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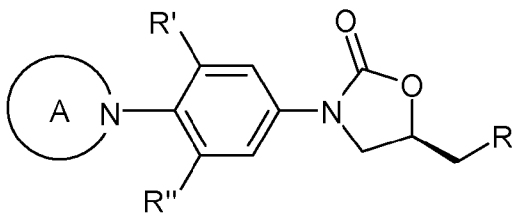
(54) Title: SUBSTITUTED PHENYLOXAZOLIDINONES FOR ANTIMICROBIAL THERAPY



(I)

(57) Abstract: The present invention relates to novel oxazolidinones (Formula I): or a pharmaceutically acceptable salt having ring A characterized by *N*-containing monocyclic, bicyclic or spirocyclic substituents, to their preparation, and to their use as drugs for treating *Mycobacterium tuberculosis* and other microbial infections, either alone or in combination with other anti-infective treatments.

SUBSTITUTED PHENYLOXAZOLIDINONES FOR ANTIMICROBIAL THERAPY

FIELD OF THE INVENTION

The invention relates generally to compounds with antibacterial activity and, more specifically, with anti-tuberculosis properties. In particular, it relates to substituted phenyloxazolidinone compounds useful for the treatment of tuberculosis in patients in need thereof.

All documents cited to or relied upon below are expressly incorporated herein by reference.

BACKGROUND OF THE INVENTION

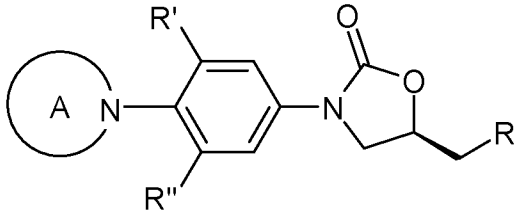
Linezolid is the first-in-class drug and was approved in 2000 for a number of clinical applications including the treatment of nosocomial and community-acquired pneumonia and skin infections caused by *Staphylococcus aureus*/Methicillin-resistant *S. aureus*, Vancomycin-resistant *Enterococci*, and *Streptococcus pneumoniae* (Pen-S). Linezolid exhibits *in vitro* bacteriostatic activity against *Mycobacterium tuberculosis*, including multidrug-resistant (MDR) and extensively drug resistant (XDR) strains, with a minimum inhibitory concentration (MIC) of less than 1 μg/ml. However, it has demonstrated only modest activity in murine models of tuberculosis. Nonetheless, Linezolid has been used off-label in combination regimens to treat multidrug-resistant tuberculosis.

Oxazolidinones currently in clinical development show bone marrow toxicity in animals after long term administration (i.e., greater than one month) that is believed to be related to mitochondrial protein synthesis (MPS) inhibition, with very narrow safety margins or no safety margins. Since the antimicrobial mode of action of this class of compounds is inhibition of microbial protein synthesis, the MPS inhibition and consequent bone marrow toxicity exhibited by these compounds is considered mechanism specific. These oxazolidinones generally show high clearance and so

require administration of high doses in clinical treatment of TB or the other indications for which they are being developed (e.g., 500 mg to 1600 mg daily) to achieve efficacious exposures. Therefore, it would be highly desirable to identify a new generation of oxazolidinones for TB treatment that would demonstrate improved potency and efficacy against TB, reduced systemic clearance to reduce the daily dose below 500 mg, and diminished MPS inhibition and related bone marrow toxicity, resulting in an improved safety margin for long term administration.

SUMMARY OF THE INVENTION

The present invention relates to novel oxazolidinones of Formula I, or a pharmaceutically acceptable salt, hydrate, or solvate thereof:



(I)

wherein,

R is independently OR_1, $OC(O)R_2$, $OC(O)NHR_2$, $OS(O_2)R_2$, $NHS(O)_2R_2$, NR_3R_4, $NHC(O)R_5$;

R' and R" are independently H, F, Cl or OMe;

each R_1 is independently H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, wherein said alkyl, cycloalkyl are optionally substituted with 1 to 4 groups selected from halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkyloxy;

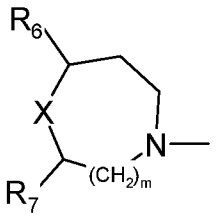
each R_2 is independently C_1-C_6 alkyl, C_3-C_8 cycloalkyl, heterocyclyl, heteroaryl or aryl, wherein said alkyl, cycloalkyl, heterocyclyl, heteroaryl, or aryl are optionally substituted with 1 to 4 groups selected from halo, hydroxyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 acyloxy, CF_3, NO_2, CN and NH_2;

each R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, heterocyclyl heteroaryl, aryl; or R_3 and R_4 taken together with the nitrogen to which they are

attached, form a 4- to 8-membered heterocyclyl or heteroaryl with 1 to 3 additional heteroatoms selected from O, S, or N, wherein said alkyl, cycloalkyl, heterocyclyl, heteroaryl, or aryl are optionally substituted with 1 to 4 groups selected from halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, CF_3, NO_2, CN;

each R_5 is independently C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_1-C_6 alkoxy, heteroaryl, aryl, wherein said alkyl, cycloalkyl, heterocyclyl, heteroaryl, or aryl are optionally substituted with 1 to 4 groups selected from halo, hydroxyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 acyloxy, CF_3, NO_2, CN and NH_2;

Ring A is selected from:



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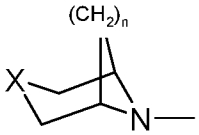

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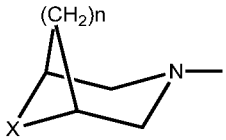
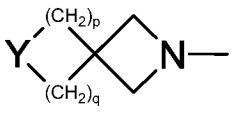


and


wherein,

each R_6 and R_7 is independently H, F, CH_3, CH_2CH_3, CF_3, phenyl;

X = O, S, SO, SO_2;

Y = O, S, SO, SO_2, and NR_8;

m is 1, or 2;

n is 1, or 2;

p is 1, or 2;

q is 1, or 2;

R_8 in independently H, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, $COCH_3$, and p-toluenesulfonyl, wherein said alkyl, cycloalkyl are optionally substituted with 1 to 4 groups selected from halo, hydroxyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 acyloxy, CF_3, NO_2, CN and NH_2.

In a further aspect, the present invention provides pharmaceutical compositions comprising at least one compound of Formula I, or a salt, hydrate, or solvate thereof, and one or more pharmaceutically acceptable carriers and/or additives.

In a further aspect, the present invention provides a method for treating microbial infections in humans by administering a therapeutically effective amount of a compound of Formula I, or a salt, hydrate, or solvate thereof to a patient in need thereof.

In a further aspect, the present invention includes pharmaceutical compositions of Formula I, or a salt, hydrate, or solvate thereof, further comprising one or more additional anti-infective treatments.

In still a further aspect, the present invention relates to a compound in accordance with Formula I or a pharmaceutically acceptable salt, hydrate, or solvate thereof for use as an anti-tuberculosis (TB) agent in a human.

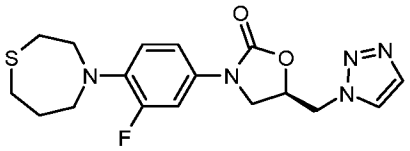
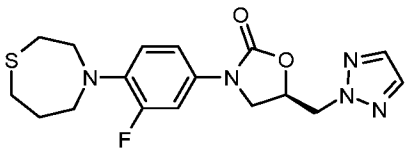
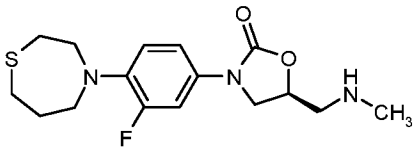
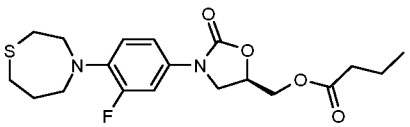
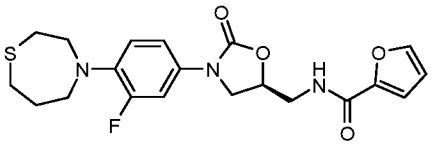
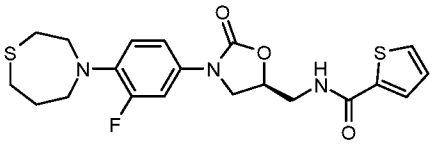
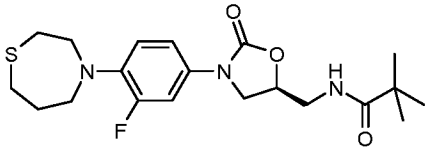
DETAILED DESCRIPTION OF THE INVENTION

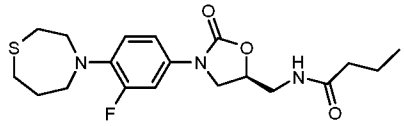
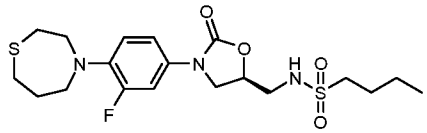
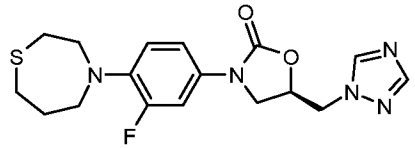
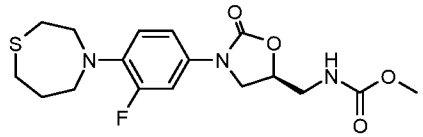
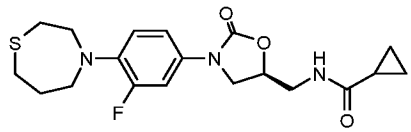
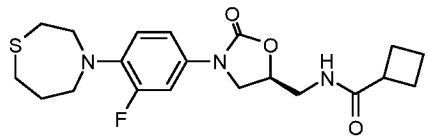
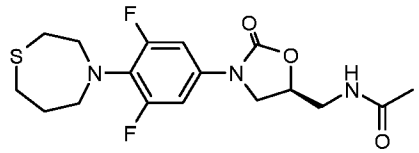
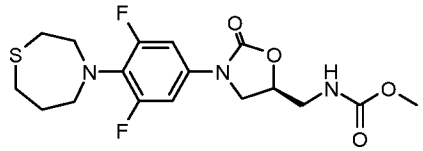
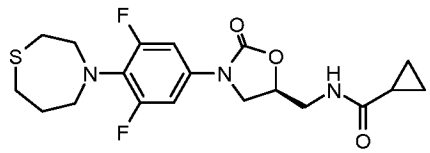
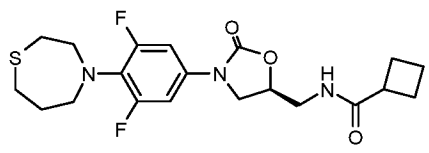
One aspect of the present invention is to provide novel compounds according to Formula I shown and described above. Specifically, the compounds of the invention are useful antimicrobial agents, effective against a number of human and veterinary pathogens, including gram-positive aerobic bacteria, *Mycobacterium tuberculosis*, *Mycobacterium avium*, and the like. As a result, this invention provides novel compounds according to Formula I, as well as pharmaceutically acceptable salts, hydrates, or solvates thereof. Values for the variables in Formula I are provided in the following paragraphs.

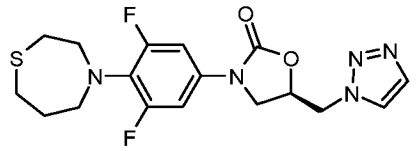
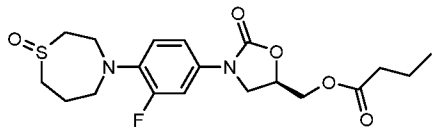
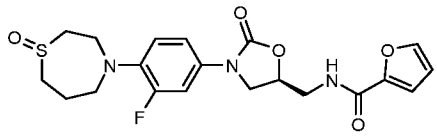
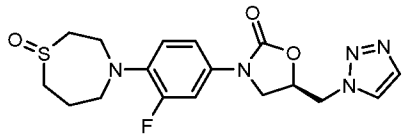
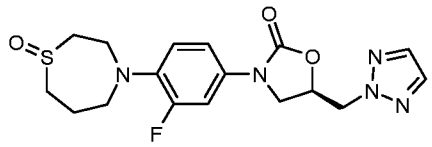
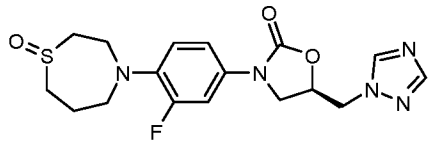
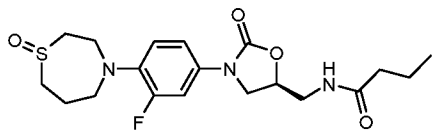
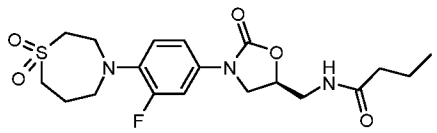
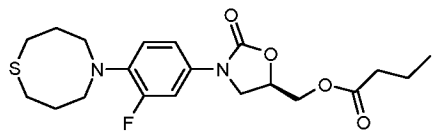
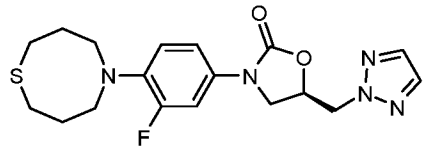
Table 1 below shows some specific examples of the compounds of the invention, by indicating their structures as well as their *in vitro* activity against *Mycobacterium tuberculosis* H37Rv strains, and *in vitro* MPS inhibition activity when tested as described in Example 9 and 10 below, respectively. As shown in Table 1 below, potent anti-tubercular agents demonstrate low MIC values (particular compounds with MIC's below 1 μg/mL). Conversely, high MPS inhibition IC_{50}'s indicate diminished mitochondrial protein synthesis activity *in vitro*, and are indicative of reduced myelosuppression toxicity *in vivo*. In certain embodiments of the invention, compounds having the best therapeutic index are those demonstrating a

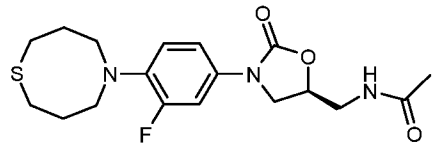
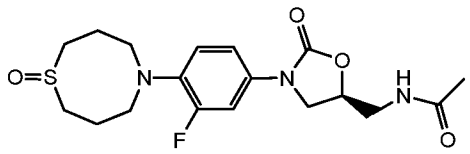
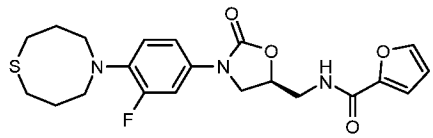
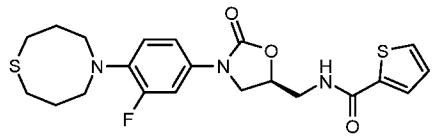
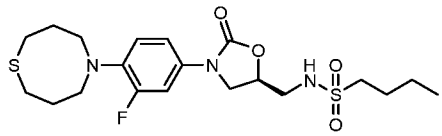
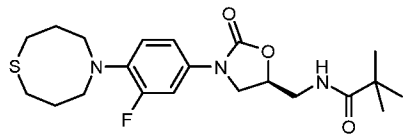
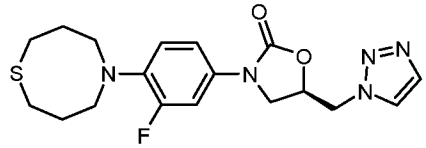
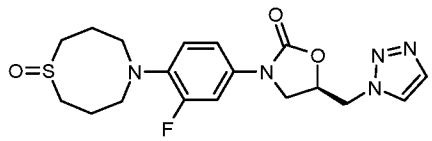
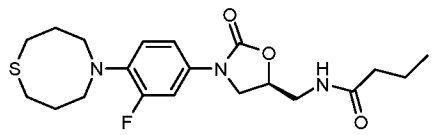
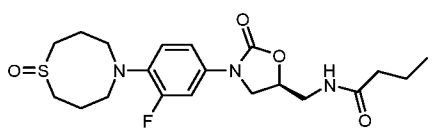
relatively lower MIC value combined a relatively higher MPS inhibition IC_{50}. Representative compounds of the invention are provided in Table 1 (wherein the entry "NA" (i.e., "not available") indicates that a particular value was not measured):

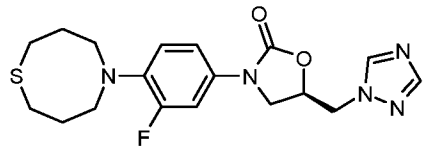
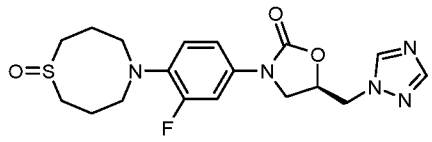
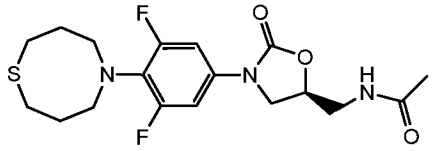
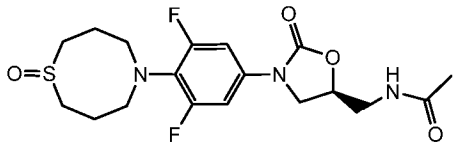
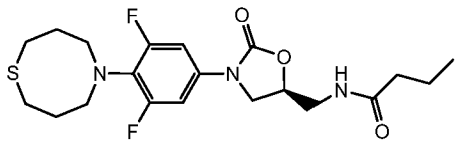
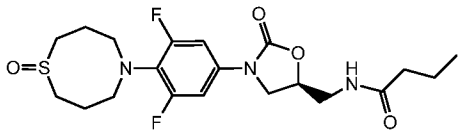
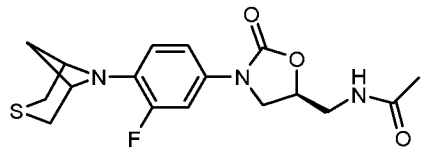
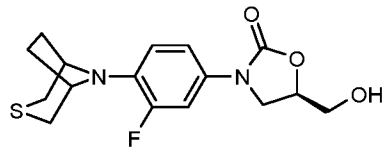
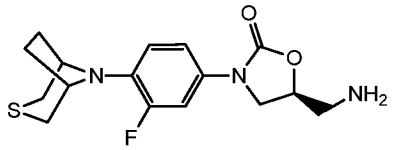
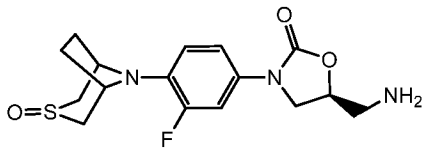
TABLE 1

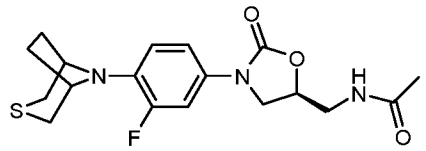
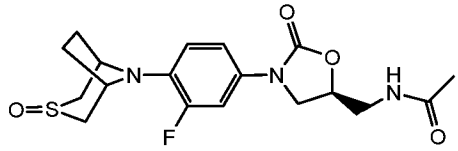
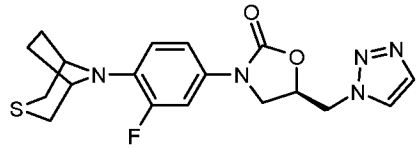
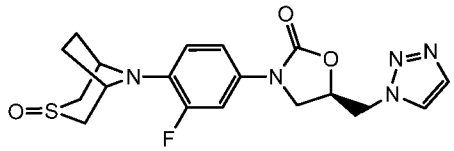
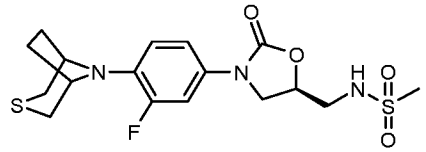
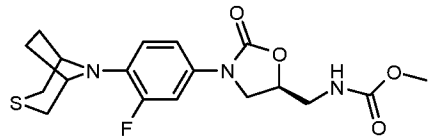
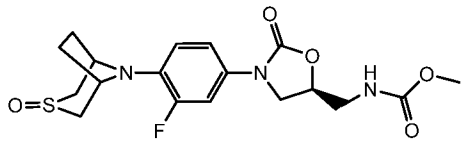
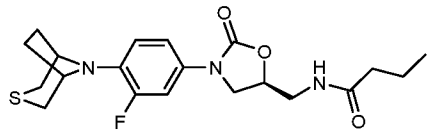
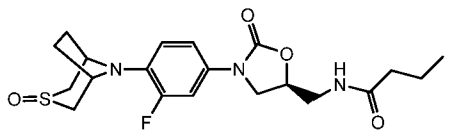
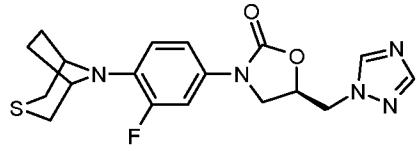
Compound	Structure	HRMS $[M+H]^+$	MIC (μg/mL) against $H_{37}Rv$	IC_{50} (μM) MPS inhibition
OTB-107		378.1396	0.03	84.85
OTB-106		378.1403	2	> 100
OTB-109		340.1484	32	NA
OTB-108		397.1613	0.125	> 100
OTB-111		420.1400	0.125	60.32
OTB-112		382.1620	0.5	> 100
OTB-115		410.1942	3.733	> 100

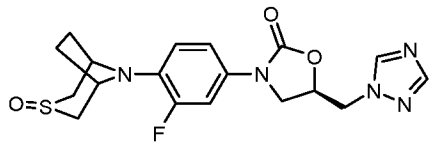
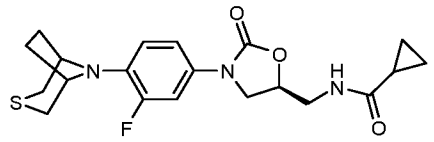
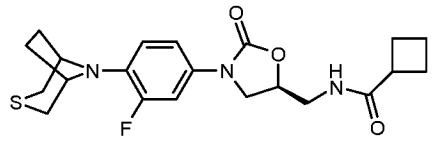
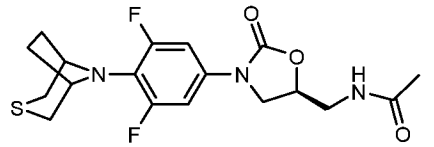
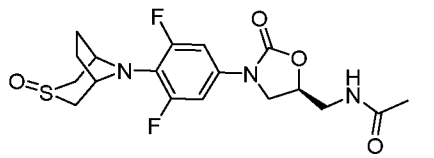
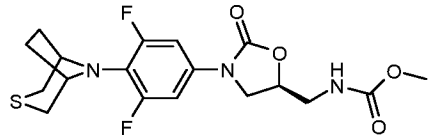
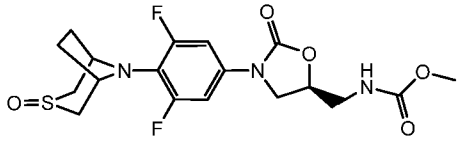
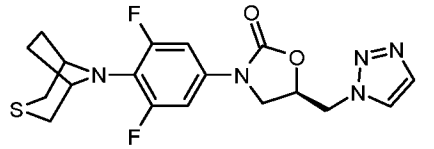
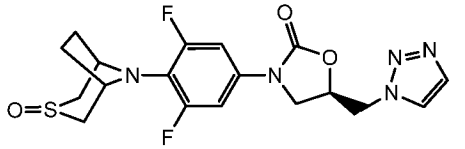
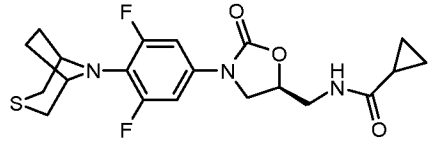
OBD-005		395.1679	0.055	15.63
OTB-116		446.1623	3.812	> 100
OTB-119		378.1421	0.456	> 100
OTB-412		384.1371	0.199	10
OTB-413		394.1580	0.108	9.13
OTB-414		408.1736	0.171	NA
OTB-407		386.1330	0.097	3.079
OTB-410		402.1287	0.125	> 100
OTB-408		412.1485	0.342	3.608
OTB-409		426.1643	0.477	8.51

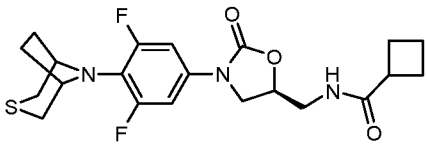
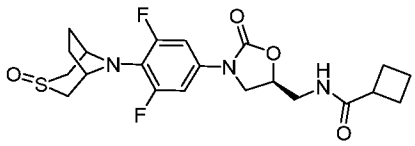
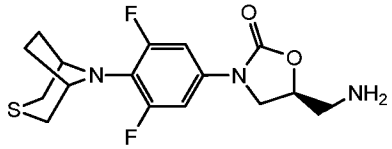
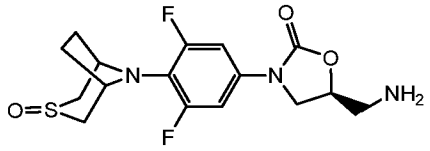
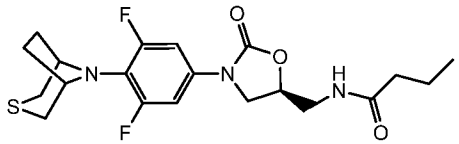
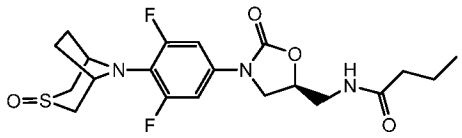
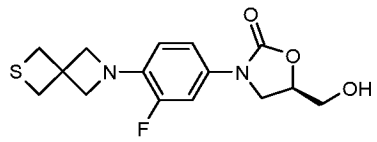
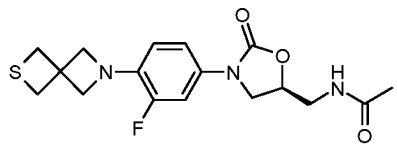
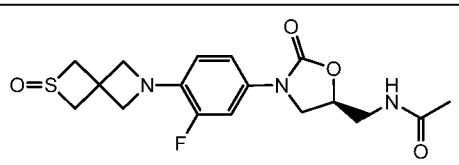
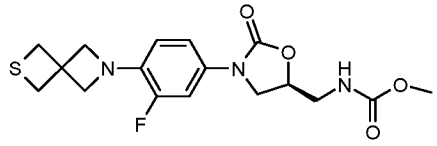
OTB-411		396.1296	0.124	8.73
OTB-126		413.1573	0.847	35.60
OTB-127		436.1371	1.234	10.15
OTB-137		394.1328	0.277	7.64
OTB-138		394.1338	7.565	> 100
OTB-140		394.1339	3.695	> 100
OBD-006		411.1628	0.49	7.485
OBD-007		427.1577	0.46	19.81
OTB-110		411.1786	0.125	> 100
OTB-113		392.1590	2	> 100

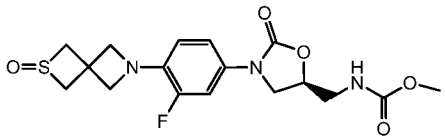
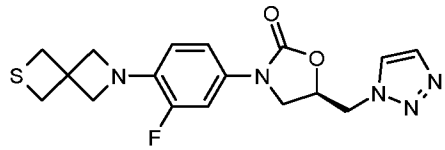
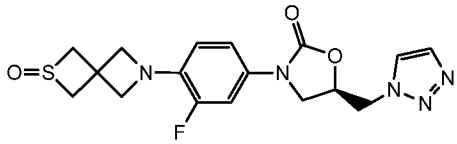
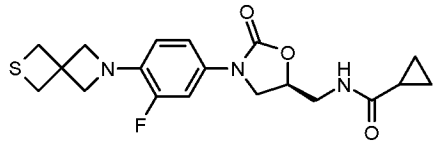
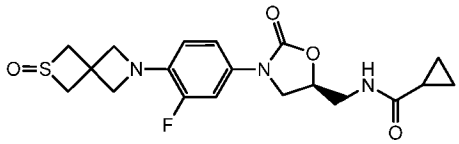
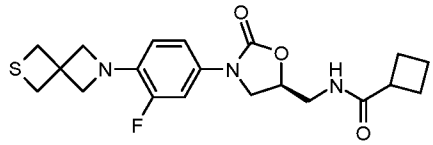
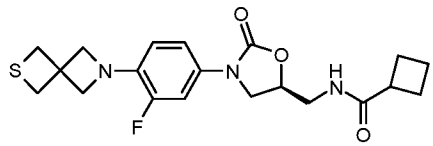
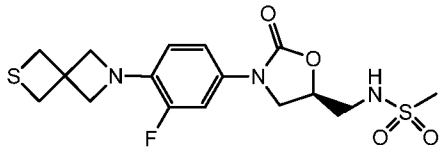
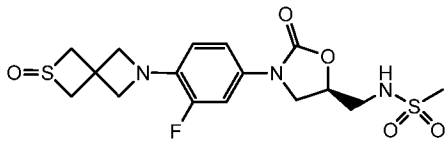
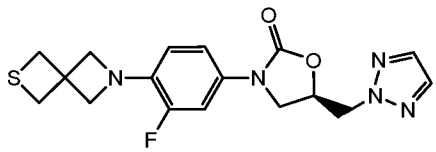
OTB-114		382.1620	0.05-0.11	28-29
OTB-124		398.1540	0.26-1.4	94->100
OTB-117		434.1581	0.665	56.32
OTB-118		450.1356	1.548	NA
OTB-120		460.1778	3.877	7.27
OTB-121		424.2096	2.785	17.63
OBD-001		391.1478	0.3	12
OBD-002		407.1427	1.6	29
OBD-003		409.1835	0.33	> 100
OBD-004		425.1785	3.338	15.76

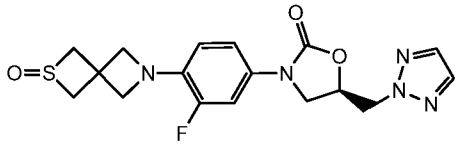
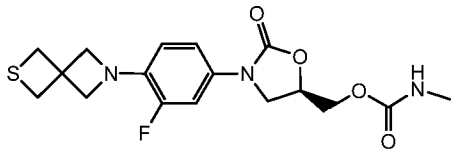
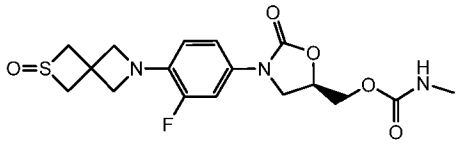
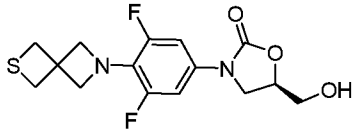
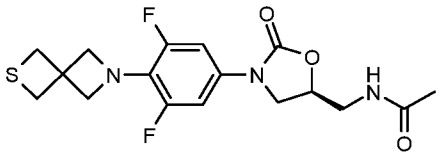
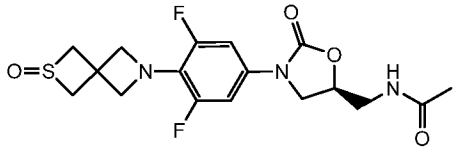
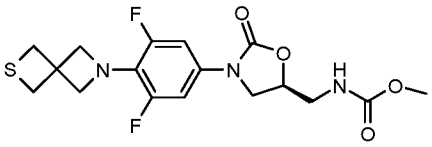
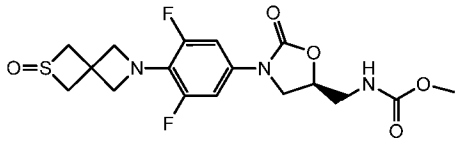
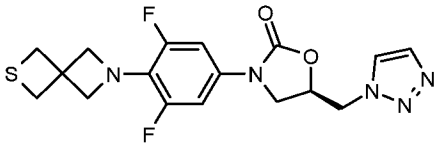
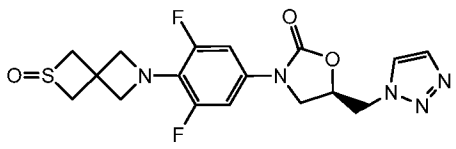
OBD-008		391.1478	3.513	29.89
OBD-009		407.1427	21.052	> 100
OBD-027			0.3	NA
OBD-240			NA	NA
OBD-026			0.4	NA
OBD-241			NA	NA
OTB-227		366.1277	0.889	15.22
OTB-501		339.1169	4.5	NA
OBD-081		407.9	0.47	77
OBD-085			1.1	>100

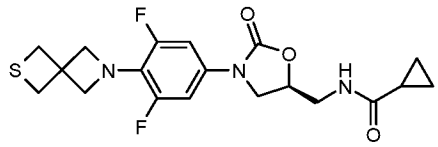
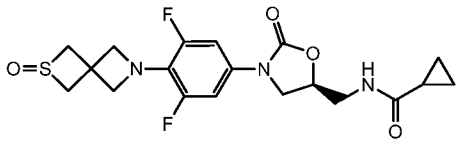
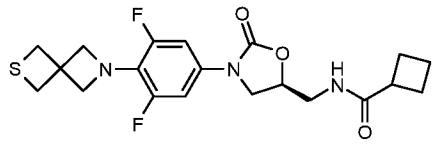
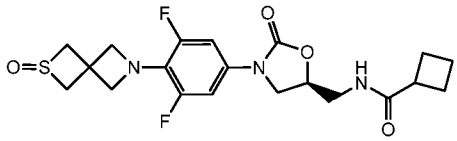
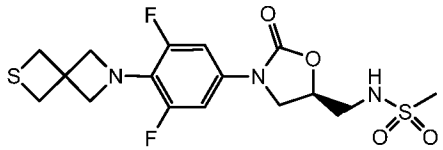
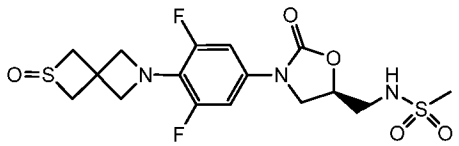
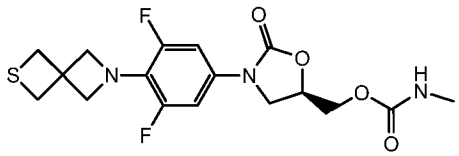
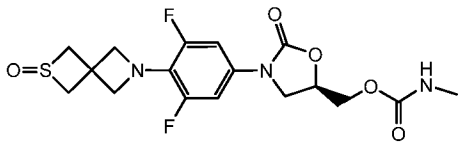
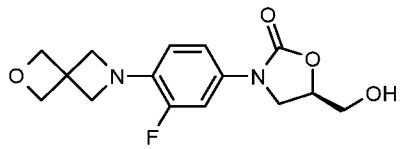
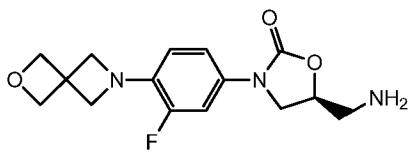
OTB-502		380.1435	0.246	13.55
OTB-503		396.1379	0.2-1.3	78->100
OTB-504		390.1385	0.5-0.7	17-> 100
OTB-505		406.1339	1.8-3.5	57->100
OTB-236		416.1097	14.256	NA
OTB-237		396.1388	0,03-0.11	15-23
OTB-518			3.5	73
OBD-016		407.1679	0.486	13
OBD-017		423.8	5.8-6.3	41
OBD-021		389.1322	27.456	NA

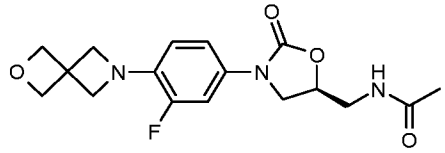
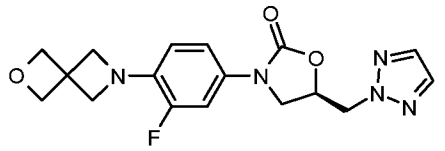
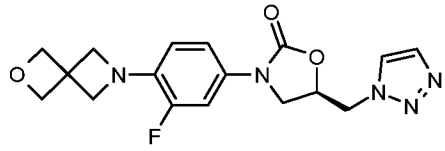
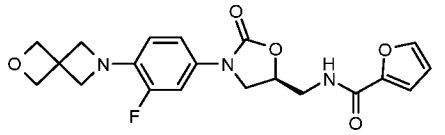
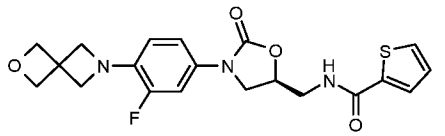
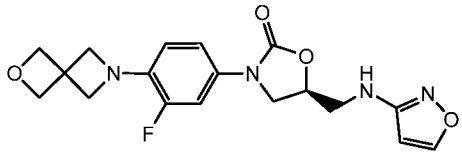
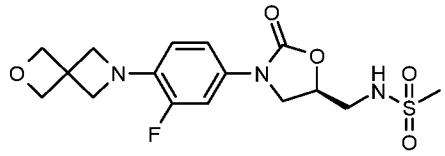
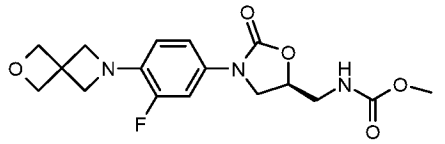
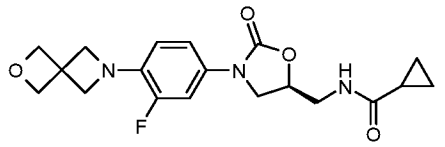
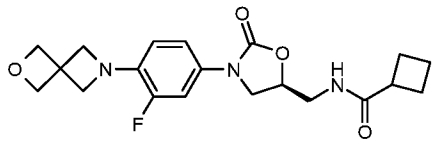
OBD-018		405.1271	> 32	NA
OTB-506		406.1527	1	8
OTB-507		420.1736	0.7	10
OTB-510		398.1329	0.03-0.22	3-7
OTB-514		414.1275	0.5	25
OTB-512		414.1278	0.063	42.47
OTB-519			0.9	51
OTB-511		408.1295	0.06-0.2	9-> 100
OTB-517			1.3-2	30-55
OTB-508		424.1484	0.2	8

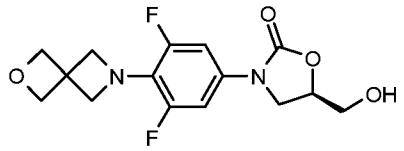
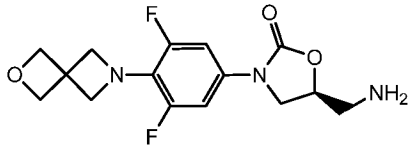
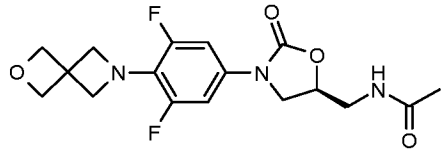
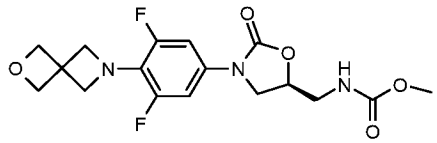
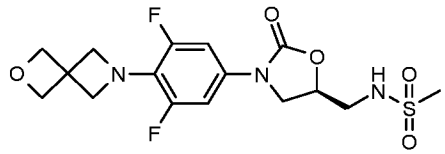
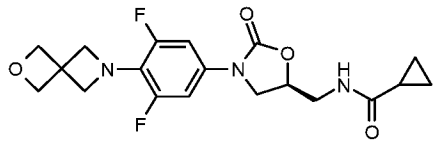
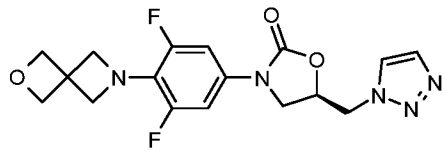
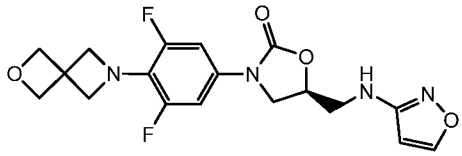
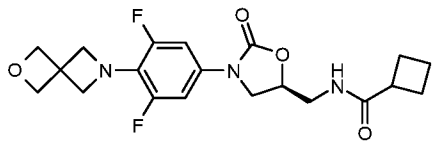
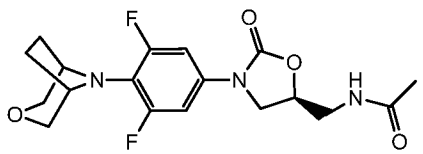
OTB-509		438.1642	0.04	5
OTB-513		454.1588	1.664	12.96
OBD-083			0.05	20
OBD-087			0.86	>100
OBD-029			0.11	>100
OBD-242			0.61	>100
OTB-260		325.1010	1.49	30.03
OTB-261		366.1274	0.12	2
OTB-523			0.5	4
OTB-515		NA	0.03-0.06	23-71

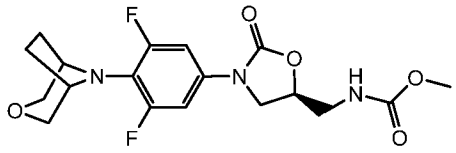
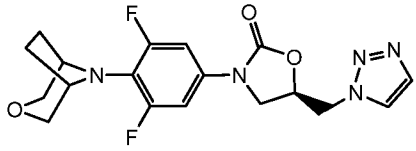
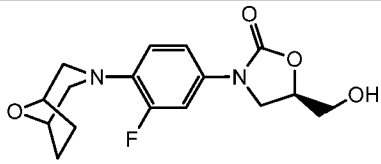
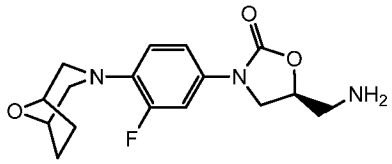
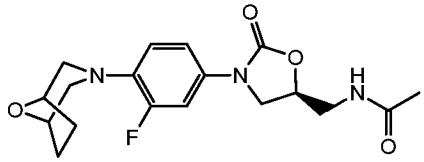
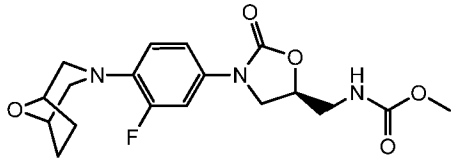
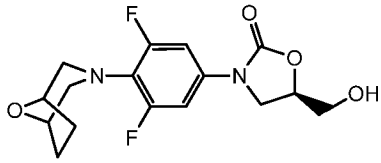
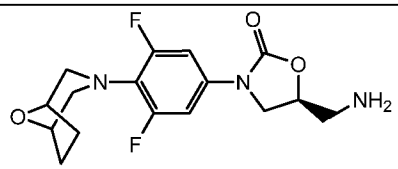
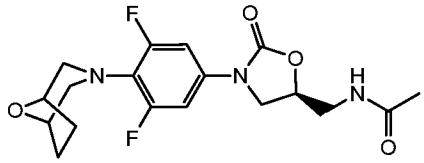
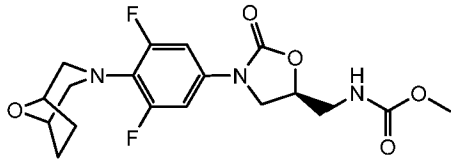
OTB-256			4	46
OTB-241		376.1231	0.116	19.81
OTB-247		392.0	1.2-1.4	10
OTB-249		392.1426	0.06-0.15	7->100
OTB-255		408.1378	1.9	10
OTB-250		428.2	0.06	10->100
OTB-254		422.1531	1.8	23
OTB-260-2A		402.1	0.82	>100
OTB-260-2B		418.0	0.49	>100
OTB-260-5A		376.1	0.44	>100

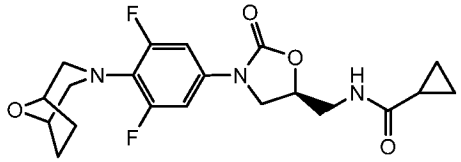
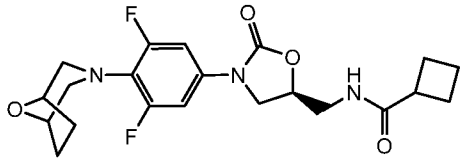
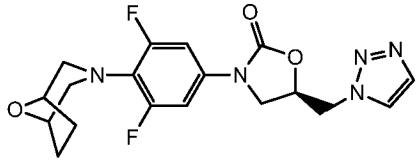
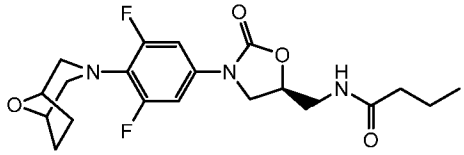
OTB-260-5B		392.1	>32	>100
OTB-260-4A		382.0	0.39	>100
OTB-260-4B		398.0	20	>100
OTB-516		343.0912	0.465	15.33
OTB-515		384.1168	0.03-0.57	14-21
OTB-520		400.1158	0.4	17
OTB-242		400.1125	0.02-0.06	23-71
OTB-253		416.1073	0.7	10
OTB-245		394.1129	0.03-0.5	25-35
OTB-522		410.1	1	38

OTB-243		410.1331	0.03	14
OTB-252		426.1278	0.7	52
OTB-244		424.1483	0.02-0.6	6->22
OTB-251		440.1441	0.9	24
OTB-516-2A		420.1	0.05	>100
OTB-516-2B		436.0	3	>100
OTB-516-4A		400.1	0.03	>100
OTB-516-4B		416.0	4.7	>100
OTB-201		309.1269	16	NA
OBD-057			0.4	67

OTB-202		350.1497	0.6-1.2	17-29
OTB-203		360.1451	> 32	NA
OTB-204		360.1451	3.2-3.7	> 100
OTB-205		402.1561	3.9	NA
OTB-206		418.1331	2.8	NA
OBD-056			1.9	17
OTB-222		386.1185	7.4	NA
OTB-223		366.1466	0.8-2.6	38->100
OTB-238		376.1652	2-4	20
OTB-239		390.1808	2.1-3.8	19-67

OTB-229		327.1135	1.9-7.4	> 100
OBD-062			0.1-0.25	21->100
OTB-230		368.1418	0.2	13
OTB-231		384.1367	0.24-0.7	37-63
OTB-232		404.1087	1.5-4	> 100
OTB-233		394.1575	0.36-1	8.4-50
OTB-234		378.1365	0.39-4	43->100
OBD-061			0.8	29
OTB-240		408.1716	0.24-0.6	19-67
OBD-051		381.9	0.6	6

OBD-052		398.0	0.95	13
OBD-055		391.8	1.3	15
OBD-112			3.5	>100
OBD-113			0.39	>100
OBD-110			0.45	7
OBD-111			0.49	7
OBD-114			1.7	>100
OBD-115			0.2=0.3	87->100
OBD-048			0.39	5
OBD-049			0.25-1	6->100

OBD-252			0.47	32.3
OBD-253			0.53	65
OBD-054			0.5	6-31
OBD-254			0.73	36

Definitions

As used herein unless otherwise indicated, "alkyl" includes branched- and straight-chain saturated aliphatic hydrocarbon groups having the specified carbon atom numbers. Commonly used abbreviations for alkyl groups are used throughout the application, e.g. methyl may be represented by conventional abbreviations including "Me" or CH_3 or a symbol that is an extended bond without defined terminal group, e.g. "ʢ—", ethyl is represented by "Et" or CH_2CH_3, propyl is represented by "Pr" or $CH_2CH_2CH_3$, butyl can be represented by "Bu" or $CH_2CH_2CH_2CH_3$, etc. "$C_{1\text{-}6}$ alkyl" (or "C_1-C_6 alkyl") means branched or linear chain alkyl groups, including all isomers, having the specified number of carbon atoms. $C_{1\text{-}6}$ alkyl includes all of the hexyl alkyl and pentyl alkyl isomers as well as n-, iso-, sec- and t-butyl, n- and isopropyl, ethyl and methyl. If no number is provided, 1-10 carbon atoms are intended for linear or branched alkyl groups. $C_{1\text{-}6}$ alkyl may be unsubstituted or substituted with 1-3 fluorine or 1-3 chlorine atoms.

"Cycloalkyl" means C_{3-10} carbocycles not containing heteroatoms. For example, cycloalkyl includes cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, decahydronaphthyl, and the like.

"Aryl" means mono- and bicyclic aromatic rings containing 6-12 carbon atoms. Examples of aryl include, but are not limited to, phenyl, naphthyl, indenyl and so on. Aryl also includes monocyclic rings fused to an aryl group. Examples include tetrahydronaphthyl, indanyl and the like.

"Heterocyclyl," unless otherwise indicated, means a 4-, 5-, 6-, 7- or 8-membered monocyclic saturated ring containing 1-2 heteroatoms selected from N, O and S, in which the point of attachment may be carbon or nitrogen. Examples of "heterocyclyl" include, but are not limited to, piperidinyl, piperazinyl, morpholinyl, pyrrolidinyl, oxazolidinyl, imidazolidinyl, and so on. The term also includes partially unsaturated monocyclic rings that are not aromatic, such as 2- or 4-pyridones attached through the nitrogen or *N*-substituted-(1*H*, 3*H*)-pyrimidine-2, 4-diones (*N*-substituted uracils). Heterocyclyl may also include such moieties in charged form, e.g., piperidinium.

"Heteroaryl" means a mono- or bicyclic aromatic ring or ring system having 5 to 10 atoms and containing 1-3 heteroatoms selected from N, O, and S. Examples include, but are not limited to, oxadiazolyl, thiadiazolyl, pyrrolyl, furanyl, triazinyl, thienyl, pyrimidyl, pyrimidinyl, pyridazinyl, pyrazinyl, isoxazolyl, triazolyl, isothiazolyl, pyrazolyl, imidazolyl, pyridyl, pyridinyl, oxazolyl, thiazolyl, tetrazolyl, and the like. Heteroaryl also includes aromatic heterocyclic groups fused to heterocycles that are non-aromatic or partially aromatic, and aromatic heterocyclic groups fused to cycloalkyl rings. Additional examples of heteroaryls include, but are not limited to, imidazopyridinyl, imidazopyridazinyl, pyrazolopyrazolyl, indazolyl, thienopyrazolyl, pyrazolopyridinyl, and imidazothiazolyl. Heteroaryl also includes such groups in charged form, such as pyridinium. In an embodiment, heteroaryl is triazolyl, imidazolyl, oxadiazolyl, pyrazolyl, oxazolyl, and pyridinyl.

"Heterocyclic alkyl," unless otherwise indicated, includes both branched- and straight-chain saturated aliphatic hydrocarbon groups which is bonded to a carbon or nitrogen atom of a heterocyclyl, as described above.

"Halogen (or halo)" includes fluorine (fluoro), chlorine (chloro), bromine (bromo) and iodine (iodo). In one embodiment, halogen is chlorine or fluorine.

Substitution by a named substituent is permitted on any atom in a ring (e.g., aryl, a heteroaryl ring, or a saturated heterocyclic ring) provided such ring substitution is chemically allowed and results in a stable compound. A "stable" compound can be prepared and isolated, and whose structure and properties remain or can be caused to remain essentially unchanged for a period of time that allows use of the compound for the described purposes.

Under standard nomenclature used throughout this disclosure, the terminal portion of the designated side chain is described first, followed by the adjacent functionality toward the point of attachment. For example, a C_{1-5} alkyl COOR is equivalent to $C_{1-5}\text{alkyl} - \overset{\overset{O}{\|}}{C}\text{-OR}$.

When a variable (e.g., R, R_x, etc.) occurs more than once in any constituent or formula, its definition on each occurrence is independent of its definition at every other occurrence. In addition, combinations of substituents and/or variables are allowed only if such combinations lead to stable compounds.

In choosing compounds of the present disclosure, one of ordinary skill in the art will recognize that the various substituents, i.e. R^1, R^2, R, etc., are to be chosen in conformity with common principles of chemical structure connectivity and stability.

The term "substituted" is used to include multiple degrees of substitution by a named substituent. Where multiple substituents are claimed, the substituted compound can be independently substituted by one or more of the disclosed substituents. By independently substituted, it is meant that the (two or more) substituents can be the identical or different.

Where a substituent or variable has multiple definitions, the substituent or variable is defined as being selected from the group consisting of the indicated definitions.

Salts:

Compounds of structural Formula I also cover the pharmaceutically acceptable salts. The compounds of the present invention may be administered in the form of a pharmaceutically acceptable salt. The term "pharmaceutically acceptable salt" means salts prepared from pharmaceutically acceptable bases or acids including inorganic or organic bases or acids. Pharmaceutically acceptable salts of basic compounds refer to non-toxic salts of the compounds of this invention which are generally prepared by mixing the free base with a suitable organic or inorganic acid. Representative salts of basic compounds of the present invention include, but are not limited to, the following: acetate, ascorbate, benzenesulfonate, benzoate, bicarbonate, bisulfate, bitartrate, borate, butyrate, camphorate, camphorsulfonate, camsylate, carbonate, clavulanate, citrate, edetate, edisylate, estolate, esylate, fumarate, gluceptate, gluconate, glutamate, hydrobromide, hydrochloride, lactobionate, laurate, malate, maleate, mandelate, mesylate, methylbromide, methylnitrate, methylsulfate, methanesulfonate, phosphate/diphosphate, polygalacturonate, propionate, salicylate, stearate, sulfate, subacetate, succinate, tannate, tartrate, teoclate, thiocyanate, tosylate, triethiodide, valerate and the like. Suitable pharmaceutically acceptable salts of acids covered by Formula I include, but are not limited to, salts generated from inorganic bases including aluminum, ammonium, calcium, copper, ferric, ferrous, lithium, magnesium, manganic, mangamous, potassium, sodium, zinc, and the like. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, cyclic amines, dicyclohexyl amines and basic ion-exchange resins, such as arginine, betaine, caffeine, choline, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine, and so on.

Solvates and hydrates of the compounds of Formula I are also included in the present invention.

The present invention also discloses processes to synthesize the compounds of Formula I, as described below.

One aspect of the invention that is of interest relates to a compound in accordance with Formula I, or a pharmaceutically acceptable salt, hydrate, or solvate thereof, for use in a method of treatment of microbial infections in humans.

Another aspect of the invention that is of interest is a method of treating microbial infections in a human patient in need of such treatment, comprising administering a therapeutically effective amount of a compound of Formula I or a pharmaceutically acceptable salt, hydrate, or solvate thereof to said patient.

In a further aspect, the present invention provides pharmaceutical compositions of Formula I, or a salt, hydrate, or solvate thereof, further comprising one or more additional anti-infective agents.

In still a further aspect, the present invention relates to a compound in accordance with Formula I or a pharmaceutically acceptable salt, hydrate, or solvate thereof for use as an anti-tuberculosis (TB) agent in a human.

While it may be possible for the compounds of the invention to be administered as the raw chemical, it is preferable to present these as a pharmaceutical composition. Thus, according to a further aspect, the present invention provides a pharmaceutical composition comprising a compound of Formula (I) or a pharmaceutically acceptable salt or solvate thereof, together with one or more pharmaceutically carriers thereof and optionally one or more other therapeutic ingredients. The carrier(s) must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not deleterious to the recipient thereof.

The formulations include those suitable for oral, parenteral (including subcutaneous, intradermal, intramuscular, intravenous and intraarticular), rectal and topical (including dermal, buccal, sublingual and intraocular) administration. The

most suitable route may depend upon the condition and disorder of the recipient. Tablets, capsules, intraocular topical formulations and parenteral solutions are common among aminoglycosides. The formulations may conveniently be presented in unit dosage form and may be prepared by any of the methods well known in the art of pharmacy. All methods include the step of bringing into association a compound of Formula (I) or a pharmaceutically acceptable salt or solvate thereof ("active ingredient") with the carrier which constitutes one or more accessory ingredients. In general, the formulations are prepared by uniformly and intimately bringing into association the active ingredient with liquid carriers or finely divided solid carriers or both and then, if necessary, shaping the product into the desired formulation.

Formulations of the present invention suitable for oral administration may be presented as discrete units such as capsules, cachets or tablets each containing a predetermined amount of the active ingredient; as a powder or granules; as a solution or a suspension in an aqueous liquid or a non-aqueous liquid; or as an oil-in-water liquid emulsion or a water-in-oil liquid emulsion. The active ingredient may also be presented as a bolus, electuary or paste.

A tablet may be made by compression or molding, optionally with one or more accessory ingredients. Compressed tablets may be prepared by compressing in a suitable machine the active ingredient in a free-flowing form such as a powder or granules, optionally mixed with a binder, lubricant, inert diluent, lubricating, surface active or dispersing agent. Molded tablets may be made by molding in a suitable machine a mixture of the powdered compound moistened with an inert liquid diluent. The tablets may optionally be coated or scored and may be formulated so as to provide sustained, delayed or controlled release of the active ingredient therein.

Formulations for parenteral administration include aqueous and non-aqueous sterile injection solutions which may contain anti-oxidants, buffers, bacteriostats and solutes which render the formulation isotonic with the blood of the intended recipient. Formulations for parenteral administration also include aqueous and non-aqueous sterile suspensions, which may include suspending agents and thickening agents.

The formulations may be presented in unit-dose of multi-dose containers, for example sealed ampoules and vials, and may be stored in a freeze-dried (lyophilized) condition requiring only the addition of a sterile liquid carrier, for example saline, phosphate-buffered saline (PBS) or the like, immediately prior to use. Extemporaneous injection solutions and suspensions may be prepared from sterile powders, granules and tablets of the kind previously described.

Preferred unit dosage formulations are those containing an effective dose, as hereinbelow recited, or an appropriate fraction thereof, of the active ingredient.

It should be understood that in addition to the ingredients particularly mentioned above, the formulations of this invention may include other agents conventional in the art having regard to the type of formulation in question, for example those suitable for oral administration may include flavoring agents.

Abbreviations

Throughout the synthetic schemes and examples below, abbreviations are used with the following meanings unless otherwise indicated:

Ac is acetate, or acetyl;

aq. is aqueous;

Ar is Aryl;

Bn is benzyl;

$BnNH_2$ is benzylamine;

Boc is *tert*-butylcarbamoyl;

br is broad;

Bu is butyl;

^{t}Bu is *tert*-butyl;

n-BuLi is n-butyllithium;

CbzCl is benzyl chloroformate;

CFU is colony forming units

CO_2 is carbon dioxide

COX-1 is cyclooxygenase I

^{c}Pr is cyclopropyl;

DCM is dichloromethane;

DIPEA is N,N-diisopropylethylamine;

DMAP is 4-dimethylaminopyridine

DMEM is Dulbecco's Modified Eagle Medium

DMF is *N*,*N*-dimethylformamide;

DMSO is dimethyl sulfoxide;

ELISA is enzyme-linked immunosorbent assay

ESI is electrospray ionization;

Et is ethyl;

Et_3N is triethylaimne;

Et_2O is diethyl ether;

EtOH is ethanol,

EtOAc is ethyl acetate;

FBS is Fetal Bovine Serum

Halo is a halogen (e.g., fluorine or chlorine);

^{1}H-NMR is proton nuclear magnetic resonance;

^{13}C-NMR is carbon nuclear magnetic resonance;

H9C2 is a cell line from rat heart myoblasts

HPLC is high performance liquid chromatography;

HRMS is high-resolution mass spectrometry;

Hz is hertz;

i is Iso;

IC_{50} is half-maximum inhibitory concentration;

Kg is kilogram;

M is molar;

Me is methyl;

μg is microgram;

MeCN is acetonitrile;

MeOH is methanol;

MsCl is methanesulfonyl chloride;

MHz is megahertz;

mm is millimeter;

μL is microliter;

mM is milimolar;

μM is micromolar;

mmol is milimoles;

MABA is microplate alamar blue assay;

MIC is minimum inhibitory concentration;

MPS is mitochondrial protein synthesis;

m/z is mass to charge ratio;

n is normal;

NEAA is non-essential amino acids

nm is nanometer;

*n*Pr is *n*-propyl;

p is para;

PE is petroleum ether;

Ph is phenyl;

Pr is propyl;

rt is room temperature;

sec is secondary;

SDH-A is succinate dehydrogenase-A

tert is tertiary;

TFA is trifluoroacetic acid;

TsCl is p-toluene sulfonyl chloride;

TMSI is trimethylsilyl iodide;

TPP is triphenylphosphine;

$TsNH_2$ is p-toluenesulfonamide;

Tosyl is p-toluenesulfonyl;

THF is tetrahydrofuran;

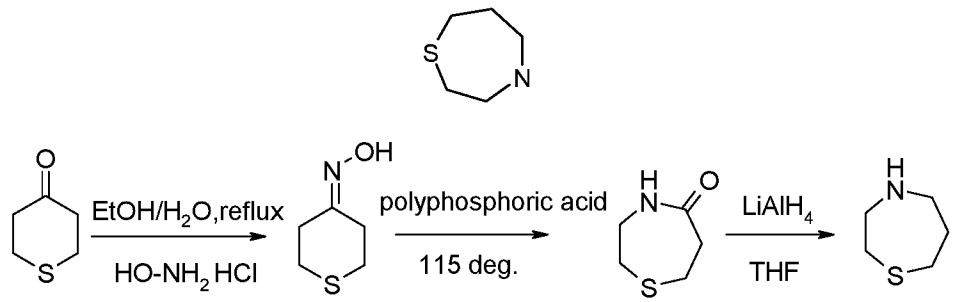
TLC is thin layer chromatography.

EXAMPLES

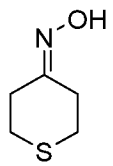
Synthetic methods for preparing the representative compounds of the present invention are illustrated in the following Examples. Starting materials are commercially available or may be made according to procedures known in the art or as illustrated herein. The following Examples are intended to help illustrate the invention, and are not intended to, nor should they be constructed to limit its scope.

Example 1

Preparation of [1, 4]Thiazepane (1a)



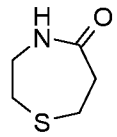
Step 1: Synthesis of Dihydro-2*H*-thiopyran-4(3*H*)-one oxime (1a-1)



To a solution of dihydro-2*H*-thiopyran-4(3H)-one (10 g, 0.086 mol) and hydroxylamine hydrochloride (10.4 g, 0.15 mol) in H_2O (100 mL) and ethanol (40 mL) was added sodium acetate (13.1 g, 0.16 mol). The mixture was refluxed for 4h, the organic solvent was removed in vacuum and the residue was cooled in an ice

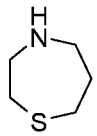
bath, 8.92 g solid was obtained in 79% yield by filtration. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.88 (m, 2H), 2.80 (m, 2H), 2.74 (m, 2H), 2.57 (m, 2H).

Step 2: Synthesis of 1,4-Thiazepan-5-one (1a-2)



The mixture of dihydro-2*H*-thiopyran-4(3*H*)-one oxime (4.01 g, 0.03 mol) in polyphosphoric acid was heated at 115□ for 15min, and cooled to rt, ice-water was added, then the mixture was extracted with EtOAc 5 times. The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum to give 2.4 g product as brown solid in 60% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.79 (brs, 1H), 3.63 (m, 2H), 2.94 (m, 2H), 2.74 (m, 4H).

