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(54) Title: PROTEIN DEGRADERS AND USES THEREOF

(57) Abstract: The present invention provides compounds, compositions thereof, and methods of using the same for the targeted degradation of proteins, and the treatment of target protein-mediated disorders.

PROTEIN DEGRADERS AND USES THEREOF

TECHNICAL FIELD OF THE INVENTION

[0001] The present invention relates to compounds and methods useful for the modulation of targeted ubiquitination, especially with respect to a variety of polypeptides and other proteins, which are degraded and/or otherwise inhibited by compounds according to the present invention. The invention also provides pharmaceutically acceptable compositions comprising compounds of the present invention and methods of using said compositions in the treatment of various disorders.

BACKGROUND OF THE INVENTION

[0002] Ubiquitin-Proteasome Pathway (UPP) is a critical pathway that regulates key regulator proteins and degrades misfolded or abnormal proteins. UPP is central to multiple cellular processes, and if defective or imbalanced, it leads to pathogenesis of a variety of diseases. The covalent attachment of ubiquitin to specific protein substrates is achieved through the action of E3 ubiquitin ligases. These ligases comprise over 500 different proteins and are categorized into multiple classes defined by the structural element of their E3 functional activity.

[0003] Cereblon (CRBN) interacts with damaged DNA binding protein 1 and forms an E3 ubiquitin ligase complex with Cullin 4 where it functions as a substrate receptor in which the proteins recognized by CRBN might be ubiquitinated and degraded by proteasomes.

[0004] Proteasome-mediated degradation of unneeded or damaged proteins plays a very important role in maintaining regular function of a cell, such as cell survival, proliferation and growth. A new role for CRBN has been identified; i.e., the binding of immunomodulatory drugs (IMiDs), e.g. thalidomide, to CRBN has now been associated with teratogenicity and also the cytotoxicity of IMiDs, including lenalidomide, which are widely used to treat multiple myeloma patients. CRBN is likely a key player in the binding, ubiquitination and degradation of factors involved in maintaining function of myeloma cells. These new findings regarding the role of CRBN in IMiD action stimulated intense investigation of CRBN's downstream factors involved in maintaining regular function of a cell (Chang and Stewart Int J Biochem Mol Biol. 2011; 2(3): 287-294).

[0005] UPP plays a key role in the degradation of short-lived and regulatory proteins important in a variety of basic cellular processes, including regulation of the cell cycle, modulation of cell surface receptors and ion channels, and antigen presentation. The pathway has been implicated in several forms of malignancy, in the pathogenesis of several genetic diseases (including cystic fibrosis, Angelman's syndrome, and Liddle syndrome), in immune surveillance/viral pathogenesis, and in the pathology of muscle wasting. Many diseases are associated with an abnormal UPP and negatively affect cell cycle and division, the cellular response to stress and to extracellular modulators, morphogenesis of neuronal networks, modulation of cell surface receptors, ion channels, the secretory pathway, DNA repair and biogenesis of organelles.

[0006] Aberrations in the process have recently been implicated in the pathogenesis of several diseases, both inherited and acquired. These diseases fall into two major groups: (a) those that result from loss of function with the resultant stabilization of certain proteins, and (b) those that result from gain of function, i.e. abnormal or accelerated degradation of the protein target.

[0007] The UPP is used to induce selective protein degradation, including use of fusion proteins to artificially ubiquitinate target proteins and synthetic small-molecule probes to induce proteasome-dependent degradation. Bifunctional compounds composed of a target protein-binding ligand and an E3 ubiquitin ligase ligand, induced proteasome-mediated degradation of selected proteins via their recruitment to E3 ubiquitin ligase and subsequent ubiquitination. These drug-like molecules offer the possibility of temporal control over protein expression. Such compounds are capable of inducing the inactivation of a protein of interest upon addition to cells or administration to an animal or human, and could be useful as biochemical reagents and lead to a new paradigm for the treatment of diseases by removing pathogenic or oncogenic proteins (Crews C, Chemistry & Biology, 2010, 17(6):551-555; Schnnekloth JS Jr., Chembiochem, 2005, 6(l):40-46).

[0008] An ongoing need exists in the art for effective treatments for disease, especially hyperplasias and cancers, such as multiple myeloma. However, non-specific effects, and the inability to target and modulate certain classes of proteins altogether, such as transcription factors, remain as obstacles to the development of effective anti-cancer agents. As such, small molecule therapeutic agents that leverage or potentiate cereblon's substrate specificity and, at the same time, are"tunable" such that a wide range of protein classes can be targetted and modulated with

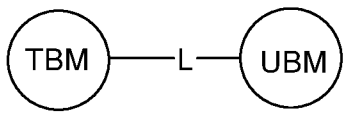
specificity would be very useful as a therapeutic. Accordingly, there remains a need to find bifunctional compounds that are protein degraders useful as therapeutic agents.

SUMMARY OF THE INVENTION

[0009] The present application relates novel bifunctional compounds, which function to recruit targeted proteins to E3 Ubiquitin Ligase for degradation, and methods of preparation and uses thereof. In particular, the present disclosure provides bifunctional compounds, which find utility as modulators of targeted ubiquitination of a variety of polypeptides and other proteins, which are then degraded and/or otherwise inhibited by the bifunctional compounds as described herein. An advantage of the compounds provided herein is that a broad range of pharmacological activities is possible, consistent with the degradation/inhibition of targeted polypeptides from virtually any protein class or family. In addition, the description provides methods of using an effective amount of the compounds as described herein for the treatment or amelioration of a disease condition, such as cancer, e.g., multiple myeloma.

[0010] The present application further relates to targeted degradation of proteins through the use of bifunctional molecules, including bifunctional molecules that link a cereblon-binding moiety to a ligand that binds the targeted protein.

[0011] The present application also relates to a bifunctional compound having the following structure:



,

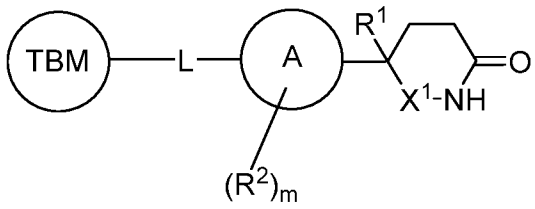
wherein,

TBM is a target binding moiety capable of binding to the targeted protein(s);

L is a bivalent moiety that connects TBM to UBM; and

UBM is a ubiquitin binding moiety capable of binding to a ubiquitin ligase such as an E3 Ubiquitin Ligase (e.g., cereblon).

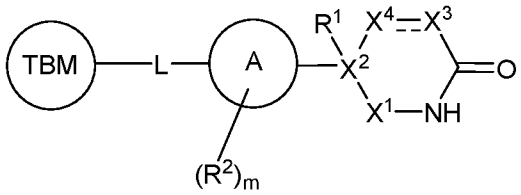
[0012] It has now been found that compounds of this invention, and pharmaceutically acceptable compositions thereof, are effective for the modulation of targeted ubiquitination. Such compounds have the general formula **I**:



I

or a pharmaceutically acceptable salt thereof, wherein each variable is as defined and described herein.

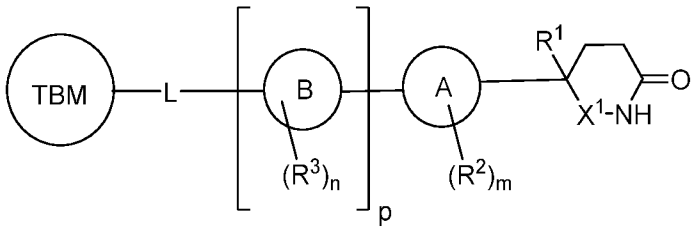
[0013] It has also been found that other compounds of this invention, and pharmaceutically acceptable compositions thereof, are effective for the modulation of targeted ubiquitination. Such compounds have the general formula **I''**:



I''

or a pharmaceutically acceptable salt thereof, wherein each variable is as defined and described herein.

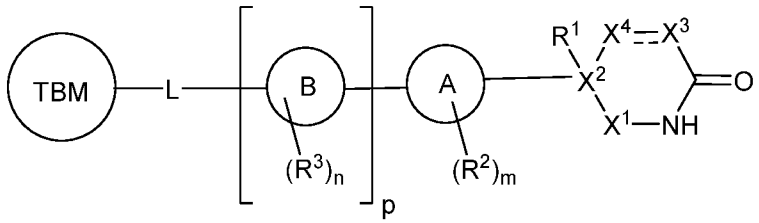
[0014] It has also been found that other compounds of this invention, and pharmaceutically acceptable compositions thereof, are effective for the modulation of targeted ubiquitination. Such compounds have the general formula **II-A**:



II-A

or a pharmaceutically acceptable salt thereof, wherein each variable is as defined and described herein.

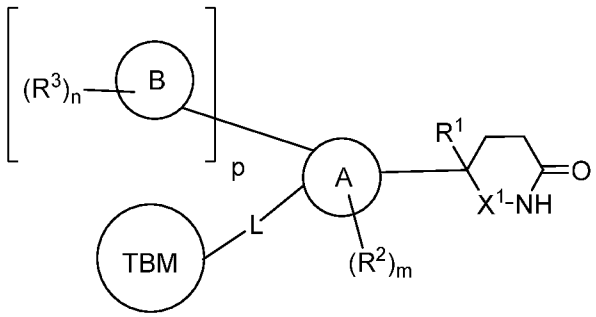
[0015] It has also been found that other compounds of this invention, and pharmaceutically acceptable compositions thereof, are effective for the modulation of targeted ubiquitination. Such compounds have the general formula **II''-A**:



II″-A

or a pharmaceutically acceptable salt thereof, wherein each variable is as defined and described herein.

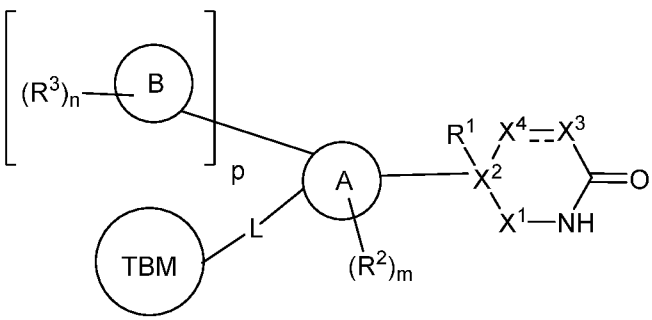
[0016] It has also been found that other compounds of this invention, and pharmaceutically acceptable compositions thereof, are effective for the modulation of targeted ubiquitination. Such compounds have the general formula **II-B**:



II-B

or a pharmaceutically acceptable salt thereof, wherein each variable is as defined and described herein.

[0017] It has also been found that other compounds of this invention, and pharmaceutically acceptable compositions thereof, are effective for the modulation of targeted ubiquitination. Such compounds have the general formula **II″-B**:



II″-B

or a pharmaceutically acceptable salt thereof, wherein each variable is as defined and described herein.

[0018] Compounds of the present invention, and pharmaceutically acceptable compositions thereof, are useful for treating a variety of diseases, disorders or conditions. Such diseases, disorders, or conditions include those described herein.

[0019] Compounds provided by this invention are also useful for the study of CRBN and targeted proteins in biological and pathological phenomena; the study of CRBN and targeted proteins occurring in bodily tissues; and the comparative evaluation of new CRBN or targeted protein ligands or other regulators of CRBN or targeted proteins *in vitro* or *in vivo*.

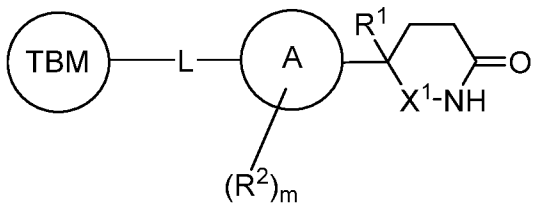
DETAILED DESCRIPTION OF CERTAIN EMBODIMENTS

1. General Description of Certain Embodiments of the Invention:

[0020] Compounds of the present invention, and compositions thereof, are useful for the modulation of targeted ubiquitination.

