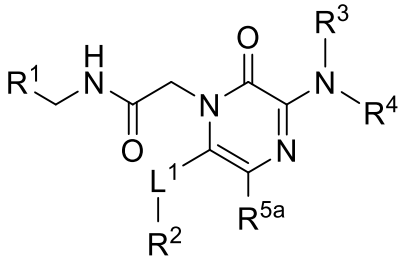
In one aspect, the present disclosure refers to a compound having the following Structure (I):

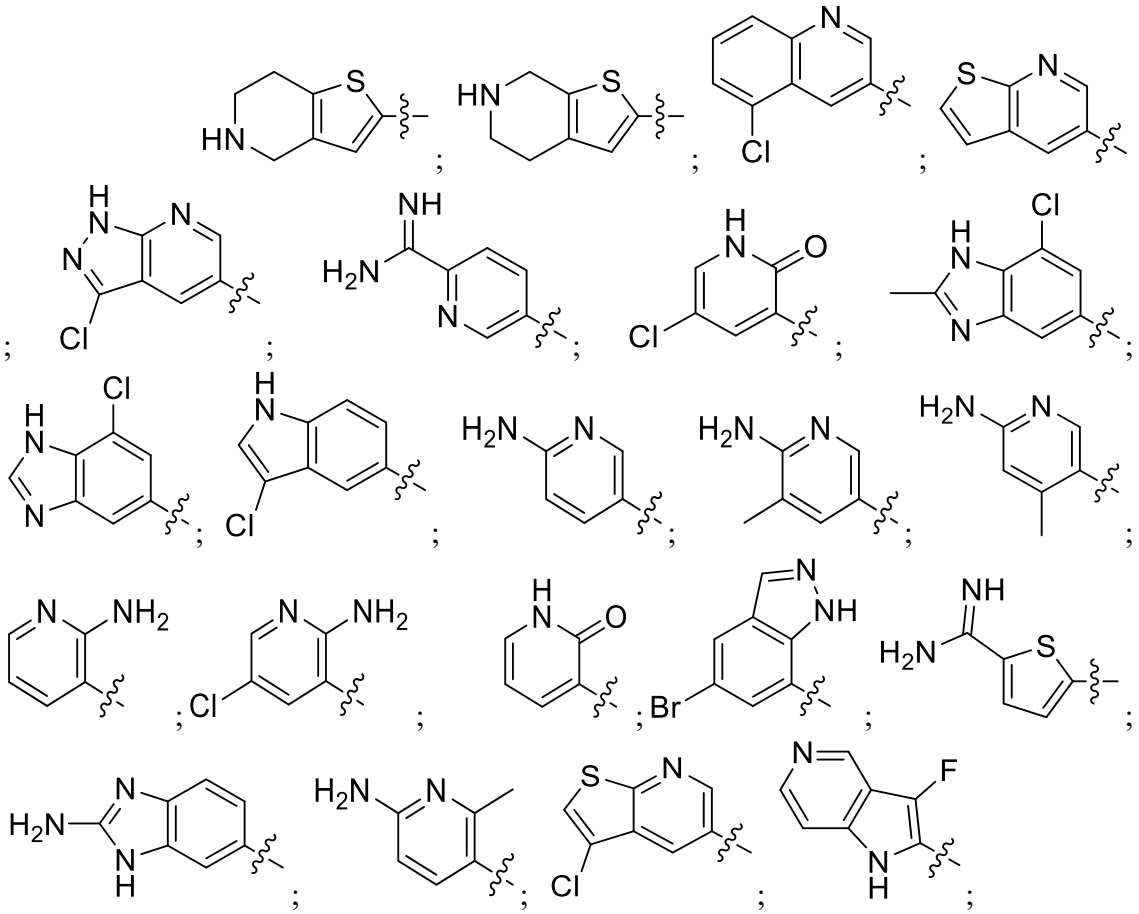


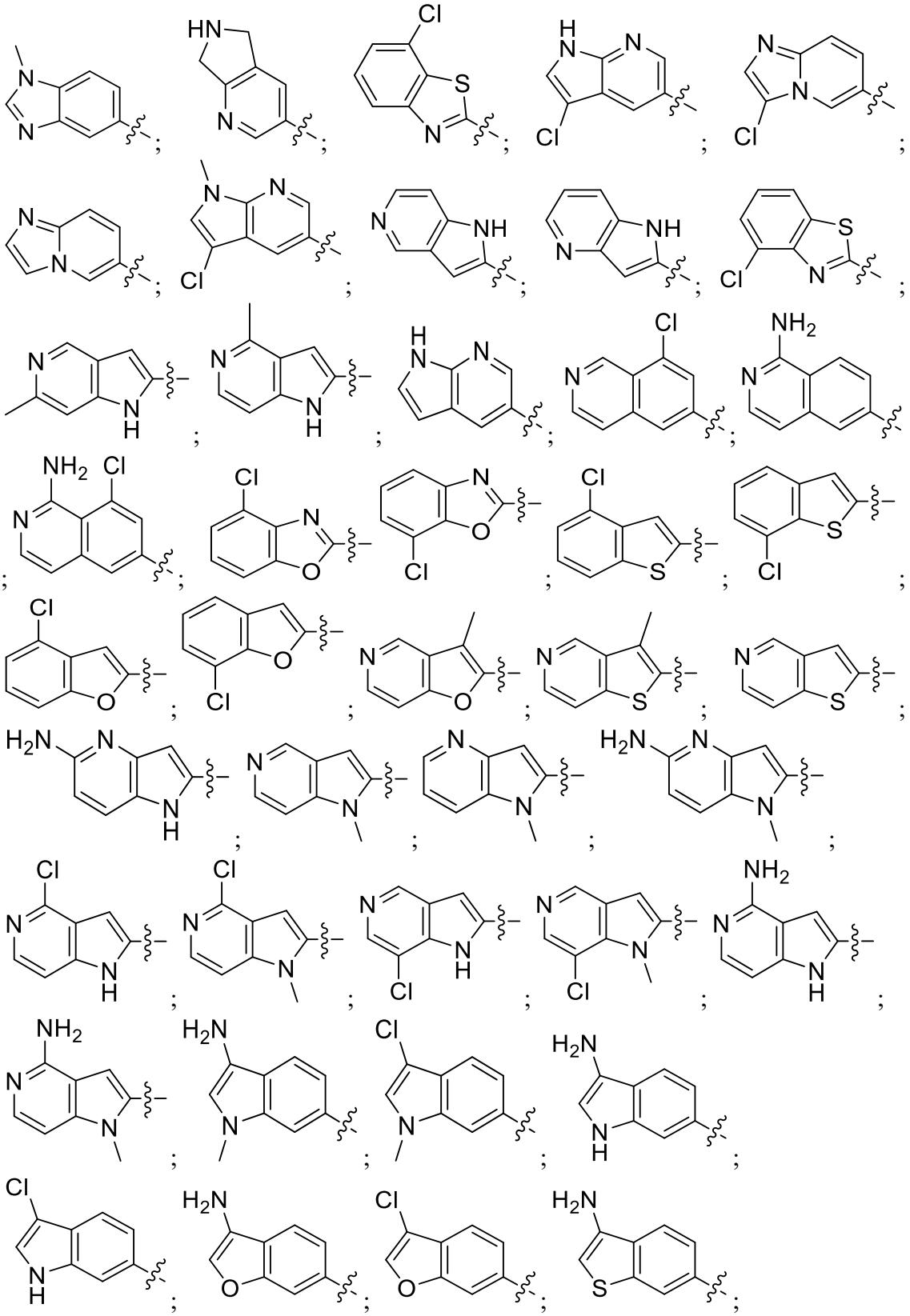
(I)

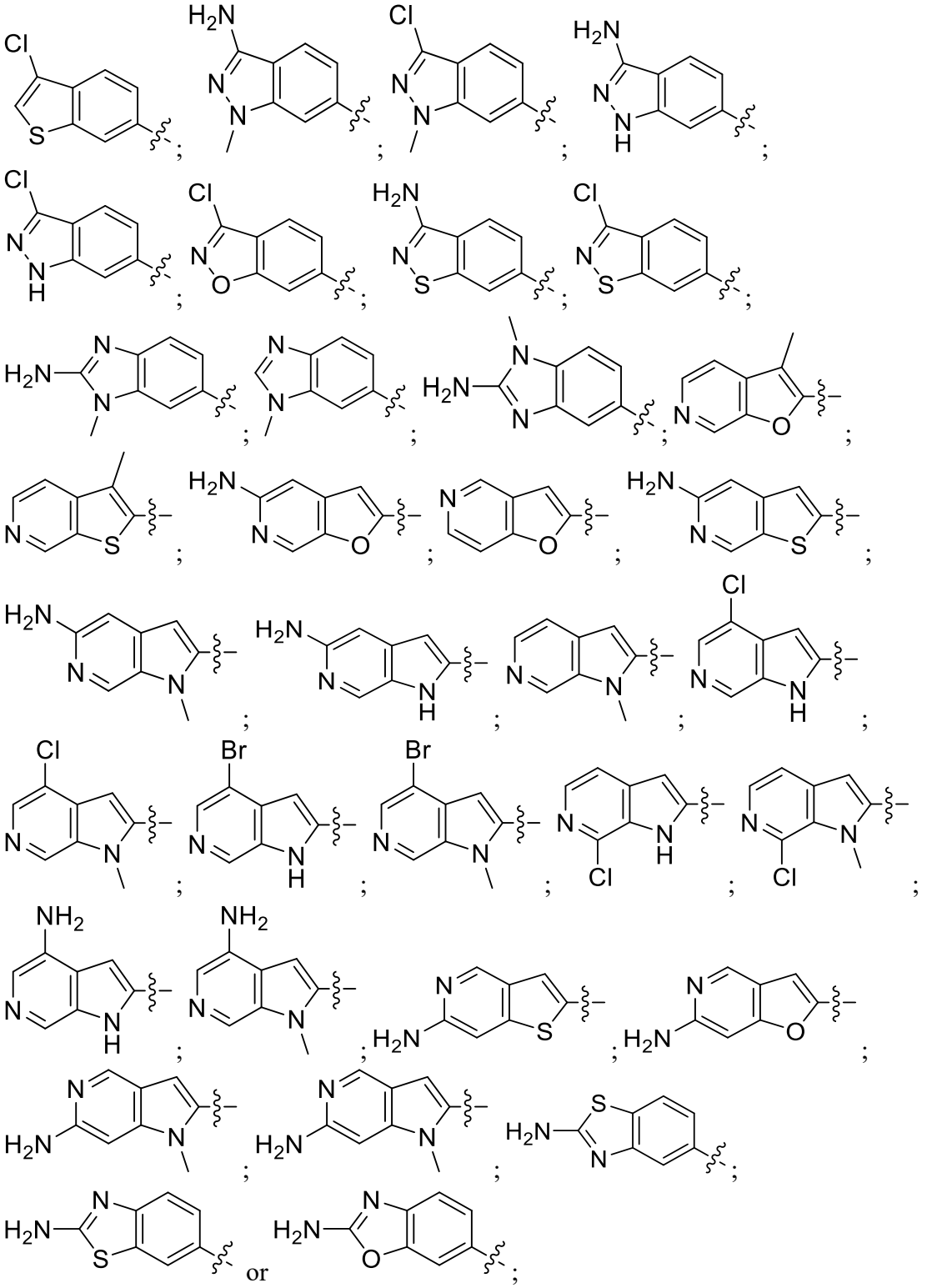
or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein:

R^1 is a substituted or unsubstituted heteroaryl,

wherein the substituted or unsubstituted heteroaryl is selected from the group consisting of:







R^2 is a substituted or unsubstituted aryl, or a substituted or unsubstituted heteroaryl,

wherein the substituted aryl of R^2 is substituted with one or more of R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} wherein R^{2a}, R^{2b}, R^{2c}, R^{2d}, and R^{2e} are each independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} deuterated alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halo, C_{1-6}

haloalkyl, aminylalkyl, hydroxyalkyl, phosphate, phosphonalkyl, phosphoalkyl, cyano, nitro, OR^a, SR^a, $C(O)R^a$, $C(O)NR^aR^b$, $C(O)OR^a$, $OC(O)R^a$, $OC(O)OR^a$, $OC(O)NR^aR^b$, NR^aR^b, $N(R^a)C(O)R^b$, $N(R^a)C(O)NR^bR^c$, $N(R^a)C(O)OR^b$, $C(=NR^a)NR^bR^c$, $C(=NOR^a)NR^bR^c$, $C(=NOC(O)R^a)NR^bR^c$, $C(=NR^a)N(R^b)C(O)OR^c$, $N(R^a)C(=NR^b)NR^cR^d$, $S(O)R^a$, $S(O)NR^aR^b$, $S(O)_2R^a$, $N(R^a)S(O)_2R^b$, $S(O)_2NR^aR^b$, substituted or unsubstituted C_{6-10} aryl, substituted or unsubstituted C_{6-10} arylalkyl, substituted or unsubstituted C_{6-10} aryloxy, substituted or unsubstituted C_{6-10} arylalkoxy, substituted or unsubstituted 5-10 membered heteroaryl, substituted or unsubstituted C_{3-10} cycloalkyl, and substituted or unsubstituted 4-10 membered heterocyclyl,

wherein R^a, R^b, R^c, and R^d, are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl, and

wherein R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} is optionally substituted with one or more substituents selected from the group consisting of halo, CN, OR^e, SR^e, $C(O)R^e$, $C(O)NR^eR^f$, $C(O)OR^e$, $OC(O)R^e$, $OC(O)NR^eR^f$, NR^eR^f, $NR^eC(O)R^f$, $NR^eC(O)NR^fR^g$, $NR^eC(O)OR^f$, $C(=NR^e)NR^fR^g$, $NR^eC(=NR^f)NR^gR^h$, $S(O)R^e$, $S(O)NR^eR^f$, $S(O)_2R^e$, $NR^eS(O)_2R^f$, $S(O)_2NR^eR^f$ and when R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} is a substituted C_{6-10} aryl, a substituted C_{6-10} arylalkyl, a substituted C_{6-10} aryloxy, a substituted C_{6-10} arylalkoxy, a substituted 5-10 membered heteroaryl, a substituted C_{3-10} cycloalkyl, and a substituted 4-10 membered heterocyclyl,

wherein R^e, R^f, R^g, and R^h are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl,

wherein the substituted heteroaryl of R^2 is substituted with one or more of R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} wherein R^{2a}, R^{2b}, R^{2c}, R^{2d}, and R^{2e} are each independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} deuterated alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halo, C_{1-6} haloalkyl, aminylalkyl, hydroxyalkyl, cyano, nitro, OR^a, SR^a, $C(O)R^a$, $C(O)NR^aR^b$, $C(O)OR^a$, $OC(O)R^a$, $OC(O)OR^a$, $OC(O)NR^aR^b$, NR^aR^b, $N(R^a)C(O)R^b$, $N(R^a)C(O)NR^bR^c$, $N(R^a)C(O)OR^b$, $C(=NR^a)NR^bR^c$, $C(=NOR^a)NR^bR^c$, $C(=NOC(O)R^a)NR^bR^c$, $C(=NR^a)N(R^b)C(O)OR^c$, $N(R^a)C(=NR^b)NR^cR^d$, $S(O)R^a$, $S(O)NR^aR^b$, $S(O)_2R^a$, $N(R^a)S(O)_2R^b$, $S(O)_2NR^aR^b$, substituted or unsubstituted C_{6-10} aryl, substituted or unsubstituted C_{6-10} arylalkyl, substituted or unsubstituted C_{6-10} aryloxy, substituted or unsubstituted C_{6-10} arylalkoxy, substituted or unsubstituted 5-10 membered heteroaryl, substituted or unsubstituted C_{3-10} cycloalkyl, and substituted or unsubstituted 4-10 membered heterocyclyl,

wherein R^a, R^b, R^c, and R^d, are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl, and

wherein R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} is optionally substituted with one or more substituents selected from the group consisting of halo, CN, OR^e, SR^e, $C(O)R^e$, $C(O)NR^eR^f$, $C(O)OR^e$, $OC(O)R^e$, $OC(O)NR^eR^f$, NR^eR^f, $NR^eC(O)R^f$, $NR^eC(O)NR^fR^g$, $NR^eC(O)OR^f$, $C(=NR^e)NR^fR^g$, $NR^eC(=NR^f)NR^gR^h$, $S(O)R^e$, $S(O)NR^eR^f$, $S(O)_2R^e$, $NR^eS(O)_2R^f$, $S(O)_2NR^eR^f$ and when R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} is a substituted C_{6-10} aryl, a substituted C_{6-10} arylalkyl, a substituted C_{6-10} aryloxy, a substituted C_{6-10} arylalkoxy, a

substituted 5-10 membered heteroaryl, a substituted C_{3-10} cycloalkyl, and a substituted 4-10 membered heterocyclyl,

wherein R^e, R^f, R^g, and R^h are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl;

R^3 is hydrogen or alkyl;

R^4 is alkyl, an arylalkyl, a heterocyclyl substituted with substituents selected from the group consisting of a phenyl or a pyridinyl, or R^3 and R^4, together with the nitrogen to which they are attached, form a 4-10 membered heterocyclyl;

R^{5a} is hydrogen or halo;

R^{5b} is hydrogen, alkyl, haloalkyl, (C=O)alkyl, (C=O)Oalkyl, (C=O)cycloalkyl, (C=O)Ocycloalkyl, (C=O)aryl, (C=O)Oaryl, (C=O)heteroaryl, (C=O)Oheteroaryl, (C=O)heterocyclyl, (C=O)Oheterocyclyl, an aryl, a heteroaryl, a cycloalkyl, a heterocyclyl, an arylalkyl, a heteroarylalkyl, a cycloalkylalkyl, or a heterocyclylalkyl;

L^1 is a direct bond, $-CH_2-$, $-S(O)_t-$, NR^{5b}, -O-, -C=C-, or -C≡C-; and

t is 0, 1, or 2, and

wherein the aryl is a 6- to 18-membered monocyclic, bicyclic, tricyclic, or tetracyclic ring system comprising at least one aromatic ring, and which can comprise fused or bridged ring systems,

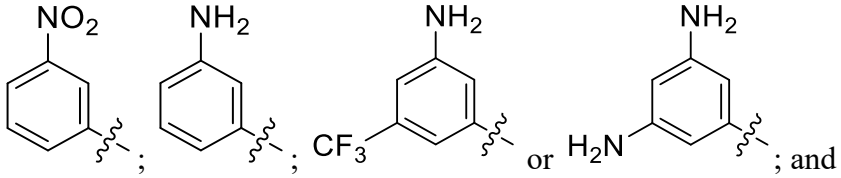
wherein the heteroaryl of R^2, R^a, R^b, R^c, R^d, R^e, R^f, R^g, R^h, and R^{5b}, are a 5- to 14-membered monocyclic, bicyclic, tricyclic, or tetracyclic ring system consisting of at least one aromatic ring, one to thirteen carbon atoms, one to six heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, and can comprise fused or bridged ring systems,

wherein the cycloalkyl is a non-aromatic 3- to 15-membered monocyclic or polycyclic ring system, which is saturated or unsaturated, and which can comprise fused or bridged ring systems, and

wherein the heterocyclyl is a 3- to 18-membered monocyclic, bicycylic, tricyclic, or tetracyclic ring system consisting of two to twelve carbon atoms and from one to six heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, and which can comprise fused, bridged, and spiro ring systems,

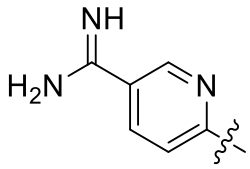
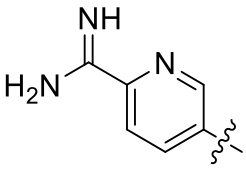
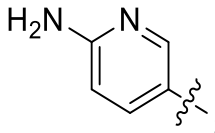
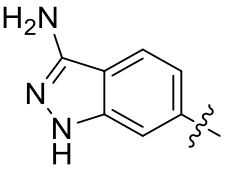
provided that:

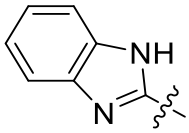
A) R^2 does not have one of the following structures:



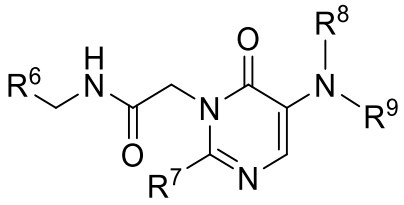
; ; or ; and

B) when R^2 is unsubstituted phenyl, R^1 does not have one of the following structures:

 ;  ;  ;  ; or

 .

