N-C₁-C₆-alkyl-, amino-C₁-C₆-alkyl-O-C₁-C₆-alkyl, C₁-C₆-alkyl-NH-
C₁-C₆-alkyl-O-C₁-C₆-alkyl-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-O-C₁-C₆-alkyl- and
C₃-C₁₂-cycloalkyl;
- R³ is selected from hydrogen, halogen, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, hydroxy-
15 C₁-C₆-alkyl, C₂-C₆-alkenyl, NO₂, CN, C₃-C₁₂-cycloalkyl, hydroxy-C₁-C₆-
alkoxy-C₁-C₆-alkyl, C₁-C₆-alkoxy and alkoxy-C₁-C₆-alkyl;
- R⁴ and R¹⁰ are each independently selected from hydrogen, halogen and C₁-C₆-alkyl;
each of R⁵, R⁶, R⁷, R⁸ and R⁹ is independently selected from hydrogen, halogen, C₁-
C₆-alkoxycarbonyl-C₁-C₆-alkoxy, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-,
20 hydroxy, C₁-C₆-alkoxy, C₁-C₆-alkylsulfanyl, C₁-C₆-alkylsulfonyloxy, halo-C₁-
C₆-alkoxy, cyano-C₁-C₆-alkoxy, C₂-C₆-alkynyloxy, C₁-C₆-alkoxy-C₂-C₆-
alkynyloxy, amino-C₂-C₆-alkynyloxy, hydroxy-C₂-C₆-alkynyloxy, halo-C₁-C₆-

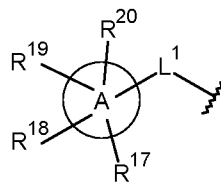
-541-

alkyl, sulfamoyl, C₁-C₆-alkylsulfamoyl, C₁-C₆-alkyl, amino-C₁-C₆-alkoxy-C₂-



C₆-alkynyloxy, amino-C₁-C₆-alkoxy and a group

each of R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ is independently selected from hydrogen, halogen, cyano, vinyl, hydroxy, amino, C₂-C₆-alkynyl, C₂-C₆-alkenyl, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-, carboxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkoxycarbonyl-NH-, carbamoyl, C₁-C₆-alkyl-NH-C(O)-, (C₁-C₆-alkyl)₂N-C(O)-, amino-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, amino-C₁-C₆-alkyl-NH-C(O)-, hydroxy-C₁-C₆-alkyl-NH-C(O)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-NH-C(O)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-NH-C(O)-, amino-C₁-C₆-alkyl-C(O)-NH-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-C(O)-NH-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-C(O)-N(C₁-C₆-alkyl)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-C(O)-N(C₁-C₆-alkyl)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-C(O)-N(C₁-C₆-alkyl)-, amino-C₁-C₆-alkyl-NH-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-, guanidino, guanidino-C₁-C₆-alkyl-C(O)-NH-, guanidino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-C₁-C₆-alkyl-NH-C(=NH)-NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, ureido-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-, hydroxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-CH(carboxy)-C₁-C₆-alkyl-C(O)-NH-, carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, amino-C₁-C₆-alkyl-, amino-C₂-C₆-alkenyl-, C₁-

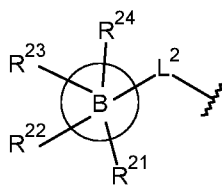


C₆-alkylimidoylamino- and a group

or any two of R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶, taken together with the carbon atom(s) to which they are attached, form a C₃-C₁₂-cycloalkyl;

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each of R^{17} , R^{18} , R^{19} and R^{20} is independently selected from hydrogen, halogen, cyano, carboxy, carboxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, oxo, imino, thiono, hydroxy- C_1 - C_6 -alkyl, cyano- C_1 - C_6 -alkyl, hydroxy, amino, C_1 - C_6 -alkyl-NH-, (C_1 - C_6 -alkyl) $_2$ N-, amino- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-, carbamimidoyl, C_1 - C_6 -alkyl-C(O)-, amino- C_1 - C_6 -alkyl-C(O)-, di- C_1 - C_6 -alkoxyphosphoryl, C_1 - C_6 -alkylsulfonyl,



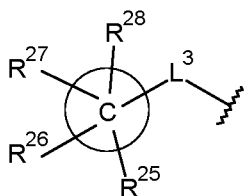
C_1 - C_6 -alkoxy, and a group

A, B and D are independently selected from C_6 - C_{14} -aryl, C_3 - C_{12} -cycloalkyl, C_2 - C_9 -heterocyclyl and C_1 - C_{13} -heteroaryl;

L^1 is selected from a covalent bond, -O-, -S-, S=O, SO₂, carbonyl, -C(O)-O-, -O-C(O)-, -C(O)-NH-, -NH-C(O)-, - C_1 - C_6 -alkyl-C(O)-NH-, - C_1 - C_6 -alkyl-NH-C(O)-, - C_1 - C_6 -alkyl-NH-C(O)- C_1 - C_6 -alkyl-, - C_1 - C_6 -alkyl-C(O)-N(C_1 - C_6 -alkyl)-, - C_1 - C_6 -alkyl-CH(OH)-, -C(O)- C_1 - C_6 -alkyl-N(C_1 - C_6 -alkyl)-C(O)-, -C(O)- C_1 - C_6 -alkyl-NH-C(O)- and -NH- C_1 - C_6 -alkyl-CH(NH₂)-C(O)-NH-;

L^2 and L^4 are independently selected from a covalent bond, -O-, - C_1 - C_6 -alkyl-, - C_1 - C_6 -alkoxy- and carbonyl;

each of R^{21} , R^{22} , R^{23} and R^{24} is independently selected from hydrogen, hydroxy, amino, halogen, cyano, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy, amino- C_1 - C_6 -alkyl-CH(OH)-C(O)-NH- and a group



C is selected from C_6 - C_{14} -aryl, C_3 - C_{12} -cycloalkyl, C_2 - C_9 -heterocyclyl and C_1 - C_{13} -heteroaryl;

L^3 is selected from a covalent bond, -O-, - C_1 - C_6 -alkyl-, - C_1 - C_6 -alkoxy- and carbonyl;

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each of R^{25} , R^{26} , R^{27} and R^{28} is independently selected from hydrogen, hydroxy, amino, halogen, cyano, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy and amino- C_1 - C_6 -alkyl; and

each of R^{29} , R^{30} , R^{31} and R^{32} is independently selected from hydrogen, C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkoxy, amino- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkoxy, amino- C_1 - C_6 -alkyl-NHC(O)-, halogen, cyano, hydroxy and amino.

2. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:

(i) R^1 is C_1 - C_6 -alkyl substituted with R^{12} , R^{13} , R^{14} , R^{15} and/or R^{16} ; and R^{11} is selected from hydrogen, halogen and C_1 - C_6 -alkyl; or

(ii) R^1 and R^{11} , taken together with the atoms to which they are attached, form a β -, γ -, δ - or ϵ -lactam;

R^2 is selected from hydrogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, cyano- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-, amino- C_1 - C_6 -alkyl-O- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-O- C_1 - C_6 -alkyl-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-O- C_1 - C_6 -alkyl- and C_3 - C_{12} -cycloalkyl;

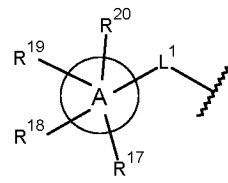
R^3 is selected from hydrogen, halogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, NO_2 , CN, C_3 - C_{12} -cycloalkyl, hydroxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy and alkoxy- C_1 - C_6 -alkyl;

R^4 and R^{10} are each independently selected from hydrogen, halogen and C_1 - C_6 -alkyl;

each of R^5 , R^6 , R^7 , R^8 and R^9 is independently selected from hydrogen, halogen, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkoxy, amino, C_1 - C_6 -alkyl-NH-, (C_1 - C_6 -alkyl) $_2$ N-, hydroxy, C_1 - C_6 -alkoxy, C_1 - C_6 -alkylsulfanyl, C_1 - C_6 -alkylsulfonyloxy, C_3 - C_{12} -cycloalkyl- C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy, C_6 - C_{14} -aryl- C_1 - C_6 -alkoxy, C_1 - C_{13} -heteroaryl- C_1 - C_6 -alkoxy, cyano- C_1 - C_6 -alkoxy, C_3 - C_{12} -cycloalkyloxy, C_2 - C_6 -alkynyloxy, C_1 - C_6 -alkoxy- C_2 - C_6 -alkynyloxy, cyano- C_3 - C_{12} -cycloalkyloxy, cyano- C_3 - C_{12} -cycloalkyl- C_1 - C_6 -alkoxy, amino- C_2 - C_6 -alkynyloxy, hydroxy- C_2 - C_6 -alkynyloxy, halo- C_1 - C_6 -alkyl, sulfamoyl, C_1 - C_6 -alkylsulfamoyl, C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkoxy- C_2 - C_6 -alkynyloxy and amino- C_1 - C_6 -alkoxy;

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R^{12} is selected from hydrogen, halogen, cyano, vinyl, hydroxy, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-, carboxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkoxycarbonyl-NH-, carbamoyl, C₁-C₆-alkyl-NH-C(O)-, (C₁-C₆-alkyl)₂N-C(O)-, aminoC₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, amino-C₁-C₆-alkyl-NH-C(O)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-NH-C(O)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-NH-C(O)-, amino-C₁-C₆-alkyl-C(O)-NH-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-C(O)-NH-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-C(O)-N(C₁-C₆-alkyl)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-C(O)-N(C₁-C₆-alkyl)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-C(O)-N(C₁-C₆-alkyl)-, amino-C₁-C₆-alkyl-NH-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-, guanidino, guanidino-C₁-C₆-alkyl-C(O)-NH-, guanidino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-C₁-C₆-alkyl-NH-C(=NH)-NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, ureido-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-, hydroxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-



NH-, C₁-C₆-alkylimidoylamino- and a group

R^{13} is selected from hydrogen, hydroxy, halogen, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N- and C₁-C₆-alkoxycarbonyl-NH-;