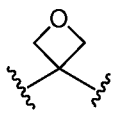
[0021] As defined herein, the terms "binder," "modulator," and "ligand" are used interchangeably and describe a compound that binds to, modulates or is a ligand for CRBN or a targeted protein.

[0022] In certain embodiments, the present invention provides a compound of formula **I**:



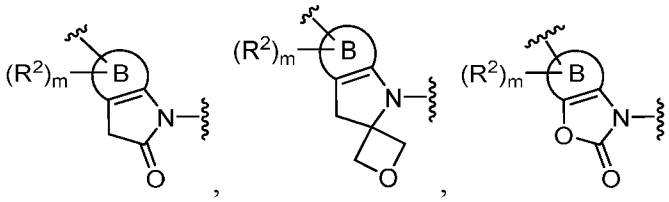
I

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–CH_2–$, –C(O)–, –C(S)–, or  ;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, or an optionally substituted C_{1-4} aliphatic;

each R^2 is independently hydrogen, $-R^6$, halogen, $-CN$, $-NO_2$, $-OR$, $-SR$, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)N(R)OR$, $-OC(O)R$, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, or $-N(R)S(O)_2R$;

Ring A is a bi- or tricyclic ring selected from  , , ,

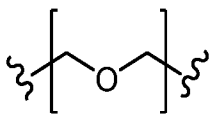
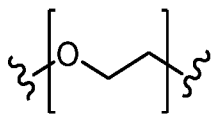
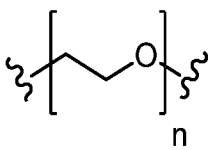
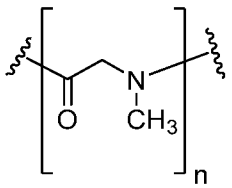
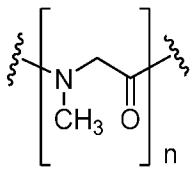
membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

R^3 is selected from hydrogen, halogen, –OR, $–N(R)_2$, or –SR;

each R^4 is independently hydrogen, $–R^6$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

R^5 is hydrogen, C_{1-4} aliphatic, or –CN;

each R^6 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -N(R)-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, $-S(O)_2-$, $-N(R)S(O)_2-$, $-S(O)_2N(R)-$, -N(R)C(O)-, -C(O)N(R)-, -OC(O)N(R)-, –N(R)C(O)O-,  ,  ,  ,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially

unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

TBM is a target binding moiety;

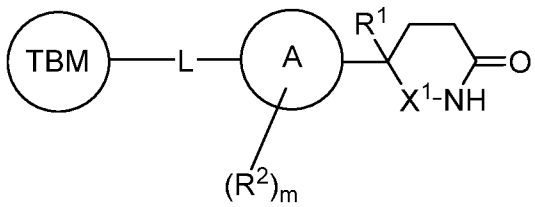
m is 0, 1, 2, 3 or 4;

each of n is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

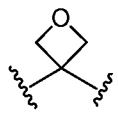
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0023] In certain embodiments, the present invention provides a compound of formula **I′**:



I′

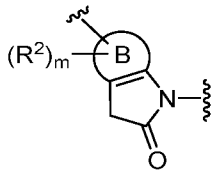
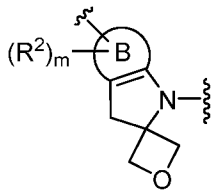
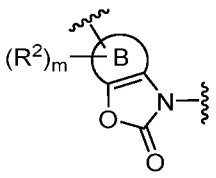
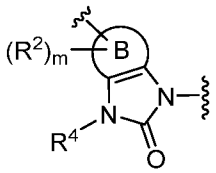
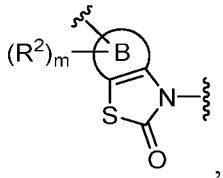
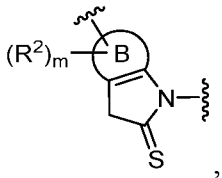
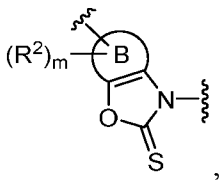
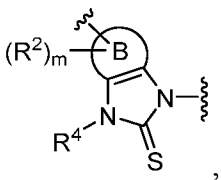
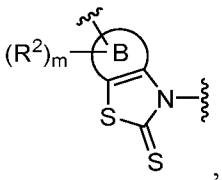
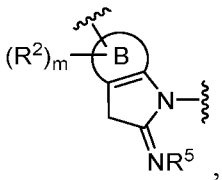
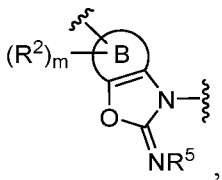
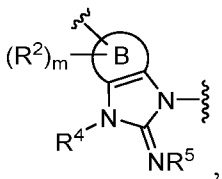
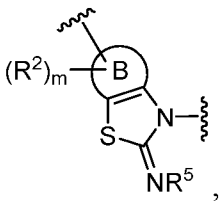
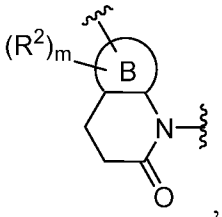
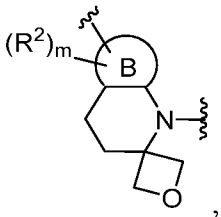
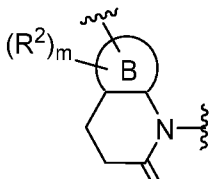
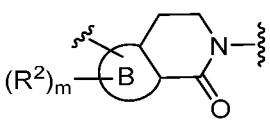
or a pharmaceutically acceptable salt thereof, wherein:

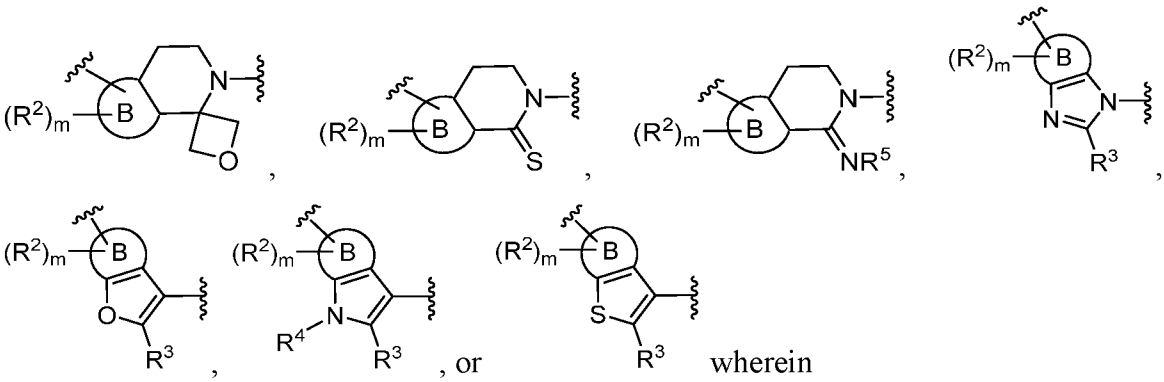
X^1 is a bivalent moiety selected from a covalent bond, $–CH_2–$, –C(O)–, –C(S)–, or  ;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, or an optionally substituted C_{1-4} aliphatic;

each R^2 is independently hydrogen, $–R^6$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$,

-C(O)N(R)OR, -OC(O)R, -OC(O)NR_2, -N(R)C(O)OR, -N(R)C(O)R, -N(R)C(O)NR_2, or –N(R)$S(O)_2$R;

Ring A is a bi- or tricyclic ring selected from  wherein Ring B is other than imidazo or benzo,   , wherein Ring B is other than benzo,  wherein Ring B is other than benzo,   ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  wherein Ring B is other than benzo, 



wherein

Ring B is a fused ring selected from 6-membered aryl containing 0-2 nitrogen atoms, 5 to 7-membered partially saturated carbocyclyl, 5 to 7-membered partially saturated heterocyclyl with 1-2 heteroatoms independently selected from nitrogen, oxygen or sulfur, or 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

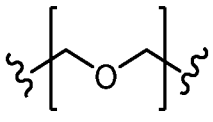
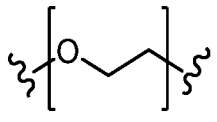
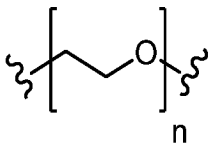
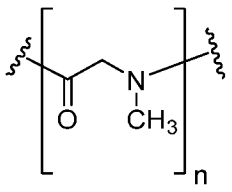
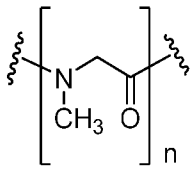
R^3 is selected from hydrogen, halogen, –OR, $–N(R)_2$, or –SR;

each R^4 is independently hydrogen, $–R^6$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

R^5 is hydrogen, C_{1-4} aliphatic, or –CN;

each R^6 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -N(R)-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, $-S(O)_2-$, $-N(R)S(O)_2-$, $-S(O)_2N(R)-$, -N(R)C(O)-, -

C(O)N(R)-, -OC(O)N(R)-, –N(R)C(O)O-,  ,  ,  ,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

TBM is a target binding moiety;

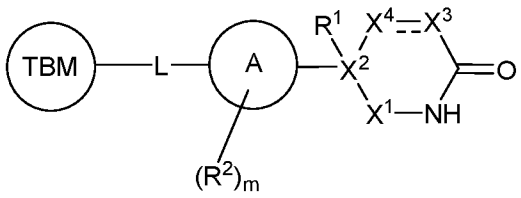
m is 0, 1, 2, 3 or 4;

each of n is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

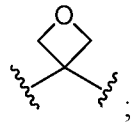
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0024] In certain embodiments, the present invention provides a compound of formula **I''**:



I″

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–C(R)_2–$, –C(O)–, –C(S)–, –P(O)(OR)–, –P(O)(R)–, $–P(O)(NR_2)–$, –S(O)–, $–S(O)_2–$, or  ;

X^2 is a carbon atom or silicon atom;

X^3 is a bivalent moiety selected from $–C(R)_2–$, –N(R)–, $–CF_2–$, –CHF–, –S–, or –O–;

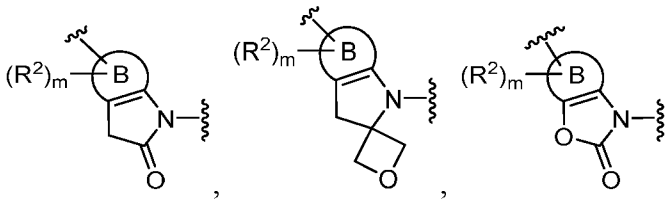
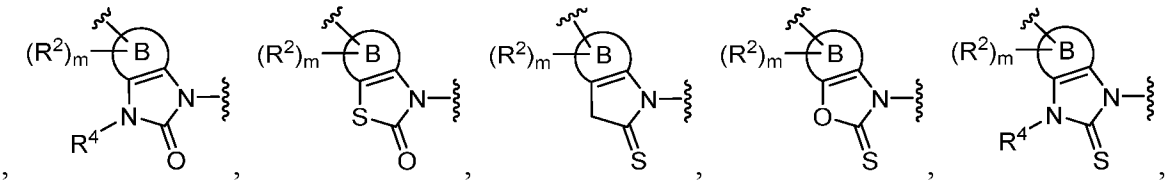
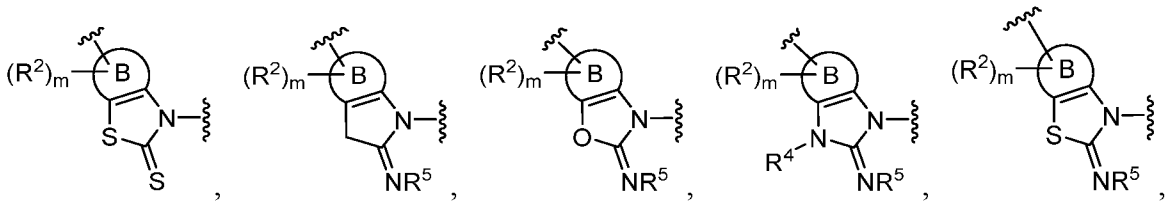
X^4 is a bivalent moiety selected from a covalent bond or $–C(R)_2–$;