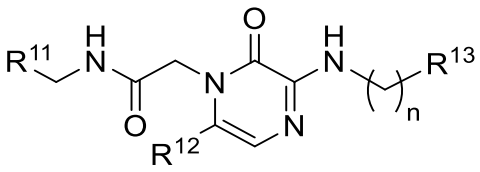
Another example provides a compound having the following Structure (II):



(II)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein R^6, R^7, R^8, and R^9 are as defined below.

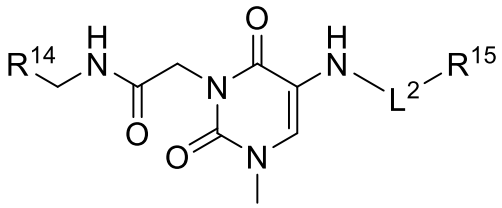
Another example provides a compound having the following Structure (III):



(III)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein R^{11}, R^{12}, R^{13}, and n are as defined below.

Another example provides a compound having the following Structure (IV):



(IV)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein R^{14}, R^{15}, and L^2 are as defined below.

Additional examples of the present disclosure provide a pharmaceutical composition comprising a compound of Structure (I), (II), (III), or (IV),

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier or excipient.

In one aspect, the present disclosure refers to a pharmaceutical composition comprising a compound or pharmaceutically acceptable salt thereof disclosed herein and a pharmaceutically acceptable carrier or excipient.

The compounds of Structures (I), (II), (III), and (IV) are useful in the treatment of MASP-2-associated diseases and disorders, and in the manufacture of medicaments for treating MASP-2-associated diseases and disorders. Accordingly, other examples of the disclosure provide methods of treating a MASP-2-associated disease and disorder comprising administering to a patient a therapeutically effective amount of a compound of Structure (I), (II), (III), or (IV), or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof.

In one aspect, the present disclosure refers to use of a compound disclosed herein, in the manufacture of a medicament for treating a MASP-2-associated disease or disorder in a subject in need thereof, wherein the MASP-2-associated disease or disorder is selected from the group consisting of thrombotic microangiopathy (TMA), a renal condition, an inflammatory reaction resulting from tissue or organ transplantation, an ischemia reperfusion injury, a complication associated with diabetes, a cardiovascular disease or disorder, an inflammatory gastrointestinal disorder, a pulmonary disorder, an ophthalmic disease or disorder, disseminated intravascular coagulation, graft-versus-host disease, veno-occlusive disease, diffuse alveolar hemorrhage, idiopathic pneumonia syndrome, capillary leak syndrome, engraftment syndrome, fluid overload, angiogenesis-dependent cancer or tumor or similar, as well as combinations thereof.

These and other aspects, objects and examples will become more apparent when read with the detailed description and figures which follow.

DETAILED DESCRIPTION

I. Definitions

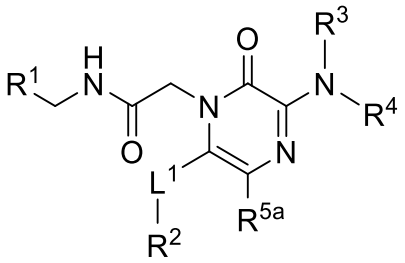
Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the subject matter of the present disclosure, suitable methods and materials are described below. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

In certain embodiments herein, reference is made to features and aspects of the disclosure, including method steps. All possible combinations of such features and aspects within the embodiments of the disclosure are included, at least to the extent that such combinations are non-contradictory. For example, if an embodiment presents aspects A, B, and C, it is understood that this also discloses embodiments including both aspects A and B, both aspects B and C, and both aspects A and C, as well as an embodiment with aspects A, B, and C.

The terms "a," "an," or "the" not only include aspects with one member, but also include aspects with more than one member. For instance, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise.

CLAIMS

1. A compound having the following Structure (I):

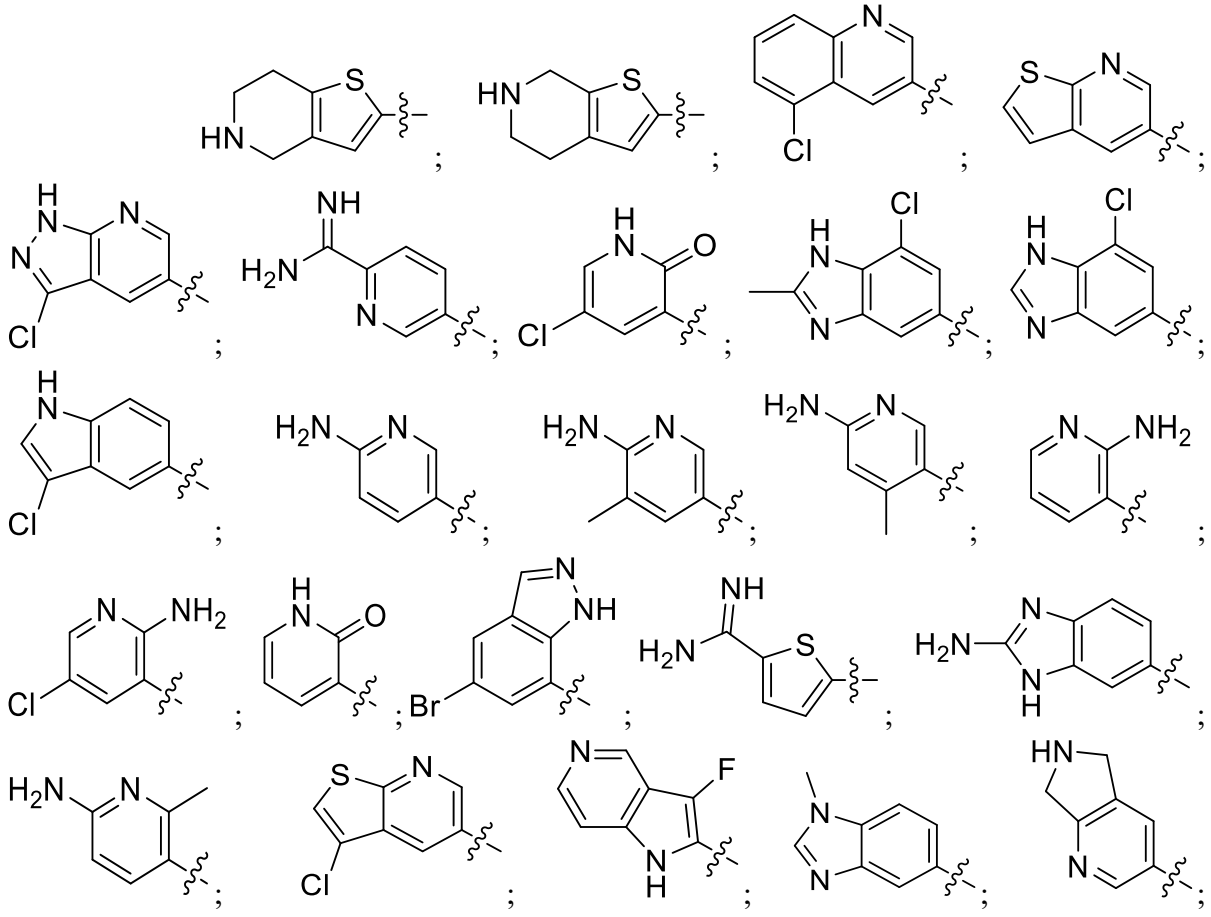


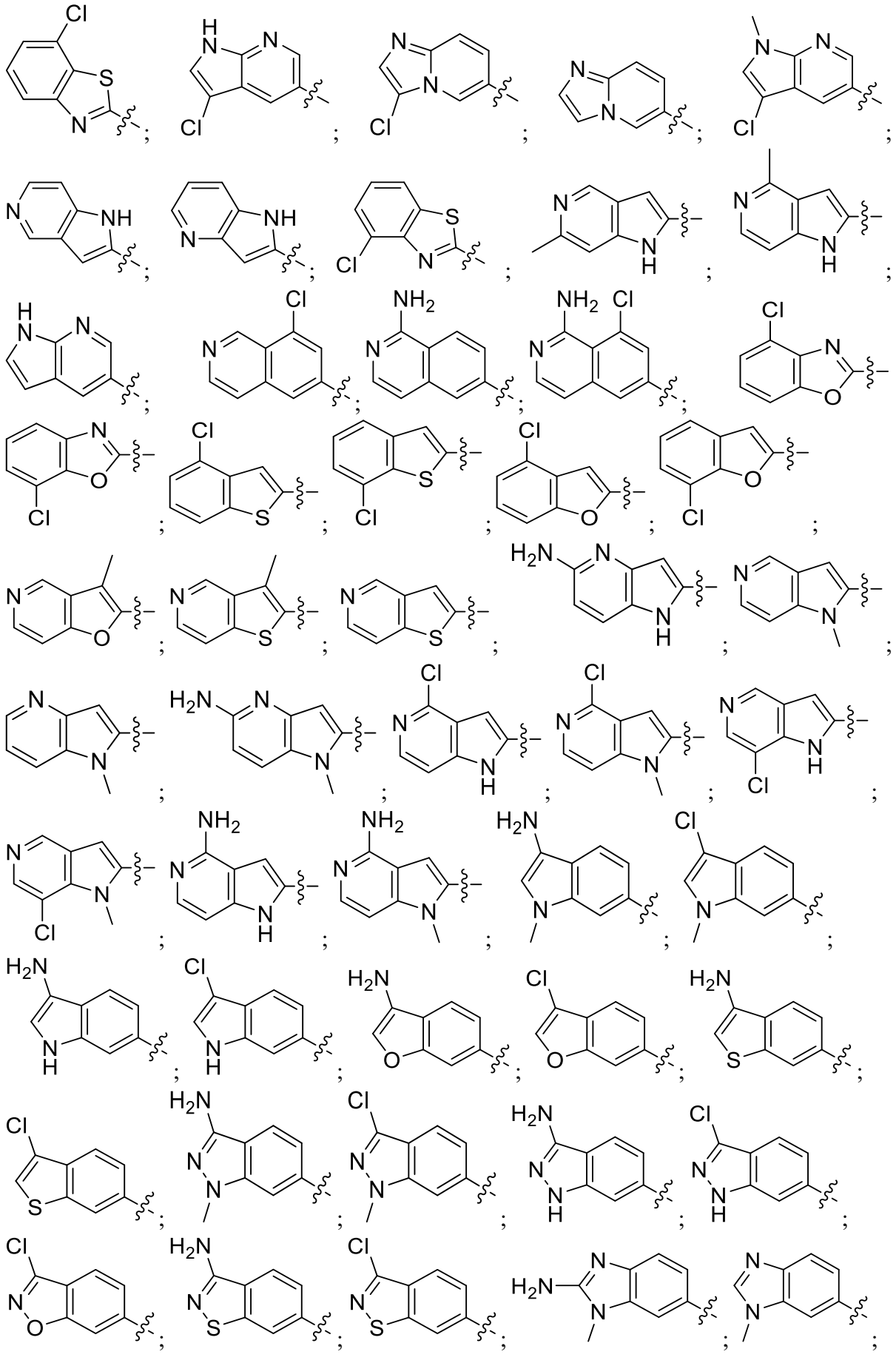
(I)

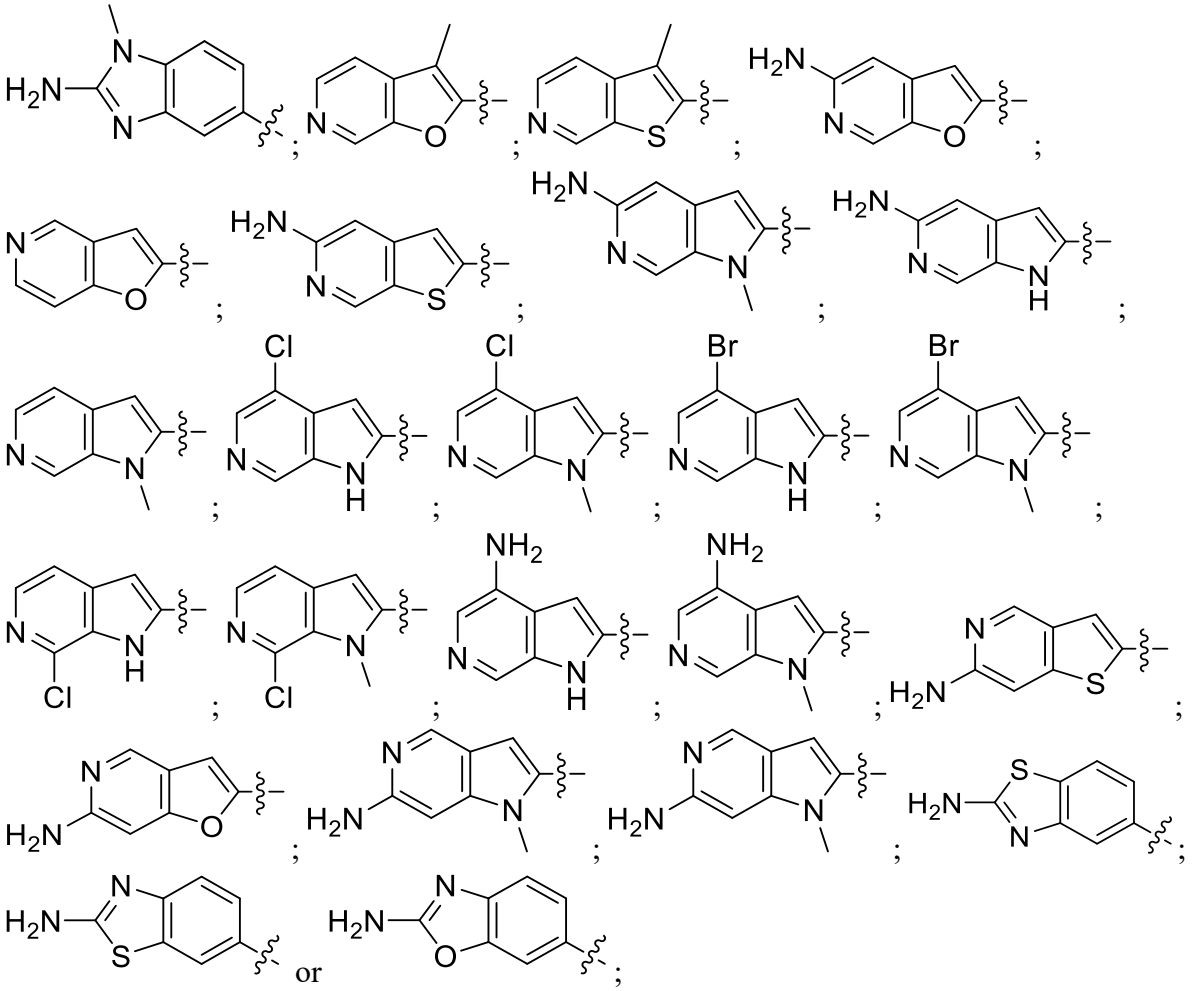
or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein:

R^1 is a substituted or unsubstituted heteroaryl,

wherein the substituted or unsubstituted heteroaryl is selected from the group consisting of:







R^2 is a substituted or unsubstituted aryl, or a substituted or unsubstituted heteroaryl,

wherein the substituted aryl of R^2 is substituted with one or more of R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} wherein R^{2a}, R^{2b}, R^{2c}, R^{2d}, and R^{2e} are each independently selected from the group consisting of $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ deuterated alkyl, $C_{2\text{-}6}$ alkenyl, $C_{2\text{-}6}$ alkynyl, halo, $C_{1\text{-}6}$ haloalkyl, aminylalkyl, hydroxyalkyl, phosphate, phosphonalkyl, phosphoalkyl, cyano, nitro, OR^a, SR^a, $C(O)R^a$, $C(O)NR^aR^b$, $C(O)OR^a$, $OC(O)R^a$, $OC(O)OR^a$, $OC(O)NR^aR^b$, NR^aR^b, $N(R^a)C(O)R^b$, $N(R^a)C(O)NR^bR^c$, $N(R^a)C(O)OR^b$, $C(=NR^a)NR^bR^c$, $C(=NOR^a)NR^bR^c$, $C(=NOC(O)R^a)NR^bR^c$, $C(=NR^a)N(R^b)C(O)OR^c$, $N(R^a)C(=NR^b)NR^cR^d$, $S(O)R^a$, $S(O)NR^aR^b$, $S(O)_2R^a$, $N(R^a)S(O)_2R^b$, $S(O)_2NR^aR^b$, substituted or unsubstituted $C_{6\text{-}10}$ aryl, substituted or unsubstituted $C_{6\text{-}10}$ arylalkyl, substituted or unsubstituted $C_{6\text{-}10}$ aryloxy, substituted or unsubstituted $C_{6\text{-}10}$ arylalkoxy, substituted or unsubstituted 5-10 membered heteroaryl, substituted or unsubstituted $C_{3\text{-}10}$ cycloalkyl, and substituted or unsubstituted 4-10 membered heterocyclyl,

wherein R^a, R^b, R^c, and R^d, are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl, and

wherein R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} is optionally substituted with one or more substituents selected from the group consisting of halo, CN, OR^e, SR^e, $C(O)R^e$, $C(O)NR^eR^f$, $C(O)OR^e$, $OC(O)R^e$, $OC(O)NR^eR^f$, NR^eR^f, $NR^eC(O)R^f$, $NR^eC(O)NR^fR^g$, $NR^eC(O)OR^f$, $C(=NR^e)NR^fR^g$, $NR^eC(=NR^f)NR^gR^h$, $S(O)R^e$, $S(O)NR^eR^f$, $S(O)_2R^e$, $NR^eS(O)_2R^f$, $S(O)_2NR^eR^f$ and when R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} is a substituted C_{6-10} aryl, a substituted C_{6-10} arylalkyl, a substituted C_{6-10} aryloxy, a substituted C_{6-10} arylalkoxy, a substituted 5-10 membered heteroaryl, a substituted C_{3-10} cycloalkyl, and a substituted 4-10 membered heterocyclyl,

wherein R^e, R^f, R^g, and R^h are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl,

wherein the substituted heteroaryl of R^2 is substituted with one or more of R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} wherein R^{2a}, R^{2b}, R^{2c}, R^{2d}, and R^{2e} are each independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} deuterated alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halo, C_{1-6} haloalkyl, aminylalkyl, hydroxyalkyl, cyano, nitro, OR^a, SR^a, $C(O)R^a$, $C(O)NR^aR^b$, $C(O)OR^a$, $OC(O)R^a$, $OC(O)OR^a$, $OC(O)NR^aR^b$, NR^aR^b, $N(R^a)C(O)R^b$, $N(R^a)C(O)NR^bR^c$, $N(R^a)C(O)OR^b$, $C(=NR^a)NR^bR^c$, $C(=NOR^a)NR^bR^c$, $C(=NOC(O)R^a)NR^bR^c$, $C(=NR^a)N(R^b)C(O)OR^c$, $N(R^a)C(=NR^b)NR^cR^d$, $S(O)R^a$, $S(O)NR^aR^b$, $S(O)_2R^a$, $N(R^a)S(O)_2R^b$, $S(O)_2NR^aR^b$, substituted or unsubstituted C_{6-10} aryl, substituted or unsubstituted C_{6-10} arylalkyl, substituted or unsubstituted C_{6-10} aryloxy, substituted or unsubstituted C_{6-10} arylalkoxy, substituted or unsubstituted 5-10 membered heteroaryl, substituted or unsubstituted C_{3-10} cycloalkyl, and substituted or unsubstituted 4-10 membered heterocyclyl,

wherein R^a, R^b, R^c, and R^d, are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl,

arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl, and

wherein R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} is optionally substituted with one or more substituents selected from the group consisting of halo, CN, OR^e, SR^e, $C(O)R^e$, $C(O)NR^eR^f$, $C(O)OR^e$, $OC(O)R^e$, $OC(O)NR^eR^f$, NR^eR^f, $NR^eC(O)R^f$, $NR^eC(O)NR^fR^g$, $NR^eC(O)OR^f$, $C(=NR^e)NR^fR^g$, $NR^eC(=NR^f)NR^gR^h$, $S(O)R^e$, $S(O)NR^eR^f$, $S(O)_2R^e$, $NR^eS(O)_2R^f$, $S(O)_2NR^eR^f$ and when R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} is a substituted C_{6-10} aryl, a substituted C_{6-10} arylalkyl, a substituted C_{6-10} aryloxy, a substituted C_{6-10} arylalkoxy, a substituted 5-10 membered heteroaryl, a substituted C_{3-10} cycloalkyl, and a substituted 4-10 membered heterocyclyl,

wherein R^e, R^f, R^g, and R^h are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl;

R^3 is hydrogen or alkyl;

R^4 is alkyl, an arylalkyl, a heterocyclyl substituted with substituents selected from the group consisting of a phenyl or a pyridinyl, or R^3 and R^4, together with the nitrogen to which they are attached, form a 4-10 membered heterocyclyl;

R^{5a} is hydrogen or halo;

R^{5b} is hydrogen, alkyl, haloalkyl, (C=O)alkyl, (C=O)Oalkyl, (C=O)cycloalkyl, (C=O)Ocycloalkyl, (C=O)aryl, (C=O)Oaryl, (C=O)heteroaryl, (C=O)Oheteroaryl, (C=O)heterocyclyl, (C=O)Oheterocyclyl, an aryl, a heteroaryl, a cycloalkyl, a heterocyclyl, an arylalkyl, a heteroarylalkyl, a cycloalkylalkyl, or a heterocyclylalkyl;

L^1 is a direct bond, $-CH_2-$, $-S(O)_t-$, NR^{5b}, -O-, -C=C-, or -C≡C-; and

t is 0, 1, or 2, and

wherein the aryl is a 6- to 18-membered monocyclic, bicyclic, tricyclic, or tetracyclic ring system comprising at least one aromatic ring, and which can comprise fused or bridged ring systems,

wherein the heteroaryl of R^2, R^a, R^b, R^c, R^d, R^e, R^f, R^g, R^h, and R^{5b}, are a 5- to 14-membered monocyclic, bicyclic, tricyclic, or tetracyclic ring system consisting of at least one

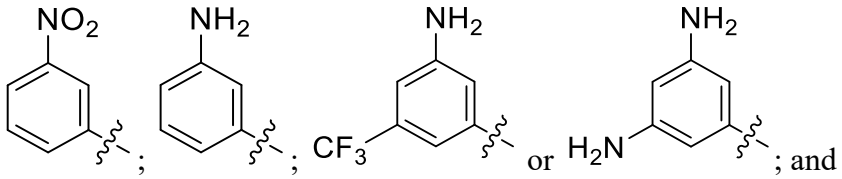
aromatic ring, one to thirteen carbon atoms, one to six heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, and can comprise fused or bridged ring systems,

wherein the cycloalkyl is a non-aromatic 3- to 15-membered monocyclic or polycyclic ring system, which is saturated or unsaturated, and which can comprise fused or bridged ring systems, and

wherein the heterocyclyl is a 3- to 18-membered monocyclic, bicyclic, tricyclic, or tetracyclic ring system consisting of two to twelve carbon atoms and from one to six heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, and which can comprise fused, bridged, and spiro ring systems,

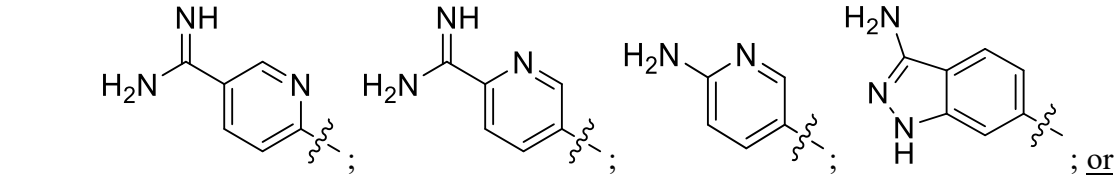
provided that:

A) R^2 does not have one of the following structures:

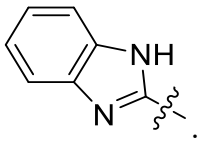


; ; or ; and

B) when R^2 is unsubstituted phenyl, R^1 does not have one of the following structures:



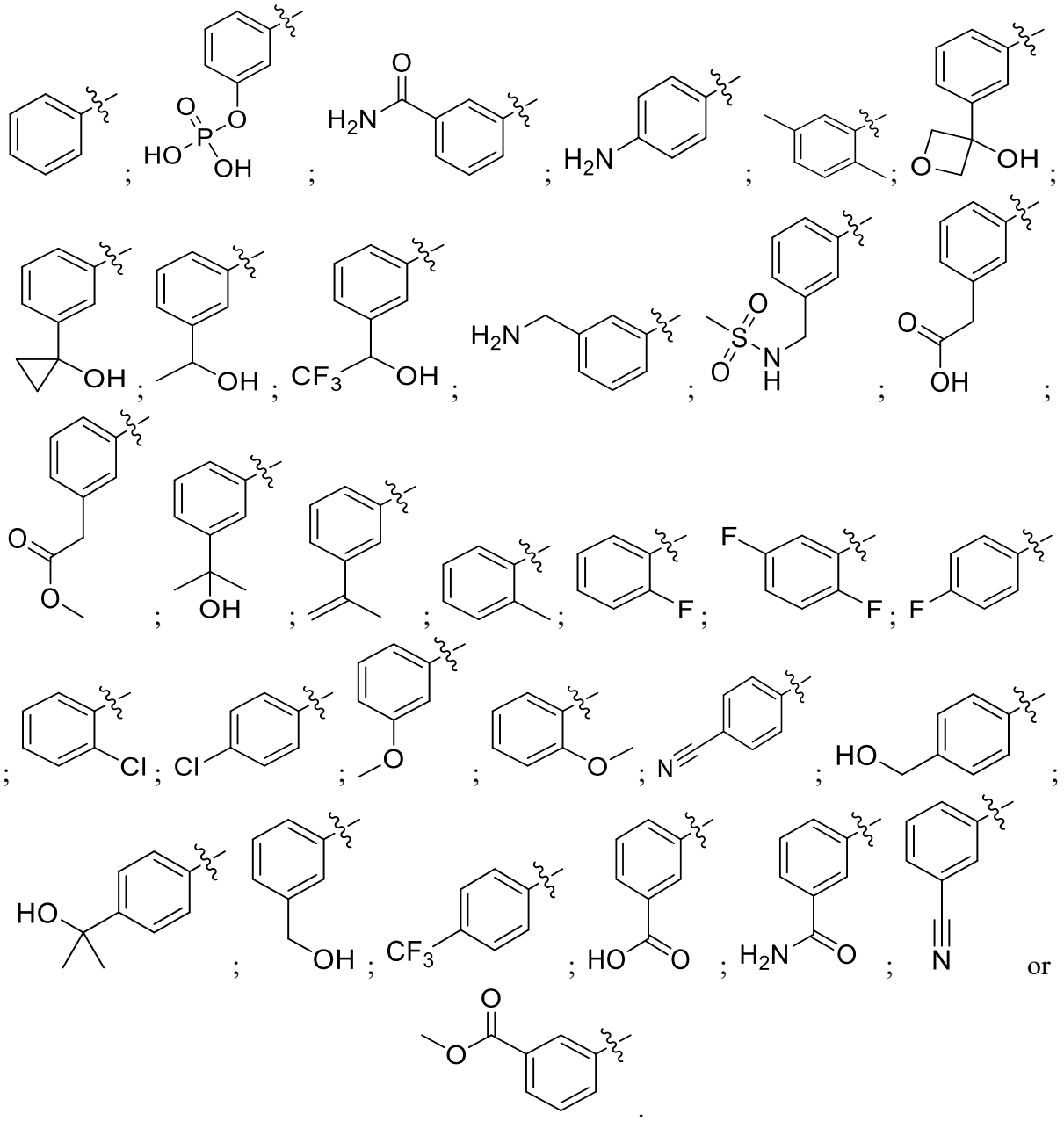
; ; ; ; or



.

2. The compound of claim 1, wherein R^2 is a substituted or unsubstituted phenyl.

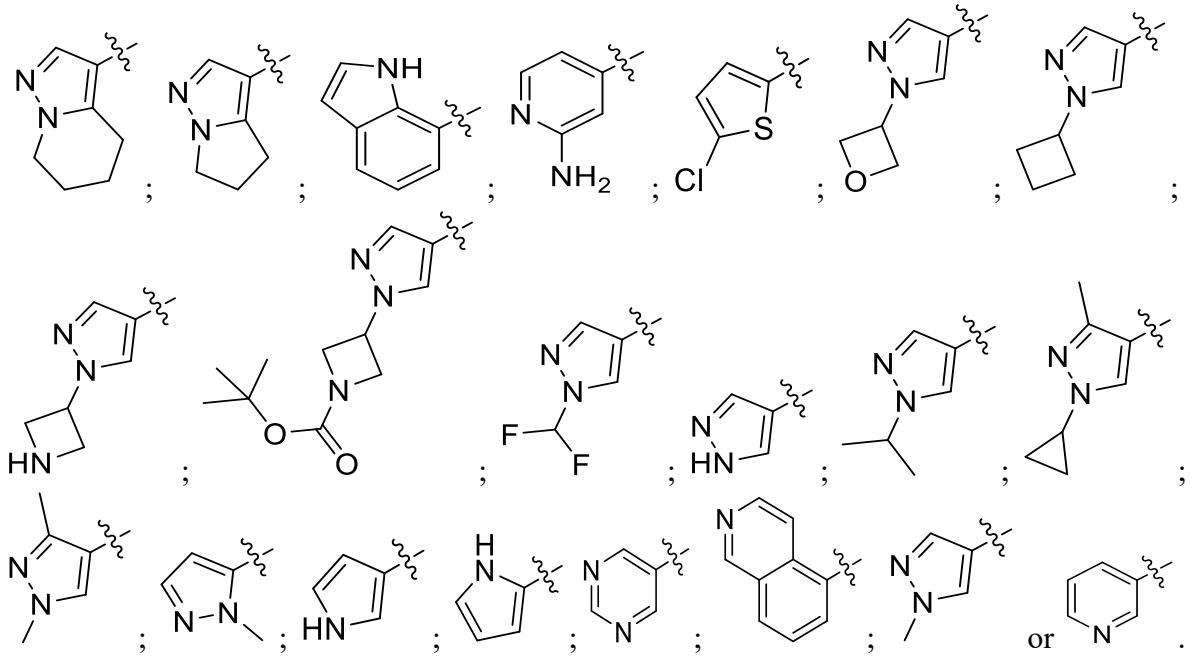
3. The compound of claim 1, wherein R^2 has one of the following structures:



4. The compound of claim 1, wherein R^2 is a substituted or unsubstituted 5-10 membered heteroaryl.

5. The compound of claim 1, wherein R^2 is a substituted or unsubstituted pyridinyl, a substituted or unsubstituted pyrrolyl, a substituted or unsubstituted pyrimidinyl, a substituted or unsubstituted isoquinolinyl, a substituted or unsubstituted pyrazolyl, a substituted or unsubstituted pyrrolopyridinyl, or a substituted or unsubstituted benzoimidazolyl.

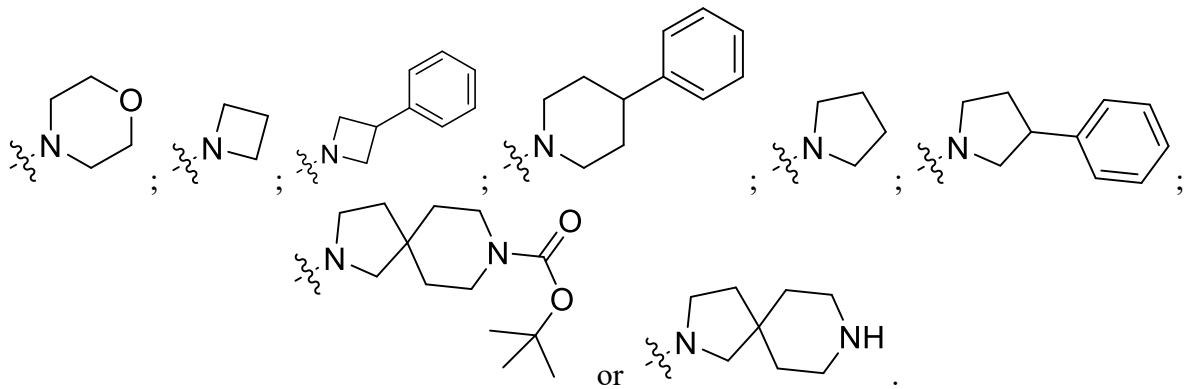
6. The compound of claim 1, wherein R^2 has one of the following structures:



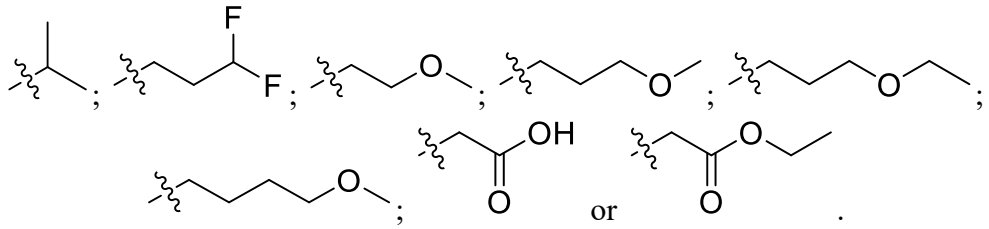
7. The compound of claim 1, wherein R^3 is hydrogen or methyl.