R^{14} is selected from hydrogen, halogen and hydroxy;

R^{15} is selected from hydrogen, halogen and hydroxy;

R^{16} is selected from hydrogen and hydroxy;

R^{17} is selected from hydrogen, carboxy, carboxy-C₁-C₆-alkyl, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, oxo, imino, hydroxy-C₁-C₆-alkyl, cyano-C₁-C₆-alkyl, hydroxy, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-, amino-C₁-C₆-alkyl, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-, carbamimidoyl, C₁-C₆-alkyl-C(O)-, di-C₁-C₆-alkoxyphosphoryl, C₁-C₆-alkylsulfonyl, and C₁-C₆-alkoxy;

R^{18} is hydrogen, hydroxy or C₁-C₆-alkyl;

R^{19} is hydrogen or hydroxy;

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R^{20} is hydrogen or hydroxy;

A is selected from C_6 - C_{14} -aryl, C_3 - C_{12} -cycloalkyl, C_2 - C_9 -heterocyclyl and C_1 - C_{13} -heteroaryl; and

L^1 is selected from a covalent bond, $-O-$, $-S-$, $S=O$, SO_2 , carbonyl, $-C(O)-O-$, $-O-C(O)-$, $-C(O)-NH-$, $-NH-C(O)-$, $-C_1-C_6$ -alkyl- $C(O)-NH-$, $-C_1-C_6$ -alkyl- $C(O)-N(C_1-C_6$ -alkyl)-, $-C_1-C_6$ -alkyl- $CH(OH)-$, $-C(O)-C_1-C_6$ -alkyl- $N(C_1-C_6$ -alkyl)- $C(O)-$, $-C(O)-C_1-C_6$ -alkyl- $NH-C(O)-$ and $-NH-C_1-C_6$ -alkyl- $CH(NH_2)-C(O)-NH-$.

3. The compound of formula (I) according to claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein:

- 10 (i) R^1 is C_1 - C_6 -alkyl substituted with R^{12} , R^{13} , R^{14} , R^{15} and/or R^{16} ; and R^{11} is selected from hydrogen and halogen; or
- (ii) R^1 and R^{11} , taken together with the atoms to which they are attached, form a δ - or ϵ -lactam.

4. The compound of formula (I) according to claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein:

15 R^1 is C_1 - C_6 -alkyl substituted with R^{12} , R^{13} , R^{14} , R^{15} and/or R^{16} ; and R^{11} is hydrogen.

5. The compound of formula (I) according to claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein:

20 R^1 is C_1 - C_6 -alkyl substituted with R^{12} , R^{13} , R^{14} , R^{15} and/or R^{16} ; and R^{11} is hydrogen;

wherein said C_1 - C_6 -alkyl is selected from methyl, ethyl, propyl, butyl, pentyl and 1-methyl-ethyl.

6. The compound of formula (I) according to any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R^2 is selected from hydrogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl- $NH-C_1-C_6$ -alkyl-, $(C_1-C_6$ -alkyl) $_2N-C_1-C_6$ -alkyl-, amino- C_1-C_6 -alkyl- $O-C_1-C_6$ -alkyl, and C_3 - C_{12} -cycloalkyl.

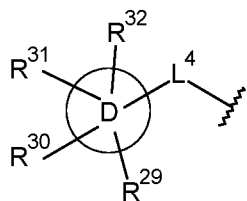
7. The compound of formula (I) according to any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R^2 is hydrogen or C_1 - C_6 -alkyl.

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8. The compound of formula (I) according to any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R^2 is hydrogen or methyl.
9. The compound of formula (I) according to any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein R^3 is selected from hydrogen,
5 halogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, NO_2 , cycloalkyl, and hydroxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl.
10. The compound of formula (I) according to any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_1 - C_6 -alkyl or halogen.
11. The compound of formula (I) according to any one of claims 1 to 8, or a
10 pharmaceutically acceptable salt thereof, wherein R^3 is selected from chloro, methyl and ethyl.
12. The compound of formula (I) according to any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, wherein R^4 is hydrogen.
13. The compound of formula (I) according to any one of claims 1 to 12, or a
15 pharmaceutically acceptable salt thereof, wherein R^5 is hydrogen, halogen or halo- C_1 - C_6 -alkyl.
14. The compound of formula (I) according to any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof, wherein R^5 is hydrogen or halogen.
15. The compound of formula (I) according to any one of claims 1 to 12, or a
20 pharmaceutically acceptable salt thereof, wherein R^5 is selected from hydrogen, fluoro and chloro.
16. The compound of formula (I) according to any one of claims 1 to 15, or a pharmaceutically acceptable salt thereof, wherein R^6 is hydrogen or halogen.
17. The compound of formula (I) according to any one of claims 1 to 15, or a
25 pharmaceutically acceptable salt thereof, wherein R^6 is hydrogen or fluoro.
18. The compound of formula (I) according to any one of claims 1 to 17, or a pharmaceutically acceptable salt thereof, wherein R^7 is selected from halogen, hydroxy, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy, cyano- C_1 - C_6 -alkoxy, amino- C_2 - C_6 -

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alkynyloxy, amino-C₁-C₆-alkoxy-C₂-C₆-alkynyloxy; and a group

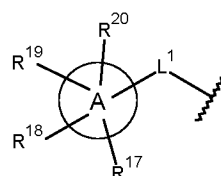


, wherein:

- D is C₁-C₁₃-heteroaryl;
 L⁴ is selected from a covalent bond, -O- and C₁-C₆-alkoxy;
 5 R²⁹ is selected from hydrogen, halogen, C₁-C₆-alkyl, C₁-C₆-alkoxy, halo-C₁-C₆-alkyl, amino-C₁-C₆-alkoxy and amino-C₁-C₆-alkyl-NH-C(O)-; and
 R³⁰, R³¹ and R³² are all hydrogen.
19. The compound of formula (I) according to any one of claims 1 to 17, or a pharmaceutically acceptable salt thereof, wherein R⁷ is selected from C₁-C₆-alkoxy, halo-C₁-C₆-alkoxy and cyano-C₁-C₆-alkoxy.
 10
20. The compound of formula (I) according to any one of claims 1 to 17, or a pharmaceutically acceptable salt thereof, wherein R⁷ is selected from methoxy, difluoromethoxy and cyanomethoxy.
21. The compound of formula (I) according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof, wherein R⁸ is hydrogen.
 15
22. The compound of formula (I) according to any one of claims 1 to 21, or a pharmaceutically acceptable salt thereof, wherein R⁹ is hydrogen.
23. The compound of formula (I) according to any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof, wherein R¹⁰ is hydrogen.
- 20 24. The compound of formula (I) according to any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, wherein
 R¹² is selected from hydrogen, halogen, vinyl, hydroxy, amino, C₂-C₆-alkynyl, (C₁-C₆-alkyl)₂N-, carboxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkoxycarbonyl-NH-, carbamoyl, C₁-C₆-alkyl-NH-C(O)-, (C₁-C₆-alkyl)₂N-C(O)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-NH-C(O)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-NH-C(O)-, amino-C₁-C₆-alkyl-NH-C(O)-,
 25

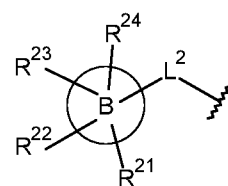
-548-

amino-C₁-C₆-alkyl-C(O)-NH-, hydroxy-C₁-C₆-alkyl-NH-C(O)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-NH-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-, guanidino, guanidino-C₁-C₆-alkyl-C(O)-NH-, guanidino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-C₁-C₆-alkyl-NH-C(=NH)-NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, ureido-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-, hydroxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-CH(carboxy)-C₁-C₆-alkyl-C(O)-NH-, carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-, carboxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, amino-C₂-C₆-alkenyl,



C₁-C₆-alkylimidoamino- and a group ; wherein:

A is selected from C₆-C₁₄-aryl, C₂-C₉-heterocyclyl and C₁-C₁₃-heteroaryl;
 L¹ is selected from a covalent bond, -O-, -S-, SO₂, carbonyl, -C(O)-O-, -C(O)-NH-, -C₁-C₆-alkyl-C(O)-NH-, -C₁-C₆-alkyl-NH-C(O)-, -C₁-C₆-alkyl-NH-C(O)-C₁-C₆-alkyl-, -C₁-C₆-alkyl-CH(OH)-, -C(O)-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)- and -NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-;
 R¹⁷ is selected from hydrogen, halogen, carboxy, carboxy-C₁-C₆-alkyl, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, oxo, imino, thiono, hydroxy-C₁-C₆-alkyl, cyano-C₁-C₆-alkyl, hydroxy, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-, carbamimidoyl, C₁-C₆-alkyl-C(O)-, amino-C₁-C₆-alkyl-C(O)-, di-C₁-C₆-



alkoxyphosphoryl, C₁-C₆-alkylsulfonyl, and a group ;

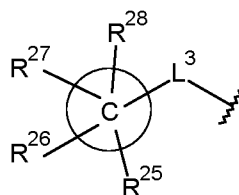
R¹⁸ is selected from hydrogen, hydroxy and C₁-C₆-alkyl;

R¹⁹ and R²⁰ are both hydrogen or hydroxy;

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B is selected from C₃-C₁₂-cycloalkyl, C₂-C₉-heterocyclyl and C₁-C₁₃-heteroaryl;

L² is selected from -O-, -C₁-C₆-alkyl- and carbonyl;



R²¹ is hydrogen or a group ;

5 R²² is hydrogen or amino-C₁-C₆-alkyl-CH(OH)-C(O)-NH-;

R²³ and R²⁴ are both independently selected from hydrogen, amino and hydroxy;

C is C₂-C₉-heterocyclyl;

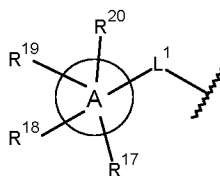
L³ is -O-;

10 R²⁵ is amino-C₁-C₆-alkyl-; and

R²⁶, R²⁷ and R²⁸ are all hydroxy.