=== is a single bond or double bond;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, $–P(O)(OR)_2$, $–P(O)(NR_2)OR$, $–P(O)(NR_2)_2$, $–Si(OH)_2R$, $–Si(OH)(R)_2$, $–Si(R)_3$, an optionally substituted C_{1-4} aliphatic, or:

R^1 and X^1 or X^4 are taken together with their intervening atoms to form a 5-7 membered saturated, partially unsaturated, carbocyclic ring or heterocyclic ring having 1-3 heteroatoms, independently selected from nitrogen, oxygen, or sulfur;

each R^2 is independently hydrogen, deuterium, $–R^6$, halogen, –CN, $–NO_2$, –OR, –SR, $–NR_2$, $–Si(OH)_2R$, $–Si(OH)(R)_2$, $–Si(R)_3$, $–S(O)_2R$, $–S(O)_2NR_2$, –S(O)R, –C(O)R, –C(O)OR, $–C(O)NR_2$, –C(O)N(R)OR, –OC(O)R, $–OC(O)NR_2$, –N(R)C(O)OR, –N(R)C(O)R, $–N(R)C(O)NR_2$, $–N(R)S(O)_2R$, $–N(R)S(O)_2NR_2$, $–P(O)(OR)_2$, $–P(O)(NR_2)OR$, or $–P(O)(NR_2)_2$;

Ring A is a bi- or tricyclic ring selected from  ,  ,  ,

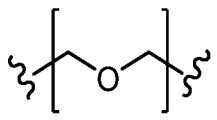
–N(R)C(O)OR, -N(R)C(O)NR_2, –N(R)$S(O)_2$R, –N(R)$S(O)_2NR_2$, –N(R)P(O)$(OR)_2$, –N(R)P(O)(OR)NR_2, –P(O)$(OR)_2$, –P(O)$(NR_2)OR$, –P(O)$(NR_2)_2$, –Si$(OH)_2$R, –Si(OH)$(R)_2$, or –Si$(R)_3$;

each R^4 is independently hydrogen, deuterium, –R^6, halogen, –$S(O)_2$R, –$S(O)_2NR_2$, –S(O)R, –C(O)R, –C(O)OR, –C(O)NR_2, –C(O)N(R)OR, –P(O)$(OR)_2$, –P(O)$(NR_2)OR$, or –P(O)$(NR_2)_2$;

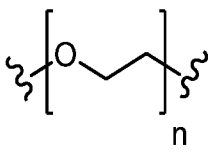
R^5 is hydrogen, deuterium, an optionally substituted C_{1-4} aliphatic, or –CN;

each R^6 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, or sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, or sulfur;

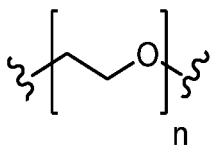
L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy–, –O–, –N(R)–, –Si$(R)_2$–, –Si(OH)(R)–, –Si$(OH)_2$–, –P(O)(OR)–, –P(O)(R)–, –P(O)(NR_2)–, –S–, –OC(O)–, –C(O)O–, –C(O)–, –S(O)–, –$S(O)_2$–, –N(R)$S(O)_2$–, –$S(O)_2$N(R)–, –N(R)C(O)–, –C(O)N(R)–, –OC(O)N(R)–, –N(R)C(O)O–,



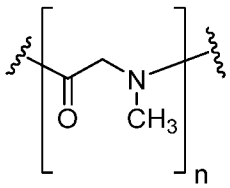
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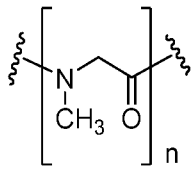
,



,



, or



, wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 3-8 membered saturated or partially unsaturated carbocyclylenyl, a 6-11 membered saturated or partially unsaturated spiro carbocyclylenyl, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-10 membered saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 6-11 membered saturated or partially unsaturated spiro

heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur;

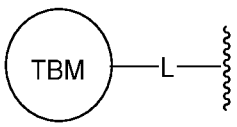
TBM is a target binding moiety;

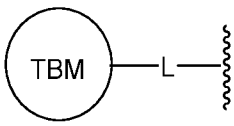
m is 0, 1, 2, 3 or 4;

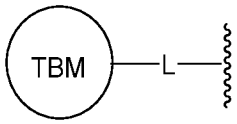
each of n is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, deuterium, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

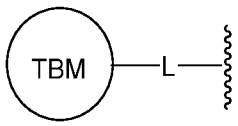
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

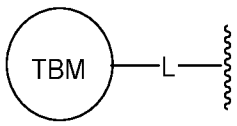
[0025] Where a point of attachment of 

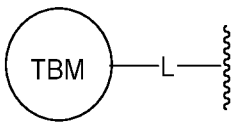
is depicted on Ring B, it is intended, and one of ordinary skill in the art would appreciate, that the point of attachment of 

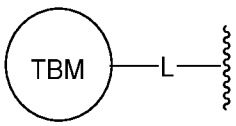
may be on Ring A and may also be at any available carbon or nitrogen atom on Ring A including the ring to which Ring B is fused. Where 

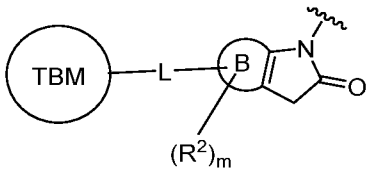
is attached to a

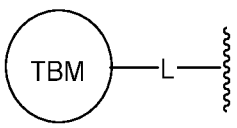
nitrogen atom bound to R^4 or R^5, R^4 or R^5 is absent and 

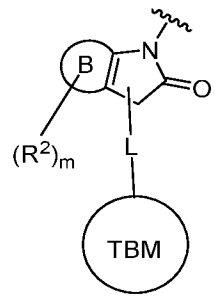
takes the place of the R^4 or R^5 group. Where 

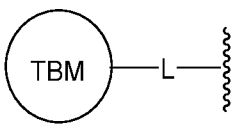
is attached to a carbon atom bound to R^3, R^3 is absent and 

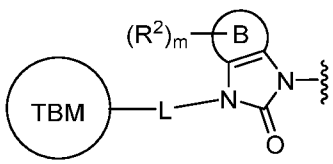
takes the place of the R^3 group. By means of example and for the purpose of clarity, when 

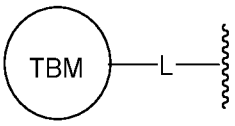
is attached to Ring B, Ring A is 

; when 

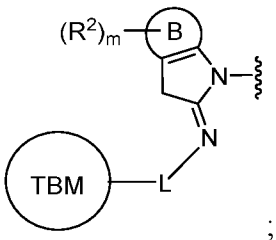
is attached to Ring A, Ring A is 

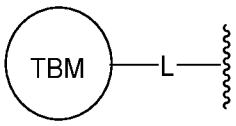
; when 

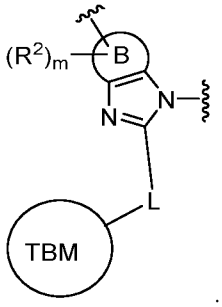
is attached to a nitrogen atom bound to R^4, Ring A is 

; when 

is attached to a nitrogen atom bound to R^5, Ring A is



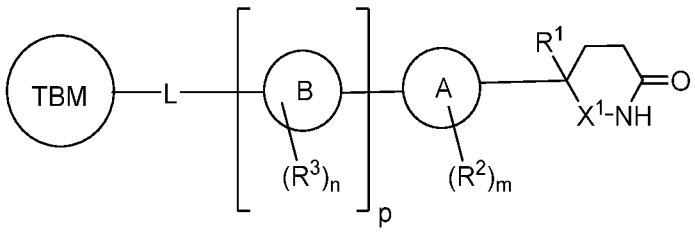
; and when 

is attached to a carbon atom bound to R^3, Ring A is 

.

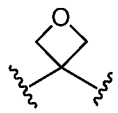
[0026] Where a point of attachment of $-(R^2)_n$ is depicted on Ring B, it is intended, and one of ordinary skill in the art would appreciate, that the point of attachment of $-(R^2)_n$ may be on Ring A and may also be at any available boron, carbon, nitrogen, or silicon atom on Ring A including the ring to which Ring B is fused. Where $-R^2$ is attached to a nitrogen atom bound to R^4 or R^5, R^4 or R^5 is absent and $-R^2$ takes the place of the R^4 or R^5 group. Where $-R^2$ is attached to a carbon atom bound to R^3, R^3 is absent and $-R^2$ takes the place of the R^3 group.

[0027] In certain embodiments, the present invention provides a compound of Formula **II-A**:



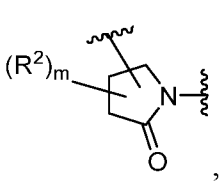
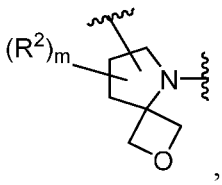
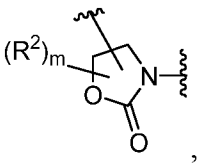
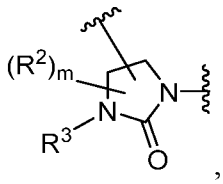
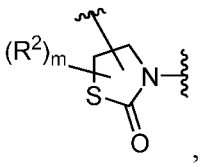
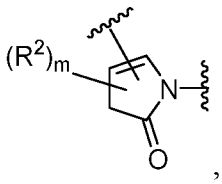
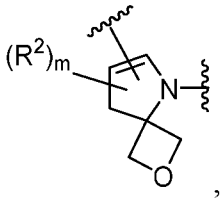
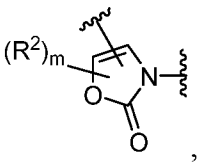
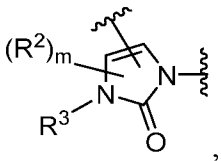
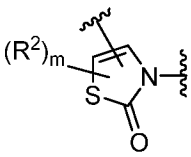
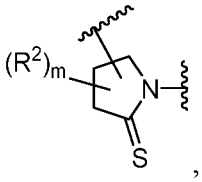
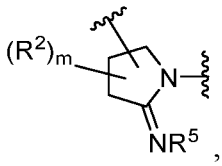
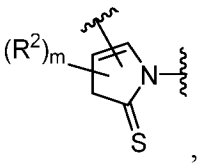
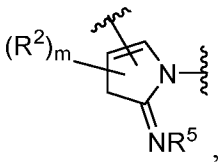
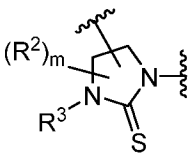
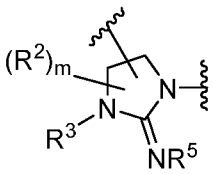
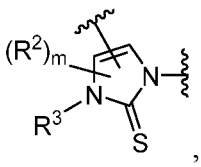
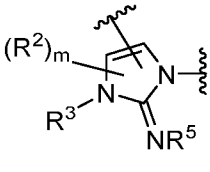
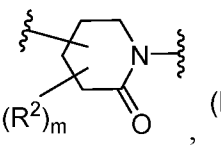
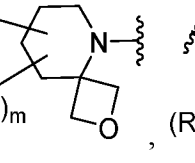
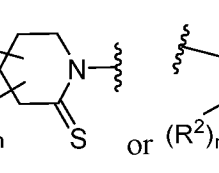
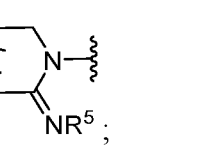
II-A