8. The compound of claim 1, wherein R^3 and R^4, together with the nitrogen to which they are attached form an optionally substituted 4-10 membered heterocyclyl.

9. The compound of claim 1, wherein R^3 and R^4, together with the nitrogen to which they are attached form one of the following structures:

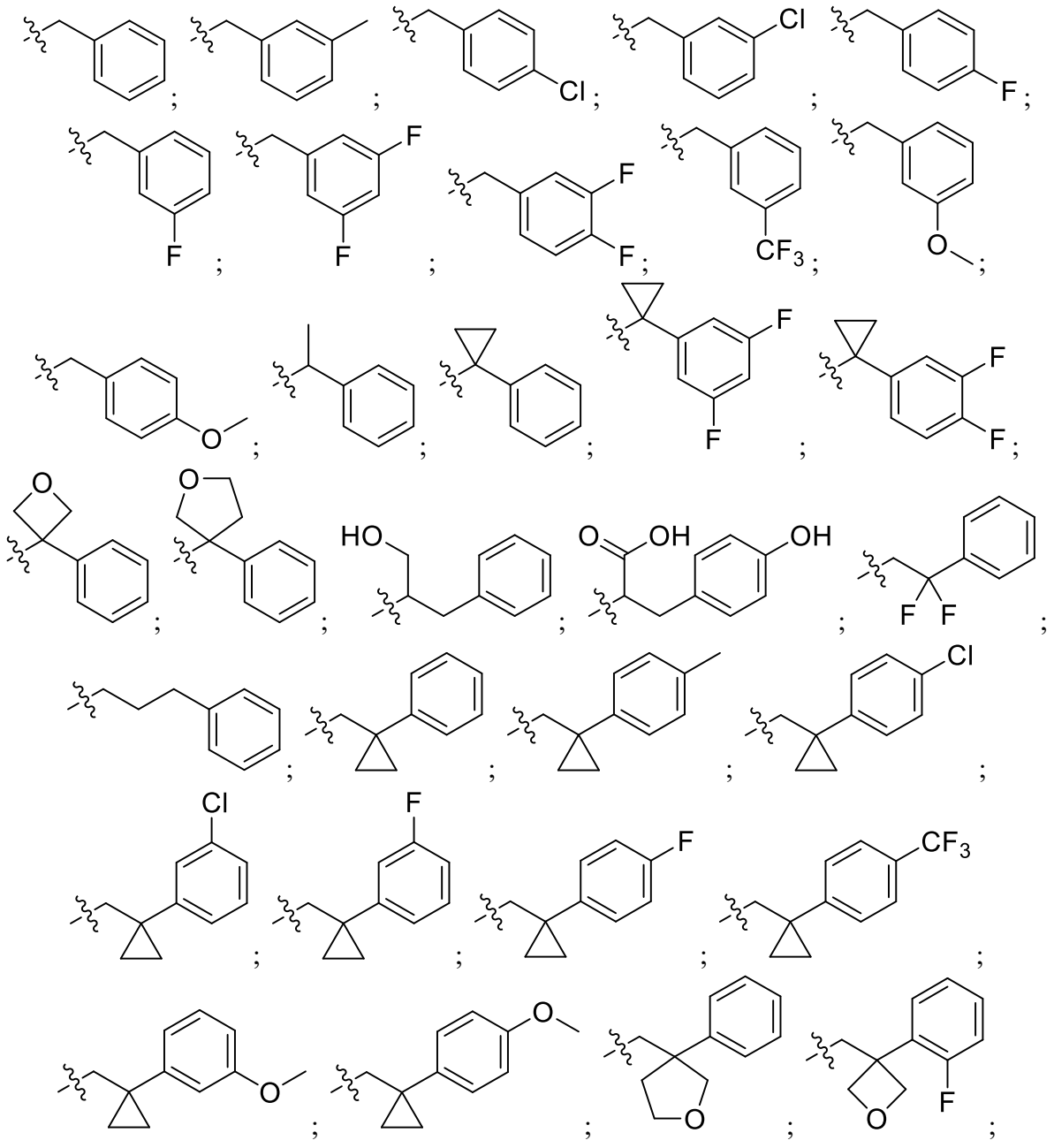


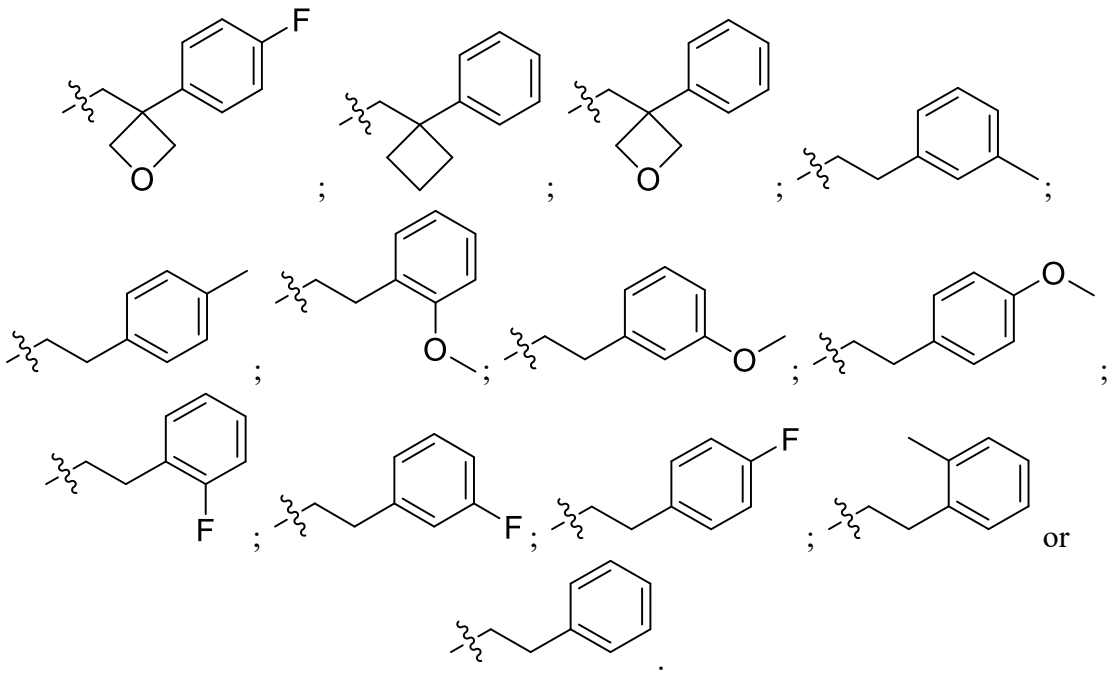
10. The compound of claim 1, wherein R^4 is methyl or has one of the following structures:



11. The compound of claim 1, wherein R^4 is a substituted or unsubstituted arylalkyl.

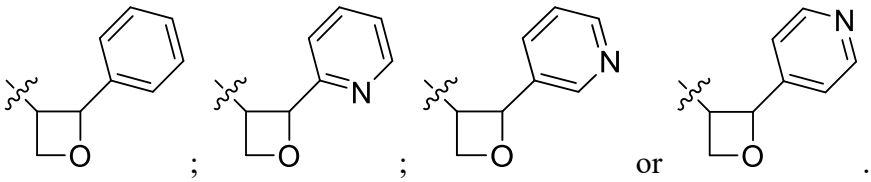
12. The compound of claim 1, wherein R^4 has the following structure:





13. The compound of claim 1, wherein R^4 is a heterocyclyl substituted with substituents selected from the group consisting of a substituted or unsubstituted phenyl or a substituted or unsubstituted pyridinyl.

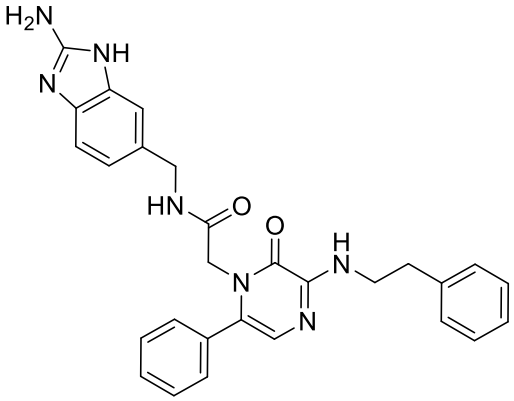
14. The compound of claim 1, wherein R^4 has one of the following structures:



15. The compound of claim 1, wherein L^1 is a direct bond, -CH_2-, or -C≡C-.

16. The compound of claim 1, wherein R^{5a} is hydrogen, F, Br, or Cl.

17. A compound of claim 1, having one of the following structures: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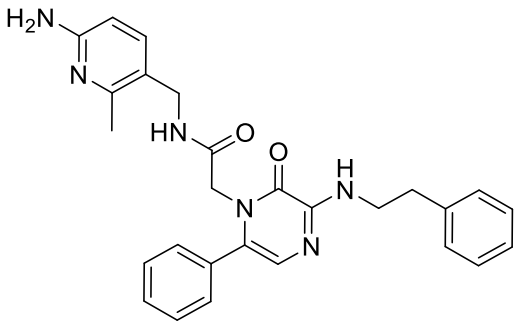
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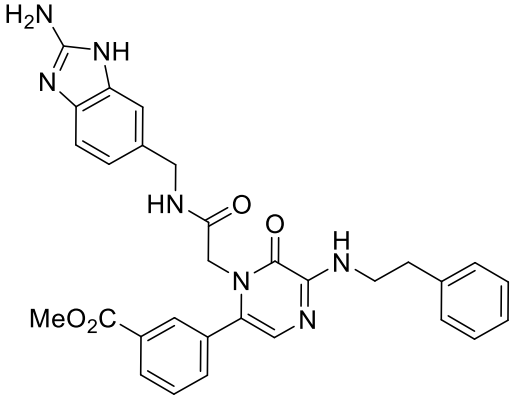
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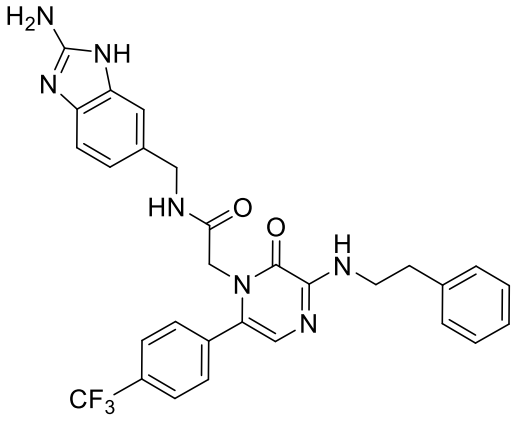
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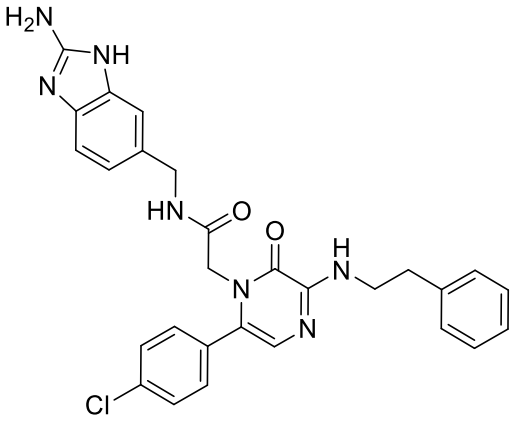
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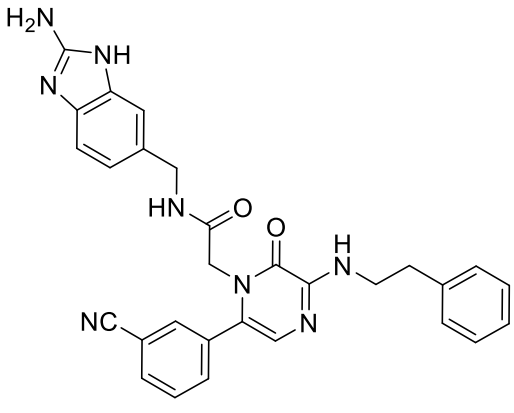
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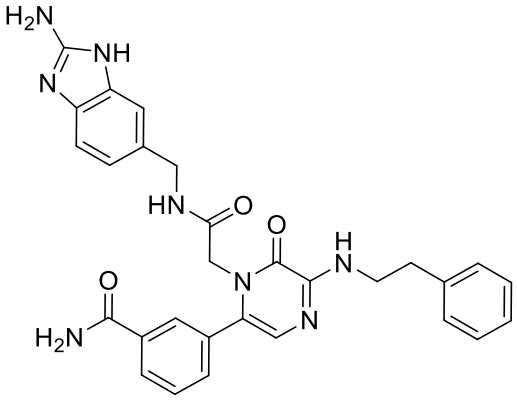
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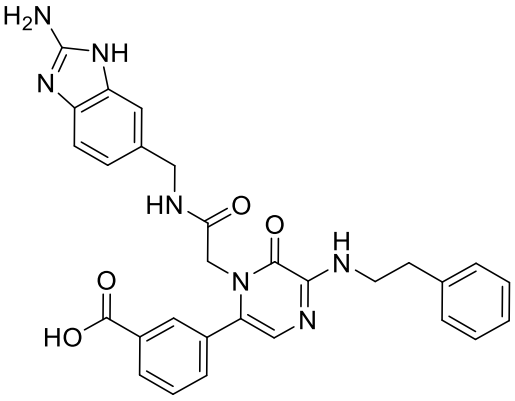
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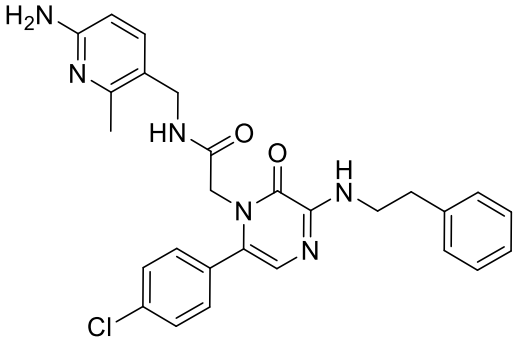
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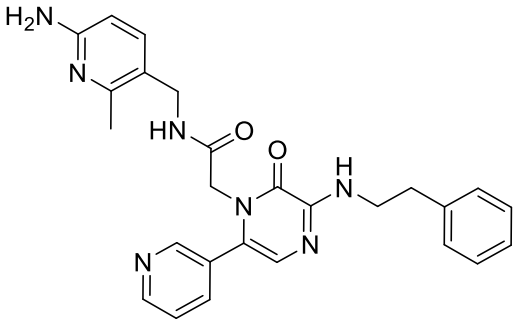
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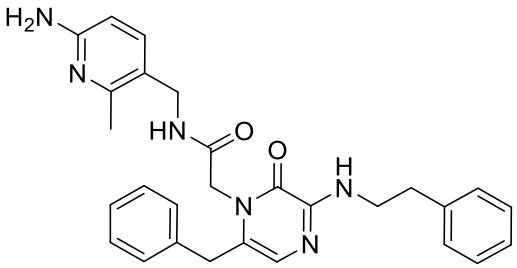
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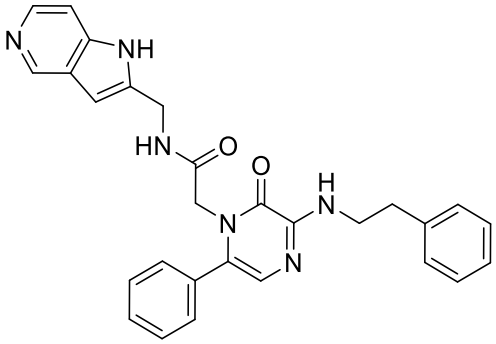
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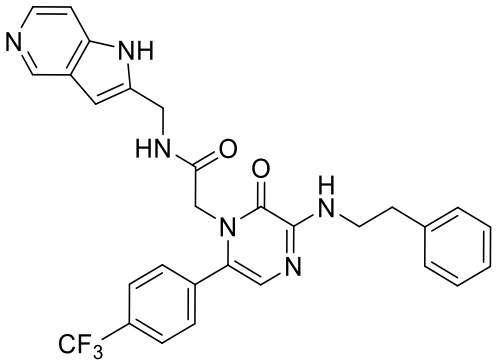
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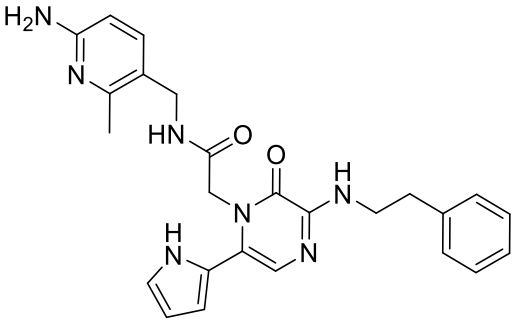
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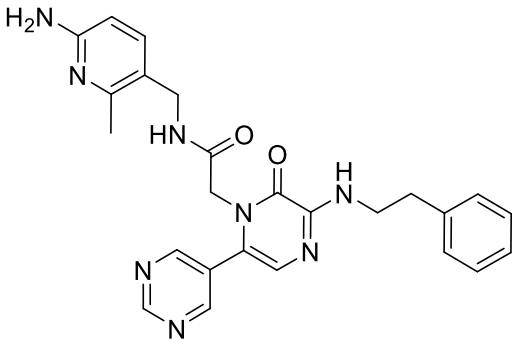
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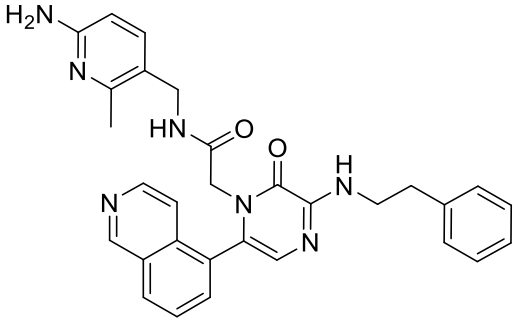
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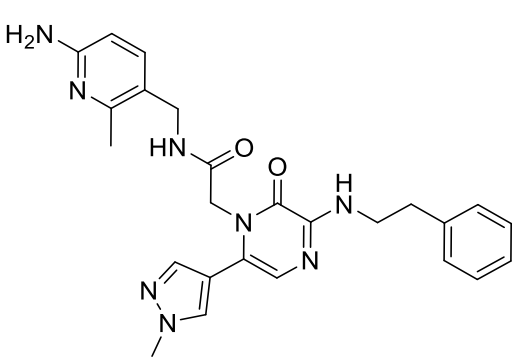
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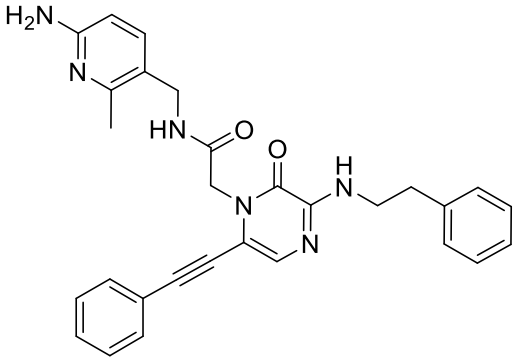
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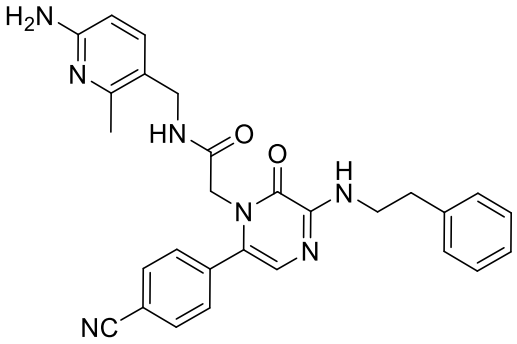
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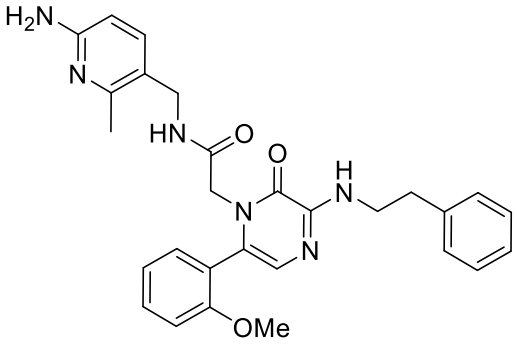
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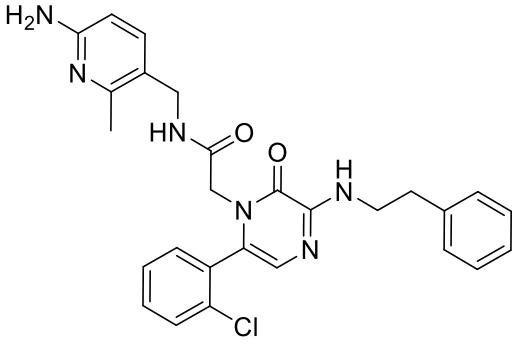
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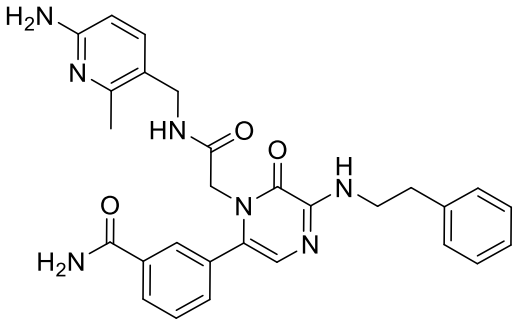
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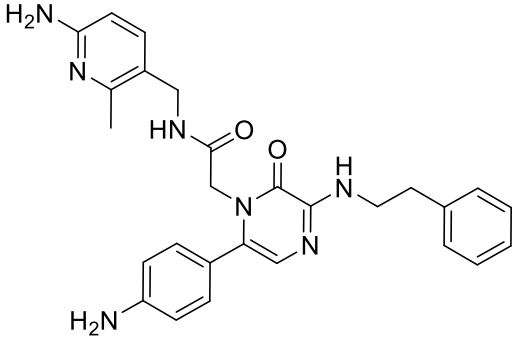
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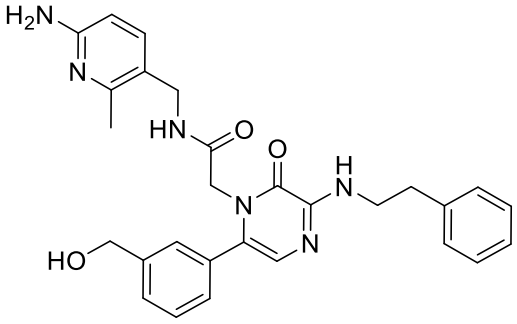
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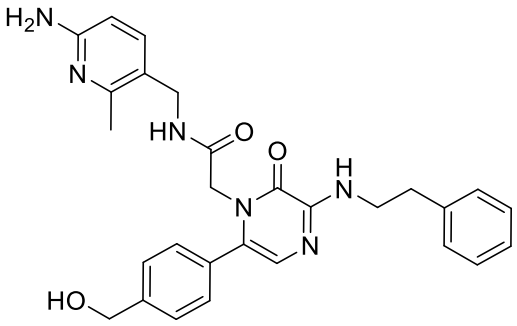
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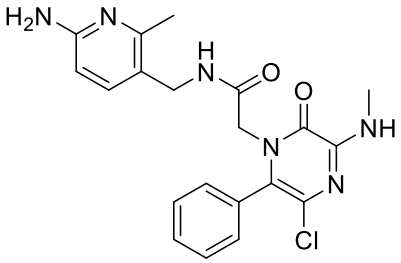
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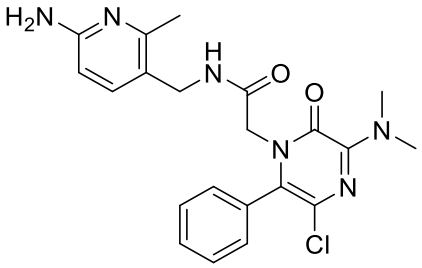
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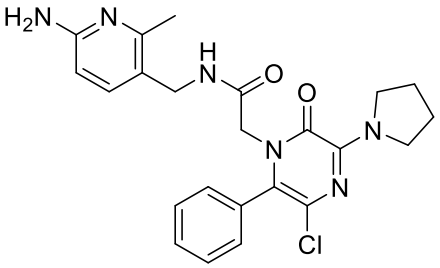
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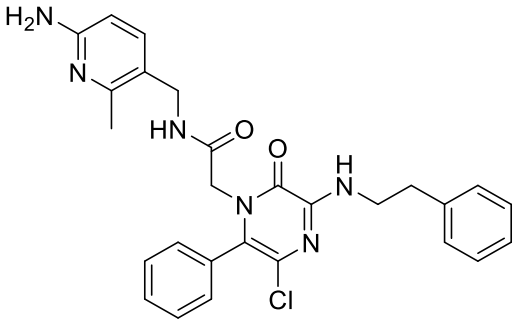
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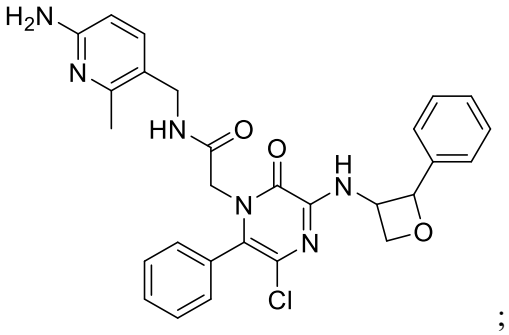
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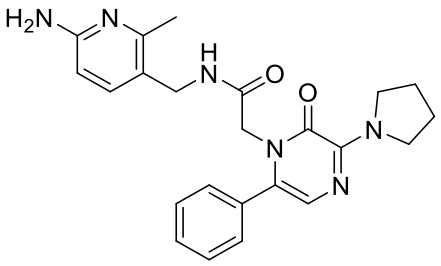
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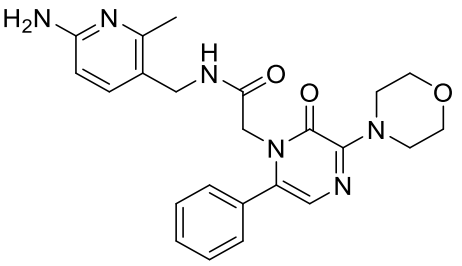
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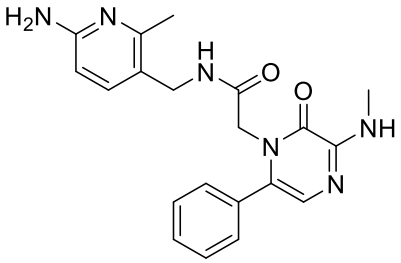
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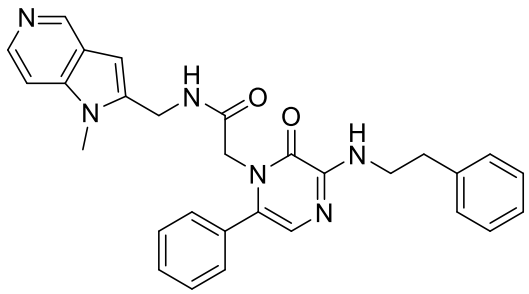
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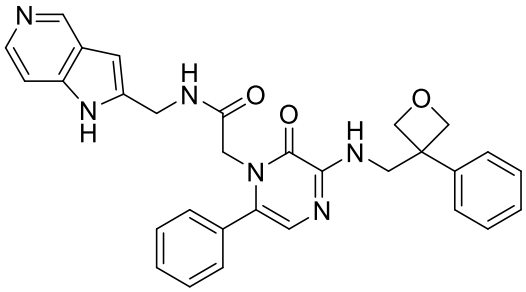
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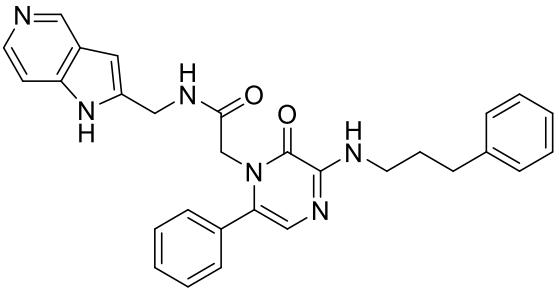
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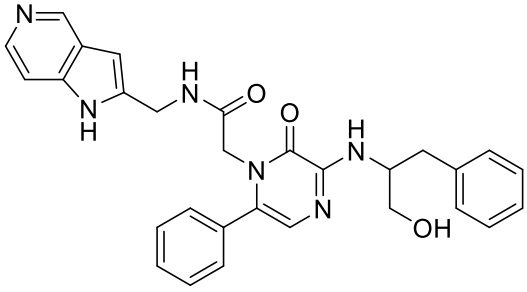
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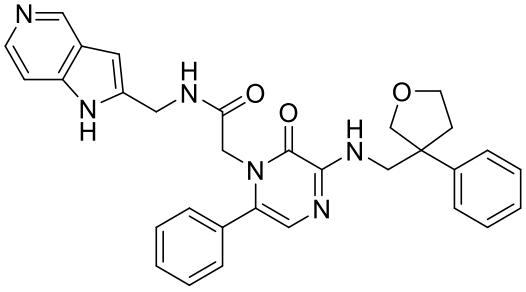