25. The compound of formula (I) according to any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, wherein R¹² is selected from C₁-C₆-alkyl-NH-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, hydroxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-,

15 amino, amino-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-NH-C(O)-NH-, guanidino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, guanidino, guanidino-C₁-C₆-



alkyl-C(O)-NH- and a group ; wherein:

A is C₂-C₉-heterocyclyl;

20 L¹ is selected from a covalent bond, -C(O)-NH- and carbonyl;

R¹⁷ is selected from hydrogen, hydroxy, C₁-C₆-alkyl, carbamimidoyl, hydroxy-C₁-C₆-alkyl and imino;

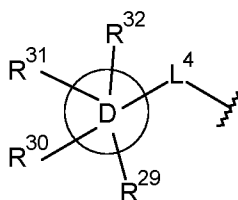
R¹⁸ is hydrogen or hydroxy; and

R¹⁹ and R²⁰ are both hydrogen.

26. The compound of formula (I) according to any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, wherein R^{12} is selected from 4-piperidyl, piperazin-1-yl, [(2R)-2-amino-5-guanidino-pentanoyl]amino, [(2S)-2-amino-5-guanidino-pentanoyl]amino, 2-aminoethylcarbamoylamino, guanidino, 5-guanidinopentanoylamino, amino, 3-aminopropylcarbamoylamino, 1-carbamimidoyl-4-piperidyl, [(2S,4S)-4-hydroxy-4-methyl-pyrrolidine-2-carbonyl]amino, [(2S)-2-amino-3-hydroxy-propanoyl]amino, (2-aminoacetyl)amino, 3-aminopropanoylamino, [(2S,3R)-2-amino-3-hydroxy-butanoyl]amino, [(2S)-2,5-diaminopentanoyl]amino, (4-amino-3-hydroxy-butanoyl)amino, [(2S)-2,6-diaminohexanoyl]amino, [(2S)-2,4-diaminobutanoyl]amino, [(2S)-2,3-diaminopropanoyl]amino, (3S)-3-(hydroxymethyl)piperazine-1-carbonyl, methyl-[2-(methylamino)ethyl]carbamoyl, (2-iminoimidazolidine-4-carbonyl)amino, [(2S,4R)-4-hydroxypyrrolidine-2-carbonyl]amino and [(2S)-2-amino-3-guanidino-propanoyl]amino.
27. The compound of formula (I) according to any one of claims 1 to 26, or a pharmaceutically acceptable salt thereof, wherein:
 R^{13} is selected from hydrogen, hydroxy, halogen, amino and C_1 - C_6 -alkoxycarbonyl-NH-; and
 R^{14} is selected from hydrogen, halogen and hydroxy; or
 R^{13} and R^{14} , taken together with the carbon atom(s) to which they are attached, form a C_3 - C_{12} -cycloalkyl.
28. The compound of formula (I) according to any one of claims 1 to 26, or a pharmaceutically acceptable salt thereof, wherein R^{13} is hydrogen.
29. The compound of formula (I) according to any one of claims 1 to 26, or a pharmaceutically acceptable salt thereof, wherein R^{14} is hydrogen.
30. The compound of formula (I) according to any one of claims 1 to 29, or a pharmaceutically acceptable salt thereof, wherein R^{15} is selected from hydrogen, halogen and hydroxy.
31. The compound of formula (I) according to any one of claims 1 to 29, or a pharmaceutically acceptable salt thereof, wherein R^{15} is hydrogen.

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32. The compound of formula (I) according to any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, wherein R^{16} is hydrogen or hydroxy.
33. The compound of formula (I) according to any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, wherein R^{16} is hydrogen.
- 5 34. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:
- (i) R^1 is C_1 - C_6 -alkyl substituted with R^{12} , R^{13} , R^{14} , R^{15} and/or R^{16} ; and R^{11} is selected from hydrogen and halogen; or
- (ii) R^1 and R^{11} , taken together with the atoms to which they are attached, form a δ -
 10 or ϵ -lactam;
- R^2 is selected from hydrogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-, (C_1 - C_6 -alkyl) $_2$ N- C_1 - C_6 -alkyl-, amino- C_1 - C_6 -alkyl-O- C_1 - C_6 -alkyl, and C_3 - C_{12} -cycloalkyl;
- R^3 is selected from hydrogen, halogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, hydroxy-
 15 C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, NO_2 , cycloalkyl, and hydroxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl;
- R^4 , R^8 , R^9 and R^{10} are all hydrogen;
- R^5 is selected from hydrogen, halogen and halo- C_1 - C_6 -alkyl;
- R^6 is hydrogen or halogen;
- 20 R^7 is selected from halogen, hydroxy, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy, cyano- C_1 - C_6 -alkoxy, amino- C_2 - C_6 -alkynyloxy, amino- C_1 - C_6 -alkoxy- C_2 - C_6 -

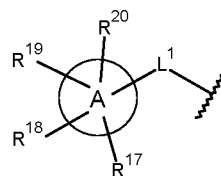


alkynyloxy; and a group , wherein:

- D is C_1 - C_{13} -heteroaryl;
- L^4 is selected from a covalent bond, $-O-$ and C_1 - C_6 -alkoxy;
- 25 R^{29} is selected from hydrogen, halogen, C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkoxy and amino- C_1 - C_6 -alkyl-NH-C(O)-;
- R^{30} , R^{31} and R^{32} are all hydrogen;

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R^{12} is selected from hydrogen, halogen, vinyl, hydroxy, amino, C₂-C₆-alkynyl, (C₁-C₆-alkyl)₂N-, carboxy, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkoxycarbonyl-NH-, carbamoyl, C₁-C₆-alkyl-NH-C(O)-, (C₁-C₆-alkyl)₂N-C(O)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-NH-C(O)-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-NH-C(O)-, amino-C₁-C₆-alkyl-NH-C(O)-, amino-C₁-C₆-alkyl-C(O)-NH-, hydroxy-C₁-C₆-alkyl-NH-C(O)-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-NH-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-C₁-C₆-alkyl-C(O)-NH-, amino-C₁-C₆-alkyl-CH(OH)-, guanidino, guanidino-C₁-C₆-alkyl-C(O)-NH-, guanidino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-C₁-C₆-alkyl-NH-C(=NH)-NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, ureido-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-, hydroxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-CH(carboxy)-C₁-C₆-alkyl-C(O)-NH-, carboxy-CH(NH₂)-C₁-C₆-alkyl-C(O)-NH-CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-, carboxy-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-CH(guanidino-C₁-C₆-alkyl)-C(O)-NH-, amino-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-, amino-C₂-C₆-alkenyl,



C₁-C₆-alkylimidoylamino- and a group ; wherein:

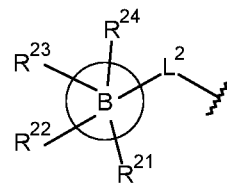
A is selected from C₆-C₁₄-aryl, C₂-C₉-heterocyclyl and C₁-C₁₃-heteroaryl;

L^1 is selected from a covalent bond, -O-, -S-, SO₂, carbonyl, -C(O)-O-, -C(O)-NH-, -C₁-C₆-alkyl-C(O)-NH-, -C₁-C₆-alkyl-NH-C(O)-, -C₁-C₆-alkyl-NH-C(O)-C₁-C₆-alkyl-, -C₁-C₆-alkyl-CH(OH)-, -C(O)-C₁-C₆-alkyl-N(C₁-C₆-alkyl)-C(O)- and -NH-C₁-C₆-alkyl-CH(NH₂)-C(O)-NH-;

R^{17} is selected from hydrogen, halogen, carboxy, carboxy-C₁-C₆-alkyl, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, oxo, imino, thiono, hydroxy-C₁-C₆-alkyl, cyano-C₁-C₆-alkyl, hydroxy, amino, C₁-C₆-alkyl-NH-, (C₁-C₆-alkyl)₂N-, C₁-C₆-alkyl-NH-C₁-C₆-alkyl-, (C₁-C₆-alkyl)₂N-C₁-C₆-alkyl-,

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carbamimidoyl, C₁-C₆-alkyl-C(O)-, amino-C₁-C₆-alkyl-C(O)-, di-C₁-C₆-



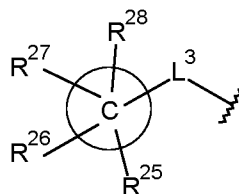
alkoxyphosphoryl, C₁-C₆-alkylsulfonyl, and a group

R¹⁸ is selected from hydrogen, hydroxy and C₁-C₆-alkyl;

R¹⁹ and R²⁰ are both hydrogen or hydroxy;

5 B is selected from C₃-C₁₂-cycloalkyl, C₂-C₉-heterocyclyl and C₁-C₁₃-heteroaryl;

L² is selected from -O-, -C₁-C₆-alkyl- and carbonyl;



R²¹ is hydrogen or a group ;

R²² is hydrogen or amino-C₁-C₆-alkyl-CH(OH)-C(O)-NH-;

10 R²³ and R²⁴ are both independently selected from hydrogen, amino and hydroxy;

C is C₂-C₉-heterocyclyl;

L³ is -O-;

R²⁵ is amino-C₁-C₆-alkyl-; and

15 R²⁶, R²⁷ and R²⁸ are all hydroxy;

R¹³ is selected from hydrogen, hydroxy, halogen, amino and C₁-C₆-alkoxycarbonyl-NH-; and

R¹⁴ is selected from hydrogen, halogen and hydroxy; or

20 R¹³ and R¹⁴, taken together with the carbon atom(s) to which they are attached, form a C₃-C₁₂-cycloalkyl;

R¹⁵ is selected from hydrogen, halogen and hydroxy; and

R¹⁶ is hydrogen or hydroxy.

35. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:

25 R¹ is C₁-C₆-alkyl substituted with R¹², R¹³, R¹⁴, R¹⁵ and/or R¹⁶;

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R^2 is hydrogen or C_1 - C_6 -alkyl;

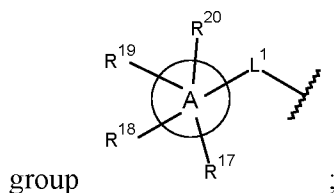
R^3 is halogen or C_1 - C_6 -alkyl;

R^4 , R^8 , R^9 , R^{10} , R^{11} , R^{13} , R^{14} , R^{15} , R^{16} , R^{19} and R^{20} are all hydrogen;

R^5 and R^6 are each independently hydrogen or halogen;

5 R^7 is selected from C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkoxy and cyano- C_1 - C_6 -alkoxy;

R^{12} is selected from C_1 - C_6 -alkyl-NH- C_1 - C_6 -alkyl-N(C_1 - C_6 -alkyl)-C(O)-, hydroxy- C_1 - C_6 -alkyl-CH(NH₂)-C(O)-NH-, amino, amino- C_1 - C_6 -alkyl-C(O)-NH-, amino- C_1 - C_6 -alkyl-CH(NH₂)-C(O)-NH-, amino- C_1 - C_6 -alkyl-CH(OH)- C_1 - C_6 -alkyl-C(O)-NH-, amino- C_1 - C_6 -alkyl-NH-C(O)-NH-, guanidino- C_1 - C_6 -alkyl-CH(NH₂)-C(O)-NH-, guanidino, guanidino- C_1 - C_6 -alkyl-C(O)-NH- and a



R^{17} is selected from hydrogen, hydroxy, C_1 - C_6 -alkyl, carbamimidoyl, hydroxy- C_1 - C_6 -alkyl and imino;

R^{18} is hydrogen or hydroxy;

15 A is C_2 - C_9 -heterocyclyl; and

L^1 is selected from a covalent bond, -C(O)-NH- and carbonyl.

36. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is C_1 - C_6 -alkyl substituted with R^{12} , R^{13} , R^{14} , R^{15} and/or R^{16} ;

20 wherein said C_1 - C_6 -alkyl is selected from methyl, ethyl, propyl, butyl, pentyl and 1-methyl-ethyl;

R^2 is hydrogen or methyl;

R^3 is selected from chloro, methyl and ethyl;

R^4 , R^8 , R^9 , R^{10} , R^{11} , R^{13} , R^{14} , R^{15} , R^{16} , R^{19} and R^{20} are all hydrogen;

25 R^5 is selected from hydrogen, fluoro and chloro;

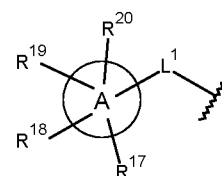
R^6 is hydrogen or fluoro;

R^7 is selected from methoxy, difluoromethoxy and cyanomethoxy;

R^{12} is selected from [(2R)-2-amino-5-guanidino-pentanoyl]amino, [(2S)-2-amino-5-guanidino-pentanoyl]amino, 2-aminoethylcarbamoylamino, guanidino, 5-

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guanidinopentanoylamino, amino, 3-aminopropylcarbamoylamino, [(2S)-2-amino-3-hydroxy-propanoyl]amino, (2-aminoacetyl)amino, 3-aminopropanoylamino, [(2S,3R)-2-amino-3-hydroxy-butanoyl]amino, [(2S)-2,5-diaminopentanoyl]amino, (4-amino-3-hydroxy-butanoyl)amino, [(2S)-2,6-diaminohexanoyl]amino, [(2S)-2,4-diaminobutanoyl]amino, [(2S)-2,3-diaminopropanoyl]amino, methyl-[2-(methylamino)ethyl]carbamoyl, [(2S)-2-



amino-3-guanidino-propanoyl]amino and a group

R^{17} is selected from hydrogen, hydroxy, methyl, carbamimidoyl, hydroxymethyl and imino;

10 R^{18} is hydrogen or hydroxy;

A is selected from 4-piperidyl, piperazin-1-yl, pyrrolidin-2-yl and imidazolidin-4-yl; and

L^1 is selected from a covalent bond, $-C(O)-NH-$ and carbonyl.

37. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound of formula (I) is selected from:

2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-piperidylmethyl)benzamide;

4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-piperidyl)ethyl]benzamide;

20 N-(6-aminohexyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;

4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-piperidyl)ethyl]benzamide;

4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(3-piperazin-1-ylpropyl)benzamide;

25 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N,2-trimethyl-benzamide;

2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;

- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethyl-benzamide;
- 2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 5 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[3-(3-oxopiperazin-1-yl)propyl]benzamide;
- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- N-(6-aminohexyl)-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 10 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)benzamide;
- 2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
- 15 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(4-pyridylmethyl)benzamide;
- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1,1-dioxothian-4-yl)methyl]benzamide;
- 2-chloro-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 20 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(5-morpholinopentyl)benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(3-piperazin-1-ylsulfonylpropyl)benzamide;
- 25 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-piperidylmethyl)benzamide;
- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(tetrahydropyran-4-ylmethyl)benzamide;
- 30 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;

- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 5 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-benzamide;
- 2-bromo-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
- 10 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-oxo-3-piperazin-1-yl-propyl)benzamide;
- 15 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(1-methyl-4-piperidyl)ethyl]benzamide;
- N-(5-aminopentyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(pyrrolidin-3-ylmethyl)benzamide;
- 20 2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 25 4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-tetrahydropyran-4-ylethyl)benzamide;
- 30 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-2-(trifluoromethyl)benzamide;
- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N,2-trimethyl-benzamide;

- 4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 2-chloro-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
- 5 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(1-methyl-4-piperidyl)methyl]benzamide;
- 4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(1-methyl-4-piperidyl)ethyl]benzamide;
- 10 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-iodo-N-methyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-piperidylmethyl)benzamide;
- 15 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[3-(2-oxopiperazin-1-yl)propyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-morpholinobutyl)benzamide;
- 2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)benzamide;
- 20 4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(4-oxo-4-piperazin-1-yl-butyl)benzamide;
- 25 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(pyrrolidin-3-ylmethyl)benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[3-(4-methyl-3-oxo-piperazin-1-yl)propyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-hydroxyethyl)-N-methyl-benzamide;
- 30 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(4-piperidyl)ethyl]benzamide;

- N-[(1-carbamimidoyl-4-piperidyl)methyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;
- 5 N-[3-(5-amino-1,3-dioxan-2-yl)propyl]-4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 10 N-(4-aminobutyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-
- 15 (4-morpholinobutyl)benzamide;
- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethylbenzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 20 N-(4-aminobutyl)-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide;
- 4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(1-methyl-4-piperidyl)ethyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-iodo-N-
- 25 methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- N-[3-(1,1-dioxo-1,4-thiazinan-4-yl)propyl]-4-[[3-(3-fluoro-4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;
- N-(4-aminobutyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylbenzamide;
- 30 2-chloro-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(4-methylpiperazin-1-yl)ethyl]benzamide;

- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- N-[2-(1-acetyl-4-piperidyl)ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 5 2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(4-piperidylmethyl)benzamide;
- N-[(5-amino-1,3-dioxan-2-yl)methyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- N-[(5-amino-1,3-dioxan-2-yl)methyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 10 N-(4-aminobutyl)-4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- N-(2-amino-2-oxo-ethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 15 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(4-morpholinobutyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(3-morpholinopropyl)benzamide;
- N,N-diethyl-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 20 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-2-vinyl-benzamide;
- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(tetrahydropyran-4-ylmethyl)benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(4-piperidylmethyl)benzamide;
- 25 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-piperidylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(2-piperazin-1-ylethyl)benzamide;
- 30 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-oxo-2-(3-oxopiperazin-1-yl)ethyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-oxo-2-piperazin-1-yl-ethyl)benzamide;

- N-[2-(4-hydroxy-1-piperidyl)-2-oxo-ethyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-piperidylmethyl)benzamide;
- 5 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-diethyl-benzamide;
- N-(2-hydroxyethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- N-(3-aminopropyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 10 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(tetrahydrofuran-3-ylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(1-methyl-4-piperidyl)methyl]benzamide;
- 15 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethyl-benzamide;
- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(1-methyl-4-piperidyl)methyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(3-oxopiperazin-1-yl)ethyl]benzamide;
- 20 N-[2-(dimethylamino)-2-oxo-ethyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-2-nitro-benzamide;
- 25 N-[2-hydroxy-1-(hydroxymethyl)ethyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)-2-vinyl-benzamide;
- N-[2-[3-[(dimethylamino)methyl]pyrrolidin-1-yl]-2-oxo-ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 30 N-[2-(1-diethoxyphosphoryl-4-piperidyl)ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;

- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(tetrahydrothiopyran-4-ylmethyl)benzamide;
- N-[4-[2-(aminomethyl)morpholin-4-yl]-4-oxo-butyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 5 N-(3-aminopropyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-isopropyl-N-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-10 (tetrahydropyran-3-ylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-piperazin-1-ylpropyl)benzamide;
- N-(2-hydroxyethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
- 15 4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(1-methyl-4-piperidyl)methyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(3-oxopiperazin-1-yl)ethyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(1,1-20 dimethyl-2-morpholino-ethyl)-2-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(tetrahydrofuran-3-ylmethyl)benzamide;
- tert-butyl N-[5-[[4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]pentyl]carbamate;
- 25 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(3-piperidylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-30 (methylamino)-2-oxo-ethyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-2-propyl-benzamide;

- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(hydroxymethyl)-N-methyl-benzamide;
N-(3-aminopropyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
5 methyl (2S)-2-amino-6-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]hexanoate;
N-(2-aminoethyl)-4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
N,N-diethyl-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-
10 benzamide;
N-(3-aminopropyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
N-(3-aminopropyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
15 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-morpholinoethyl)benzamide;
4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-morpholinoethyl)benzamide;
4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-
20 N-(tetrahydropyran-4-ylmethyl)benzamide;
2-cyclopropyl-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(morpholin-2-ylmethyl)benzamide;
25 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(morpholin-2-ylmethyl)benzamide;
4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-
30 N-[2-(1-methylsulfonyl-4-piperidyl)ethyl]benzamide;
N-(3-aminopropyl)-4-[[3-(4-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;

- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-[rac-(2R,6S)-2,6-dimethylmorpholin-4-yl]ethyl]benzamide;
- 2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-[2-(1-piperidyl)ethyl]benzamide;
- 5 6-[[3-(2-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3,4-dihydro-2H-isoquinolin-1-one;
- N-(2-aminoethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 10 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(pyrrolidin-3-ylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)-2-vinyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(morpholin-3-ylmethyl)benzamide;
- 15 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-[rac-(2R,6S)-2,6-dimethylmorpholin-4-yl]ethyl]benzamide;
- N-(2-aminoethyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 20 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(4-methylpiperazin-1-yl)-2-oxo-ethyl]benzamide;
- N-[2-(dimethylamino)-2-oxo-ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-hydroxyethoxymethyl)-N-methyl-benzamide;
- 25 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-morpholino-2-oxo-ethyl)benzamide;
- N-[2-[4-(2,2-difluoroethyl)piperazin-1-yl]ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(morpholin-2-ylmethyl)benzamide;
- 30 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-2-[(E)-prop-1-enyl]benzamide;

- 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-hydroxyethyl)benzamide;
- 2-chloro-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-pyridylmethyl)benzamide;
- 5 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(2,2-dimethylmorpholin-4-yl)ethyl]-N,2-dimethyl-benzamide;
- methyl (2S)-2-(tert-butoxycarbonylamino)-6-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]hexanoate;
- 10 N-[2-(dimethylamino)ethyl]-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(piperazin-2-ylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-
- 15 [2-(3-oxomorpholin-4-yl)ethyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(2-oxopiperazin-1-yl)ethyl]benzamide;
- N-(2-aminoethyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 20 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperidylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[1-(hydroxymethyl)-2-morpholino-ethyl]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-
- 25 (2-morpholino-2-oxo-ethyl)benzamide;
- 4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(4-piperidylmethyl)benzamide;
- N-(2-aminoethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 30 N-[(2S)-2-aminopropyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(morpholin-3-ylmethyl)benzamide;

- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-morpholino-2-oxo-ethyl)benzamide;
- 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(dimethylamino)ethyl]-N-methyl-benzamide;
- 5 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[3-(1-piperidyl)propyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-[methyl-[2-(4-methylpiperazin-1-yl)-2-oxo-ethyl]amino]-2-oxo-ethyl]benzamide;
- 10 N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-
- 15 (hydroxymethyl)-N,N-dimethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(dimethylamino)ethyl]-N,2-dimethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(4-hydroxy-4-piperidyl)methyl]-N,2-dimethyl-benzamide;
- 20 4-[3-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]piperazine-2-carboxylic acid;
- N-(3-aminopropyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(4-
- 25 hydroxy-4-piperidyl)methyl]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-bis(2-hydroxyethyl)-2-methyl-benzamide;
- 4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-(dimethylamino)propyl]benzamide;
- 30 N-(2-aminoethyl)-4-[[3-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(1-piperidyl)ethyl]benzamide;

- N-(2-aminoethyl)-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(1-piperidyl)ethyl]benzamide;
- 5 N-[(2R)-2-aminopropyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)-N-(2,2,2-trifluoroethyl)benzamide;
- N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 10 N-[(1R)-2-amino-1-methyl-ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[2-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]acetyl]piperazine-2-carboxylic acid;
- 15 4-[[4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]butanoic acid;
- (2S)-2-amino-6-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]hexanoic acid;
- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 20 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(4-pyridyl)ethyl]benzamide;
- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(3-piperazin-1-ylpropyl)benzamide;
- 25 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(5-piperazin-1-ylpentyl)benzamide;
- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-[2-(4-piperidyl)ethyl]benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(5-oxo-5-piperazin-1-yl-pentyl)benzamide;
- 30 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-pyridylmethyl)benzamide;

- 6-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-3,4-dihydroisoquinolin-1-one;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(pyrimidin-4-ylmethyl)benzamide;
- 5 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(3-piperazin-1-ylpropyl)benzamide;
- N-(3-aminopropyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-10 (pyrrolidin-3-ylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-ethyl-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-imidazol-1-ylethyl)-N,2-dimethyl-benzamide;
- 15 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1S)-1-(hydroxymethyl)-2-(1H-imidazol-5-yl)ethyl]-2-methyl-benzamide;
- N-(azetidin-3-ylmethyl)-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- N-(3-aminopropyl)-2-ethyl-4-[[3-(2-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 20 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(4-hydroxy-4-piperidyl)ethyl]-2-methyl-benzamide;
- 2-[2-(dimethylamino)ethyl]-6-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3,4-dihydroisoquinolin-1-one;
- 25 N-[3-(azetidin-1-yl)propyl]-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(1H-imidazol-2-yl)ethyl]-N,2-dimethyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-[2-(methylaminomethyl)morpholin-4-yl]ethyl]benzamide;
- 30 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(3-hydroxyazetidin-3-yl)methyl]-2-methyl-benzamide;

- N-[2-[2-[(dimethylamino)methyl]morpholin-4-yl]ethyl]-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- N-(3-aminopropyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-benzamide;
- 5 N-(3-aminopropyl)-4-[[3-(4-chloro-2-fluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-cyclopropyl-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- N-(2,2-difluoroethyl)-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-(2-piperazin-1-ylethyl)benzamide;
- 10 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(4-hydroxy-4-piperidyl)methyl]-2-methyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(3-hydroxypyrrolidin-3-yl)methyl]-2-methyl-benzamide;
- 15 4-[[3-[4-(4-aminobut-2-ynoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(3-aminopropyl)-2-ethyl-benzamide;
- 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(2R,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]benzamide;
- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-hydroxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 N-[3-(2-aminoethylcarbamoylamino)propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 N-[2-[[[(2S)-2-amino-5-(4,5-dihydro-1H-imidazol-2-ylamino)pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-guanidinobutyl)-2-methyl-benzamide;
- 10 N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(1-carbamimidoyl-4-piperidyl)methyl]-4-[[3-(3-chloro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 N-[(2R)-2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(2S)-2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 3-[4-[2-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]ethyl]-1-piperidyl]propanoic acid;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(3-imidazol-1-ylpropyl)benzamide;
- 25 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-(5-guanidinopentanoylamino)ethyl]benzamide;
- N-(5-aminopentyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(2-oxo-1H-pyridin-4-yl)methyl]benzamide;
- 30 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1-methyl-6-oxo-3-pyridyl)methyl]benzamide;

- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(oxetan-3-ylmethyl)benzamide;
- N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 N-[(1-carbamimidoyl-4-piperidyl)methyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(3-hydroxypropyl)benzamide;
- 10 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[2-(dimethylamino)acetyl]amino]ethyl]-2-ethyl-benzamide;
- 2-chloro-4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(4-pyridyl)ethyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-(5-methyl-4H-1,2,4-triazol-3-yl)ethyl]benzamide;
- 15 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1-methyl-2-oxo-4-pyridyl)methyl]benzamide;
- N-[3-(3-aminopropylcarbamoylamino)propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 N-[(1-carbamimidoyl-4-piperidyl)methyl]-2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(1-methylazetidin-3-yl)methyl]benzamide;
- N-[(1-carbamimidoyl-4-piperidyl)methyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-(4-pyridyl)propyl]benzamide;
- N-(3-aminopropyl)-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(3-pyrrolidin-1-ylpropyl)benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-(4-piperidyl)ethyl]benzamide;

- 6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-[2-(methylamino)ethyl]-3,4-dihydroisoquinolin-1-one;
- 3-[4-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethyl]-1-piperidyl]propanoic acid;
- 5 2-chloro-4-[[3-[3-chloro-4-(cyanomethoxy)-2-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(4-pyridyl)ethyl]benzamide;
- 2-(3-aminopropyl)-6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3,4-dihydroisoquinolin-1-one;
- N-(4-aminobutyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-hydroxyethyl)-3,4-dihydroisoquinolin-1-one;
- N-[(1R)-2-[[2-(2S)-2-amino-5-guanidino-pentanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-
- 15 benzamide;
- N-[2-[[2-(2S)-2-amino-5-ureido-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[2-(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-
- 20 ethyl-benzamide;
- N-(3-amino-2-hydroxy-propyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(1R)-3-amino-1-methyl-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 N-(2-amino-1,1-dimethyl-ethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(2-hydroxy-3-pyrrolidin-1-yl-propyl)benzamide;
- N-(3-amino-1,1-dimethyl-propyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 N-[2-(3-aminopropylcarbamoylamino)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- 2-chloro-4-[[3-[4-(1-cyanoethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-piperazin-1-ylethyl)benzamide;
N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 N-[(3S)-3-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]butyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-(3-aminopropyl)-4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(triazolo[4,5-b]pyridin-3-yloxy)ethyl]benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-[3-[(2S)-3-oxoaziridin-2-yl]propanoylamino]ethyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-(1-methyltetrazol-5-yl)sulfanylethyl]benzamide;
- 15 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[2-[3-[(2S)-1-methyl-3-oxo-aziridin-2-yl]propanoylamino]ethyl]benzamide;
N-[2-(2-aminoethylcarbamoylamino)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 N-(2-aminoethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
1-[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-N-[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]piperidine-4-carboxamide;
- N-[(3R)-3-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]butyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(3-hydroxyazetidin-3-yl)methyl]benzamide;
- 30 methyl (2S)-3-amino-2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propanoate;