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $-CH_2-$, $-C(O)-$, $-C(S)-$, or 

;

R^1 is hydrogen, deuterium, halogen, $-CN$, $-OR$, $-SR$, $-S(O)R$, $-S(O)_2R$, $-NR_2$, or an optionally substituted C_{1-4} aliphatic;

Ring A is a mono- or bicyclic ring selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , , , , , , or ;

each R^2 is independently hydrogen, $-R^4$, halogen, –CN, $-NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $-C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $-N(R)S(O)_2R$;

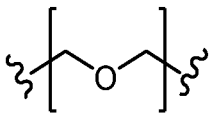
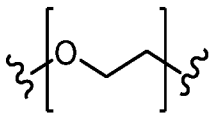
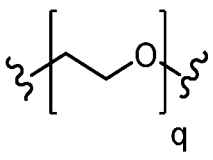
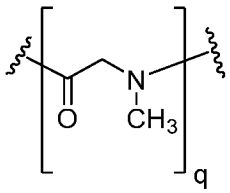
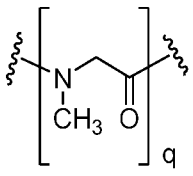
Ring B is selected from a 6-membered aryl containing 0-2 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each R^3 is independently hydrogen, $-R^4$, halogen, –CN, $-NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $-C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $-N(R)S(O)_2R$;

each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms

independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^5 is hydrogen, C_{1-4} aliphatic, or –CN;

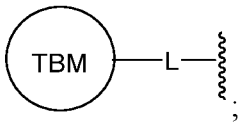
L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -N(R)-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, -$S(O)_2$-, -N(R)$S(O)_2$-, -$S(O)_2$N(R)-, -N(R)C(O)-, -C(O)N(R)-, -OC(O)N(R)-, –N(R)C(O)O-,  ,  ,  ,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

TBM is a target binding moiety;

m is 0, 1, or 2;

n is 0, 1, 2, 3, or 4;

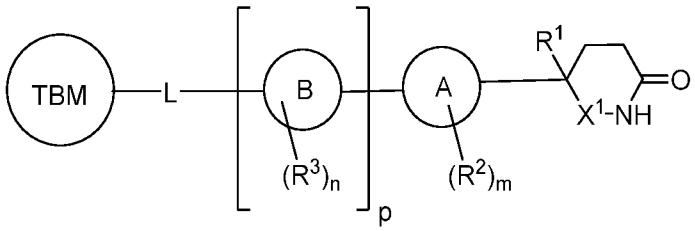
p is 0 or 1, wherein when p is 0, the bond connecting Ring A and Ring B is connected to  ;

each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

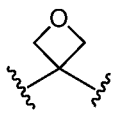
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0028] In certain embodiments, the present invention provides a compound of formula **II′-A**:

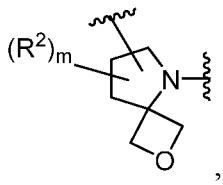
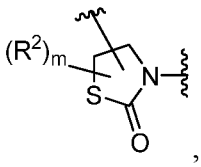
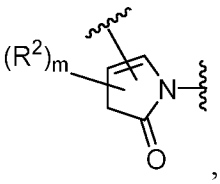
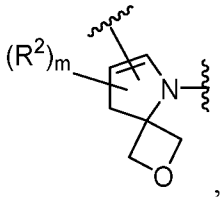
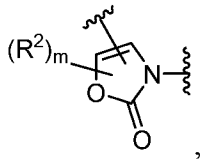
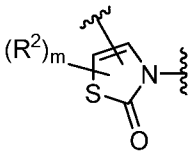
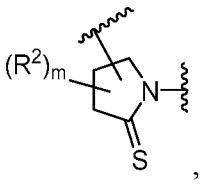
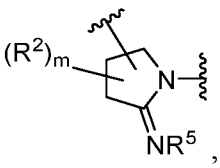
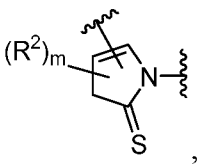
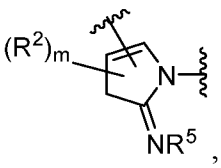
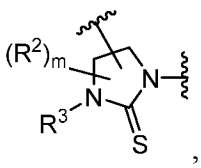
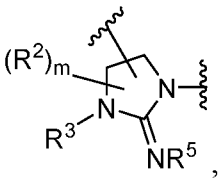
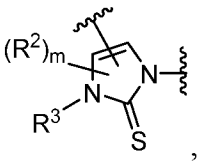
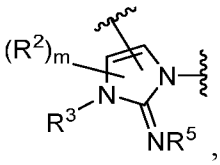
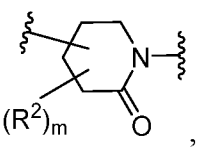
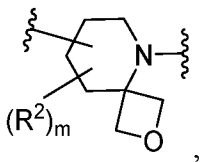
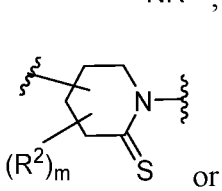
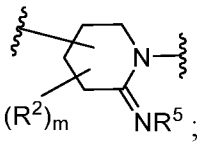
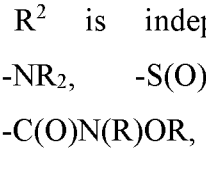


II′-A

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–CH_2–$, –C(O)–, –C(S)–, or  ;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, or an optionally substituted C_{1-4} aliphatic;

Ring A is a mono- or bicyclic ring selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , , , , , ,  ,  , , , , ,  , or ;

each R^2 is independently hydrogen, $-R^4$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

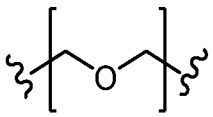
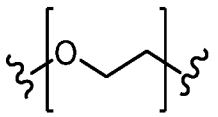
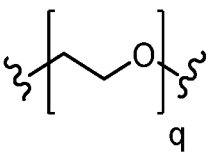
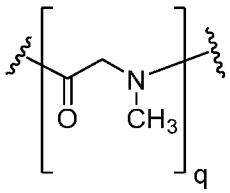
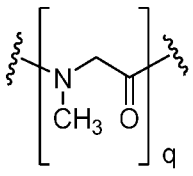
Ring B is selected from a 6-membered aryl containing 0-2 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each R^3 is independently hydrogen, $-R^4$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms

independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^5 is hydrogen, C_{1-4} aliphatic, or –CN;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -N(R)-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, -$S(O)_2$-, -N(R)$S(O)_2$-, -$S(O)_2$N(R)-, -N(R)C(O)-, -C(O)N(R)-, -OC(O)N(R)-, –N(R)C(O)O-,  ,  ,  ,  , or  , wherein:

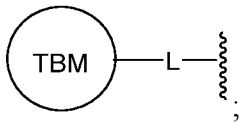
each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

TBM is a target binding moiety;

m is 0, 1, or 2;

n is 0, 1, 2, 3, or 4;

p is 0 or 1, wherein when p is 0, the bond connecting Ring A and Ring B is connected to



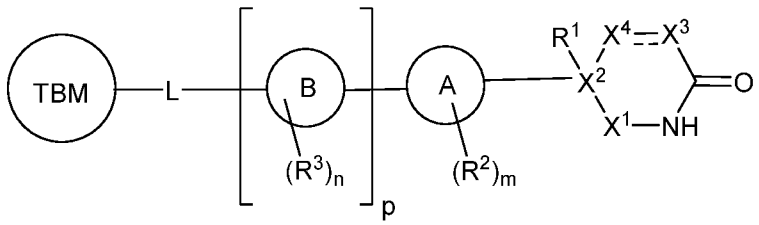
;

each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

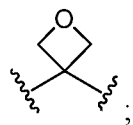
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0029] In certain embodiments, the present invention provides a compound of Formula **II''-A**:



II''-A

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–C(R)_2–$, –C(O)–, –C(S)–, –P(O)(OR)–, –P(O)(R)–, $–P(O)(NR_2)–$, $–S(O)–$, $–S(O)_2–$, or 

;

X^2 is a carbon atom or silicon atom;

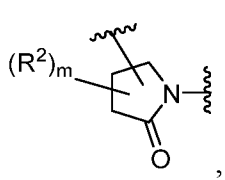
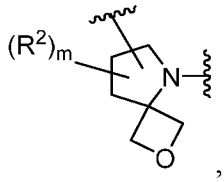
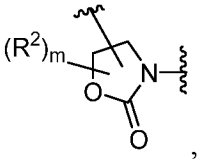
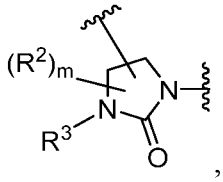
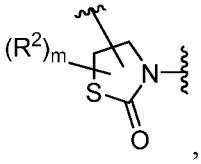
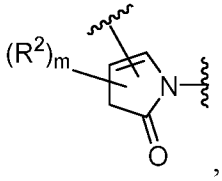
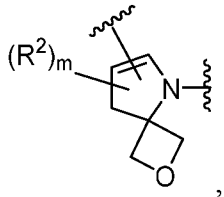
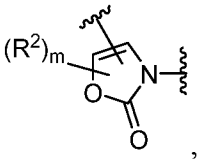
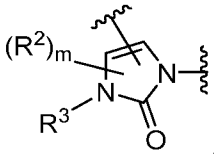
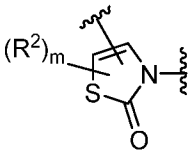
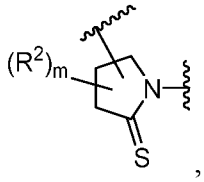
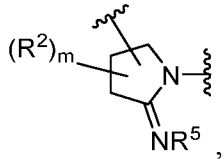
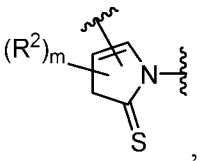
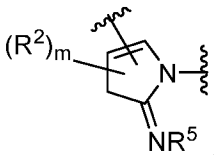
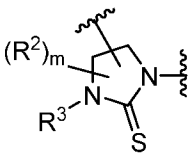
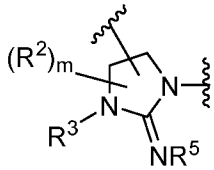
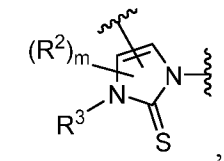
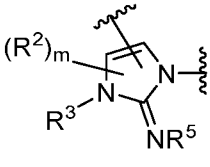
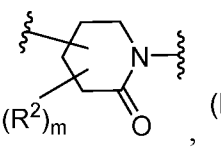
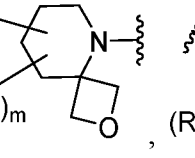
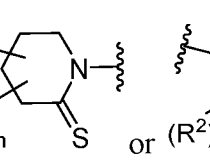
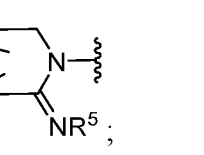
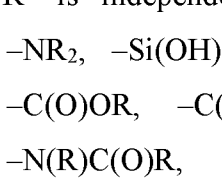
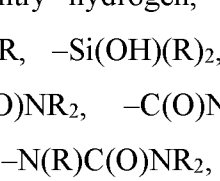
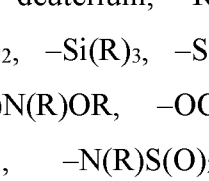
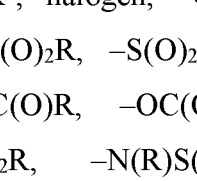
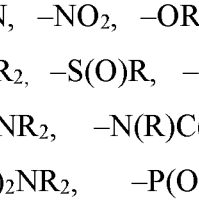
X^3 is a bivalent moiety selected from $–C(R)_2–$, $–N(R)–$, $–CF_2–$, –CHF–, –S–, or –O–;