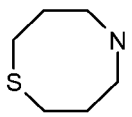
Step 3: Synthesis of 1,4-Thiazepane (1a)

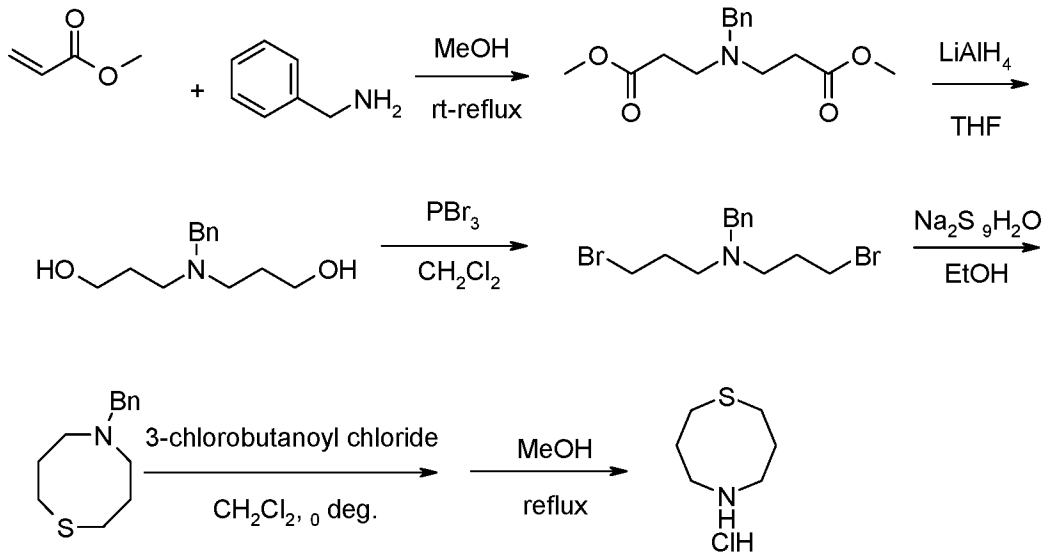


To a solution of 1,4-thiazepan-5-one (2.07 g, 15.7 mmol) in dry THF was added $LiAlH_4$ (0.66 g, 17.3 mmol) at 0□, then the mixture was stirred at rt for 4h. H_2O (0.7 mL), 15% NaOH (0.7 mL) and H_2O (2.1 mL) were added to the reaction in successively. The mixture was filtrated to give 1.77 g product in 96% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.07 (m, 2H), 2.98 (m, 2H), 2.75 (m, 4H), 1.93 (m, 2H).

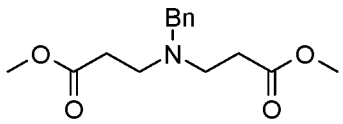
Example 2

Preparation of 1,5-Thiazocane hydrochloride (1b)



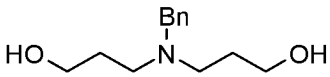


Step 1: Synthesis of Dimethyl 3,3'-(benzylazanediyl)dipropanoate (1b-1)



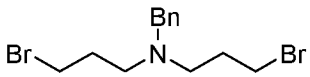
A solution of benzylamine (10.7 g, 0.1 mol) in MeOH (50 mL) was added in dropwise to a solution of methyl acrylate (18.9 g, .022 mol) in MeOH (100 mL) at rt. The result mixture was refluxed for 8h, and evaporated in vacuum to give 27.9 g product in quantitative yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.28 (m., 5H), 3.64 (s, 2H), 3.59 (s, 6H), 2.80 (m, 4H), 2.47 (m, 4H).

Step 2: Synthesis of 3,3'-(Benzylazanediyl)bis(propan-1-ol) (1b-2)



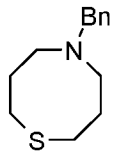
To a solution of dimethyl 3,3'-(benzylazanediyl)dipropanoate (4.47 g, 16.0 mmol) in dry THF was added $LiAlH_4$ (0.77 g, 20.2 mmol) at 0□, then the mixture was stirred at rt for 24h. MeOH (1.5 mL), 15% NaOH (1.0 mL) and H_2O (1.0 mL) were added to the reaction in successively. The mixture was filtrated to give 3.4 g product in 91% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.31 (m, 5H), 3.68 (t, J = 5.6 Hz, 5.6 Hz, 4H), 3.57 (s, 2H), 2.63 (t, J = 6.4 Hz, 6.0 Hz, 4H), 1.76 (m, 4H).

Step 3: Synthesis of *N*-Benzyl-3-bromo-*N*-(3-bromopropyl)propan-1-amine (1b-3)



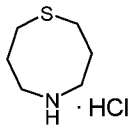
To a solution of 3,3'-(benzylazanediyl)bis(propan-1-ol) (447 mg, 2.0 mmol) in dry CH_2Cl_2 was added PBr3 in dropwise at 0□, then the mixture was stirred at rt for 12h. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layer was washed with sat. $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. The 0.43 g product was obtained as yellow oil in 61% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.27 (m, 5 H), 3.56 (s, 2 H), 3.44 (t, *J* = 6.8 Hz, 6.4 Hz, 4 H), 2.58 (t, *J* = 6.4 Hz, 6.4 Hz, 4 H), 2.02 (m, 4 H).

Step 4: Synthesis of 5-Benzyl-1,5-thiazocane (1b-4)



To a solution of N-benzyl-3-bromo-N-(3-bromopropyl)propan-1-amine (1.0 g, 2.9 mmol) in ethanol was added $Na_2S{\cdot}9H_2O$ (697 mg, 2.9 mmol). The mixture was refluxed for 18 h. The mixture was then cooled to r.t., and the solvent was removed in vacuum. To the residue was added H_2O and Et_2O. The aqueous layer was extracted with Et_2O, and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under vacuum. The crude product was used without purification.

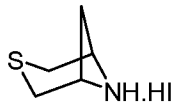
Step 5: Synthesis of 1,5-Thiazocane hydrochloride (1b)

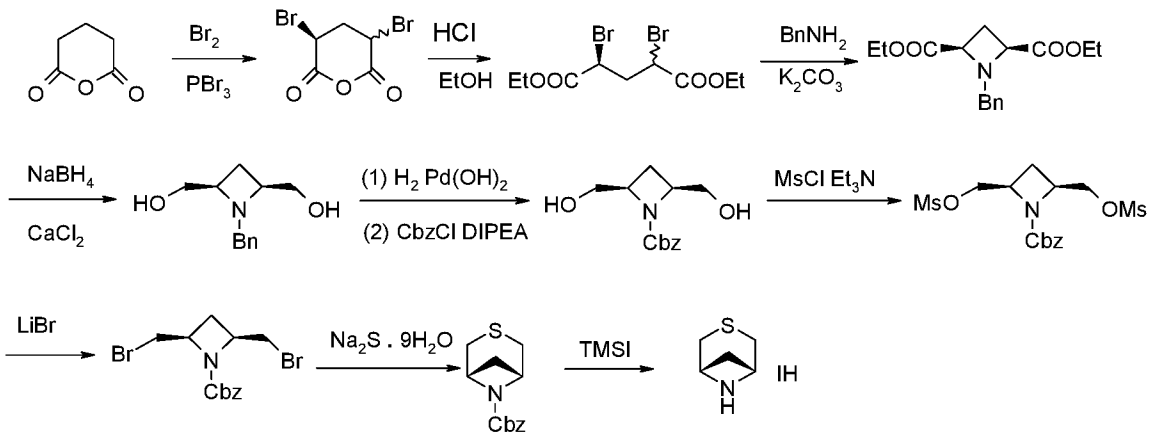


To a solution of 5-benzyl-1,5-thiazocane (8.6 g, 39 mmol) in CH_2Cl_2 was added (6.15 g, 43 mmol) at 0□. The mixture was stirred at rt for 6 h. the solvent was evaporated in vacuum and the residue was refluxed in MeOH for 3h. The mixture was concentrated and washed with Et_2O. The crude product was used without purification.

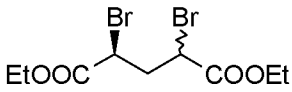
Example 3

Preparation of (1*R*,5*S*)-3-thia-6-azabicyclo[3.1.1]heptane (1c)



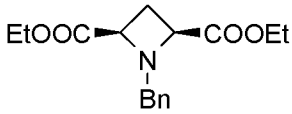


Step 1: Synthesis of diethyl 2,4-dibromopentanedioate (1c-1)



To a solution of dihydro-2*H*-pyran-2,6(3*H*)-dione (11.4 g, 0.1mol) and PBr_3 (0.1 mL) was added Br_2 (32 g, 0.2 mol) dropwise at 100°C, the mixture was stirred at 100°C for 7h and cooled to rt. HCl/EtOH (10mL) was added to the reaction mixture and stirred overnight at rt. After EtOH was evaporated, Et_2O was added to the residue and washed with sat. $NaHCO_3$ and brine, dried over Na_2SO_4, concentrated to give 32 g product was used for next step without purification.

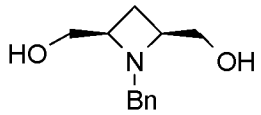
Step 2: Synthesis of (2*R*,4*S*)-diethyl 1-benzylazetidine-2,4-dicarboxylate (1c-2)



A mixture of (2*R*,4*S*)-diethyl 2,4-dibromopentanedioate (54 g, 156 mmol), benzylamine (17 g, 159 mmol) and K_2CO_3 (25.9 g, 187.2 mmol) in toluene was

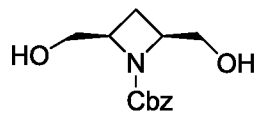
refluxed for 24h. the mixture was washed with brine, dried over and concentrated. The crude product was purified by chromatography on silica gel to give 18.39 g product in 41% yield. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{22}NO_4$: 292.1549; found: 292.1542.

Step 3: Synthesis of ((2*R*,4*S*)-1-benzylazetidine-2,4-diyl)dimethanol (1c-3)



To a solution of (2*R*,4*S*)-diethyl 1-benzylazetidine-2,4-dicarboxylate (0.8 g, 2.75 mmol) in EtOH/MeOH (9:1; 10 mL) was added $CaCl_2$ (0.92 g, 8.25 mmol) at r.t. To the resulting stirred mixture was then added $NaBH_4$ (0.63 g, 16.5 mmol) in portions. The reaction mixture was stirred for overnight at r.t. Subsequently H_2O (5 mL) was added, and the mixture was stirred for 30 min. The mixture was then concentrated in vacuum, and partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the organic layers were combined, washed with brine (10 mL), dried over Na_2SO_4, and concentrated in vacuo to give 0.25 g product as yellow oil. This product was used in the next step without further purification. MS (ESI): *m/z* $[M + H]^+$: 208.1477.

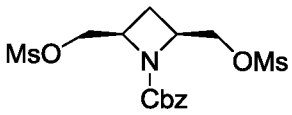
Step 4: Synthesis of (2*R*,4*S*)-benzyl 2,4-bis(hydroxymethyl)azetidine-1-carboxylate (1c-4)



To a solution of ((2*R*,4*S*)-1-benzylazetidine-2,4-diyl)dimethanol (0.52 g, 2.9 mmol) in MeOH (10 mL) was added $Pd(OH)_2$ (0.13 g), and the mixture was stirred for 2 h under H_2 at r.t. The suspension was filtered through a short pad of Celite and eluted with additional MeOH. The solvent was removed in vacuo. The residue was dissolved in anhydrous CH_2Cl_2 (30 mL). To the resulting solution was added DIPEA (0.37 g, 2.9 mmol), and then CbzCl (0.44 g, 2.56 mmol) dropwise. The mixture was

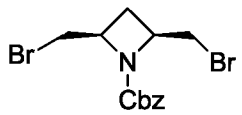
stirred for 2 h at r.t., and then quenched with H_2O (50 mL). The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford 0.33 g product as a yellow oil in 45% yield.

Step 5: Synthesis of (2*R*,4*S*)-benzyl-2,4-bis(((methylsulfonyl)oxy)methyl)azetidine-1-carboxylate (1c-5)



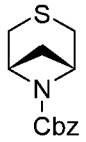
To a solution of (2*R*,4*S*)-benzyl 2,4-bis(hydroxymethyl)azetidine-1-carboxylate (51 mg, 0.2 mmol) in CH_2Cl_2(15 mL) was added Et_3N (61 mg, 0.6 mmol), and then MsCl (70 mg, 0.6 mmol) dropwise. The mixture was stirred for 5 h at r.t., and the reaction mixture was washed with 1N HCl and brine, dried over Na_2SO_4, and concentrated. The crude product was purified by chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford 65 mg product as a yellow oil in 80% yield.
HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{22}NO_8S_2$: 408.0787; found: 408.0780.

Step 6: Synthesis of (2*R*,4*S*)-benzyl-2,4-bis(bromomethyl)azetidine-1-carboxylate (1c-6)



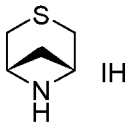
A mixture of (2*R*,4*S*)-benzyl-2,4-bis(((methylsulfonyl)oxy)methyl)azetidine-1-carboxylate (65 mg, 0.16 mmol) and LiBr (139 mg, 1.6 mmol) in acetone (15mL) was refluxed for 10h. The reaction mixture was evaporated, the residue was added H_2O (20 mL) and Et_2O (20 mL). The aqueous layer was extracted with Et_2O (2 × 20 mL), and the combined organic layer was washed with brine (10 mL), dried over Na_2SO_4 and concentrated under vacuum to give 51 mg product as yellow oil in 85% yield. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_{15}Br_2NO_2$: 375.9548; found: 375.9558.

Step 7: Synthesis of (1*R*,5*S*)-benzyl 3-thia-6-azabicyclo[3.1.1]heptane-6-carboxylate (1c-7)



To a solution of (2*R*,4*S*)-benzyl 2,4-bis(bromomethyl)azetidine-1-carboxylate (0.77 g, 2.05 mmol) in DMF (5 mL) was added $Na_2S·9H_2O$ (0.59 g, 2.46 mmol). The mixture was stirred at rt for 45min. To the solution was added H_2O (20 mL) and EtOAc (25 mL). The aqueous layer was extracted with EtOAc (2 × 20 mL), and the combined organic layer was washed with brine (10 mL), dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by chromatography on silica gel (20–30% EtOAc in PE) to give 0.15 g product as a colorless oil in 28.7% yield. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_{17}NO_2S$: 250.0902; found: 250.0900.

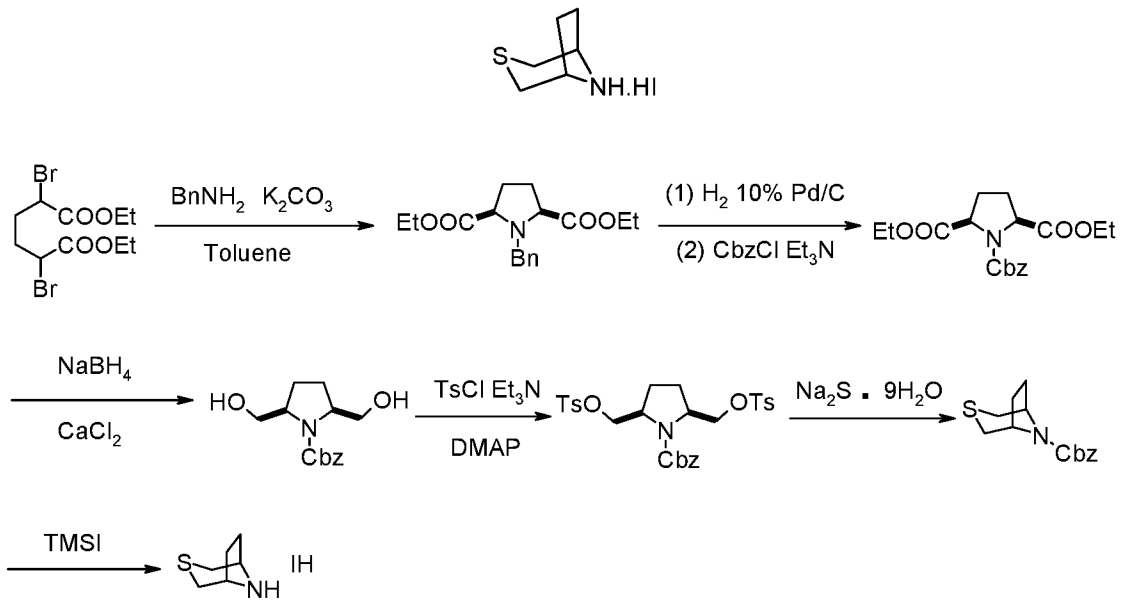
Step 8: Synthesis of (1*R*,5*S*)-3-thia-6-azabicyclo[3.1.1]heptane iodate (1c)



To a solution of (1*R*, 5*S*)-benzyl-3-thia-6-azabicyclo[3.1.1]heptane-6-carboxylate (0.19 g, 0.8 mmol) in anhydrous CH_2Cl_2 (20 mL) was added TMSI (0.39 g, 1.9 mmol) under Ar at 0 °C. The resulting mixture was stirred at rt for 2 h, and MeOH (5 mL) was added to the reaction dropwise. The result solution was stirred for additional 0.5 h, and then evaporated to remove the solvent. The residue was washed with PE/EtOAc (2:1) to give 0.24 g crude product as a brown solid and was used without purification.

Example 4

Preparation of (1*R*, 5*S*)-3-Thia-8-azabicyclo[3.2.1]octane iodate (1d)

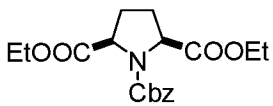


Step 1: Synthesis of *cis*-Diethyl 1-benzylpyrrolidine-2,5-dicarboxylate (1d-1)

To a stirred solution of diethyl 2,5-dibromohexanedioate (10.8 g, 30 mmol) and benzylamine (3.2 g, 30 mmol) in toluene (45 mL) and H_2O (9 mL) was added K_2CO_3 (5 g, 36 mmol) at r.t. The mixture was refluxed for 20 h under Ar, and then poured into H_2O (30 mL). The aqueous layer was extracted with EtOAc (2 × 20 mL), the combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and purified by chromatography on silica gel (10–20% EtOAc in PE) to afford 6.1 g product as a yellow oil in 67% yield.

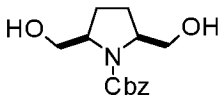
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.35–7.22 (m, 5 H), 4.06–4.00 (m, 4 H), 3.97 (s, 2 H), 3.46 (brs, 2 H), 2.08–2.04 (m, 4 H), 1.19 (t, J = 7.1 Hz, 6 H). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{24}NO_4$: 306.1705; found: 306.1695.

Step 2: Synthesis of *cis*-1-Benzyl 2,5-diethyl pyrrolidine-1,2,5-tricarboxylate (1d-2)



To a solution of cis-diethyl 1-benzylpyrrolidine-2,5-dicarboxylate (5.4 g, 17.7 mmol) in MeOH (100 mL) was added 10% Pd/C (0.54 g), and the mixture was shaken in a Parr Shaker for 4 h at 50 psi under H_2 at r.t. The suspension was filtered through a short pad of Celite and eluted with additional MeOH. The solvent was removed in vacuo. The residue was dissolved in anhydrous CH_2Cl_2 (50 mL), and cooled to 0 °C. To the resulting solution was added Et_3N (2.2 g, 21.6 mmol), and then CbzCl (3.7 g, 21.6 mmol) dropwise. The mixture was stirred overnight at r.t., and then quenched with H_2O (50 mL). The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by chromatography on silica gel (5–20% EtOAc in PE) to afford 5.22 g product as a yellow oil in 84% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.33–7.29 (m, 5 H), 5.19–5.10 (m, 2 H), 4.47 (m, 1 H), 4.40 (m, 1 H), 4.22 (q, J = 7.2 Hz, 2 H), 4.09 (q, J = 6.8 Hz, 2 H), 2.25–2.14 (m, 4 H), 1.28 (t, J = 6.8 Hz, 3 H), 1.17 (t, J = 6.8 Hz, 3 H). HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{18}H_{24}NO_6$: 350.1604; found: 350.1649.

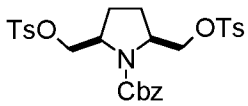
Step 3: Synthesis of *cis*-Benzyl 2,5-bis(hydroxymethyl)pyrrolidine-1-carboxylate (1d-3)



To a solution of *cis*-1-benzyl 2,5-diethyl pyrrolidine-1,2,5-tricarboxylate (5.75 g, 16.4 mmol) in EtOH/MeOH (10:1; 300 mL) was added $CaCl_2$ (5.5 g, 49.2 mmol) at r.t. To the resulting stirred mixture was then added $NaBH_4$ (3.75 g, 98.4 mmol) in portions. The reaction mixture was stirred for overnight at r.t. Subsequently H_2O (50 mL) was added, and the mixture was stirred for 30 min. The mixture was then concentrated in vacuo, and partitioned between H_2O (100 mL) and EtOAc (100 mL). The aqueous layer was extracted with EtOAc (2 × 50 mL), and the organic layers were combined, washed with brine (10 mL), dried over Na_2SO_4, and concentrated in vacuo to give 4.57 g product as colorless oil. This product was used in the next step without further purification.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.39–7.33(m, 5 H), 5.16 (s, 2 H), 4.09–3.82 (m, 4 H), 3.56 (d, *J* = 8.1 Hz, 2 H), 2.91 (brs, 2 H), 2.04–1.97 (m, 4 H). HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{14}H_{19}NNaO_4$: 288.1206; found: 288.1196.

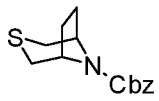
Step 4: Synthesis of *cis*-Benzyl 2,5-bis(tosyloxymethyl)pyrrolidine-1-carboxylate (1d-4)



A solution of compound *cis*-benzyl 2,5-bis(hydroxymethyl)pyrrolidine-1-carboxylate (4.35 g, 16.4 mmol), Et_3N (3.65 g, 36.1 mmol), and DMAP (4.01 g, 32.8 mmol) in CH_2Cl_2 (50 mL) was cooled to 0 °C. To this mixture was added p-toluenesulfonyl chloride (6.88 g, 36.1 mmol) in one portion and the resulting mixture was stirred overnight at r.t. The mixture was then washed with water and brine, dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by flash column chromatography (30–40% EtOAc in PE) to give 8.97 g product as a semi-solid in 95% yield.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.73 (brs, 4 H), 7.36–7.29 (m, 9 H), 5.03–4.96 (m, 2 H), 4.15–3.89 (m, 6 H), 2.44 (s, 6 H), 1.87–1.83 (m, 4 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (rotamers): 165.30, 154.49, 144.90, 135.88, 132.61, 129.90, 128.55, 128.19, 127.89, 69.16, 68.87, 67.28, 57.30, 56.56, 26.61, 25.44, 21.63. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{28}H_{32}NO_8S_2$: 574.1564; found: 574.1547.

Step 5: Synthesis of (1*R*, 5*S*)-Benzyl-3-thia-8-azabicyclo[3.2.1]octane-8-carboxylate (1d-5)

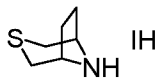


To a solution of *cis*-benzyl 2,5-bis(tosyloxymethyl)pyrrolidine-1-carboxylate (4.1 g, 7.1 mmol) in ethanol (25 mL) and H_2O (25 mL) was added $Na_2S{\cdot}9H_2O$ (5.12 g, 21.3 mmol). The mixture was refluxed for 5 h. The mixture was then cooled to r.t., and

the solvent was removed in vacuo. To the residue was added H_2O (20 mL) and EtOAc (25 mL). The aqueous layer was extracted with EtOAc (2 × 20 mL), and the combined organic layer was washed with brine (10 mL), dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by chromatography on silica gel (20–30% EtOAc in PE) to give 1.38 g product as a colorless oil in 73% yield.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.37–7.30 (m, 5 H), 5.16 (s, 2 H), 4.52–4.47 (m, 2 H), 3.22 (d, *J* = 11.6 Hz, 1 H), 3.11 (d, *J* = 10.8 Hz, 1 H), 2.12 (d, *J* = 12.8 Hz, 2 H), 2.06 (d, *J* = 1.2 Hz, 4 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 152.95, 136.59, 128.40, 127.93, 127.80, 66.73, 53.94, 32.72, 32.08, 28.82, 27.99. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{14}H_{18}NO_2S$: 264.1058; found: 264.1113.

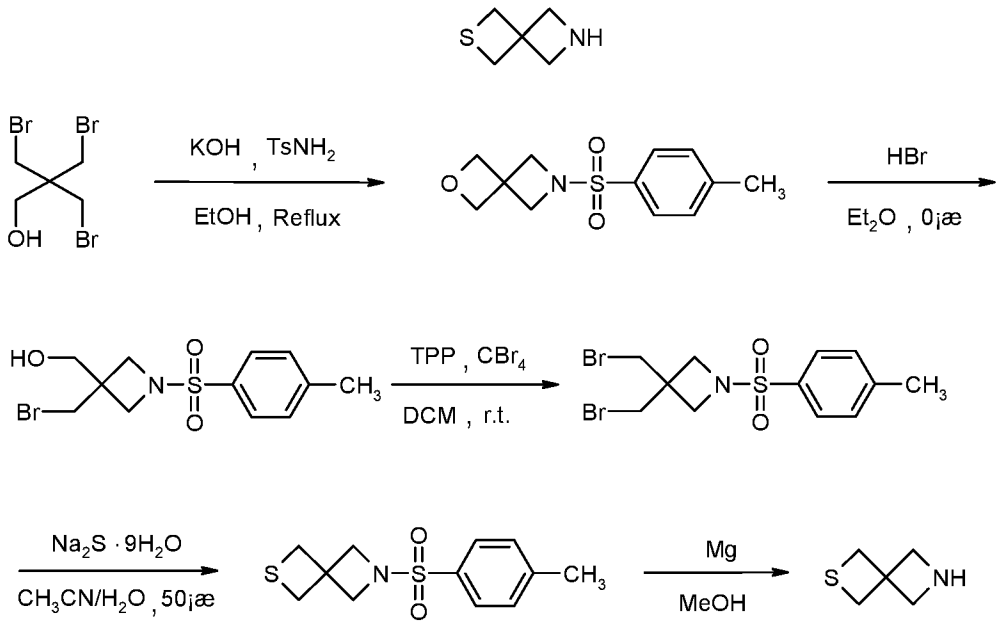
Step 6: Synthesis of (1*R*, 5*S*)-3-Thia-8-azabicyclo[3.2.1]octane iodate (1d)



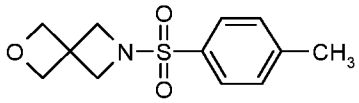
To a solution of (1*R*, 5*S*)-benzyl-3-thia-8-azabicyclo[3.2.1]octane-8-carboxylate (0.24 g, 0.91 mmol) in anhydrous CH_2Cl_2 (20 mL) was added TMSI (0.44 g, 2.18 mmol) under Ar at 0 °C. The resulting mixture was stirred at rt for 0.5 h, and MeOH (0.26 mL) was added to the reaction dropwise. The result solution was stirred for additional 0.5 h, and then evaporated to remove the solvent. The residue was washed with PE/EtOAc (1:2) to give 0.21 g product as a yellow solid in 91% yield. Mp: 208–210□. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.92 (brs, 1 H), 8.72 (brs, 1 H), 4.38 (s, 2 H), 3.78 (d, *J* = 14.0 Hz, 2 H), 2.41–2.35 (m, 4 H), 2.24–2.22 (d, *J* = 7.6 Hz, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 55.67, 31.42, 27.23. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_6H_{12}NS$: 130.0685; found: 130.0686.

Example 5

Preparation of 2-Thia-6-aza-spiro[3.3]heptane (1e)

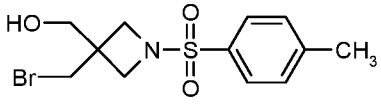


Step 1: Synthesis of 6-Tosyl-2-oxa-6-azaspiro[3.3]heptane (1e-1)



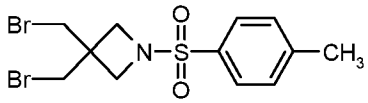
To a solution of KOH (9.04 g, 161 mmol) and 3-bromo-2,2-bis(bromomethyl)propan-1-ol (15.3 g, 47.0 mmol) in 500 mL ethanol was added *p*-tosylamide (17.9 g, 104 mmol) at room temperature and the reaction mixture was refluxed for 20 h. The solvent was removed by evaporation, 100 mL 8% NaOH solution was added and the suspension was stirred for another 2 h. The mixture was filtered and the white filter cake was rinsed with water until the washing water was neutral. The filter cake was dried to give the title product. Yield: 6.1 g (40.2 %). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.71 (d, J = 8.0 Hz, 2 H), 7.37 (d, J = 8.0 Hz, 2 H), 4.59 (s, 4 H), 3.91 (s, 4 H), 2.46 (s, 3 H). HRMS (ESI-TOF$^+$): *m/z* [M + H]$^+$ calcd for $C_{12}H_{16}NO_3S$: 254.0825; found: 254.0851.

Step 2: Synthesis of (3-(bromomethyl)-1-tosylazetidin-3-yl)methanol (1e-2)



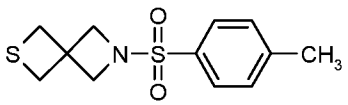
To a suspension of 6-(*p*-toluenesulfonyl)-2-oxa-6-azaspiro[3.3]heptane (1e-1) (9.79 g, 38.7 mmol) in Et_2O (200 mL) at 0 °C was added a solution of hydrobromic acid (ca. 33% in AcOH) in dropwise. The resulting solution was stirred at room temperature for 30 min, it was adjusted to pH=8 with 1mol/L NaOH. The phases were separated and the aqueous phase was extracted with Et_2O (3×100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated *in vacuo* to afford the title compound as a colorless solid. Yield: 10.0 g (77.4%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.74 (d, *J* = 8.0 Hz, 2 H), 7.39 (d, *J* = 8.0 Hz, 2 H), 3.68 (s, 2 H), 3.68 (s, 2 H), 3.62 (d, *J* = 8.4 Hz, 2 H), 3.55 (d, *J* = 8.4 Hz, 2 H), 3.45 (s, 2 H), 2.47 (s, 3 H).

Step 3: Synthesis of 3,3-bis(bromomethyl)-1-tosylazetidine (1e-3)



(3-(Bromomethyl)-1-tosylazetidin-3-yl)methanol (1e-2) (10.0 g, 30.0 mmol) was dissolved in CH_2Cl_2 and CBr_4 (16.4 g, 49.4 mmol) was added. The resulting solution was cooled to 0 °C and PPh_3 (17.9 g, 104 mmol) was added. The reaction mixture was stirred at room temperature overnight. The mixture was concentrated under reduced pressure and the residue was purified by chromatography on silica gel (5 - 10% EtOAc in PE) to give the pure title compound. Yield: 8.85 g (74.8%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.73 (d, *J* = 8.0 Hz, 2 H), 7.39 (d, *J* = 8.0 Hz, 2 H), 3.59 (s, 4 H), 3.53 (s, 4 H), 2.47 (s, 3 H).

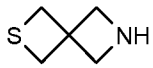
Step 4: Synthesis of 6-tosyl-2-thia-6-azaspiro[3.3]heptane (1e-4)



To a solution of 3,3-bis(bromomethyl)-1-tosylazetidine (1e-3) (8.82 g, 7.9 mmol) in a mixture of CH_3CN (90 mL) and H_2O (9 mL) was added $Na_2S{\cdot}9H_2O$ (10.7 g, 44.7 mmol) and the reaction mixture was stirred at 50 °C for 4 h, then it was concentrated

to dryness. EtOAc (100 mL) and $NaHCO_3$ solution (100 mL) were added, and the phases were separated. The aqueous phase was extracted with EtOAc (2×100 mL). The organic phase was washed with brine, dried (Na_2SO_4), filtered, and concentrated *in vacuo* to give the title compound. Yield: 5.46 g (90.1%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.71 (d *J* = 8.0 Hz, 2 H), 7.37 (d *J* = 8.0 Hz, 2 H), 3.78 (s, 4 H), 3.14 (s, 4 H), 2.46(s, 3 H). HRMS (ESI-TOF$^+$): *m/z* $[M + H]^+$ calcd for $C_{12}H_{16}NO_2S_2$: 270.0622; found: 270.0621.

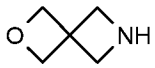
Step 5: Synthesis of 2-thia-6-azaspiro[3.3]heptane (1e)

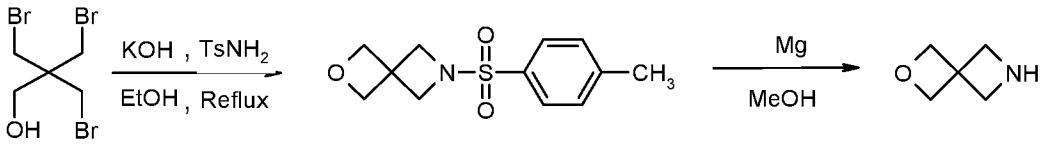


6-Tosyl-2-thia-6-azaspiro[3.3]heptane (1e-4) (2.0 g, 7.9 mmol) was dissolved in MeOH (40 mL). To the resulting solution was added magnesium powder (1.0g), and the reaction mixture was sonicated at RT for about 3 hrs. The reaction mixture was concentrated *in vacuo*, the crude product was used in next step without purification.

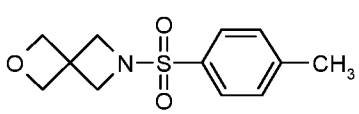
Example 6

Preparation of 2-Oxa-6-aza-spiro[3.3]heptane (1f)



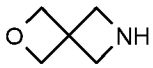


Step 1: Synthesis of 6-Tosyl-2-oxa-6-azaspiro[3.3]heptane



This product was synthesized as described in Example 5, StepSStep 1.

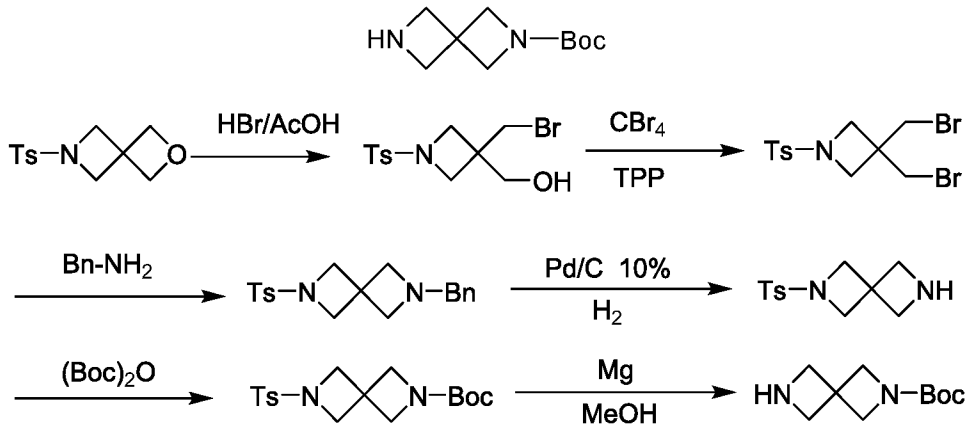
Step 2: Synthesis of 2-oxa-6-azaspiro[3.3]heptane (1f)



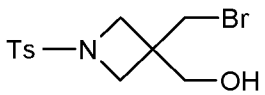
6-Tosyl-2-oxa-6-azaspiro[3.3]heptane (6.3 g, 25.0 mmol) was dissolved in MeOH (50 mL). To the resulting solution was added magnesium powder (6.0g), and the reaction mixture was sonicated at RT for about 3 hrs. The reaction mixture was concentrated *in vacuo*, the crude product was used in next step without purification.

Example 7

Preparation of N-Boc protected 2, 6-Diaza-spiro[3.3]heptane (1g)



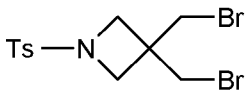
Step 1: Synthesis of (3-(Bromomethyl)-1-(*p*-toluenesulfonyl)azetidin-3-yl)methanol (1g-1)



To a suspension of 6-(*p*-toluenesulfonyl)-2-oxa-6-azaspiro[3.3]heptane (6.25 g, 24.7 mmol) (obtained according to Example 5 step 1) in Et_2O (100 mL) at 0 °C was dropwise added over a period of 15 min a solution of hydrobromic acid (ca. 33% in AcOH; 4.1 mL, 24.7 mmol) in Et_2O (5 mL). The resulting mixture was warmed to room temperature and stirred for 45 min. The resulting colorless solution was poured into a saturated aqueous solution of $NaHCO_3$ (100 mL). The organic phase was

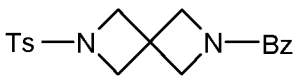
separated and the aqueous phase was extracted with Et_2O (100 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford the title compound 7.74g as a colorless solid. The crude product was pure enough for further transformations.

Step 2: Synthesis of 3,3-Bis(bromomethyl)-1-(*p*-toluenesulfonyl)azetidine (1g-2)



The above crude product 1g-1 (7.74 g, 23.1 mmol) was dissolved in CH_2Cl_2 (100 mL) and CBr_4 (13.7 g, 41.2 mmol) was added in one portion. The resulting solution was cooled to 0 °C and PPh_3 (26.26 g, 41.2 mmol) was added in one portion. The reaction mixture turned to a dark orange solution, which was stirred at 0 °C for 1.5 h, then warmed to room temperature and stirred for further 8 h. The mixture was concentrated under reduced pressure to afford a dark orange oil, which was purified by chromatography (hexanes : EtOAc 4:1) to give the title compound 7.61g. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.73 (d, J = 8.4 Hz, 2 H), 7.40 (d, J = 7.6 Hz, 2 H), 3.60 (s, 4 H), 3.53 (s, 4 H), 2.48 (s, 3 H).

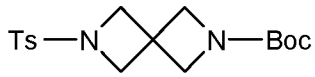
Step 3: Synthesis of 2-Benzyl-6-(*p*-toluenesulfonyl)-2,6-diazaspiro[3.3]heptane (1g-3)



Dibromide 1g-2 (7.61 g, 19.1 mmol) was dissolved in CH_3CN (100 mL). Benzylamine (4.1 g, 38.3 mmol) and DIPEA (12.4 g, 95.5 mmol) were added to the above mixture and the reaction mixture was heated to reflux for 3 d. Then the yellowish solution was cooled to room temperature and concentrated to about 1/6 of the initial volume. The residue was partitioned between CH_2Cl_2 (100 mL) and 1 mol/L NaOH (100 mL). The organic phase was separated and the aqueous layer was extracted with CH_2Cl_2 (50 mL). The combined organic layers were dried ($MgSO_4$),

filtered, and concentrated *in vacuo*. The residue was purified by chromatography (hexanes : EtOAc : Et3N 1:1:1% to 1:2:1% gradient) to afford the title compound 4.0 g. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.69 (d, J = 8.2 Hz, 2 H), 7.34 (d, J = 8.2 Hz, 2 H), 7.32-7.11 (m, 5 H), 3.82 (s, 4 H), 3.47 (s, 2 H), 3.13 (s, 4 H), 2.44 (s, 3 H).

Step 4: Synthesis of *tert*-Butyl 6-(p-toluenesulfonyl)-2,6-diazaspiro[3.3]heptane-2-carboxylate (1g-5)



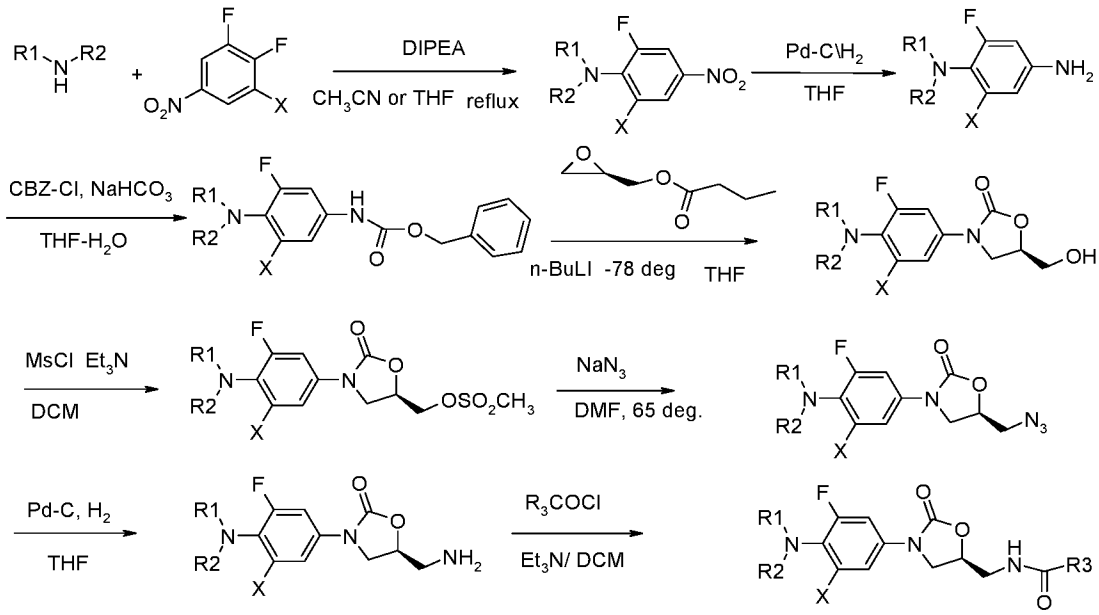
Benzyl azetidine 1g-3 (2.70 g, 7.88 mmol) was dissolved in MeOH (40 mL), and Pd/C (10% on charcoal; 0.54 g) was added to the above mixture. A hydrogen atmosphere (50 PSI) was built up and the mixture was heated to 45 °C and stirred at this temperature for 48 h. Then the reaction mixture was cooled to room temperature and filtered over celite. The filter cake was washed thoroughly with MeOH (2 × 20 mL). To the above solution of the intermediate Ts-protected azetidine (1g-4) in MeOH (ca. 80 mL) was added Boc_2O (1.77 g, 7.88 mmol). The resulting solution was stirred at room temperature for 1 h and concentrated *in vacuo*. The residue was purified by chromatography (hexanes : EtOAc 1:1 to 1:2 gradient) to furnish the pure title compound. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.71 (d, J = 7.6 Hz, 2 H), 7.37 (d, J = 8.0 Hz, 2 H), 3.85 (s, 4 H), 3.84 (s, 4 H), 2.46 (s, 3 H), 1.39 (s, 9 H).

Step 5: Synthesis of *tert*-Butyl 2,6-diazaspiro[3.3]heptane-2-carboxylate (1g)

The above product 1g-5 (3.50 g, 10.0 mmol) was dissolved in MeOH (30 mL). Mg powder (1.92 g, 80.0 mmol) was added, and the mixture was sonicated for 6 h. The reaction mixture was concentrated *in vacuo* to afford a dark gray solid, which can be . used for the further reaction without purification.

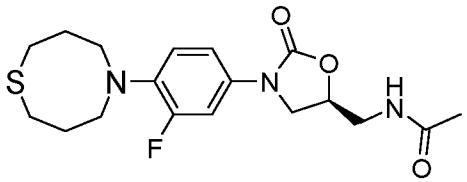
Example 8

General Synthetic Methods: preparation of oxazolidinone compounds

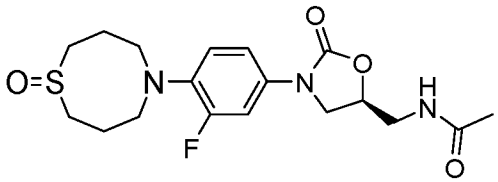


wherein,  represents ring A as previously defined in Formula I; X = H, or F.

General procedures for the preparation of (*S*)-N-((3-(3-fluoro-4-(1,5-thiazocan-5-yl) phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide (OTB-114) and its sulfoxide (OTB-124), are provided below.

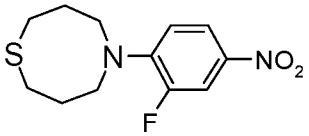


OTB-114



OTB-124

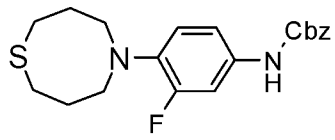
Step A: 5-(2-Fluoro-4-nitrophenyl)-1,5-thiazocane



A solution of 3,4-difluoronitrobenzene (4.92 g, 31 mmol) and *N*,*N*-diisopropylethylamine (8.81 g, 68 mmol) in CH_3CN (30 mL) was treated with

1,5-thiazocane hydrochloride (5.2 g, 31 mol) at ambient temperature and the reaction mixture heated to reflux for 24 h. The reaction mixture was cooled to rt and concentrated. The residue was diluted with H_2O and CH_2Cl_2, aqueous layer was extracted with CH_2Cl_2 (50mL*3). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by chromatography on silica gel (PE/CH_2Cl_2=10:1) to give 3.36 g (40%) of the title compound as a yellow solid.^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.92 (m, 2H), 6.80 (t, *J* = 9.2 Hz, 8.8 Hz, 1H), 3.67 (t, *J* = 6.0 Hz, 5.6 Hz, 4H), 2.72 (t, *J* = 5.6 Hz, 6.0 Hz, 4H), 2.08 (m, 4H).

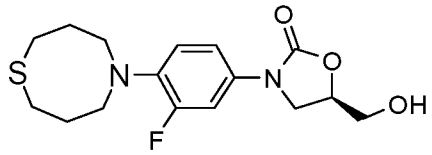
Step B: Benzyl(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)carbamate



To a solution of 5-(2-fluoro-4-nitrophenyl)-1,5-thiazocane (3.0 g, 12.5 mmol) in MeOH/THF was added 10% Pd/C (0.3 g), and the mixture was shaken 4 h under H_2 at r.t. The suspension was filtered through a short pad of Celite and eluted with additional MeOH. The solvent was removed in vacuo. The residue was dissolved in THF/H_2O (50 mL). To the resulting solution was added $NaHCO_3$ (2.12 g, 25.2 mmol), and then CbzCl (2.58 g, 15.1 mmol) dropwise. The mixture was stirred overnight at r.t., and concentrated. The residue was added H_2O (50 mL) and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by chromatography on silica gel (PE/EtOAc=5:1) to afford 4.6 g product as a colorless solid in 98% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.30 (m, 5H), 6.96 (m, 2H), 6.76 (s, 1H), 4.11 (m, 2H), 3.30 (m, 4H), 2.74 (m, 4H), 1.93 (m, 4H)。

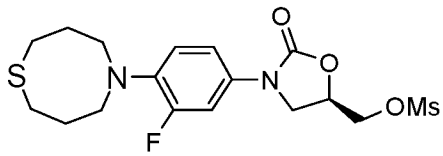
Step C:

(*R*)-[3-[3-Fluoro-4-(1,5-thiazocane-5-yl)phenyl]-2-oxo-5-oxazolidinyl]methanol



A solution of benzyl(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)carbamate (2.44 g, 6.5 mmol) in dry THF (20 mL) was cooled to -78 °C (dry ice/acetone bath) under N_2. *n*-Butyllithium (2.5 M solution in hexanes, 2.9 mL, 7.2 mmol) was added to the reaction mixture over 10 min. The resultant light yellow solution was stirred at -78 °C for 50 min and then treated with (*R*)-(-)-glycidyl butyrate (0.95 mL, 6.9 mmol) dropwise. The reaction mixture was stirred for an additional 30 min at -78 °C, and then the cooling bath was removed. The reaction mixture was allowed to warm to ambient temperature overnight. Saturated aqueous NH_4Cl (50 mL) was added to the reaction mixture. The reaction mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by by chromatography on silica gel (PE/EtOAc=1:2) to afford 1.33 g product as a colorless solid in 59% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.37 (dd, *J* = 14.8 Hz, 2.4 Hz, 1H), 7.09 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 7.00 (m, 1H), 4.73 (m, 1H), 3.95 (m, 3H), 3.76 (m, 1H), 3.35 (m, 4H), 2.74 (m, 4H), 1.97 (m, 4H).

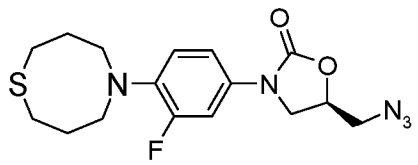
Step D: (*R*)-[3-[3-Fluoro-4-(1,5-thiazocane-5-yl)phenyl]-2-oxo-5-oxazolidinyl] methyl methanesulfonate



A solution of (*R*)-[3-[3-Fluoro-4-(1,5-thiazocane-5-yl)phenyl]-2-oxo-5-oxazolidinyl] methanol (1.0 g, 2.94 mmol) in dry CH_2Cl_2 was cooled with an ice bath and treated with Et_3N (446 mg, 4.41 mmol) and methanesulfonyl chloride (404 mg, 3.53 mmol). The mixture was stirred for 2h at rt, and was washed with H_2O, saturated aqueous $NaHCO_3$, and brine. The organic layer was then dried over Na_2SO_4, filtered, and

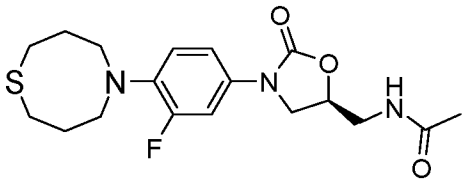
concentrated. The product was used in next step without purification.

Step E: (*R*)-[3-[3-Fluoro-4-(1,5-thiazocane-5-yl)phenyl]-2-oxo-5-oxazolidinyl] methyl azide



A solution of (*R*)-[3-[3-Fluoro-4-(1,5-thiazocane-5-yl)phenyl]-2-oxo-5-oxazolidinyl] methyl methanesulfonate (859 mg, 2.1 mmol) in dry DMF was treated with solid NaN_3 (683 mg, 10.5 mmol) at rt. The mixture was then heated to 65 °C for 8 h, after cooling to rt; the reaction mixture was quenched with H_2O and was extracted with EtOAc. The combined organic layer was washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated. The product was used in next step without purification.

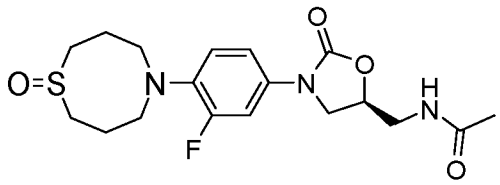
Step F: (*S*)-N-((3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl) methyl)acetamide



To a solution of (*R*)-[3-[3-fluoro-4-(1,5-thiazocane-5-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl azide (216 mg, 0.59 mmol) in MeOH/THF was added 10% Pd/C (22 mg), and the mixture was shaken 4 h under H_2 at r.t. The suspension was filtered through a short pad of Celite and eluted with additional MeOH. The solvent was removed in vacuo. The residue was dissolved in CH_2Cl_2 and was treated with Et_3N (121 mg, 1.2 mmol) and AcCl (56 mg, 1.2 mmol). The reaction mixture was quenched with H_2O and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH=100:1) to afford 0.1 g

product as a colorless solid in 44% yield. mp 78-80 °C. $[\alpha]_D^{20}$ -15.4 (*c* 0.25, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.34 (m, 1H), 7.02 (m, 2H), 6.23 (m, 1H), 4.75 (m, 1H), 4.00 (t, *J* = 8.8 Hz, 8.8 Hz, 1H), 3.73 (m, 2H), 3.64 (m, 1H), 3.36 (t, *J* = 6.4 Hz, 6.0 Hz, 4H), 2.73 (m, 4H), 2.04 (s, 3H), 1.97 (m, 4H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 171.4, 155.2 (d, *J* = 243.5 Hz), 154.4, 134.5, 130.2, 119.9, 114.3, 108.3 (d, *J* = 26.8 Hz), 71.9 , 48.1, 47.8, 42.0, 31.9, 29.7, 23.1. HR-MS (ESI-TOF): m/z $[M+H]^+$ calcd for $C_{18}H_{25}O_3N_3FS$: 382.1595; found: 382.1620.

Step G: (*S*)-*N*-[[3-(3-fluoro-4-(1-oxido-1,5-thiazocan-5-yl)phenyl)-2-oxo-oxazolidin-5-yl]methyl]acetamide



A solution of sodium metaperiodate (30 mg, 0.14 mmol) in H_2O (2 mL) was cooled to 0 °C. (S)-N-((3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl) methyl)acetamide (50 mg, 0.13 mmol) was added and then MeOH (3 mL). The reaction mixture was stirred at 0 °C for 2 h, and was concentrated. H_2O was added to the residue and then extracted with CH_2Cl_2 The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH=100:1) to afford 39 mg product as a colorless solid in 75% yield. mp 69-70 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.46 (dd, *J* = 2.8 Hz, 14.8 Hz, 1H), 7.14 (t, *J* = 9.2 Hz, 8.8 Hz, 1H), 7.07 (m, 1H), 6.15 (m, 1H), 4.78 (m, 1H), 4.03 (t, *J* = 9.2 Hz, 8.8 Hz, 1H), 3.74 (m, 3H), 3.31 (m, 1H), 3.18 (m, 4H), 2.98 (m, 2H), 2.17 (m, 4H), 2.03 (s, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 171.0, 154.2, 134.0, 128.5, 127.3, 122.6, 113.9, 108.1 (d, *J* = 26.9 Hz), 71.9, 53.1, 51.7, 47.7, 42.0, 29.7, 25.0, 23.2. HR-MS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{25}O_4N_3FS$: 398.1544; found: 398.1540.

Example 9

In Vitro Assay for Antimicrobial Susceptibility

Antimicrobial susceptibility testing was performed in 96-well microplates. Initial drug dilutions (6.4 mg/ml) were prepared in dimethyl sulfoxide, and subsequent two-fold dilutions were performed in 0.1 ml of 7H9 broth media (BD) in the microplates. The final drug concentrations were about 0.008 μg/ml. Every concentration of test compounds was added to two wells. Control wells consisted of bacteria and positive drug (Linezolid). Plates were incubated at 37°C. The final bacterial titers were 1×10^6 CFU/ml for $H_{37}Rv$. Starting at day 7 of incubation, 20μl of 10× Alamar blue solution (Life Technologies) and 12.5μl of 20% Tween 80 (Sigma-Aldrich) were added to each well and the plates were reincubated at 37°C. Wells were observed at 24h and the colors of all were recorded. Visual MICs were defined as the lowest amount of drug that prevented a color change from blue to pink. Fluorescence was measured in a microplate fluorometer in bottom-reading mode with excitation at 530 nm and emission at 590 nm. For fluorometric MICs, the lowest drug concentration effecting an inhibition of ≥90% was considered the MIC. The MIC results are provided in Table 1 above.

Example 10

In Vitro Assay for MPS Inhibition

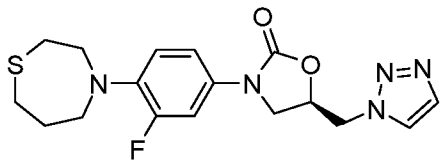
H9C2 cells were incubated in DMEM (Hyclone, GE LifeSciences) with 10% FBS (Gibco, Life Technologies) and 1× Glutamine (Gibco, Life Technologies) and NEAA (Gibco, Life Technologies) at 37°C, 5% CO2 at 1500 cells/well in a 384-well plate. Test compound was added after 18 hr incubation, and then incubated for 5 days. COX-1 protein (cyclooxygenase I) and SDH-A (succinate dehydrogenase-A) formation reduction were measured by ELISA assay (MitoBiogenesisTM In-Cell ELISA Kit (Colorimetric, Abcam). MPS assay results are provided in Table 1 above.

Example 11

Specific Compounds Synthesized According to General Methods

OTB-107

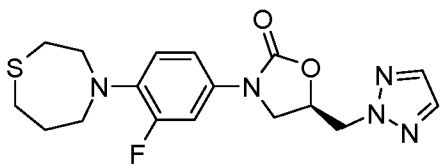
(*R*)-5-[(1*H*-1,2,3-Triazol-1-yl)methyl]-3-[3-fluoro-4-(1,4-thiazepan-4-yl)phenyl]oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.94 (s, 1 H), 7.75 (s, 1 H), 7.17 (dd, *J* = 15.2 Hz, 1.2 Hz, 1 H), 6.89 (dd, *J* = 8.8 Hz, 1.6 Hz, 1 H), 6.82 (t, *J* = 9.6 Hz, 8.8 Hz, 1 H), 5.03 (m, 1 H), 4.78 (s, 2 H), 4.10 (t, *J* = 9.2 Hz, 8.8 Hz, 1 H), 3.87 (m, 1 H), 3.68 (m, 4 H), 2.87 (m, 2 H), 2.68 (t, *J* = 6.4 Hz, 6.0 Hz, 2 H), 2.06 (m, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 153.4, 151.0, 134.3, 124.9, 116.8, 115.1, 108.7 (d, *J* = 27.3 Hz), 70.2, 56.1, 51.9, 51.3, 47.4, 34.0, 31.5, 30.3. HR-MS (ESI): m/z $[M + H]^+$ calcd for $C_{17}H_{21}O_2N_5FS$: 378.1395; found: 378.1396.

OTB-106

(*R*)-5-[(2*H*-1,2,3-Triazol-2-yl)methyl]-3-[3-fluoro-4-(1,4-thiazepan-4-yl)phenyl]oxazolidin-2-one

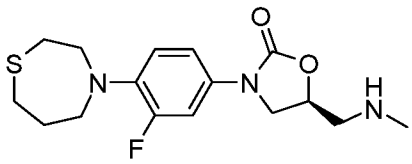


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.65 (s, 2 H), 7.27 (m, 1 H), 7.01 (dd, *J* = 8.8 Hz, 1.6 Hz, 1 H), 6.84 (t, *J* = 9.2 Hz, 9.2 Hz, 1 H), 5.11 (m. 1 H), 4.85 (dd, *J* = 14 Hz, 4.8 Hz, 1 H), 4.74 (dd, *J* = 14 Hz, 6.8 Hz, 1 H), 4.05 (t, *J* = 9.2 Hz, 8.8 Hz, 1 H), 3.95 (m, 1 H), 3.67 (m, 4 H), 2.87 (m, 2 H), 2.69 (t, *J* = 6.4 Hz, 6.0 Hz, 2 H), 2.06 (m, 2 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 153.7, 152.4 (d, *J* = 241.8 Hz), 135.0, 134.7, 129.1, 116.9 (d, *J* = 5.1 Hz), 114.7 (d, *J* = 2.9 Hz), 108.4 (d, *J* = 27.4 Hz), 69.9, 56.2,

56.1, 51.4, 48.2, 34.1, 31.6, 30.4. HR-MS (ESI): m/z $[M + H]^+$ calcd for $C_{17}H_{21}O_2N_5FS$: 378.1395; found: 378.1403.

OTB-109

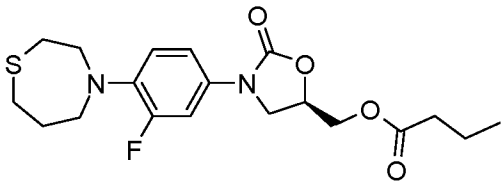
(*S*)-3-[3-Fluoro-4-(1,4-thiazepan-4-yl)phenyl]-5-[(methylamino)methyl]oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.30 (dd, *J* = 15.6 Hz, 2.4 Hz, 1 H), 7.06 (d, *J* = 8.8 Hz, 1 H), 6.82 (t, *J* = 9.6 Hz, 9.6 Hz, 1 H), 4.83 (m, 1 H), 4.02 (t, *J* = 8.8 Hz, 8.4 Hz, 1 H), 3.79 (t, *J* = 8.0 Hz, 7.2 Hz, 1 H), 3.67 (m, 4 H), 2.97 (m, 2 H), 2.87 (m, 2 H), 2.68 (m, 2 H), 2.54 (s, 3 H), 2.05 (m, 2 H). HR-MS (ESI): m/z $[M + H]^+$ calcd for $C_{16}H_{23}O_2N_3FS$: 340.1490; found: 340.1484.

OTB-108

(*R*)-[3-[3-Fluoro-4-(1,4-thiazepan-4-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl butyrate

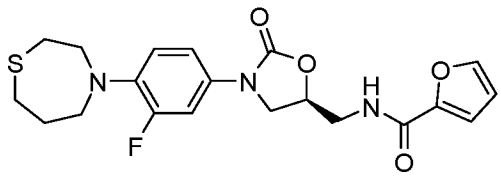


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.34 (dd, *J* = 15.6 Hz, 2.4 Hz, 1 H), 7.05 (dd, *J* = 9.2 Hz, 2.0 Hz, 1 H), 6.89 (m, 1 H), 4.84 (m, 1 H), 4.37 (dd, *J* = 16.0 Hz, 4.0 Hz, 1 H), 4.31 (dd, *J* = 12.0 Hz, 4.8 Hz, 1 H), 4.06 (t, *J* = 9.2 Hz, 8.8 Hz, 1 H), 3.76 (m, 1 H), 3.68 (m, 4 H), 2.89 (m, 2 H), 2.70 (t, *J* = 6.4 Hz, 6.0 Hz, 2 H), 2.34 (t, *J* = 7.6 Hz, 7.2 Hz, 2 H), 2.08 (m, 2 H), 1.65 (m, 2 H), 0.94 (t, *J* = 7.6 Hz, 7.2 Hz, 3 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 173.3, 154.4, 152.7 (d, *J* = 241.6 Hz), 134.9 (d, *J* = 8.3 Hz), 129.5 (d, *J* = 10.1 Hz), 117.2 (d, *J* = 5.4 Hz), 114.7 (d, *J* = 2.9 Hz), 108.5 (d,

J = 27.5 Hz), 70.2, 64.1, 56.3, 51.7, 47.5, 36.0, 34.4, 31.9, 30.7, 18.4, 13.7. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{19}H_{26}O_4N_2FS$: 397.1592; found: 397.1613.

OTB-111

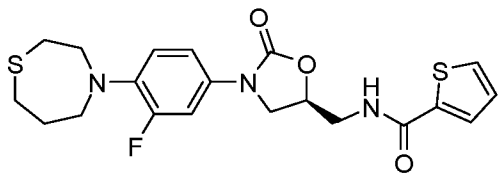
(*S*)-*N*-[(3-[3-Fluoro-4-(1,4-thiazepan-4-yl)phenyl]-2-oxo-oxazolidin-5-yl)methyl]furan-2-carboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.47 (s, 1 H), 7.32 (dd, *J* = 16.0 Hz, 2.0 Hz, 1 H), 7.14 (d, *J* = 3.2 Hz, 1 H), 7.01 (dd, *J* = 8.8 Hz, 1.6 Hz, 1 H), 6.87 (m, 1 H), 6.81 (m, 1 H), 6.52 (s, 1 H), 4.82 (m, 1 H), 4.04 (t, *J* = 9.2 Hz, 8.8 Hz, 1 H), 3.89 (m, 1 H), 3.76 (m, 2 H), 3.67 (m, 4 H), 2.88 (m, 2 H), 2.69 (t, *J* = 6.4 Hz, 6.0 Hz, 2 H), 2.07 (m, 2 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 159.0, 154.4, 152.6 (d, *J* = 241.9 Hz), 147.1, 144.5, 134.5, 129.3, 117.2, 115.1, 114.7, 112.3, 108.5 (d, *J* = 27.4 Hz), 71.9, 56.3, 51.7, 47.9, 41.6, 34.1, 31.7, 30.5. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{20}H_{23}O_4N_3FS$: 420.1388; found: 420.1400.

OTB-112

(*S*)-*N*-[(3-[3-Fluoro-4-(1,4-thiazepan-4-yl)phenyl]-2-oxo-oxazolidin-5-yl)methyl]thiophene-2-carboxamide

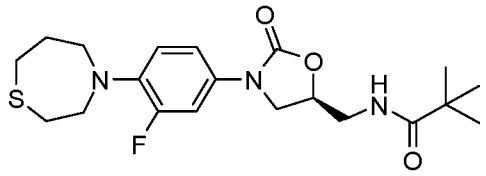


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.34 (m, 1 H), 7.02 (m, 2 H), 6.23 (m, 1 H), 4.75 (m, 1 H), 4.00 (t, *J* = 8.8 Hz, 8.8 Hz, 1 H), 3.73 (m, 2 H), 3.64 (m, 1 H), 3.36 (t, *J* = 6.4 Hz, 6.0 Hz, 4 H), 2.73 (m, 4 H), 2.04 (s, 3 H), 1.97 (m, 4 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 171.4, 155.2 (d, *J* = 243.5 Hz), 154.4, 134.5, 130.2, 119.9, 114.3, 108.3 (d,

J = 26.8 Hz), 71.9 , 48.1, 47.8, 42.0, 31.9, 29.7, 23.1. HR-MS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{18}H_{25}O_3N_3FS$: 382.1595; found: 382.1620.