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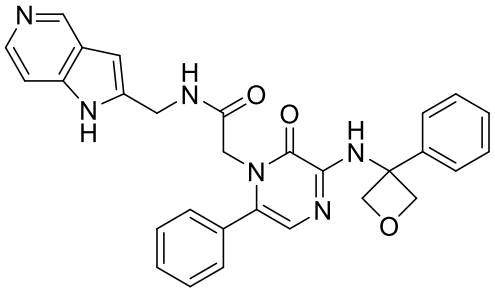
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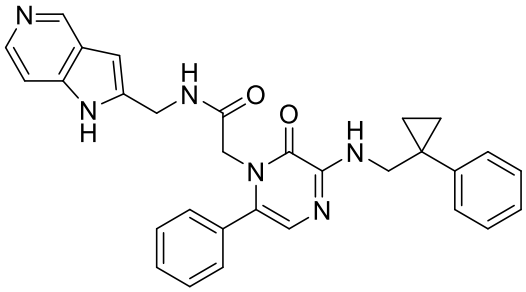
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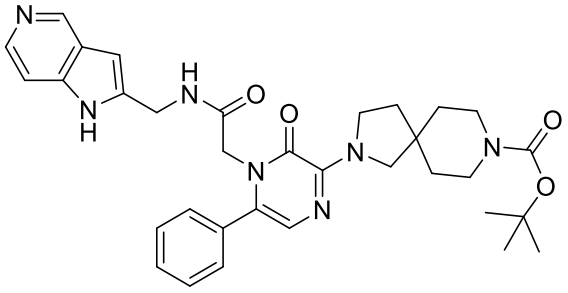
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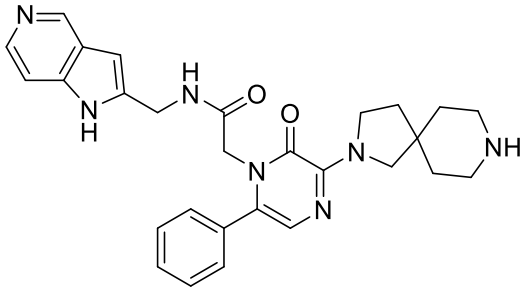
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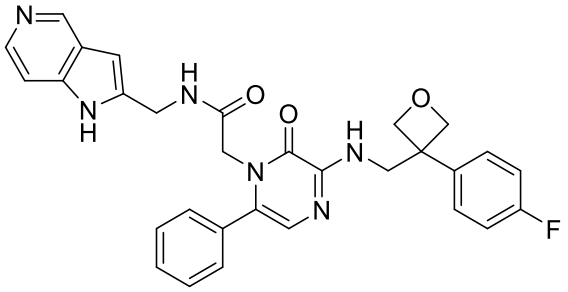
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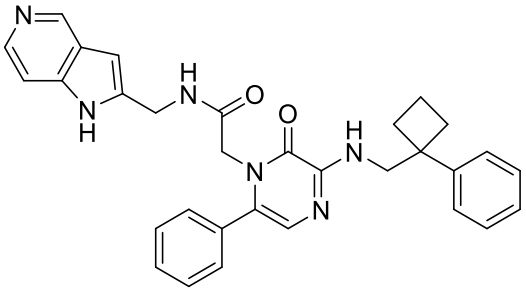
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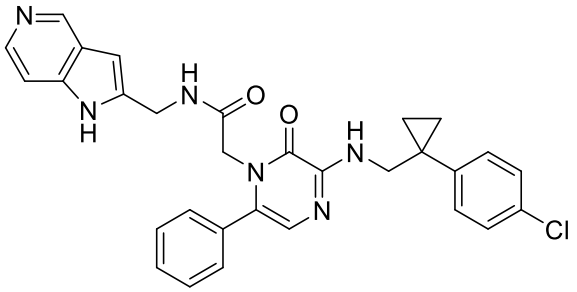
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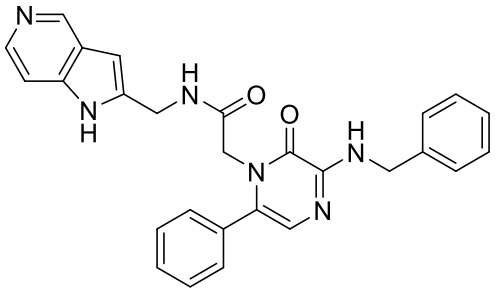
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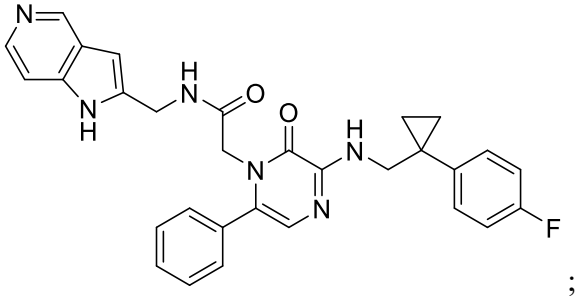
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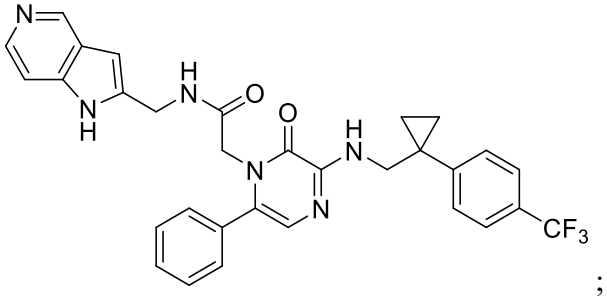
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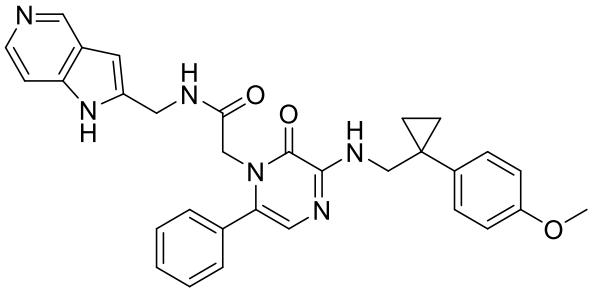
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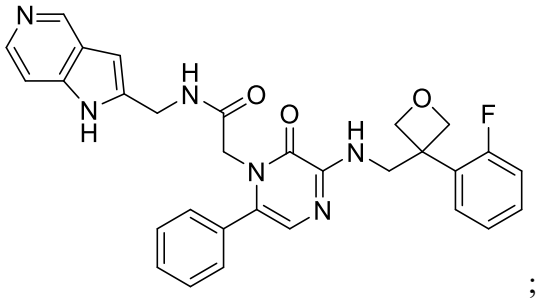
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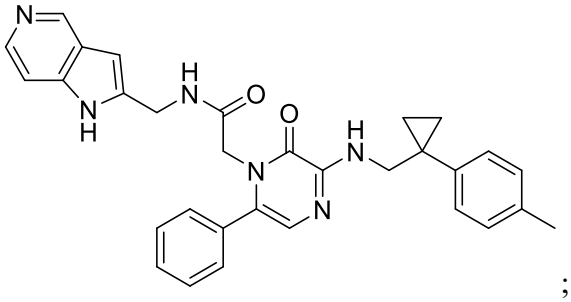
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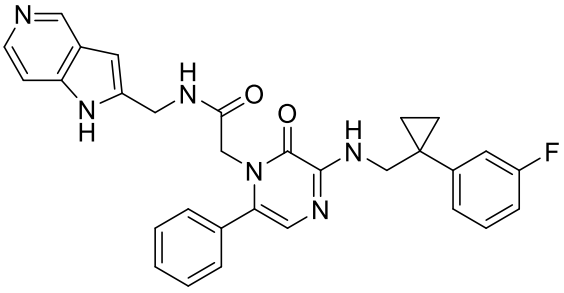
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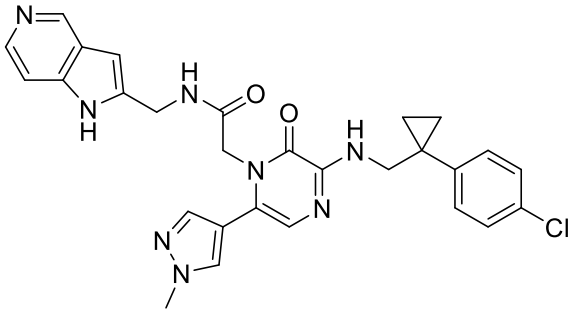
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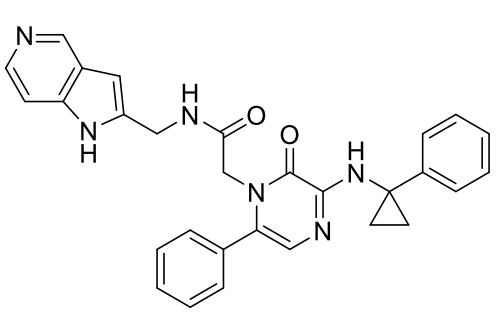
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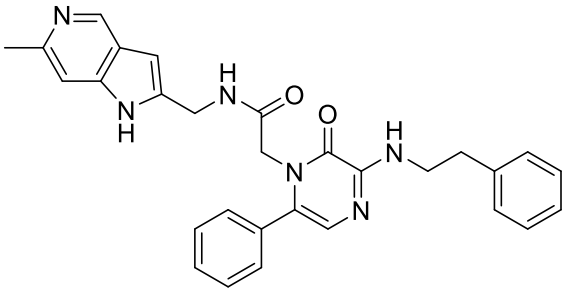
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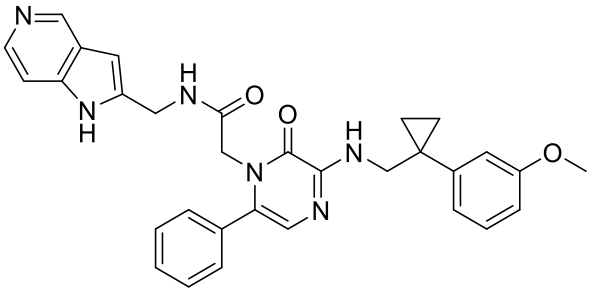
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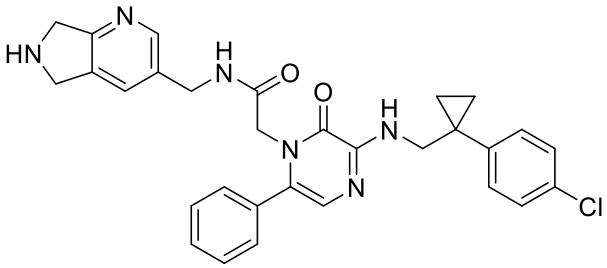
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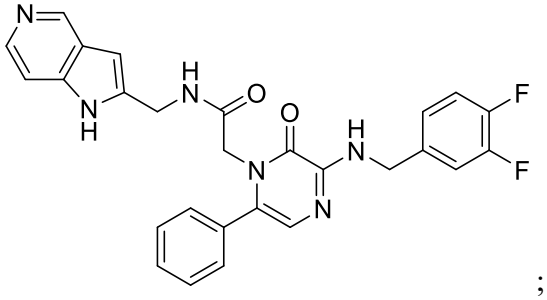
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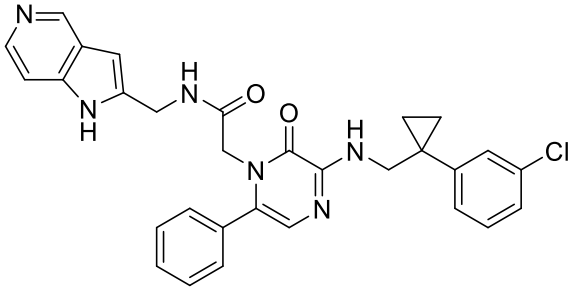
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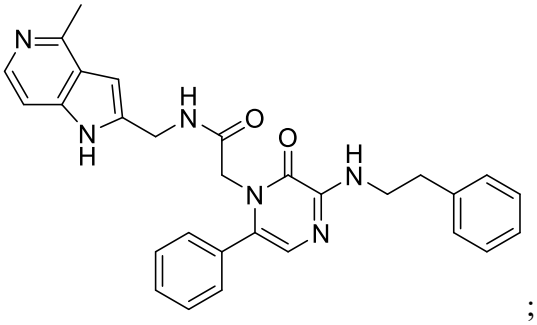
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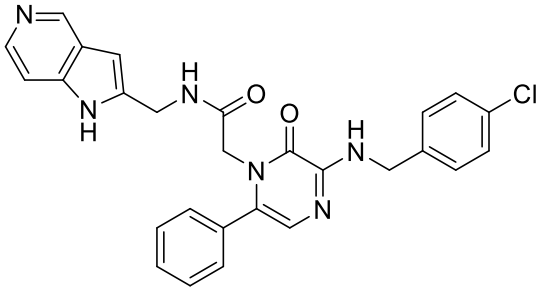
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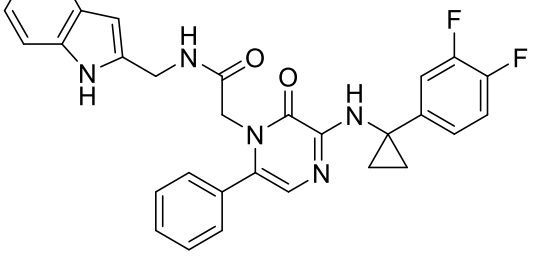
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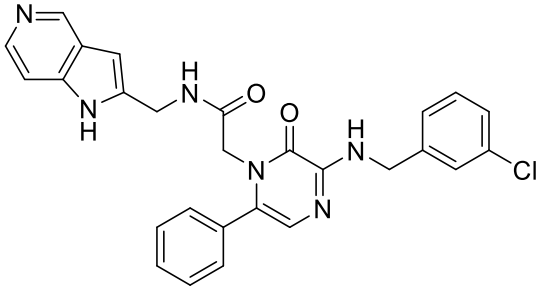
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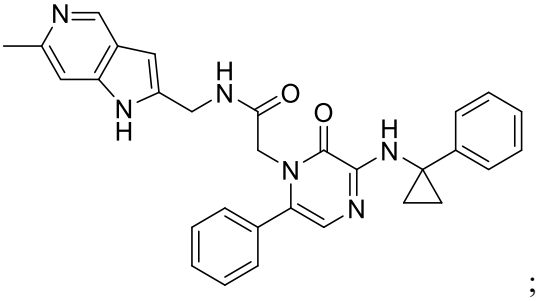
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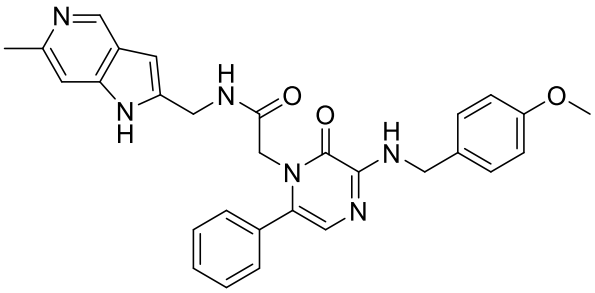
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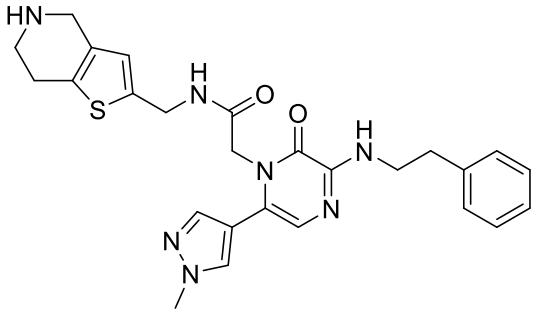
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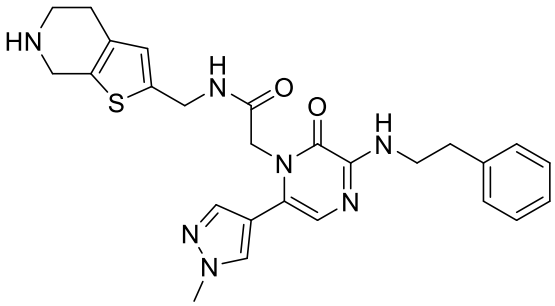
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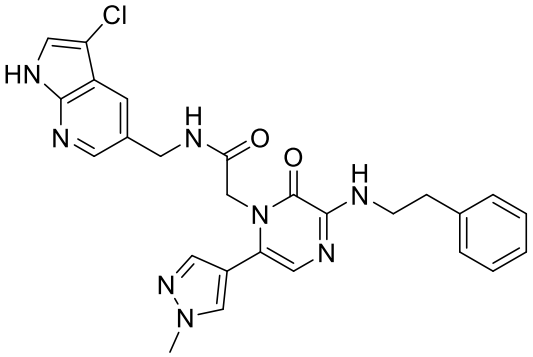
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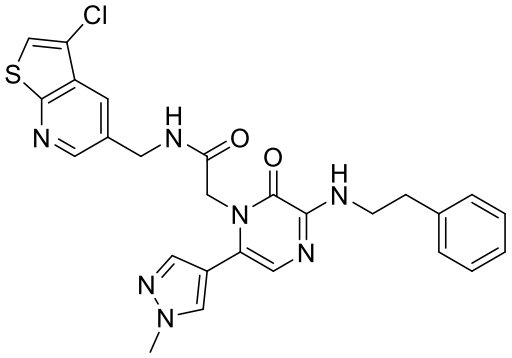
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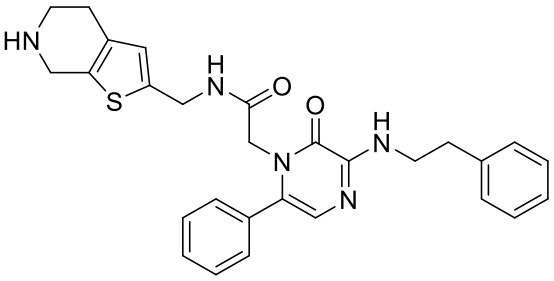
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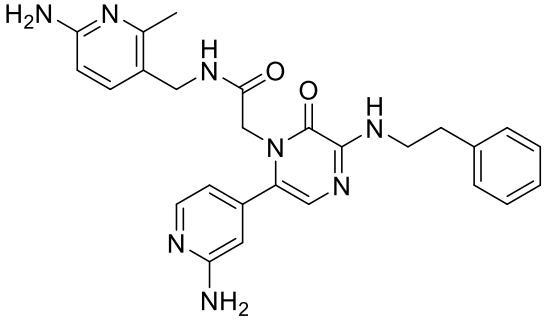
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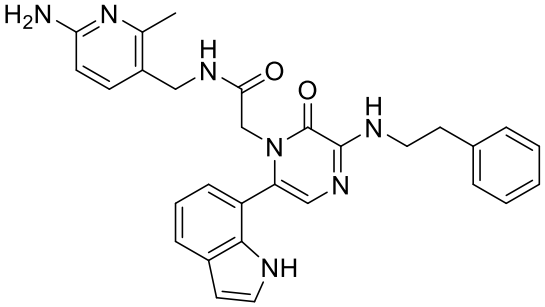
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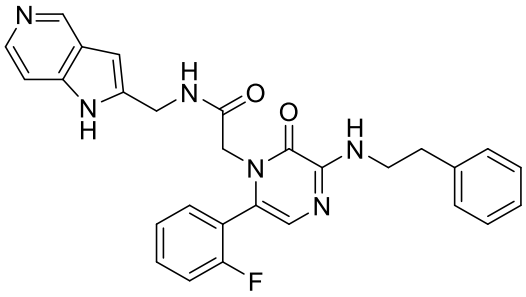
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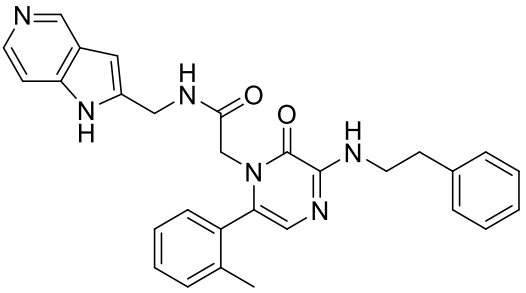
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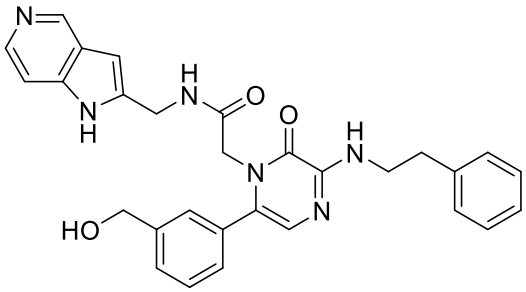
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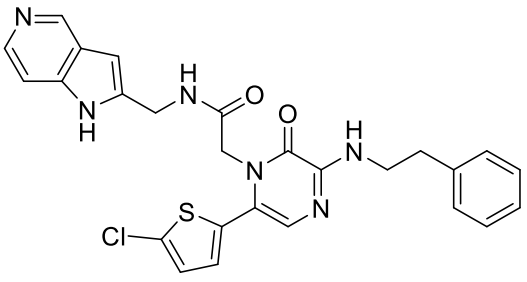
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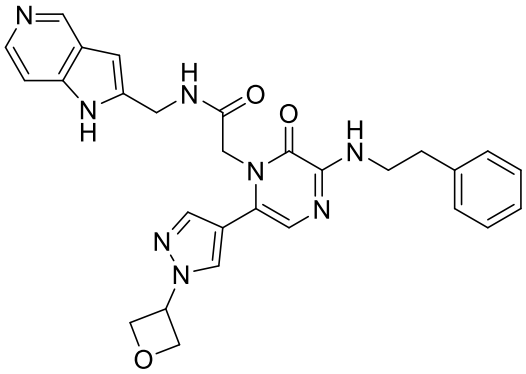