X^4 is a bivalent moiety selected from a covalent bond or $–C(R)_2–$;

=== is a single bond or double bond;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, $–P(O)(OR)_2$, $–P(O)(NR_2)OR$, $–P(O)(NR_2)_2$, $–Si(OH)_2R$, $–Si(OH)(R)_2$, $–Si(R)_3$, an optionally substituted C_{1-4} aliphatic, or:

R^1 and X^1 or X^4 are taken together with their intervening atoms to form a 5-7 membered saturated, partially unsaturated, carbocyclic ring or heterocyclic ring having 1-3 heteroatoms, independently selected from nitrogen, oxygen, or sulfur;

Ring A is a mono- or bicyclic ring selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  or  ;

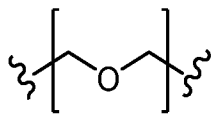
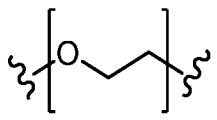
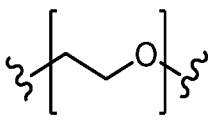
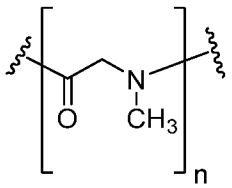
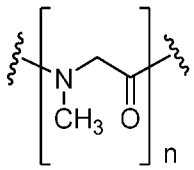
each R^2 is independently hydrogen, deuterium, $-R^6$, halogen, $-CN$, $-NO_2$, $-OR$, $-SR$, $-NR_2$, $-Si(OH)_2R$, $-Si(OH)(R)_2$, $-Si(R)_3$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)N(R)OR$, $-OC(O)R$, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, $-N(R)S(O)_2R$, $-N(R)S(O)_2NR_2$, $-P(O)(OR)_2$, $-P(O)(NR_2)OR$, or $-P(O)(NR_2)_2$;

Ring B is selected from a 6-membered aryl containing 0-3 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, or sulfur;

each R^3 is selected from hydrogen, deuterium, halogen, –CN, $–NO_2$, –OR, $–NR_2$, –SR, $–S(O)_2R$, $–S(O)_2NR_2$, –S(O)R, –C(O)R, –C(O)OR, $–C(O)NR_2$, –C(O)NR(OR), –OC(O)R, $–OC(O)NR_2$, $–OP(O)(OR)_2$, $–OP(O)(NR_2)_2$, $–OP(O)(OR)NR_2$, –N(R)C(O)R, –N(R)C(O)OR, $-N(R)C(O)NR_2$, $–N(R)S(O)_2R$, $–N(R)S(O)_2NR_2$, $–N(R)P(O)(OR)_2$, $–N(R)P(O)(OR)NR_2$, $–P(O)(OR)_2$, $–P(O)(NR_2)OR$, $–P(O)(NR_2)_2$, $–Si(OH)_2R$, $–Si(OH)(R)_2$, or $–Si(R)_3$;

each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^5 is hydrogen, deuterium, an optionally substituted C_{1-4} aliphatic, or –CN;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy–, –O–, –N(R)–, $–Si(R)_2–$, –Si(OH)(R)–, $–Si(OH)_2–$, –P(O)(OR)–, –P(O)(R)–, $–P(O)(NR_2)–$, –S–, –OC(O)–, –C(O)O–, –C(O)–, –S(O)–, $–S(O)_2–$, $–N(R)S(O)_2–$, $–S(O)_2N(R)–$, –N(R)C(O)–, –C(O)N(R)–, –OC(O)N(R)–, –N(R)C(O)O–,  ,  ,  ,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 3-8 membered saturated or partially unsaturated carbocyclylenyl, a 6-11 membered saturated or partially unsaturated spiro carbocyclylenyl, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-10 membered saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 6-11 membered saturated or partially unsaturated spiro

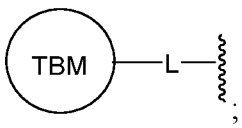
heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur;

TBM is a target binding moiety;

m is 0, 1, or 2;

n is 0, 1, 2, 3, or 4;

p is 0 or 1, wherein when p is 0, the bond connecting Ring A and Ring B is connected to



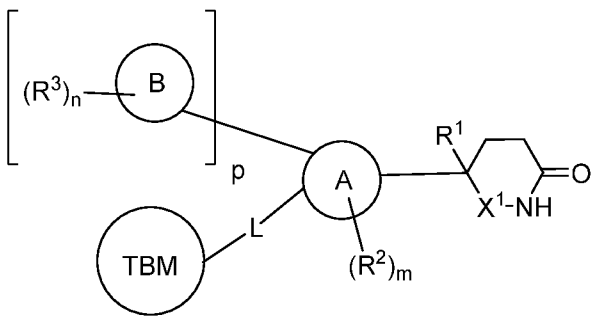
;

each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

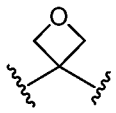
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0030] In certain embodiments, the present invention provides a compound of Formula **II-B**:

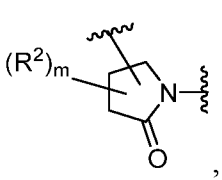
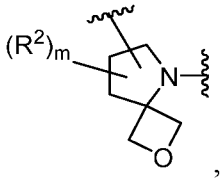
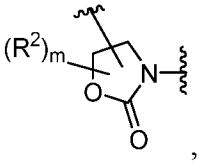
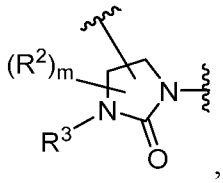
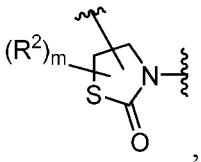
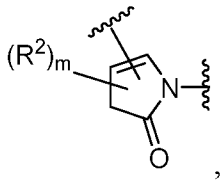
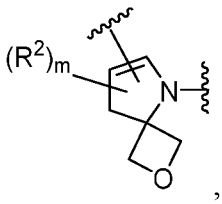
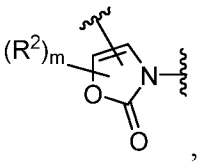
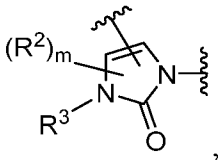
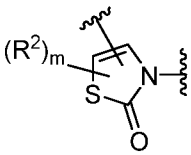
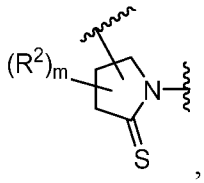
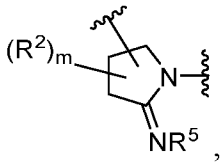
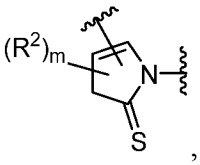
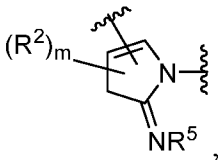
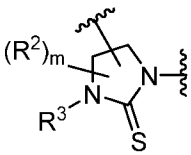
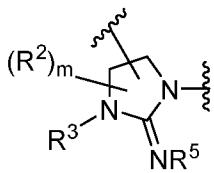
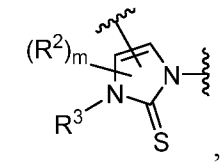
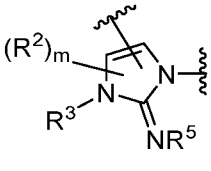
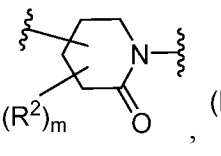
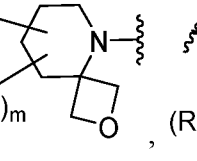
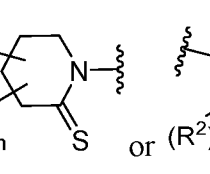
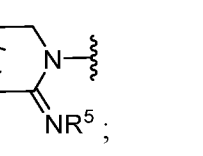
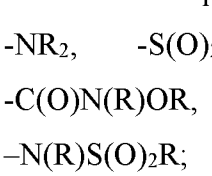
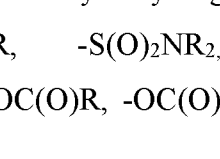
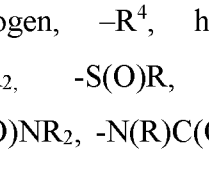
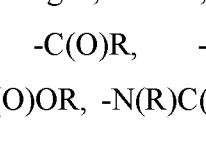
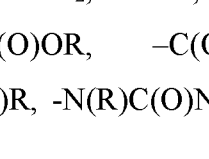


II-B

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–CH_2–$, –C(O)–, –C(S)–, or  ;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, or an optionally substituted C_{1-4} aliphatic;

Ring A is a mono- or bicyclic ring selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , or  ;

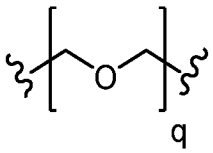
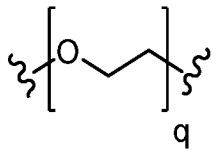
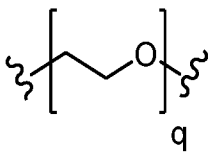
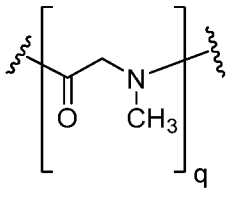
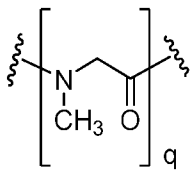
each R^2 is independently hydrogen, $–R^4$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

Ring B is selected from a 6-membered aryl containing 0-2 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each R^3 is independently hydrogen, $-R^4$, halogen, –CN, $-NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $-C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $-N(R)S(O)_2R$;

each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^5 is hydrogen, C_{1-4} aliphatic, or –CN;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -N(R)-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, $-S(O)_2-$, $-N(R)S(O)_2-$, $-S(O)_2N(R)-$, -N(R)C(O)-, -C(O)N(R)-, -OC(O)N(R)-, –N(R)C(O)O-,  ,  ,  ,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently

selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

TBM is a target binding moiety;

m is 0, 1, or 2;

n is 0, 1, 2, 3, or 4;

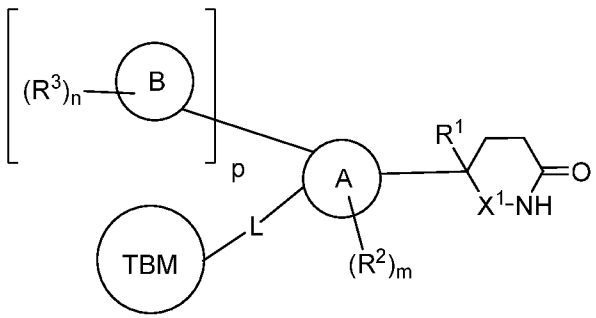
p is 0 or 1;

each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0031] In certain embodiments, the present invention provides a compound of formula **II′-B**:

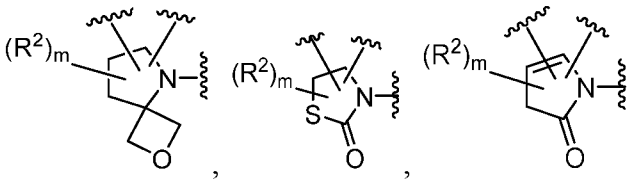
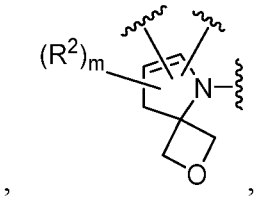
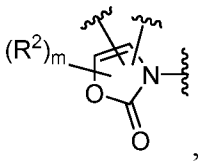
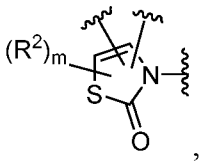
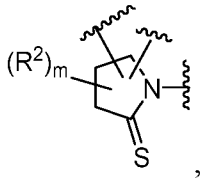
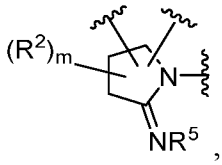
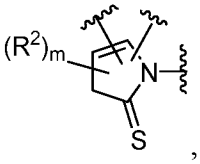
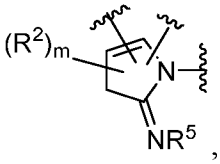
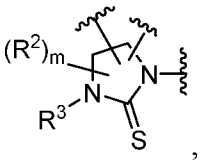
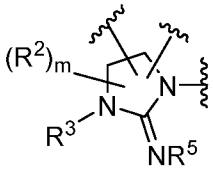
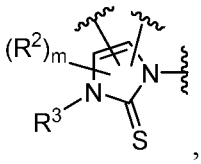
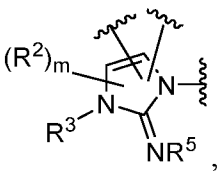
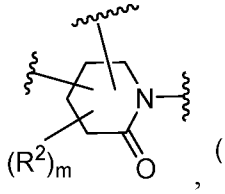
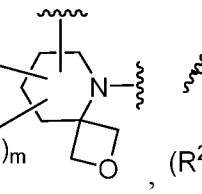
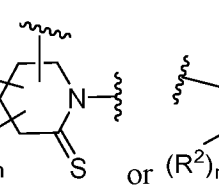
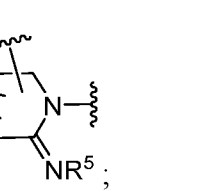
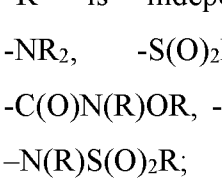
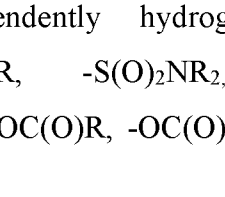
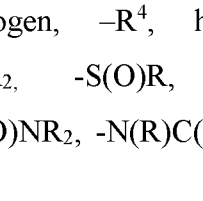
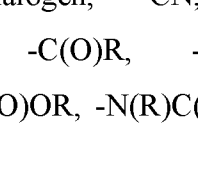
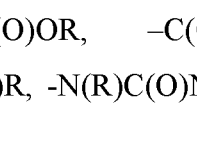


II′-B

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $-CH_2-$, $-C(O)-$, $-C(S)-$, or  ;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, $-S(O)R$, $-S(O)_2R$, $-NR_2$, or an optionally substituted C_{1-4} aliphatic;

Ring A is a mono- or bicyclic ring selected from  , , ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , or ;

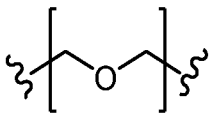
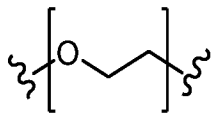
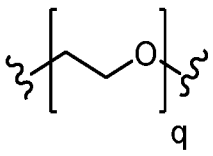
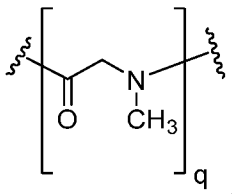
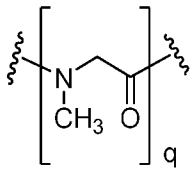
each R^2 is independently hydrogen, $-R^4$, halogen, –CN, $-NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $-C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, or $-N(R)S(O)_2R$;

Ring B is selected from a 6-membered aryl containing 0-2 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each R^3 is independently hydrogen, $-R^4$, halogen, –CN, $-NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $-C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, or $-N(R)S(O)_2R$;

each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^5 is hydrogen, C_{1-4} aliphatic, or –CN;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -N(R)-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, -$S(O)_2$-, -N(R)$S(O)_2$-, -$S(O)_2$N(R)-, -N(R)C(O)-, -C(O)N(R)-, -OC(O)N(R)-, –N(R)C(O)O-,  ,  ,  ,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

TBM is a target binding moiety;

m is 0, 1, or 2;

n is 0, 1, 2, 3, or 4;

p is 0 or 1;

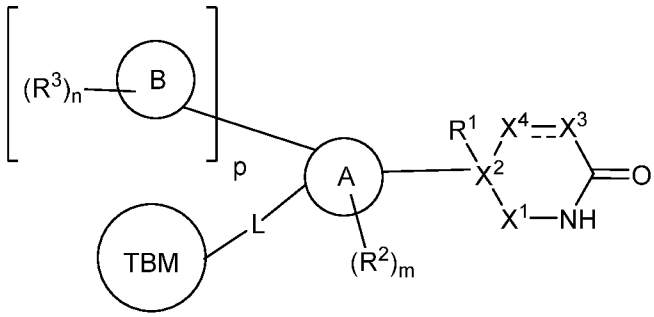
each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms

independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

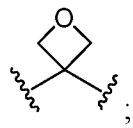
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0032] In certain embodiments, the present invention provides a compound of Formula **II″-B**:



II″-B

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–C(R)_2–$, –C(O)–, –C(S)–, –P(O)(OR)–, –P(O)(R)–, $–P(O)(NR_2)–$, $–S(O)–$, $–S(O)_2–$, or  ;

X^2 is a carbon atom or silicon atom;

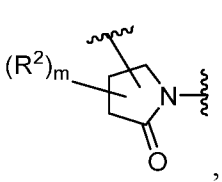
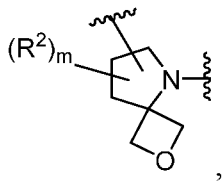
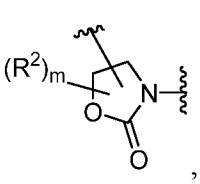
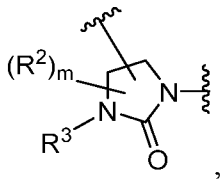
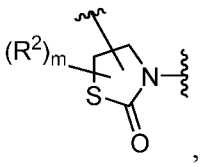
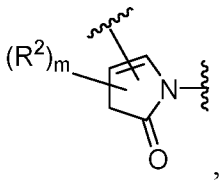
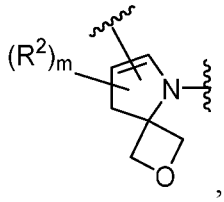
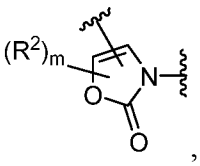
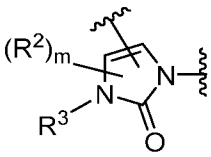
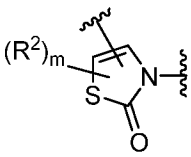
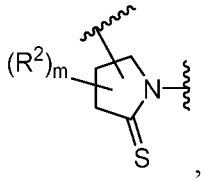
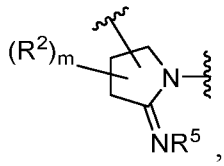
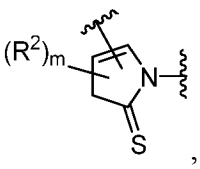
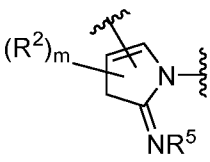
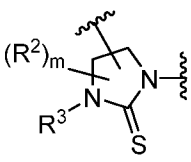
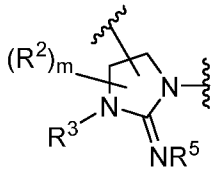
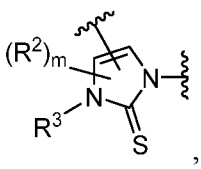
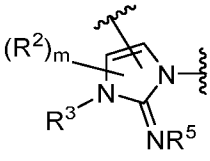
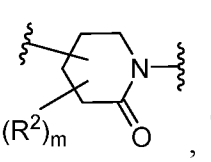
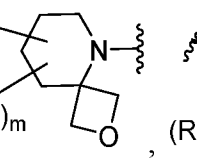
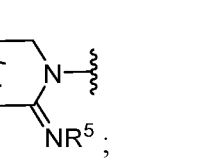
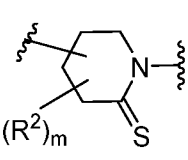
X^3 is a bivalent moiety selected from $–C(R)_2–$, $–N(R)–$, $–CF_2–$, –CHF–, –S–, or –O–;

X^4 is a bivalent moiety selected from a covalent bond or $–C(R)_2–$;

⚌ is a single bond or double bond;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, $–P(O)(OR)_2$, $–P(O)(NR_2)OR$, $–P(O)(NR_2)_2$, $–Si(OH)_2R$, $–Si(OH)(R)_2$, $–Si(R)_3$, an optionally substituted C_{1-4} aliphatic, or:

R^1 and X^1 or X^4 are taken together with their intervening atoms to form a 5-7 membered saturated, partially unsaturated, carbocyclic ring or heterocyclic ring having 1-3 heteroatoms, independently selected from nitrogen, oxygen, or sulfur;

Ring A is a mono- or bicyclic ring selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , ,  , , , ,  , or ;

each R^2 is independently hydrogen, deuterium, $-R^6$, halogen, $-CN$, $-NO_2$, $-OR$, $-SR$, $-NR_2$, $-Si(OH)_2R$, $-Si(OH)(R)_2$, $-Si(R)_3$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)N(R)OR$, $-OC(O)R$, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, $-N(R)S(O)_2R$, $-N(R)S(O)_2NR_2$, $-P(O)(OR)_2$, $-P(O)(NR_2)OR$, or $-P(O)(NR_2)_2$;

Ring B is selected from a 6-membered aryl containing 0-3 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

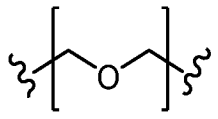
each R^3 is selected from hydrogen, deuterium, halogen, $-CN$, $-NO_2$, $-OR$, $-NR_2$, $-SR$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)NR(OR)$, $-OC(O)R$, $-OC(O)NR_2$, $-OP(O)(OR)_2$, $-OP(O)(NR_2)_2$, $-OP(O)(OR)NR_2$, $-N(R)C(O)R$, $-N(R)C(O)OR$, $-N(R)C(O)NR_2$, $-N(R)S(O)_2R$, $-N(R)S(O)_2NR_2$, $-N(R)P(O)(OR)_2$,

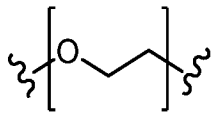
–N(R)P(O)(OR)NR_2, –P(O)$(OR)_2$, –P(O)(NR_2)OR, –P(O)$(NR_2)_2$, –Si$(OH)_2$R, –Si(OH)$(R)_2$, or –Si$(R)_3$;

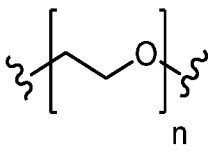
each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

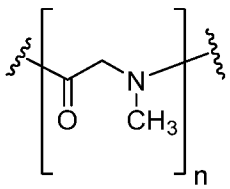
R^5 is hydrogen, deuterium, an optionally substituted C_{1-4} aliphatic, or –CN;

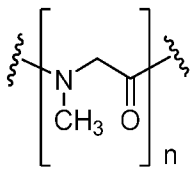
L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy–, –O–, –N(R)–, –Si$(R)_2$–, –Si(OH)(R)–, –Si$(OH)_2$–, –P(O)(OR)–, –P(O)(R)–, –P(O)(NR_2)–, –S–, –OC(O)–, –C(O)O–, –C(O)–, –S(O)–, –S$(O)_2$–, –N(R)S$(O)_2$–, –S$(O)_2$N(R)–, –N(R)C(O)–, –C(O)N(R)–, –OC(O)N(R)–, –N(R)C(O)O–,