OTB-115

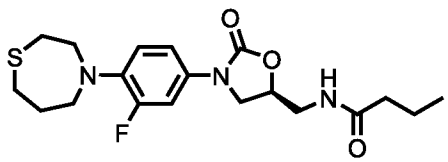
(*S*)-*N*-[[3-(3-Fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxo-oxazolidin-5-yl]methyl]pivalamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.34 (dd, *J* = 15.6 Hz, 2.0 Hz, 1 H), 7.01 (dd, *J* = 8.8 Hz, 2.4 Hz, 1 H), 6.89 (m, 1 H), 6.12 (m, 1 H), 4.74 (m, 1 H), 3.99 (t, *J* = 9.2 Hz, 8.8 Hz, 1 H), 3.74 (m, 1 H), 3.67 (m, 6 H), 2.89 (t, *J* = 5.6 Hz, 5.2 Hz, 2 H), 2.70 (t, *J* = 6.4 Hz, 6.4 Hz, 2 H), 2.08 (m, 2 H), 1.17 (s, 9H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 179.7, 154.6, 152.7 (d, *J* = 241.6 Hz), 134.8, 129.5, 117.2 (d, *J* = 5.4 Hz), 114.7 (d, *J* = 2.9 Hz), 108.5 (d, *J* = 27.6 Hz), 72.1, 56.3, 51.7, 48.0, 42.4, 39.0, 34.4, 31.9, 30.7, 27.7. HR-MS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{20}H_{29}O_3N_3FS$: 410.1908; found: 410.1942.

OBD-005

(*S*)-*N*-((3-(3-Fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)butyramide

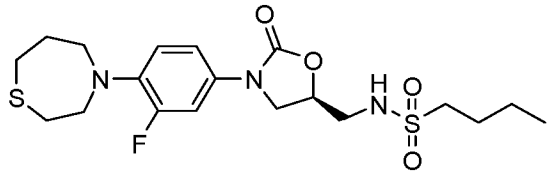


^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.42-7.23 (m, 2 H), 7.01 (dd, *J* = 8.9, 2.3 Hz, 1 H), 6.04 (s, 1 H), 4.75 (ddd, *J* = 9.0, 7.9, 4.6 Hz, 1 H), 4.00 (t, *J* = 9.0 Hz, 1 H), 3.79-3.05 (m, 7 H), 2.91 (dd, *J* = 16.2, 10.1 Hz, 2 H), 2.70 (t, *J* = 6.3 Hz, 2 H), 2.28-2.13 (m, 2 H), 2.13-1.97 (m, 2 H), 1.82-1.25 (m, 3 H), 0.92 (t, *J* = 7.4 Hz, 3 H), 0.01 (s, 1 H).

LC-MS (ESI): *m/z* = 395.9 [M+H]$^+$.

OTB-116

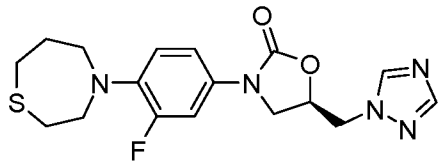
(*R*)-*N*-[[3-(3-Fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxo-oxazolidin-5-yl]methyl]butane-1-sulfonamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.33 (d, *J* = 15.6 Hz, 1 H), 7.05 (d, *J* = 8.8 Hz, 1 H), 6.88 (m, 1 H), 4.92 (t, *J* = 6.8 Hz, 6.4 Hz, 1 H), 4.78 (m, 1 H), 4.02 (t, *J* = 9.2 Hz, 8.8 Hz, 1 H), 3.90 (m, 1 H), 3.69 (m, 4 H), 3.54 (m, 1 H), 3.43 (m, 1 H), 3.07 (m, 2 H), 2.94 (m, 2 H), 2.69 (m, 2 H), 2.08 (m, 2 H), 1.79 (m, 2 H), 1.46 (m, 2 H), 0.95 (t, *J* = 7.2 Hz, 7.2 Hz, 3 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 154.2, 152.5 (d, *J* = 241.8 Hz), 134.8 (d, *J* = 8.3 Hz), 129.2 (d, *J* = 10.5 Hz), 117.2, 115.0, 108.6 (d, *J* = 27.5 Hz), 71.5, 56.3, 53.2, 51.6, 47.5, 45.5, 34.1, 31.7, 30.5, 25.6, 21.5, 13.5. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{19}H_{29}O_4N_3FS_2$: 446.1578; found: 446.1623.

OTB-119

(*R*)-5-[(1*H*-1,2,4-Triazol-1-yl)methyl]-3-[3-fluoro-4-(1,4-thiazepan-4-yl)phenyl]oxazolidin-2-one

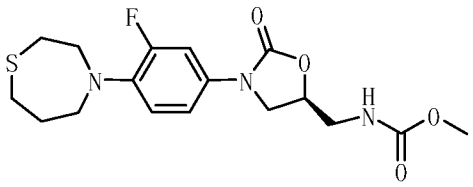


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.24 (s, 1 H), 7.96 (s, 1 H), 7.22 (m, 1 H), 6.97 (m, 1 H), 6.89 (m, 1 H), 5.02 (m, 1 H), 4.54 (d, *J* = 4.8 Hz, 2 H), 4.10 (t, *J* = 9.2 Hz, 9.2 Hz, 1 H), 3.94 (m, 1 H), 3.68 (m, 4 H), 2.89 (m, 2 H), 2.70 (m, 2 H), 2.08 (m, 2 H). HR-MS (ESI-TOF): *m/z* $[M + H]^+$ calcd for $C_{17}H_{21}O_2N_5FS$: 378.1395; found: 378.1421.

OTB-412

Methyl (*S*)-((3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxo-oxazolidin-5-yl)

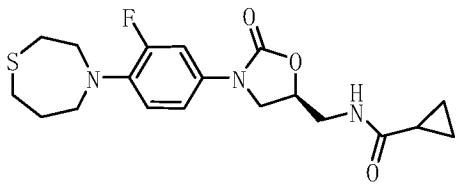
methyl) carbamate



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.29-7.33 (m, 1 H), 7.03-7.05 (m, 1 H), 6.82 (t, J = 8.8 Hz, 1 H), 5.10 (m, 1 H), 4.73 (m, 1 H), 3.99 (t, J = 9.9 Hz, 1 H), 3.69-3.74 (m, 1 H), 3.67 (s, 3 H), 3.66-3.67 (m, 4 H), 3.61 (m, 1 H), 3.50-3.55 (m, 1 H), 2.87 (m, 1 H), 2.68 (m, 2 H), 2.04-2.07 (m, 2 H). ^{13}C-NMR (150 MHz, $CDCl_3$) δ: 157.5, 154.3, 153.3, 151.7, 134.8, 134.7, 129.3, 129.2, 117.0, 117.0, 114.7, 114.7, 108.5, 108.4, 71.7, 56.2, 56.2, 51.5, 47.7, 43.7, 34.3, 31.8, 30.6. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{17}H_{23}O_4N_3FS$: 384.1388; found: 384.1371.

OTB-413

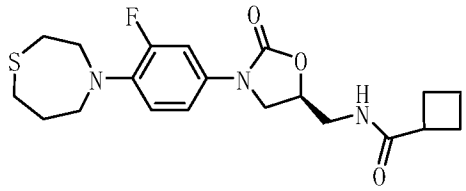
(*S*)-N-((3-(3-Fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)cyclopropanecarboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.29-7.33 (m, 1 H), 7.03-7.00 (m, 1 H), 6.81 (t, J = 9.6 Hz, 1 H), 6.09 (m, 1 H), 4.74 (m, 1 H), 3.98 (t, J = 8.8 Hz, 1 H), 3.73-3.74 (m, 1 H), 3.67-3.71 (m, 4 H), 3.62-3.66 (m, 1 H), 2.87 (t, J = 4.8 Hz, 2 H), 2.68 (t, J = 10.0 Hz, 2 H), 2.04-2.07 (m, 2 H), 1.36-1.43 (m, 1 H), 1.05-1.07 (m, 1 H), 0.93-0.97 (m, 2 H), 0.77-0.78 (m, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$) δ: 174.5, 154.5, 153.3, 151.7, 134.8, 134.7, 129.2, 129.2, 117.0, 114.7, 108.6, 108.4, 72.0, 56.2, 51.5, 47.8, 42.1, 34.3, 31.8, 30.6, 14.7, 7.7. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{19}H_{25}O_3N_3FS$: 394.1595; found: 394.1580.

OTB-414

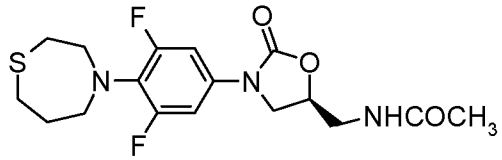
(*S*)-N-((3-(3-Fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)cyclobutanecarboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.29-7.34 (m, 1 H), 7.03-7.00 (m, 1 H), 6.82 (t, J = 9.6 Hz, 1 H), 5.84 (m, 1 H), 4.75 (m, 1 H), 3.99 (t, J = 8.8 Hz, 1 H), 3.72-3.76 (m, 1 H), 3.67-3.71 (m, 4H), 3.63-3.66 (m, 1 H), 3.14-3.23 (m, 2 H), 2.68 (m, 1 H), 1.89-2.35 (m, 10 H). ^{13}C-NMR (150 MHz, $CDCl_3$) δ: 180.2, 176.0, 154.5, 134.8, 134.8, 129.2, 129.1, 117.0, 117.0, 114.7, 114.7, 108.5, 108.4, 72.0, 56.2, 56.2, 51.5, 51.5, 47.9, 42.0, 39.7, 37.8, 34.3, 31.8, 30.6, 25.2, 18.4. HR-MS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{20}H_{27}O_3N_3FS$: 408.1752; found: 408.1736.

OTB-407

(*S*)-N-((3-(3,5-Difluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)acetamide

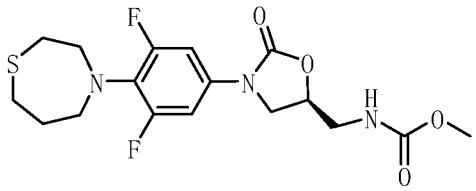


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.07 (d, J = 10.4 Hz, 2 H), 6.08 (m, 1 H), 4.76-4.77 (m, 1 H), 3.98 (t, J = 9.2 Hz, 1 H), 3.59-3.70 (m, 3 H), 3.45-3.48 (m, 4 H), 2.89 (t, J = 6.0 Hz, 2 H), 2.77-2.80 (m, 2 H), 2.02 (s, 3 H). ^{13}C-NMR (150 MHz, $CDCl_3$) δ: 171.1, 159.8, 159.7, 158.1, 158.1, 154.0, 133.3, 126.0, 102.5, 102.3, 71.9, 58.8, 54.1, 47.5, 41.9, 36.1, 31.8, 31.6, 23.1. HR-MS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{17}H_{22}O_3N_3F_2S$: 386.1344; found: 386.1330.

OTB-410

Methyl (*S*)-((3-(3,5-difluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxo-oxazolidin-5-yl)

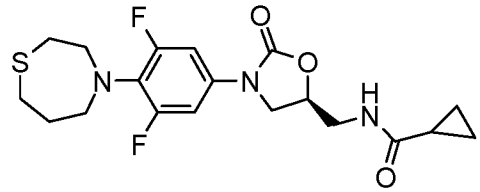
methyl)carbamate



^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.09 (d, J = 10.0 Hz, 2 H), 5.09 (m, 1 H), 4.76 (m, 1 H), 3.99 (t, J = 9.0 Hz, 1 H), 3.74-3.76 (m, 1 H), 3.73 (s, 3 H), 3.61 (m, 1 H), 3.52-3.55 (m, 1 H), 3.46-3.47 (m, 4 H), 2.90 (t, J = 6.0 Hz, 1 H), 2.78-2.80 (m, 2 H), 1.94-1.98 (m, 2 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 157.5, 154.3, 153.3, 151.7, 134.8, 134.7, 129.3, 129.2, 117.0, 117.0, 114.7, 114.7, 108.4, 108.4, 71.3, 56.2, 56.2, 51.5, 47.8, 43.7, 34.3, 31.8, 30.6. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{17}H_{22}O_4N_3F_2S$: 402.1297; found: 402.1287.

OTB-408

(*S*)-5-((Cyclopropylamino)methyl)-3-(3,5-difluoro-4-(1,4-thiazepan-4-yl)phenyl)oxazolidin-2-one

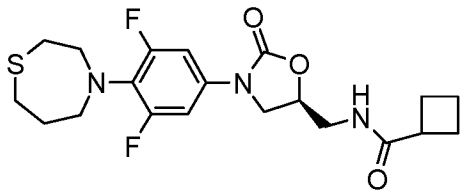


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.07 (d, J = 10.8 Hz, 2 H), 6.06 (m, 1 H), 4.76 (m, 1 H), 3.96 (t, J = 8.8 Hz, 1 H), 3.66-3.75 (m, 3 H), 3.43-3.47 (m, 3 H), 2.89 (t, J = 9.2 Hz, 2 H), 2.78-2.80 (m, 3 H), 1.94-1.97 (m, 2 H), 1.37-1.39 (m, 1 H), 0.97 (m, 1 H), 0.93 (m, 1 H), 0.77-0.79 (m, 2 H). ^{13}C-NMR (150 MHz, $CDCl_3$) δ: 174.7, 159.8, 159.7, 158.2, 158.1, 154.0, 133.4, 126.0, 102.6, 102.4, 72.0, 58.8, 54.1, 47.5, 42.0, 36.1, 31.8, 31.6, 14.7, 7.8, 7.7. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{19}H_{24}O_3N_3F_2S$: 412.1501; found: 412.1485.

OTB-409

(*S*)-5-((Cyclobutylamino)methyl)-3-(3,5-difluoro-4-(1,4-thiazepan-4-yl)phenyl)oxaz

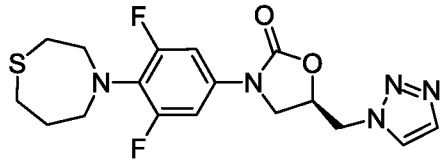
olidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.07 (d, J = 10.8 Hz, 2 H), 5.81 (m, 1 H), 4.75 (m, 1 H), 3.98 (t, J = 8.8 Hz, 1 H), 3.72-3.76 (m, 1 H), 3.64-3.66 (m, 2 H), 3.45-3.46 (m, 3 H), 3.01 (t, J = 8.8 Hz, 1 H), 2.90 (t, J = 6.4 Hz, 2 H), 2.77-2.80 (m, 2 H), 2.13-2.26 (m, 4 H), 1.92-1.96 (m, 3 H). ^{13}C-NMR (150 MHz, $CDCl_3$) δ: 176.0, 159.8, 159.8, 158.2, 158.1, 154.0, 133.3, 126.0, 102.5, 102.3, 72.0, 58.8, 54.1, 47.5, 41.9, 39.7, 36.1, 31.8, 31.6, 25.4, 25.3, 18.1. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{20}H_{26}O_3N_3F_2S$: 426.1658; found: 426.1643.

OTB-411

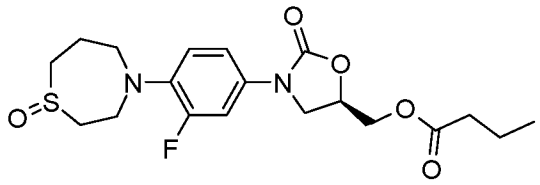
(*R*)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3,5-difluoro-4-(1,4-thiazepan-4-yl)phenyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.76 (d, J = 11.2 Hz, 2 H), 6.95 (d, J = 10.4 Hz, 2 H), 5.04-5.07 (m, 1 H), 4.78 (d, J = 4.0 Hz, 2 H), 4.10 (t, J = 9.2 Hz, 1 H), 3.86-3.90 (m, 1 H), 3.44-3.46 (m, 4 H), 2.88 (t, J = 6.4 Hz, 2 H), 2.76-2.79 (m, 2 H), 1.91-1.97 (m, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 159.8, 159.8, 157.9, 157.8, 153.0, 134.6, 125.1, 102.8, 102.5, 70.3, 58.7, 54.0, 51.9, 47.1, 36.1, 31.8, 31.6. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{17}H_{20}O_2N_5F_2S$: 396.1300; found: 396.1296.

OTB-126

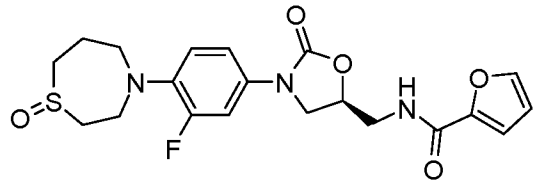
[(5*R*)-3-[3-Fluoro-4-(1-oxido-1,4-thiazepan-4-yl)phenyl)-2-oxo-oxazolidin-5-yl]methyl butyrate



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.45 (dd, *J* = 14.8 Hz, 1.6 Hz, 1 H), 7.07 (dd, *J* = 8.8 Hz, 2.4 Hz, 1 H), 6.96 (t, *J* = 9.2 Hz, 9.2 Hz, 1 H), 4.85 (m, 1 H), 4.37 (dd, *J* = 12.0 Hz, 4.0 Hz, 1 H), 4.30 (dd, *J* = 12.4 Hz, 4.8 Hz, 1 H), 4.07 (m, 1 H), 3.78 (m, 2 H), 3.40 (m, 2 H), 3.19 (m, 4 H), 2.98 (m, 1 H), 2.72 (m, 1 H), 2.33 (t, *J* = 7.6 Hz, 7.2 Hz, 2 H), 2.04 (m, 1 H), 1.63 (m, 2 H), 0.92 (t, *J* = 7.6 Hz, 7.2 Hz, 3 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 173.2, 154.1, 154.0 (d, *J* = 241.8 Hz), 136.6, 131.4, 118.1 (d, *J* = 4.3 Hz), 114.0, (d, *J* = 2.9 Hz), 107.8 (d, *J* = 26.9 Hz), 70.1, 63.9, 52.8, 49.6, 47.2, 46.4, 43.7, 35.8, 18.3, 16.2, 13.6. HR-MS (ESI-TOF): *m/z* $[M + H]^+$ calcd for $C_{19}H_{26}O_5N_2FS$: 413.1541; found: 413.1573.

OTB-127

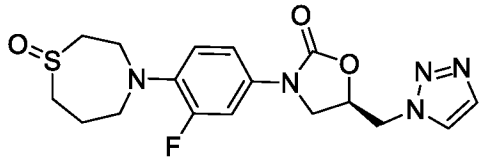
N-[[(5*S*)-3-(3-Fluoro-4-(1-oxido-1,4-thiazepan-4-yl)phenyl)-2-oxo-oxazolidin-5-yl] methyl]furan-2-carboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.47 (s, 1 H), 7.42 (m, 1 H), 7.14 (d, *J* = 3.2 Hz, 1 H), 7.04 (m, 1 H), 6.87 (m, 2 H), 6.51 (m, 1 H), 4.85 (m, 1 H), 4.05 (m, 1 H), 3.81 (m, 4 H), 3.38 (m, 2 H), 3.15 (m, 2 H), 3.04 (m, 3 H), 2.70 (m, 1 H), 2.03 (m, 1 H). HR-MS (ESI-TOF): *m/z* $[M + H]^+$ calcd for $C_{20}H_{23}O_5N_3FS$: 436.1337; found: 436.1371.

OTB-137

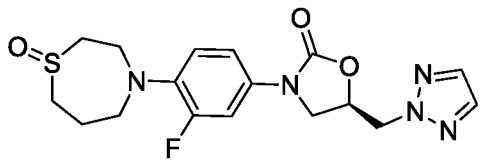
(5*R*)-5-((1*H*-1,2,3-Triazol-1-yl)methyl)-3-(3-fluoro-4-(1-oxido-1,4-thiazepan-4-yl)phenyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.79 (s, 1 H), 7.75 (s, 1 H), 7.30-7.25 (m, 1 H), 6.91-6.89 (m, 2 H), 5.07-5.02 (m, 1 H), 4.78 (d, *J* = 4.0 Hz, 2 H), 4.11 (t, *J* = 9.2 Hz, 1 H), 3.93-3.88 (m, 1 H), 3.82-3.76 (m, 1 H), 3.43-3.36 (m, 2 H), 3.24-2.91 (m, 4 H), 2.75-2.69 (m, 1 H), 2.04-2.02 (m, 2 H). HR-MS (ESI): m/z $[M + H]^+$ calcd for $C_{17}H_{21}O_3N_5FS$: 394.1344; found: 394.1328.

OTB-138

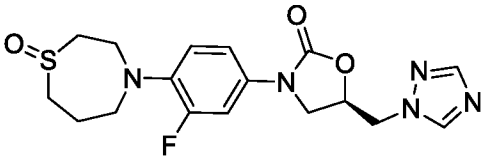
(5*R*)-5-((2*H*-1,2,3-Triazol-2-yl)methyl)-3-(3-fluoro-4-(1-oxido-1,4-thiazepan-4-yl)phenyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.65 (s, 2 H), 7.39 (d, *J* = 14.4 Hz, 1 H), 7.04-6.98 (m, 2 H), 5.15-5.09 (m, 1 H), 4.86 (dd, *J* = 14.0, 4.4 Hz, 1 H), 4.75 (dd, *J* = 14.0, 6.8 Hz, 1 H), 4.06 (dt, *J* = 9.2, 2.4 Hz, 1 H), 4.00-3.96 (m, 1 H), 3.86-3.82 (m, 1 H), 3.46-3.38 (m, 2 H), 3.29-3.08 (m, 3 H), 3.02-2.96 (m, 1 H), 2.76-2.71 (m, 1 H), 2.04-2.02 (m, 2 H). HR-MS (ESI): m/z $[M + H]^+$ calcd for $C_{17}H_{21}O_3N_5FS$: 394.1344; found: 394.1338.

OTB-140

(5*R*)-5-((1*H*-1,2,4-Triazol-1-yl)methyl)-3-(3-fluoro-4-(1-oxido-1,4-thiazepan-4-yl)phenyl)oxazolidin-2-one

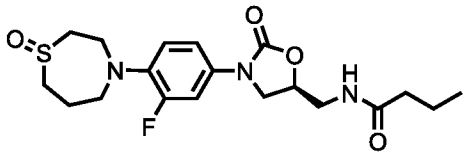


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.24 (s, 1 H), 7.94 (s, 1 H), 7.35 (d, *J* = 14.4 Hz, 1 H), 7.0-6.96 (m, 2 H), 5.02-4.99 (m, 1 H), 4.55 (d, *J* = 4.4 Hz, 2 H), 4.10 (dt, *J* = 8.8,

2.0 Hz, 1 H), 3.99-3.95 (m, 1 H), 3.86-3.82 (m, 1 H), 3.45-3.38 (m, 2 H), 3.29-3.09 (m, 3 H), 3.00-2.94 (m, 1 H), 2.77-2.71 (m, 1 H), 2.07-2.03 (m, 2 H). HR-MS (ESI): m/z $[M + H]^+$ calcd for $C_{17}H_{21}O_3N_5FS$: 394.1344; found: 394.1339.

OBD-006

N-(((5*S*)-3-(3-Fluoro-4-(1-oxido-1,4-thiazepan-4-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)butyramide

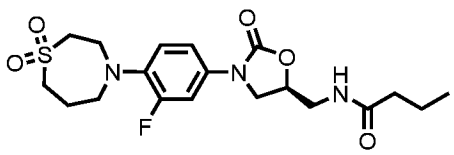


^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.52 (d, *J* = 15.0 Hz, 1 H), 7.16 (s, 1 H), 7.03 (d, *J* = 8.7 Hz, 1 H), 5.99 (s, 1 H), 4.78 (s, 1 H), 4.02 (t, *J* = 8.8 Hz, 2 H), 3.88-3.56 (m, 3 H), 3.55-2.92 (m, 7 H), 2.77 (s, 1 H), 2.20 (t, *J* = 7.1 Hz, 3 H), 1.64 (dd, *J* = 14.9, 7.4 Hz, 2 H), 0.91 (t, *J* = 7.4 Hz, 3 H).

LC-MS (ESI): *m/z* = 411.8 $[M+H]^+$.

OBD-007

(*S*)-*N*-((3-(4-(1,1-Dioxido-1,4-thiazepan-4-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide

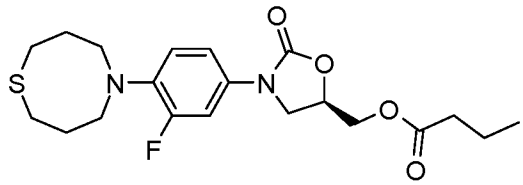


^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.51 (d, *J* = 14.7 Hz, 1 H), 7.10 (d, *J* = 9.9 Hz, 2 H), 5.92 (s, 1 H), 4.78 (s, 1 H), 4.03 (t, *J* = 9.0 Hz, 1 H), 3.87-3.39 (m, 7 H), 3.27 (d, *J* = 5.7 Hz, 2 H), 2.39 (d, *J* = 6.2 Hz, 2 H), 2.20 (t, *J* = 7.2 Hz, 2 H), 1.64 (dd, *J* = 14.8, 7.4 Hz, 2 H), 0.92 (t, *J* = 7.3 Hz, 3 H).

LC-MS (ESI): *m/z* = 427.8 $[M+H]^+$.

OTB-110

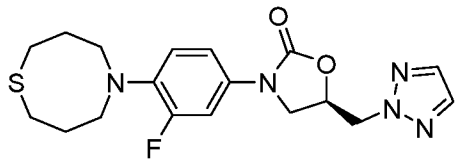
(*R*)-[3-[3-Fluoro-4-(1,5-thiazocan-5-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl butyrate



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.36 (dd, *J* = 14.8 Hz, 4.0 Hz, 1 H), 7.09 (dd, *J* = 8.8 Hz, 2.4 Hz, 1 H), 7.04 (t, *J* = 10.4 Hz, 9.2 Hz, 1 H), 4.85 (m, 1 H), 4.37 (m, 1 H), 4.31 (m, 1 H), 4.08 (m, 1 H), 3.78 (m, 1 H), 3.37 (m, 4 H), 2.75 (m, 4 H), 2.34 (t, *J* = 7.6 Hz, 7.2 Hz, 2 H), 1.97 (m, 4 H), 1.64 (m, 2 H), 0.93 (t, 7.6 Hz, *J* = 7.2 Hz, 3 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 173.3, 155.4 (d, *J* = 243.5 Hz), 154.3, 134.5 (d, *J* = 8.3 Hz), 131.1 (d, *J* = 10.1 Hz), 128.2, 127.1, 120.0 (d, *J* = 4.9 Hz), 114.3 (d, *J* = 3.0 Hz), 108.4 (d, *J* = 26.8 Hz), 70.2, 64.0, 48.1, 47.4, 36.0, 32.1, 29.8, 18.4, 13.7. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{20}H_{28}O_4N_2FS$: 411.1748; found: 411.1786.

OTB-113

(*R*)-5-[(2*H*-1,2,3-triazol-2-yl)methyl]-3-[3-fluoro-4-(1,5-thiazocan-5-yl)phenyl]oxazolidin-2-one

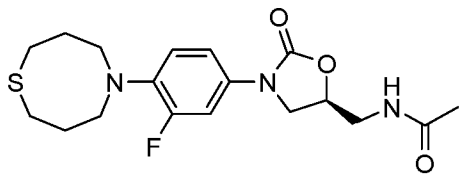


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.65 (s, 2 H), 7.30 (d, *J* = 14.8 Hz, 1 H), 7.03 (m, 2 H), 5.10 (m, 1 H), 4.85 (dd, *J* = 14.0 Hz, 4.8 Hz, 1 H), 4.74 (dd, *J* = 14.0 Hz, 7.2 Hz, 1 H), 4.06 (t, *J* = 9.2 Hz, 8.8 Hz, 1 H), 3.97 (m, 1 H), 3.37 (t, *J* = 6.0 Hz, 6.0 Hz, 4 H), 2.73 (m, 4 H), 1.97 (m, 4 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 155.2 (d, *J* = 243.5 Hz), 135.2, 134.4 (d, *J* = 8.1 Hz), 130.8 (d, *J* = 10.3 Hz), 119.8 (d, *J* = 4.9 Hz), 114.5 (d, *J* = 3.1 Hz), 108.4 (d, *J* = 26.6 Hz), 70.0, 56.3, 48.3, 47.9, 31.9, 29.6. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{18}H_{23}O_2N_5FS$: 392.1551; found:

392.1590.

OTB-114

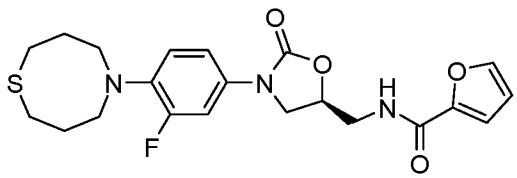
(*R*)-[3-[3-Fluoro-4-(1,5-thiazocan-5-yl)phenyl]-2-oxo-5-oxazolidinyl]methyl acetamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.34 (m, 1 H), 7.02 (m, 2 H), 6.23 (m, 1 H), 4.75 (m, 1 H), 4.00 (t, *J* = 8.8 Hz, 8.8 Hz, 1 H), 3.73 (m, 2 H), 3.64 (m, 1 H), 3.36 (t, *J* = 6.4 Hz, 6.0 Hz, 4 H), 2.73 (m, 4 H), 2.04 (s, 3 H), 1.97 (m, 4 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 171.4, 155.2 (d, *J* = 243.5 Hz), 154.4, 134.5, 130.2, 119.9, 114.3, 108.3 (d, *J* = 26.8 Hz), 71.9 , 48.1, 47.8, 42.0, 31.9, 29.7, 23.1. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{18}H_{25}O_3N_3FS$: 382.1595; found: 382.1620.

OTB-117

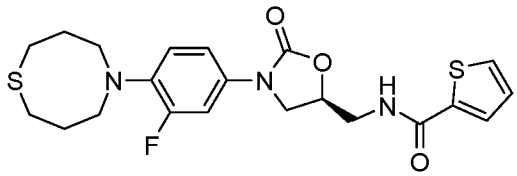
(*S*)-*N*-[[3-(3-Fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxo-oxazolidin-5-yl]methyl]furan-2-carboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.47 (s, 1 H), 7.36 (d, *J* = 14.4 Hz, 1 H), 7.14 (d, *J* = 3.2 Hz, 1 H), 7.01 (m, 2 H), 6.78 (m, 1 H), 6.51 (m, 1 H), 4.84 (m, 1 H), 4.05 (t, *J* = 9.2 Hz, 8.8 Hz, 1 H), 3.88 (m, 1 H), 3.80 (m, 2 H), 3.36 (t, *J* = 6.0 Hz, 6.0 Hz, 4 H), 2.73 (m, 4 H), 1.96 (m, 4 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 159.0, 155.2 (d, *J* = 243.6 Hz), 154.3, 147.1, 144.5, 134.3, 130.9, 119.8, 115.1, 114.3 (d, *J* = 3.0 Hz), 112.3, 108.4 (d, *J* = 26.8 Hz), 71.9, 47.9, 41.5, 31.9, 29.6. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{21}H_{25}O_4N_3FS$: 434.1544; found: 434.1581.

OTB-118

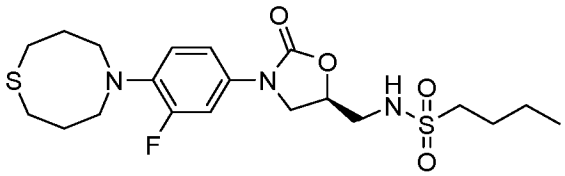
(*S*)-*N*-[[3-(3-Fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxo-oxazolidin-5-yl]methyl]thiophene-2-carboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.54 (m, 1 H), 7.52 (m, 1 H), 7.34 (m, 1 H), 7.10 (m, 1 H), 7.04 (m, 1 H), 7.00 (m, 1 H), 6.57 (t, *J* = 6.0 Hz, 6.0 Hz, 1 H), 4.86 (m, 1 H), 4.07 (t, *J* = 9.2 Hz, 8.8 Hz, 1 H), 4.07 (m, 1 H), 3.82 (m, 2 H), 3.36 (t, *J* = 6.0 Hz, 6.0 Hz, 4 H), 2.74 (m, 4 H), 1.96 (m, 4 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 162.7, 155.2 (d, *J* = 243.5 Hz), 154.5, 137.9, 130.8, 128.7, 127.8, 119.8, 114.5 (d, *J* = 3.0 Hz), 108.5 (d, *J* = 26.8 Hz), 72.1, 48.0, 42.5, 31.9, 29.6. HR-MS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{21}H_{25}O_4N_4FS_2$: 450.1316; found: 450.1356.

OTB-120

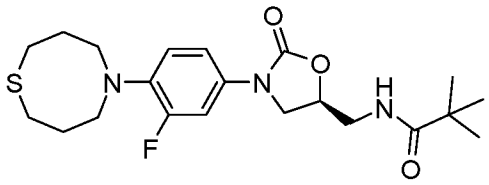
(*R*)-*N*-[[3-(3-Fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxo-oxazolidin-5-yl]methyl]butane-1-sulfonamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.42 (d, *J* = 14.4 Hz, 1 H), 7.08 (m, 2 H), 4.94 (m, 1 H), 4.79 (m, 1 H), 4.04 (t, *J* = 8.8 Hz, 8.8 Hz, 1 H), 3.93 (m, 1 H), 3.55 (m, 1 H), 3.43 (m, 5 H), 3.07 (m, 2 H), 2.76 (m, 4 H), 2.01 (m, 4 H), 1.80 (m, 2 H), 1.45 (m, 2 H), 0.95 (t, *J* = 7.6 Hz, 7.2 Hz, 3 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 155.2 (d, *J* = 243.6 Hz), 154.2, 134.5, 130.7, 119.8 (d, *J* = 4.9 Hz), 114.5 (d, *J* = 3.0 Hz), 108.5 (d, *J* = 26.8 Hz), 71.5, 53.1, 47.9, 47.4, 45.5, 31.9, 29.6, 25.6, 21.5, 13.5. HR-MS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{20}H_{31}O_4N_3FS_2$: 460.1735; found: 460.1778.

OTB-121

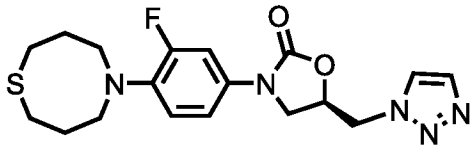
(*S*)-*N*-[[3-(3-Fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxo-oxazolidin-5-yl]methyl]pivalamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.39 (d, *J* = 14.4 Hz, 1 H), 7.04 (m, 2 H), 6.11 (m, 1 H), 4.74 (m, 1 H), 4.00 (t, *J* = 9.2 Hz, 8.8 Hz, 1 H), 3.76 (m, 1 H), 3.67 (m, 2 H), 3.39 (m, 4 H), 2.74 (m, 4 H), 1.98 (m, 4 H), 1.17 (s, 9 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 179.6, 155.2 (d, *J* = 243.6 Hz), 154.4, 134.3 (d, *J* = 8.0 Hz), 130.9 (d, *J* = 5.4 Hz), 128.8, 119.8 (d, *J* = 4.9 Hz), 114.2 (d, *J* = 2.9 Hz), 108.2 (d, *J* = 26.9 Hz), 72.0, 47.9, 47.8, 42.2, 38.9, 31.9, 29.6, 27.5. HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{21}H_{31}O_3N_3FS$: 424.2065; found: 424.2096.

OBD-001

(*R*)-5-((1*H*-1,2,3-Triazol-1-yl)methyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one

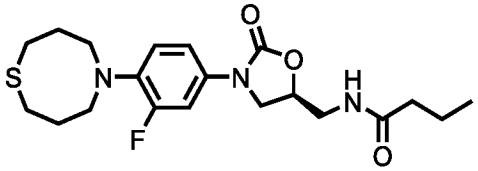


^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.76 (d, *J* = 17.6 Hz, 2 H), 7.41-7.09 (m, 1 H), 7.11-6.73 (m, 2 H), 5.04 (d, *J* = 3.0 Hz, 1 H), 4.78 (d, *J* = 3.4 Hz, 2 H), 4.12 (t, *J* = 9.2 Hz, 1 H), 3.88 (dd, *J* = 9.2, 6.1 Hz, 1 H), 3.36 (t, *J* = 6.0 Hz, 3 H), 2.92-2.59 (m, 4 H), 2.01 (dd, *J* = 27.9, 7.3 Hz, 4 H).

LC-MS (ESI): *m/z* = 391.9 $[M+H]^+$.

OBD-003

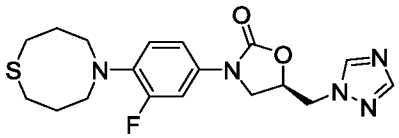
(*S*)-*N*-((3-(3-Fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)butyramide



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.50 (s, 2 H), 7.03 (d, *J* = 6.1 Hz, 1 H), 5.99 (s, 1 H), 4.77 (d, *J* = 5.7 Hz, 1 H), 4.02 (t, *J* = 9.0 Hz, 2 H), 3.70 (ddd, *J* = 20.7, 15.2, 7.7 Hz, 4 H), 3.48 (s, 4 H), 2.95-2.68 (m, 4 H), 2.20 (t, *J* = 7.2 Hz, 3 H), 2.06 (d, *J* = 6.1 Hz, 4 H), 1.64 (dd, *J* = 14.8, 7.4 Hz, 4 H), 0.91 (t, *J* = 7.4 Hz, 4 H).
LC-MS (ESI): *m/z* = 409.9 $[M+H]^+$.

OBD-008

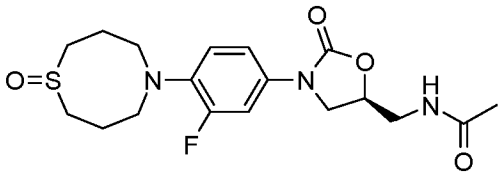
(*R*)-5-((1*H*-1,2,4-Triazol-1-yl)methyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.24 (s, 1 H), 7.97 (s, 1 H), 7.00 (s, 2 H), 5.12-4.91 (m, 1 H), 4.56 (d, *J* = 4.7 Hz, 2 H), 4.24-3.83 (m, 2 H), 3.38 (t, *J* = 6.0 Hz, 4 H), 2.95-2.59 (m, 4 H), 1.98 (s, 5 H).
LC-MS (ESI): *m/z* = 391.9 $[M+H]^+$.

OTB-124

(*S*)-*N*-[[3-(3-Fluoro-4-(1-oxido-1,5-thiazocan-5-yl)phenyl)-2-oxo-oxazolidin-5-yl]methyl]acetamide

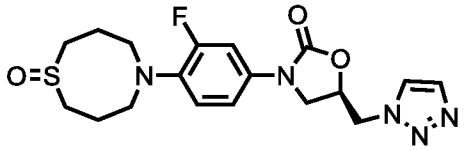


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.46 (dd, *J* = 2.8 Hz, 14.8 Hz, 1 H), 7.14 (t, *J* = 9.2

Hz, 8.8 Hz, 1 H), 7.07 (m, 1 H), 6.15 (m, 1 H), 4.78 (m, 1 H), 4.03 (t, *J* = 9.2 Hz, 8.8 Hz, 1 H), 3.74 (m, 3 H), 3.31 (m, 1 H), 3.18 (m, 4 H), 2.98 (m, 2 H), 2.17 (m, 4 H), 2.03 (s, 3 H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 171.0, 154.2, 134.0, 128.5, 127.3, 122.6, 113.9, 108.1 (d, *J* = 26.9 Hz), 71.9, 53.1, 51.7, 47.7, 42.0, 29.7, 25.0, 23.2. HR-MS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{25}O_4N_3FS$: 398.1544; found: 398.1540.

OBD-002

(*R*)-5-((1*H*-1,2,3-Triazol-1-yl)methyl)-3-(3-fluoro-4-(1-oxido-1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one

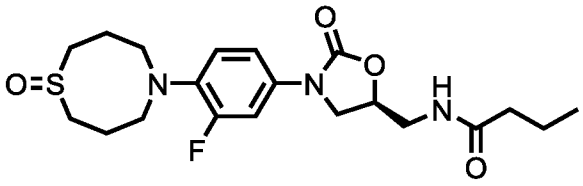


^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.92-7.67 (m, 2 H), 7.32 (d, *J* = 16.8 Hz, 1 H), 7.12 (t, *J* = 9.0 Hz, 1 H), 6.96 (d, *J* = 8.1 Hz, 1 H), 5.07 (s, 1 H), 4.81 (d, *J* = 4.0 Hz, 2 H), 4.15 (t, *J* = 9.0 Hz, 1 H), 4.01-3.83 (m, 1 H), 3.32 (d, *J* = 14.2 Hz, 5 H), 3.11-2.87 (m, 2 H), 2.59 (s, 2 H), 2.19 (s, 4 H).

LC-MS (ESI): *m/z* = 407.8 $[M+H]^+$.

OBD-004

(*S*)-*N*-((3-(3-Fluoro-4-(1-oxido-1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)butyramide

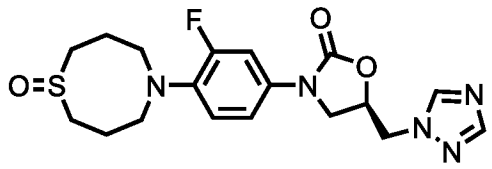


^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.44 (dd, *J* = 14.7, 2.4 Hz, 1 H), 7.19-6.99 (m, 2 H), 6.44 (s, 1 H), 4.84-4.71 (m, 1 H), 4.02 (t, *J* = 8.9 Hz, 1 H), 3.78 (dd, *J* = 9.0, 6.6 Hz,

1 H), 3.66 (t, *J* = 4.6 Hz, 2 H), 3.38-3.09 (m, 6 H), 2.99 (dd, *J* = 12.6, 6.3 Hz, 2 H), 2.20 (dd, *J* = 9.4, 5.3 Hz, 6 H), 1.71-1.56 (m, 2 H), 0.91 (dd, *J* = 9.6, 5.1 Hz, 3 H). LC-MS (ESI): *m/z* = 425.8 $[M+H]^+$.

OBD-009

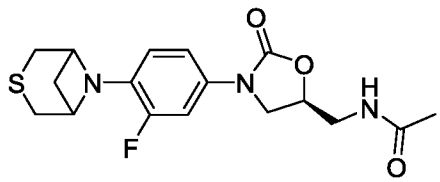
(*R*)-5-((1*H*-1,2,4-Triazol-1-yl)methyl)-3-(3-fluoro-4-(1-oxido-1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.24 (s, 1 H), 7.93 (s, 1 H), 7.41-7.20 (m, 1 H), 7.19-6.92 (m, 2 H), 5.10-4.92 (m, 1 H), 4.56 (d, *J* = 4.7 Hz, 2 H), 4.12 (t, *J* = 9.0 Hz, 1 H), 3.97 (dd, *J* = 9.2, 6.2 Hz, 1 H), 3.28 (dd, *J* = 13.0, 6.9 Hz, 2 H), 3.12 (dd, *J* = 12.5, 5.9 Hz, 4 H), 3.02-2.83 (m, 2 H), 2.22-1.99 (m, 5 H), 1.26 (d, *J* = 9.4 Hz, 4 H). LC-MS (ESI): *m/z* = 407.8 $[M+H]^+$.

OTB-227

N-(((5S)-3-(4-(3-Thia-6-azabicyclo[3.1.1]heptan-6-yl)-3-fluorophenyl)-2-oxo-oxazolidin-5-yl)methyl)acetamide

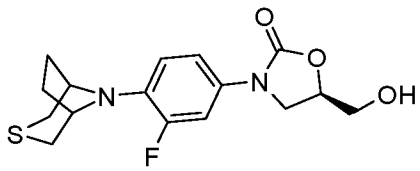


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.36 (d, *J* = 14.4 Hz, 1 H), 7.05 (d, *J* = 8.4 Hz, 1 H), 6.60 (t, *J* = 9.2 Hz, 1 H), 6.35 (brs, 1 H), 4.76-4.74 (m, 1 H), 4.56-4.54 (m, 2 H), 4.00 (t, *J* = 9.2 Hz, 1 H), 3.76-3.65 (m, 2 H), 3.62-3.57 (m, 1 H), 3.43 (d, *J* = 12.0 Hz, 2 H), 2.93-2.87 (m, 1 H), 2.74 (d, *J* = 12.0 Hz, 2 H), 2.09 (s, 1 H), 2.03 (s, 3 H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.1, 154.5, 151.8 (d, J = 238.5 Hz), 131.9 (d, J = 11.8 Hz), 129.2 (d, J = 9.5 Hz), 115.2 (d, J = 6.2 Hz), 114.7 (d, J = 2.8 Hz), 108.0 (d, J = 24.9 Hz), 71.9, 60.8, 47.8, 41.9, 29.4, 25.3, 23.2. HRMS (ESI-TOF+): m/z [M + H]$^+$ calcd for $C_{17}H_{21}FN_3O_3S$: 366.1288; found: 366.1277.

OTB-501

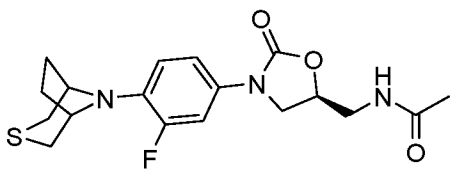
(*R*)-3-(4-((1*R*,5*S*)-3-Thia-8-azabicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-5-(hydroxy methyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.39 (d, J = 12.8 Hz, 1 H), 7.16 (d, J = 8.8 Hz, 1 H), 6.90 (t, J = 9.2 Hz, 1 H), 4.74 (m, 1 H), 4.43 (s, 2 H), 3.99-3.96 (m, 3 H), 3.79-3.75 (m, 1 H), 3.48 (d, J = 13.2 Hz, 2 H), 2.21-2.10 (m, 6 H). HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{16}H_{20}N_2O_3FS$: 339.1179; found: 339.1169.

OTB-502

N-(((*S*)-3-(4-((1*R*,5*S*)-3-Thia-8-azabicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-2-oxoo xazolidin-5-yl)methyl)acetamide

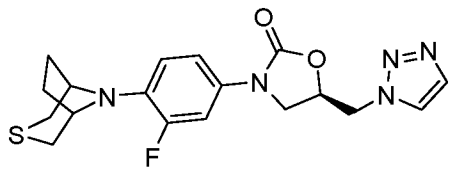


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.36 (dd, J = 15.2, 2.4 Hz, 1 H), 7.06 (dd, J = 8.8, 1.8 Hz, 1 H), 6.83 (t, J = 9.2 Hz, 1 H), 6.18 (s, 1 H), 4.77–4.75 (m, 1 H), 4.40 (s, 2 H), 4.00 (t, J = 8.8 Hz, 1 H), 3.76–3.72 (m, 2 H), 3.68-3.62 (m, 1 H), 3.37 (d, J = 12.8 Hz, 2 H), 2.26–2.04 (m, 6 H), 2.02 (s, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.1, 154.5, 152.8 (d, J = 241.7 Hz), 132.2 (d, J = 8.6 Hz), 130.2 (d, J = 10.4 Hz), 118.1 (d, J = 5.0 Hz), 114.7, 108.4 (d, J = 27.2 Hz), 71.9 , 57.4, 47.8, 42.0, 30.2, 28.4, 23.1. HR-MS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{18}H_{23}N_3O_3FS$: 380.1444;

found: 380.1435.

OTB-504

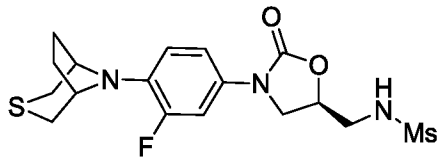
(*R*)-5-((1*H*-1,2,3-Triazol-1-yl)methyl)-3-(4-((1*R*,5*S*)-3-thia-8-azabicyclo[3.2.1]octan -8-yl)-3-fluorophenyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.80 (s, 1 H), 7.76 (s, 1 H), 7.24 (m, 1 H), 6.96 (d, *J* = 8.8 Hz, 1 H), 6.83 (t, *J* = 8.8 Hz, 1 H), 5.07–5.04 (m, 1 H), 4.79 (s, 2 H), 4.40 (s, 2 H), 4.11 (t, *J* = 8.0 Hz, 1 H), 3.90–3.87 (m, 1 H), 3.42 (d, *J* = 12.8 Hz, 2 H), 2.20–2.07 (m, 6 H). HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{18}H_{21}N_5O_2FS$: 390.1400; found: 390.1385.

OTB-236

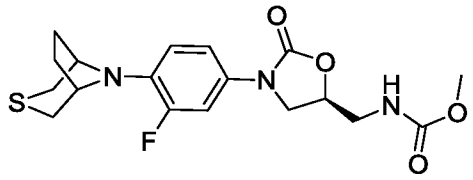
N-(((*R*)-3-(4-((1*R*,5*S*)-3-Thia-8-azabicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-2-oxo-oxazolidin-5-yl)methyl)methanesulfonamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.47-7.41 (m, 1 H), 7.13 (d, *J* = 9.6 Hz, 1 H), 7.02 (t, *J* = 9.6 Hz, 1 H), 4.76-4.70 (m, 1 H), 4.34 (s, 2 H), 4.08 (t, *J* = 9.2 Hz, 1 H), 3.76 (t, *J* = 8.8 Hz, 1 H), 3.29-3.26 (m, 2 H), 3.11 (d, *J* = 12.8 Hz, 2 H), 2.93 (s, 3 H), 2.11 (d, *J* = 12.4 Hz, 2 H), 2.02 (s, 4 H). HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{17}H_{23}N_3O_4FS_2$: 416.1114; found: 416.1097.

OTB-237

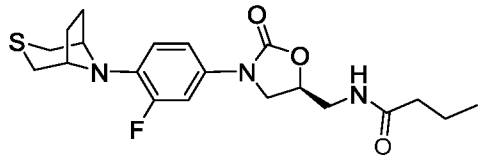
Methyl (((*S*)-3-(4-((1*R*,5*S*)-3-thia-8-azabicyclo[3.2.1]octan-8-yl)-3-fluorophenyl) -2-Oxo-oxazolidin-5-yl)methyl)carbamate



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.36 (d, *J* = 15.2 Hz, 1 H), 7.07 (d, *J* = 8.8 Hz, 1 H), 6.81 (t, *J* = 9.2 Hz, 1 H), 5.18 (brs, 1 H), 4.74 (brs, 1 H), 4.39 (s, 2 H), 4.01 (t, *J* = 8.8 Hz, 1 H), 3.76 (t, *J* = 7.6 Hz, 1 H), 3.69 (s, 3 H), 3.56-3.51 (m, 1 H), 3.33 (d, *J* = 12.8 Hz, 2 H), 2.18-2.07 (m, 6 H). HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{18}H_{23}N_3O_4FS$: 396.1393; found: 396.1388.

OBD-016

N-(((*S*)-3-(4-((1*R*,5*S*)-3-Thia-8-azabicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-2-oxoo xazolidin-5-yl)methyl)butyramide

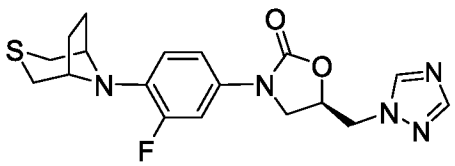


^{1}H-NMR (300 MHz, DMSO-d_6) δ: 8.18 (s, 1 H), 7.42 (d, *J* = 16.0 Hz, 1 H), 7.35-6.88 (m, 2 H), 4.71 (s, 1 H), 4.35 (s, 2 H), 4.07 (t, *J* = 8.7 Hz, 1 H), 3.77-3.57 (m, 1 H), 3.51-3.27 (m, 2 H), 3.12 (d, *J* = 12.4 Hz, 2 H), 2.09 (dd, *J* = 20.9, 12.2 Hz, 8 H), 1.47 (dd, *J* = 14.0, 7.1 Hz, 2 H), 0.80 (dd, *J* = 8.0, 6.7 Hz, 3 H).

LC-MS (ESI): *m/z* = 407.9 $[M+H]^+$.

OBD-021

(*R*)-5-((1*H*-1,2,4-Triazol-1-yl)methyl)-3-(4-((1*R*,5*S*)-3-thia-8-azabicyclo[3.2.1]octan -8-yl)-3-fluorophenyl)oxazolidin-2-one

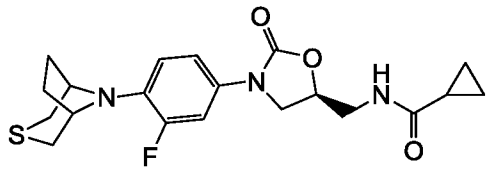


^{1}H-NMR (300 MHz, DMSO-d_6) δ: 8.57 (s, 1 H), 8.01 (s, 1 H), 7.36 (dd, J = 15.8, 2.1 Hz, 1 H), 7.18-6.92 (m, 2 H), 5.06 (dd, J = 8.9, 4.8 Hz, 1 H), 4.72-4.52 (m, 2 H), 4.36 (s, 2 H), 4.17 (t, J = 9.1 Hz, 1 H), 3.84 (dt, J = 49.3, 24.7 Hz, 1 H), 3.12 (d, J = 12.8 Hz, 2 H), 2.16 (s, 1 H), 2.11 (s, 1 H), 2.04 (s, 4 H).

LC-MS (ESI): m/z = 389.9 $[M+H]^+$.

OTB-506

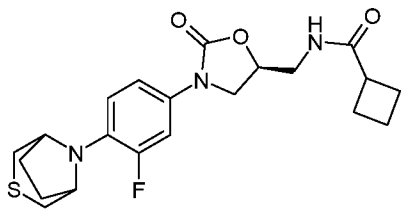
N-(((*S*)-3-(4-((1*R*,5*S*)-3-Thia-8-azabicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-2-oxo-oxazolidin-5-yl)methyl)cyclopropanecarboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.37 (d, J = 13.6 Hz, 1 H), 7.07 (d, J = 7.6 Hz, 1 H), 6.85 (brs, 1 H), 6.22 (t, J = 6.0 Hz, 1 H), 4.79–4.73 (m, 1 H), 4.41 (brs, 2 H), 3.99 (t, J = 7.2 Hz, 1 H), 3.77–3.64 (m, 3 H), 3.39 (d, J = 12.8 Hz, 2 H), 2.20–2.09 (m, 6 H), 1.43–1.37 (m, 1 H), 0.98–0.90 (m, 2 H), 0.82–0.75 (m, 2 H). HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{20}H_{25}N_3O_3FS$: 406.1595; found: 406.1527.

OTB-507

N-(((S)-3-(4-((1*R*,5*S*)-3-Thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-2-oxo-oxazolidin-5-yl)methyl)cyclobutanecarboxamide

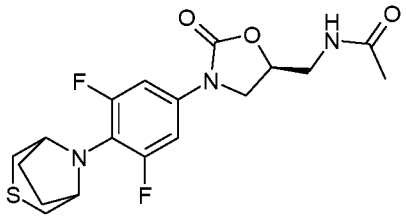


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.45 (d, J = 12.4 Hz, 1 H), 7.17 (d, J = 8.8 Hz, 1 H), 7.05 (t, J = 8.8 Hz, 1 H) 5.95 (m, 1 H), 4.78 (m, 1 H), 4.51 (brs, 2 H), 4.00 (t, J = 9.2

Hz, 1 H), 3.84-3.74 (m, 3 H), 3.66 (m, 2 H), 3.02 (m, 1 H), 2.28-2.15 (m, 10 H), 1.95 (m, 1 H), 1.85 (m, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 175.9, 154.3, 153.0 (d, J = 242.9 Hz), 131.2, 127.0, 118.6 (d, J = 4.4 Hz), 114.5 (d, J = 2.9 Hz), 108.3 (d, J = 27.1 Hz), 71.9, 58.2, 47.7, 41.9, 39.6, 30.3, 28.3, 25.4, 25.3, 18.1. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{21}H_{27}N_3O_3SF$: 420.1757; found: 420.1736.

OTB-510

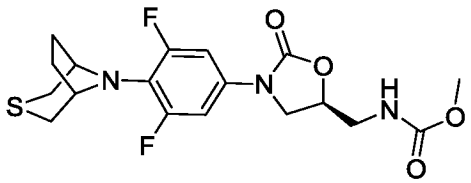
N-(((S)-3-(4-((1*R*,5*S*)-3-Thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxo-oxazolidin-5-yl)methyl)acetamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.08 (m, 2 H), 6.00 (m, 1 H), 4.76 (m, 1 H), 4.24 (brs, 2 H), 3.97 (t, J = 8.8 Hz, 1 H), 3.75-3.60 (m, 3 H), 3.38 (m, 2 H), 2.21 (m, 2 H), 2.14 (s, 4 H), 2.03 (s, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.2, 155.3 (dd, J = 241.5, 9.5 Hz), 154.1, 130.6 (t, J = 13.6 Hz), 122.9 (t, J = 12.4 Hz), 102.9 (dd, J = 20.7, 11.3 Hz), 71.9, 60.4, 47.4, 41.9, 33.7, 29.2, 23.1. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{22}N_3O_3SF_2$: 398.1350; found: 398.1329.

OTB-512

Methyl (((S)-3-(4-((1*R*,5*S*)-3-thia-8-azabicyclo[3.2.1]octan-8-yl)-3,5-difluoro phenyl)-2-oxo-oxazolidin-5-yl)methyl)carbamate

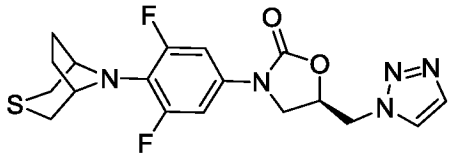


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.09 (m, 2 H), 5.08 (m, 1 H), 4.76 (m, 1 H), 4.24 (brs, 2 H), 3.98 (t, J = 8.8 Hz, 1 H), 3.75-3.50 (m, 6 H), 3.38 (m, 2 H), 2.20 (m, 2 H), 2.14

(s, 4 H).^{13}C-NMR (100 MHz, $CDCl_3$) δ: 157.5, 155.3 (dd, *J* = 241.6, 9.4 Hz), 153.9, 130.7 (t, *J* = 13.6 Hz), 122.9 (t, *J* = 12.3 Hz), 102.9 (dd, *J* = 20.7, 11.3 Hz), 71.8, 60.4, 52.6, 47.3, 43.6, 33.7, 29.2. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{22}N_3O_4SF_2$: 414.1294; found: 414.1278.

OTB-511

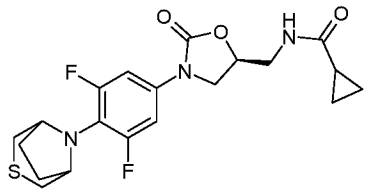
(*R*)-5-((1H-1,2,3-Triazol-1-yl)methyl)-3-(4-((1*R*,5*S*)-3-thia-8-azabicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.78 (s, 1 H), 7.76 (s, 1 H), 6.94 (d, *J* = 11.6 Hz, 2 H), 5.07-5.04 (m, 1 H), 4.79 (d, *J* = 3.6 Hz, 2 H), 4.20 (brs, 2 H), 4.09 (t, *J* = 8.8 Hz, 1 H), 3.88-3.83 (m, 1 H), 3.32 (d, *J* = 12.8 Hz, 2 H), 2.19-2.11 (m, 6 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 155.3 (d, *J* = 242.1 Hz), 155.2 (d, *J* = 242.1 Hz), 153.1, 134.5, 129.9 (t, *J* = 13.6 Hz), 125.1, 123.3 (t, *J* = 12.3 Hz), 103.3 (dd, *J* = 20.7, 11.2 Hz), 70.3, 60.4, 52.0, 47.2, 33.8, 29.2. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{20}N_5O_2SF_2$: 408.1300; found: 408.1295.

OTB-508

N-(((*S*)-3-(4-((1*R*,5*S*)-3-Thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxo-oxazolidin-5-yl)methyl)cyclopropanecarboxamide

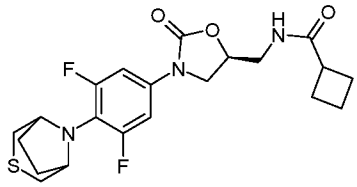


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.05 (m, 2 H), 6.12 (m, 1 H), 4.76 (m, 1 H), 4.21 (brs, 2 H), 3.95 (t, *J* = 9.2 Hz, 1 H), 3.72-3.65 (m, 3 H), 3.34 (m, 2 H), 2.21-2.12 (m, 6 H), 1.37 (m, 1 H), 0.99-0.75 (m, 4 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 174.8, 155.3 (dd, *J* = 241.7, 9.5 Hz), 154.2, 130.5 (t, *J* = 13.6 Hz), 123.0 (t, *J* = 12.5 Hz), 103.0 (dd, *J*

= 20.8, 11.4 Hz), 72.1, 60.4, 47.5, 41.9, 33.8, 29.2, 14.6, 7.8, 7.7. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{20}H_{24}N_3O_3SF_2$: 420.1506; found: 424.1484.

OTB-509

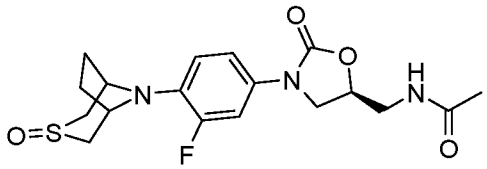
N-(((*S*)-3-(4-((1*R*,5*S*)-3-Thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxo-oxazolidin-5-yl)methyl)cyclobutanecarboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.09 (m, 2 H), 5.78 (m, 1 H), 4.75 (m, 1 H), 4.23 (brs, 2 H), 3.97 (t, *J* = 8.8 Hz, 1 H), 3.73 (m, 1 H), 3.65 (m, 2 H), 3.36 (m, 2 H), 2.99 (m, 1 H), 2.27-2.14 (m, 9 H), 1.97 (m, 1 H), 1.85 (m, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 176.0, 155.3 (dd, *J* = 243.4, 9.5 Hz), 154.1, 130.6 (t, *J* = 13.5 Hz), 122.9 (t, *J* = 12.2 Hz), 102.9 (dd, *J* = 20.7, 11.4 Hz), 72.0, 60.4, 47.5, 41.8, 33.7, 29.2, 25.4, 25.3, 18.1. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{21}H_{26}N_3O_3SF_2$: 438.1663; found: 438.1642.

OTB-503

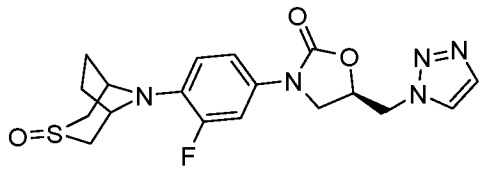
N-(((5*S*)-3-(3-Fluoro-4-((1*R*,5*S*)-3-oxido-3-thia-8-azabicyclo[3.2.1]octan-8-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)acetamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.45 (dd, *J* = 16.0, 2.8 Hz, 1 H), 7.12 (dd, *J* = 8.8, 2.0 Hz, 1 H), 6.83 (t, *J* = 9.2 Hz, 1 H), 6.14 (s, 1 H), 4.78–4.77 (m, 1 H), 4.61 (s, 2 H), 4.00 (t, *J* = 8.8 Hz, 1 H), 3.77–3.64 (m, 3 H), 3.45 (d, *J* = 9.6 Hz, 2 H), 2.85 (d, *J* = 12.4 Hz, 2 H), 2.22–2.20 (m, 2 H), 2.03 (s, 3 H), 1.92–1.88 (m, 2 H). HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{18}H_{23}N_3O_4FS$: 396.1388; found: 396.1379.