- N-[2-[1-(2-cyanoethyl)-4-piperidyl]ethyl]-4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethylbenzamide;
- 5 N-[(1S)-2-[[2S)-2-amino-5-guanidino-pentanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;
- N-[3-[[2S)-2-amino-5-guanidino-pentanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;
- 10 N-(3-amino-2,2-dimethyl-propyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;
- (2S)-2-amino-6-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]hexanoic acid;
- methyl (2R)-3-amino-2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propanoate;
- 15 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(3-hydroxypyrrolidin-3-yl)methyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-[1-[2-(dimethylamino)ethyl]tetrazol-5-yl]sulfanylpropyl]-N,2-dimethylbenzamide;
- N-[2-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]piperazine-1-carboxamide;
- 20 N-[2-[[2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,4-dichlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;
- 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[3-(1-methyltetrazol-5-yl)sulfanylpropyl]benzamide;
- 25 N-[2-[(3S)-3-amino-2-oxo-1-piperidyl]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethylbenzamide;
- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(1H-tetrazol-5-yl)ethyl]benzamide;
- (2S)-4-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethylcarbonyl]piperazine-2-carboxylic acid;
- 30 (2S)-2-amino-6-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]hexanoic acid;

- (2S)-4-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethylcarbamoyl]piperazine-2-carboxylic acid;
N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
5 4-[[3-[4-(4-aminobut-2-ynoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,N,2-trimethyl-benzamide;
N-[(1S)-3-amino-1-methyl-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
4-[3-[[2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]amino]propyl]piperazine-2-carboxylic acid;
10 N-[3-amino-1-(difluoromethyl)propyl]-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,4-dichlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
15 (2R)-4-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethylcarbamoyl]piperazine-2-carboxylic acid;
(2R)-4-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethylcarbamoyl]piperazine-2-carboxylic acid;
N-[2-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]piperidine-4-carboxamide;
20 N-(3-aminopropyl)-2-(2,2-difluoroethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
N-(3-amino-1-ethyl-propyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
25 N-(3-amino-1-methyl-propyl)-4-[[3-(4-chloro-2,3-difluoro-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
(2S)-2-amino-5-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propylamino]-5-oxo-pentanoic acid;
4-[[3-[4-(4-aminobut-2-ynoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-[2-(1-methyl-4-piperidyl)ethyl]benzamide;
30 N-[3-amino-1-(trifluoromethyl)propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-[(1R)-2-amino-1-phenyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
methyl (2S)-4-amino-2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]butanoate;
- 5 (2S,4S)-N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-hydroxy-4-methyl-pyrrolidine-2-carboxamide;
(2S,4S)-N-[3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-4-methyl-pyrrolidine-2-carboxamide;
- 10 N-[2-[[[(2S)-2-amino-3-hydroxy-propanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[(2-aminoacetyl)amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[[[(2S,3R)-2-amino-3-hydroxy-butanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 4-[[N-[(4S)-4-amino-5-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethylamino]-5-oxo-pentyl]carbamimidoyl]amino]butanoic acid;
rac-(4S)-4-amino-5-[[2-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propylamino]-1-(guanidinomethyl)-2-oxo-ethyl]amino]-5-oxo-pentanoic acid;
- 25 N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,5-diaminopentanoyl]amino]ethyl]-2-ethyl-benzamide;
- 30 N-[2-(4-aminobutanoylamino)ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[(4-amino-3-hydroxy-butanoyl)amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- 4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,6-diaminohexanoyl]amino]ethyl]-2-ethyl-benzamide];
- 4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,4-diaminobutanoyl]amino]ethyl]-2-ethyl-benzamide];
- 5 4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,3-diaminopropanoyl]amino]ethyl]-2-ethyl-benzamide];
- N-[(1R)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 N-[3-(3-aminopropanoylamino)-2-hydroxy-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- (4S)-4-amino-5-[[[(1S)-1-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propylcarbamoyl]-4-guanidino-butyl]amino]-5-oxo-pentanoic acid;
- 15 N-[3-[(2-aminoacetyl)amino]propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[3-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-3-oxo-propyl]benzamide;
- 20 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[4-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-4-oxo-butyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[6-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-6-oxo-hexyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[5-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-5-oxo-pentyl]benzamide;
- 25 4-[[3-[4-[4-(2-aminoethoxy)but-2-ynoxy]-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(3-aminopropyl)-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-[methyl-[2-(methylamino)ethyl]amino]-2-oxo-ethyl]benzamide;
- 30 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[3-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl]oxypropyl]benzamide;

- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(difluoromethyl)benzamide;
- N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propyl]-2-imino-imidazolidine-4-carboxamide;
- 5 (2S,4R)-N-[3-[[4-[[3-(4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- (2S,4R)-N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-
- 10 carboxamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(2-piperazin-1-ylethyl)benzamide;
- N-[3-[[[(2S)-2-amino-3-guanidino-propanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 N-[2-(4-aminobutanoylamino)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- (2S,4S)-N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-4-methyl-pyrrolidine-2-carboxamide;
- 20 [4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-phenyl]-[4-[(2S,4R)-4-hydroxy-4-methyl-pyrrolidine-2-carbonyl]piperazin-1-yl]methanone;
- (2S,4R)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- 25 N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- (2S,4R)-N-[2-[[4-[[3-(4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- 30 (2S,4S)-N-[2-[[4-[[3-(4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-ethyl-4-hydroxy-pyrrolidine-2-carboxamide;

- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-(ethanimidoylamino)-1-methyl-ethyl]-2-ethyl-benzamide;
N-[3-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
5 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-[[2-(dimethylamino)acetyl]amino]propyl]-2-ethyl-benzamide;
N-[2-[(2-aminoacetyl)amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
10 [2-hydroxy-3-[[rac-(2S)-2-amino-3-guanidino-propanoyl]amino]propyl]benzamide;
(2S,4R)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethyl]-4-hydroxy-pyrrolidine-2-carboxamide;
(2S,4S)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-
15 yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-ethyl-4-hydroxy-pyrrolidine-2-carboxamide;
(2S,4S)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-hydroxy-4-methyl-pyrrolidine-2-carboxamide;
20 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[3-[2-(dimethylamino)ethylamino]-3-oxo-propyl]-2-ethyl-benzamide;
N-[2-[[[(2S)-2-amino-3-hydroxy-propanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
3-[[2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-
25 yl]amino]benzoyl]-methyl-amino]propyl pyridine-4-carboxylate;
N-[3-[(2-aminoacetyl)amino]-2-hydroxy-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[(1R)-3-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]-1-methyl-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-
30 benzamide;
N-[2-[(4-amino-3-hydroxy-butanoyl)amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-[2-[[[(2S)-2,6-diaminohexanoyl]amino]-1,1-dimethyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(3-hydroxypropyl)-3,4-dihydroisoquinolin-1-one;
5 N-allyl-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
2-chloro-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-piperidylmethyl)benzamide;
N-[(2-aminothiazol-5-yl)methyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
10 2-[4-[[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]methyl]-1-piperidyl]-2-methyl-propanoic acid;
N-[[1-(azetidin-3-ylmethyl)-4-piperidyl]methyl]-4-[[3-[2,3-difluoro-4-[3-(trifluoromethyl)-1H-pyrazol-4-yl]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
15 1-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethyl]pyrrolidine-3-carboxamide;
2-[4-[[[4-[[3-[2,3-difluoro-4-(3-methyl-1H-pyrazol-4-yl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]methyl]-1-piperidyl]acetic acid;
20 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(4-pyridylmethyl)benzamide;
N-[[1-(azetidin-3-ylmethyl)-4-piperidyl]methyl]-4-[[3-[2,3-difluoro-4-(3-methyl-1H-pyrazol-4-yl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
2-[4-[[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]methyl]-1-piperidyl]acetic acid;
25 2-[4-[[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]methyl]-1-piperidyl]acetic acid;
N-(5-aminopentyl)-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
30 4-[[3-[2,3-difluoro-4-(1H-triazol-5-yloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[1-(pyrrolidin-3-ylmethyl)-4-piperidyl]methyl]benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[1-(2-pyrrolidin-2-ylethyl)-4-piperidyl]methyl]benzamide;

- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
[(1-methylpyrazol-4-yl)methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
[[1-(3-pyridylmethyl)-4-piperidyl]methyl]benzamide;
- 5 1-(azetidin-3-ylmethyl)-N-[(2S)-2-[[4-[[3-[4-(difluoromethoxy)-2,3-difluoro-
phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-
benzoyl]amino]propyl]piperidine-4-carboxamide;
- N-[(2S)-2-[[4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-
8-yl]amino]-2-ethyl-benzoyl]amino]propyl]piperidine-4-carboxamide;
- 10 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
[[1-[2-oxo-2-(pyrrolidin-3-ylmethylamino)ethyl]-4-piperidyl]methyl]benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-
2-ethyl-N-(pyrrolidin-3-ylmethyl)benzamide;
- 4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-
2-ethyl-N-[[1-(pyrrolidin-3-ylmethyl)-4-piperidyl]methyl]benzamide;
- 15 4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-
2-ethyl-N-(4-piperidylmethyl)benzamide;
- N-[[1-(azetidin-3-ylmethyl)-4-piperidyl]methyl]-4-[[3-[4-(difluoromethoxy)-2,3-
difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
[[1-(piperidine-4-carbonyl)-4-piperidyl]methyl]benzamide;
- N-[3-[[4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-
yl]amino]-2-ethyl-benzoyl]amino]propyl]-1-(pyrrolidin-3-ylmethyl)piperidine-4-
carboxamide;
- 25 N-[3-[[4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-
yl]amino]-2-ethyl-benzoyl]amino]propyl]piperidine-4-carboxamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
(4-piperidylmethyl)benzamide;
- 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-
2-ethyl-N-(3-oxo-3-piperazin-1-yl-propyl)benzamide;
- 30 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
prop-2-ynyl-benzamide;