,


,


,


, or


, wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 3-8 membered saturated or partially unsaturated carbocyclylenyl, a 6-11 membered saturated or partially unsaturated spiro carbocyclylenyl, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-10 membered saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 6-11 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-6 membered

heteroarylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur;

TBM is a target binding moiety;

m is 0, 1, or 2;

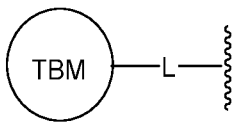
n is 0, 1, 2, 3, or 4;

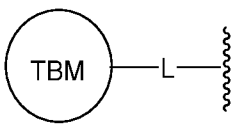
p is 0 or 1;

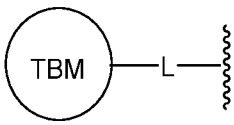
each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

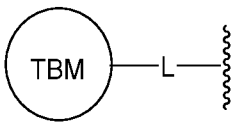
each R is independently hydrogen, deuterium, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0033] Where a point of attachment of 

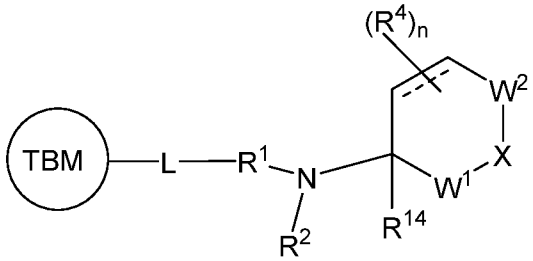
is depicted on Ring A, it is intended, and one of ordinary skill in the art would appreciate, that the point of attachment of 

may be at any available carbon or nitrogen atom on Ring A. Where 

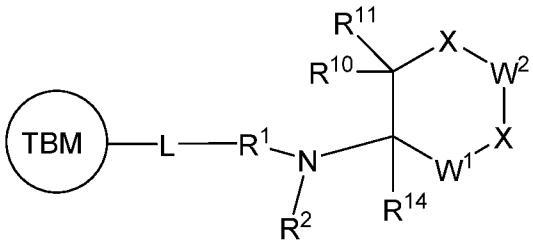
is attached to a nitrogen atom bound to R^3 or R^5, R^3 or R^5 is absent and 

takes the place of the R^3 or R^5 group.

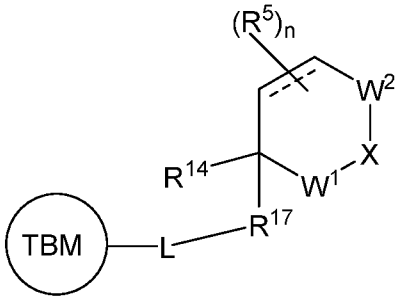
[0034] In certain embodiments, the present invention provides a compound of Formula **III-A**, **III-B**, or **III-C**:



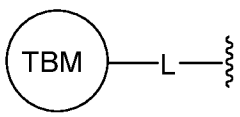
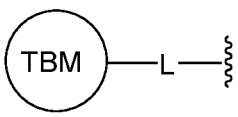
III-A



III-B



III-C

or a pharmaceutically acceptable salt thereof, wherein L and TBM are as defined above and described herein, and wherein each of the variables R^1, R^2, R^4, R^5, R^{10}, R^{11}, R^{14}, R^{17}, W^1, W^2, X and n is as defined in WO 2017/197051 which is herein incorporated by reference in its entirety and wherein  is attached to R^1, the ring formed by combining R^1 and R^2, or R^{17} at the site of attachment of R^{12} as defined in WO 2017/197051 such that  takes the place of the R^{12} substituent.

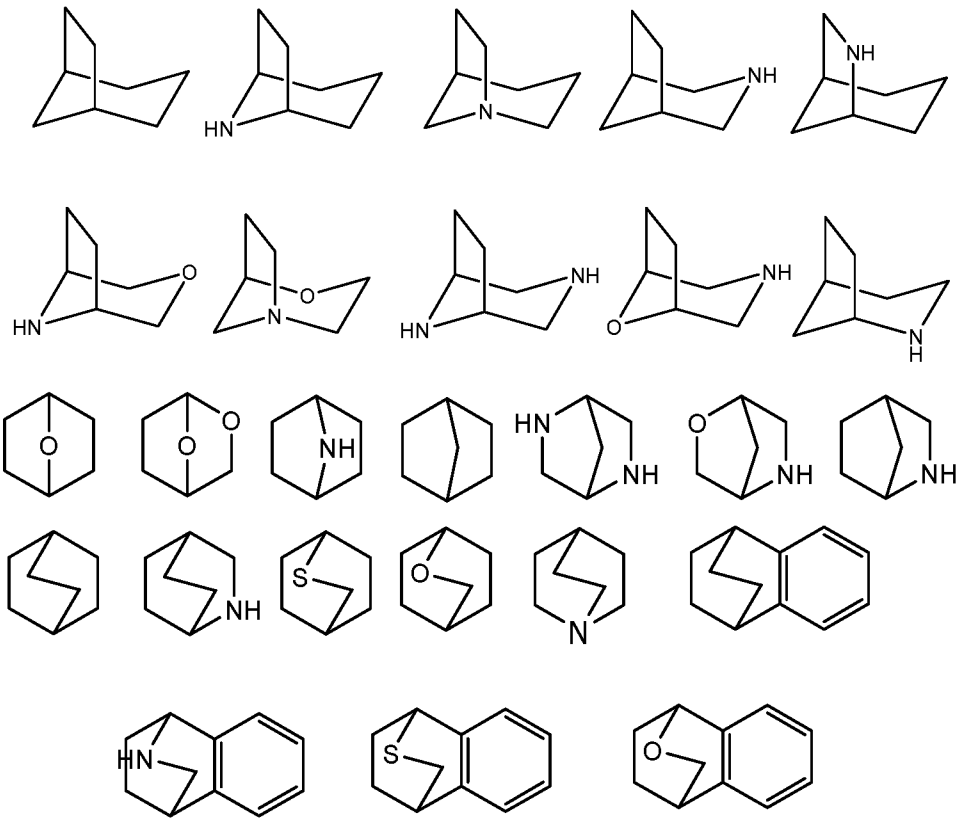
2. Compounds and Definitions:

[0035] Compounds of the present invention include those described generally herein, and are further illustrated by the classes, subclasses, and species disclosed herein. As used herein, the following definitions shall apply unless otherwise indicated. For purposes of this invention, the chemical elements are identified in accordance with the Periodic Table of the Elements, CAS version, Handbook of Chemistry and Physics, 75th Ed. Additionally, general principles of organic chemistry are described in "Organic Chemistry", Thomas Sorrell, University Science Books, Sausalito: 1999, and "March's Advanced Organic Chemistry", 5th Ed., Ed.: Smith, M.B. and March, J., John Wiley & Sons, New York: 2001, the entire contents of which are hereby incorporated by reference.

[0036] The term "aliphatic" or "aliphatic group", as used herein, means a straight-chain (i.e., unbranched) or branched, substituted or unsubstituted hydrocarbon chain that is completely saturated or that contains one or more units of unsaturation, or a monocyclic hydrocarbon or bicyclic hydrocarbon that is completely saturated or that contains one or more units of unsaturation, but which is not aromatic (also referred to herein as "carbocycle," "cycloaliphatic" or "cycloalkyl"), that has a single point of attachment to the rest of the molecule. Unless otherwise specified, aliphatic groups contain 1-6 aliphatic carbon atoms. In some embodiments, aliphatic groups contain 1-5 aliphatic carbon atoms. In other embodiments, aliphatic groups contain 1-4 aliphatic carbon atoms. In still other embodiments, aliphatic groups contain 1-3 aliphatic carbon atoms, and in yet other embodiments, aliphatic groups contain 1-2 aliphatic carbon atoms. In some embodiments, "cycloaliphatic" (or "carbocycle" or "cycloalkyl") refers to a monocyclic C_3-C_6 hydrocarbon that is completely saturated or that contains one or more units of unsaturation, but which is not aromatic, that has a single point of attachment to the rest of the molecule. Suitable aliphatic groups include, but are not limite to, linear or branched, substituted or unsubstituted alkyl, alkenyl, alkynyl groups and hybrids thereof such as (cycloalkyl)alkyl, (cycloalkenyl)alkyl or (cycloalkyl)alkenyl.

[0037] As used herein, the term "bridged bicyclic" refers to any bicyclic ring system, i.e. carbocyclic or heterocyclic, saturated or partially unsaturated, having at least one bridge. As defined by IUPAC, a "bridge" is an unbranched chain of atoms or an atom or a valence bond

connecting two bridgeheads, where a "bridgehead" is any skeletal atom of the ring system which is bonded to three or more skeletal atoms (excluding hydrogen). In some embodiments, a bridged bicyclic group has 7-12 ring members and 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur. Such bridged bicyclic groups are well known in the art and include those groups set forth below where each group is attached to the rest of the molecule at any substitutable carbon or nitrogen atom. Unless otherwise specified, a bridged bicyclic group is optionally substituted with one or more substituents as set forth for aliphatic groups. Additionally or alternatively, any substitutable nitrogen of a bridged bicyclic group is optionally substituted. Exemplary bridged bicyclics include:



[0038] The term "lower alkyl" refers to a C_{1-4} straight or branched alkyl group. Exemplary lower alkyl groups are methyl, ethyl, propyl, isopropyl, butyl, isobutyl, and tert-butyl.

[0039] The term "lower haloalkyl" refers to a C_{1-4} straight or branched alkyl group that is substituted with one or more halogen atoms.

[0040] The term "heteroatom" means one or more of oxygen, sulfur, nitrogen, phosphorus, or silicon (including, any oxidized form of nitrogen, sulfur, phosphorus, or silicon; the quaternized

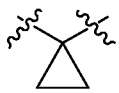
form of any basic nitrogen or; a substitutable nitrogen of a heterocyclic ring, for example N (as in 3,4-dihydro-2*H*-pyrrolyl), NH (as in pyrrolidinyl) or NR^+ (as in N-substituted pyrrolidinyl)).

[0041] The term "unsaturated," as used herein, means that a moiety has one or more units of unsaturation.

[0042] As used herein, the term "bivalent C_{1-8} (or C_{1-6}) saturated or unsaturated, straight or branched, hydrocarbon chain", refers to bivalent alkylene, alkenylene, and alkynylene chains that are straight or branched as defined herein.

[0043] The term "alkylene" refers to a bivalent alkyl group. An "alkylene chain" is a polymethylene group, i.e., $–(CH_2)_n–$, wherein n is a positive integer, preferably from 1 to 6, from 1 to 4, from 1 to 3, from 1 to 2, or from 2 to 3. A substituted alkylene chain is a polymethylene group in which one or more methylene hydrogen atoms are replaced with a substituent. Suitable substituents include those described below for a substituted aliphatic group.

[0044] The term "alkenylene" refers to a bivalent alkenyl group. A substituted alkenylene chain is a polymethylene group containing at least one double bond in which one or more hydrogen atoms are replaced with a substituent. Suitable substituents include those described below for a substituted aliphatic group.

[0045] As used herein, the term "cyclopropylenyl" refers to a bivalent cyclopropyl group of the following structure:  .

[0046] The term "halogen" means F, Cl, Br, or I.

[0047] The term "aryl" used alone or as part of a larger moiety as in "aralkyl," "aralkoxy," or "aryloxyalkyl," refers to monocyclic or bicyclic ring systems having a total of five to fourteen ring members, wherein at least one ring in the system is aromatic and wherein each ring in the system contains 3 to 7 ring members. The term "aryl" may be used interchangeably with the term "aryl ring." In certain embodiments of the present invention, "aryl" refers to an aromatic ring system which includes, but not limited to, phenyl, biphenyl, naphthyl, anthracyl and the like, which may bear one or more substituents. Also included within the scope of the term "aryl," as it is used herein, is a group in which an aromatic ring is fused to one or more non–aromatic rings, such as indanyl, phthalimidyl, naphthimidyl, phenanthridinyl, or tetrahydronaphthyl, and the like.