OTB-505

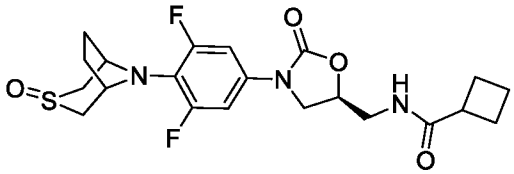
(5*R*)-5-((1*H*-1,2,3-Triazol-1-yl)methyl)-3-(3-fluoro-4-((1*R*,5*S*)-3-oxido-3-thia-8-aza bicyclo[3.2.1]octan-8-yl)phenyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.79 (s, 1 H), 7.75 (s, 1 H), 7.30 (dd, *J* = 15.2, 2.0 Hz, 1 H), 6.98 (d, *J* = 8.4 Hz, 1 H), 6.79 (t, *J* = 9.2 Hz, 1 H), 5.07–5.05 (m, 1 H), 4.79 (s, 2 H), 4.58 (s, 2 H), 4.12 (t, *J* = 9.2 Hz, 1 H), 3.91–3.89 (m, 1 H), 3.43 (d, *J* = 11.6 Hz, 2 H), 2.88–2.81 (m, 2 H), 2.21–2.18 (m, 2 H), 1.89–1.87 (m, 2 H). HR-MS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{18}H_{21}N_5O_3FS$: 406.1349; found: 406.1339.

OTB-513

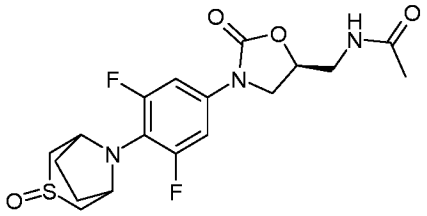
N-(((5*S*)-3-(3,5-Difluoro-4-((1*R*,5*S*)-3-oxido-3-thia-8-azabicyclo[3.2.1]octan-8-yl)ph enyl)-2-oxo-oxazolidin-5-yl)methyl)cyclobutanecarboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.12 (d, *J* = 12.0 Hz, 2 H), 5.97 (brs, 1 H), 4.77-4.75 (m, 1 H), 4.45 (s, 2 H), 3.97 (t, *J* = 8.8 Hz, 1 H), 3.74 (t, *J* = 8.4 Hz, 1 H), 3.66 (t, *J* = 5.2 Hz, 2 H), 3.54 (d, *J* = 9.2 Hz, 2 H), 3.02 (m, 1 H), 2.91 (d, *J* = 12.0 Hz, 2 H), 2.26-2.11 (m, 6 H), 1.99-1.92 (m, 1 H), 1.87-1.85 (m, 3 H). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{21}H_{26}N_3O_4SF_2$: 454.1606; found: 454.1588.

OTB-514

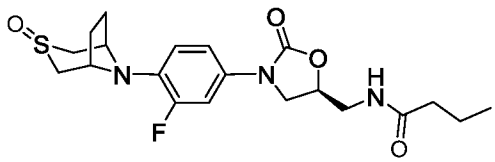
N-(((5*S*)-3-(3,5-Difluoro-4-((1*R*,5*S*)-3-oxido-3-thia-8-azabicyclo[3.2.1]octan-8-yl)ph enyl)-2-oxo-oxazolidin-5-yl)methyl) acetamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.12 (d, *J* = 12.0 Hz, 2 H), 6.15 (brs, 1 H), 4.81-4.75 (m, 1 H), 4.45 (s, 2 H), 3.98 (t, *J* = 8.8 Hz, 1 H), 3.74-3.63 (m, 3 H), 3.56 (d, *J* = 9.2 Hz, 2 H), 2.92 (d, *J* = 12.4 Hz, 2 H), 2.20-2.17 (m, 2 H), 2.03 (s, 3 H), 1.89-1.83 (m, 2 H). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{22}N_3O_4SF_2$: 414.1293; found: 414.1275.

OBD-017

N-(((5*S*)-3-(3-Fluoro-4-((1*R*,5*S*)-3-oxido-3-thia-8-azabicyclo[3.2.1]octan-8-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)butyramide

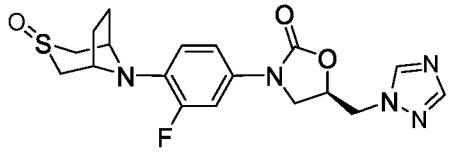


^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.39 (dd, *J* = 15.8, 2.3 Hz, 1 H), 7.03 (d, *J* = 6.1 Hz, 2 H), 6.78 (t, *J* = 9.3 Hz, 1 H), 4.72 (s, 1 H), 4.55 (s, 2 H), 3.94 (t, *J* = 8.9 Hz, 1 H), 3.81-3.66 (m, 1 H), 3.58 (s, 2 H), 3.42 (d, *J* = 10.3 Hz, 2 H), 2.77 (d, *J* = 11.9 Hz, 2 H), 2.17 (dd, *J* = 25.1, 17.8 Hz, 4 H), 1.84 (d, *J* = 7.9 Hz, 2 H), 1.56 (dd, *J* = 14.5, 7.2 Hz, 2 H), 0.83 (t, *J* = 7.4 Hz, 3 H).

LC-MS (ESI): *m/z* = 423.8 $[M+H]^+$.

OBD-018

(5*R*)-5-((1*H*-1,2,4-Triazol-1-yl)methyl)-3-(3-fluoro-4-((1*R*,5*S*)-3-oxido-3-thia-8-azabicyclo[3.2.1]octan-8-yl)phenyl)oxazolidin-2-one

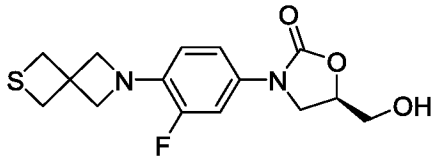


^{1}H-NMR (300 MHz, DMSO-d_6) δ: 12.17 (s, 1 H), 8.69 (d, J = 2.9 Hz, 1 H), 8.20 – 8.03 (m, 1 H), 7.44 (d, J = 16.2 Hz, 1 H), 7.28-7.02 (m, 2 H), 5.08 (dd, J = 8.5, 5.1 Hz, 1 H), 4.68-4.52 (m, 4 H), 4.20 (t, J = 9.1 Hz, 1 H), 3.91 (dd, J = 8.7, 6.0 Hz, 1 H), 3.56 (d, J = 11.1 Hz, 2 H), 2.48 (d, J = 12.3 Hz, 2 H), 2.06 (d, J = 5.1 Hz, 2 H), 1.79 (d, J = 7.6 Hz, 2 H).

LC-MS (ESI): m/z = 405.8 $[M+H]^+$.

OTB-260

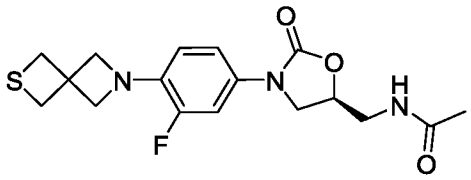
(*R*)-3-(3-Fluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ:7.38 (d, J = 14.0 Hz, 1 H), 7.04 (d, J = 8.0 Hz, 1 H), 6.55 (t, J = 8.8 Hz, 1 H), 4.72 (brs, 1 H), 4.02 (s, 4 H), 3.99-3.89 (m, 3 H), 3.76-3.73 (m, 1 H), 3.42 (s, 4 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 154.8, 152.2 (d, J = 240.8 Hz), 135.9 (d, J = 11.7 Hz), 130.2 (d, J = 9.3 Hz), 114.6 (d, J = 5.2 Hz), 114.5 (d, J = 3.1 Hz), 107.6 (d, J = 23.8 Hz), 72.8, 66.8, 62.8, 46.7, 44.3, 36.8. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{15}H_{18}FN_2O_3S$: 325.1022; found: 325.1010.

OTB-261

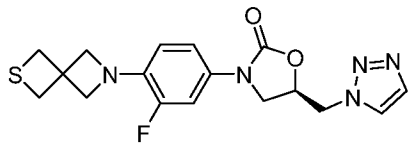
(*S*)-*N*-((3-(3-Fluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)acetamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.33 (d, *J* = 14.0 Hz, 1 H), 6.99 (d, *J* = 8.4 Hz, 1 H), 6.48 (t, *J* = 8.8 Hz, 1 H), 6.20 (brs, 1 H), 4.75-4.73 (m, 1 H), 3.98-3.96 (m, 5 H), 3.73-3.66 (m, 2 H), 3.62-3.57 (m, 1 H), 3.41 (s, 4 H), 2.01 (s, 3 H). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{21}FN_3O_3S$: 366.1288; found: 366.1274.

OTB-241

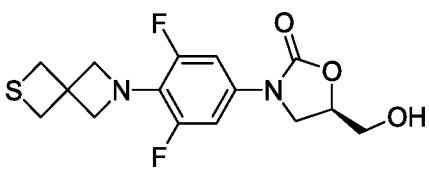
(*R*)-5-((1H-1,2,3-Triazol-1-yl)methyl)-3-(3-fluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.79 (s, 1 H), 7.75 (s, 1 H), 7.22 (dd, *J* = 13.6, 2.0 Hz, 1 H), 6.88 (d, *J* = 8.8 Hz, 1 H), 6.51 (t, *J* = 9.2 Hz, 1 H), 5.06-5.00 (m, 1 H), 4.78-4.77 (m, 2 H), 4.08 (t, *J* = 9.2 Hz, 1 H), 4.01 (s, 4 H), 3.89-3.85 (m, 1 H), 3.40 (s, 4 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 153.6, 152.0 (d, *J* = 243.1 Hz), 136.3 (d, *J* = 11.1 Hz), 134.5, 129.1 (d, *J* = 9.0 Hz), 125.1, 115.0 (d, *J* = 3.2 Hz), 114.5 (d, *J* = 5.2 Hz), 108.1 (d, *J* = 23.6 Hz), 70.4, 66.7, 52.1, 47.7, 44.3, 36.8. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{19}FN_5O_2S$: 376.1244; found: 376.1231.

OTB-516

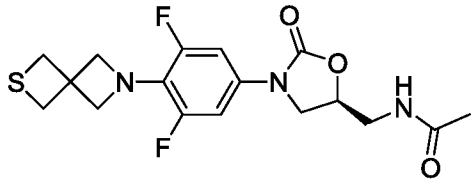
(*R*)-3-(3,5-Difluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-5-(hydroxymethyl) oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.03 (d, *J* = 12.0 Hz, 2 H), 4.74-4.70 (m, 1 H), 4.18 (s, 4 H), 3.98 (dd, *J* = 12.8, 3.2 Hz, 1 H), 3.93-3.85 (m, 2 H), 3.75 (dd, *J* = 12.4, 4.0 Hz, 1 H), 3.41 (s, 4 H). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{17}N_2O_3SF_2$: 343.0922; found: 343.0912.

OTB-515

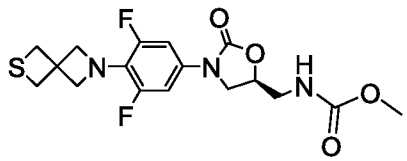
(*S*)-*N*-((3-(3,5-Difluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)acetamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.98 (d, *J* = 11.6 Hz, 2 H), 5.99 (brs, 1 H), 4.74-4.72 (m, 1 H), 4.16 (s, 4 H), 3.94 (t, *J* = 8.8 Hz, 1 H), 3.71-3.65 (m, 2 H), 3.61-3.55 (m, 1 H), 3.40 (s, 4 H), 2.01 (s, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.1, 154.2, 152.6 (dd, *J* = 240.6, 11.1 Hz), 153.1, 134.5, 128.5 (t, *J* = 12.6 Hz), 124.7 (t, *J* = 13.3 Hz), 102.8 (dd, *J* = 18.2, 10.7 Hz), 71.9, 68.7, 47.6, 45.2, 42.0, 36.5, 23.1. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{20}N_3O_3SF_2$: 384.1188; found: 384.1168.

OTB-242

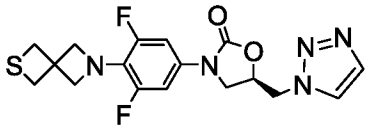
Methyl (*S*)-((3-(3,5-difluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)carbamate



^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.00 (d, *J* = 11.6 Hz, 2 H), 5.16 (brs, 1 H), 4.81–4.67 (m, 1 H), 4.16 (s, 4 H), 3.94 (t, *J* = 8.8 Hz, 1 H), 3.68 (s, 3 H), 3.56–3.50 (m, 3 H), 3.40 (s, 4 H). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{20}F_2N_3O_4S$: 400.1143; found: 400.1125.

OTB-245

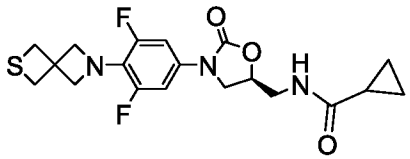
(*R*)-5-((1H-1,2,3-Triazol-1-yl)methyl)-3-(3,5-difluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)oxazolidin-2-one



^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (s, 1 H), 7.74 (s, 1 H), 6.87 (d, *J* = 11.6 Hz, 2 H), 5.03–5.01 (m, 1 H), 4.77–4.76 (m, 2 H), 4.15 (s, 4 H), 4.06 (t, *J* = 9.2 Hz, 1 H), 3.86–3.82 (m, 1 H), 3.41 (s, 4 H). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{18}F_2N_5O_2S$: 394.1149; found: 394.1129.

OTB-243

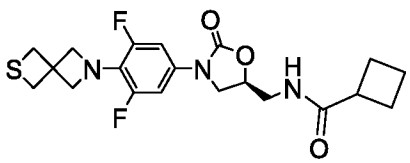
(*S*)-*N*-((3-(3,5-Difluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)cyclopropanecarboxamide



^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.98 (d, *J* = 11.6 Hz, 2 H), 6.25–6.24 (m, 1 H), 4.77–4.71 (m, 1 H), 4.16 (s, 4 H), 3.92 (t, *J* = 8.8 Hz, 1 H), 3.71 – 3.56 (m, 3 H), 3.40 (s, 4 H), 1.40–1.38 (m, 1 H), 1.04–0.87 (m, 2 H), 0.82–0.73 (m, 2 H). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{22}F_2N_3O_3S$: 410.1350; found: 410.1331.

OTB-244

(*S*)-*N*-((3-(3,5-Difluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)cyclobutanecarboxamide

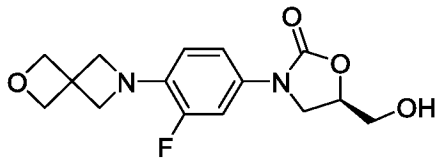


^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.99 (d, *J* = 11.6 Hz, 2 H), 5.83 (brs, 1 H), 4.82–4.68

(m, 1 H), 4.17 (s, 4 H), 3.93 (t, *J* = 8.8 Hz, 1 H), 3.72–3.64 (m, 3 H), 3.40 (s, 4 H), 3.03–2.96 (m, 1 H), 2.26–1.85 (m, 6 H). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{20}H_{24}F_2N_3O_3S$: 424.1506; found:.424.1483

OTB-201

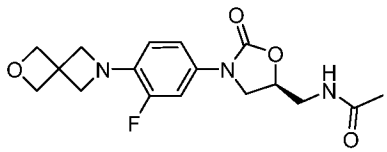
(*R*)-3-(3-Fluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ:7.42 (dd, *J* = 14.0, 2.0 Hz, 1 H), 7.03 (dd, *J* = 8.8, 2.0 Hz, 1 H), 6.62 (t, *J* = 8.8 Hz, 1 H), 4.85 (s, 4 H), 4.73 (m, 1 H), 4.17 (s, 4 H), 4.00-3.95 (m, 2 H), 3.93-3.89 (m, 1 H), 3.77-3.74 (m, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 155.2, 152.3 (d, *J* = 240.7 Hz), 135.9 (d, *J* = 11.3 Hz), 130.4 (d, *J* = 8.9 Hz), 114.7 (d, *J* = 3.0 Hz), 114.6 (d, *J* = 5.6 Hz), 107.8 (d, *J* = 23.8 Hz), 81.3, 73.2, 63.1, 62.9, 46.9, 40.1. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{18}FN_2O_4$: 309.1251; found: 309.1269.

OTB-202

(*S*)-*N*-((3-(3-Fluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)acetamide

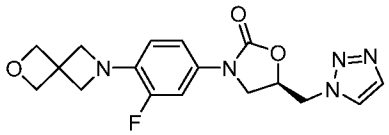


^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.35 (d, *J* = 14.1 Hz, 1 H), 7.00 (d, *J* = 8.7 Hz, 1 H), 6.51 (t, *J* =9.0 Hz, 1 H), 6.03(s, 1 H), 4.84 (s, 4 H), 4.74 (m, 1 H), 4.12 (s, 4 H), 3.99 (t, *J* =8.7 Hz, 1 H), 3.73-3.69 (m, 2 H), 3.61 (m, 1 H), 2.02 (s, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.4, 154.8, 152.4 (d, *J* = 240.8 Hz), 136.1 (d, *J* = 11.9 Hz), 130.1 (d, *J* = 9.2 Hz), 114.7 (d, *J* = 3.1 Hz), 114.6 (d, *J* = 5.0 Hz), 107.9 (d, *J* = 23.6 Hz),

81.2, 72.1, 63.1, 48.1, 42.2, 40.1, 23.4. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{21}FN_3O_4$: 350.1516; found: 350.1497.

OTB-203

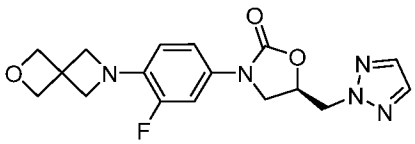
(*R*)-5-((1H-1,2,3-Triazol-1-yl)methyl)-3-(3-fluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.78 (s, 1 H), 7.75 (s, 1 H), 7.18 (d, *J* = 13.6 Hz, 1 H), 6.88 (d, *J* = 8.8 Hz, 1 H), 6.46 (t, *J* = 9.2 Hz, 1 H), 5.03 (m, 1 H), 4.83 (s, 4 H), 4.78 (m, 2 H), 4.10-4.07 (m, 5 H), 3.91-3.85 (m, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 153.6, 152.1 (d, *J* = 241.4 Hz), 136.1 (d, *J* = 10.6 Hz), 134.5, 129.2 (d, *J* = 9.3 Hz), 125.1, 115.0 (d, *J* = 2.9 Hz), 114.5 (d, *J* = 4.7 Hz), 108.1 (d, *J* = 23.7 Hz), 81.0, 70.4, 62.9, 52.1, 47.7, 39.8. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{19}FN_5O_3$: 360.1472; found: 360.1451.

OTB-204

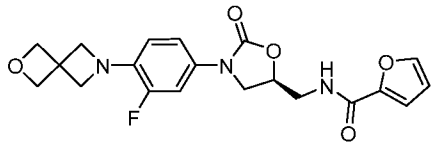
(*R*)-5-((2H-1,2,3-Triazol-2-yl)methyl)-3-(3-fluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.65 (s, 2 H), 7.31 (d, *J* = 14.4, 2.4 Hz,1 H), 6.99 (d, *J* = 8.4 Hz, 1 H), 6.59 (t, *J* = 9.2 Hz, 1 H), 5.14-5.07 (m, 1 H), 4.88-4.83 (m, 5 H), 4.77-4.71 (m, 1 H), 4.16 (s, 4 H), 4.07-4.02 (m, 1 H), 3.98-3.92 (m, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 158.99, 154.38, 147.08, 144.53, 135.18, 115.11, 114.43, 112.30, 107.91, 107.87, 81.04, 71.85, 70.04, 62.91, 48.38, 48.02, 41.57, 39.85. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{19}FN_5O_3$: 360.1472; found: 360.1451.

OTB-205

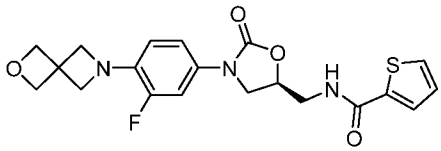
(*S*)-*N*-((3-(3-Fluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)furan-2-carboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.46 (s, 1 H), 7.32 (dd, *J* = 14.0, 2.4 Hz, 1 H), 7.14 (d, *J* = 3.2 Hz, 1 H), 7.00 (d, *J* = 8.4 Hz, 1 H), 6.81 (t, *J* = 6.4 Hz, 1 H), 6.51 (d, *J* = 3.2 Hz, 1 H), 6.45 (t, *J* = 9.2 Hz, 1 H), 4.83 (brs, 5 H), 4.08 (s, 4 H), 4.03 (t, *J* = 8.8 Hz, 1 H), 3.92-3.85 (m, 1 H), 3.79-3.73 (m, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 159.2, 154.6, 152.4 (d, *J* = 240.8 Hz), 147.3, 144.7, 136.5, 130.5 (d, *J* = 9.4 Hz), 115.3, 114.7 (d, *J* = 3.1 Hz), 112.5, 109.9, 107.9 (d, *J* = 23.9 Hz), 81.2, 72.1, 63.1, 48.2, 41.8, 40.1. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{20}H_{21}FN_3O_5$: 402.1465; found: 402.1561.

OTB-206

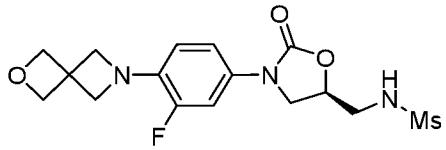
(*S*)-*N*-((3-(3-Fluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)thiophene-2-carboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.53 (d, *J* = 3.2 Hz, 1 H), 7.50 (d, *J* = 4.8 Hz, 1 H), 7.32 (d, *J* = 14.0 Hz, 1 H), 7.09-6.96 (m, 2 H), 6.66 (m, 1 H), 6.45 (t, *J* = 9.2 Hz, 1 H), 4.82 (s, 4 H), 4.09-4.01 (m, 6 H), 3.81-3.79 (m, 1 H), 3.78-3.73 (m, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 162.9, 154.7, 152.5 (d, *J* = 241.1 Hz), 150.1, 140.8, 138.1, 130.9, 128.9, 128.0, 114.9 (d, *J* = 2.8 Hz), 114.2 (d, *J* = 3.2 Hz), 108.1 (d, *J* = 23.9 Hz), 81.20 72.2, 63.2, 48.3, 42.7, 40.0. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{20}H_{21}FN_3O_4S$: 418.1237; found: 418.1331.

OTB-222

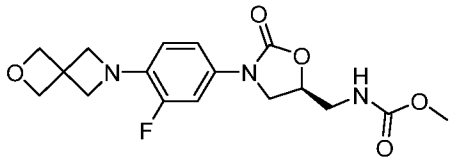
(*R*)-*N*-((3-(3-Fluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)methanesulfonamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.44-7.35 (m, 1 H), 7.07- 6.97 (m, 1 H), 6.69-6.59 (m, 1 H), 4.98-4.91 (m, 1 H), 4.85 (s, 4 H), 4.81-4.75 (m, 1 H), 4.24-4.14 (m, 4 H), 4.13-4.09 (m, 1 H), 4.06-3.98 (m, 1 H), 3.92-3.86 (m, 1 H), 3.63-3.53 (m, 1 H), 3.47-3.36 (m, 1 H), 3.03 (s, 3 H). ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 154.5, 151.7 (d, J = 237.7 Hz), 135.9 (d, J = 11.0 Hz), 130.5 (d, J = 9.4 Hz), 115.2 (d, J = 5.4 Hz), 115.1 (d, J = 2.8 Hz), 107.3 (d, J = 23.8 Hz), 80.2, 71.7, 62.7, 47.6, 45.5. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{21}FN_3O_5S$: 386.1186; found: 386.1185.

OTB-223

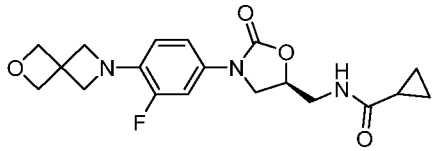
Methyl (*S*)-((3-(3-fluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)carbamate



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.39 (d, J = 14.0 Hz, 1 H), 7.01 (d, J = 8.8 Hz, 1 H), 6.61 (t, J = 9.2 Hz, 1 H), 5.11 (brs, 1 H), 4.84 (s, 4 H), 4.73 (brs, 1 H), 4.16 (s, 4 H), 3.99 (t, J = 8.8 Hz, 1 H), 3.77-3.75 (m, 1 H), 3.68 (s, 3 H), 3.64-3.60 (m, 1 H), 3.55-3.50 (m, 1 H). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{21}FN_3O_5$: 366.1465; found: 366.1466.

OTB-238

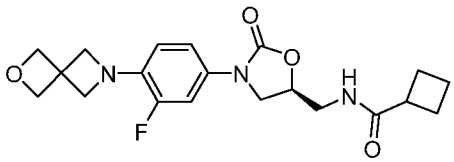
(*S*)-*N*-((3-(3-Fluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)cyclopropanecarboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.35 (dd, *J* = 14.0, 2.4 Hz, 1 H), 7.00 (d, *J* = 8.4 Hz, 1 H), 6.51 (t, *J* = 9.2 Hz, 1 H), 6.13 (brs, 1 H), 4.84 (s, 4 H), 4.75-4.73 (m, 1 H), 4.12 (s, 4 H), 3.97 (t, *J* = 8.8 Hz, 1 H), 3.75-3.65 (m, 3 H), 1.39-1.36 (m, 1 H), 0.97-0.91 (m, 2 H), 0.79-0.75 (m, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 174.8, 154.6, 151.6 (d, *J* = 240.8 Hz), 136.0 (d, *J* = 11.3 Hz), 129.8 (d, *J* = 9.2 Hz), 114.5 (d, *J* = 3.1 Hz), 114.6 (d, *J* = 3.1 Hz), 114.3 (d, *J* = 5.2 Hz), 107.8 (d, *J* = 23.8 Hz), 81.1, 72.1, 62.9, 47.9, 42.0, 39.9, 14.6, 7.7. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{23}FN_3O_4$: 376.1673; found: 376.1652.

OTB-239

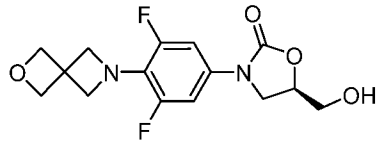
(*S*)-*N*-((3-(3-Fluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)cyclobutanecarboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.49 (d, *J* = 14.4 Hz, 1 H), 7.01 (d, *J* = 8.4 Hz, 1 H), 6.85 (t, *J* = 9.2 Hz, 1 H), 5.82 (brs, 1 H), 4.86 (s, 4 H), 4.76 (brs, 1 H), 4.27 (s, 4 H), 4.00 (t, *J* = 9.2 Hz, 1 H), 3.78-3.65 (m, 3 H), 3.03-2.99 (m, 1 H), 2.26-2.13 (m, 4 H), 1.99-1.85 (m, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 176.0, 154.5, 152.1 (d, *J* = 240.9 Hz), 136.0 (d, *J* = 11.2 Hz), 129.8 (d, *J* = 9.2 Hz), 114.4 (d, *J* = 3.1 Hz), 114.3 (d, *J* = 5.2 Hz), 107.7 (d, *J* = 23.9 Hz), 81.1, 71.9, 62.8, 47.9, 41.9, 39.7, 25.4, 25.3, 18.2. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{20}H_{25}FN_3O_4$: 390.1829; found: 390.1808.

OTB-229

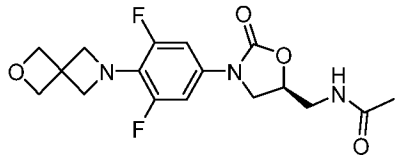
(*R*)-3-(3,5-Difluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.03 (d, *J* = 10.8 Hz, 2 H), 4.82 (s, 4 H), 4.72 (brs, 1 H), 4.28 (s, 4 H), 3.99-3.85 (m, 3 H), 3.75-3.72 (m, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 154.6, 152.6 (dd, *J* = 240.2, 10.8 Hz), 128.9 (t, *J* = 12.8 Hz), 124.3 (t, *J* = 13.3 Hz), 102.8 (dd, *J* = 18.2, 10.7 Hz), 81.0, 72.9, 64.9, 62.6, 46.3, 40.8. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{15}H_{17}F_2N_2O_4$: 327.1156; found: 327.1135.

OTB-230

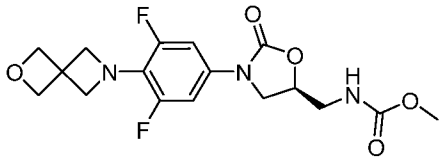
(*S*)-*N*-((3-(3,5-Difluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)acetamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.97 (d, *J* = 10.0 Hz, 2 H), 6.49 (brs, 1 H), 4.81 (s, 4 H), 4.75 (brs, 1 H), 4.27 (s, 4 H), 3.94 (t, *J* = 8.8 Hz, 1 H), 3.70-3.63 (m, 3 H), 2.02 (s, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.2, 154.2, 152.5 (dd, *J* = 240.5, 10.9 Hz), 128.6 (t, *J* = 12.6 Hz), 124.5 (t, *J* = 13.4 Hz), 102.8 (dd, *J* = 18.2, 10.6 Hz), 80.9, 71.9, 64.9, 47.5, 41.9, 40.8, 23.1. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{17}H_{20}F_2N_3O_4$: 368.1422; found: 368.1418.

OTB-231

Methyl (*S*)-((3-(3,5-difluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)carbamate

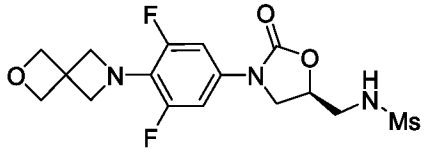


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.04 (d, *J* = 10.8 Hz, 2 H), 5.08 (brs, 1 H), 4.83 (s, 4 H), 4.74 (brs, 1 H), 4.34 (s, 4 H), 3.96 (t, *J* = 9.2 Hz, 1 H), 3.72-3.51 (m, 6 H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 157.5, 154.0, 152.6 (dd, J = 240.4, 10.9 Hz), 128.7 (t, J = 12.8 Hz), 124.5 (t, J = 13.5 Hz), 102.8 (dd, J = 23.3, 15.7 Hz), 80.9, 71.7, 64.8, 52.6, 47.4, 43.6, 40.8. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{20}F_2N_3O_5$: 384.1371; found: 384.1367.

OTB-232

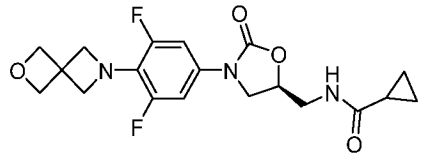
(*R*)-*N*-((3-(3,5-Difluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)methanesulfonamide



^{1}H-NMR (400 MHz, DMSO-d_6) δ: 7.8 (d, J = 12.4 Hz, 2 H), 4.74-4.69 (m, 5 H), 4.23 (s, 4 H), 4.06 (t, J = 8.8 Hz, 1 H), 3.74-3.70 (m, 1 H), 3.31-3.27 (m, 2 H), 2.94 (s, 3 H). ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 154.3, 152.2 (dd, J = 237.8, 11.3 Hz), 129.5 (t, J = 13.0 Hz), 124.4 (t, J = 13.6 Hz), 102.9 (dd, J = 18.2, 10.5 Hz), 80.0, 71.8, 64.7, 47.4, 45.5, 40.7. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{20}F_2N_3O_5S$: 404.1092; found: 404.1087.

OTB-233

(*S*)-*N*-((3-(3,5-Difluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)cyclopropanecarboxamide

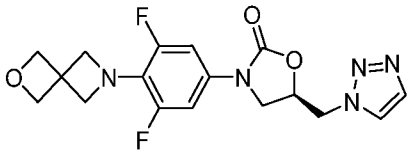


^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.98 (d, J = 10.0 Hz, 2 H), 6.36 (brs, 1 H), 4.82 (s, 4 H), 4.75 (brs, 1 H), 4.28 (s, 4 H), 3.93 (t, J = 8.8 Hz, 1 H), 3.72-3.65 (m, 3 H), 1.42-1.40 (m, 1 H), 0.96-0.88 (m, 2 H), 0.77-0.75 (m, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 174.9, 154.4, 152.5 (dd, J = 240.4, 10.3 Hz), 128.6 (t, J = 12.7 Hz), 124.4 (t, J = 13.4 Hz), 102.8 (dd, J = 18.2, 10.6 Hz), 80.9, 72.2, 64.8, 47.6, 41.9, 40.8, 14.5, 7.7.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{22}F_2N_3O_4$: 394.1578; found: 394.1575.

OTB-234

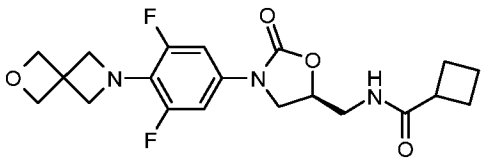
(*R*)-5-((1H-1,2,3-Triazol-1-yl)methyl)-3-(3,5-difluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)oxazolidin-2-one



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.77 (s, 1 H), 7.75 (s, 1 H), 6.86 (d, *J* = 11.6 Hz, 2 H), 5.03-5.02 (m, 1 H), 4.81 (s, 4 H), 4.77-4.76 (m, 2 H), 4.27 (s, 4 H), 4.06 (t, *J* = 9.2 Hz, 1 H), 3.86-3.82 (m, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 153.2, 152.4 (dd, *J* = 240.7, 11.0 Hz), 134.5, 127.8 (t, *J* = 12.8 Hz), 125.1, 124.8 (t, *J* = 13.3 Hz), 103.1 (dd, *J* = 18.1, 10.7 Hz), 80.9, 70.4, 64.8, 52.0, 47.3, 40.8. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{18}F_2N_5O_3$: 378.1378; found: 378.1365.

OTB-240

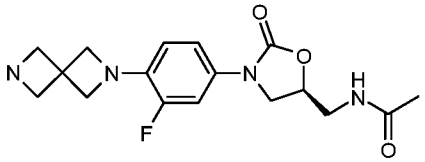
(*S*)-*N*-((3-(3,5-Difluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)cyclobutanecarboxamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.00 (d, *J* = 12.0 Hz, 2 H), 5.87 (t, *J* = 6.0 Hz, 1 H), 4.82 (s, 4 H), 4.77-4.71 (m, 1 H), 4.28 (s, 4 H), 3.94 (t, *J* = 8.8 Hz, 1 H), 3.72-3.64 (m, 3 H), 3.03-2.99 (m, 1 H), 2.26-2.13 (m, 4 H), 1.99-1.82 (m, 2 H). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{20}H_{24}F_2N_3O_4$: 408.1735; found: 408.1716.

OTB-701

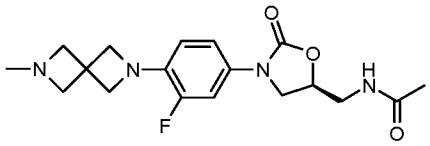
(*R*)-*N*-((3-(3-Fluoro-4-(2,6-diazaspiro[3.3]heptan-2-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)acetamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38 (d, *J* = 14.4 Hz, 1 H), 7.09 (d, *J* = 8.4 Hz, 1 H), 6.58 (t, *J* = 9.2 Hz, 1 H), 4.76 (m, 2 H), 4.30 (s, 4 H), 4.10 (s, 4 H), 3.76 (m, 1 H), 3.54 (m, 2 H), 1.96 (s, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.6, 155.4, 153.2, 150.8, 135.6, 130.5, 114.4, 107.3, 72.0, 62.2, 55.0, 48.0, 41.7, 37.2, 21.0. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{17}H_{22}FN_4O_3$:349.1671; found: 349.1662.

OTB-702

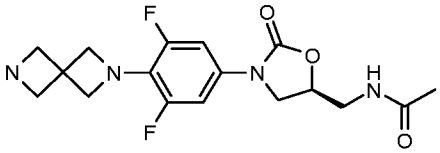
(*R*)-*N*-((3-(3-Fluoro-4-(6-methyl-2,6-diazaspiro[3.3]heptan-2-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)acetamide



^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.36 (d, *J* = 14.4 Hz, 1 H), 7.08 (d, *J* = 8.8 Hz, 1 H), 6.57 (t, *J* = 9.2 Hz, 1 H), 4.75 (m, 1 H), 4.10 (t, *J* = 9.2 Hz, 1 H), 4.01 (s, 4 H), 3.74 (m, 1 H), 3,73 (s, 4 H), 3.53 (m, 2 H), 2.52 (s, 3 H), 1.96 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.6, 155.4, 153.2, 150.8, 136.1, 130.3, 114.4, 107.3, 72.0, 64.9, 62.6, 48.0, 43.0, 41.7, 34.8, 21.0. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{18}H_{24}FN_4O_3$: 363.1827, found: 363.1819.

OTB-704

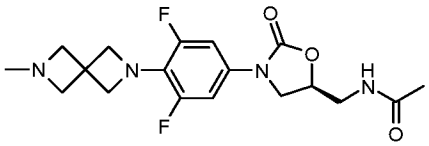
(*R*)-*N*-((3-(3,5-Difluoro-4-(2,6-diazaspiro[3.3]heptan-2-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)acetamide



^{1}H-NMR (400 MHz, CD_3OD) δ: 7.12 (d, *J* = 9.6 Hz, 2 H), 4.76, (m, 1 H), 4.30 (s, 4 H), 4.24 (s, 4 H), 4.06 (m, 1 H), 3.73 (m, 1 H), 3.53 (m, 2 H), 1.96 (s, 3 H). ^{13}C NMR (100 MHz, CD_3OD) δ: 172.6, 155.0, 153.7, 151.3, 129.6, 129.4, 102.7, 102.5, 72.0, 64.3, 55.0, 48.0, 41.6, 38.3, 21.0. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{17}H_{21}F_2N_4O_3$: 367.1583 , found: 367.1576.

OTB-705

(*R*)-*N*-((3-(3,5-Difluoro-4-(6-methyl-2,6-diazaspiro[3.3]heptan-2-yl)phenyl)-2-oxo-oxazolidin-5-yl)methyl)acetamide

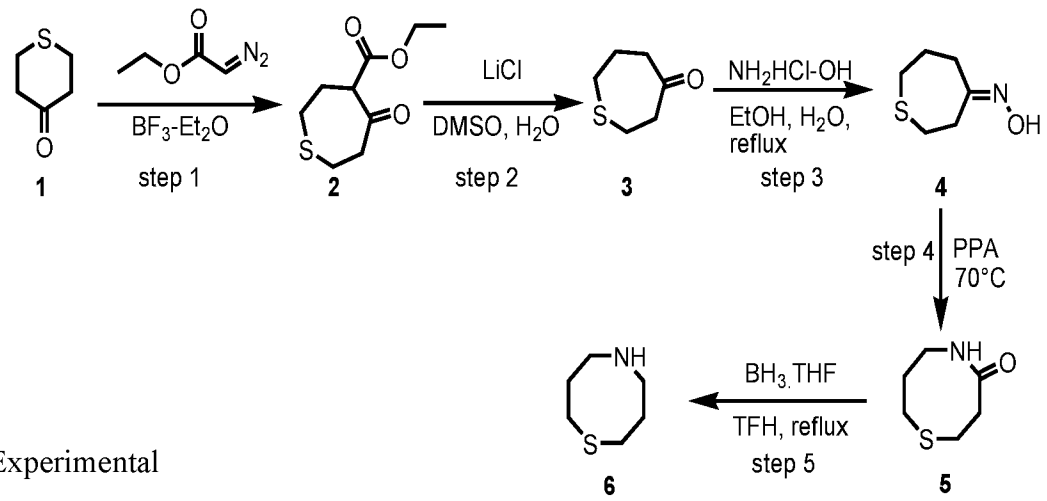


^{1}H-NMR (400 MHz, CD_3OD) δ: 7.12 (d, *J* = 10.0 Hz, 2 H), 4.75 (m, 1 H), 4.22 (s, 4 H), 4.05 (m, 1 H), 3.78 (s, 4 H), 3.73 (m, 1 H), 3.53 (m, 2 H), 2.55 (s, 3 H), 1.96 (s, 3 H). ^{13}C-NMR (100 MHz, CD_3OD) δ: 172.6, 155.0, 153.7, 151.3, 129.4, 102.8, 72.0, 64.7, 64.6, 48.0, 42.7, 41.7, 22.4, 21.0. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{18}H_{23}F_2N_4O_3$: 381.1733, found: 381.1725.

Example 12

Synthesis of Additional Embodiments of the Invention

Procedures for preparation of (6):



Experimental

Ethyl 5-oxothiepane-4-carboxylate (2).

To a solution of tetrahydrothiopyran-4-one (100 g, 862 mmol) in Et_2O (150 mL) was added BF_3-Et_2O (120 mL, 948 mmol) at -30 °C, then the reaction mixture was stirred at -30 °C for 2 h under a nitrogen gas atmosphere, after that the solution of ethyl 2-diazoacetate (147 g, 1293 mmol) in Et_2O (100 mL) was added to the mixture at -30 °C, then the mixture was warmed to room temperature and stirred for overnight. Quenched with K_2CO_3, the solvent was concentrated and dried to give ethyl 5-oxothiepane-4-carboxylate (2) (80 g, 46%) as brown oil.

Thiepan-4-one (3).

A mixture of ethyl 5-oxothiepane-4-carboxylate (2) (80 g, 396 mmol) and lithium chloride (16.6 g, 396 mmol) in DMSO (100 mL) and H_2O (5 drop) was stirred at 180°C for 2 h. The reaction mixture was cooled to room temperature and poured into ice water, extracted with EA, the organic layer was concentrated under reduced pressure to afford thiepan-4-one (3) (15.9 g crude, 31%) as brown solid.

(Z)-Thiepan-4-one oxime (4).

To a solution of thiepan-4-one (3) (15.9 g, 122 mmol) in EtOH (150 mL) and H_2O (50 mL) was added with NH_2OH-HCl (8.47 g, 122 mmol), then the reaction mixture was stirred at 75 °C for 4 h under a nitrogen gas atmosphere, then mixture was

concentrated and dried to give (Z)-thiepan-4-one oxime (4) (9.97 g, 56%) as brown solid.

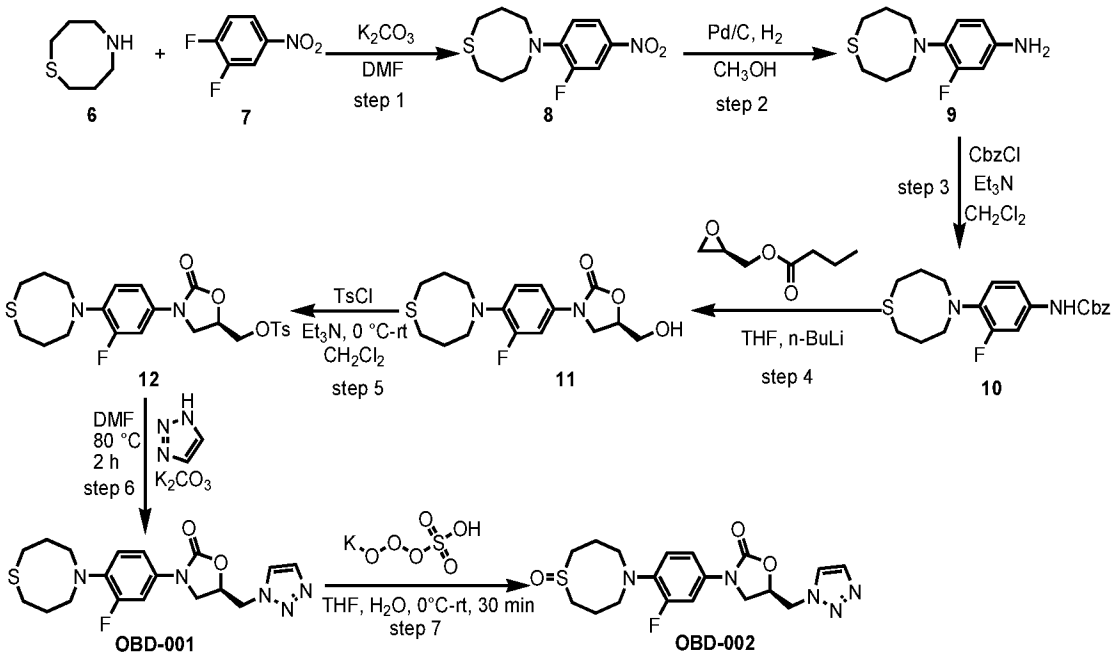
1,5-Thiazocan-4-one (5).

A mixture of (Z)-thiepan-4-one oxime (4) (9.97 g, 68.7 mmol) and polyphosphoric acid (50 g) was stirred at 70 °C for 2 h. The reaction mixture was cooled to room temperature and poured into ice water, adjusted pH = 8 using potassium carbonate solution, extracted with EA, the organic layer was concentrated under reduced pressure to afford 1,5-thiazocan-4-one (5) (3 g crude, 30%) as brown solid.

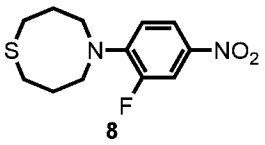
1,5-Thiazocane (6).

To a solution of 1,5-thiazocan-4-one (5) (3 g, 20.7 mmol) in THF (100 mL) was added BH_3 (31 mL, 31.1 mmol) in THF at 0 °C, followed by refluxing for 12 h. The reaction was quenched with CH_3OH (50 mL). The solvent was evaporated to afford 1,5-thiazocane (6) as a white oil (1.7 g, 63%), and the crude material was used for next reaction without further purification.

LC-MS (ESI) m/z = 132 $[M+H]^+$.



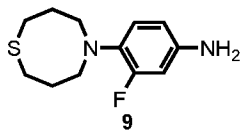
Step 1: Preparation of 5-(2-fluoro-4-nitrophenyl)-1,5-thiazocane (8):



8

To a solution of 1,5-thiazocane (6) (1 g, 7.6 mmol) and 1,2-difluoro-4-nitrobenzene (1.2 g, 7.6 mmol) in DMF (10 mL) was added K_2CO_3 (1.05 g, 7.6 mmol) at 25°C then the reaction mixture was stirred at 80°C for 2 h under a nitrogen gas atmosphere, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 3: 1) to afford 5-(2-fluoro-4-nitrophenyl)-1,5-thiazocane (8) (1.5 g, 74%) as a yellow solid. LC-MS (ESI) *m/z* = 271 $[M+H]^+$.

Step 2: 3-Fluoro-4-(1,5-thiazocan-5-yl)benzenamine (9):

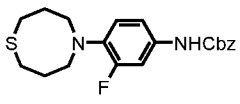


9

To a solution of 5-(2-fluoro-4-nitrophenyl)-1,5-thiazocane (8) (1.5 g, 5.7 mmol) and Palladium carbon (200 mg) in MeOH (15 mL), then under a hydrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. The filtrate was concentrated under reduced pressure to afford 3-fluoro-4-(1,5-thiazocan-5-yl)benzenamine (9) (1.2 g, 91%) as a white oil., and the crude material was used for next reaction without further purification.

LC-MS (ESI) *m/z* = 241 $[M+H]^+$.

Step 3: Benzyl 3-fluoro-4-(1,5-thiazocan-5-yl)phenylcarbamate (10):



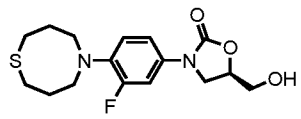
10

Benzyl carbonochloridate (1.76 g, 10.4 mmol) was added to a suspension of 3-fluoro-4-(1,5-thiazocan-5-yl)benzenamine (9) (1.2 g, 5.2 mmol) and triethylamine (1.05 g, 10.4 mmol) in DCM (200 mL) at -20 °C under a nitrogen gas atmosphere, then reaction mixture was stirred at 0 °C for 30 min, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 10: 1) to afford benzyl 3-fluoro-4-(1,5-thiazocan-5-yl)phenylcarbamate (10) (740 mg, 38%) as a white solid.

LC-MS (ESI) *m/z* = 375 $[M+H]^+$.

Step 4:

(*R*)-3-(3-Fluoro-4-(1,5-thiazocan-5-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one (11):



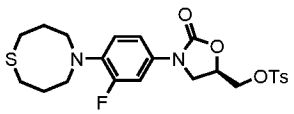
11

To a solution of benzyl 3-fluoro-4-(1,5-thiazocan-5-yl)phenylcarbamate (10) (740 mg, 1.97 mmol) in THF (10 mL) at – 78 °C under a nitrogen gas atmosphere was added n-BuLi (1.3 ml, 2.96 mmol), then the mixture was stirred at -78°C for 30 min, after that the solution of (*R*)-oxiran-2-ylmethyl butyrate (427 mg, 2.96 mmol) in THF was added to the mixture at -78 °C, then warmed to room temperature and stirred for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 70: 1) to afford

(*R*)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one (11) (382 mg, 57%) as a white solid.

LC-MS (ESI) *m/z* = 341 $[M+H]^+$.

Step 5: (*R*)-(3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (12):

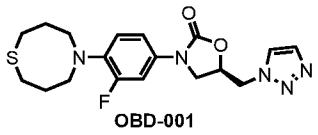


12

4-methylbenzene-1-sulfonyl chloride (418 mg, 2.2 mmol) was added to a suspension of (*R*)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one (11) (382 mg, 1.1 mmol) and Et_3N (222 mg, 2.2 mmol) in DCM (10 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford (*R*)-(3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (12) (407 mg, 75%) as a white solid.

LC-MS (ESI) *m/z* = 495 $[M+H]^+$.

Step 6: (*R*)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (OBD-001):



OBD-001

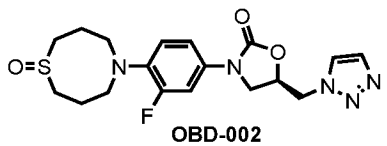
To a solution of

(*R*)-(3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (12) (200 mg, 0.4 mmol) and 1H-1,2,3-triazole (56 mg, 0.8 mmol) in DMF (5 mL) was added K_2CO_3 (110 mg, 0.8 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 2 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 2: 1) to afford (*R*)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxaz olidin-2-one (OBD-001) (70 mg, 45%) as a white solid.

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.76 (d, J = 17.6 Hz, 2H), 7.41 – 7.09 (m, 1H), 7.11 – 6.73 (m, 2H), 5.04 (d, J = 3.0 Hz, 1H), 4.78 (d, J = 3.4 Hz, 2H), 4.12 (t, J = 9.2 Hz, 1H), 3.88 (dd, J = 9.2, 6.1 Hz, 1H), 3.36 (t, J = 6.0 Hz, 3H), 2.92 – 2.59 (m, 4H), 2.01 (dd, J = 27.9, 7.3 Hz, 4H).

LC-MS (ESI) *m/z* = 391.9 $[M+H]^+$.

Step 7: Preparation of (OBD-002):



OBD-002

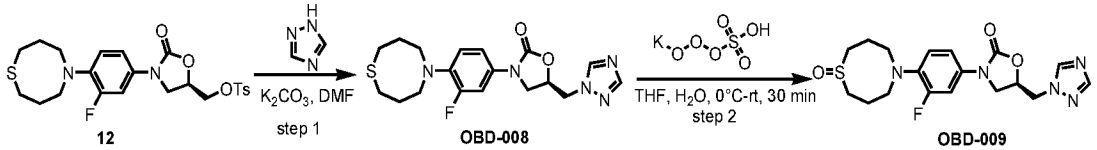
To a solution of

(*R*)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxaz olidin-2-one (OBD-001) (50 mg, 0.13 mmol) in THF (10 mL) and 10 drops water was added potassium peroxomonosulfate (80 mg, 0.13 mmol) at 0 °C, then the reaction mixture was stirred at 0 °C for 2 h, monitored by TLC. Quenched with sodium thiosulfate, and the crude material was purified by silica gel column

chromatography (DCM: MeOH = 80: 1) to afford (OBD-002) (22 mg, 41%) as a white solid.

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.92 – 7.67 (m, 2H), 7.32 (d, J = 16.8 Hz, 1H), 7.12 (t, J = 9.0 Hz, 1H), 6.96 (d, J = 8.1 Hz, 1H), 5.07 (s, 1H), 4.81 (d, J = 4.0 Hz, 2H), 4.15 (t, J = 9.0 Hz, 1H), 4.01 – 3.83 (m, 1H), 3.32 (d, J = 14.2 Hz, 5H), 3.11 – 2.87 (m, 2H), 2.59 (s, 2H), 2.19 (s, 4H).

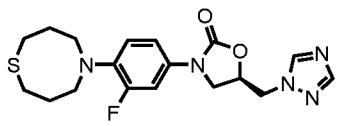
LC-MS (ESI) *m/z* = 407.8 $[M+H]^+$.



12 OBD-008 OBD-009

Step 1:

(*R*)-5-((1H-1,2,4-triazol-1-yl)methyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (OBD-008):



OBD-008

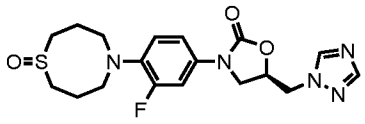
To a solution of (*R*)-(3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (12) (200 mg, 0.4 mmol) and 1H-1,2,4-triazole (56 mg, 0.8 mmol) in DMF (5 mL) was added K_2CO_3 (110 mg, 0.8 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 2 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 2: 1) to afford (*R*)-5-((1H-1,2,4-triazol-1-yl)methyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (OBD-008) (84 mg, 54%) as a white solid.

^{1}H NMR (301 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.97 (s, 1H), 7.00 (s, 2H), 5.12 – 4.91

(m, 1H), 4.56 (d, J = 4.7 Hz, 2H), 4.24 – 3.83 (m, 2H), 3.38 (t, J = 6.0 Hz, 4H), 2.95 – 2.59 (m, 4H), 1.98 (s, 5H).

LC-MS (ESI) *m/z* = 391.9 $[M+H]^+$.

Step 2: Preparation of (OBD-009):

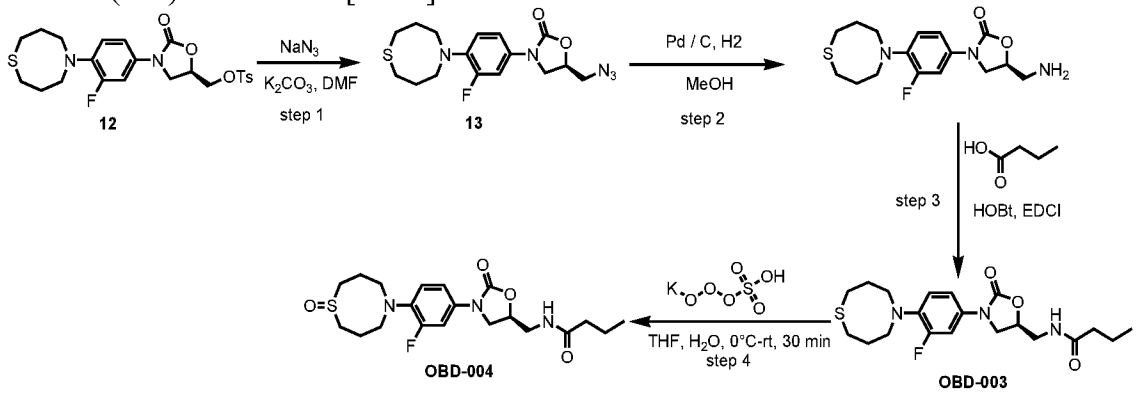


OBD-009

To a solution of (*R*)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (OBD-008) (50 mg, 0.13 mmol) in THF (10 mL) and 10 drops water was added potassium peroxomonosulfate (80 mg, 0.13 mmol) at 0 °C, then the reaction mixture was stirred at 0 °C for 2 h, monitored by TLC. Quenched with sodium thiosulfate, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 80: 1) to afford (OBD-009) (22 mg, 41%) as a white solid.

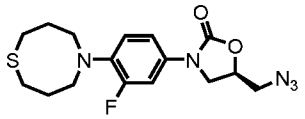
^{1}H NMR (301 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.93 (s, 1H), 7.41 – 7.20 (m, 1H), 7.19 – 6.92 (m, 2H), 5.10 – 4.92 (m, 1H), 4.56 (d, J = 4.7 Hz, 2H), 4.12 (t, J = 9.0 Hz, 1H), 3.97 (dd, J = 9.2, 6.2 Hz, 1H), 3.28 (dd, J = 13.0, 6.9 Hz, 2H), 3.12 (dd, J = 12.5, 5.9 Hz, 4H), 3.02 – 2.83 (m, 2H), 2.22 – 1.99 (m, 5H), 1.26 (d, J = 9.4 Hz, 4H).

LC-MS (ESI) *m/z* = 407.8 $[M+H]^+$.



Step 1:

(*R*)-5-(azidomethyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (13):



13

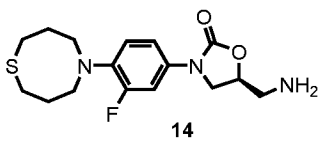
To a solution of

(*R*)-(3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (12) (800 mg, 1.62 mmol) and sodium azide (105 mg, 1.62 mmol) in DMF (10 mL) was added K_2CO_3 (447 g, 3.24 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 1 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (PE: EA = 2: 1) to afford (*R*)-5-(azidomethyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (13) (470 mg, 80%) as a white solid.

LC-MS (ESI) *m/z* = 366 $[M+H]^+$.

Step 2:

(*S*)-5-(aminomethyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (14):



14

To a solution of

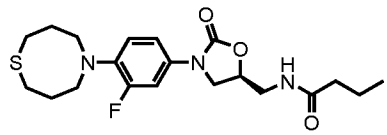
(*R*)-5-(azidomethyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (13) (470 mg, 1.3 mmol) in MeOH (10 mL) was added palladium carbon (100 mg) at 25°C, then the reaction mixture was stirred at room temperature for overnight under a hydrogen gas atmosphere, monitored by TLC. The filtrate was concentrated under

reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford (*S*)-5-(aminomethyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (14) (374 mg, 85%) as a white solid.

LC-MS (ESI) $m/z = 340$ $[M+H]^+$.

Step 3:

(*S*)-N-((3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-005):



OBD-003

To a solution of

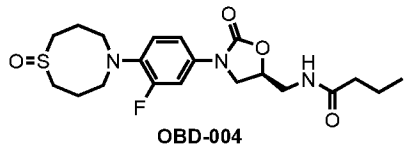
(*S*)-5-(aminomethyl)-3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (14) (374 mg, 1.1 mmol) and butyric acid (97 mg, 1.1 mmol) in DCM (10 mL) were added HOBt (223 mg, 1.65 mmol), EDCI (420 mg, 2.2 mmol) and DIPEA (284 mg, 2.2 mmol) at 25 °C, then the reaction mixture was stirred at 25 °C for 2 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 80: 1) to afford

(*S*)-N-((3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-003) (252 mg, 56%) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (s, 2H), 7.03 (d, J = 6.1 Hz, 1H), 5.99 (s, 1H), 4.77 (d, J = 5.7 Hz, 1H), 4.02 (t, J = 9.0 Hz, 2H), 3.70 (ddd, J = 20.7, 15.2, 7.7 Hz, 4H), 3.48 (s, 4H), 2.95 – 2.68 (m, 4H), 2.20 (t, J = 7.2 Hz, 3H), 2.06 (d, J = 6.1 Hz, 4H), 1.64 (dd, J = 14.8, 7.4 Hz, 4H), 0.91 (t, J = 7.4 Hz, 4H).

LC-MS (ESI) $m/z = 409.9$ $[M+H]^+$.

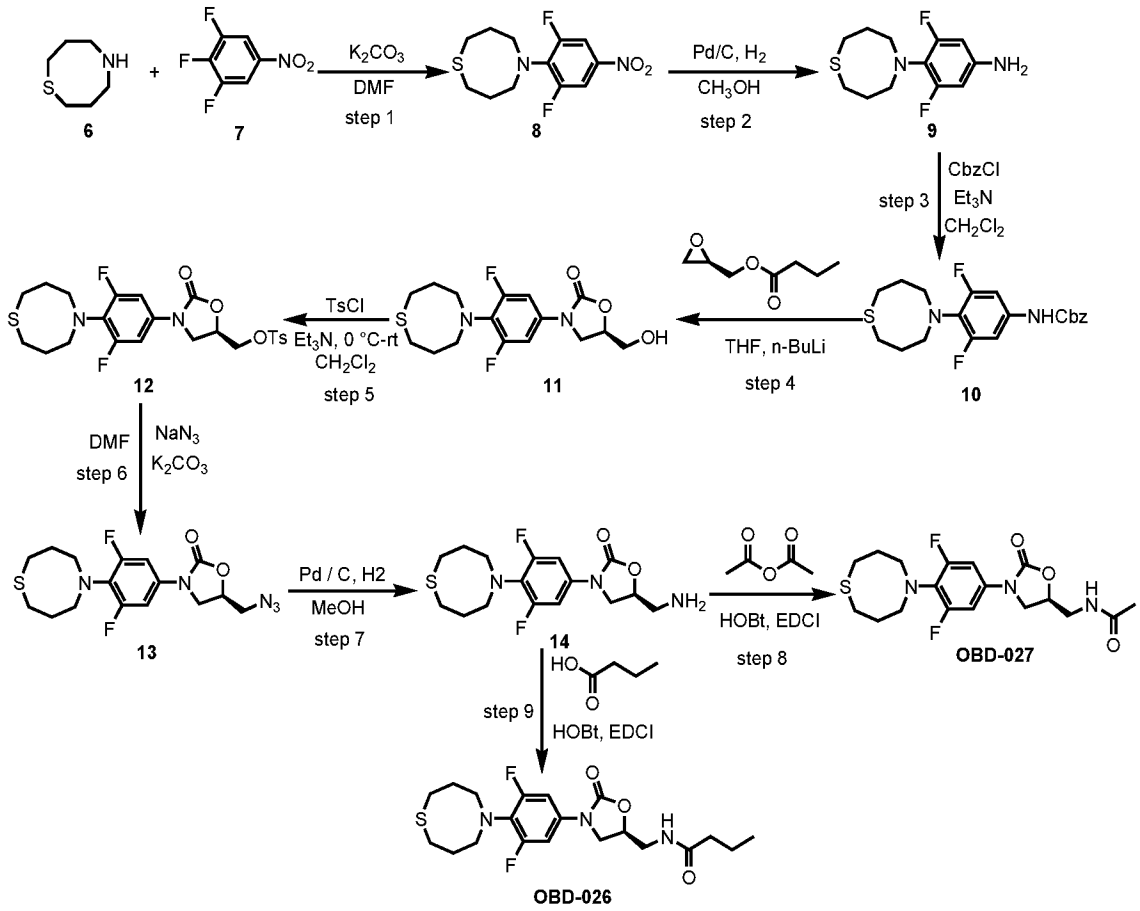
Step 4: Preparation of (OBD-004):



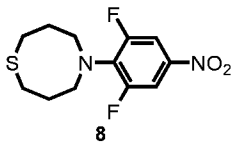
OBD-004

To a solution of (*S*)-N-((3-(3-fluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-003) (150 mg, 0.37 mmol) in THF (10 mL) and 10 drops water was added potassium peroxomonosulfate (225 mg, 0.37 mmol) at 0 °C, then the reaction mixture was stirred at 0 °C for 2 h, monitored by TLC. Quenched with sodium thiosulfate, and the crude material was purified by prep-HPLC to afford (OBD-004) (48 mg, 31%) as a white solid.