- N-(8-aminooctyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(1R)-1-(aminomethyl)-2-hydroxy-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-benzamide;
- 2-ethyl-4-[[3-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-benzamide;
- N-[(E)-4-aminobut-2-enyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(6-imidazol-1-yl)hexyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[6-(1-piperidyl)hexyl]benzamide;
- 15 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[5-([1,2,4]triazolo[4,3-a]pyridin-3-yl)pentyl]benzamide;
- N-[[1-(2-aminoacetyl)azetidin-3-yl]methyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-20 [[(3S,4R)-4-hydroxypyrrolidin-3-yl]methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-25 [[(3S)-pyrrolidin-3-yl]methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-30 [[(3R)-pyrrolidin-3-yl]methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(3-hydroxypyrrolidin-3-yl)methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-(pyrrolidin-2-yl)methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(3-fluoroazetidin-3-yl)methyl]benzamide;
- 30 N-(2-amino-3-hydroxy-propyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-(2-amino-2-methyl-propyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(2-aminobutyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 N-[(2S)-2-aminopropyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(7-aminoheptyl)-2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- N-[3-[(2R,3R,4R,5R,6R)-3-amino-4,5-dihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl]oxypropyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 N-(4-aminobutyl)-2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- N-(7-aminoheptyl)-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 15 N-(7-aminoheptyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(7-aminoheptyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 20 N-(4-aminobutyl)-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- N-(4-aminobutyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(4-aminobutyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 25 4-[[3-[4-[[5-(2-aminoethoxy)-2-pyridyl]oxy]-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-benzamide;
- 4-[[3-[4-[[5-(3-aminopropoxy)-2-pyridyl]oxy]-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-benzamide;
- 30 4-[[3-[4-[[5-(3-aminopropoxy)-2-pyridyl]oxy]-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N,N-dimethyl-benzamide;
- 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1R)-1-methyl-2-(2-methylpropanimidoylamino)ethyl]benzamide;

- N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
N-(3-aminopropyl)-6-[4-[8-[3-ethyl-4-(methylcarbamoyl)anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]pyridine-3-carboxamide;
- 5 N-[(1R)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
N-[(1S)-2-amino-1-methyl-ethyl]-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 10 N-[(1R)-2-amino-1-methyl-ethyl]-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(1S)-1-methyl-2-(2-methylpropanimidoylamino)ethyl]benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[(1R)-1-methyl-2-(2-methylpropanimidoylamino)ethyl]benzamide;
- 15 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1R)-2-(ethanimidoylamino)-1-methyl-ethyl]benzamide;
2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1S)-1-methyl-2-(2-methylpropanimidoylamino)ethyl]benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-
- 20 N-[(1S)-1-methyl-2-(2-methylpropanimidoylamino)ethyl]benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-N-[(1R)-1-methyl-2-(2-methylpropanimidoylamino)ethyl]benzamide;
N-(6-aminohexyl)-2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 25 N-(5-aminopentyl)-2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
N-(6-aminohexyl)-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- 30 N-(6-aminohexyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-(6-aminohexyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;

- N-(5-aminopentyl)-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- N-(5-aminopentyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzamide;
- 5 N-(2-aminoethyl)-6-[4-[8-[3-ethyl-4-(methylcarbamoyl)anilino]imidazo[1,2-a]pyrazin-3-yl]-2,3-difluoro-phenoxy]pyridine-3-carboxamide;
- N-[(1S)-1-(aminomethyl)propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1S)-2-(ethanimidoylamino)-1-methyl-ethyl]-2-methyl-benzamide;
- 10 2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1S)-2-(ethanimidoylamino)-1-methyl-ethyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1R)-2-(ethanimidoylamino)-1-methyl-ethyl]-2-methyl-benzamide;
- 15 N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-[2,3-difluoro-4-(1H-pyrazol-3-ylmethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[1-[[[(2S)-2,6-diaminohexanoyl]amino]methyl]cyclopropyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2,3-dihydroxypropyl)-2-ethyl-benzamide;
- 20 N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-thiazol-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-pent-4-ynyl-benzamide;
- 25 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[(1S)-2-(ethanimidoylamino)-1-methyl-ethyl]-2-ethyl-benzamide;
- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3-fluoro-2-methyl-benzamide;
- 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[6-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-6-oxo-hexyl]benzamide;
- 30 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[5-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-5-oxo-pentyl]benzamide;

- 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[4-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-4-oxo-butyl]benzamide;
- 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[3-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-3-oxo-propyl]benzamide;
- 5 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-2-oxo-ethyl]benzamide;
- (2S,4R)-N-[(2R)-2-amino-3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- 10 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-methyl-benzamide;
- 4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N,N-dimethyl-benzamide;
- (2S,4R)-N-[(2S)-2-amino-3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- 15 (2S,4R)-N-[(2S)-2-amino-3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- (2S,4R)-N-[(2S)-2-amino-3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- 20 (2S,4R)-N-[(2R)-2-amino-3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- N-(2-aminoethyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-fluoro-6-methyl-benzamide;
- 25 N-(2-aminoethyl)-4-[[3-[2,3-difluoro-4-(4-methoxypyrimidin-2-yl)oxy-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[(1R)-2-[(2S)-2,6-diaminohexanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-
- 30 [2-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-2-oxo-ethyl]benzamide;
- N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-[2,3-difluoro-4-(6-methoxypyrimidin-4-yl)oxy-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-[2,3-difluoro-4-(4-methoxypyrimidin-2-yl)oxy-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
rac-(4S)-4-amino-5-[[2-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethylamino]-1-(guanidinomethyl)-2-oxo-ethyl]amino]-5-oxo-pentanoic acid;
- 5 N-[(1R)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
(3R,4R)-N-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-3-hydroxy-piperidine-4-carboxamide;
- 10 N-[(1S)-2-[[2-(2R)-2-amino-4-guanidino-butanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[(1S)-2-[[2-(2S)-2-amino-4-guanidino-butanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 N-[(1S)-2-[[2-(2S)-2-amino-4-guanidino-butanoyl]amino]-1-methyl-ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[(1S)-2-[[2-(2S)-2-amino-4-guanidino-butanoyl]amino]-1-methyl-ethyl]-4-[[3-[2,3-difluoro-4-(4-methylpyrimidin-2-yl)oxy-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 N-[5-[[2-(2R,3S,4S,5R,6R)-4-amino-6-[(1S,2S,3R,4S,6R)-4-amino-6-[(2S)-4-amino-2-hydroxy-butanoyl]amino]-3-[(2R,3R,4S,5S,6R)-6-(aminomethyl)-3,4,5-trihydroxy-tetrahydropyran-2-yl]oxy-2-hydroxy-cyclohexoxy]-3,5-dihydroxy-tetrahydropyran-2-yl]methylamino]-5-oxo-pentyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 N-[(1S)-2-[[2-(2S)-2,6-diaminohexanoyl]amino]-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[(1S)-2-amino-1-methyl-ethyl]-4-[[3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 (3R,4R)-N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-3-hydroxy-piperidine-4-carboxamide;

- N-[2-[[[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-methoxy-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 N-[2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-methoxy-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[2,3-difluoro-4-[(5-methoxy-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-methoxy-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[2-(azetidin-1-yl)ethylamino]-2-oxo-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 N-[2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(4-methylpyrimidin-2-yl)oxy-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[4-[2-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]ethyl]piperazin-1-yl]butanoic acid;
- 4-[4-[2-[[4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]-methyl-amino]ethyl]-1-piperidyl]butanoic acid;
- 20 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[3-[(2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl]oxypropyl]benzamide;
- N-[2-[[[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 N-[2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2R)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 N-[2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-(3-aminopropyl)-2-chloro-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-6-fluoro-benzamide;
- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2,6-difluoro-benzamide;
- 5 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[2-(dimethylamino)ethylamino]-2-oxo-ethyl]-2-ethyl-benzamide;
- N-[2-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-4-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-(2,3-difluoro-4-pyrimidin-2-yloxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-(2-aminoethylamino)-2-oxo-ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 N-[2-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-fluoro-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-[2-(methylamino)ethylamino]-2-oxo-ethyl]benzamide;
- 20 N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-fluoro-6-methyl-benzamide;
- N-[2-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[2,3-difluoro-4-[(5-fluoro-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]ethyl]-4-[[3-[2,3-difluoro-4-[(5-fluoro-2-pyridyl)oxy]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-(2-hydroxyethylamino)-2-oxo-ethyl]benzamide;
- N-[2-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2S)-2-amino-4-guanidino-butanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 N-(3-aminopropyl)-4-[[3-[2,3-difluoro-4-(4-hydroxybut-2-ynoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-(5-aminopentyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2,3-difluoro-4-(2-pyridyloxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 10 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2-amino-4-guanidino-butanoyl]amino]propyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2,3-diaminopropanoyl]amino]propyl]benzamide;
- 15 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2,4-diaminobutanoyl]amino]propyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2,5-diaminopentanoyl]amino]propyl]benzamide;
- 20 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2,6-diaminohexanoyl]amino]propyl]benzamide;
- N-[3-[(4-amino-3-hydroxy-butanoyl)amino]-2-hydroxy-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[3-(4-aminobutanoylamino)-2-hydroxy-propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 25 4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[[4-(hydroxymethyl)-2-oxo-oxazolidin-4-yl]methyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-methyl-3-[[rac-(2S)-2-amino-3-guanidino-propanoyl]amino]propyl]benzamide;
- 30 (2S)-2-amino-5-[[[(1S)-1-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propyl]carbamoyl]-4-guanidino-butyl]amino]-5-oxo-pentanoic acid;