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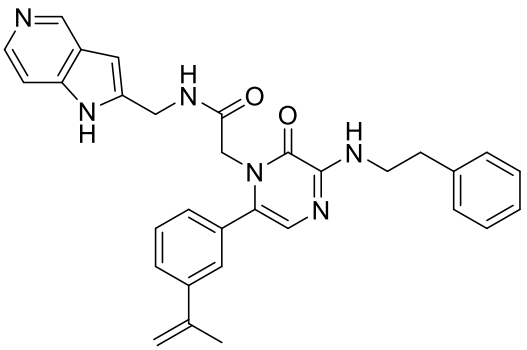
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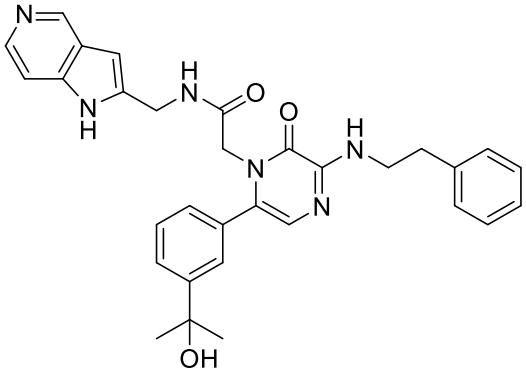
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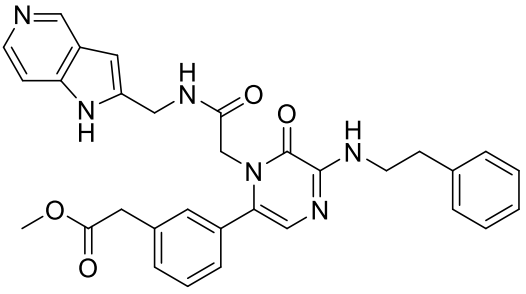
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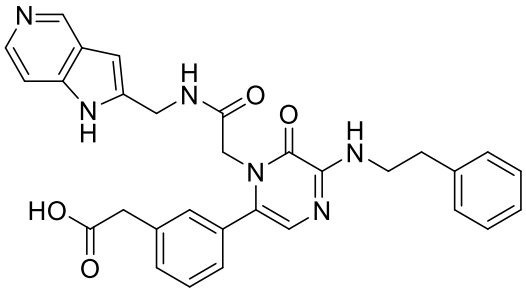
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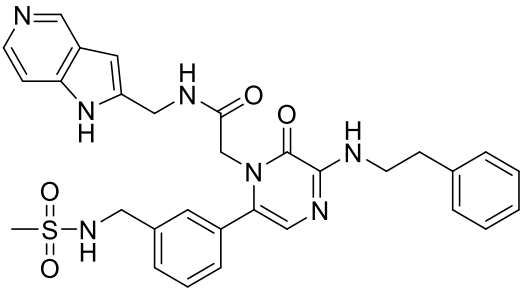
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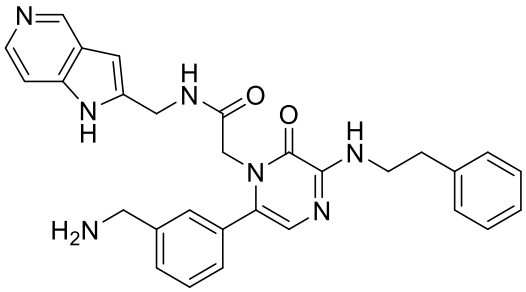
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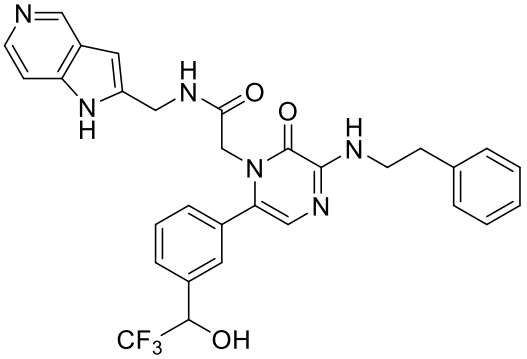
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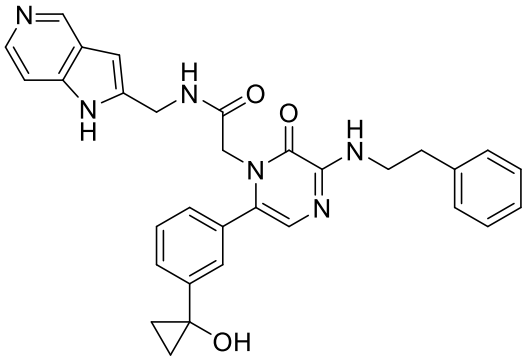
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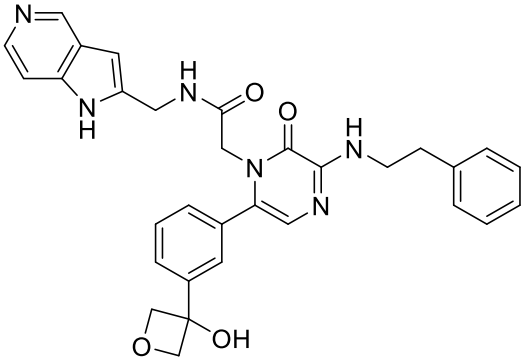
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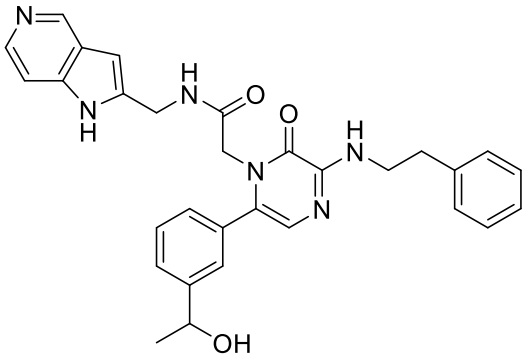
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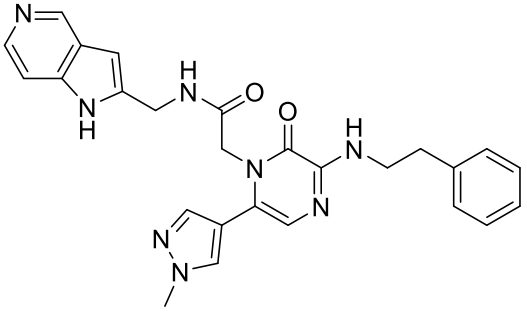
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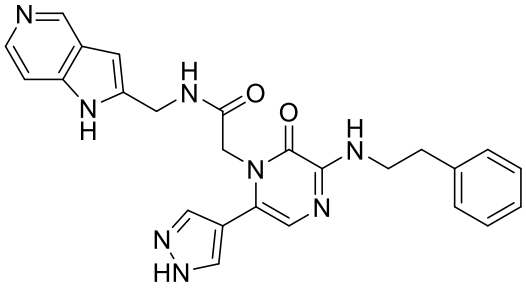
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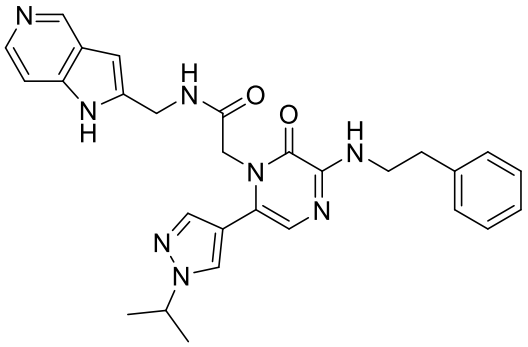
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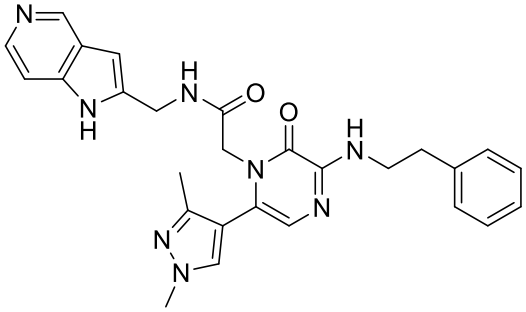
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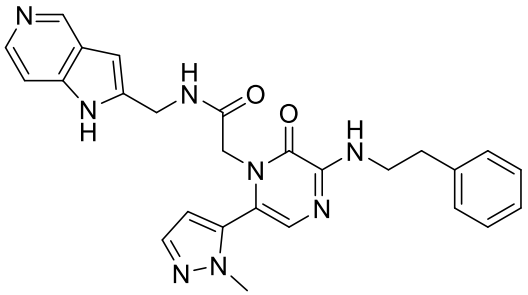
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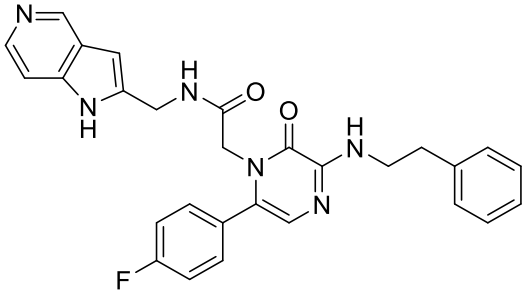
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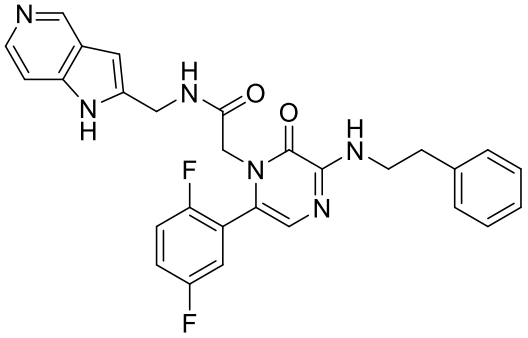
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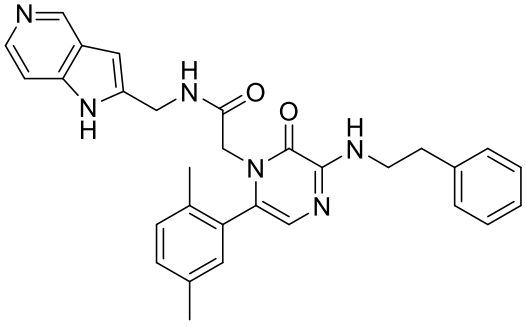
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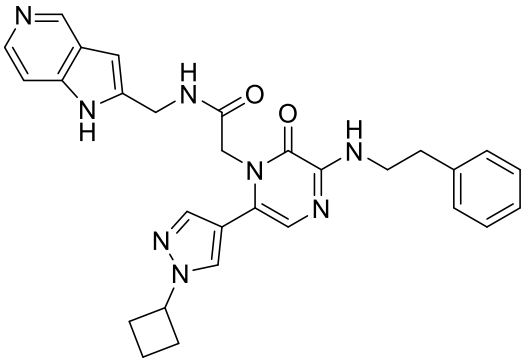
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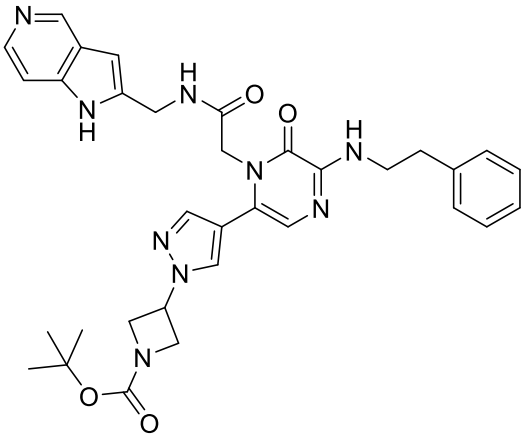
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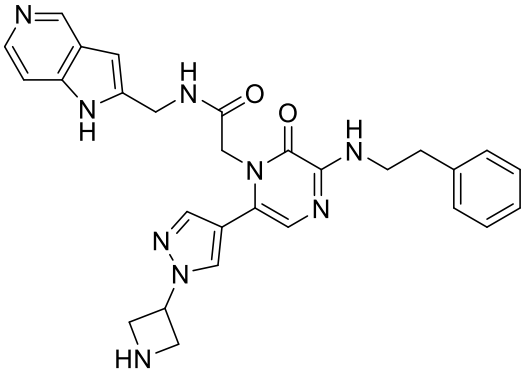
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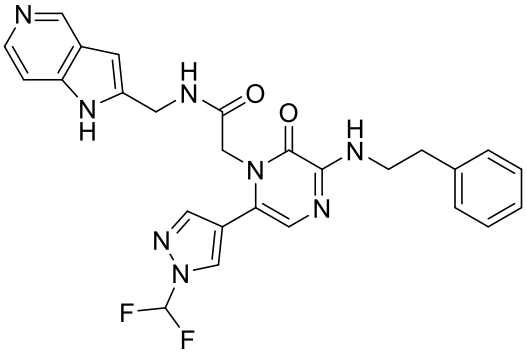
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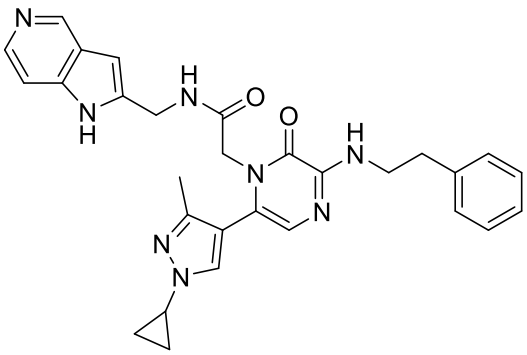
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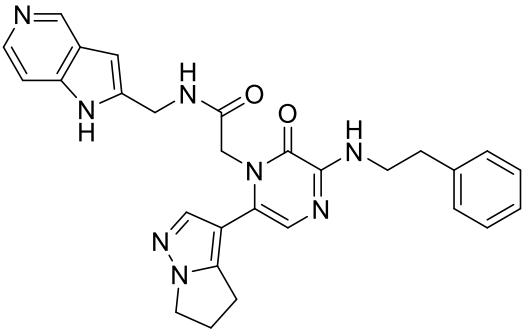
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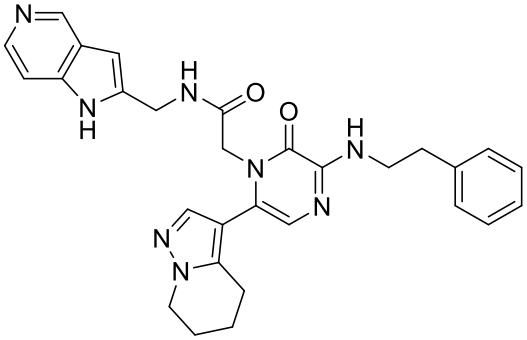
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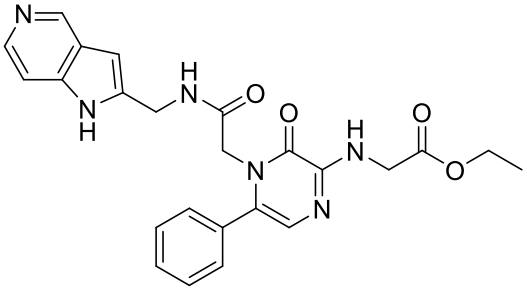
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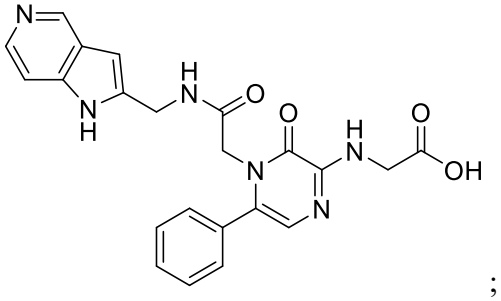
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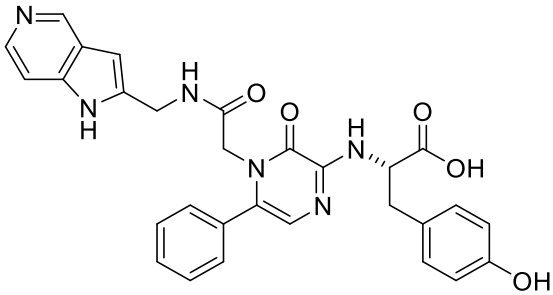
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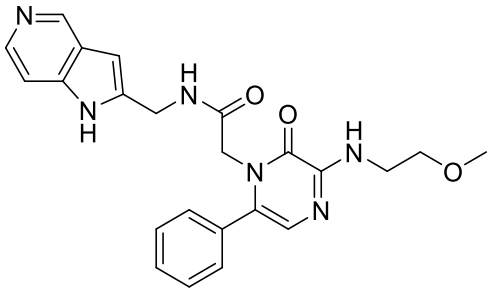
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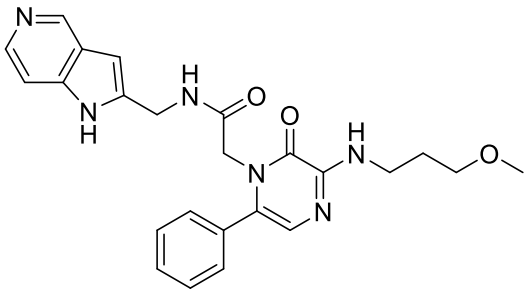
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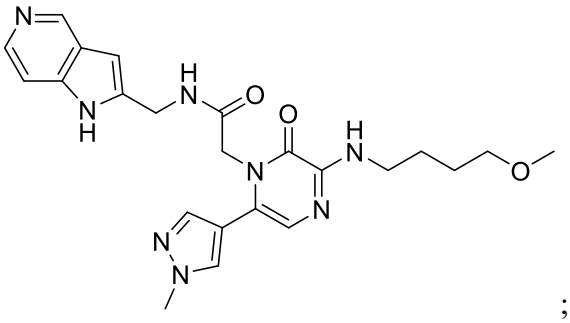
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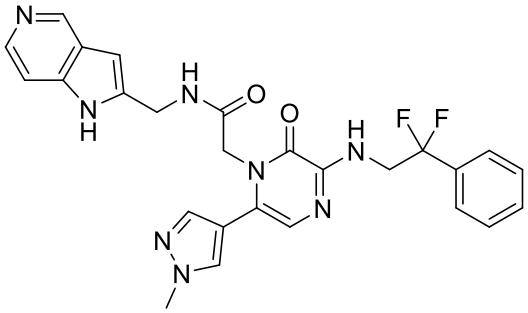
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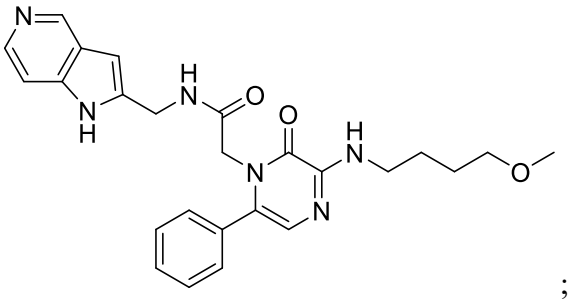
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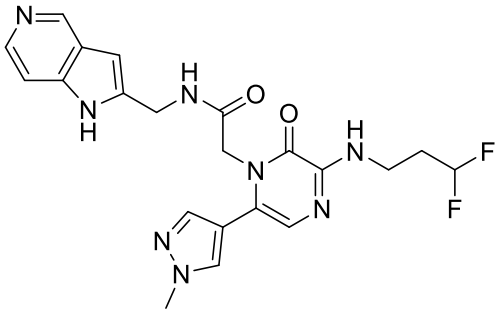
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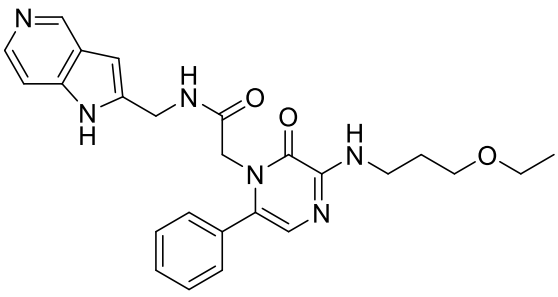
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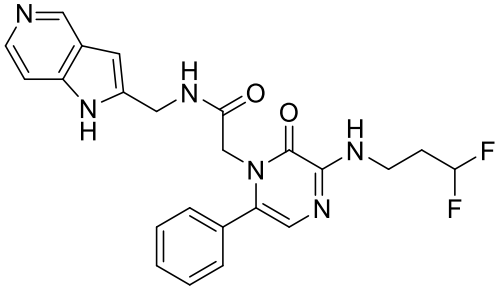
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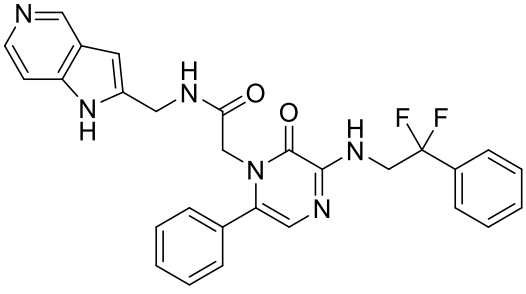
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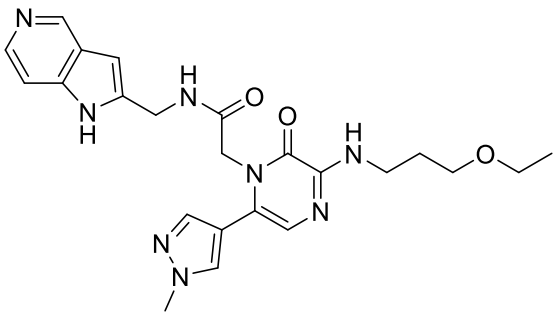
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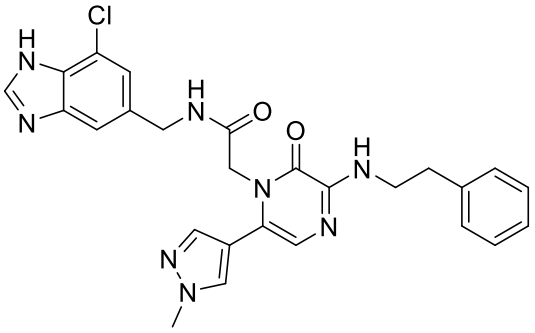