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.44 (dd, J = 14.7, 2.4 Hz, 1H), 7.19 – 6.99 (m, 2H), 6.44 (s, 1H), 4.84 – 4.71 (m, 1H), 4.02 (t, J = 8.9 Hz, 1H), 3.78 (dd, J = 9.0, 6.6 Hz, 1H), 3.66 (t, J = 4.6 Hz, 2H), 3.38 – 3.09 (m, 6H), 2.99 (dd, J = 12.6, 6.3 Hz, 2H), 2.20 (dd, J = 9.4, 5.3 Hz, 6H), 1.71 – 1.56 (m, 2H), 0.91 (dd, J = 9.6, 5.1 Hz, 3H).
LC-MS (ESI) *m/z* = 425.8 $[M+H]^+$.

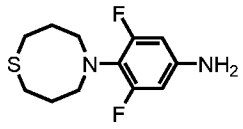


Step 1: Preparation of 5-(2,6-difluoro-4-nitrophenyl)-1,5-thiazocane (8):



To a solution of 1,5-thiazocane (6) (1 g, 7.6 mmol) and 1,2,3-trifluoro-5-nitrobenzene (1.35 g, 7.6 mmol) in DMF (10 mL) was added K_2CO_3 (2.1 g, 15.2 mmol) at 25°C then the reaction mixture was stirred at 80°C for 2 h under a nitrogen gas atmosphere, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 3: 1) to afford 5-(2,6-difluoro-4-nitrophenyl)-1,5-thiazocane (8) (1.64 g, 75%) as a yellow solid. LC-MS (ESI) *m/z* = 289 $[M+H]^+$.

Step 2: 3,5-Difluoro-4-(1,5-thiazocan-5-yl)benzenamine (9):

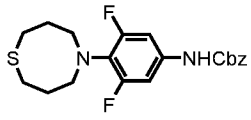


9

To a solution of 5-(2,6-difluoro-4-nitrophenyl)-1,5-thiazocane (8) (1.64 g, 5.7 mmol) and Palladium carbon (200 mg) in MeOH (15 mL), then under a hydrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. The filtrate was concentrated under reduced pressure to afford 3,5-difluoro-4-(1,5-thiazocan-5-yl)benzenamine (9) (1.4 g, 94%) as a white oil, and the crude material was used for next reaction without further purification.

LC-MS (ESI) m/z = 259 $[M+H]^+$.

Step 3: Benzyl 3,5-difluoro-4-(1,5-thiazocan-5-yl)phenylcarbamate (10):



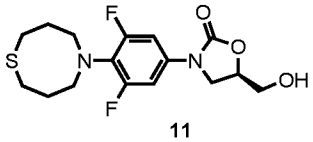
10

Benzyl carbonochloridate (1.87 g, 10.6 mmol) was added to a suspension of 3,5-difluoro-4-(1,5-thiazocan-5-yl)benzenamine (9) (1.4 g, 5.3 mmol) and triethylamine (1.07 g, 10.6 mmol) in DCM (200 mL) at -20 °C under a nitrogen gas atmosphere, then reaction mixture was stirred at 0 °C for 30 min, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 10: 1) to afford benzyl 3,5-difluoro-4-(1,5-thiazocan-5-yl)phenylcarbamate (10) (872 mg, 42%) as a white solid.

LC-MS (ESI) m/z = 393 $[M+H]^+$.

Step 4:

(*R*)-3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one (11):



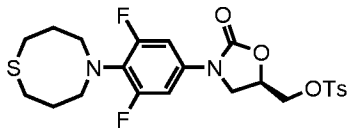
11

To a solution of benzyl 3,5-difluoro-4-(1,5-thiazocan-5-yl)phenylcarbamate (10) (872 mg, 2.23 mmol) in THF (10 mL) at – 78 °C under a nitrogen gas atmosphere was added n-BuLi (1.4 ml, 3.34 mmol), then the mixture was stirred at -78°C for 30 min, after that the solution of (*R*)-oxiran-2-ylmethyl butyrate (480 mg, 3.34 mmol) in THF was added to the mixture at -78°C, then warmed to room temperature and stirred for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 70: 1) to afford (*R*)-3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one (11) (519 mg, 65%) as a white solid.

LC-MS (ESI) *m/z* = 359 $[M+H]^+$.

Step 5:

(*R*)-(3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (12):



12

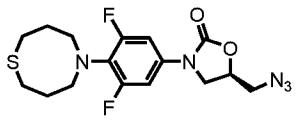
4-methylbenzene-1-sulfonyl chloride (550 mg, 2.9 mmol) was added to a suspension of

(*R*)-3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one (11) (519 mg, 1.45 mmol) and Et_3N (292 mg, 2.9 mmol) in DCM (10 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford (*R*)-(3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (12) (594 mg, 80%) as a white solid.

LC-MS (ESI) *m/z* = 513 $[M+H]^+$.

Step 6:

(*R*)-5-(azidomethyl)-3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (13):



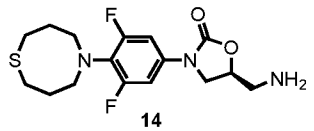
13

To a solution of (*R*)-(3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (12) (594 g, 1.2 mmol) and sodium azide (75 mg, 1.2 mmol) in DMF (10 mL) was added K_2CO_3 (160 mg, 2.4 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 1 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (PE: EA = 2: 1) to afford (*R*)-5-(azidomethyl)-3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (13) (400 mg, 87%) as a white solid.

LC-MS (ESI) m/z = 384 $[M+H]^+$.

Step 7:

(*S*)-5-(aminomethyl)-3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (14):



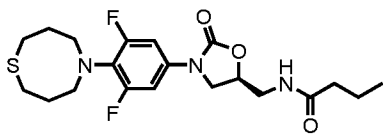
14

To a solution of (*R*)-5-(azidomethyl)-3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (13) (400 g, 1.04 mmol) in MeOH (10 mL) was added palladium carbon (100 mg) at 25°C, then the reaction mixture was stirred at room temperature for overnight under a hydrogen gas atmosphere, monitored by TLC. The filtrate was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford (*S*)-5-(aminomethyl)-3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (14) (331 g, 89 %) as a white solid.

LC-MS (ESI) m/z = 358 $[M+H]^+$.

Step 8:

(*S*)-N-((3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl) butyramide (OBD-026):



OBD-026

To a solution of (*S*)-5-(aminomethyl)-3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (14) (165 mg, 0.46 mmol) and butyric acid (52 mg, 0.46 mmol) in DCM (10 mL) were added HOBt (95 mg, 0.7 mmol), EDCI (175 mg, 0.92 mmol) and DIPEA (118

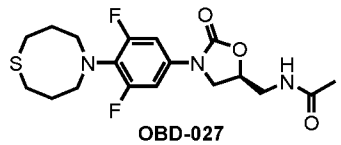
mg, 0.92 mmol) at 25 °C, then the reaction mixture was stirred at 25 °C for 2 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 80: 1) to afford (*S*)-N-((3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)-2-oxooxazolidin-5-yl)methyl) butyramide (OBD-026) (82 mg, 42%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.14 (d, *J* = 11.1 Hz, 1H), 5.93 (s, 1H), 4.81 (s, 1H), 4.02 (t, *J* = 8.9 Hz, 1H), 3.70 (s, 2H), 3.31 (s, 3H), 2.87 (s, 2H), 2.22 (s, 2H), 1.90 (s, 5H), 1.66 (d, *J* = 7.3 Hz, 2H), 0.93 (t, *J* = 7.4 Hz, 2H).

LC-MS (ESI) m/z = 428 $[M+H]^+$.

Step 9:

N-(((S)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-027):



OBD-027

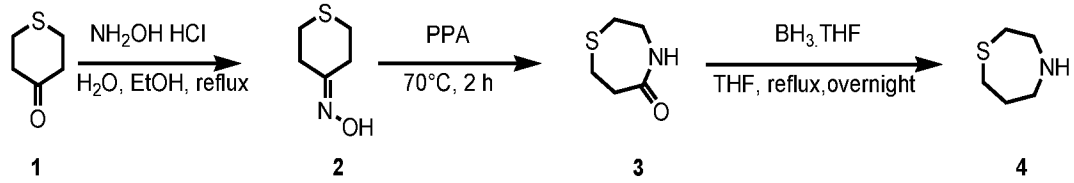
To a solution of (*S*)-5-(aminomethyl)-3-(3,5-difluoro-4-(1,5-thiazocan-5-yl)phenyl)oxazolidin-2-one (14) (165 mg, 0.46 mmol) and butyric acid (52 mg, 0.46 mmol) in DCM (10 mL) were added HOBt (95 mg, 0.7 mmol), EDCI (175 mg, 0.92 mmol) and DIPEA (118 mg, 0.92 mmol) at 25 °C, then the reaction mixture was stirred at 25 °C for 2 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 80: 1) to afford

N-(((*S*)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-027) (82 mg, 45%) as a white solid.

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.23 – 6.85 (m, 2H), 6.00 (s, 1H), 4.90 – 4.66 (m, 1H), 4.17 – 3.86 (m, 1H), 3.71 (s, 2H), 3.28 (s, 2H), 2.84 (s, 3H), 2.04 (s, 3H), 1.88 (s, 5H).

LC-MS (ESI) m/z = 400 $[M+H]^+$.

The synthesis route:



Experimental

Tetrahydrothiopyran-4-one oxime (2).

To a solution of tetrahydrothiopyran-4-one (20 g, 172 mmol) in EtOH (150 mL) and H_2O (50 mL) was added with NH_2OH-HCl (11.9 g, 172 mmol), then the reaction mixture was stirred at 75 °C for 4 h under a nitrogen gas atmosphere, then mixture was concentrated and dried to give tetrahydrothiopyran-4-one oxime (2) (14.7 g, 66%) as brown solid.

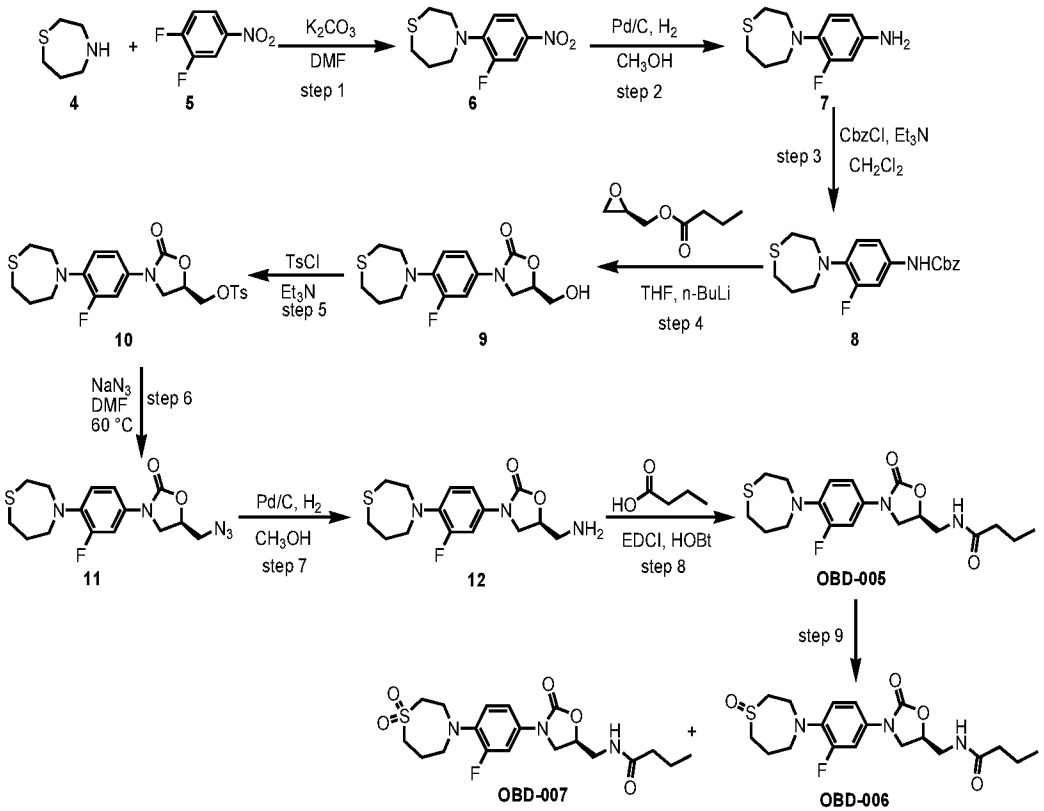
1,4-Thiazepan-5-one (3).

A mixture of tetrahydrothiopyran-4-one oxime (2) (14.7 g, 112 mmol) and polyphosphoric acid (50 g) was stirred at 70 °C for 2 h. The reaction mixture was cooled to room temperature and poured into ice water, adjusted pH = 8 using potassium carbonate solution, extracted with EA, the organic layer was concentrated under reduced pressure to afford 1,4-thiazepan-5-one (3) (11.9 g crude, 81%) as brown solid.

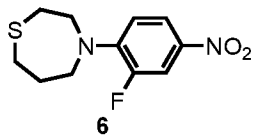
1,4-Thiazepane (4).

To a solution of 1,4-thiazepan-5-one (3) (11.9 g, 105 mmol) in THF (100 mL) was added BH_3(158 mL, 158 mol) in THF at 0 °C, followed by refluxing for 12 h. The reaction was quenched with CH_3OH (50 mL). The solvent was evaporated to afford 1,4-thiazepane (4) as a white oil (10.7 g, 87%), and the crude material was used for next reaction without further purification.

LC-MS (ESI) m/z = 118 $[M+H]^+$.



Step 1: Preparation of 4-(2-fluoro-4-nitrophenyl)-1,4-thiazepane (6):

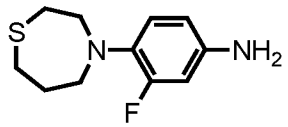


To a solution of 1,4-thiazepane (4) (7 g, 59.8 mmol) and 1,2-difluoro-4-nitrobenzene (10.4 g, 65.8 mmol) in DMF (10 mL) was added K_2CO_3 (16.5 g, 119.6 mmol) at

25°C and then reaction mixture was stirred at 80°C for 2 h under a nitrogen gas atmosphere, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 3: 1) to afford 4-(2-fluoro-4-nitrophenyl)-1,4-thiazepane (6) (10 g, 65%) as a yellow solid.

LC-MS (ESI) m/z = 257 $[M+H]^+$.

Step 2: 3-Fluoro-4-(1,4-thiazepan-4-yl)benzenamine (7):

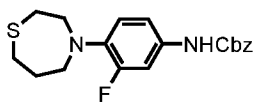


7

To a solution of 4-(2-fluoro-4-nitrophenyl)-1,4-thiazepane (6) (8 g, 31.2 mmol) and Palladium carbon (500 mg) in MeOH (15 mL), then the reaction mixture was stirred at room temperature for overnight under a hydrogen gas atmosphere, monitored by TLC. The filtrate was concentrated under reduced pressure to afford 3-fluoro-4-(1,4-thiazepan-4-yl)benzenamine (7) (6.4 g, 93%) as a white oil, and the crude material was used for next reaction without further purification.

LC-MS (ESI) m/z = 227 $[M+H]^+$.

Step 3: Benzyl 3-fluoro-4-(1,4-thiazepan-4-yl)phenylcarbamate (8):



8

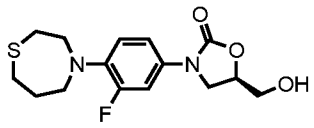
Benzyl carbonochloridate (9.6 g, 56.6 mmol) was added to a suspension of 3-fluoro-4-(1,4-thiazepan-4-yl)benzenamine (7) (6.4 g, 28.3 mmol) and triethylamine (5.7 g, 56.6 mmol) in DCM (200 mL) at -20 °C under a nitrogen gas atmosphere, then reaction mixture was stirred at 0 °C for 30 min, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was

concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 10: 1) to afford benzyl 3-fluoro-4-(1,4-thiazepan-4-yl)phenylcarbamate (8) (2.34 g, 23%) as a white oil.

LC-MS (ESI) m/z = 361 $[M+H]^+$.

Step 4:

(*R*)-3-(3-Fluoro-4-(1,4-thiazepan-4-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one (9):

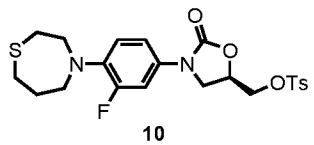


9

To a solution of benzyl 3-fluoro-4-(1,4-thiazepan-4-yl)phenylcarbamate (8) (2.34 g, 6.5 mmol) in THF (10 mL) at – 78 °C under a nitrogen gas atmosphere was added n-BuLi (4 ml, 9.7 mmol), then the mixture was stirred at -78°C for 30 min, after that the solution of (R)-oxiran-2-ylmethyl butyrate (1.4 g, 9.7 mmol) in THF was added to the mixture at -78°C, then warmed to room temperature and stirred for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 70: 1) to afford (*R*)-3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one (9) (1.16 g, 55%) as a white solid.

LC-MS (ESI) m/z = 327 $[M+H]^+$.

Step 5: (*R*)-(3-(3-Fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (10):



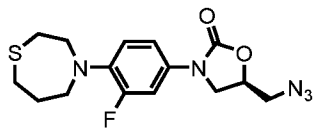
10

4-Methylbenzene-1-sulfonyl chloride (1.4 g, 7.2 mmol) was added to a suspension of (*R*)-3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)-5-(hydroxymethyl)oxazolidin-2-one (9) (1.16 g, 3.6 mmol) and Et_3N (727 mg, 7.2 mmol) in DCM (10 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford (*R*)-(3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (10) (1.41 g, 41%) as a white solid.

LC-MS (ESI) *m/z* = 481 $[M+H]^+$.

Step 1:

(*R*)-5-(azidomethyl)-3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)oxazolidin-2-one (11):



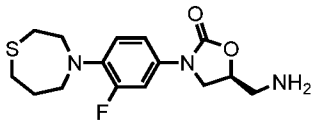
11

To a solution of (*R*)-(3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (10) (1.41 g, 2.95 mmol) and sodium azide (190 mg, 2.95 mmol) in DMF (10 mL) was added K_2CO_3 (814 g, 5.9 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 1 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (PE: EA = 2: 1) to afford (*R*)-5-(azidomethyl)-3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)oxazolidin-2-one (11) (830 mg, 80%) as a white solid.

LC-MS (ESI) m/z = 352 $[M+H]^+$.

Step 2:

(*S*)-5-(aminomethyl)-3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)oxazolidin-2-one (12):



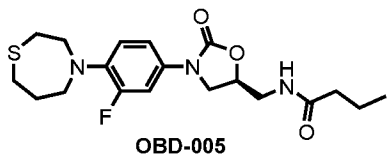
12

To a solution of (*R*)-5-(azidomethyl)-3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)oxazolidin-2-one (11) (830 mg, 2.4 mmol) in MeOH (10 mL) was added palladium carbon (100 mg) at 25°C, then the reaction mixture was stirred at room temperature for overnight under a hydrogen gas atmosphere, monitored by TLC. The filtrate was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford (*S*)-5-(aminomethyl)-3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)oxazolidin-2-one (12) (654 mg, 85%) as a white solid.

LC-MS (ESI) m/z = 326 $[M+H]^+$.

Step 3:

(*S*)-N-((3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-005):



OBD-005

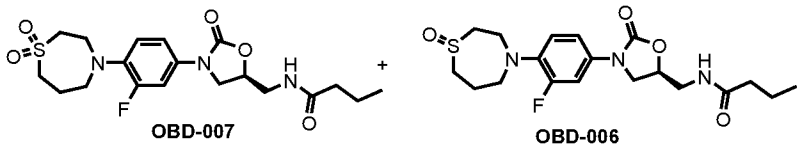
To a solution of (*S*)-5-(aminomethyl)-3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)oxazolidin-2-one (12) (654 mg, 2 mmol) and butyric acid (177 mg, 2 mmol) in DCM (10 mL) were added

HOBt (405 mg, 3 mmol), EDCI (764 mg, 4 mmol) and DIPEA (516 mg, 4 mmol) at 25 °C, then the reaction mixture was stirred at 25 °C for 2 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 80: 1) to afford (*S*)-N-((3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-005) (286 mg, 34%) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.23 (m, 2H), 7.01 (dd, J = 8.9, 2.3 Hz, 1H), 6.04 (s, 1H), 4.75 (ddd, J = 9.0, 7.9, 4.6 Hz, 1H), 4.00 (t, J = 9.0 Hz, 1H), 3.79 – 3.05 (m, 7H), 2.91 (dd, J = 16.2, 10.1 Hz, 2H), 2.70 (t, J = 6.3 Hz, 2H), 2.28 – 2.13 (m, 2H), 2.13 – 1.97 (m, 2H), 1.82 – 1.25 (m, 3H), 0.92 (t, J = 7.4 Hz, 3H), 0.01 (s, 1H).

LC-MS (ESI) *m/z* = 395.9 $[M+H]^+$.

Step 4: Preparation of (OBD-006 and OBD-007):



To a solution of (*S*)-N-((3-(3-fluoro-4-(1,4-thiazepan-4-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-005) (150 mg, 0.38 mmol) in THF (10 mL) and 10 drops water was added potassium peroxomonosulfate (233 mg, 0.38 mmol) at 0 °C, then the reaction mixture was stirred at 0 °C for 2 h, monitored by TLC. Quenched with sodium thiosulfate, and the crude material was purified by prep-HPLC to afford (OBD-006) (50 mg, 32%) as a white solid and (OBD-007) (24 mg, 15%) as a white solid.

(OBD-006)

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.52 (d, J = 15.0 Hz, 1H), 7.16 (s, 1H), 7.03 (d, J = 8.7 Hz, 1H), 5.99 (s, 1H), 4.78 (s, 1H), 4.02 (t, J = 8.8 Hz, 2H), 3.88 – 3.56 (m, 3H), 3.55 – 2.92 (m, 7H), 2.77 (s, 1H), 2.20 (t, J = 7.1 Hz, 3H), 1.64 (dd, J = 14.9, 7.4 Hz, 2H), 0.91 (t, J = 7.4 Hz, 3H).

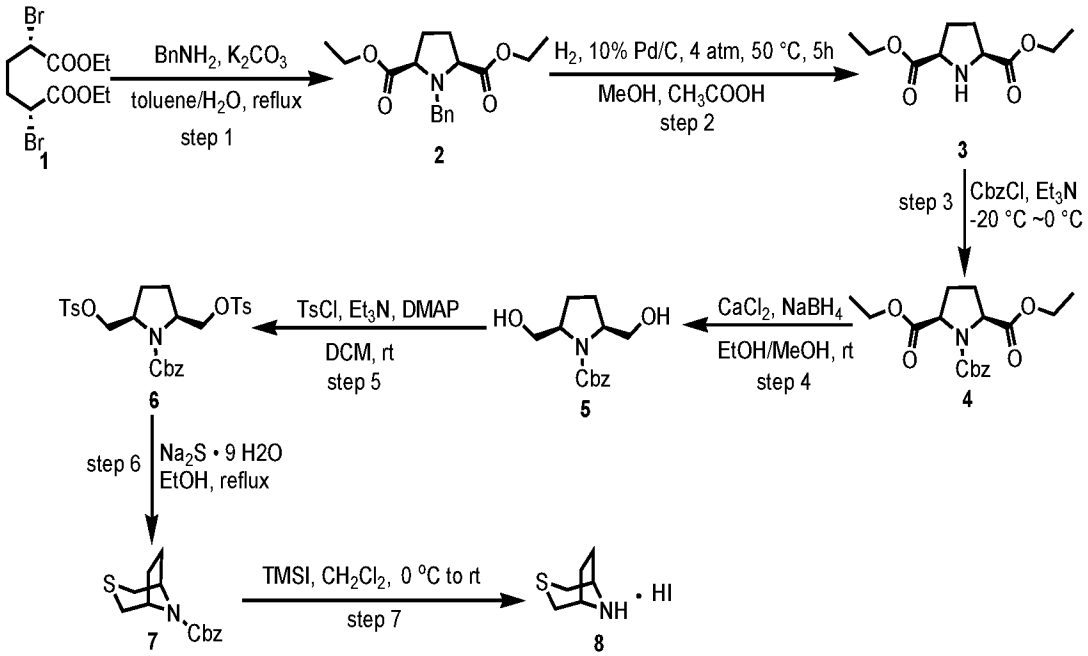
LC-MS (ESI) *m/z* = 411.8 $[M+H]^+$.

(OBD-007)

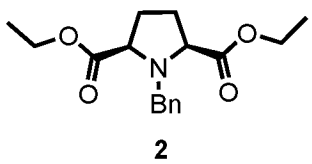
^{1}H NMR (301 MHz, $CDCl_3$) δ 7.51 (d, J = 14.7 Hz, 1H), 7.10 (d, J = 9.9 Hz, 2H), 5.92 (s, 1H), 4.78 (s, 1H), 4.03 (t, J = 9.0 Hz, 1H), 3.87 – 3.39 (m, 7H), 3.27 (d, J = 5.7 Hz, 2H), 2.39 (d, J = 6.2 Hz, 2H), 2.20 (t, J = 7.2 Hz, 2H), 1.64 (dd, J = 14.8, 7.4 Hz, 2H), 0.92 (t, J = 7.3 Hz, 3H).

LC-MS (ESI) *m/z* = 427.8 $[M+H]^+$.

Procedures for preparation of R:



Step 1: Preparation of (2*S*,5*R*)-diethyl 1-benzylpyrrolidine-2,5-dicarboxylate (2):

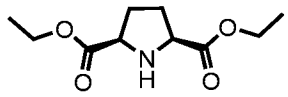


2

The mixture of (2*R*,5*S*)-diethyl 2,5-dibromohexanedioate (1) (100 g, 278 mmol), $BnNH_2$ (44.6 g, 416 mmol) and K_2CO_3 (76.84 g, 556 mmol) in toluene/H_2O was stirred at 110°C for overnight, monitored by TLC. The mixture was extracted with EtOAc, washed with water and brine and then dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford (2*S*,5*R*)-diethyl 1-benzylpyrrolidine-2,5-dicarboxylate (2) (63.75 g, 75%) as a white oil.

LC-MS (ESI) *m/z* = 306 $[M+H]^+$.

Step 2: (2*S*,5*R*)-diethyl pyrrolidine-2,5-dicarboxylate (3):

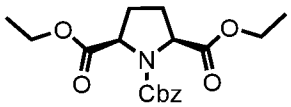


3

To a solution of (2*S*,5*R*)-diethyl 1-benzylpyrrolidine-2,5-dicarboxylate (2) (63.75 g, 209 mmol) and Palladium carbon (2 g) in MeOH (15 mL) was added CH_3COOH (5 mL), then the reaction mixture was stirred at 50°C under a hydrogen gas atmosphere, 4atm for 5 h, monitored by TLC. The filter was concentrated under reduced pressure, and the crude material was used for next reaction without further purification.

LC-MS (ESI) *m/z* = 216 $[M+H]^+$.

Step 3: (2*S*,5*R*)-1-benzyl 2,5-diethyl pyrrolidine-1,2,5-tricarboxylate (4):



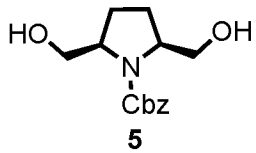
4

To a solution of (2*S*,5*R*)-diethyl pyrrolidine-2,5-dicarboxylate (3) (62 g, 288 mmol) and Et_3N (58 g, 577 mmol) in DCM (100 mL) was added benzyl carbonochloridate (98 g, 577 mmol) at -20 °C under a nitrogen gas atmosphere, then the reaction mixture was stirred at rt for 5 h, monitored by TLC. The mixture was extracted with DCM, washed with water and brine and then dried over anhydrous sodium sulfate,

filtered, and concentrated under reduced pressure to afford (2*S*,5*R*)-1-benzyl 2,5-diethyl pyrrolidine-1,2,5-tricarboxylate (4) (80 g, 80%) as a white oil.

LC-MS (ESI) *m/z* = 350 $[M+H]^+$.

Step 4: (2*S*,5*R*)-benzyl 2,5-bis(hydroxymethyl)pyrrolidine-1-carboxylate (5):

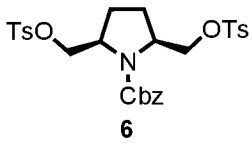


5

$CaCl_2$ (76 g, 688 mmol) and $NaBH_4$ (43 g, 1146 mmol) were added to a stirred solution of (2*S*,5*R*)-1-benzyl 2,5-diethyl pyrrolidine-1,2,5-tricarboxylate (4) (80 g, 229 mmol) in EtOH-MeOH (9:1; 200 mL) at rt under a nitrogen gas atmosphere, then the reaction mixture was stirred for 5 h, monitored by TLC. H_2O (5 mL) was added, and the mixture was stirred tor a turther 15 min. The mixture was then concentrated in vacuo. The mixture was extracted with EtOAc, then dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford (2*S*,5*R*)-benzyl 2,5-bis(hydroxymethyl)pyrrolidine-1-carboxylate (5) (32 g, 52%) as a white oil.

LC-MS (ESI) *m/z* = 266 $[M+H]^+$.

Step 5: (2*S*,5*R*)-benzyl 2,5-bis(tosyloxymethyl)pyrrolidine-1-carboxylate (6):



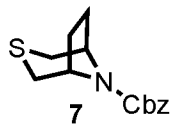
6

4-methylbenzene-1-sulfonyl chloride (92 g, 483 mmol) was added to a stirred solution of (2S,5R)-benzyl 2,5-bis(hydroxymethyl)pyrrolidine-1-carboxylate (5) (32 g, 121 mmol) and Et_3N in DCM(200 mL) at 0 °C under a nitrogen gas atmosphere, then the reaction mixture was allowed to warm to room temperature and stirred for 5 h, monitored by TLC. The mixture was extracted with DCM, then dried over

anhydrous sodium sulfate, filtered, and concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 2: 1) to afford (2*S*,5*R*)-benzyl 2,5-bis(tosyloxymethyl)pyrrolidine-1-carboxylate (6) (30 g, 43%) as a white solid.

LC-MS (ESI) *m/z* = 574 $[M+H]^+$.

Step 6: 8-benzyl-3-thia-8-aza-bicyclo[3.2.1]octane-1-carboxylate (7):

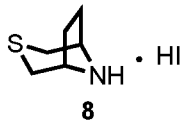


7

Sodium sulfide hydrate (38 g, 157 mmol) was added to a stirred solution of (2*S*,5*R*)-benzyl 2,5-bis(tosyloxymethyl)pyrrolidine-1-carboxylate (6) (30 g, 50 mmol) in EtOH (50 mL) and water (50 mL) at room temperature, then the reaction mixture was stirred at 90 °C for 2 h, monitored by TLC. The mixture was extracted with DCM, then dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 10: 1) to afford 8-benzyl-3-thia-8-aza-bicyclo[3.2.1]octane-1-carboxylate (7) (10 g, 73%) as a white solid.

LC-MS (ESI) *m/z* = 264 $[M+H]^+$.

Step 7: 3-thia-8-aza-bicyclo[3.2.1]octane hydrogen iodide (8):

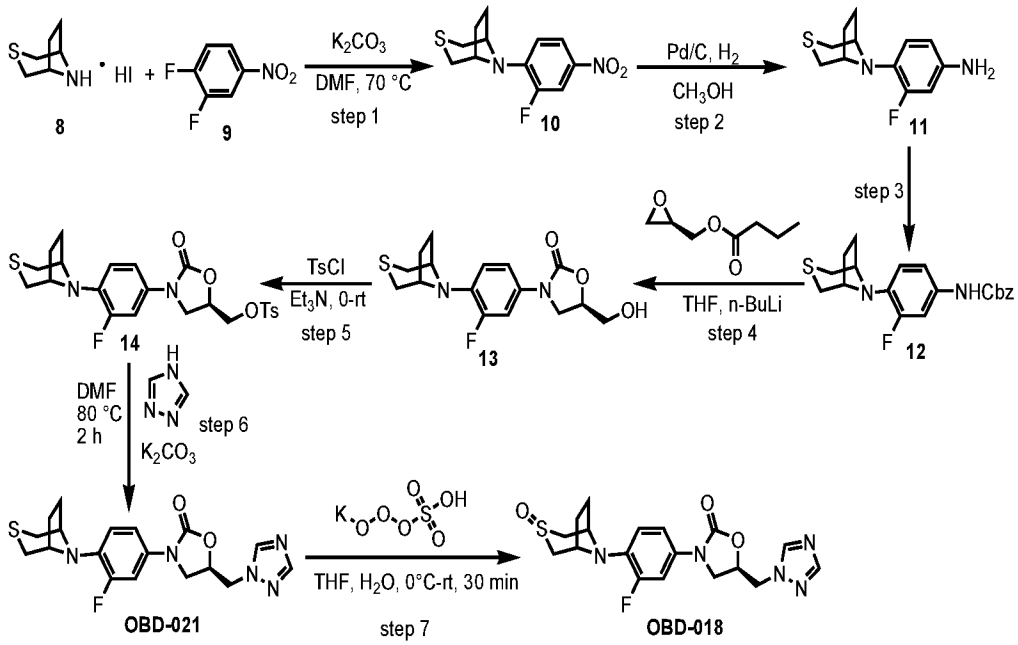


8

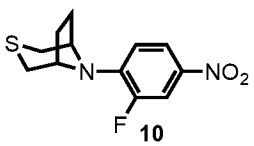
Iodotrimethylsilane (15 g, 75 mmol) was added to a stirred solution of 8-benzyl-3-thia-8-aza-bicyclo[3.2.1]octane-1-carboxylate (7) (10 g, 38 mmol) in DCM (200 mL) at 0 °C under a nitrogen gas atmosphere, then the reaction mixture was allowed to warm to room temperature and stirred for 30 min, monitored by TLC.

The mixture was extracted with DCM, then dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 15: 1) to afford 3-thia-8-aza-bicyclo[3.2.1]octane hydrogen iodide (8) (8.13 g, 84%) as a brown solid.

LC-MS (ESI) m/z = 130 $[M+H]^+$



Step 1: Preparation of 8-(2-fluoro-4-nitrophenyl)-3-thia-8-aza-bicyclo[3.2.1]octane (10):

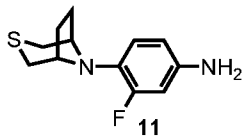


To a solution of 3-thia-8-aza-bicyclo[3.2.1]octane hydrogen iodide (8) (5.58 g, 21.7 mmol) and 1,2-difluoro-4-nitrobenzene (3.8 g, 23.8 mmol) in DMF (10 mL) was added K_2CO_3 (6 g, 43.4 mmol) at 25°C under a nitrogen gas atmosphere and the reaction mixture was stirred at 80°C for 2 h, monitored by TLC. The mixture was

concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 3: 1) to afford 8-(2-fluoro-4-nitrophenyl)-3-thia-8-aza-bicyclo[3.2.1]octane (10) (4.89 g, 84%) as a yellow solid.

LC-MS (ESI) m/z = 269 $[M+H]^+$.

Step 2: 4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorobenzenamine (11):

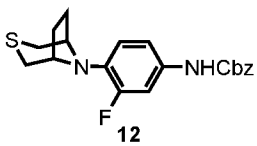


11

To a solution of 8-(2-fluoro-4-nitrophenyl)-3-thia-8-aza-bicyclo[3.2.1]octane (10) (4.89 g, 18.2 mmol) and Palladium carbon (200 mg) in MeOH (15 mL), then under a hydrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. The filtrate was concentrated under reduced pressure to afford 4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorobenzenamine (11) (4.08 g, 94%) as a white oil, and the crude material was used for next reaction without further purification.

LC-MS (ESI) m/z = 239 $[M+H]^+$.

Step 3: Benzyl 4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenylcarbamate (12):



12

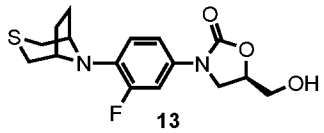
Carbonic acid, 2,5-dioxo-1-pyrrolidinyl phenylmethyl ester (6.38 g, 25.6 mmol) was added to a suspension of

4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorobenzenamine (11) (4.08 g, 17.1 mmol) in THF (30 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at 50°C for 5 h, monitored by TLC. The mixture was

concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 10: 1) to afford benzyl 4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenylcarbamate (12) (4.34 g, 68%) as a white solid.

LC-MS (ESI) m/z = 373 $[M+H]^+$.

Step 4: (5R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (13):



13

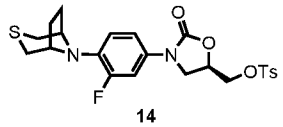
To a solution of benzyl 4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenylcarbamate (12) (4.34 g, 11.6 mmol) in THF (10 mL) at – 78 °C under a nitrogen gas atmosphere was added n-BuLi (7.3 ml, 17.5 mmol), then the mixture was stirred at -78°C for 30 min, after that the solution of (*R*)-oxiran-2-ylmethyl butyrate (2.5 g, 17.4 mmol) in THF was added to the mixture at -78°C, then warmed to room temperature and stirred for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 70: 1) to afford (5*R*)-3-(4-(3-thia-8-aza-bicyclo[3.2.1] Octan-8-yl)-3-fluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (13) (3.03 g, 77%) as a white solid.

LC-MS (ESI) m/z = 339 $[M+H]^+$.

Step 5:

((*R*)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-2-oxooxazolidin

-5-yl)methyl 4-methylbenzenesulfonate (14):



14

4-methylbenzene-1-sulfonyl chloride (3.41 g, 17.9 mmol) was added to a suspension of

(5*R*)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-5-(hydroxymethyl)

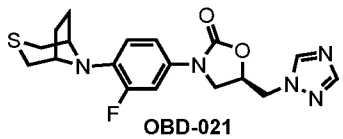
oxazolidin-2-one (13) (3.03 g, 8.9 mmol) and Et_3N (1.8 g, 17.9 mmol) in DCM (10 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford

((R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-2-oxooxazolidin -5-yl)methyl 4-methylbenzenesulfonate (14) (3.74 g, 85%) as a white solid.

LC-MS (ESI) *m/z* = 493 $[M+H]^+$.

Step 6:

(5*R*)-5-((1H-1,2,4-triazol-1-yl)methyl)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl) -3-fluorophenyl)oxazolidin-2-one (OBD-021):



OBD-021

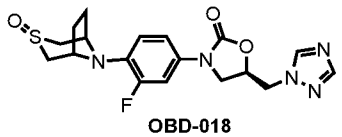
To a solution of ((*R*)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (14) (500 mg, 1 mmol) and 1H-1,2,4-triazole (140 mg, 2 mmol) in DMF (10 mL) was added K_2CO_3 (280 mg, 2 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 2 h under a nitrogen

gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 2: 1) to afford (5*R*)-5-((1H-1,2,4-triazol-1-yl)methyl)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)oxazolidin-2-one (OBD-021) (177 mg, 45%) as a white solid.

^{1}H NMR (300 MHz, DMSO-d_6) δ 8.57 (s, 1H), 8.01 (s, 1H), 7.36 (dd, J = 15.8, 2.1 Hz, 1H), 7.18 – 6.92 (m, 2H), 5.06 (dd, J = 8.9, 4.8 Hz, 1H), 4.72 – 4.52 (m, 2H), 4.36 (s, 2H), 4.17 (t, J = 9.1 Hz, 1H), 3.84 (dt, J = 49.3, 24.7 Hz, 1H), 3.12 (d, J = 12.8 Hz, 2H), 2.16 (s, 1H), 2.11 (s, 1H), 2.04 (s, 4H).

LC-MS (ESI) *m/z* = 390 $[M+H]^+$.

Step 7: Preparation of (OBD-018):

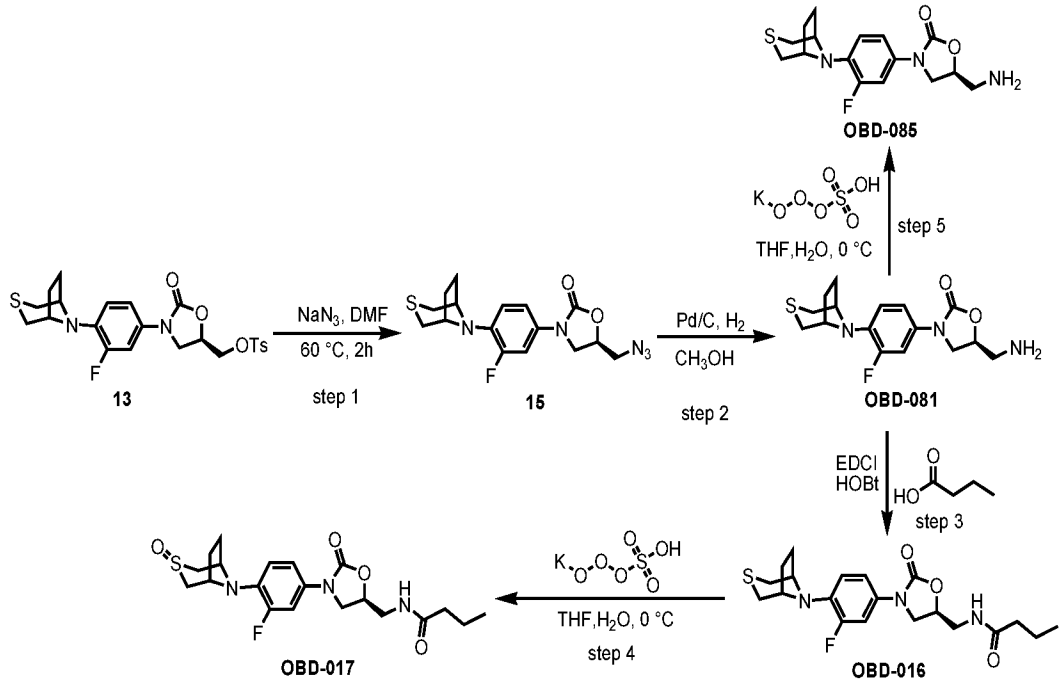


OBD-018

To a solution of (5*R*)-5-((1H-1,2,4-triazol-1-yl)methyl)-3-(4-(3-thia-8-aza-bicyclo[3.2.1] octan-8-yl)-3-fluorophenyl)oxazolidin-2-one (OBD-021) (100 mg, 0.26 mmol) in THF (10 mL) and 10 drops water was added potassium peroxomonosulfate (157 mg, 0.26 mmol) at 0 °C, then the reaction mixture was stirred at 0 °C for 2 h, monitored by TLC. Quenched with sodium thiosulfate, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 80: 1) to afford (OBD-018) (52 mg, 50%) as a white solid.

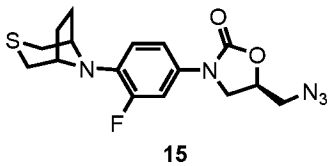
^{1}H NMR (300 MHz, DMSO-d_6) δ 12.17 (s, 1H), 8.69 (d, *J* = 2.9 Hz, 1H), 8.20 – 8.03 (m, 1H), 7.44 (d, *J* = 16.2 Hz, 1H), 7.28 – 7.02 (m, 2H), 5.08 (dd, *J* = 8.5, 5.1 Hz, 1H), 4.68 – 4.52 (m, 4H), 4.20 (t, *J* = 9.1 Hz, 1H), 3.91 (dd, *J* = 8.7, 6.0 Hz, 1H), 3.56 (d, *J* = 11.1 Hz, 2H), 2.48 (d, *J* = 12.3 Hz, 2H), 2.06 (d, *J* = 5.1 Hz, 2H), 1.79 (d, *J* = 7.6 Hz, 2H).

LC-MS (ESI) m/z = 405.8 $[M+H]^+$.



Step 1:

(5*R*)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-5-(azidomethyl)oxazolidin-2-one (15):



15

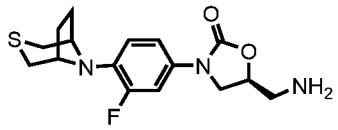
To a solution of ((*R*)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (14) (2 g, 4 mmol) and sodium azide (265 mg, 4 mmol) in DMF (10 mL) was added K_2CO_3 (1.1 g, 8 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 1 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (PE: EA = 2: 1) to afford (5R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)

-3-fluorophenyl)-5-(azidomethyl)oxazolidin-2-one (15) (1.01 g, 70%) as a white solid.

LC-MS (ESI) *m/z* = 364 $[M+H]^+$.

Step 2:

(5*S*)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-5-(aminomethyl)oxazolidin-2-one (OBD-081):



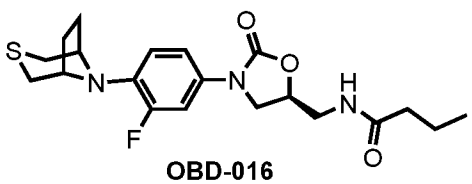
OBD-081

To a solution of (5R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl) -3-fluorophenyl)-5-(azidomethyl)oxazolidin-2-one (15) (1.01 g, 2.8 mmol) in MeOH (10 mL) was added palladium carbon (100 mg) at 25°C, then the reaction mixture was stirred at room temperature for overnight under a hydrogen gas atmosphere, monitored by TLC. The filtrate was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford (5S)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-5-(aminomethyl)oxazolidin-2-one (OBD-081) (800 mg, 85%) as a white solid.

LC-MS (ESI) *m/z* = 338 $[M+H]^+$.

Step 3:

N-(((*S*)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-016):



OBD-016

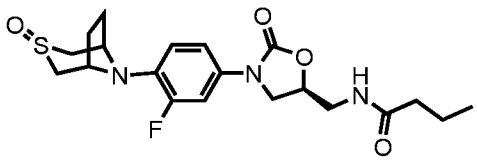
To a solution of

(5S)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-5-(aminomethyl)oxazolidin-2-one (OBD-081) (200 mg, 0.59 mmol) and butyric acid (52 mg, 0.59 mmol) in DCM (10 mL) were added HOBt (95 mg, 0.7 mmol), EDCI (170 mg, 0.88 mmol) and DIPEA (115 mg, 0.88 mmol) at 25 °C, then the reaction mixture was stirred at 25 °C for 2 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 80: 1) to afford N-(((*S*)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-016) (156 mg, 65%) as a white solid.

^{1}H NMR (300 MHz, DMSO-d_6) δ 8.18 (s, 1H), 7.42 (d, J = 16.0 Hz, 1H), 7.35 – 6.88 (m, 2H), 4.71 (s, 1H), 4.35 (s, 2H), 4.07 (t, J = 8.7 Hz, 1H), 3.77 – 3.57 (m, 1H), 3.51 – 3.27 (m, 2H), 3.12 (d, J = 12.4 Hz, 2H), 2.09 (dd, J = 20.9, 12.2 Hz, 8H), 1.47 (dd, J = 14.0, 7.1 Hz, 2H), 0.80 (dd, J = 8.0, 6.7 Hz, 3H).

LC-MS (ESI) m/z = 407.9 $[M+H]^+$.

Step 4: Preparation of (OBD-017):



OBD-017

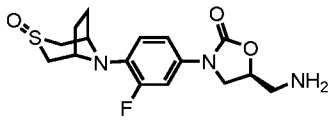
To a solution of N-(((S)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-016) (100 mg, 0.25 mmol) in THF (10 mL) and 10 drops water was added potassium peroxomonosulfate (157 mg, 0.26 mmol) at 0 °C, then the reaction mixture was stirred at 0 °C for 2 h, monitored by TLC. Quenched with sodium thiosulfate, and the crude material was purified by prep-HPLC to afford (OBD-017) (16 mg, 15%) as a white solid.

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.39 (dd, J = 15.8, 2.3 Hz, 1H), 7.03 (d, J = 6.1 Hz,

2H), 6.78 (t, J = 9.3 Hz, 1H), 4.72 (s, 1H), 4.55 (s, 2H), 3.94 (t, J = 8.9 Hz, 1H), 3.81 – 3.66 (m, 1H), 3.58 (s, 2H), 3.42 (d, J = 10.3 Hz, 2H), 2.77 (d, J = 11.9 Hz, 2H), 2.17 (dd, J = 25.1, 17.8 Hz, 4H), 1.84 (d, J = 7.9 Hz, 2H), 1.56 (dq, J = 14.5, 7.2 Hz, 2H), 0.83 (t, J = 7.4 Hz, 3H).

LC-MS (ESI) m/z = 423.8 $[M+H]^+$.

Step 4: Preparation of (OBD-085):

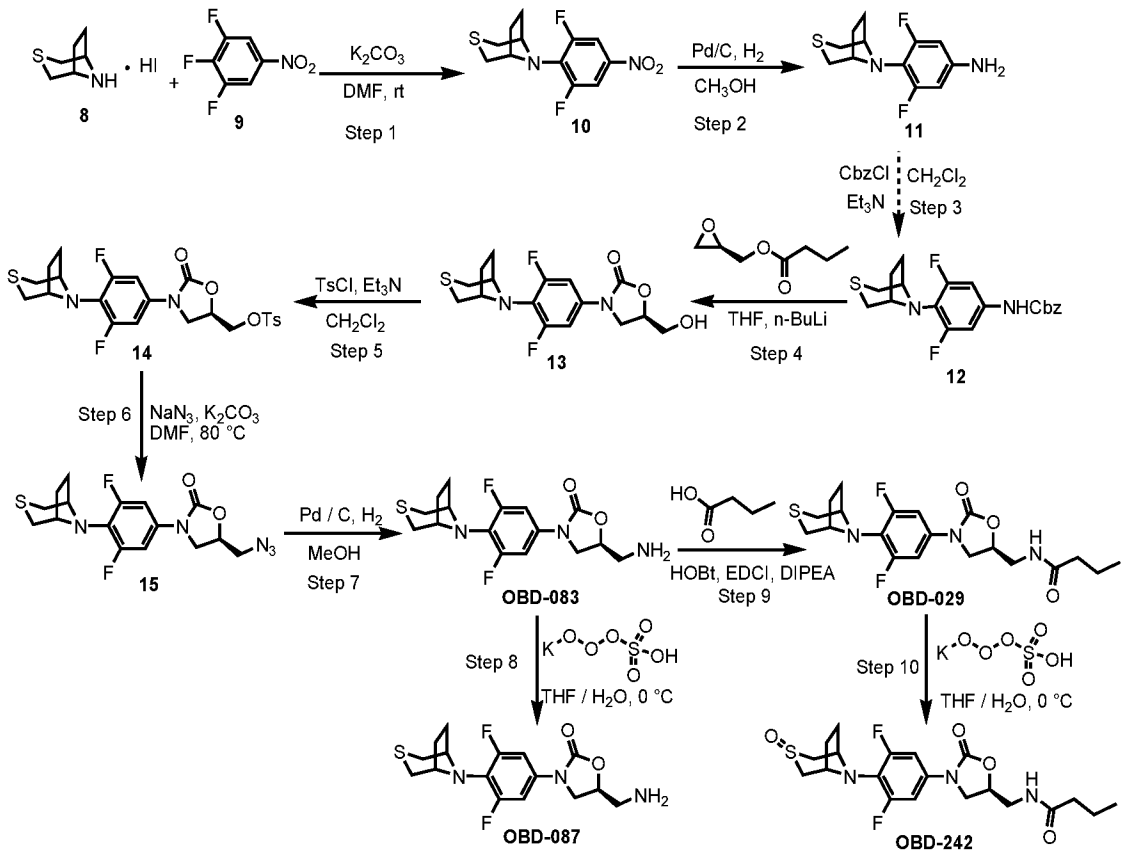


OBD-085

To a solution of (5S)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3-fluorophenyl)-5-(aminomethyl)oxazolidin-2-one (OBD-081) (100 mg, 0.29 mmol) in THF (10 mL) and 10 drops water was added potassium peroxomonosulfate (182 mg, 0.29 mmol) at 0 °C, then the reaction mixture was stirred at 0 °C for 2 h, monitored by TLC. Quenched with sodium thiosulfate, and the crude material was purified by prep-HPLC to afford (OBD-085) (28 mg, 28%) as a white solid.

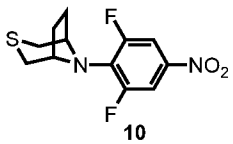
^{1}H NMR (400 MHz, DMSO-d_6) δ 7.52 (dd, J = 16.4, 2.2 Hz, 1H), 7.24 (dd, J = 8.9, 2.0 Hz, 1H), 7.13 (t, J = 9.6 Hz, 1H), 4.58 (dd, J = 14.1, 4.9 Hz, 3H), 4.04 (t, J = 8.9 Hz, 1H), 3.84 (dd, J = 8.7, 6.5 Hz, 1H), 3.56 (d, J = 10.0 Hz, 2H), 2.81 (dd, J = 9.3, 4.9 Hz, 2H), 2.46 (s, 2H), 2.17 – 1.99 (m, 2H), 1.79 (dd, J = 17.3, 9.5 Hz, 4H).

LC-MS (ESI) m/z = 354 $[M+H]^+$.



Step 1: Preparation of

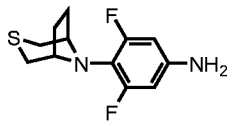
8-(2,6-difluoro-4-nitrophenyl)-3-thia-8-aza-bicyclo[3.2.1]octane (10):



To a solution of 3-thia-8-aza-bicyclo[3.2.1]octane hydrogen iodide (8) (5.0 g, 19.4 mmol) and 1,2,3-trifluoro-5-nitrobenzene (4.13 g, 23.3 mmol) in DMF (10 mL) was added K_2CO_3 (5.35 g, 38.8 mmol) at 25°C then the reaction mixture was stirred at 80°C for 2 h under a nitrogen gas atmosphere, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 3: 1) to afford 8-(2,6-difluoro-4-nitrophenyl)-3-thia-8-aza-bicyclo[3.2.1]octane (10) (3.6 g, 65%) as a yellow solid.

LC-MS (ESI) *m/z* = 287 $[M+H]^+$.

Step 2: 4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorobenzenamine (11):

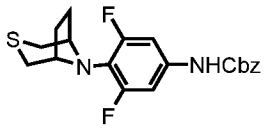


11

To a solution of 8-(2-fluoro-4-nitrophenyl)-3-thia-8-aza-bicyclo[3.2.1]octane (10) (3.6 g, 12.5 mmol) and Palladium carbon (200 mg) in MeOH (15 mL), then under a hydrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. The filtrate was concentrated under reduced pressure to afford 4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorobenzenamine (11) (2.9 g, 90%) as a white oil, and the crude material was used for next reaction without further purification.

LC-MS (ESI) *m/z* = 257 $[M+H]^+$.

Step 3: benzyl
4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenylcarbamate (12):



12

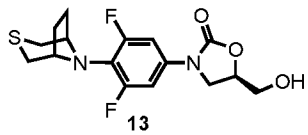
Carbonic acid, 2,5-dioxo-1-pyrrolidinyl phenylmethyl ester (5.57 g, 22.4 mmol) was added to a suspension of
4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorobenzenamine (11) (2.9 g, 11.2 mmol) in THF (30 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at 50°C for 5 h, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 10: 1) to afford benzyl

4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenylcarbamate (12) (3.0 g, 68%) as a white solid.

LC-MS (ESI) *m/z* = 391 $[M+H]^+$.

Step 4:

(5R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (13):



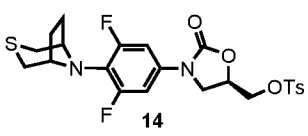
13

To a solution of benzyl 4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenylcarbamate (12) (3.0 g, 7.7 mmol) in THF (10 mL) at – 78 °C under a nitrogen gas atmosphere was added n-BuLi (4.8 ml, 11.5 mmol), then the mixture was stirred at -78°C for 30 min, after that the solution of (R)-oxiran-2-ylmethyl butyrate (1.66 g, 11.5 mmol) in THF was added to the mixture at -78°C, then warmed to room temperature and stirred for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 70: 1) to afford (5R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (13) (2.3 g, 84%) as a white solid.

LC-MS (ESI) *m/z* = 357 $[M+H]^+$.

Step 5:

((R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (14):



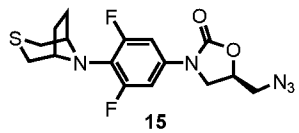
14

4-methylbenzene-1-sulfonyl chloride (2.45 g, 13 mmol) was added to a suspension of (5R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (13) (2.3 g, 6.5 mmol) and Et_3N (1.3 g, 13 mmol) in DCM (10 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford ((R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (14) (2.81 g, 85%) as a white solid.

LC-MS (ESI) *m/z* = 511 $[M+H]^+$.

Step 6:

(5R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(azidomethyl)oxazolidin-2-one (15):



15

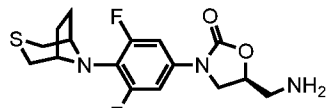
To a solution of ((R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (14) (2.81 g, 5.52 mmol) and sodium azide (360 mg, 5.52 mmol) in DMF (10 mL) was added K_2CO_3 (1.52 mg, 11.04 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 1 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (PE: EA = 2: 1) to afford

(5R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(azidomethy l)oxazolidin-2-one (15) (1.85 g, 88%) as a white solid.

LC-MS (ESI) *m/z* = 382 $[M+H]^+$.

Step 7:

(5S)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(aminometh yl)oxazolidin-2-one (OBD-083):



OBD-083

To a solution of

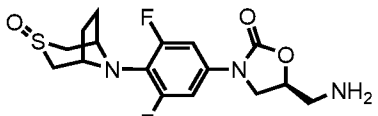
(5R)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(azidomethy l)oxazolidin-2-one (15) (1.85 g, 4.87 mmol) in MeOH (10 mL) was added palladium carbon (100 mg) at 25°C, then the reaction mixture was stirred at room temperature for overnight under a hydrogen gas atmosphere, monitored by TLC. The filtrate was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford

(5S)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(aminometh yl)oxazolidin-2-one (OBD-083) (1.6 g, 90 %) as a white solid.

^{1}H NMR (400 MHz, DMSO) δ 7.34 – 7.15 (m, 2H), 4.59 (td, J = 11.0, 5.0 Hz, 1H), 4.10 (s, 2H), 3.99 (t, J = 8.9 Hz, 1H), 3.79 (dd, J = 8.9, 6.4 Hz, 1H), 3.11 (dd, J = 12.6, 1.6 Hz, 2H), 2.79 (qd, J = 13.7, 4.9 Hz, 2H), 2.26 (dd, J = 12.4, 3.3 Hz, 2H), 2.01 (s, 4H), 1.72 (d, J = 59.8 Hz, 2H).

LC-MS (ESI) *m/z* = 356 $[M+H]^+$.

Step 8: Preparation of (OBD-087):



OBD-087

To a solution of

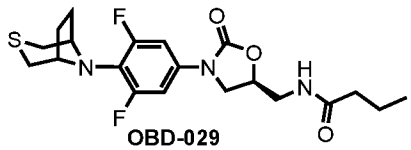
(5S)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(aminomethyl)oxazolidin-2-one (OBD-083) (100 mg, 0.28 mmol) in THF (10 mL) and 10 drops water was added potassium peroxomonosulfate (173 mg, 0.28 mmol) at 0 °C, then the reaction mixture was stirred at 0 °C for 2 h, monitored by TLC. Quenched with sodium thiosulfate, and the crude material was purified by prep-HPLC to afford (OBD-087) (31 mg, 30 %) as a white solid.

^{1}H NMR (400 MHz, DMSO) δ 7.32 (t, J = 9.4 Hz, 2H), 4.61 (dd, J = 8.8, 6.0 Hz, 0H), 4.34 (s, 1H), 4.02 (t, J = 8.9 Hz, 1H), 3.82 (dd, J = 8.9, 6.4 Hz, 1H), 3.68 (dd, J = 12.4, 3.7 Hz, 1H), 2.81 (qd, J = 13.7, 4.9 Hz, 1H), 2.58 (d, J = 11.6 Hz, 1H), 2.12 – 1.98 (m, 1H), 1.78 (q, J = 6.9 Hz, 2H).

LC-MS (ESI) m/z = 372 $[M+H]^+$.

Step 9:

N-(((S)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-029):



OBD-029

To a solution of

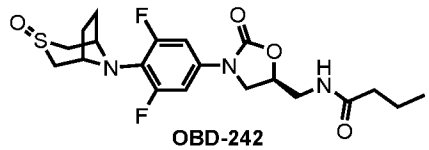
(5S)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(aminomethyl)oxazolidin-2-one (OBD-083) (200 mg, 0.56 mmol) and butyric acid (52 mg, 0.59 mmol) in DCM (10 mL) were added HOBt (95 mg, 0.7 mmol), EDCI (170 mg, 0.88 mmol) and DIPEA (115 mg, 0.88 mmol) at 25 °C, then the reaction mixture was stirred at 25 °C for 2 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 80: 1) to afford

N-(((S)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-029) (119 mg, 50%) as a white solid.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.18 (s, 1H), 7.22 (d, J = 12.2 Hz, 2H), 4.73 (d, J = 3.6 Hz, 1H), 4.07 (dd, J = 19.1, 10.0 Hz, 3H), 3.68 (dd, J = 9.1, 6.2 Hz, 1H), 3.41 (s, 2H), 3.12 (d, J = 11.3 Hz, 2H), 2.26 (dd, J = 12.4, 3.0 Hz, 2H), 2.05 (dd, J = 16.8, 9.5 Hz, 6H), 1.47 (dd, J = 14.7, 7.3 Hz, 2H), 0.79 (t, J = 7.4 Hz, 3H).

LC-MS (ESI) m/z = 426 $[M+H]^+$.

Step 10: Preparation of (OBD-242):

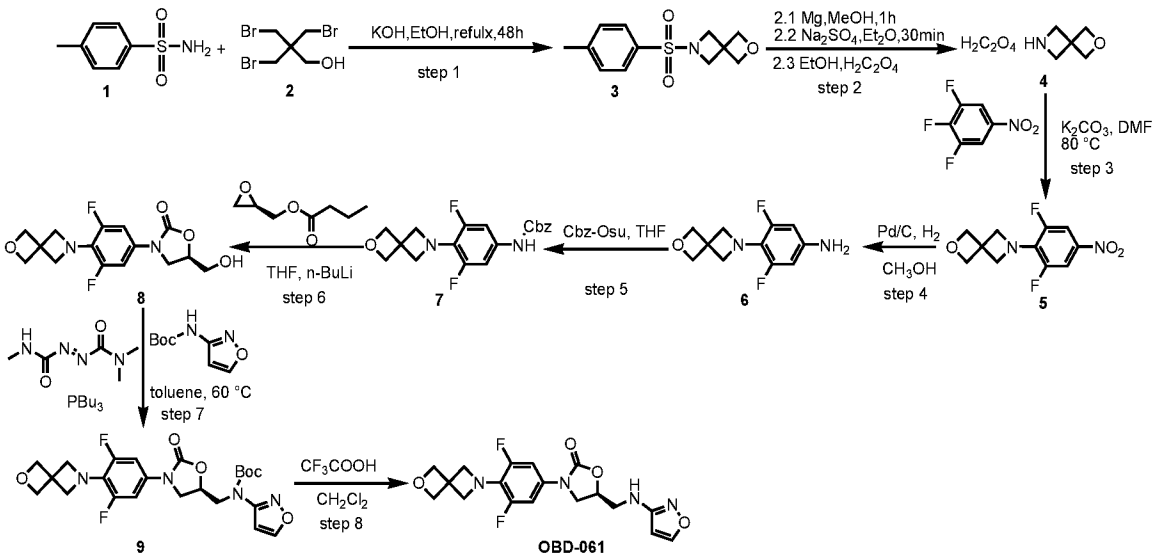


OBD-242

To a solution of N-(((S)-3-(4-(3-thia-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl)butyramide (OBD-029) (100 mg, 0.23 mmol) in THF (10 mL) and 10 drops water was added potassium peroxomonosulfate (144 mg, 0.23 mmol) at 0 °C, then the reaction mixture was stirred at 0 °C for 2 h, monitored by TLC. Quenched with sodium thiosulfate, and the crude material was purified by prep-HPLC to afford (OBD-242) (30 mg, 15%) as a white solid.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.19 (d, J = 5.6 Hz, 1H), 7.28 (d, J = 12.7 Hz, 3H), 4.77 – 4.69 (m, 1H), 4.34 (s, 2H), 4.07 (t, J = 9.0 Hz, 1H), 3.67 (d, J = 9.0 Hz, 3H), 3.40 (dd, J = 11.0, 5.5 Hz, 1H), 2.56 (d, J = 11.9 Hz, 1H), 2.06 (t, J = 7.3 Hz, 4H), 1.82 – 1.72 (m, 2H), 1.51 – 1.40 (m, 2H), 0.78 (t, J = 7.4 Hz, 3H).