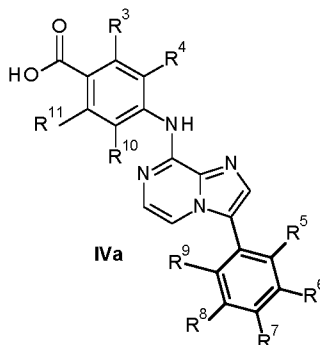
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-methyl-3-[[rac-(2S)-2-amino-5-guanidino-pentanoyl]amino]propyl]benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-hydroxy-3-[[rac-(2S)-2-amino-5-guanidino-pentanoyl]amino]propyl]benzamide;
4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[2-(dimethylamino)ethylamino]-2-oxo-ethyl]-2-ethyl-benzamide;
(2S)-2-[[[(2S)-2,6-diaminohexanoyl]amino]-5-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propylamino]-5-oxo-pentanoic acid;
N-(3-amino-1-methyl-propyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-methyl-3-[[rac-(2S)-2-amino-4-guanidino-butanoyl]amino]propyl]benzamide;
N-[2-[[[(2S)-2,3-diaminopropanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[[[(2S)-2,4-diaminobutanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[[[(2S)-2,6-diaminohexanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[[[(2S)-2,5-diaminopentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-[3-(2-methyl-5,6-dioxo-3-thioxo-1,2,4-triazinan-4-yl)propyl]benzamide;
2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-[3-[(2-methyl-5,6-dioxo-1H-1,2,4-triazin-3-yl)sulfanyl]propyl]benzamide;
N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-prop-2-ynoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
N-[2-[[[(2S,3R)-2-amino-3-hydroxy-butanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;

- N-(3-aminopropyl)-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-(2-fluoroethyl)benzamide;
 6-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-3,4-dihydroisoquinolin-1-one; and
 5 7-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2,3,4,5-tetrahydro-2-benzazepin-1-one.
38. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound of formula (I) is selected from:
- 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-piperidylmethyl)benzamide;
 10 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N,2-dimethyl-N-(2-piperazin-1-ylethyl)benzamide;
 2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;
 15 2-chloro-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-N-(2-piperazin-1-ylethyl)benzamide;
 N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[2-chloro-4-(cyanomethoxy)-3-fluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
 20 N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
 N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
 25 N-[3-(2-aminoethylcarbamoylamino)propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
 N-[2-[[[(2S)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-(2-chloro-3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
 4-[[3-[4-(difluoromethoxy)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(4-guanidinobutyl)-2-methyl-benzamide;
 30 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-(5-guanidinopentanoylamino)ethyl]benzamide;

- N-(5-aminopentyl)-4-[[3-[4-(difluoromethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[3-(3-aminopropylcarbamoylamino)propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 5 N-[(1-carbamimidoyl-4-piperidyl)methyl]-2-chloro-4-[[3-(3-fluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]benzamide;
- (2S,4S)-N-[2-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]ethyl]-4-hydroxy-4-methyl-pyrrolidine-2-carboxamide;
- 10 (2S,4S)-N-[3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-4-methyl-pyrrolidine-2-carboxamide;
- N-[2-[[[(2S)-2-amino-3-hydroxy-propanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 15 N-[2-[(2-aminoacetyl)amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-(3-aminopropanoylamino)ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2S,3R)-2-amino-3-hydroxy-butanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 20 (cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[[[(2R)-2-amino-5-guanidino-pentanoyl]amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,5-diaminopentanoyl]amino]ethyl]-2-ethyl-benzamide;
- 25 N-[2-(4-aminobutanoylamino)ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- N-[2-[(4-amino-3-hydroxy-butanoyl)amino]ethyl]-4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide;
- 30 4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,6-diaminohexanoyl]amino]ethyl]-2-ethyl-benzamide;
- 4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,4-diaminobutanoyl]amino]ethyl]-2-ethyl-benzamide;

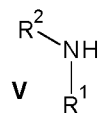
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- 4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-[2-[[[(2S)-2,3-diaminopropanoyl]amino]ethyl]-2-ethyl-benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[3-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-3-oxo-propyl]benzamide;
- 5 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[4-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-4-oxo-butyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[6-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-6-oxo-hexyl]benzamide;
- 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[5-[(3S)-3-(hydroxymethyl)piperazin-1-yl]-5-oxo-pentyl]benzamide;
- 10 4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-N-[2-[methyl-[2-(methylamino)ethyl]amino]-2-oxo-ethyl]benzamide;
- N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzoyl]amino]propyl]-2-imino-imidazolidine-4-carboxamide;
- 15 (2S,4R)-N-[3-[[4-[[3-[4-(cyanomethoxy)-2,3-difluoro-phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-carboxamide;
- (2S,4R)-N-[3-[[4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methyl-benzoyl]amino]propyl]-4-hydroxy-pyrrolidine-2-
- 20 carboxamide; and
- N-[3-[[[(2S)-2-amino-3-guanidino-propanoyl]amino]propyl]-4-[[3-(2,3-difluoro-4-methoxy-phenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-ethyl-benzamide.
39. A process of manufacturing the compounds of formula (I) described herein, comprising:
- 25 (i) reacting an ester carboxylic acid **IVa**, wherein R³ to R¹¹ are as defined in any one of claims 1-38,



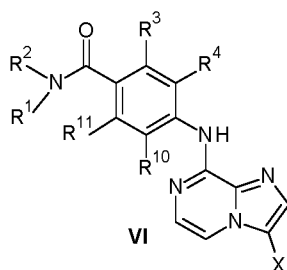
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with an amine **V**, wherein R^1 and R^2 are as defined in any one of claims 1-38,

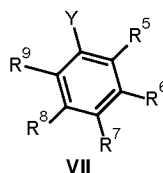


in the presence of a coupling reagent (such as HATU, TBTU, and the like) and a base (such as DIPEA, NEt_3 , and the like), to form said compound of formula (I); or

- (ii) reacting a compound **VI**, wherein R^1 to R^4 , R^{10} and R^{11} are as defined in any one of claims 1-38 and X is halogen,



with a boronic acid **VII**, wherein R^5 to R^9 are as defined in any one of claims 1-38 and Y is a boronic acid or a boronic acid ester,



in the presence of a transition metal catalyst (such as $\text{PdCl}_2(\text{dppf})\text{-CH}_2\text{Cl}_2$ adduct, $\text{Pd}(\text{PPh}_3)_4$, and the like) and a base (such as K_3PO_4 , NaOtBu , and the like),

to form said compound of formula (I).

40. A compound of formula (I) according to any one of claims 1 to 38, when manufactured according to the process of claim 39.

41. A compound of formula (I) according to any one of claims 1 to 38 and 40, or a pharmaceutically acceptable salt thereof, for use as therapeutically active substance.

42. A pharmaceutical composition comprising a compound of formula (I) according to any one of claims 1 to 38 and 40, or a pharmaceutically acceptable salt thereof, and a therapeutically inert carrier.

43. A compound of formula (I) according to any of claims 1 to 38 and 40, or a pharmaceutically acceptable salt thereof, for use as antibiotic.
44. A compound of formula (I) according to any of claims 1 to 38 and 40, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of nosocomial infections and resulting diseases.
45. A compound of formula (I) according to any of claims 1 to 38 and 40, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of infections and resulting diseases caused by Gram-negative bacteria.
46. The compound for use according to claim 45, wherein said Gram-negative bacteria are selected from *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter species* and *E. coli*.
47. The compound for use according to claim 46, wherein said Gram-negative bacteria are *Acinetobacter baumannii*.
48. A compound of formula (I) according to any of claims 1 to 38 and 40, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of infections and resulting diseases caused by *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter species* or *E. coli*, or a combination thereof.
49. A method for the treatment or prevention of infections and resulting diseases caused by *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter species* or *E. coli*, or a combination thereof, which method comprises administering a compound of formula (I) according to any of claims 1 to 38 and 40, or a pharmaceutically acceptable salt thereof, to a mammal.
50. Use of a compound of formula (I) according to any of claims 1 to 38 and 40, or a pharmaceutically acceptable salt thereof, as an antibiotic.
51. Use of a compound of formula (I) according to any of claims 1 to 38 and 40, or a pharmaceutically acceptable salt thereof, for the treatment or prevention of infections and resulting diseases caused by *Enterococcus faecium*, *Staphylococcus aureus*,

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Klebsiella pneumoniae, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*,
Enterobacter species or *E. coli*, or a combination thereof.

52. The use of a compound of formula (I) according to any of claims 1 to 38 and 40, or a
pharmaceutically acceptable salt thereof, for the preparation of medicaments useful
5 for the treatment or prevention of infections and resulting diseases caused by
Enterococcus faecium, *Staphylococcus aureus*, *Klebsiella pneumoniae*,
Acinetobacter baumannii, *Pseudomonas aeruginosa*, *Enterobacter species* or *E.*
coli, or a combination thereof.

53. The invention as described hereinbefore.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2019/085217

A. CLASSIFICATION OF SUBJECT MATTER INV. C07D487/04 A61P31/04 A61K31/519 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C07D A61P		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data, CHEM ABS Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2012/168733 A1 (UCL BUSINESS PLC [GB]; BIRKBECK COLLEGE [GB] ET AL.) 13 December 2012 (2012-12-13) page 116 - page 123; claims; examples 1-5 ----- -/--	1-53
☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents :		
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INTERNATIONAL SEARCH REPORT

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CORONA P ET AL: "4-Substituted anilino imidazo[1,2-a] and triazolo[4,3-a]quinoxalines. Synthesis and evaluation of in vitro biological activity", EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, ELSEVIER, AMSTERDAM, NL, vol. 41, no. 9, 1 September 2006 (2006-09-01), pages 1102-1107, XP024993886, ISSN: 0223-5234, DOI: 10.1016/J.EJMECH.2006.05.015 [retrieved on 2006-09-01] the whole document -----	1-53
A	HONGBO ZENG ET AL: "Discovery of novel imidazo[1,2-]pyrazin-8-amines as Brk/PTK6 inhibitors", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, PERGAMON, AMSTERDAM, NL, vol. 21, no. 19, 26 July 2011 (2011-07-26), pages 5870-5875, XP028286385, ISSN: 0960-894X, DOI: 10.1016/J.BMCL.2011.07.101 [retrieved on 2011-08-03] the whole document -----	1-53

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WO 2012168733	A1	13-12-2012	NONE