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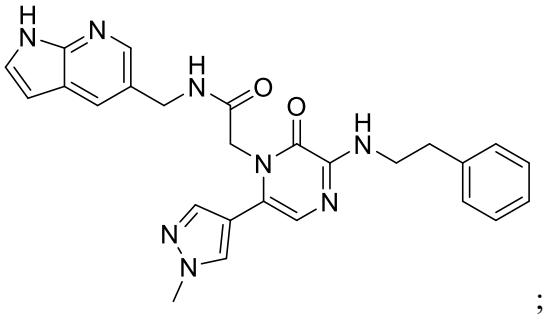
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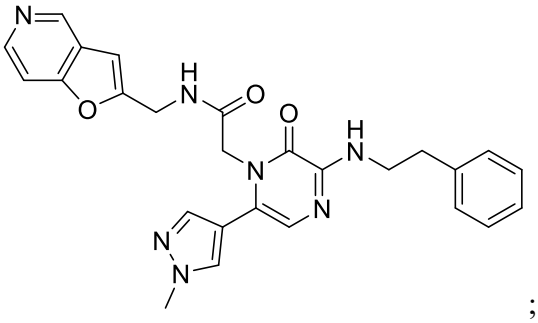
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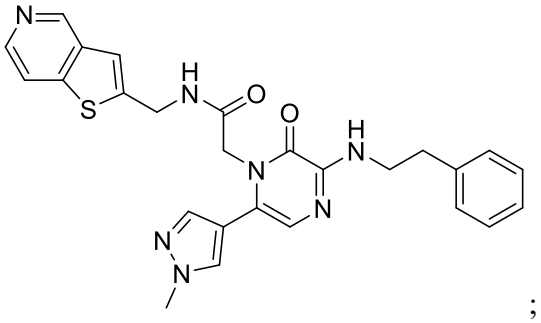
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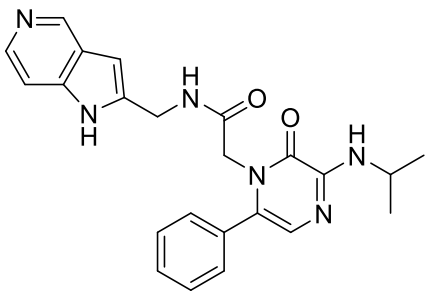
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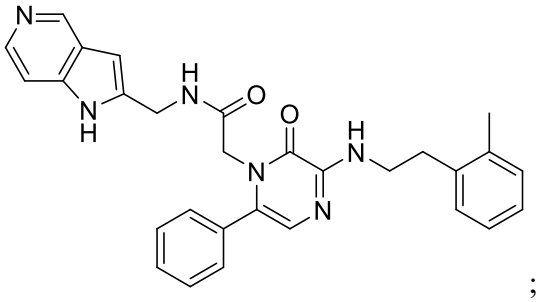
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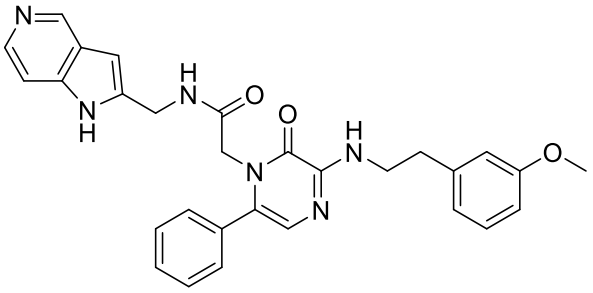
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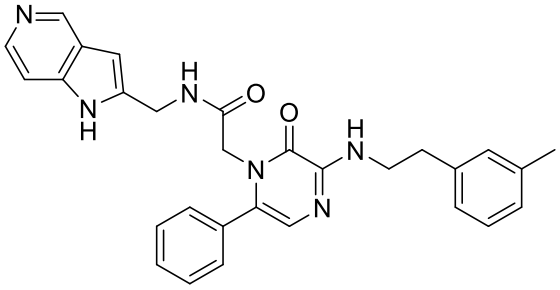
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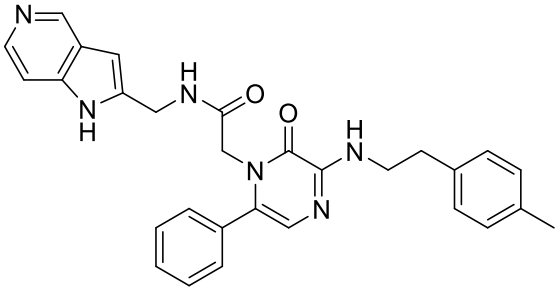
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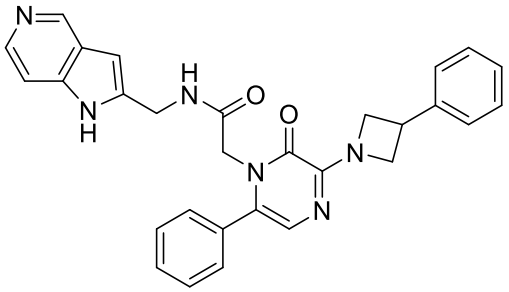
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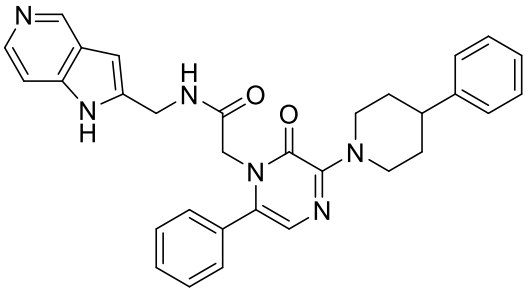
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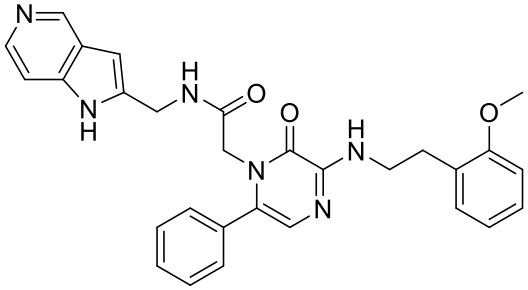
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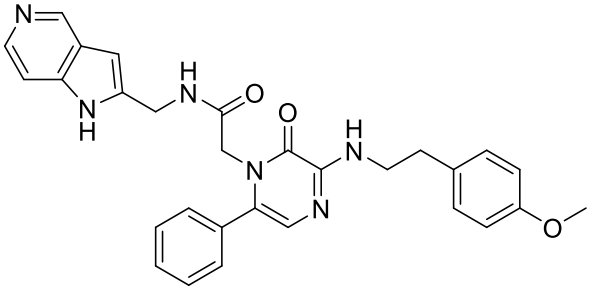
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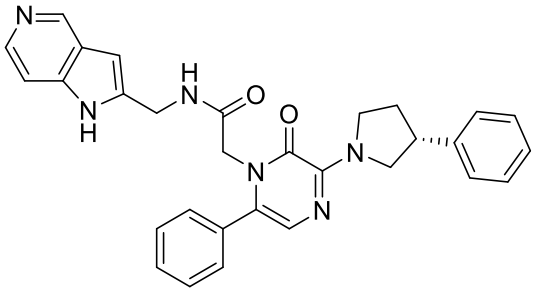
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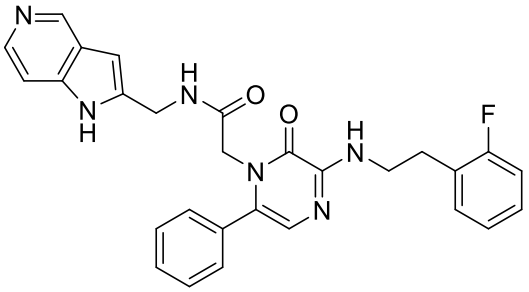
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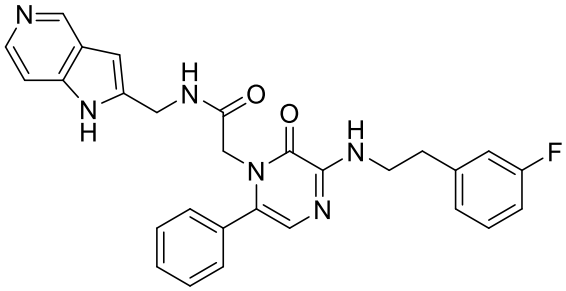
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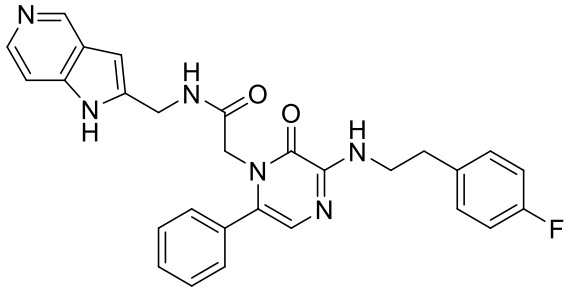
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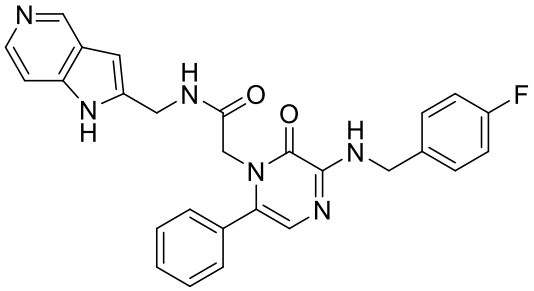
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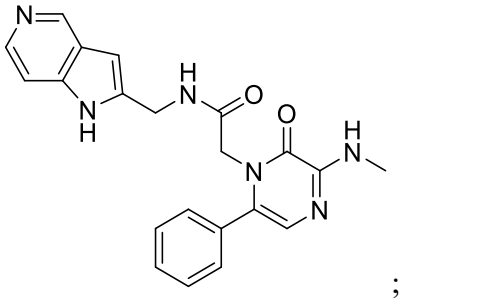
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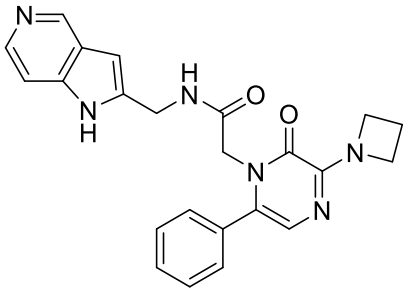
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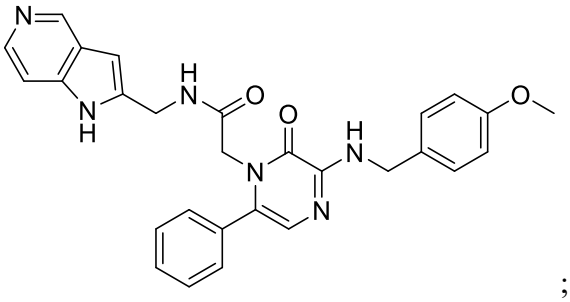
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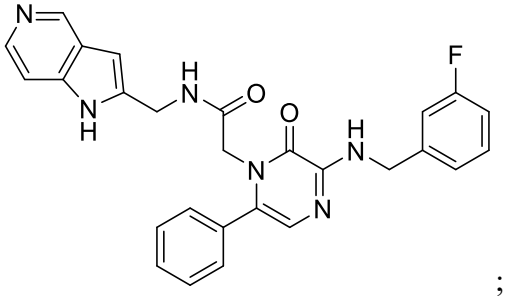
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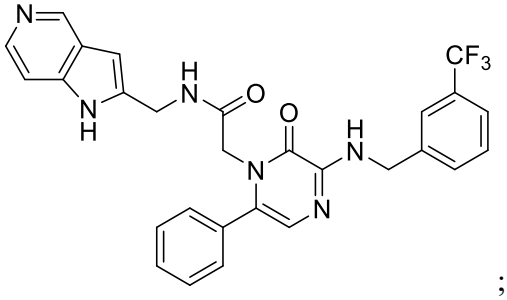
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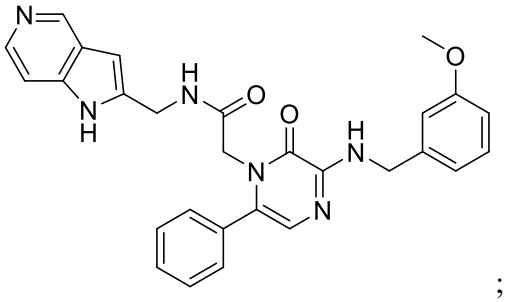
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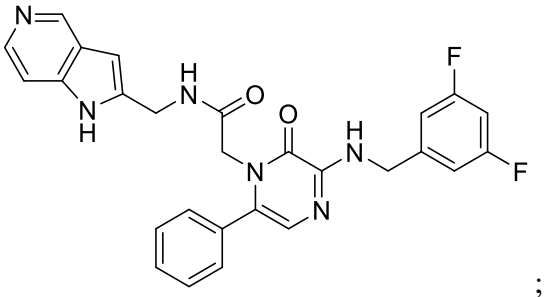
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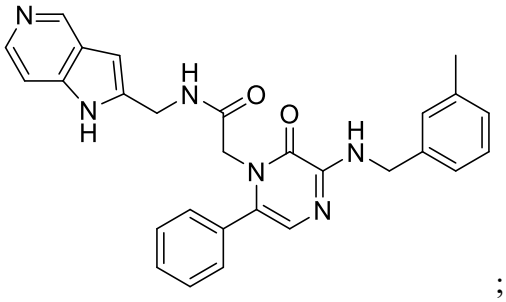
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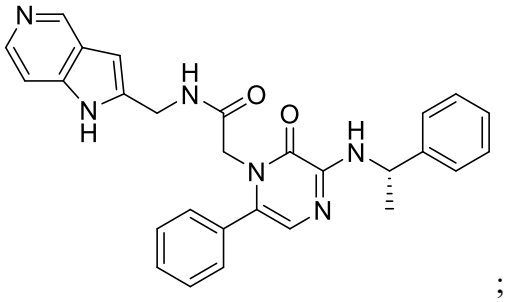
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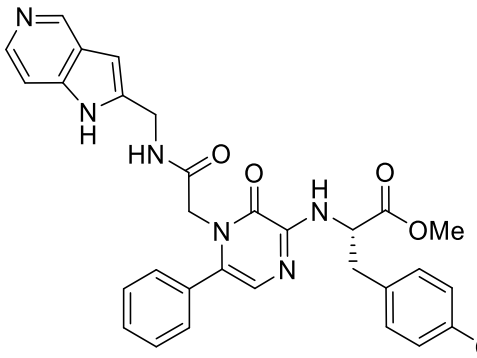
or ,

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof.

18. A pharmaceutical composition comprising a compound or pharmaceutically acceptable salt thereof of claim 1 and a pharmaceutically acceptable carrier or excipient.

19. Use of a compound of claim 1, in the manufacture of a medicament for treating a MASP-2-associated disease or disorder in a subject in need thereof, wherein the MASP-2-associated disease or disorder is selected from the group consisting of thrombotic microangiopathy (TMA), a renal condition, an inflammatory reaction resulting from tissue or organ transplantation, an ischemia reperfusion injury, a complication associated with diabetes, a cardiovascular disease or disorder, an inflammatory gastrointestinal disorder, a pulmonary disorder, an ophthalmic disease or disorder, disseminated intravascular coagulation, graft-versus-host disease, veno-occlusive disease, diffuse alveolar hemorrhage, idiopathic pneumonia syndrome, capillary leak syndrome, engraftment syndrome, fluid overload, angiogenesis-dependent cancer or tumor or similar, as well as combinations thereof.