LC-MS (ESI) m/z = 442 $[M+H]^+$.



Step 1: Preparation of (3):

To a solution of p-toluenesulfonamide (57 g, 330 mmol) and potassium hydroxide (49.8 g, 890 mmol) in ethanol (1000 mL) was added 3-bromo-2,2-bis(bromomethyl)propan-1-ol (90 g, 270 mmol) at 25°C then the reaction mixture was stirred at 100°C for 48 h. The mixture was concentrated under reduced pressure, and the crude material was poured into solution of potassium hydroxide (75 mL) and stirred for 2 h, to afford filter cake (3) (10 g, 59%) as a white solid.

LC-MS (ESI) m/z = 254 $[M+H]^+$.

Step 2: Preparation of (4):

A mixture of (3) (10 g, 39.5 mmol) and magnesium (6.7 g) in methanol (15 mL) was sonicated for 1 h at 40 °C, after that the solvent was removed under reduced pressure to afford a viscous grey residue, Et2O and sodium sulfate were added and the resulting grey mixture was stirred vigorously for 30 min before filtration. A solution of oxalic acid in ethanol was added to the filtrate. A think white precipitate formed

instantly, which was target product (4) (3.7 g, 50%), and the crude material was used for next reaction without further purification.

Step 3: Preparation of (5):

To a solution of (4) (3.7 g, 19.5 mmol) and 1,2,3-trifluoro-5-nitrobenzene (3.81 g, 21.5 mmol) in DMF (10 mL) was added K_2CO_3 (5.38 g, 39 mmol) at 25°C then the reaction mixture was stirred at 80°C for 2 h under a nitrogen gas atmosphere, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 3: 1) to afford (5) (1.9 g, 38%) as a yellow solid.
LC-MS (ESI) m/z = 257 $[M+H]^+$.

Step 4: Preparation of (6):

To a solution of (5) (1.9 g, 7.4 mmol) and Palladium carbon (200 mg) in methanol (15 mL), then under a hydrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. The filtrate was concentrated under reduced pressure to afford (6) (1.5 g, 90%) as a white oil, and the crude material was used for next reaction without further purification.

LC-MS (ESI) m/z = 227 $[M+H]^+$.

Step 5: Preparation of (7):

Carbonic acid, 2,5-dioxo-1-pyrrolidinyl phenylmethyl ester (3.3 g, 13.3 mmol) was added to a suspension of (6) (1.5 g, 6.7 mmol) in THF (30 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at 50°C for 5 h, monitored by TLC. The mixture was concentrated under reduced pressure, and the

crude material was purified by silica gel column chromatography (EA: PE = 10: 1) to afford (7) (1.6 g, 68%) as a white solid.

LC-MS (ESI) m/z = 361 $[M+H]^+$.

Step 6: Preparation of (8):

To a solution of (7) (1.6 g, 4.6 mmol) in THF (10 mL) at – 78 °C under a nitrogen gas atmosphere was added n-BuLi (2.8 ml, 6.8 mmol), then the mixture was stirred at -78°C for 30 min, after that the solution of (R)-oxiran-2-ylmethyl butyrate (980 mg, 6.8 mmol) in THF was added to the mixture at -78°C, then warmed to room temperature and stirred for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 70: 1) to afford (8) (1.2 g, 84%) as a white solid.

LC-MS (ESI) m/z = 327 $[M+H]^+$.

Step 7: Preparation of (9):

(E)-N1,N1,N2-trimethyldiazene-1,2-dicarboxamide (443 mg, 2.6 mmol) was added to a suspension of (8) (560 mg, 1.7 mmol), tert-butyl isoxazol-3-ylcarbamate (380 mg, 2.1 mmol) and tributylphosphine (521 mg, 2.6 mmol) in toluene (30 mL) at 0 °C under a nitrogen gas atmosphere and then the reaction mixture was stirred at 60 °C for overnight, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 10: 1) to afford (9) (309 mg, 37%) as a white solid.

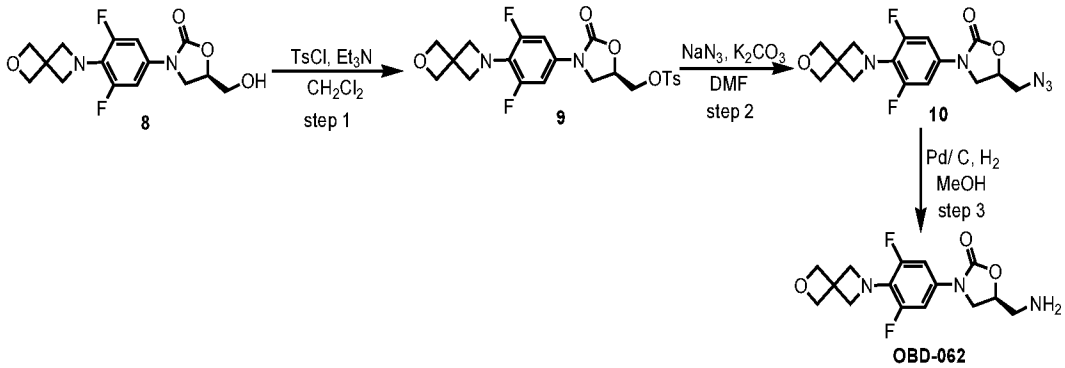
LC-MS (ESI) m/z = 493 $[M+H]^+$.

Step 8: Preparation of (OBD-061):

To a solution of (9) (309 g, 0.6 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added trifluoroacetic acid (1 ml), then the mixture was stirred at 0 °C for 30 min, monitored by TLC. Quenched with ammonium chloride, extracted with CH_2Cl_2, the organic layer was concentrated under reduced pressure, and the crude material was purified by prep-HPLC to afford (OBD-061) (93 mg, 38 %) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.01 (d, J = 12.1 Hz, 2H), 5.85 (d, J = 1.7 Hz, 1H), 4.92 (s, 1H), 4.82 (s, 4H), 4.29 (s, 4H), 3.99 (s, 2H), 3.75 (s, 2H), 3.60 (s, 2H)

LC-MS (ESI) m/z = 392.9 $[M+H]^+$.



Step 1: Preparation of (9):

4-methylbenzene-1-sulfonyl chloride (2.45 g, 13 mmol) was added to a suspension of (8) (2.3 g, 6.5 mmol) and Et_3N (1.3 g, 13 mmol) in DCM (10 mL) at 0 °C and then the reaction mixture was stirred at room temperature for overnight under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and

the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford (9) (2.65 g, 85%) as a white solid.

LC-MS (ESI) *m/z* = 481 $[M+H]^+$.

Step 2: Preparation of (10):

To a solution of (9) (2.65 g, 5.52 mmol) and sodium azide (360 mg, 5.52 mmol) in DMF (10 mL) was added K_2CO_3 (1.52 mg, 11.04 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 1 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (PE: EA = 2: 1) to afford (10) (1.7 g, 88%) as a white solid.

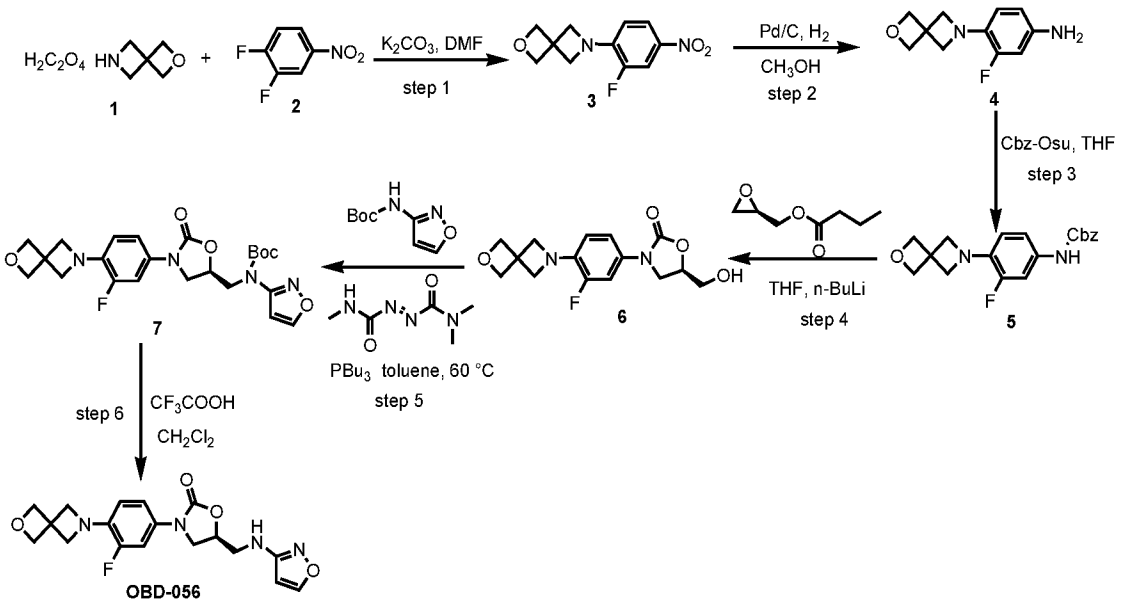
LC-MS (ESI) *m/z* = 352 $[M+H]^+$.

Step 3: Preparation of (OBD-062):

To a solution of (10) (1.7 g, 4.86 mmol) in MeOH (10 mL) was added palladium carbon (100 mg) at 25°C, then the reaction mixture was stirred at room temperature for overnight under a hydrogen gas atmosphere, monitored by TLC. The filtrate was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford (OBD-062) (1.3 g, 85 %) as a white solid.

^1H NMR (400 MHz, DMSO-d_6) δ 7.34 – 6.98 (m, 2H), 4.70 (s, 4H), 4.59 (dt, J = 11.3, 5.1 Hz, 1H), 4.23 (d, J = 2.2 Hz, 4H), 3.99 (dd, J = 20.9, 12.0 Hz, 1H), 3.78 (dd, J = 8.9, 6.4 Hz, 1H), 2.80 (ddd, J = 24.5, 13.6, 4.9 Hz, 2H), 1.99 (s, 2H).

LC-MS (ESI) m/z = 326.1 $[M+H]^+$.



Step 1: Preparation of (3):

To a solution of (1) (3.7 g, 19.5 mmol) and 1,2-difluoro-4-nitrobenzene (3.41 g, 21.5 mmol) in DMF (10 mL) was added K_2CO_3 (5.38 g, 39 mmol) at 25°C then the reaction mixture was stirred at 80°C for 2 h under a nitrogen gas atmosphere, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 3: 1) to afford (3) (1.7 g, 38%) as a yellow solid.

LC-MS (ESI) m/z = 239 $[M+H]^+$.

Step 2: Preparation of (4):

To a solution of (3) (1.7 g, 7.4 mmol) and Palladium carbon (200 mg) in methanol (15 mL), then under a hydrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. The filtrate was concentrated

under reduced pressure to afford (4) (1.4 g, 90%) as a white oil, and the crude material was used for next reaction without further purification.

LC-MS (ESI) m/z = 209 $[M+H]^+$.

Step 3: Preparation of (7):

Carbonic acid, 2,5-dioxo-1-pyrrolidinyl phenylmethyl ester (3.3 g, 13.3 mmol) was added to a suspension of (6) (1.4 g, 6.7 mmol) in THF (30 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at 50°C for 5 h, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 10: 1) to afford (7) (1.6 g, 70%) as a white solid.

LC-MS (ESI) m/z = 343 $[M+H]^+$.

Step 4: Preparation of (8):

To a solution of (7) (1.6 g, 4.7 mmol) in THF (10 mL) at – 78 °C under a nitrogen gas atmosphere was added n-BuLi (2.9 ml, 7.0 mmol), then the mixture was stirred at -78°C for 30 min, after that the solution of (R)-oxiran-2-ylmethyl butyrate (1 g, 7.0 mmol) in THF was added to the mixture at -78°C, then warmed to room temperature and stirred for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 70: 1) to afford (8) (1.2 g, 84%) as a white solid.

LC-MS (ESI) m/z = 309 $[M+H]^+$.

Step 5: Preparation of (9):

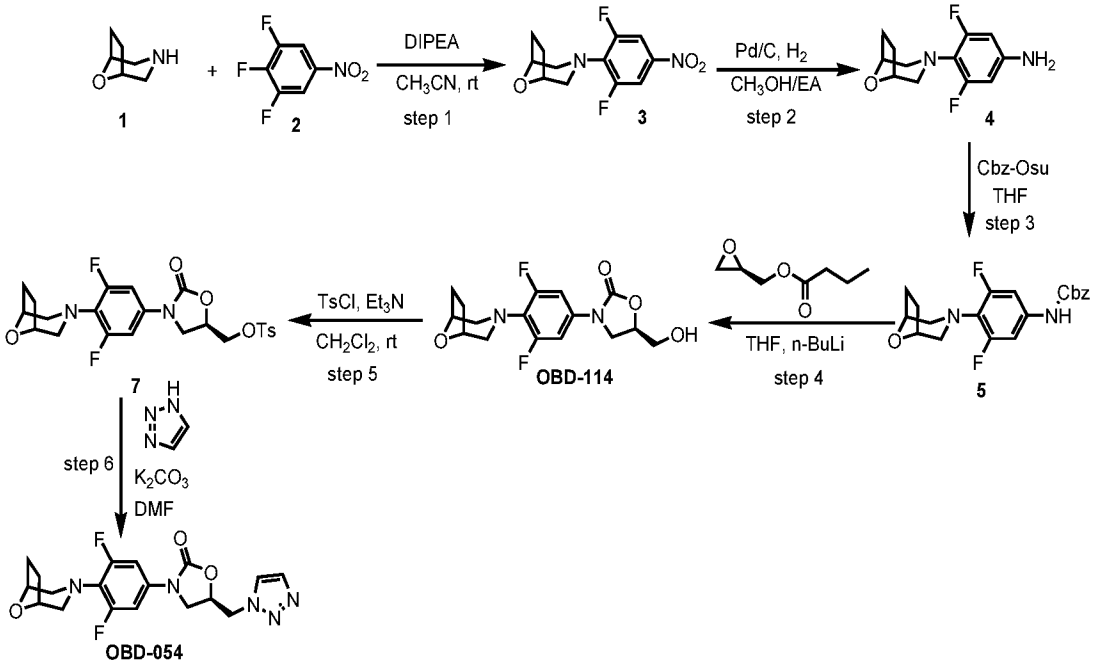
(E)-N_1,N_1,N_2-trimethyldiazene-1,2-dicarboxamide (443 mg, 2.6 mmol) was added to a suspension of (8) (523 mg, 1.7 mmol), tert-butyl isoxazol-3-ylcarbamate (380 mg, 2.1 mmol) and tributylphosphine (521 mg, 2.6 mmol) in toluene (30 mL) at 0 °C under a nitrogen gas atmosphere and then the reaction mixture was stirred at 60 °C for overnight, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 10: 1) to afford (9) (298 mg, 37%) as a white solid.

LC-MS (ESI) *m/z* = 475 $[M+H]^+$.

Step 6: Preparation of (OBD-056):

To a solution of (9) (298 mg, 0.6 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added trifluoroacetic acid (1 ml), then the mixture was stirred at 0 °C for 30 min, monitored by TLC. Quenched with ammonium chloride, extracted with CH_2Cl_2, the organic layer was concentrated under reduced pressure, and the crude material was purified by prep-HPLC to afford (OBD-056) (84 mg, 38 %) as a white solid.
^{1}H NMR (301 MHz, $CDCl_3$) δ 7.39 (d, J = 14.4 Hz, 1H), 7.25 (s, 1H), 7.04 (d, J = 8.6 Hz, 1H), 6.83 (t, J = 8.9 Hz, 1H), 5.14 (s, 1H), 4.73 (s, 1H), 4.39 (s, 2H), 4.00 (t, J = 8.8 Hz, 1H), 3.84 – 3.42 (m, 8H), 3.05 (dd, J = 23.2, 11.2 Hz, 5H), 2.13 – 1.88 (m, 5H).

LC-MS (ESI) m/z = 375 $[M+H]^+$.



Step 1: Preparation of

3-(2,6-difluoro-4-nitrophenyl)-8-oxa-3-aza-bicyclo[3.2.1]octane (3):

To a solution of 8-oxa-3-aza-bicyclo[3.2.1]octane (1) (5.0 g, 44.2 mmol) and 1,2,3-trifluoro-5-nitrobenzene (8.6 g, 48.6 mmol) in DMF (10 mL) was added K_2CO_3 (12.2 g, 88.4 mmol) at 25°C then the reaction mixture was stirred at 80°C for 2 h under a nitrogen gas atmosphere, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 3: 1) to afford 3-(2,6-difluoro-4-nitrophenyl)-8-oxa-3-aza-bicyclo[3.2.1]octane (3) (9.3 g, 78%) as a yellow solid.

LC-MS (ESI) m/z = 271 $[M+H]^+$.

Step 2: Preparation of

4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorobenzenamine (4):

To a solution of 3-(2,6-difluoro-4-nitrophenyl)-8-oxa-3-aza-bicyclo[3.2.1]octane (3) (9.3 g, 34.4 mmol) and Palladium carbon (1 g) in MeOH (15 mL), then under a hydrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. The filtrate was concentrated under reduced pressure to afford 4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorobenzenamine (4) (7.8 g, 95%) as a white oil, and the crude material was used for next reaction without further purification.

LC-MS (ESI) m/z = 241 $[M+H]^+$.

Step 3: Preparation of benzyl
4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenylcarbamate (5):

Carbonic acid, 2,5-dioxo-1-pyrrolidinyl phenylmethyl ester (12 g, 48.7 mmol) was added to a suspension of
4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorobenzenamine (4) (7.8 g, 32.5 mmol) in THF (100 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at 50°C for 5 h, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 10: 1) to afford benzyl
4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenylcarbamate (5) (8.2 g, 68%) as a white solid.

LC-MS (ESI) m/z = 375 $[M+H]^+$.

Step 4: Preparation of
3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (OBD-114):

To a solution of benzyl 4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenylcarbamate (5) (8.2 g, 22.1 mmol) in THF (10 mL) at – 78 °C under a nitrogen gas atmosphere was added n-BuLi (13.8 ml, 33.1 mmol), then the mixture was stirred at -78°C for 30 min, after that the solution of (R)-oxiran-2-ylmethyl butyrate (4.7 g, 33.1 mmol) in THF was added to the mixture at -78°C, then warmed to room temperature and stirred for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 70: 1) to afford 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (OBD-114) (4.5 g, 60%) as a white solid.

LC-MS (ESI) m/z = 341 $[M+H]^+$.

Step 5: Preparation of (3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (7):

4-methylbenzene-1-sulfonyl chloride (5 g, 26.6 mmol) was added to a suspension of 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (OBD-114) (4.5 g, 13.3 mmol) and Et_3N (2.7 g, 26.6 mmol) in DCM (10 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford (3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (7) (5.58 g, 85%) as a white solid.

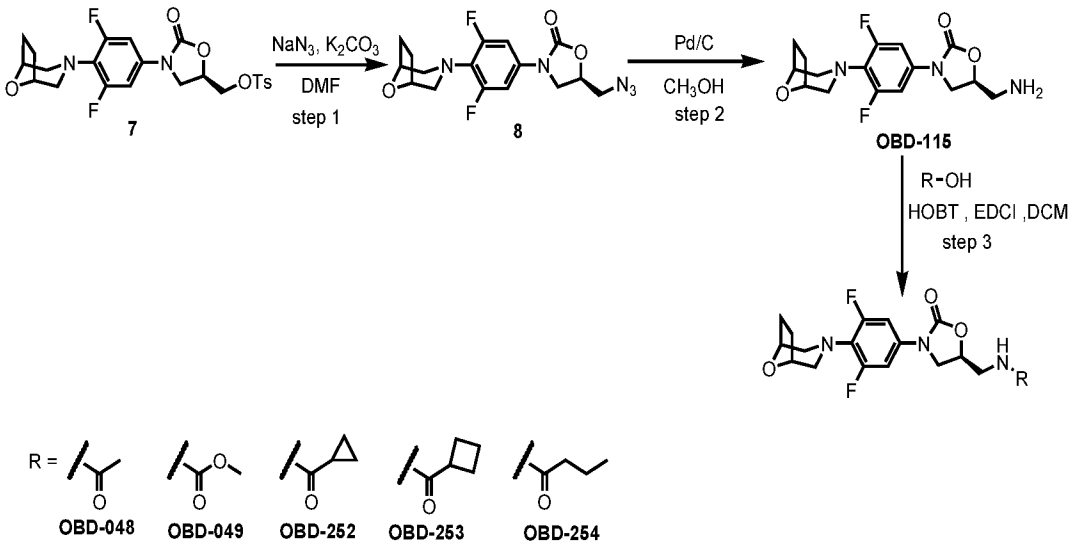
LC-MS (ESI) m/z = 495 $[M+H]^+$.

Step 6: Preparation of 5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-di fluorophenyl)oxazolidin-2-one (OBD-054):

To a solution of (3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (7) (300 mg, 0.6 mmol) and 1H-1,2,3-triazole (42 mg, 0.6 mmol) in DMF (10 mL) was added K_2CO_3 (166 mg, 1.2 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 1 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by prep-HPLC to afford 5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-di fluorophenyl)oxazolidin-2-one (OBD-054) (82 mg, 35%) as a white solid.

^{1}H NMR (300 MHz, DMSO-d_6) δ 8.14 (d, J = 1.0 Hz, 1H), 7.73 (d, J = 1.0 Hz, 1H), 7.17 (d, J = 11.7 Hz, 2H), 5.11 (d, J = 3.5 Hz, 1H), 4.79 (d, J = 5.0 Hz, 2H), 4.18 (dd, J = 23.1, 13.7 Hz, 3H), 3.91 – 3.70 (m, 1H), 3.23 (d, J = 10.9 Hz, 3H), 2.72 (d, J = 10.7 Hz, 3H), 2.07 – 1.61 (m, 7H).

LC-MS (ESI) m/z = 392 $[M+H]^+$.



Step 1: Preparation of 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-5-(azidomethyl)oxazolidin-2-one (8):

To a solution of (3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (7) (4 g, 8 mmol) and sodium azide (526 mg, 8 mmol) in DMF (10 mL) was added K_2CO_3 (2.2 mg, 16 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 1 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (PE: EA = 2: 1) to afford 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-5-(azidomethyl)oxazolidin-2-one (8) (2.57 g, 88%) as a white solid.

LC-MS (ESI) m/z = 366 $[M+H]^+$.

Step 2: Preparation of 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-5-(aminomethyl)oxazolidin-2-one (OBD-115):

To a solution of 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-5-(azidomethyl)oxazolidin-2-one (8) (2.57 g, 7 mmol) in MeOH (10 mL) was added palladium carbon (300 mg) at 25°C, then the reaction mixture was stirred at room temperature for overnight under a hydrogen gas atmosphere, monitored by TLC. The filtrate was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford

3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-5-(aminomethyl)ox azolidin-2-one (OBD-115) (2.1 g, 85 %) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.20 (m, 2H), 4.62 (td, *J* = 10.9, 4.9 Hz, 1H), 4.28 (s, 2H), 4.02 (t, *J* = 8.9 Hz, 1H), 3.81 (dd, *J* = 8.9, 6.3 Hz, 1H), 3.27 (d, *J* = 10.4 Hz, 2H), 2.81 (ddd, *J* = 28.3, 18.6, 7.7 Hz, 4H), 2.21 (s, 2H), 2.04 – 1.94 (m, 2H), 1.88 – 1.71 (m, 2H).

LC-MS (ESI) *m/z* = 340 $[M+H]^+$.

Step 3: Preparation of (OBD-048, 049, 252, 253, 254):

To a solution of

3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorophenyl)-5-(aminomethyl)ox azolidin-2-one (OBD-115) (200 mg, 0.59 mmol) and R-OH (0.59 mmol) in DCM (10 mL) were added HOBt (119 mg, 0.88 mmol), EDCI (225 mg, 1.18 mmol) and DIPEA (152 mg, 1.18 mmol) at 25 °C, then the reaction mixture was stirred at 25 °C for 2 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 80: 1) to afford (OBD-048, 049, 252, 253, 254) as a white solid.

OBD-048

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (d, *J* = 10.9 Hz, 2H), 5.98 (s, 1H), 4.75 (s, 1H), 4.33 (s, 2H), 3.98 (t, *J* = 8.8 Hz, 1H), 3.68 (dd, *J* = 19.8, 11.0 Hz, 3H), 3.45 (d, *J* = 10.9 Hz, 3H), 2.78 (d, *J* = 11.1 Hz, 2H), 2.11 (d, *J* = 6.6 Hz, 3H), 1.98 (d, *J* = 24.1 Hz, 6H).

LC-MS (ESI) m/z = 426 $[M+H]^+$.

OBD-049

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.06 (d, J = 11.0 Hz, 2H), 5.15 (s, 1H), 4.75 (s, 1H), 4.32 (s, 2H), 3.97 (t, J = 9.0 Hz, 2H), 3.80 – 3.70 (m, 4H), 3.56 (d, J = 5.9 Hz, 2H), 3.42 (s, 2H), 2.77 (d, J = 11.1 Hz, 2H), 2.10 (d, J = 6.4 Hz, 2H), 1.92 (d, J = 5.0 Hz, 2H).

LC-MS (ESI) m/z = 397.7 $[M+H]^+$.

OBD-252

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.07 (d, *J* = 11.0 Hz, 2H), 6.19 (s, 1H), 4.77 (s, 1H), 4.35 (s, 2H), 3.97 (t, *J* = 8.9 Hz, 1H), 3.78 – 3.62 (m, 3H), 3.46 (d, *J* = 10.1 Hz, 2H), 2.79 (d, *J* = 11.1 Hz, 2H), 2.12 (d, *J* = 6.5 Hz, 2H), 1.94 (d, *J* = 4.5 Hz, 2H), 1.43 – 1.33 (m, 1H), 0.95 (dd, *J* = 9.5, 4.4 Hz, 2H), 0.78 (d, *J* = 6.4 Hz, 2H).

LC-MS (ESI) m/z = 408.1 $[M+H]^+$.

OBD-253

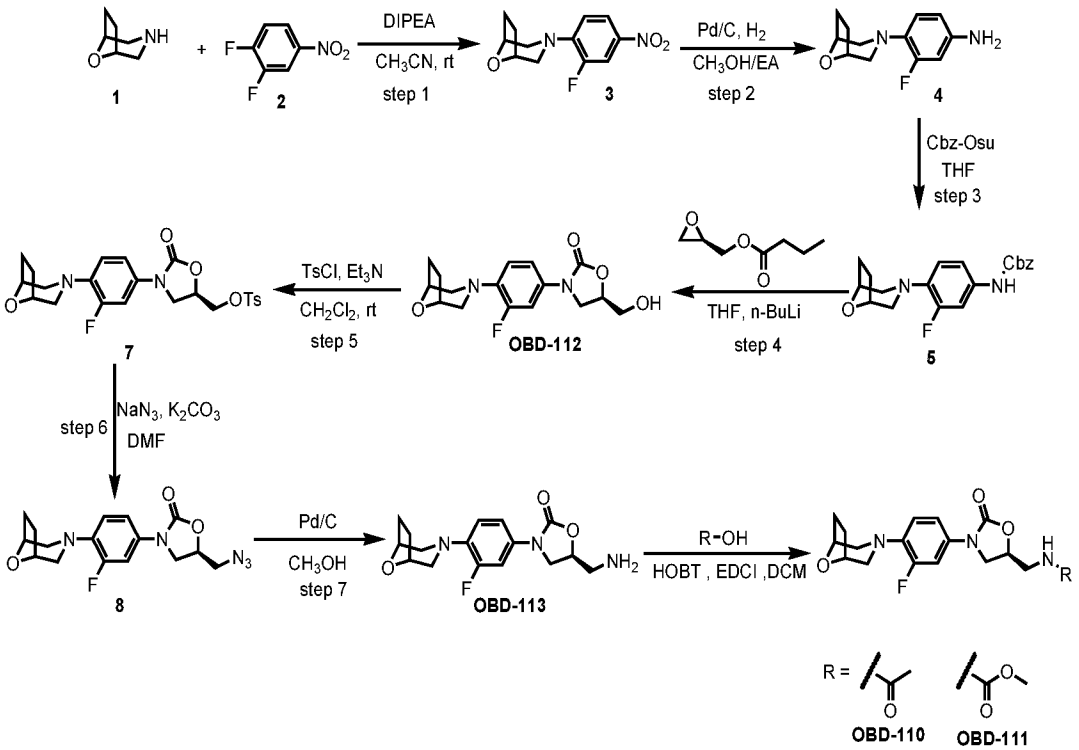
^{1}H NMR (301 MHz, $CDCl_3$) δ 7.07 (d, *J* = 11.0 Hz, 2H), 5.88 (s, 1H), 4.76 (s, 1H), 4.34 (s,2H), 3.98 (t, *J* = 9.0 Hz, 1H), 3.79 – 3.59 (m, 3H), 3.45 (d, *J* = 10.8 Hz, 2H), 3.12 – 2.97 (m, 1H), 2.79 (d, *J* = 11.3 Hz, 2H), 2.38 – 2.10 (m, 6H), 2.00 – 1.79 (m, 4H).

LC-MS (ESI) m/z = 422.1 $[M+H]^+$.

OBD-254

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.17 – 6.96 (m, 2H), 6.07 (s, 1H), 4.78 (s, 1H), 4.34 (s, 2H), 3.98 (t, *J* = 8.9 Hz, 1H), 3.82 – 3.64 (m, 3H), 3.45 (d, *J* = 10.0 Hz, 2H), 2.79 (d, *J* = 11.2 Hz, 2H), 2.38 – 2.06 (m, 4H), 1.98 – 1.78 (m, 2H), 1.63 (dq, *J* = 14.7, 7.3 Hz, 2H), 1.26 (s, 1H), 0.90 (t, *J* = 7.4 Hz, 3H).

LC-MS (ESI) m/z = 410.1 $[M+H]^+$.



Step 1: Preparation of 3-(2-fluoro-4-nitrophenyl)-8-oxa-3-aza-bicyclo[3.2.1]octane (3):

To a solution of 8-oxa-3-aza-bicyclo[3.2.1]octane (1) (5.0 g, 44.2 mmol) and 1,2-difluoro-4-nitrobenzene (7.7 g, 48.6 mmol) in DMF (10 mL) was added K_2CO_3 (12.2 g, 88.4 mmol) at 25°C then the reaction mixture was stirred at 80°C for 2 h under a nitrogen gas atmosphere, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 5: 1) to afford 3-(2-fluoro-4-nitrophenyl)-8-oxa-3-aza-bicyclo[3.2.1]octane (3) (9.1 g, 82%) as a yellow solid.

LC-MS (ESI) *m/z* = 253 $[M+H]^+$.

Step 2: Preparation of 4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorobenzenamine (4):

To a solution of 3-(2-fluoro-4-nitrophenyl)-8-oxa-3-aza-bicyclo[3.2.1]octane (3) (3) (9.1 g, 36.2 mmol) and Palladium carbon (1 g) in MeOH (15 mL), then under a hydrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. The filtrate was concentrated under reduced pressure to afford 4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorobenzenamine (4) (7.3 g, 91%) as a white oil, and the crude material was used for next reaction without further purification.

LC-MS (ESI) m/z = 223 $[M+H]^+$.

Step 3: Preparation of benzyl
4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenylcarbamate (5):

Carbonic acid, 2,5-dioxo-1-pyrrolidinyl phenylmethyl ester (16.4 g, 65.88 mmol) was added to a suspension of
4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorobenzenamine (4) (7.3 g, 32.9 mmol) in THF (100 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at 50°C for 5 h, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (PE: EA = 10: 1) to afford benzyl
4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenylcarbamate (5) (7.1 g, 61%) as a white solid.

LC-MS (ESI) m/z = 357 $[M+H]^+$.

Step 4: Preparation of
3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (OBD-112):

To a solution of benzyl 4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenylcarbamate (5) (7.1 g, 20.1 mmol) in THF (10 mL) at – 78 °C under a nitrogen gas atmosphere was added n-BuLi (12.5 ml, 30.1 mmol), then the mixture was stirred at -78°C for 30 min, after that the solution of (R)-oxiran-2-ylmethyl butyrate (4.3 g, 30.1 mmol) in THF was added to the mixture at -78°C, then warmed to room temperature and stirred for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 70: 1) to afford 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (OBD-112) (3.9 g, 60%) as a white solid.

^{1}H NMR (301 MHz, DMSO-d_6) δ 7.46 (dd, J = 15.4, 2.5 Hz, 1H), 7.14 (d, J = 6.5 Hz, 1H), 7.03 – 6.84 (m, 1H), 5.18 (s, 1H), 4.64 (d, J = 3.3 Hz, 1H), 4.31 (s, 2H), 4.00 (t, J = 9.0 Hz, 1H), 3.81 – 3.72 (m, 1H), 3.57 (d, J = 24.9 Hz, 2H), 3.00 (d, J = 11.2 Hz, 3H), 2.85 (d, J = 10.9 Hz, 2H), 2.08 – 1.63 (m, 5H).

LC-MS (ESI) m/z = 323 $[M+H]^+$.

Step 5: Preparation of (3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl) methyl 4-methylbenzenesulfonate (7):

4-methylbenzene-1-sulfonyl chloride (2.3 g, 24 mmol) was added to a suspension of 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (OBD-112) (3.9 g, 12 mmol) and Et_3N (1.2 g, 24 mmol) in DCM (10 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced

pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford (3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl) methyl 4-methylbenzenesulfonate (7) (4.86 g, 85%) as a white solid.

LC-MS (ESI) m/z = 477 $[M+H]^+$.

Step 6: Preparation of 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)-5-(azidomethyl)oxazoli din-2-one (8):

To a solution of (3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)-2-oxooxazolidin-5-yl) methyl 4-methylbenzenesulfonate (7) (4.86 g, 10.2 mmol) and sodium azide (663 mg, 10.2 mmol) in DMF (10 mL) was added K_2CO_3 (1.4 g, 20.4 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 1 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (PE: EA = 2: 1) to afford 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)-5-(azidomethyl)oxazoli din-2-one (8) (2.97 g, 84%) as a white solid.

LC-MS (ESI) m/z = 348 $[M+H]^+$.

Step 7: Preparation of 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)-5-(aminomethyl)oxazol idin-2-one (OBD-113):

To a solution of

3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)-5-(azidomethyl)oxazolidin-2-one (8) (2.97 g, 8.5 mmol) in MeOH (10 mL) was added palladium carbon (300 mg) at 25°C, then the reaction mixture was stirred at room temperature for overnight under a hydrogen gas atmosphere, monitored by TLC. The filtrate was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)-5-(aminomethyl)oxazolidin-2-one (OBD-113) (2.2 g, 81 %) as a white solid.

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.53 – 7.35 (m, 1H), 7.09 (d, J = 8.9 Hz, 1H), 6.96 – 6.73 (m, 1H), 4.66 (s, 1H), 4.40 (s, 1H), 4.00 (t, J = 8.7 Hz, 1H), 3.89 – 3.74 (m, 1H), 3.06 (dd, J = 21.9, 11.0 Hz, 6H), 2.27 – 1.85 (m, 4H).

LC-MS (ESI) m/z = 322 $[M+H]^+$.

Step 8: Preparation of (OBD-110, 111):

To a solution of 3-(4-(8-oxa-3-aza-bicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)-5-(aminomethyl)oxazolidin-2-one (OBD-113) (200 mg, 0.62 mmol) and R-OH (0.62 mmol) in DCM (10 mL) were added HOBt (126 mg, 0.96 mmol), EDCI (237 mg, 1.24 mmol) and DIPEA (160 mg, 1.24 mmol) at 25 °C, then the reaction mixture was stirred at 25 °C for 2 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 80: 1) to afford (OBD-110, 111) as a white solid.

OBD-110

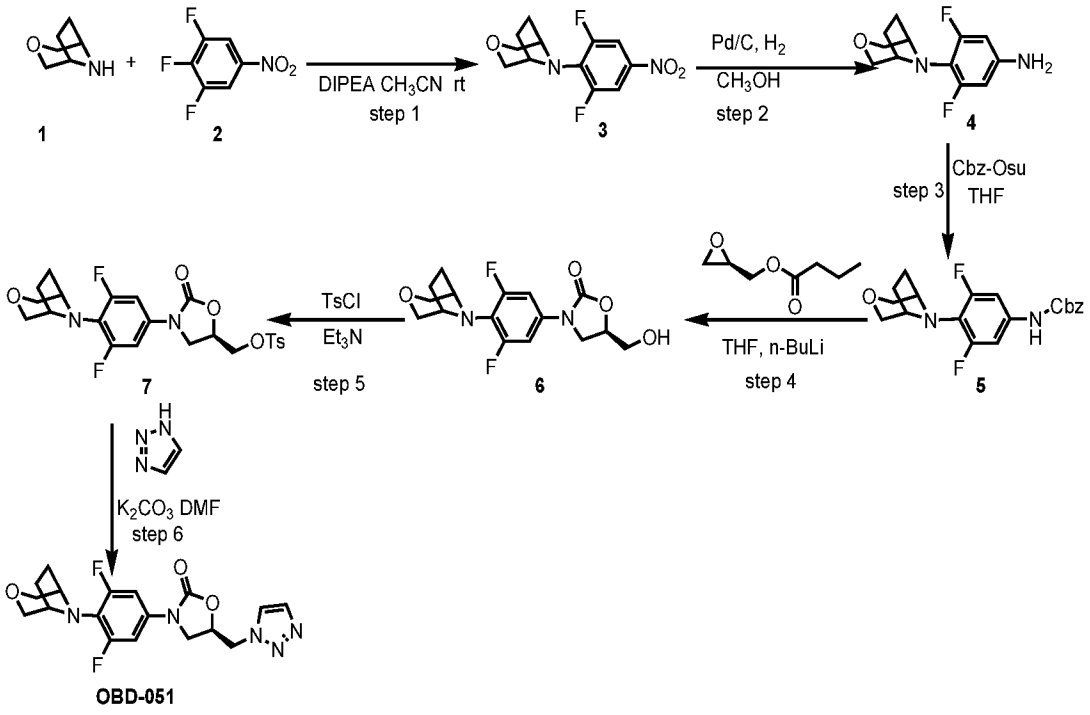
^{1}H NMR (301 MHz, $CDCl_3$) δ 7.51 – 7.32 (m, 1H), 7.02 (d, J = 8.5 Hz, 1H), 6.83 (t, J = 9.1 Hz, 1H), 6.07 (s, 1H), 4.74 (s, 1H), 4.39 (s, 2H), 4.00 (t, J = 8.9 Hz, 1H), 3.85 – 3.49 (m, 3H), 3.05 (dd, J = 23.2, 10.6 Hz, 4H), 2.32 – 1.67 (m, 8H).

LC-MS (ESI) m/z = 426 $[M+H]^+$.

OBD-111

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.03 (s, 1H), 6.17 (s, 0H), 5.20 – 5.02 (m, 1H), 4.85 – 4.62 (m, 1H), 4.41 (s, 1H), 4.01 (s, 1H), 3.68 (s, 3H), 3.09 (d, *J* = 7.9 Hz, 2H), 2.05 (d, *J* = 42.7 Hz, 3H), 1.83 – 1.35 (m, 3H).

LC-MS (ESI) m/z = 397.7 $[M+H]^+$.



Step 1: Preparation of

8-(2,6-difluoro-4-nitrophenyl)-3-oxa-8-aza-bicyclo[3.2.1]octane (3):

To a solution of 3-oxa-8-aza-bicyclo[3.2.1]octane (1) (5.0 g, 44.2 mmol) and 1,2,3-trifluoro-5-nitrobenzene (8.6 g, 48.6 mmol) in DMF (10 mL) was added K_2CO_3 (12.2 g, 88.4 mmol) at 25°C then the reaction mixture was stirred at 80°C for

2 h under a nitrogen gas atmosphere, monitored by TLC. The mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (EA: PE = 3: 1) to afford 8-(2,6-difluoro-4-nitrophenyl)-3-oxa-8-aza-bicyclo[3.2.1]octane (3) (9.3 g, 78%) as a yellow solid.

LC-MS (ESI) m/z = 271 $[M+H]^+$.

Step 2: Preparation of 4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorobenzenamine (4):

To a solution of 3-(2,6-difluoro-4-nitrophenyl)-8-oxa-3-aza-bicyclo[3.2.1]octane (3) (9.3 g, 34.4 mmol) and Palladium carbon (1 g) in MeOH (15 mL), then under a hydrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. The filtrate was concentrated under reduced pressure to afford 4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorobenzenamine (4) (7.8 g, 95%) as a white oil, and the crude material was used for next reaction without further purification.

LC-MS (ESI) m/z = 241 $[M+H]^+$.

Step 3: Preparation of benzyl 4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenylcarbamate (5):

Carbonic acid, 2,5-dioxo-1-pyrrolidinyl phenylmethyl ester (12 g, 48.7 mmol) was added to a suspension of 4-(3-oxa-8-aza-bicyclo[3.2.1]octan-3-yl)-3,5-difluorobenzenamine (4) (7.8 g, 32.5 mmol) in THF (100 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at 50°C for 5 h, monitored by TLC. The mixture was

concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (PE: EA = 10: 1) to afford benzyl 4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenylcarbamate (5) (8.2 g, 68%) as a white solid.

LC-MS (ESI) m/z = 375 $[M+H]^+$.

Step 4: Preparation of (5R)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (6):

To a solution of benzyl 4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenylcarbamate (5) (8.2 g, 22.1 mmol) in THF (10 mL) at – 78 °C under a nitrogen gas atmosphere was added n-BuLi (13.8 ml, 33.1 mmol), then the mixture was stirred at -78°C for 30 min, after that the solution of (R)-oxiran-2-ylmethyl butyrate (4.7 g, 33.1 mmol) in THF was added to the mixture at -78°C, then warmed to room temperature and stirred for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 70: 1) to afford (5R)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (6) (4.5 g, 60%) as a white solid.

LC-MS (ESI) m/z = 341 $[M+H]^+$.

Step 5: Preparation of ((R)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (7):

4-methylbenzene-1-sulfonyl chloride (5 g, 26.6 mmol) was added to a suspension of (5R)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (6) (4.5 g, 13.3 mmol) and Et_3N (2.7 g, 26.6 mmol) in DCM (10 mL) at 0 °C under a nitrogen gas atmosphere and the reaction mixture was stirred at room temperature for overnight, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford ((R)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (7) (5.58 g, 85%) as a white solid.

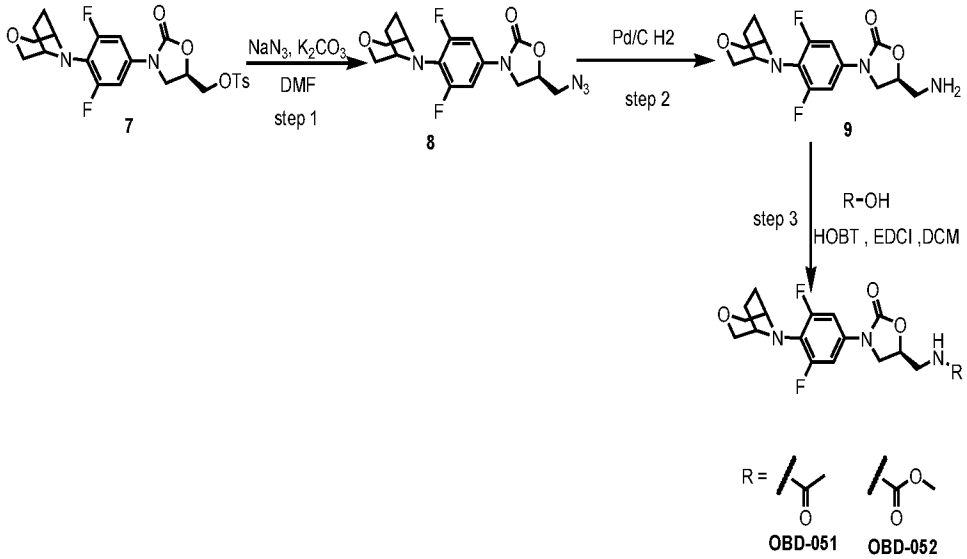
LC-MS (ESI) m/z = 495 $[M+H]^+$.

Step 6: Preparation of (5R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)oxazolidin-2-one (OBD-055):

To a solution of ((R)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (7) (300 mg, 0.6 mmol) and 1H-1,2,3-triazole (42 mg, 0.6 mmol) in DMF (10 mL) was added K_2CO_3 (166 mg, 1.2 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 1 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by prep-HPLC to afford (5R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)oxazolidin-2-one (OBD-055) (82 mg, 35%) as a white solid.

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.76 (d, J = 5.7 Hz, 2H), 6.94 (d, J = 12.1 Hz, 2H), 5.06 (s, 1H), 4.78 (d, J = 4.1 Hz, 1H), 4.08 (t, J = 9.0 Hz, 1H), 3.90 (t, J = 8.9 Hz, 4H), 3.58 (d, J = 10.4 Hz, 2H), 2.04 (t, J = 8.0 Hz, 4H), 1.76 (s, 2H).

LC-MS (ESI) m/z = 391.8 $[M+H]^+$.



Step 1: Preparation of (5R)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(azidomethyl)oxazolidin-2-one (8):

To a solution of ((R)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-2-oxooxazolidin-5-yl)methyl 4-methylbenzenesulfonate (7) (4 g, 8 mmol) and sodium azide (526 mg, 8 mmol) in DMF (10 mL) was added K_2CO_3 (2.2 g, 16 mmol) at 25°C, then the reaction mixture was stirred at 80°C for 1 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with EA, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (PE: EA = 2: 1) to afford (5R)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(azidomethyl)oxazolidin-2-one (8) (2.4 g, 82%) as a white solid.

LC-MS (ESI) m/z = 366 $[M+H]^+$.

Step 2: Preparation of (5S)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(aminomethyl)oxazolidin-2-one (9):

To a solution of (5R)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(azidomethyl)oxazolidin-2-one (8) (2.4 g, 6.5 mmol) in MeOH (10 mL) was added palladium carbon (300 mg) at 25°C, then the reaction mixture was stirred at room temperature for overnight under a hydrogen gas atmosphere, monitored by TLC. The filtrate was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 50: 1) to afford (5S)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(aminomethyl)oxazolidin-2-one (9) (1.9 g, 86 %) as a white solid.
LC-MS (ESI) m/z = 340 $[M+H]^+$.

Step 3: Preparation of (OBD-051, 052):

To a solution of (5S)-3-(4-(3-oxa-8-aza-bicyclo[3.2.1]octan-8-yl)-3,5-difluorophenyl)-5-(aminomethyl)oxazolidin-2-one (9) (200 mg, 0.59 mmol) and R-OH (0.59 mmol) in DCM (10 mL) were added HOBt (119 mg, 0.88 mmol), EDCI (224 mg, 1.18 mmol) and DIPEA (152 mg, 1.18 mmol) at 25 °C, then the reaction mixture was stirred at 25 °C for 2 h under a nitrogen gas atmosphere, monitored by TLC. Quenched with ammonium chloride, extracted with DCM, the organic layer was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (DCM: MeOH = 80: 1) to afford (OBD-051, 052) as a white solid.

OBD-051

^{1}H NMR (301 MHz, $CDCl_3$) δ 6.99 (t, *J* = 9.3 Hz, 2H), 5.38 (s, 1H), 4.84 – 4.69 (m, 1H), 3.98 – 3.86 (m, 4H), 3.75 – 3.60 (m, 4H), 2.24 – 1.97 (m, 8H).

LC-MS (ESI) m/z = 381.9 $[M+H]^+$.

OBD-052

^{1}H NMR (301 MHz, $CDCl_3$) δ 7.06 (d, *J* = 12.4 Hz, 2H), 5.10 (s, 1H), 4.75 (s, 1H), 4.02 – 3.86 (m, 4H), 3.68 (s, 2H), 3.58 (d, *J* = 9.6 Hz, 2H), 2.02 (d, *J* = 7.7 Hz, 2H), 1.80 (s, 4H), 0.98 (d, *J* = 6.7 Hz, 3H).

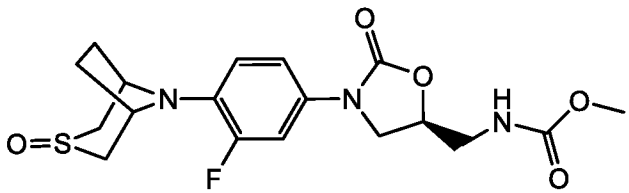
LC-MS (ESI) m/z = 398.0 $[M+H]^+$.

Example 13

Synthesis of Additional Embodiments of the Invention

In a manner similar to those disclosed in Examples 8 and 12 above, the following compounds were made:

OTB-518

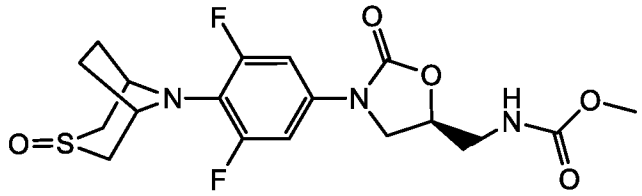


Methyl (((5*S*)-3-(3-fluoro-4-((1R,5S)-3-oxido-3-thia-8-azabicyclo[3.2.1]octan-8-yl)phenyl)-2-oxooxazolidin-5-yl)
methyl)carbamate

1H-NMR (400 MHz, CDCl3) δ: 7.45 (d, J = 16.4 Hz, 1 H), 7.12 (d, J = 7.6 Hz, 1 H), 6.83 (t, J = 9.2 Hz, 1 H), 5.17-5.12 (m, 1 H), 4.80-4.74 (m, 1 H), 4.62 (brs, 2 H), 4.02 (t, J = 8.4 Hz, 1 H), 3.77 (t, J = 8.0 Hz, 1 H), 3.69-3.53 (m, 4 H), 3.45 (d, J = 10.4 Hz, 2 H), 2.86 (d, J = 12.0 Hz, 2 H), 2.22 (m, 2 H), 1.90-1.88 (m, 2 H).

HRMS (ESI): m/z [M + H]+ calcd for $C_{18}H_{23}FN_3O_5S$: 412.1344; found: 412.1359

OTB-519

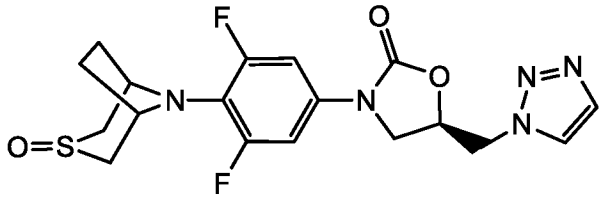


Methyl (((5*S*)-3-(3,5-difluoro-4-((1R,5S)-3-oxido-3-thia-8-azabicyclo[3.2.1]octan-8-yl)phenyl)-2-oxooxazolidin-5-yl)
methyl)carbamate

1H-NMR (400 MHz, CDCl3) δ: 7.13 (d, J = 12.4 Hz, 2 H), 5.10 (m, 1 H), 4.80-4.74 (m, 1 H), 4.46 (brs, 2 H), 3.98 (t, J = 8.8 Hz, 1 H), 3.76-3.69 (m, 4 H), 3.60-3.49 (m, 3 H), 2.94 (d, J = 12.0 Hz, 2 H), 2.20-2.18 (m, 2 H), 1.87-1.85 (m, 2 H).

HRMS (ESI): m/z [M + H]+ calcd for $C_{18}H_{22}F_2N_3O_5S$: 430.1248; found: 430.1259

OTB-517

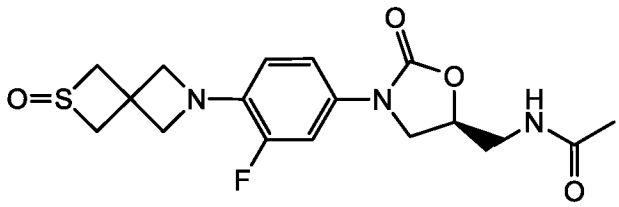


(5*R*)-5-((1H-1,2,3-Triazol-1-yl)methyl)-3-(3,5-difluoro-4-((1R,5S)-3-oxido-3-thia-8-azabicyclo[3.2.1]
octan-8-yl)phenyl)oxazolidin-2-one

1H-NMR (400 MHz, CDCl3) δ: 7.79 (s, 1 H), 7.77 (s, 1 H), 6.98 (d, J = 12.0 Hz, 2 H), 5.10-5.04 (m, 1 H), 4.79 (d, J = 4.0 Hz, 2 H), 4.43 (brs, 2 H), 4.10 (t, J = 9.2 Hz, 1 H), 3.91-3.87 (m, 1 H), 3.55 (d, J = 12.4 Hz, 2 H), 2.92 (d, J = 10.4 Hz, 2 H), 2.19-2.16 (m, 2 H), 1.88-1.83 (m, 2 H).

HRMS (ESI): m/z [M + H]+ calcd for $C_{18}H_{20}F_2N_5O_3S$: 424.1249; found: 424.1271

OTB-523

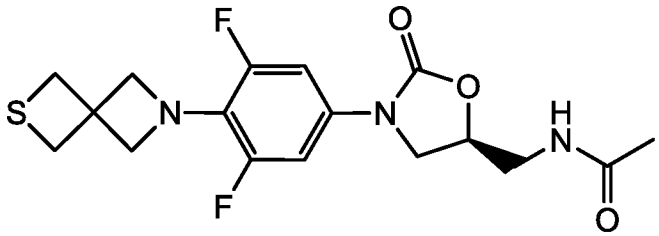


(*S*)-N-((3-(3-Fluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl) methyl)acetamide

1H-NMR (400 MHz, CDCl3) δ: 7.34 (d, J = 14.0 Hz, 1 H), 7.01 (d, J = 8.8 Hz, 1 H), 6.41 (t, J = 8.8 Hz, 1 H), 6.12 (t, J = 6.0 Hz, 1 H), 4.76-4.73 (m, 1 H), 4.01-3.90 (m, 7 H), 3.74-3.66 (m, 2 H), 3.62-3.56 (m, 1 H), 3.45-3.40 (m, 2 H), 2.02 (s, 3 H).

HRMS (ESI): m/z [M + H]+ calcd for C17H21FN3O4S: 382.1237; found: 382.1217

OTB-515

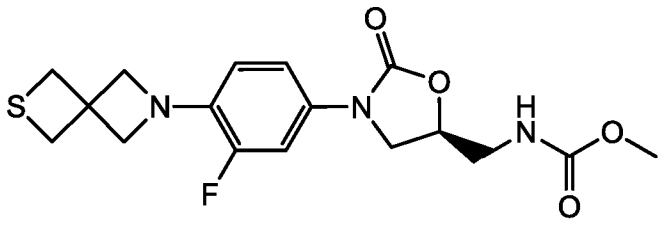


(*S*)-N-((3-(3,5-Difluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl) methyl)acetamide

HNMR (400 MHz, CDCl3) δ: 7.03-6.94 (m, 2 H), 6.09 (t, J = 5.6 Hz, 1 H), 4.75 (q, J = 3.2 Hz, J = 2.8 Hz, 1 H), 4.16 (s, 4 H), 3.95 (t, J = 8.8 Hz, 1 H), 3.72-3.61 (m, 3 H), 3.40 (s, 4 H), 2.03 (s, 3 H).

m/z [M + Na]+ calcd for $C_{17}H_{19}F_2N_3O_3S$:383.1115; found: 384.0

OTB-248

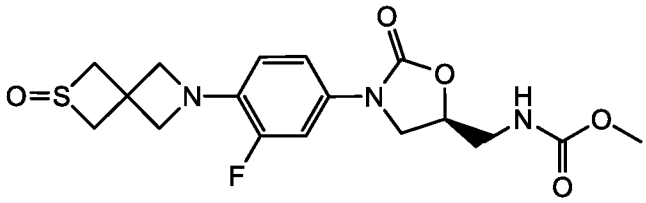


(*S*)-Methyl
((3-(3-fluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)carbamate

HNMR (400 MHz, CDCl3) δ: 7.33 (q, J = 2.0 Hz, J = 11.6 Hz, 2 H), 7.01 (d, J = 2.0 Hz, 1 H), 6.44 (t, J = 9.2 Hz, 1 H), 5.15 (bs, 1 H), 4.77-4.73 (m, 1 H), 4.01-3.97 (m, 4 H), 3.76-3.52 (m, 6 H), 3.42 (s, 4 H).

m/z [M + Na]+ calcd for $C_{17}H_{20}FN_3O_4S$:381.1159; found: 404.1

OTB-256

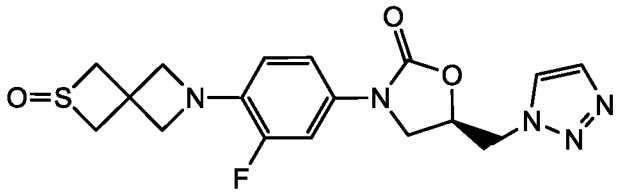


(*S*)-Methyl ((3-(3-fluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl) methyl)carbamate

1H-NMR (400 MHz, CDCl3) δ: 7.51 (d, J = 14.4 Hz, 1 H), 7.04 (d, J = 8.4 Hz, 1 H), 6.80 (t, J = 8.8 Hz, 1 H), 5.09 (brs, 1 H), 4.76 (brs, 1 H), 4.16 (d, J = 13.2 Hz, 4 H), 4.01-3.98 (m, 3 H), 3.77–3.75 (m, 1 H), 3.69 (s, 3 H), 3.61-3.55 (m, 2 H), 3.46-3.44 (m, 2 H).

HRMS (ESI): m/z [M + H]+ calcd for $C_{17}H_{21}FN_3O_5S$: 398.1186; found: 398.1166

OTB-247

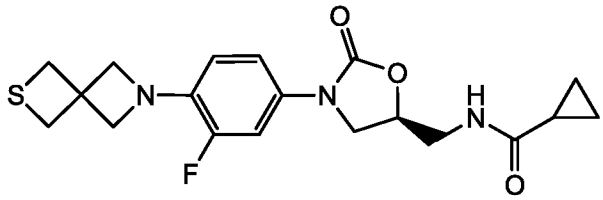


(*R*)-5-((1H-1,2,3-Triazol-1-yl)methyl)-3-(3-fluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl) phenyl)oxazolidin-2-one

HNMR(400 MHz, CDCl3) δ: 7.78 (d, J = 0.8 Hz, 1H), 7.74 (d, J = 0.8 Hz, 1H), 7.18 (dd, J = 13.6, 2.4 Hz, 1H), 6.87 (dd, J = 8.8, 1.6 Hz, 1H), 6.37 (t, J = 9.2 Hz, 1H), 5.04 - 5.00 (m, 1H), 4.77 (d, J = 3.6 Hz, 2H), 4.08 (t, J = 9.2 Hz, 1H), 3.96 (dd, J = 10.4, 1.6 Hz, 4H), 3.92 - 3.89 (m, 3H), 3.42 - 3.39 (m, 2H).

m/z [M + H]+ calcd for $C_{17}H_{18}FN_5O_3S$: 391.1114; found: 392.0

OTB-249

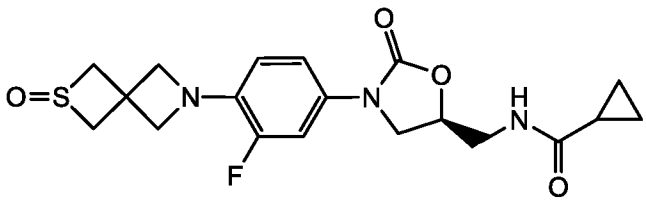


(*S*)-N-((3-(3-Fluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl) methyl)cyclopropanecarboxamide

1H-NMR (400 MHz, CDCl3) δ: 7.33 (d, J = 14.0 Hz, 1 H), 6.99 (d, J = 8.8 Hz, 1 H), 6.47 (t, J = 9.2 Hz, 1 H), 6.13 (brs, 1 H), 4.73 (m, 1 H), 3.98-3.95 (m, 5 H), 3.73-3.66 (m, 3 H), 3.42 (s, 4 H), 1.39-1.37 (m, 1 H), 0.97-0.91 (m, 2 H), 0.78-0.76 (m, 2 H).

HRMS (ESI): m/z [M + H]+ calcd for $C_{19}H_{23}FN_3O_3S$: 392.1444; found: 392.1426

OTB-255

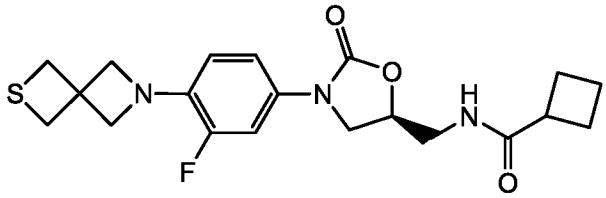


(*S*)-N-((3-(3-Fluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl) methyl)cyclopropanecarboxamide

1H-NMR (400 MHz, CDCl3) δ: 7.35 (d, J = 14.0 Hz, 1 H), 7.01 (d, J = 8.4 Hz, 1 H), 6.44 (t, J = 9.2 Hz, 1 H), 6.13 (brs, 1 H), 4.74 (m, 1 H), 4.00-3.91 (m, 7 H), 3.75-3.62 (m, 3 H), 3.47-3.41 (m, 2 H), 1.38-1.37 (m, 1 H), 0.97-0.92 (m, 2 H), 0.78-0.76 (m, 2 H).

HRMS (ESI): m/z [M + H]+ calcd for C19H23FN3O4S: 408.1393; found: 408.1378

OTB-250

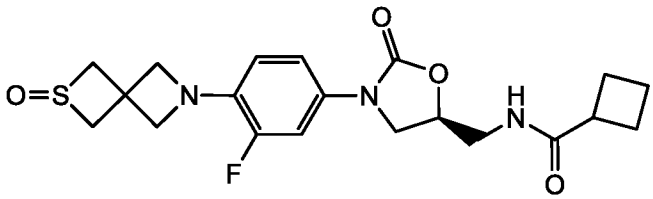


(*S*)-N-((3-(3-Fluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl) methyl)cyclobutanecarboxamide

HNMR (400 MHz, CDCl3) δ: 7.76 (d, J = 8.8 Hz, 2 H), 6.92-6.83 (m, 2 H), 5.04 (m, 1 H), 4.78 (q, J = 0.8 Hz, J = 3.2 Hz 2 H), 4.15 (t, J = 2.4 Hz, 4 H), 3.85 (t, J = 6.0 Hz, 1 H), 3.72-3.63 (m, 3 H), 3.40 (s, 4 H), 3.05-2.99 (m, 1 H), 2.24-2.13 (m, 4 H), 1.97-1.60 (m ,2 H).

m/z [M + Na]+ calcd for $C_{20}H_{24}FN_3O_3S$: 405.1522; found: 428.2

OTB-254

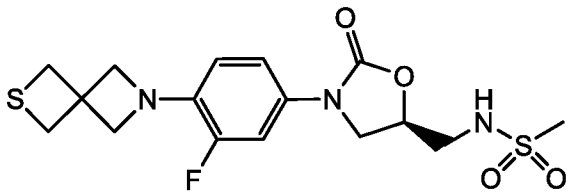


(S)-N-((3-(3-fluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl) methyl)cyclobutanecarboxamide

1H-NMR (400 MHz, CDCl3) δ: 7.36 (d, J = 14.4 Hz, 1 H), 7.00 (d, J = 8.0 Hz, 1 H), 6.47 (t, J = 9.2 Hz, 1 H), 5.80 (brs, 1 H), 4.73 (brs, 1 H), 4.00 (d, J = 12.0 Hz, 4 H), 3.95-3.92 (m, 3 H), 3.76-3.72 (m, 1 H), 3.65-3.62 (m, 2 H), 3.47-3.41 (m, 2 H), 3.02-2.96 (m, 1 H), 2.26-2.13 (m, 4 H), 1.98-1.84 (m, 2 H).

HRMS (ESI): m/z [M + H]+ calcd for $C_{20}H_{25}FN_3O_4S$: 422.1549; found: 422.1531

OTB-260-2A

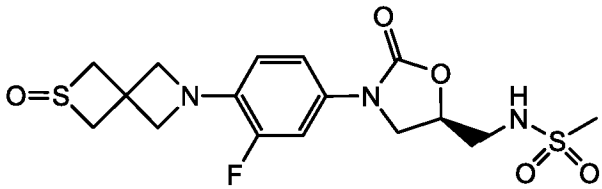


(*R*)-N-((3-(3-Fluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl)methyl) methanesulfonamide

HNMR (400 MHz, CDCl3) δ: 7.04 - 6.95 (m, 2H), 5.05 (s, 1H), 4.80 - 4.77 (m, 1H), 4.15 (t, J = 2.4 Hz, 4H), 3.97 (t, J = 8.8 Hz, 1H), 3.86 (dd, J = 6.4, 8.8 Hz, 1H), 3.56 (dd, J = 3.6, 14.4 Hz, 1H), 3.43 - 3.39 (m, 5H), 3.01 (s, 3H).

m/z [M + H]+ calcd for $C_{16}H_{20}FN_3O_4S_2$: 401.0879; found: 402.1

OTB-260-2B

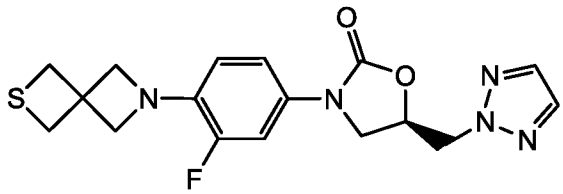


(*R*)-N-((3-(3-Fluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl) methyl)methanesulfonamide

HNMR (400 MHz, $CDCl_3$) δ: 7.32 (dd, J = 14.0, 2.4 Hz, 1H), 7.04 - 7.02 (m, 1H), 6.41 (t, J = 9.6 Hz, 1H), 4.86 - 4.77 (m, 2H), 4.04 - 3.95 (m, 8H), 3.93 (dd, J = 9.6, 3.2 Hz, 1H), 3.43 - 3.40 (m, 3H), 3.02 (s, 3H).

m/z [M + H]+ calcd for $C_{16}H_{20}FN_3O_5S_2$: 417.0828; found: 418.0

OTB-260-5A

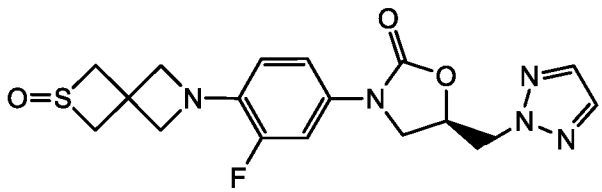


(*R*)-5-((2H-1,2,3-Triazol-2-yl)methyl)-3-(3-fluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl) phenyl)oxazolidin-2-one

HNMR (400 MHz, $CDCl_3$) δ: 7.64 (s, 2H), 7.24 - 7.21 (m, 1H), 6.99 (dd, J = 8.8, 1.6 Hz, 1H), 6.41 (t, J = 9.6 Hz, 1H), 5.12 - 5.06 (m, 1H), 4.87 - 4.82 (m, 1H), 4.75 - 4.72 (m, 1H), 4.05 - 4.01 (m, 1H), 3.96 - 3.93 (m, 5H), 3.40 (s, 4H).

m/z [M + H]+ calcd for $C_{17}H_{18}FN_5O_2S$: 375.1165; found: 376.1

OTB-260-5B

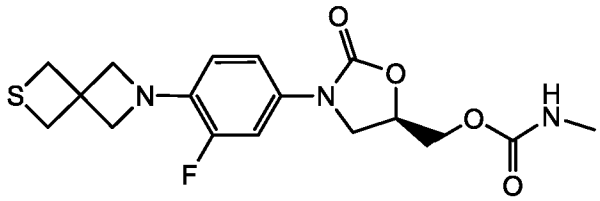


(*R*)-5-((2H-1,2,3-Triazol-2-yl)methyl)-3-(3-fluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl) phenyl)oxazolidin-2-one

HNMR (400 MHz, $CDCl_3$) δ: 7.64 (s, 2H), 7.27 - 7.23 (m, 1H), 6.99 (dd, J = 8.8, 2.0 Hz, 1H), 6.39 (t, J = 9.2 Hz, 1H), 5.11 - 5.06 (m, 1H), 4.87 - 4.82 (m, 1H), 4.76 - 4.70 (m, 1H), 4.06 - 4.03 (m, 1H), 3.98 - 3.90 (m, 7H), 3.43 - 3.40 (m, 2H).

m/z [M + H]+ calcd for $C_{17}H_{18}FN_5O_3S$: 391.1114; found: 392.1

OTB-260-4A

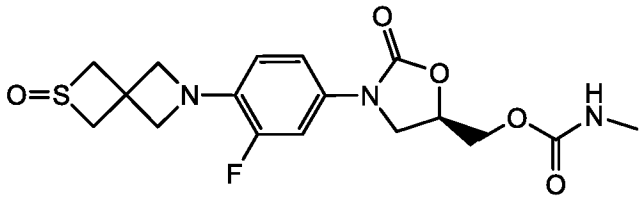


(*R*)-(3-(3-Fluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl)methyl methylcarbamate

HNMR (400 MHz, $CDCl_3$) δ: 7.33 (dd, J = 2.4, 13.6 Hz, 1H), 7.04 (dd, J = 1.6, 8.4 Hz, 1H), 6.44 (t, J = 9.2 Hz, 1H), 4.88 - 4.72 (m, 2H), 4.33 (t, J = 4.0 Hz, 2H), 4.02 (t, J = 9.2 Hz, 1H), 3.97 (d, J = 1.6 Hz, 4H), 3.77 (dd, J = 6.4, 8.8 Hz, 1H), 3.42 (s, 4H), 2.80 (d, J = 4.8 Hz, 3H).

m/z [M + H]+ calcd for $C_{17}H_{20}FN_3O_4S$: 381.1159; found: 382.0

OTB-260-4B

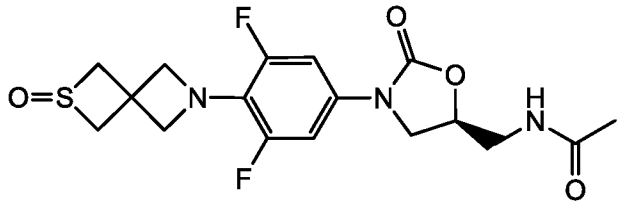


(*R*)-(3-(3-Fluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl)methyl methylcarbamate

HNMR (400 MHz, $CDCl_3$) δ: 7.35 (dd, J = 2.0, 11.6 Hz, 1H), 7.06 (d, J = 8.4 Hz, 1H), 6.42 (t, J = 9.2 Hz, 1H), 4.89 - 4.70 (m, 2H), 4.42 - 4.26 (m, 2H), 4.08 - 3.88 (m, 7H), 3.84 - 3.71 (m, 1H), 3.47 - 3.37 (m, 2H), 2.81 (m, 3H).

m/z [M + H]+ calcd for $C_{17}H_{20}FN_3O_5S$: 397.1108; found: 398.0

OTB-520

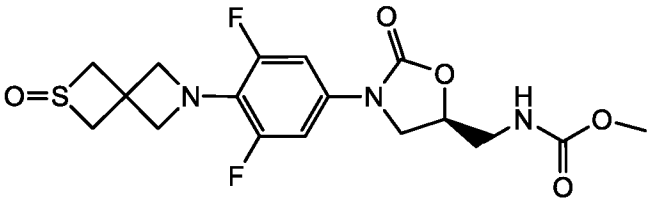


(*S*)-N-((3-(3,5-Difluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)acetamide

1H-NMR (400 MHz, CDCl3) δ: 7.02 (d, J = 12.0 Hz, 2 H), 5.92 (brs, 1 H), 4.75-4.74 (m, 1 H), 4.16 (d, J = 12.0 Hz, 4 H), 3.97-3.90 (m, 2 H), 3.72-3.65 (m, 4 H), 3.41-3.37 (m, 2 H), 2.02 (s, 3 H).

HRMS (ESI): m/z [M + H]+ calcd for $C_{17}H_{20}F_2N_3O_4S$: 400.1143; found: 400.1158

OTB-253

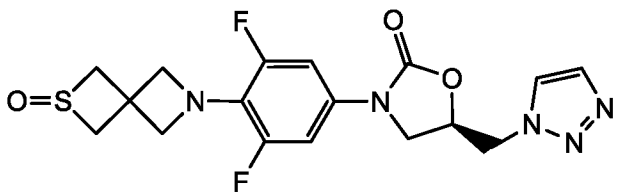


(*S*)-Methyl ((3-(3,5-difluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)carbamate

1H-NMR (400 MHz, CDCl3) δ: 7.00 (d, J = 10.8 Hz, 2H), 5.36 (m, 1H), 4.72 (m, 1H), 4.14 (d, J = 12.0 Hz, 4H), 3.92 (m, 3H), 3.69 (m, 1H), 3.67 (s, 3H), 3.52 (m, 2H), 3.39 (d, J = 12.4 Hz, 2H).

HRMS (ESI) calcd for $C_{17}H_{20}F_2N_3O_5S$ [M+H]+ 416.1086, found: 416.1073

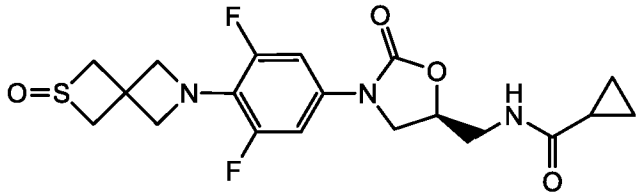
OTB-522



HNMR (400 MHz, $CDCl_3$) δ: 7.75 (d, J = 8.0 Hz, 2H), 6.92 - 6.83 (m, 2H), 5.05 - 5.01 (m, 1H), 4.77 (d, J = 4.0 Hz, 2H), 4.15 (dt, J = 11.6, 2.4 Hz, 4H), 4.05 (t, J = 9.2 Hz, 1H), 3.92 - 3.89 (m, 3H), 3.40 - 3.37 (m, 2H).

m/z [M + H]+ calcd for $C_{17}H_{17}F_2N_5O_3S$: 409.1020; found: 410.1

OTB-252

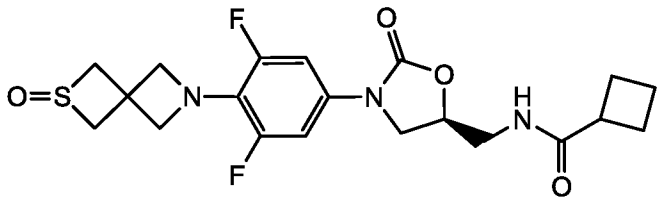


(*S*)-N-((3-(3,5-Difluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)cyclopropanecarboxamide

1H-NMR (400 MHz, CDCl3) δ: 6.98 (d, J = 11.6 Hz, 2H), 6.60 (m, 1H), 4.73 (m, 1H), 4.13 (d, J = 12.4 Hz, 4H), 3.91 (m, 3H), 3.70 (m, 1H), 3.64 (m, 2H), 3.79 (d, J = 10.4 Hz, 2H),1.41 (m, 1H), 0.94 (m, 1H), 0.87 (m, 1H), 0.74 (m, 2H)

HRMS (ESI) calcd for $C_{19}H_{22}F_2N_3O_4S$ [M+H]+ 426.1294, found: 426.1278

OTB-251

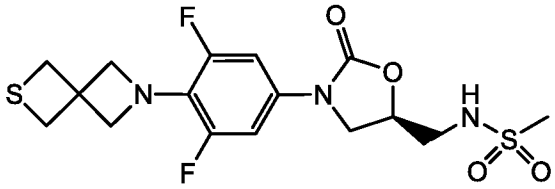


(*S*)-N-((3-(3,5-Difluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)cyclobutanecarboxamide

1H-NMR (400 MHz, CDCl3) δ: 6.99 (d, J = 10.4 Hz, 2H), 6.06 (m, 1H), 4.74 (m, 1H), 4.14 (d, J = 12.4 Hz, 4H), 3.93 (m, 3H), 3.70 (m, 1H), 3.62 (m, 2H), 3.38 (d, J = 12.4 Hz, 2H), 3.00 (m, 1H), 2.21 (m, 1H), 2.11 (m, 3H), 1.92 (m, 1H), 1.83 (m, 1H)

HRMS (ESI) calcd for $C_{20}H_{24}F_2N_3O_4S$ [M+H]+ 440.1450, found: 440.1441

OTB-516-2A

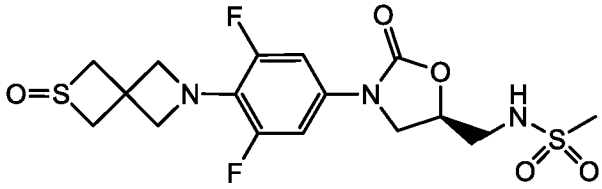


(*R*)-N-((3-(3,5-Difluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)methanesulfonamide

HNMR (400 MHz, CDCl3) δ: 7.04 - 6.95 (m, 2H), 5.05 (s, 1H), 4.80 - 4.77 (m, 1H), 4.15 (t, J = 2.4 Hz, 4H), 3.97 (t, J = 8.8 Hz, 1H), 3.86 (dd, J = 6.4, 8.8 Hz, 1H), 3.56 (dd, J = 3.6, 14.4 Hz, 1H), 3.43 - 3.39 (m, 5H), 3.01 (s, 3H).

m/z [M + H]+ calcd for $C_{16}H_{19}F_2N_3O_4S_2$: 419.0785; found: 420.1

OTB-516-2B

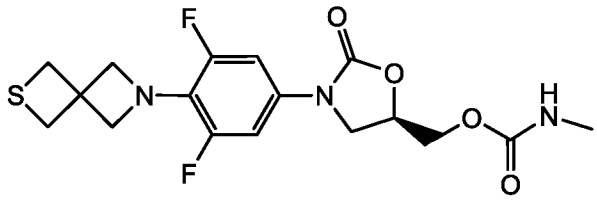


(*R*)-N-((3-(3,5-Difluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl)methyl)methanesulfonamide

HNMR (400 MHz, CDCl3) δ: 7.03 - 7.00 (m, 2H), 4.81 - 4.78 (m, 2H), 4.18 - 4.14 (m, 4H), 3.98 - 3.93 (m, 1H), 3.91 - 3.85 (m, 3H), 3.60-3.41 (m, 4H), 3.40 - 3.37 (m, 3H), 3.02 (s,3H).

m/z [M + H]+ calcd for $C_{16}H_{19}F_2N_3O_5S_2$: 435.0734; found: 436.0

OTB-516-4A

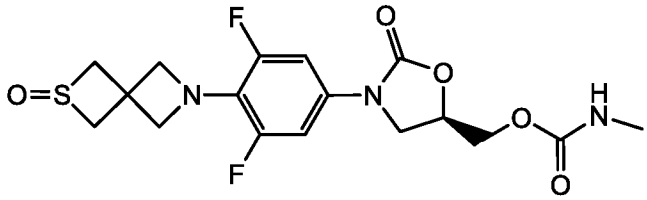


(*R*)-(3-(3,5-Difluoro-4-(2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl)methyl methylcarbamate

HNMR (400 MHz, $CDCl_3$) δ: 7.08 - 6.91 (m, 2H), 4.91 - 4.70 (m, 2H), 4.38 - 4.28 (m, 2H), 4.16 (t, J = 2.4 Hz, 4H), 3.98 (t, J = 9.2 Hz, 1H), 3.74 (dd, J = 6.4, 8.8 Hz, 1H), 3.43 - 3.37 (m, 4H), 2.81 (d, J = 4.8 Hz, 3H).

m/z [M + H]+ calcd for $C_{17}H_{19}F_2N_3O_4S$: 399.1064; found: 400.1

OTB-516-4B

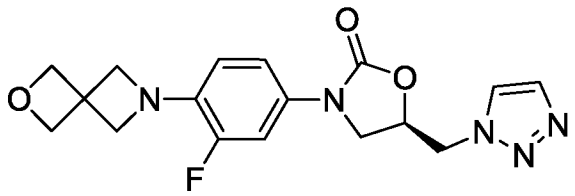


(*R*)-(3-(3,5-Difluoro-4-(2-oxido-2-thia-6-azaspiro[3.3]heptan-6-yl)phenyl)-2-oxooxazolidin-5-yl) methyl methylcarbamate

HNMR (400 MHz, $CDCl_3$) δ: 7.10 - 6.95 (m, 2H), 4.89 - 4.69 (m, 2H), 4.30 - 4.36 (m, 2H), 4.17 (d, J = 11.6 Hz, 4H), 4.02 - 3.89 (m, 3H), 3.74 (dd, J = 6.4, 8.6 Hz, 1H), 3.44 - 3.33 (m, 2H), 2.81 (d, J = 4.8 Hz, 3H).

m/z [M + H]+ calcd for $C_{17}H_{19}F_2N_3O_5S$: 415.1013; found: 416.0

OTB-204



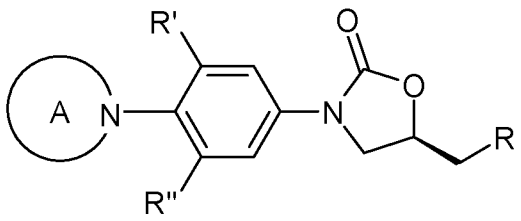
(*R*)-5-((1H-1,2,3-tTriazol-1-yl)methyl)-3-(3-fluoro-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)phenyl)oxazolidin-2-one

1H-NMR (400 MHz, CDCl3) δ: 7.65 (s, 2 H), 7.31 (d, J = 14.4, 2.4 Hz,1 H), 6.99 (d, J = 8.4 Hz, 1 H), 6.59 (t, J = 9.2 Hz, 1 H), 5.14-5.07 (m, 1 H), 4.88-4.83 (m, 5H), 4.77-4.71 (m, 1 H), 4.16 (s, 4 H), 4.07-4.02 (m, 1 H), 3.98-3.92 (m, 1 H)

HRMS (ESI): m/z [M + H]+calcd for $C_{17}H_{19}FN_5O_3$: 360.1472; found: 360.1451

The invention will be further described, without limitation, by the following numbered paragraphs:

1. A compound of Formula I, or a pharmaceutically acceptable salt, hydrate, or solvate of:



(I)

wherein:

R is independently OR_1, $OC(O)R_2$, $OC(O)NHR_2$, $OS(O_2)R_2$, $NHS(O)_2R_2$, NR_3R_4, $NHC(O)R_5$;

R' and R'' are independently H, F, Cl or OMe;

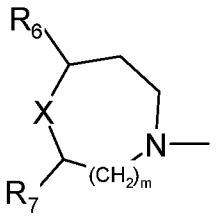
each R_1 is independently H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, wherein said alkyl, cycloalkyl are optionally substituted with 1 to 4 groups selected from halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkyloxy;

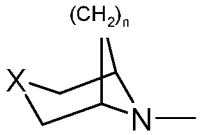
each R_2 is independently C_1-C_6 alkyl, C_3-C_8 cycloalkyl, heterocyclyl, heteroaryl or aryl, wherein said alkyl, cycloalkyl, heterocyclyl, heteroaryl, or aryl are optionally substituted with 1 to 4 groups selected from halo, hydroxyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 acyloxy, CF_3, NO_2, CN and NH_2;

each R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, heterocyclyl heteroaryl, aryl; or R_3 and R_4 taken together with the nitrogen to which they are attached, form a 4- to 8-membered heterocyclyl or heteroaryl with 1 to 3 additional heteroatoms selected from O, S, or N, wherein said alkyl, cycloalkyl, heterocyclyl, heteroaryl, or aryl are optionally substituted with 1 to 4 groups selected from halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, CF_3, NO_2, CN;

each R_5 is independently C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_1-C_6 alkoxy, heteroaryl, aryl, wherein said alkyl, cycloalkyl, heterocyclyl, heteroaryl, or aryl are optionally substituted with 1 to 4 groups selected from halo, hydroxyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 acyloxy, CF_3, NO_2, CN and NH_2;

Ring A is selected from:



,


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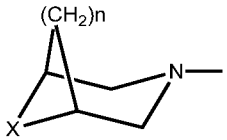
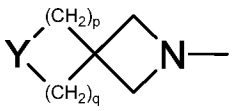


and


wherein,

each R_6 and R_7 is independently H, F, CH_3, CH_2CH_3, CF_3, phenyl;

X = O, S, SO, SO_2;

Y = O, S, SO, SO_2, and NR_8;

m is 1, or 2;

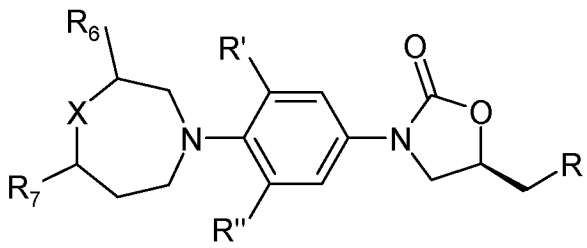
n is 1, or 2;

p is 1, or 2;

q is 1, or 2;

R_8 in independently H, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, $COCH_3$, and p-toluenesulfonyl, wherein said alkyl, cycloalkyl are optionally substituted with 1 to 4 groups selected from halo, hydroxyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 acyloxy, CF_3, NO_2, CN and NH_2.

2. The compound of paragraph 1, wherein the compound is represented by Formula II:



II

wherein,

R is independently OR_1, $OC(O)R_2$, NR_3R_4, $NHS(O)_2R_2$, $NHC(O)R_5$;

R' and R'' are independently H, or F;

R_1 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

R_2 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, phenyl; or R_3 and R_4 taken together with the nitrogen to which they are attached to form morpholine, thiamorpholine, piperazine and triazole;

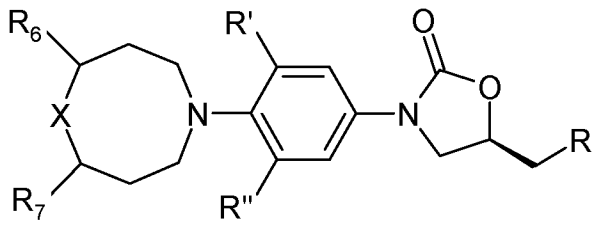
R_5 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, 5- or 6-membered heteroaryl or phenyl;

R_6 and R_7 is independently H, F, CH_3, CH_2CH_3, CF_3;

X = O, S, SO, SO_2; when X = S, SO, SO_2, R' = H, R'' = F, R_5 can not be CH_3;

3. The compound of paragraph 1, wherein the compound is represented by Formula

III:



III

wherein,

R is independently OR_1, $OC(O)R_2$, NR_3R_4, $NHS(O)_2R_2$, $NHC(O)R_5$;

R' and R'' are independently H, or F;

R_1 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

R_2 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

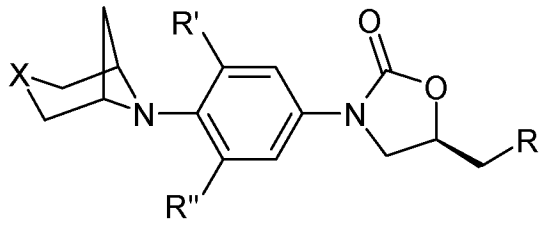
R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, or phenyl; or R_3 and R_4 taken together with the nitrogen to which they are attached to form morpholine, thiamorpholine, piperazine and triazole;

R_5 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, 5- or 6-membered heteroaryl or phenyl;

R_6 and R_7 is independently H, F, CH_3, CH_2CH_3, CF_3;

X = O, S, SO, SO_2;

4. The compound of paragraph 1, wherein the compound is represented by Formula IV:



IV

wherein,

R is independently OR_1, $OC(O)R_2$, NR_3R_4, $NHS(O)_2R_2$, $NHC(O)R_5$;

R' and R'' are independently H, or F;

R_1 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

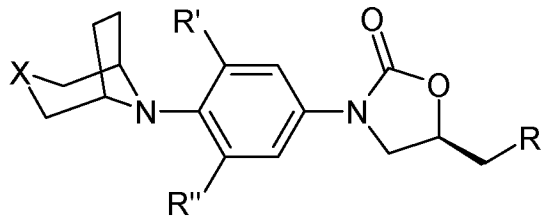
R_2 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, 5- or 6-membered heteroaryl or phenyl; or R_3 and R_4 taken together with the nitrogen to which they are attached, to form morpholine, thiamorpholine, piperazine and triazole;

R_5 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, 5- or 6-membered heteroaryl or phenyl; and

X = O, S, SO, SO_2.

5. The compound of paragraph 1, wherein the compound is represented by Formula V:



V

wherein,

R is independently OR_1, $OC(O)R_2$, NR_3R_4, $NHS(O)_2R_2$, $NHC(O)R_5$;

R' and R'' are independently H, or F;

R_1 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

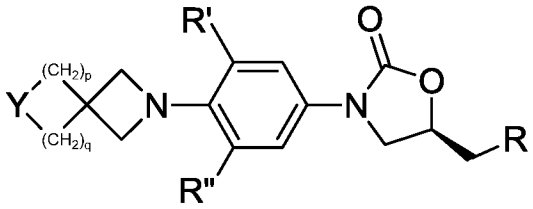
R_2 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, 5- or 6-membered heteroaryl or phenyl; or R_3 and R_4 taken together with the nitrogen to which they are attached, to form morpholine, thiamorpholine, piperazine and triazole;

R_5 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, 5- or 6-membered heteroaryl or phenyl; and

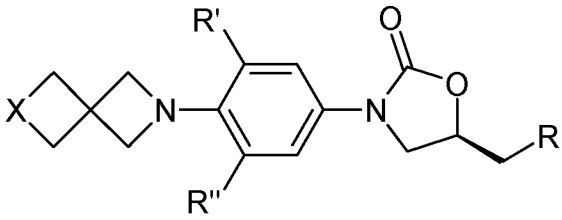
X = O, S, SO, SO_2.

6. The compound of paragraph 1, wherein the compound is represented by Formula VI:

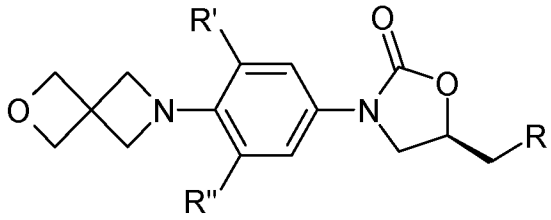


VI.

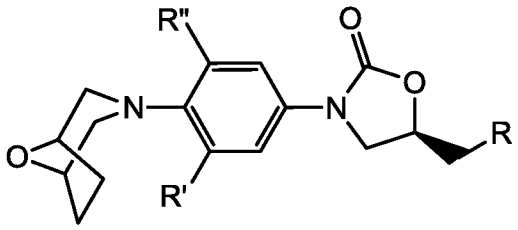
7. The compound of paragraph 6, wherein the compound is represented by Formula VII, Formula VIII, or Formula IX:



VII



VIII



IX

wherein,

R is independently OR_1, $OC(O)R_2$, NR_3R_4, $NHS(O)_2R_2$, $NHC(O)R_5$;

R' and R'' are independently H, or F;

R_1 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

R_2 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

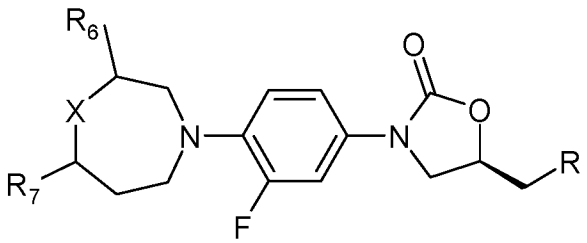
R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, 5- or 6-membered

heteroaryl or phenyl; or R_3 and R_4 taken together with the nitrogen to which they are attached, to form morpholine, thiamorpholine, piperazine and triazole;

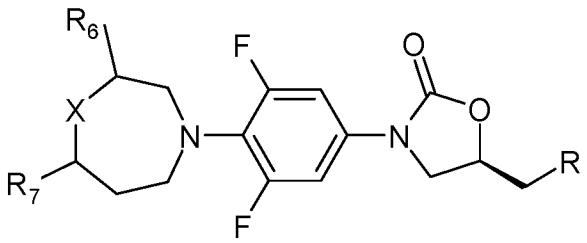
R_5 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, 5- or 6-membered heteroaryl or phenyl; and

X = O, S, SO, SO_2.

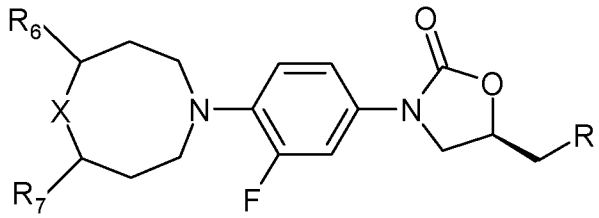
8. The compound of paragraph1, the compound is represented by Formula IIa, IIb, IIIa, IIIb, IVa, IVb, Va, Vb, VIIa, VIIb, VIIIa, VIIIb, IXa, or IXb:



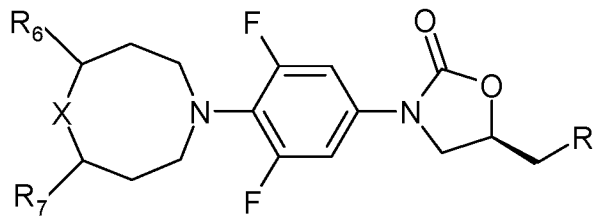
IIa



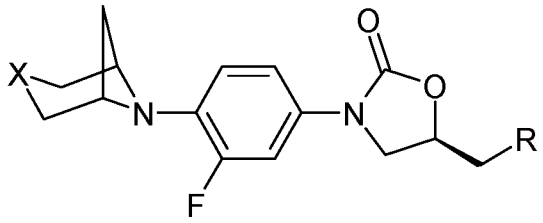
IIb



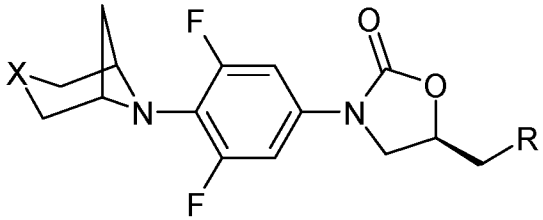
IIIa



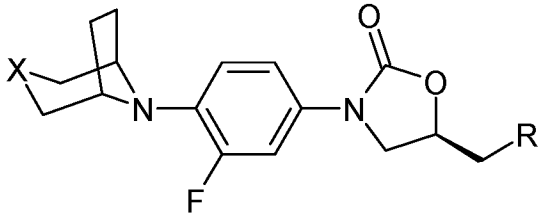
IIIb



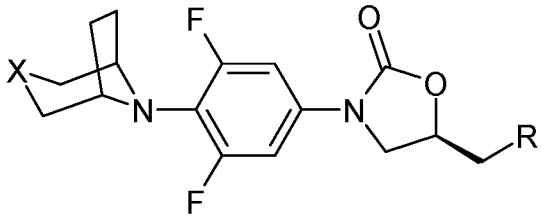
IVa



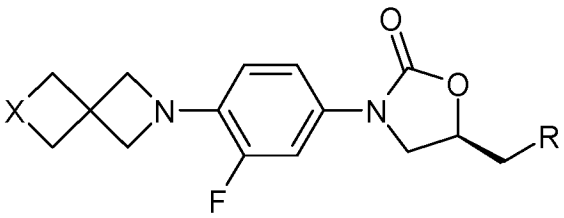
IVb



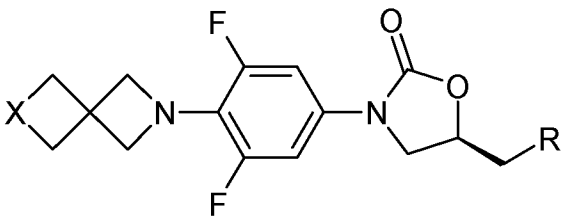
Va



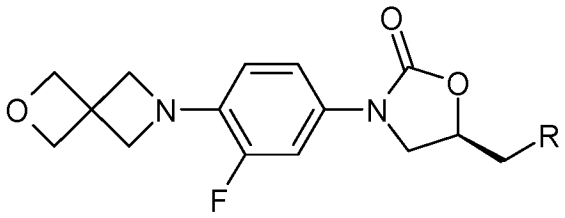
Vb



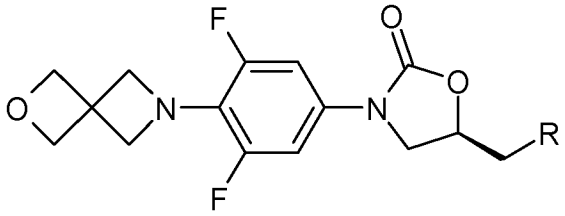
VIIa



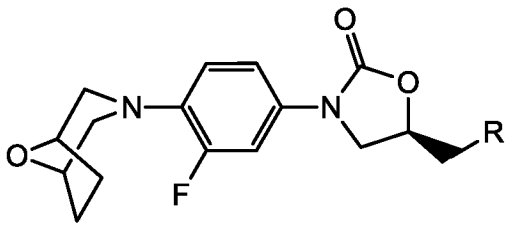
VIIb



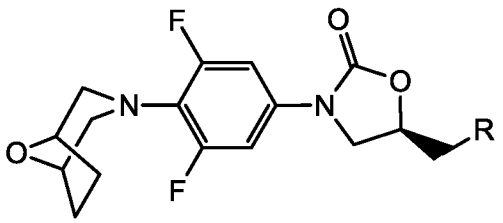
VIIIa



VIIIb



IXa



IXb

wherein,

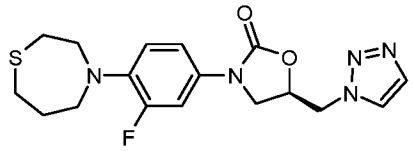
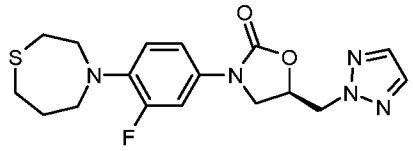
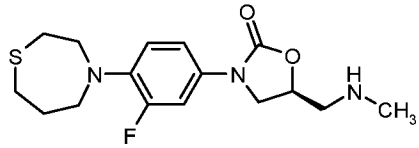
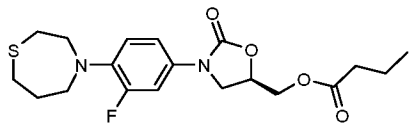
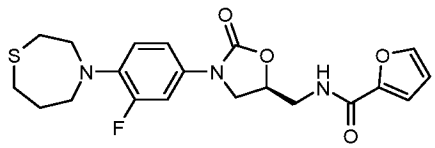
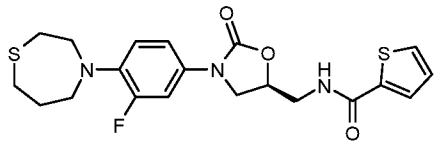
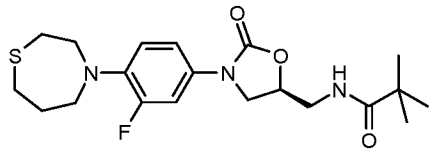
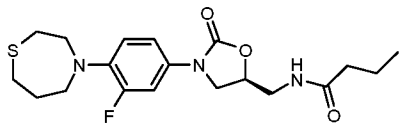
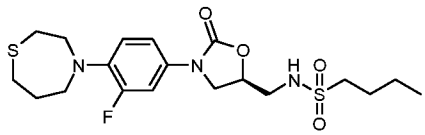
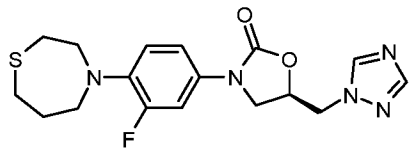
R is independently OH, OCH_3, OCH_2CH_3, $OC(O)CH_3$, NH_2, $NHCH_3$, NHC_6H_5, 1,2,3-triazole, 1,2,4-triazole, 1,2,5-triazole, $NHS(O)_2R_2$, $NHC(O)R_5$;

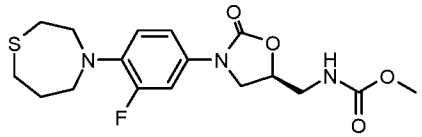
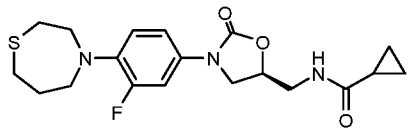
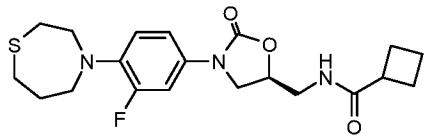
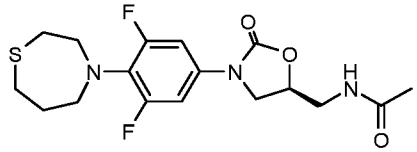
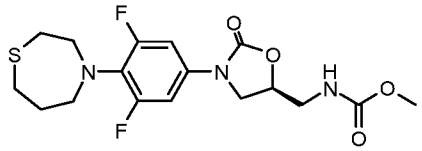
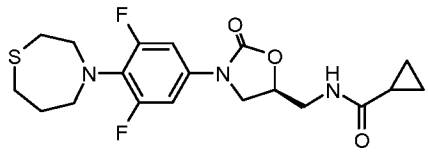
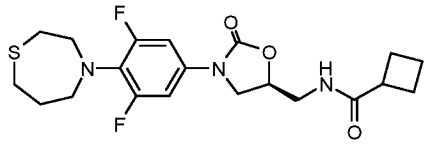
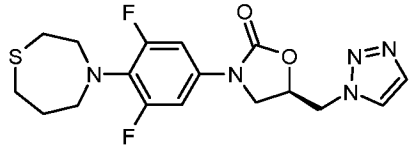
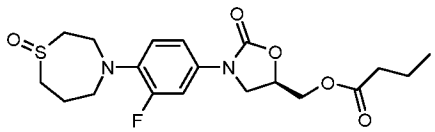
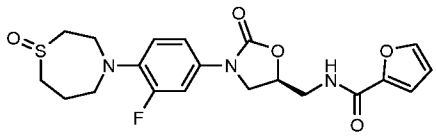
R_2 is independently C_1-C_6 alkyl;

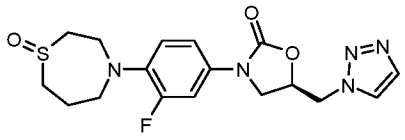
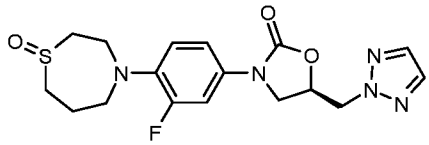
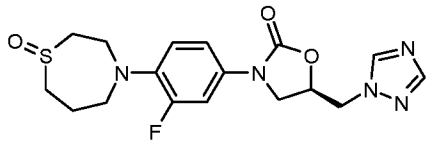
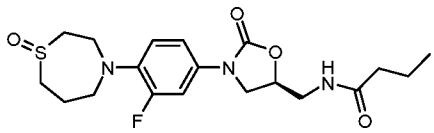
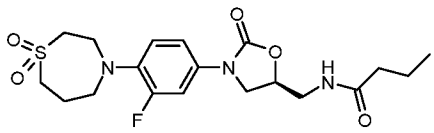
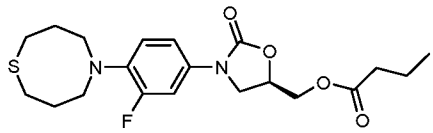
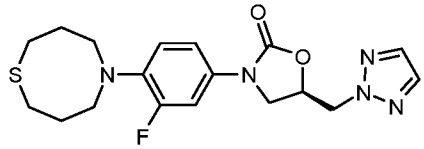
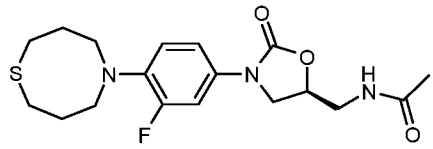
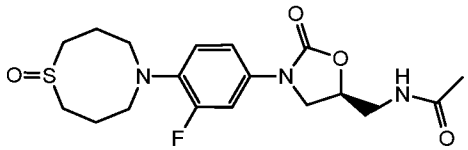
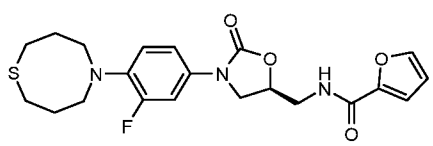
R_5 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, furan, thiophene or phenyl; in Formula IIa, R_5 can not be CH_3; and

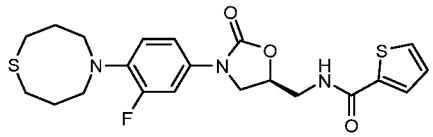
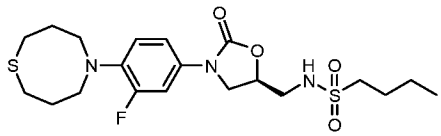
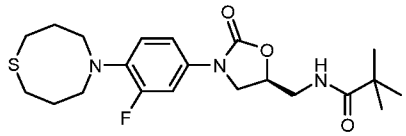
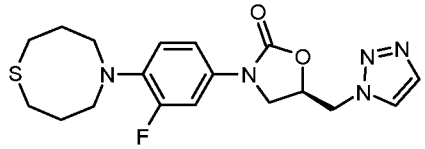
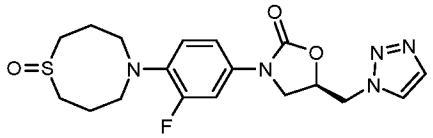
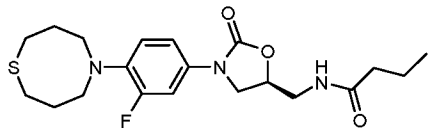
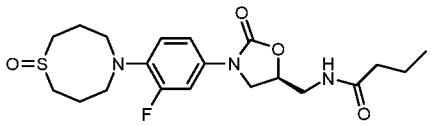
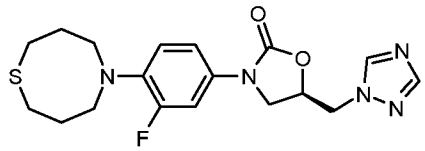
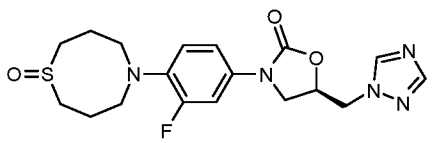
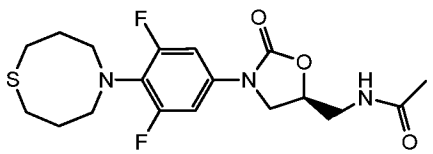
X = O, S, SO, SO_2.

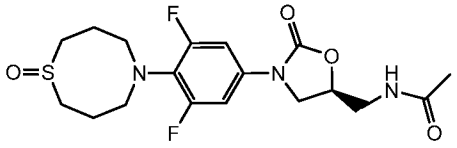
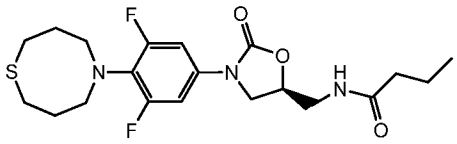
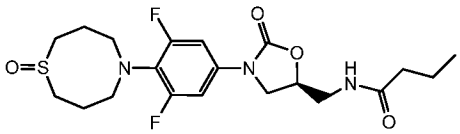
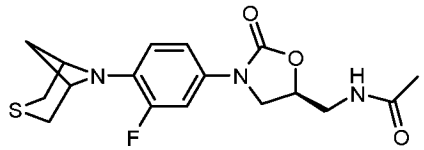
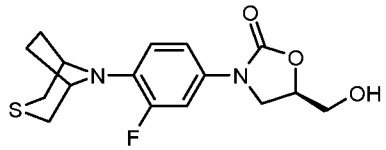
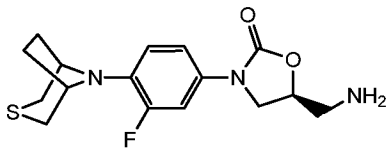
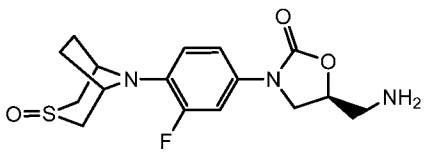
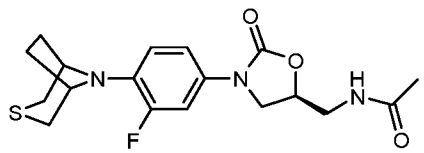
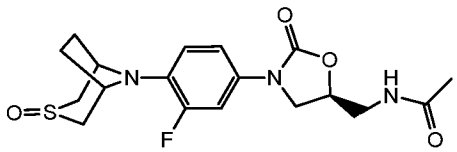
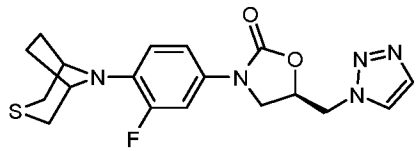
9. The compound of paragraph 1, wherein the compound is:

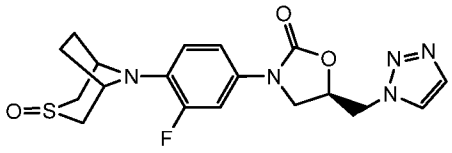
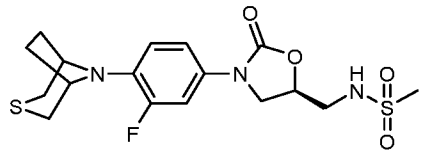
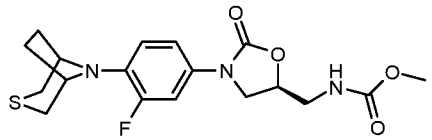
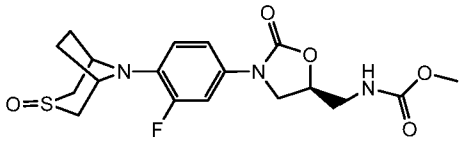
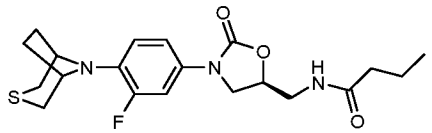
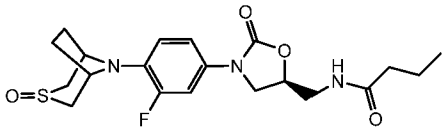
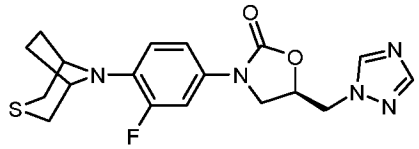
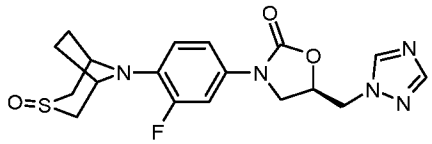
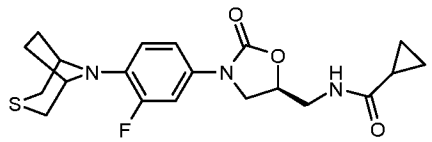
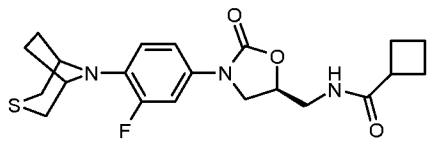
OTB-107	
OTB-106	
OTB-109	
OTB-108	
OTB-111	
OTB-112	
OTB-115	
OBD-005	
OTB-116	
OTB-119	

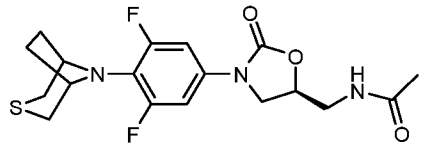
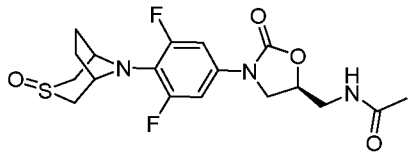
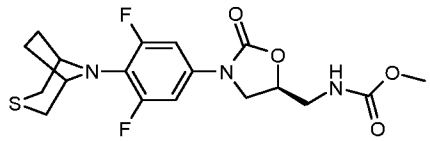
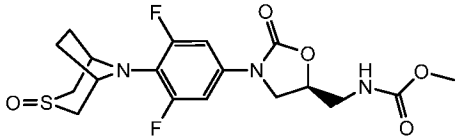
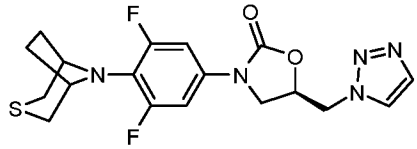
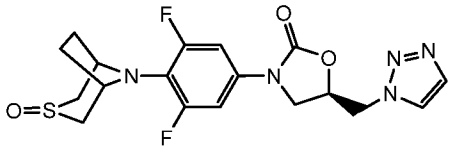
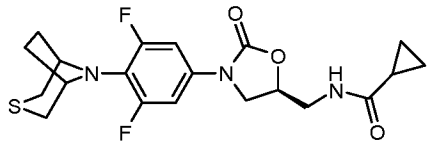
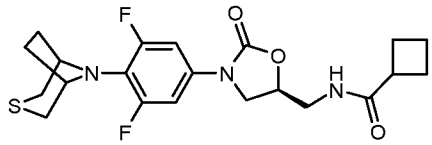
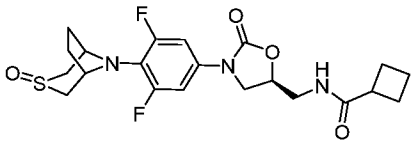
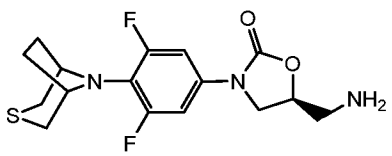
OTB-412	
OTB-413	
OTB-414	
OTB-407	
OTB-410	
OTB-408	
OTB-409	
OTB-411	
OTB-126	
OTB-127	

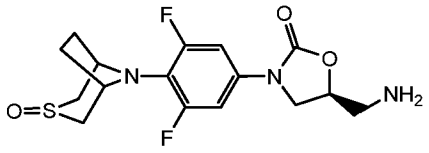
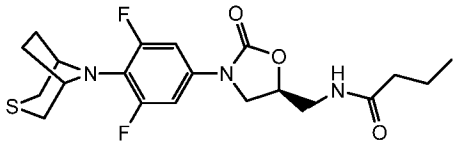
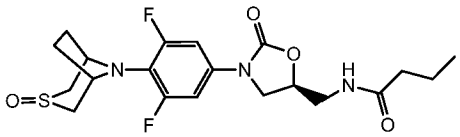
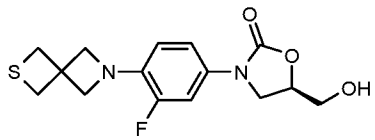
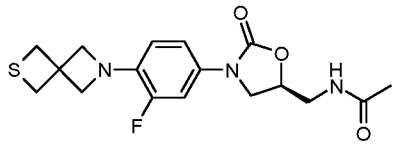
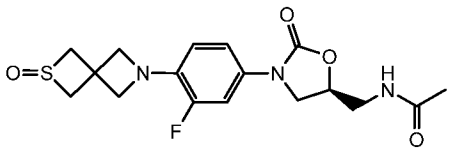
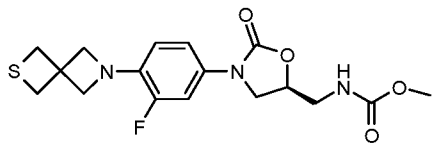
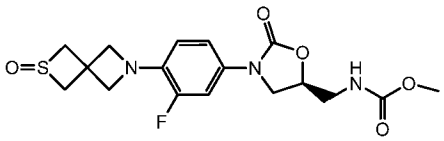
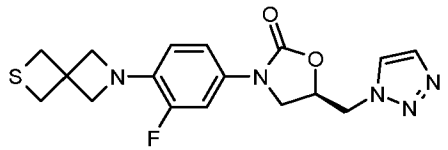
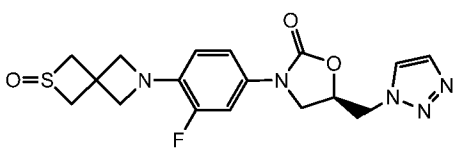
OTB-137	
OTB-138	
OTB-140	
OBD-006	
OBD-007	
OTB-110	
OTB-113	
OTB-114	
OTB124	
OTB-117	

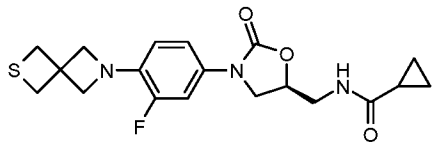
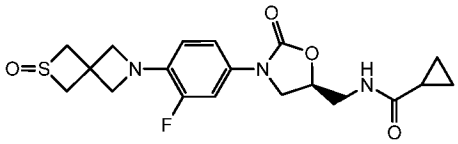
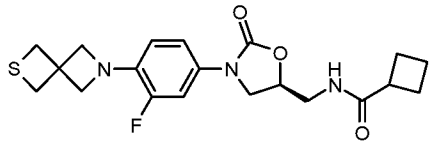
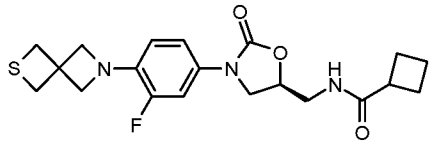
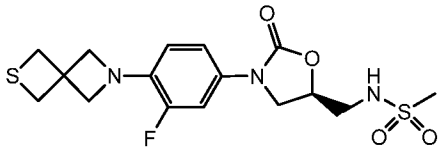
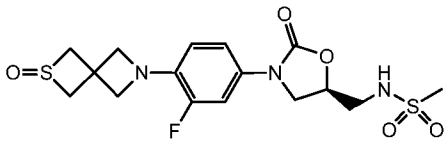
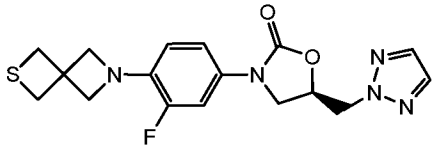
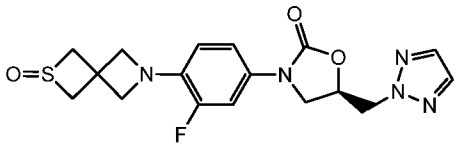
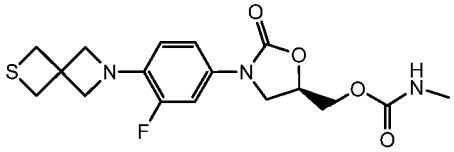
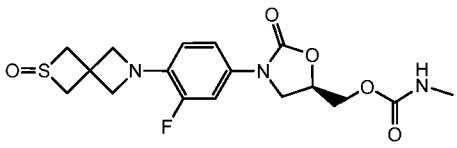
OTB-118	
OTB-120	
OTB-121	
OBD-001	
OBD-002	
OBD-003	
OBD-004	
OBD-008	
OBD-009	
OBD-027	

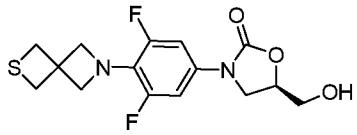
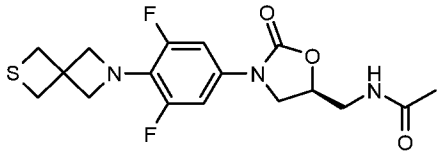
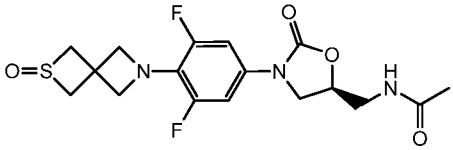
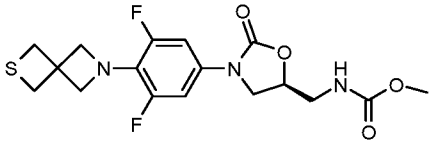
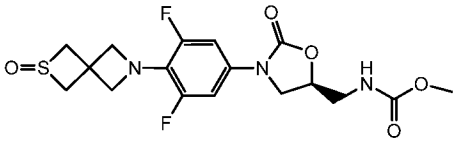
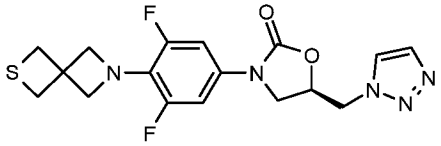
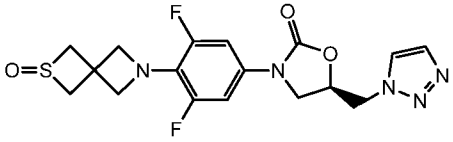
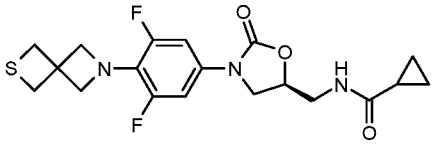
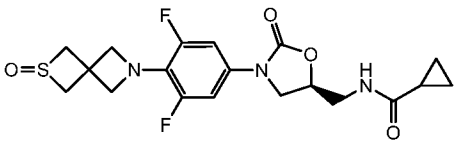
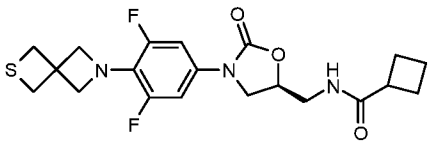
OBD-240	
OBD-026	
OBD-241	
OTB-227	
OTB-501	
OBD-081	
OBD-085	
OTB-502	
OTB-503	
OTB-504	

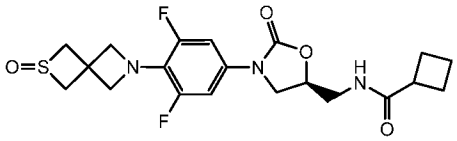
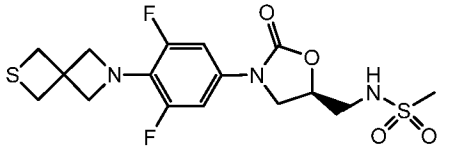
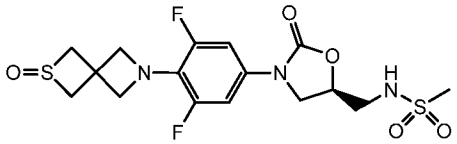
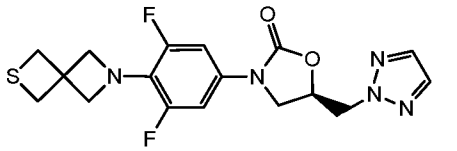
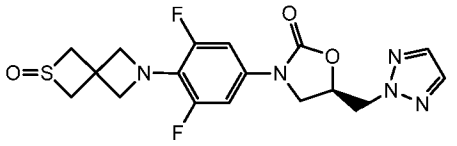
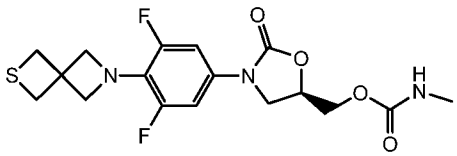
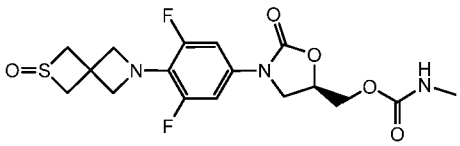
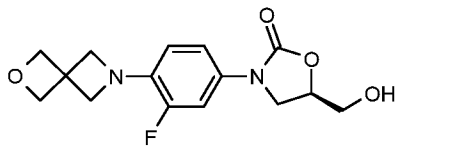
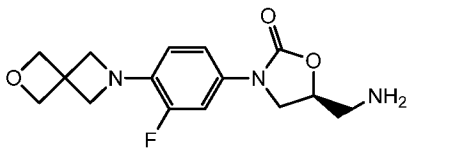
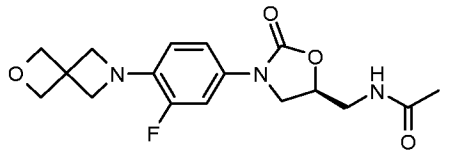
OTB-505	
OTB-236	
OTB-237	
OTB-518	
OBD-016	
OBD-017	
OBD-021	
OBD-018	
OTB-506	
OTB-507	

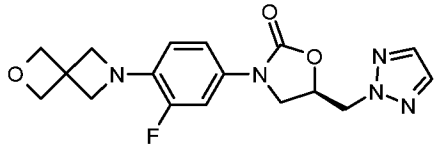
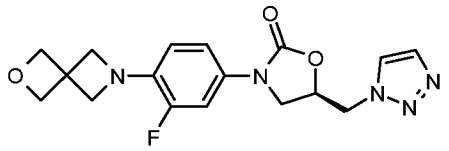
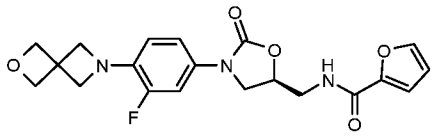
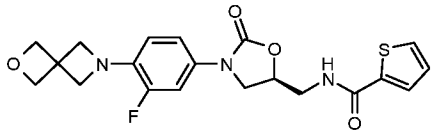
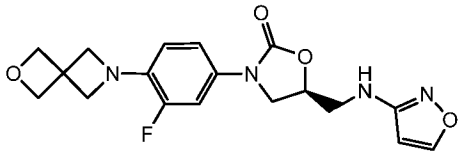
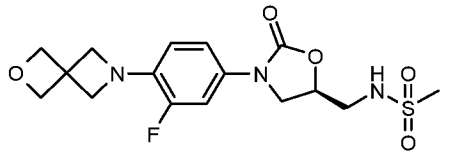
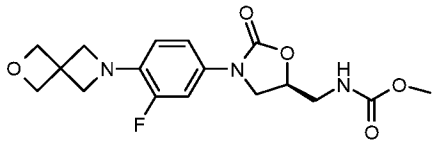
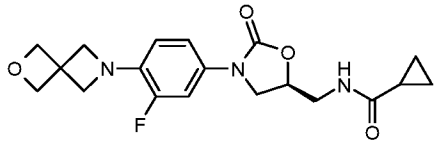
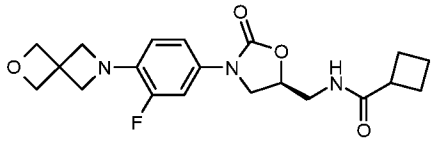
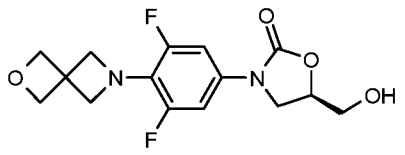
OTB-510	
OTB-514	
OTB-512	
OTB-519	
OTB-511	
OTB-517	
OTB-508	
OTB-509	
OTB-513	
OBD-083	

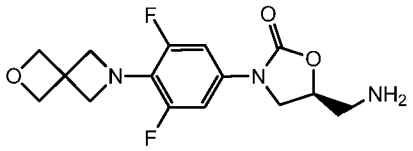
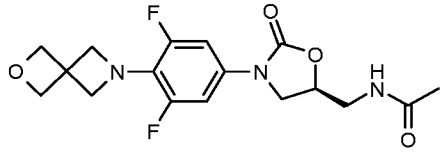
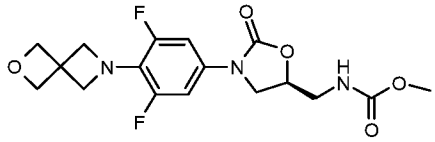
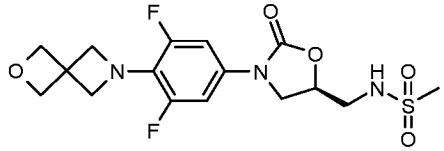
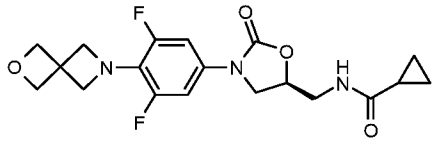
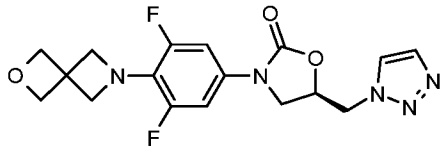
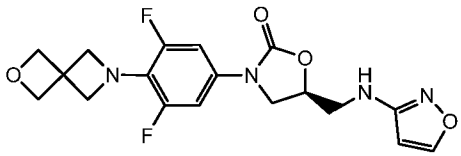
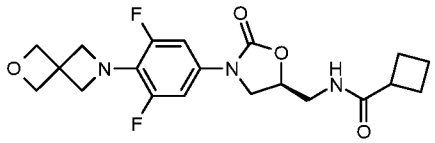
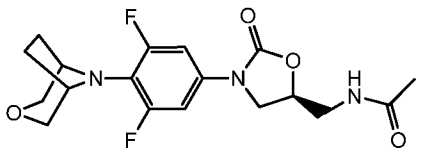
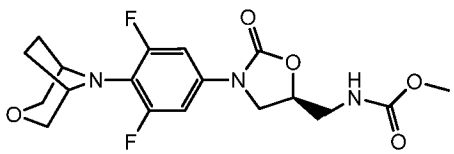
OBD-087	
OBD-029	
OBD-242	
OTB-260	
OTB-261	
OTB523	
OTB-515	
OTB-256	
OTB-241	
OTB-247	

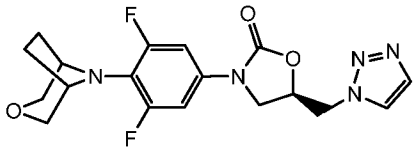
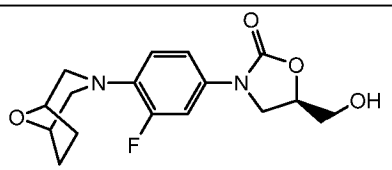
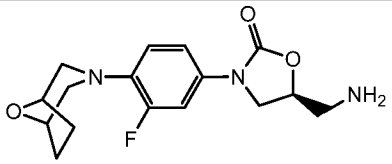
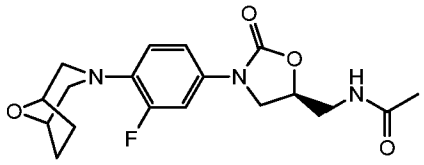
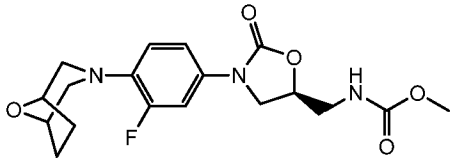
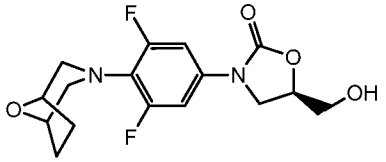
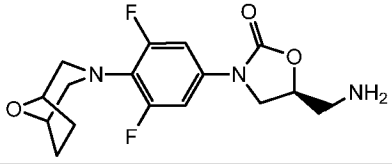
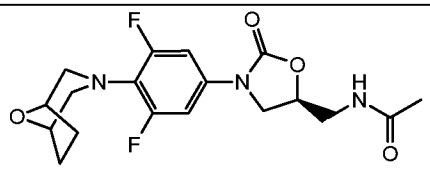
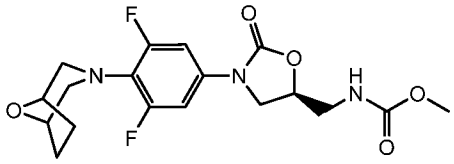
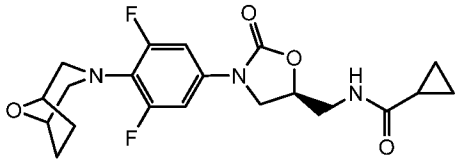
OTB-249	
OTB-255	
OTB-250	
OTB-254	
OTB-260 -2A	
OTB-260 -2B	
OTB-260 -5A	
OTB-260 -5B	
OTB-260 -4A	
OTB-260 -4B	

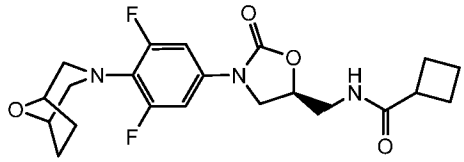
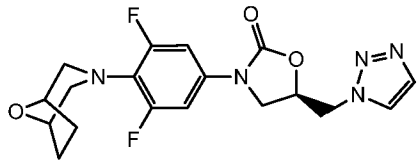
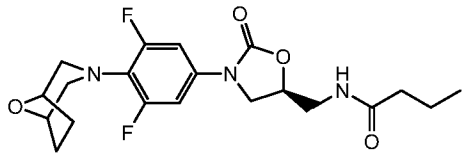
OTB-516	
OTB-515	
OTB-520	
OTB-242	
OTB-253	
OTB-245	
OTB-522	
OTB-243	
OTB-252	
OTB-244	

OTB-251	
OTB-516 -2A	
OTB-516 -2B	
OTB-516 -6A	
OTB-516 -6B	
OTB-516 -4A	
OTB-516 -4B	
OTB-201	
OBD-057	
OTB-202	

OTB-203	
OTB-204	
OTB-205	
OTB-206	
OBD-056	
OTB-222	
OTB-223	
OTB-238	
OTB-239	
OTB-229	

OBD-062	
OTB-230	
OTB-231	
OTB-232	
OTB-233	
OTB-234	
OBD-061	
OTB-240	
OBD-051	
OBD-052	

OBD-055	
OBD-112	
OBD-113	
OBD-110	
OBD-111	
OBD-114	
OBD-115	
OBD-048	
OBD-049	
OBD-252	

OBD-253	
OBD-054	 and
OBD-254	 .

10. A pharmaceutical composition comprising at least one compound of Formula I, or a salt, hydrate, or solvate thereof, and one or more pharmaceutically acceptable carriers and/or additives.

11. The pharmaceutical compositions Formula I, or a salt, hydrate, or solvate thereof, further comprising one or more additional anti-infective treatments.

12. A method of preventing and treating microbial infections in humans by administering a therapeutically effective amount of a compound of Formula I, or a salt, hydrate, or solvate thereof to a patient in need thereof.

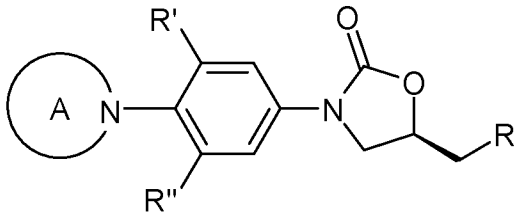
13. The method of paragraph 12, wherein the microbial infection is caused by *Mycobacterium tuberculosis*.

* * *

It is to be understood that the invention is not limited to the particular embodiments of the invention described above, as variations of the particular embodiments may be made and still fall within the scope of the appended claims.

WHAT IS CLAIMED IS:

1. A compound of Formula I, or a pharmaceutically acceptable salt, hydrate, or solvate of:



(I)

wherein:

R is independently OR_1, $OC(O)R_2$, $OC(O)NHR_2$, $OS(O_2)R_2$, $NHS(O)_2R_2$, NR_3R_4, $NHC(O)R_5$;

R' and R'' are independently H, F, Cl or OMe;

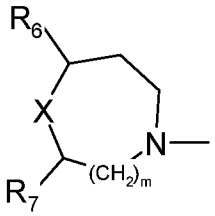
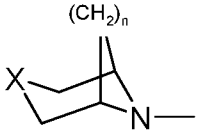
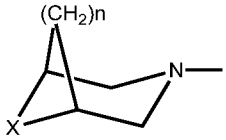
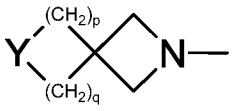
each R_1 is independently H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, wherein said alkyl, cycloalkyl are optionally substituted with 1 to 4 groups selected from halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkyloxy;

each R_2 is independently C_1-C_6 alkyl, C_3-C_8 cycloalkyl, heterocyclyl, heteroaryl or aryl, wherein said alkyl, cycloalkyl, heterocyclyl, heteroaryl, or aryl are optionally substituted with 1 to 4 groups selected from halo, hydroxyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 acyloxy, CF_3, NO_2, CN and NH_2;

each R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, heterocyclyl heteroaryl, aryl; or R_3 and R_4 taken together with the nitrogen to which they are attached, form a 4- to 8-membered heterocyclyl or heteroaryl with 1 to 3 additional heteroatoms selected from O, S, or N, wherein said alkyl, cycloalkyl, heterocyclyl, heteroaryl, or aryl are optionally substituted with 1 to 4 groups selected from halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, CF_3, NO_2, CN;

each R_5 is independently C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_1-C_6 alkoxy, heteroaryl, aryl, wherein said alkyl, cycloalkyl, heterocyclyl, heteroaryl, or aryl are optionally substituted with 1 to 4 groups selected from halo, hydroxyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 acyloxy, CF_3, NO_2, CN and NH_2;

Ring A is selected from:




and


wherein,

each R_6 and R_7 is independently H, F, CH_3, CH_2CH_3, CF_3, phenyl;

X = O, S, SO, SO_2;

Y = O, S, SO, SO_2, and NR_8;

m is 1, or 2;

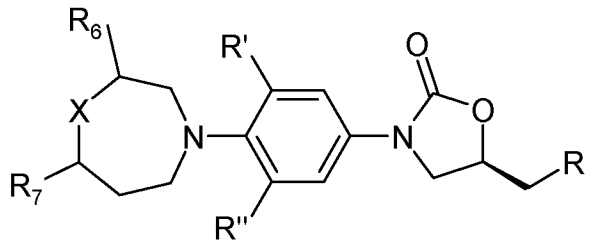
n is 1, or 2;

p is 1, or 2;

q is 1, or 2;

R_8 in independently H, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, $COCH_3$, and p-toluenesulfonyl, wherein said alkyl, cycloalkyl are optionally substituted with 1 to 4 groups selected from halo, hydroxyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 acyloxy, CF_3, NO_2, CN and NH_2.

2. The compound of claim 1, wherein the compound is represented by Formula II:



II

wherein,

R is independently OR_1, $OC(O)R_2$, NR_3R_4, $NHS(O)_2R_2$, $NHC(O)R_5$;

R' and R'' are independently H, or F;

R_1 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

R_2 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

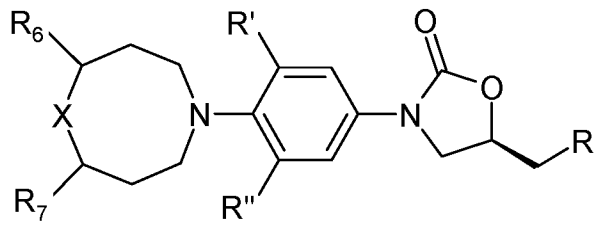
R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, phenyl; or R_3 and R_4 taken together with the nitrogen to which they are attached to form morpholine, thiamorpholine, piperazine and triazole;

R_5 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, 5- or 6-membered heteroaryl or phenyl;

R_6 and R_7 is independently H, F, CH_3, CH_2CH_3, CF_3;

X = O, S, SO, SO_2; when X = S, SO, SO_2, R' = H, R'' = F, R_5 can not be CH_3;

3. The compound of claim 1, wherein the compound is represented by Formula III:



III

wherein,

R is independently OR_1, $OC(O)R_2$, NR_3R_4, $NHS(O)_2R_2$, $NHC(O)R_5$;

R' and R'' are independently H, or F;

R_1 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

R_2 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

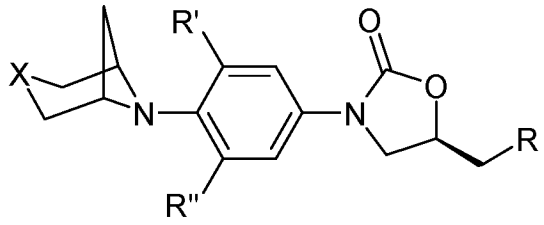
R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, or phenyl; or R_3 and R_4 taken together with the nitrogen to which they are attached to form morpholine, thiamorpholine, piperazine and triazole;

R_5 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, 5- or 6-membered heteroaryl or phenyl;

R_6 and R_7 is independently H, F, CH_3, CH_2CH_3, CF_3;

X = O, S, SO, SO_2;

4. The compound of claim 1, wherein the compound is represented by Formula IV:



IV

wherein,

R is independently OR_1, $OC(O)R_2$, NR_3R_4, $NHS(O)_2R_2$, $NHC(O)R_5$;

R' and R'' are independently H, or F;

R_1 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

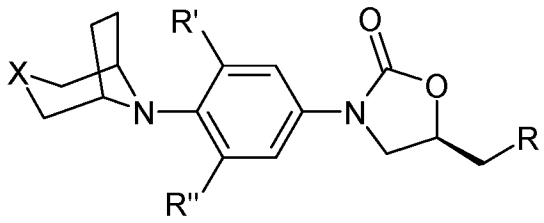
R_2 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, 5- or 6-membered heteroaryl or phenyl; or R_3 and R_4 taken together with the nitrogen to which they are attached, to form morpholine, thiamorpholine, piperazine and triazole;

R_5 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, 5- or 6-membered heteroaryl or phenyl; and

X = O, S, SO, SO_2.

5. The compound of claim 1, wherein the compound is represented by Formula V:



V

wherein,

R is independently OR_1, $OC(O)R_2$, NR_3R_4, $NHS(O)_2R_2$, $NHC(O)R_5$;

R' and R'' are independently H, or F;

R_1 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

R_2 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

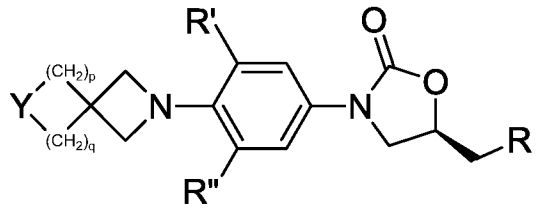
R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, 5- or 6-membered heteroaryl or phenyl; or R_3 and R_4 taken together with the nitrogen to which they are

attached, to form morpholine, thiamorpholine, piperazine and triazole;

R_5 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, 5- or 6-membered heteroaryl or phenyl; and

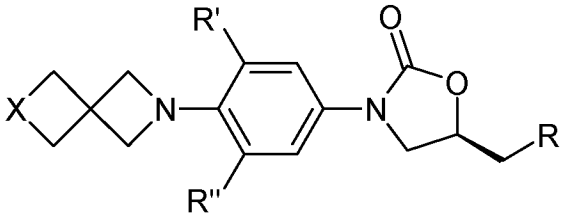
X = O, S, SO, SO_2.

6. The compound of claim 1, wherein the compound is represented by Formula VI:

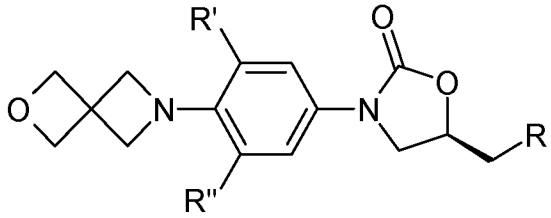


VI.

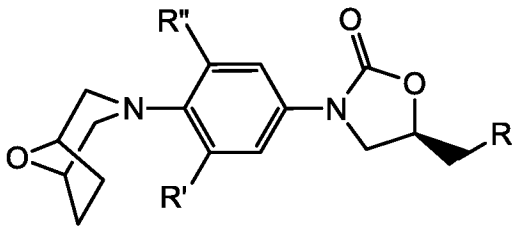
7. The compound of claim 6, wherein the compound is represented by Formula VII, Formula VIII, or Formula IX:



VII



VIII



IX

wherein,

R is independently OR_1, $OC(O)R_2$, NR_3R_4, $NHS(O)_2R_2$, $NHC(O)R_5$;

R' and R'' are independently H, or F;

R_1 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

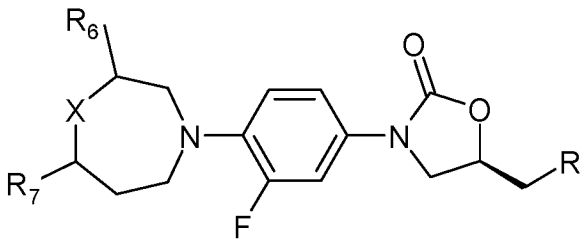
R_2 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl;

R_3 and R_4 is independently H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, 5- or 6-membered heteroaryl or phenyl; or R_3 and R_4 taken together with the nitrogen to which they are attached, to form morpholine, thiamorpholine, piperazine and triazole;

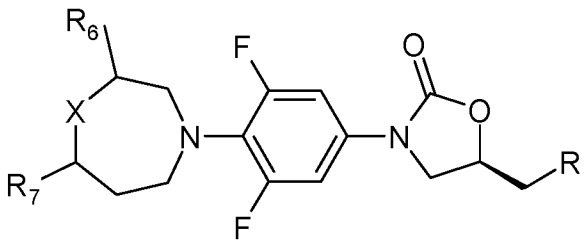
R_5 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, 5- or 6-membered heteroaryl or phenyl; and

X = O, S, SO, SO_2.

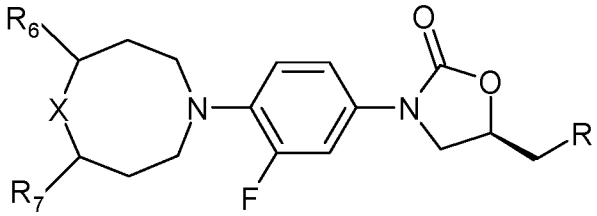
8. The compound of claim1, the compound is represented by Formula IIa, IIb, IIIa, IIIb, IVa, IVb, Va, Vb, VIIa, VIIb, VIIIa, VIIIb, IXa, or IXb:



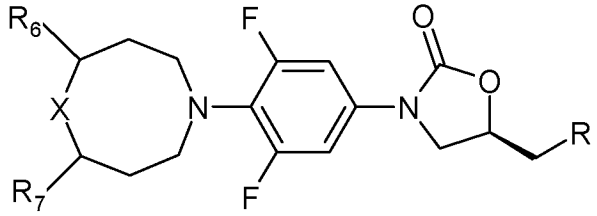
IIa



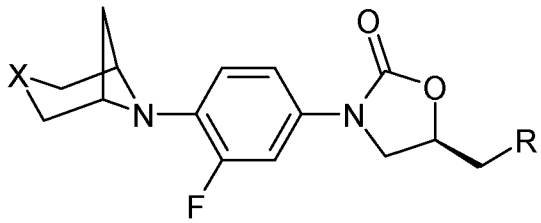
IIb



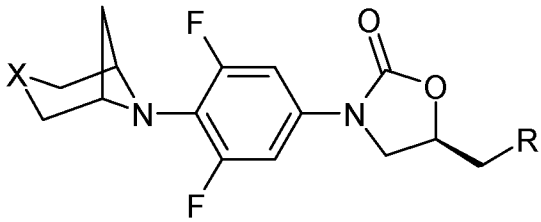
IIIa



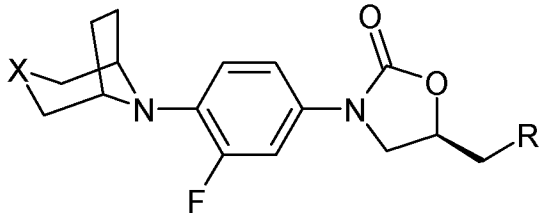
IIIb



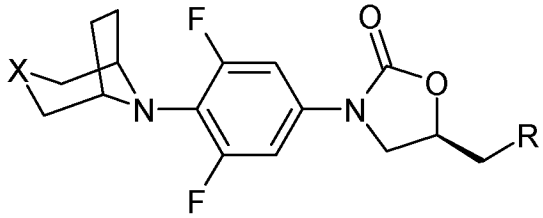
IVa



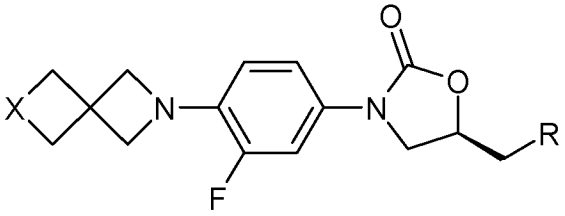
IVb



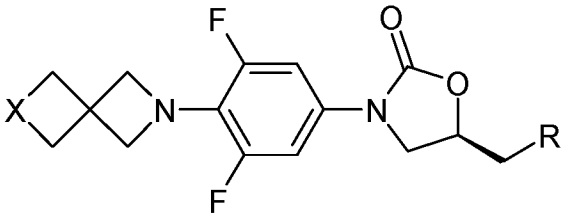
Va



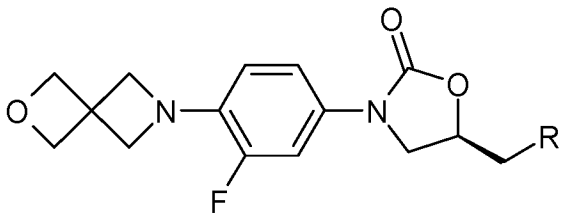
Vb



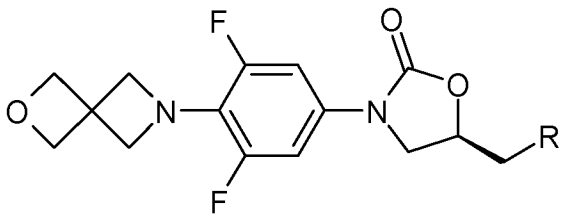
VIIa



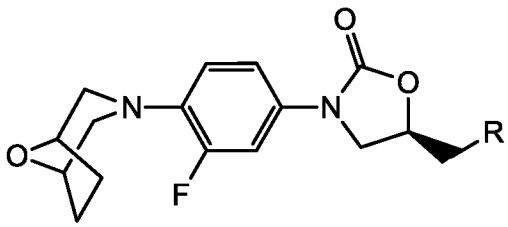
VIIb



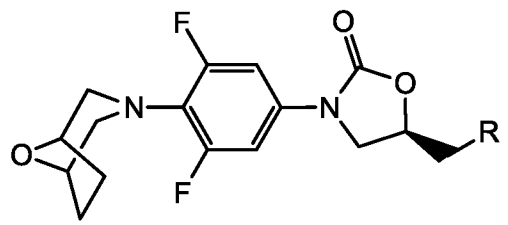
VIIIa



VIIIb



IXa



IXb

wherein,

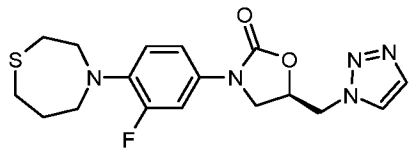
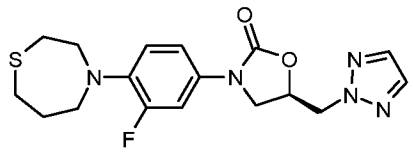
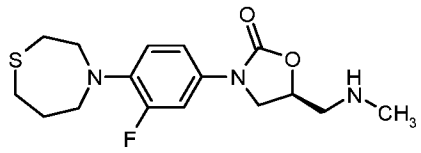
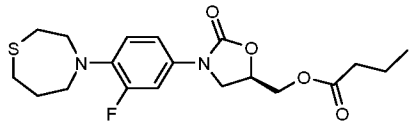
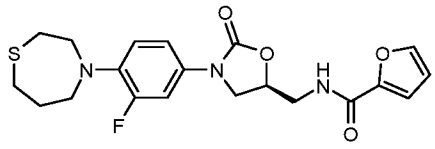
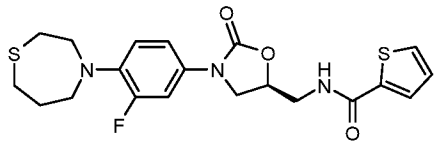
R is independently OH, OCH_3, OCH_2CH_3, $OC(O)CH_3$, NH_2, $NHCH_3$, NHC_6H_5, 1,2,3-triazole, 1,2,4-triazole, 1,2,5-triazole, $NHS(O)_2R_2$, $NHC(O)R_5$;

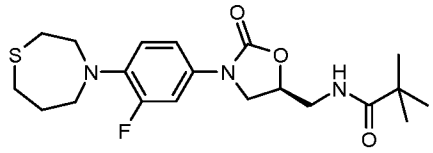
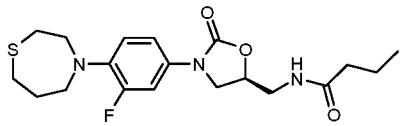
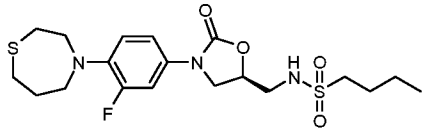
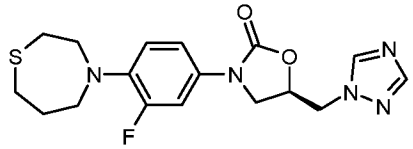
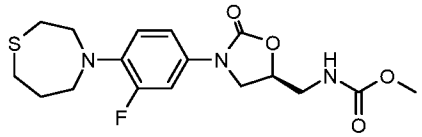
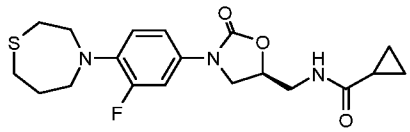
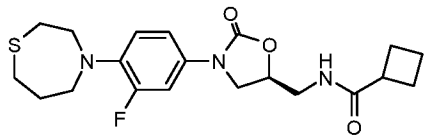
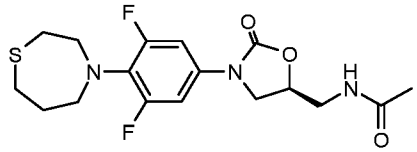
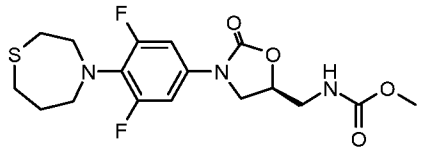
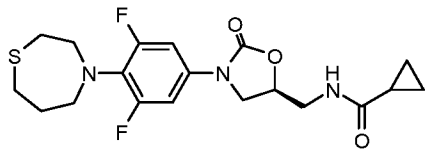
R_2 is independently C_1-C_6 alkyl;

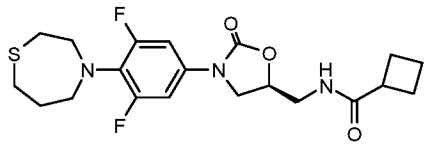
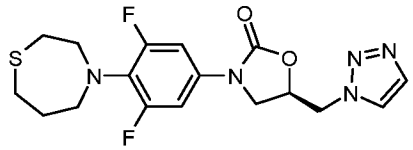
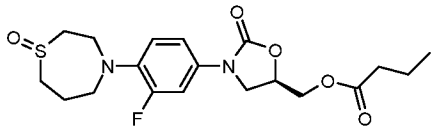
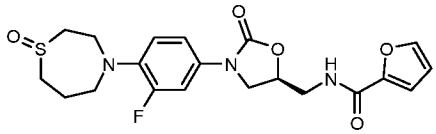
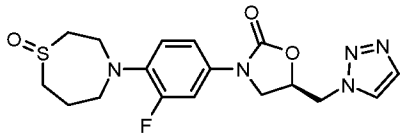
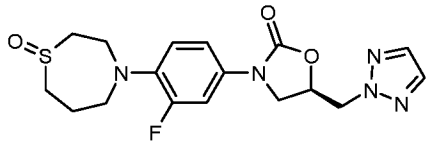
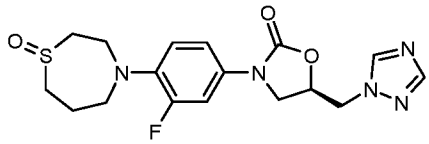
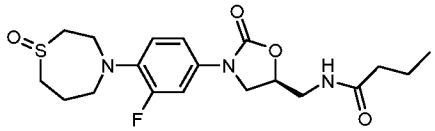
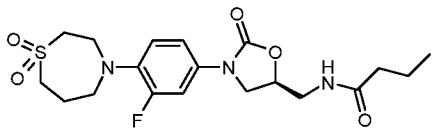
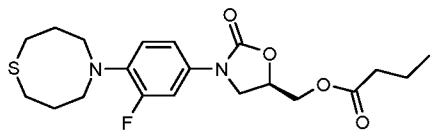
R_5 is independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, furan, thiophene or phenyl; in Formula IIa, R_5 can not be CH_3; and

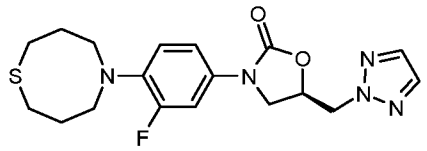
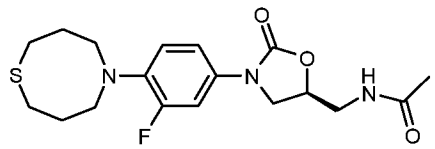
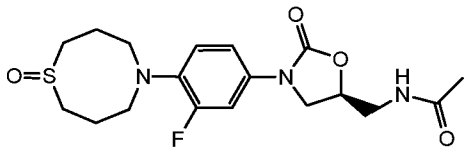
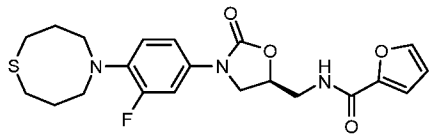
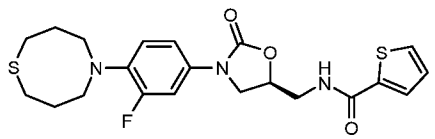
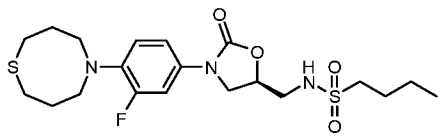
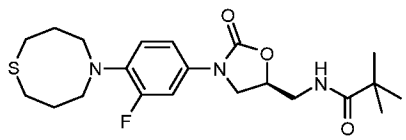
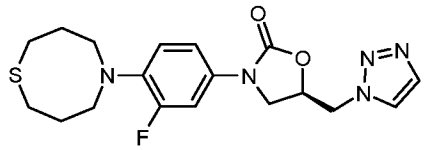
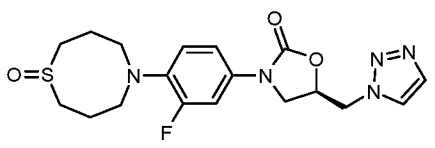
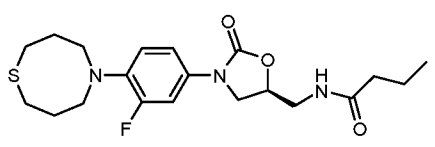
X = O, S, SO, SO_2.

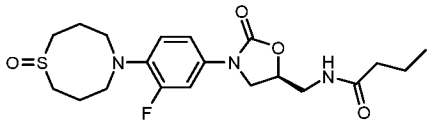
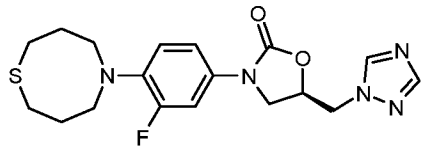
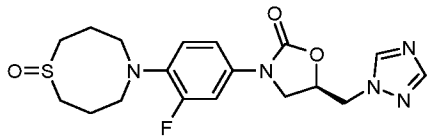
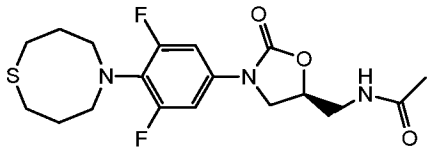
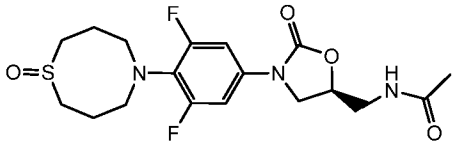
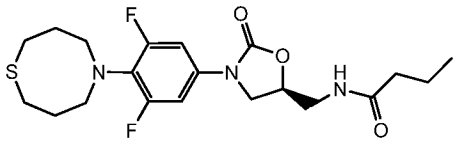
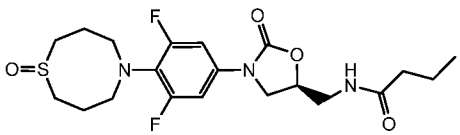
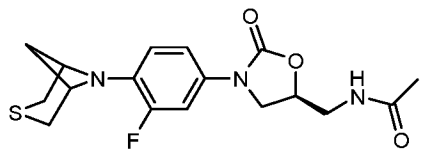
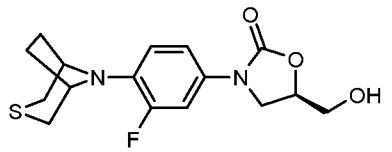
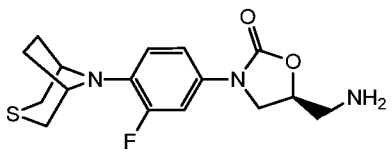
9. The compound of claim 1, wherein the compound is:

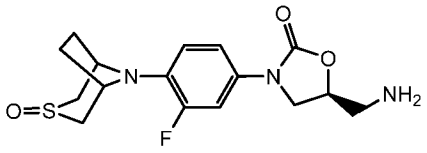
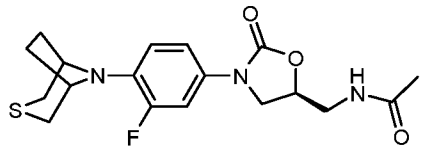
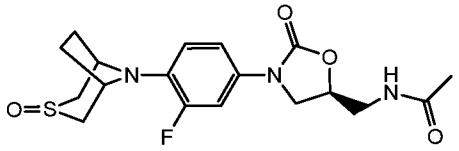
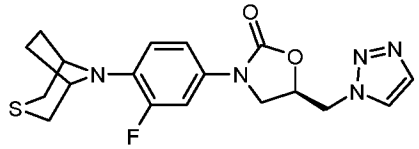
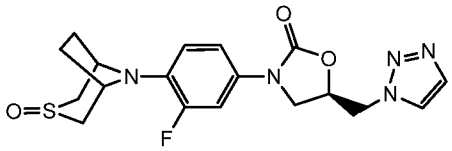
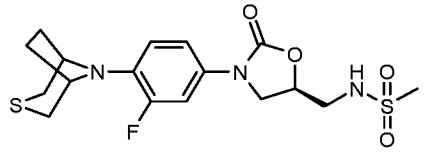
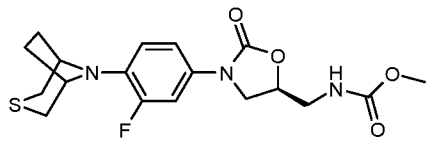
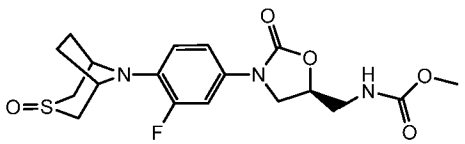
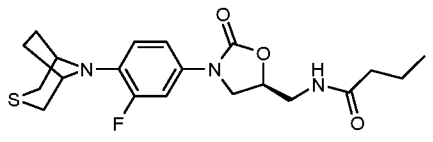
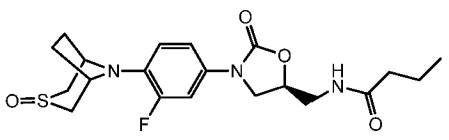
OTB-107	
OTB-106	
OTB-109	
OTB-108	
OTB-111	
OTB-112	

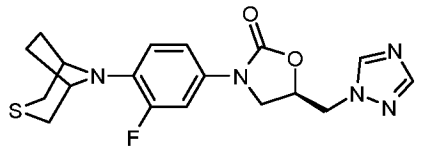
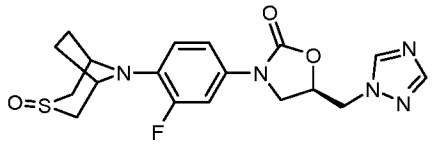
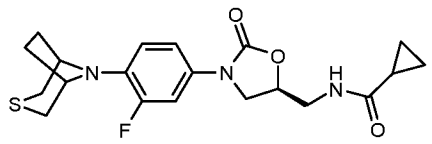
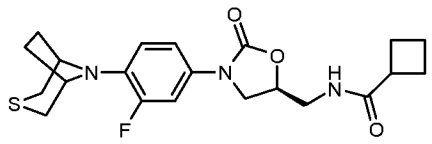
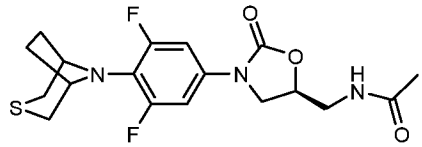
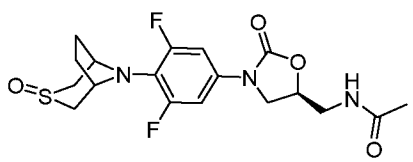
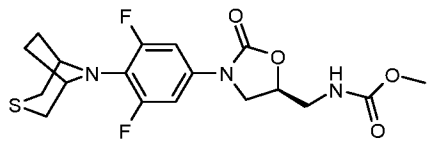
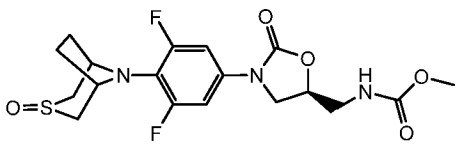
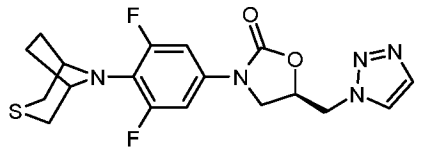
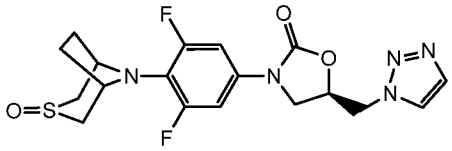
OTB-115	
OBD-005	
OTB-116	
OTB-119	
OTB-412	
OTB-413	
OTB-414	
OTB-407	
OTB-410	
OTB-408	

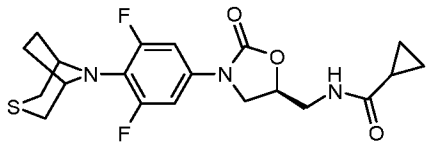
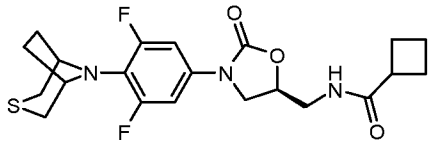
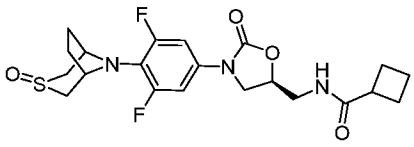
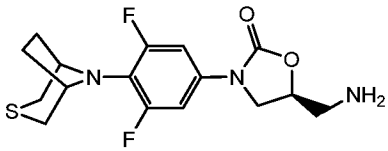
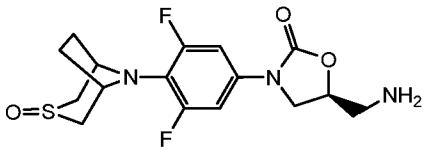
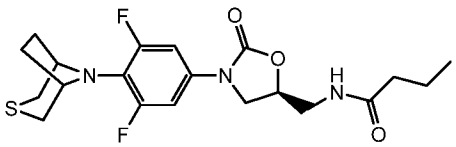
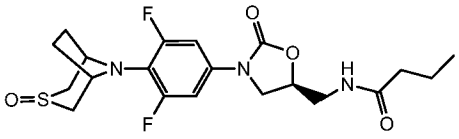
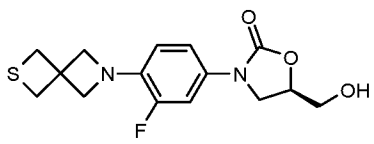
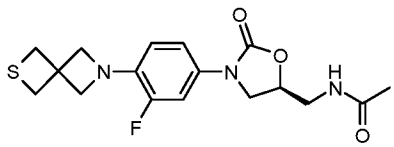
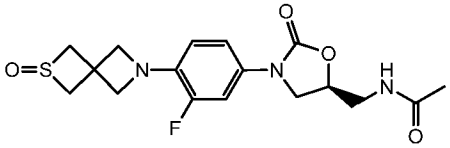
OTB-409	
OTB-411	
OTB-126	
OTB-127	
OTB-137	
OTB-138	
OTB-140	
OBD-006	
OBD-007	
OTB-110	

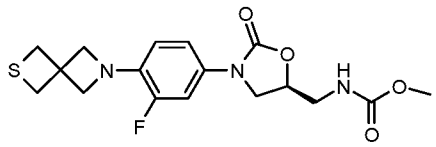
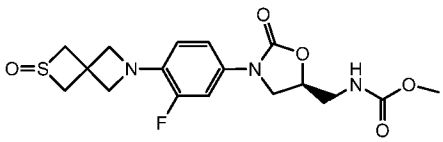
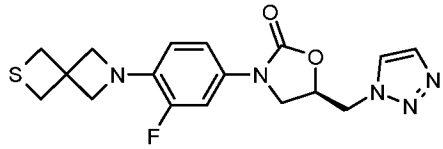
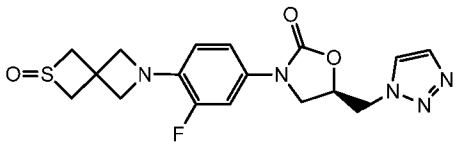
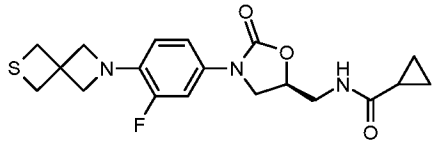
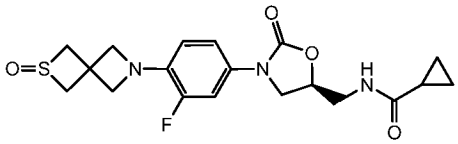
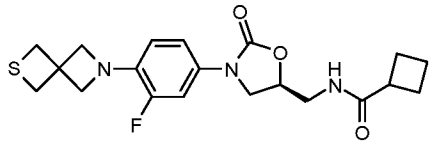
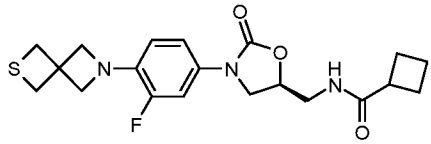
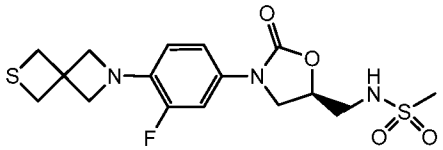
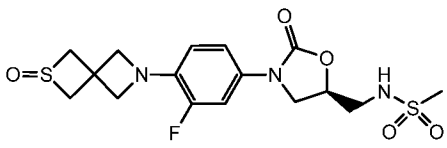
OTB-113	
OTB-114	
OTB124	
OTB-117	
OTB-118	
OTB-120	
OTB-121	
OBD-001	
OBD-002	
OBD-003	

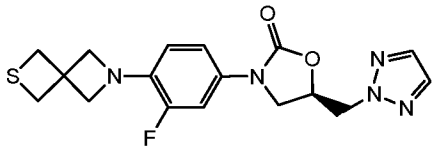
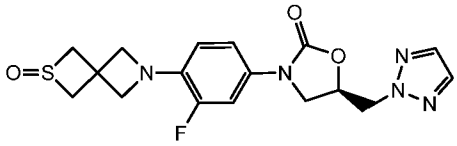
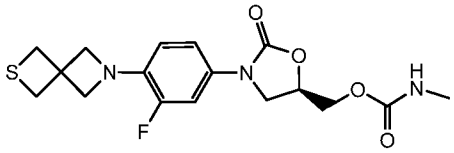
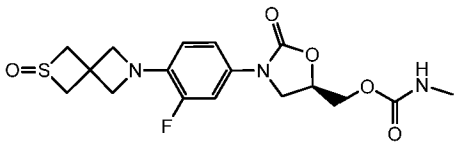
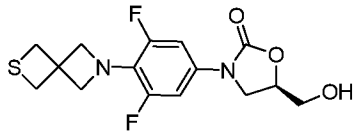
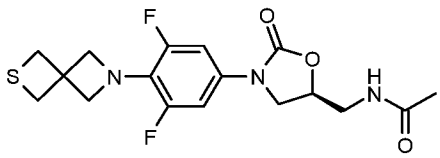
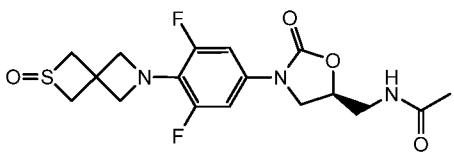
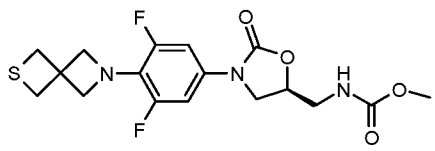
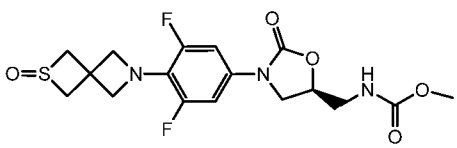
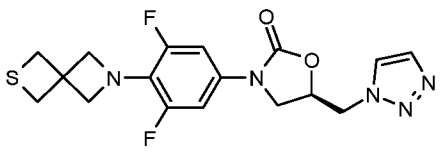
OBD-004	
OBD-008	
OBD-009	
OBD-027	
OBD-240	
OBD-026	
OBD-241	
OTB-227	
OTB-501	
OBD-081	

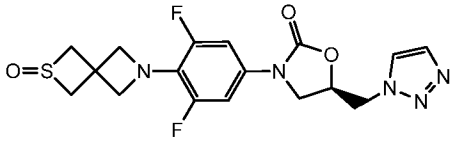
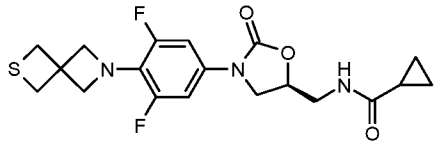
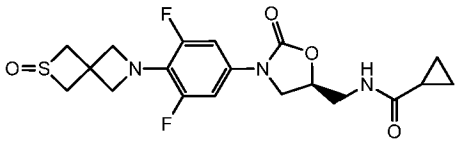
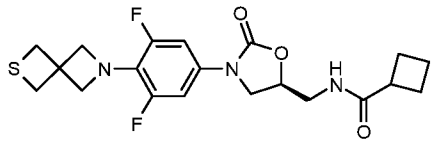
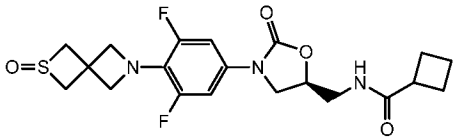
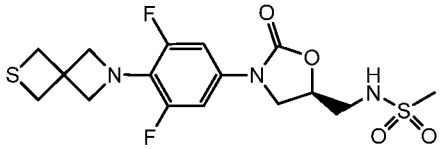
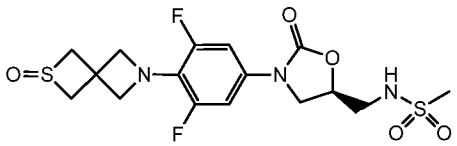
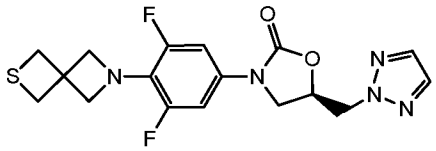
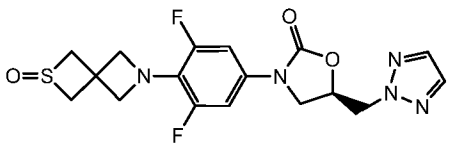
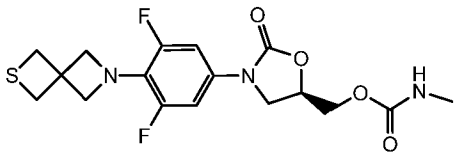
OBD-085	
OTB-502	
OTB-503	
OTB-504	
OTB-505	
OTB-236	
OTB-237	
OTB-518	
OBD-016	
OBD-017	

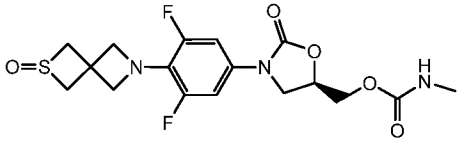
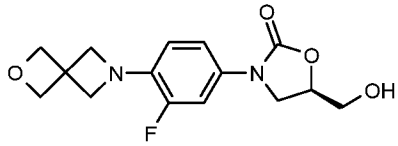
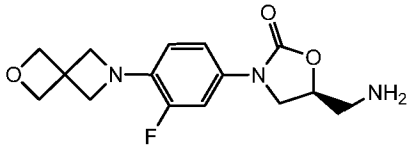
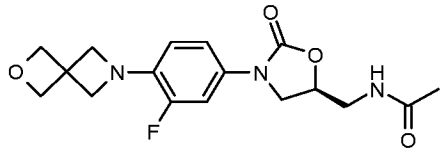
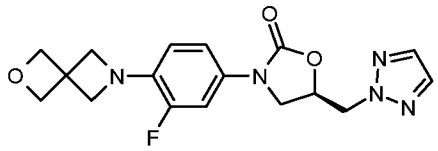
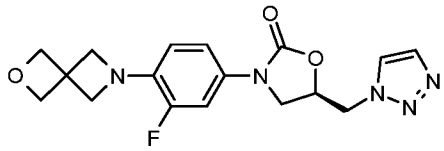
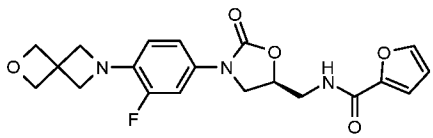
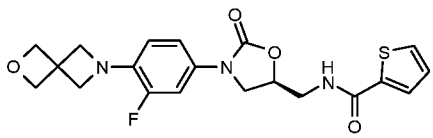
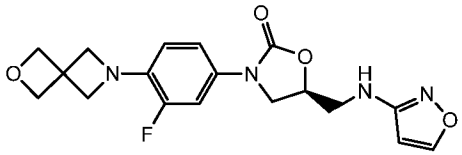
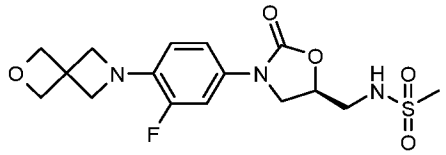
OBD-021	
OBD-018	
OTB-506	
OTB-507	
OTB-510	
OTB-514	
OTB-512	
OTB-519	
OTB-511	
OTB-517	

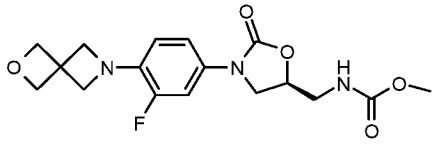
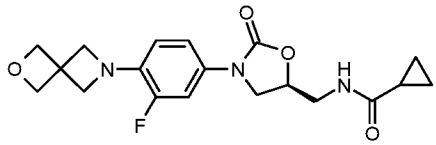
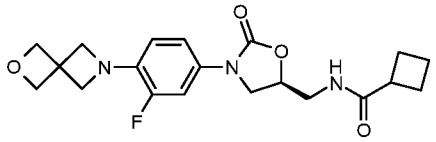
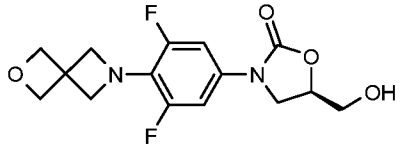
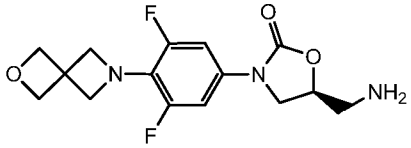
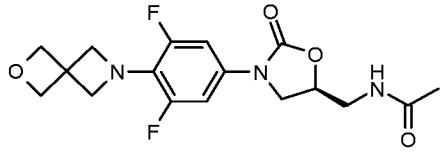
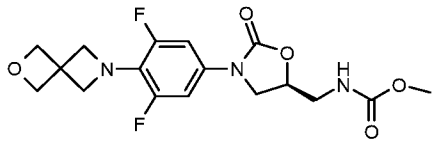
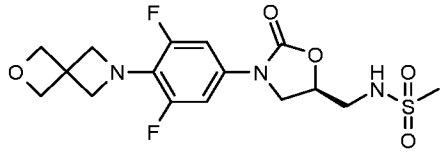
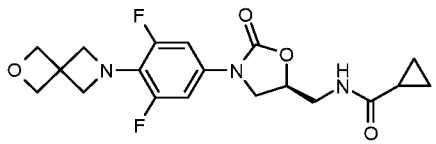
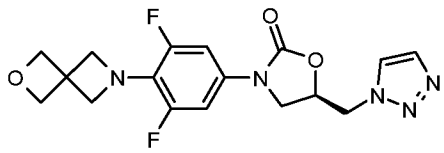
OTB-508	
OTB-509	
OTB-513	
OBD-083	
OBD-087	
OBD-029	
OBD-242	
OTB-260	
OTB-261	
OTB523	

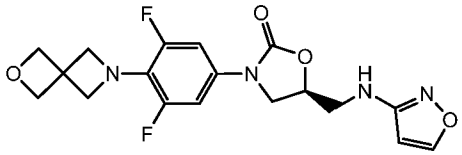
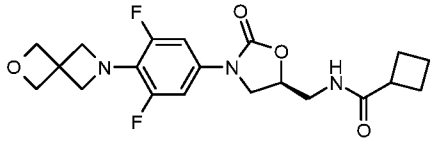
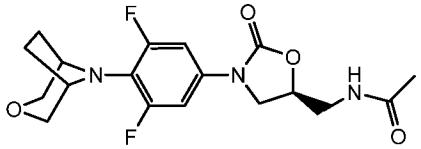
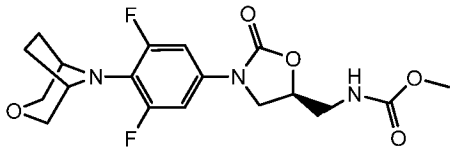
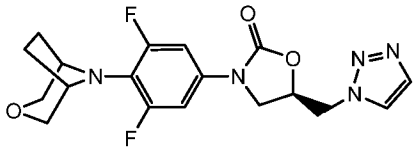
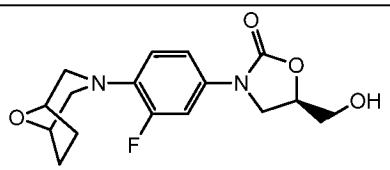
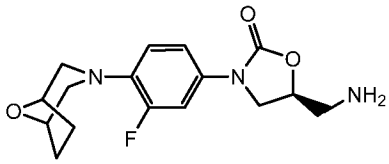
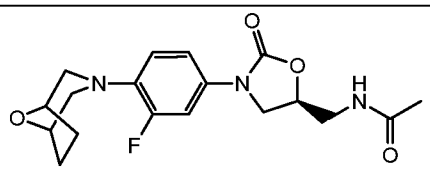
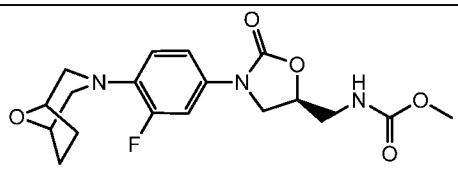
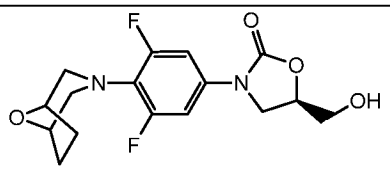
OTB-515	
OTB-256	
OTB-241	
OTB-247	
OTB-249	
OTB-255	
OTB-250	
OTB-254	
OTB-260 -2A	
OTB-260 -2B	

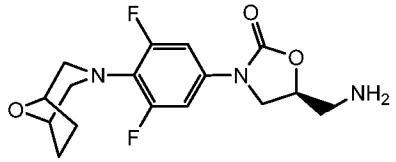
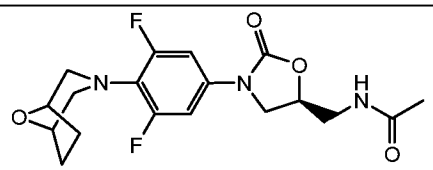
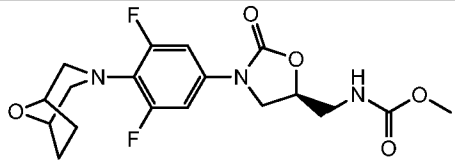
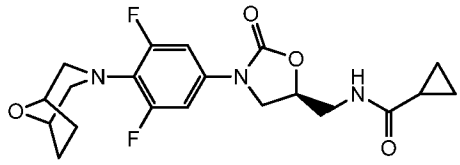
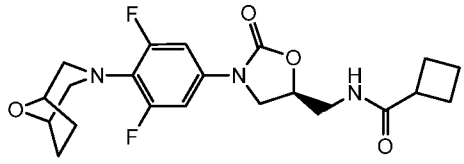
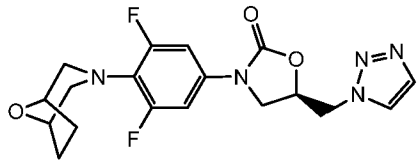
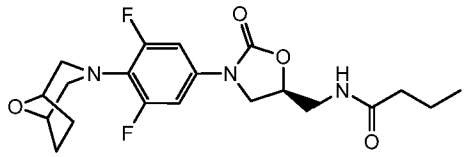
OTB-260 -5A	
OTB-260 -5B	
OTB-260 -4A	
OTB-260 -4B	
OTB-516	
OTB-515	
OTB-520	
OTB-242	
OTB-253	
OTB-245	

OTB-522	
OTB-243	
OTB-252	
OTB-244	
OTB-251	
OTB-516 -2A	
OTB-516 -2B	
OTB-516 -6A	
OTB-516 -6B	
OTB-516 -4A	

OTB-516 -4B	
OTB-201	
OBD-057	
OTB-202	
OTB-203	
OTB-204	
OTB-205	
OTB-206	
OBD-056	
OTB-222	

OTB-223	
OTB-238	
OTB-239	
OTB-229	
OBD-062	
OTB-230	
OTB-231	
OTB-232	
OTB-233	
OTB-234	

OBD-061	
OTB-240	
OBD-051	
OBD-052	
OBD-055	
OBD-112	
OBD-113	
OBD-110	
OBD-111	
OBD-114	

OBD-115	
OBD-048	
OBD-049	
OBD-252	
OBD-253	
OBD-054	 and
OBD-254	 .

10. A pharmaceutical composition comprising at least one compound of Formula I, or a salt, hydrate, or solvate thereof, and one or more pharmaceutically acceptable carriers and/or additives.

11. The pharmaceutical compositions Formula I, or a salt, hydrate, or solvate thereof, further comprising one or more additional anti-infective treatments.

12. A method of preventing and treating microbial infections in humans by administering a therapeutically effective amount of a compound of Formula I, or a salt, hydrate, or solvate thereof to a patient in need thereof.

13. The method of claim 12, wherein the microbial infection is caused by *Mycobacterium tuberculosis*.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US16/42486

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 31/422; A61P 31/04; C07D 263/20 (2016.01)
CPC - C07D 413/10, 417/02, 417/10
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)
IPC(8): A61K 31/422; A61P 31/04; C07D 263/20 (2016.01)
CPC: C07D 413/10, 417/02, 417/10

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)
PATSEER (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, Other Countries (INPADOC), RU, AT, CH, TH, BR, PH); EBSCO; Google Scholar; IP.com; SureChEMBL; KEYWORDS: phenyl oxazolidinone*, treat* bacter* infect*, M tuberculosis, oxazolidin 2 one, thiazepan 4 yl, 1 1 dioxido 1 4 thiazepan 4 yl, thiazocan*, oxazocan*, spirocycl*, azaspiro heptan*, azabicycl* heptan*, azabicycl* octan*

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2009/0281088 A1 (DING, CZ et al.) 12 November 2009; paragraphs [0008]-[0010], [0014], [0022]-[0023], [0073], [0102], [0283]	1-3, 6, 8-13
Y	US 2004/0077626 A1 (HESTER JR, JB et al.) 22 April 2004; paragraphs [0002]-[0003], [0177]	1-2, 8-13
Y	US 2011/0053916 A1 (WANG, T et al.) 03 March 2011; paragraphs [0002], [0006], [0015], [0026], [0195], [0209]	1, 3
Y	US 6,090,820 A (BARBACHYN, MR et al.) 18 July 2000; column 2, lines 20-52; column 4, lines 10-14, 10-40	1, 6
A	WO 2004/033451 A1 (PHARMACIA & UPJOHN COMPANY) 22 April 2004; page 2, lines 1-18; page 43, lines 4-12	4-5
A	WO 96/15130 A1 (THE UPJOHN COMPANY) 23 May 1996; page 2, lines 4-16; page 3, lines 5-23; page 4, lines 1-5	4-5
A	US 2010/0069449 A1 (OH, CH et al.) 18 March 2010; paragraphs [0015]-[0016], [0071]	7
A	US 2008/0119533 A1 (TUROS, E et al.) 22 May 2008; abstract; claim 1	7

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
31 August 2016 (31.08.2016)	19 SEP 2016
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US16/42486

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	GADEKAR, PK et al., Design, synthesis and biological evaluation of novel azaspiro analogs of linezolid as antibacterial and antitubercular agents, European Journal of Medicinal Chemistry 122, pages 475-487, 07 July 2016; [retrieved on 2016-08-28]. Retrieved from the Internet: <URL: https://www.researchgate.net/publication/305082525_Design_synthesis_and_biological_evaluation_of_novel_azaspiro_analogs_of_linezolid_as_antibacterial_and_antitubercular_agents> <DOI: 10.1016/j.ejmech.2016.07.001>; abstract; page 477, Table 1, compound 18	1, 7