[0048] The terms "heteroaryl" and "heteroar–," used alone or as part of a larger moiety, e.g., "heteroaralkyl," or "heteroaralkoxy," refer to groups having 5 to 10 ring atoms, preferably 5, 6, or 9 ring atoms; having 6, 10, or 14 π electrons shared in a cyclic array; and having, in addition to carbon atoms, from one to five heteroatoms. The term "heteroatom" refers to nitrogen, oxygen, or sulfur, and includes any oxidized form of nitrogen or sulfur, and any quaternized form of a basic nitrogen. Heteroaryl groups include, without limitation, thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, thiadiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolizinyl, purinyl, naphthyridinyl, and pteridinyl. The terms "heteroaryl" and "heteroar–", as used herein, also include groups in which a heteroaromatic ring is fused to one or more aryl, cycloaliphatic, or heterocyclyl rings, where the radical or point of attachment is on the heteroaromatic ring. Nonlimiting examples include indolyl, isoindolyl, benzothienyl, benzofuranyl, dibenzofuranyl, indazolyl, benzimidazolyl, benzthiazolyl, quinolyl, isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, 4*H*–quinolizinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, phenoxazinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, and pyrido[2,3–b]–1,4–oxazin–3(4H)–one. A heteroaryl group may be mono– or bicyclic. The term "heteroaryl" may be used interchangeably with the terms "heteroaryl ring," "heteroaryl group," or "heteroaromatic," any of which terms include rings that are optionally substituted. The term "heteroaralkyl" refers to an alkyl group substituted by a heteroaryl, wherein the alkyl and heteroaryl portions independently are optionally substituted.

[0049] As used herein, the terms "heterocycle," "heterocyclyl," "heterocyclic radical," and "heterocyclic ring" are used interchangeably and refer to a stable 5– to 7–membered monocyclic or 7–10–membered bicyclic heterocyclic moiety that is either saturated or partially unsaturated, and having, in addition to carbon atoms, one or more, preferably one to four, heteroatoms, as defined above. When used in reference to a ring atom of a heterocycle, the term "nitrogen" includes a substituted nitrogen. As an example, in a saturated or partially unsaturated ring having 0–3 heteroatoms selected from oxygen, sulfur or nitrogen, the nitrogen may be N (as in 3,4–dihydro–2*H*–pyrrolyl), NH (as in pyrrolidinyl), or $^{+}$NR (as in *N*–substituted pyrrolidinyl).

[0050] A heterocyclic ring can be attached to its pendant group at any heteroatom or carbon atom that results in a stable structure and any of the ring atoms can be optionally substituted. Examples of such saturated or partially unsaturated heterocyclic radicals include, without

limitation, tetrahydrofuranyl, tetrahydrothiophenyl pyrrolidinyl, piperidinyl, pyrrolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, decahydroquinolinyl, oxazolidinyl, piperazinyl, dioxanyl, dioxolanyl, diazepinyl, oxazepinyl, thiazepinyl, morpholinyl, 2-oxa-6-azaspiro[3.3]heptane, and quinuclidinyl. The terms "heterocycle," "heterocyclyl," "heterocyclyl ring," "heterocyclic group," "heterocyclic moiety," and "heterocyclic radical," are used interchangeably herein, and also include groups in which a heterocyclyl ring is fused to one or more aryl, heteroaryl, or cycloaliphatic rings, such as indolinyl, 3*H*–indolyl, chromanyl, phenanthridinyl, or tetrahydroquinolinyl. A heterocyclyl group may be mono– or bicyclic. The term "heterocyclylalkyl" refers to an alkyl group substituted by a heterocyclyl, wherein the alkyl and heterocyclyl portions independently are optionally substituted.

[0051] As used herein, the term "partially unsaturated" refers to a ring moiety that includes at least one double or triple bond. The term "partially unsaturated" is intended to encompass rings having multiple sites of unsaturation, but is not intended to include aryl or heteroaryl moieties, as herein defined.

[0052] As described herein, compounds of the invention may contain "optionally substituted" moieties. In general, the term "substituted," whether preceded by the term "optionally" or not, means that one or more hydrogens of the designated moiety are replaced with a suitable substituent. Unless otherwise indicated, an "optionally substituted" group may have a suitable substituent at each substitutable position of the group, and when more than one position in any given structure may be substituted with more than one substituent selected from a specified group, the substituent may be either the same or different at every position. Combinations of substituents envisioned by this invention are preferably those that result in the formation of stable or chemically feasible compounds. The term "stable," as used herein, refers to compounds that are not substantially altered when subjected to conditions to allow for their production, detection, and, in certain embodiments, their recovery, purification, and use for one or more of the purposes disclosed herein.

[0053] Suitable monovalent substituents on a substitutable carbon atom of an "optionally substituted" group are independently halogen; $–(CH_2)_{0–4}R°$; $–(CH_2)_{0–4}OR°$; $-O(CH_2)_{0-4}R^o$, $–O–(CH_2)_{0–4}C(O)OR°$; $–(CH_2)_{0–4}CH(OR°)_2$; $–(CH_2)_{0–4}SR°$; $–(CH_2)_{0–4}Ph$, which may be substituted with R°; $–(CH_2)_{0–4}O(CH_2)_{0–1}Ph$ which may be substituted with R°; –CH=CHPh, which may be

substituted with R°; –$(CH_2)_{0-4}O(CH_2)_{0-1}$-pyridyl which may be substituted with R°; –NO_2; –CN; –N_3; -$(CH_2)_{0-4}N(R°)_2$; –$(CH_2)_{0-4}N(R°)C(O)R°$; –$N(R°)C(S)R°$; –$(CH_2)_{0-4}N(R°)C(O)NR°_2$; -$N(R°)C(S)NR°_2$; –$(CH_2)_{0-4}N(R°)C(O)OR°$; –$N(R°)N(R°)C(O)R°$; -$N(R°)N(R°)C(O)NR°_2$; -$N(R°)N(R°)C(O)OR°$; –$(CH_2)_{0-4}C(O)R°$; –$C(S)R°$; –$(CH_2)_{0-4}C(O)OR°$; –$(CH_2)_{0-4}C(O)SR°$; -$(CH_2)_{0-4}C(O)OSiR°_3$; –$(CH_2)_{0-4}OC(O)R°$; –$OC(O)(CH_2)_{0-4}SR°$; -$SC(S)SR°$; –$(CH_2)_{0-4}SC(O)R°$; –$(CH_2)_{0-4}C(O)NR°_2$; –$C(S)NR°_2$; –$C(S)SR°$; -$(CH_2)_{0-4}OC(O)NR°_2$; -$C(O)N(OR°)R°$; –$C(O)C(O)R°$; –$C(O)CH_2C(O)R°$; –$C(NOR°)R°$; -$(CH_2)_{0-4}SSR°$; –$(CH_2)_{0-4}S(O)_2R°$; –$(CH_2)_{0-4}S(O)_2OR°$; –$(CH_2)_{0-4}OS(O)_2R°$; –$S(O)_2NR°_2$; -$(CH_2)_{0-4}S(O)R°$; -$N(R°)S(O)_2NR°_2$; –$N(R°)S(O)_2R°$; –$N(OR°)R°$; –$C(NH)NR°_2$; –$P(O)_2R°$; -$P(O)R°_2$; -$OP(O)R°_2$; –$OP(O)(OR°)_2$; –$SiR°_3$; –($C_{1-4}$ straight or branched alkylene)O–$N(R°)_2$; or –(C_{1-4} straight or branched alkylene)C(O)O–$N(R°)_2$, wherein each R° may be substituted as defined below and is independently hydrogen, C_{1-6} aliphatic, –CH_2Ph, –$O(CH_2)_{0-1}Ph$, -CH_2-(5-6 membered heteroaryl ring), or a 5–6–membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or, notwithstanding the definition above, two independent occurrences of R°, taken together with their intervening atom(s), form a 3–12–membered saturated, partially unsaturated, or aryl mono– or bicyclic ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, which may be substituted as defined below.

[0054] Suitable monovalent substituents on R° (or the ring formed by taking two independent occurrences of R° together with their intervening atoms), are independently halogen, –$(CH_2)_{0-2}R^•$, –(halo$R^•$), –$(CH_2)_{0-2}OH$, –$(CH_2)_{0-2}OR^•$, –$(CH_2)_{0-2}CH(OR^•)_2$; -O(halo$R^•$), –CN, –N_3, –$(CH_2)_{0-2}C(O)R^•$, –$(CH_2)_{0-2}C(O)OH$, –$(CH_2)_{0-2}C(O)OR^•$, –$(CH_2)_{0-2}SR^•$, –$(CH_2)_{0-2}SH$, –$(CH_2)_{0-2}NH_2$, –$(CH_2)_{0-2}NHR^•$, –$(CH_2)_{0-2}NR^•_2$, –NO_2, –$SiR^•_3$, –$OSiR^•_3$, -$C(O)SR^•$, –(C_{1-4} straight or branched alkylene)$C(O)OR^•$, or –$SSR^•$ wherein each $R^•$ is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently selected from C_{1-4} aliphatic, –CH_2Ph, –$O(CH_2)_{0-1}Ph$, or a 5–6–membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur. Suitable divalent substituents on a saturated carbon atom of R° include =O and =S.

[0055] Suitable divalent substituents on a saturated carbon atom of an "optionally substituted" group include the following: =O, =S, $=NNR^*_2$, $=NNHC(O)R^*$, $=NNHC(O)OR^*$, $=NNHS(O)_2R^*$, $=NR^*$, $=NOR^*$, $–O(C(R^*_2))_{2–3}O–$, or $–S(C(R^*_2))_{2–3}S–$, wherein each independent occurrence of R^* is selected from hydrogen, $C_{1–6}$ aliphatic which may be substituted as defined below, or an unsubstituted 5–6–membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur. Suitable divalent substituents that are bound to vicinal substitutable carbons of an "optionally substituted" group include: $–O(CR^*_2)_{2–3}O–$, wherein each independent occurrence of R^* is selected from hydrogen, $C_{1–6}$ aliphatic which may be substituted as defined below, or an unsubstituted 5–6–membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

[0056] Suitable substituents on the aliphatic group of R^* include halogen, $–R^\bullet$, -(halo$R^\bullet$), -OH, $–OR^\bullet$, –O(halo$R^\bullet$), –CN, –C(O)OH, $–C(O)OR^\bullet$, $–NH_2$, $–NHR^\bullet$, $–NR^\bullet_2$, or $–NO_2$, wherein each $R^\bullet$ is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently $C_{1–4}$ aliphatic, $–CH_2Ph$, $–O(CH_2)_{0–1}Ph$, or a 5–6–membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

[0057] Suitable substituents on a substitutable nitrogen of an "optionally substituted" group include $–R^\dagger$, $–NR^\dagger_2$, $–C(O)R^\dagger$, $–C(O)OR^\dagger$, $–C(O)C(O)R^\dagger$, $–C(O)CH_2C(O)R^\dagger$, $-S(O)_2R^\dagger$, $-S(O)_2NR^\dagger_2$, $–C(S)NR^\dagger_2$, $–C(NH)NR^\dagger_2$, or $–N(R^\dagger)S(O)_2R^\dagger$; wherein each $R^\dagger$ is independently hydrogen, $C_{1–6}$ aliphatic which may be substituted as defined below, unsubstituted –OPh, or an unsubstituted 5–6–membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or, notwithstanding the definition above, two independent occurrences of $R^\dagger$, taken together with their intervening atom(s) form an unsubstituted 3–12–membered saturated, partially unsaturated, or aryl mono– or bicyclic ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

[0058] Suitable substituents on the aliphatic group of $R^\dagger$ are independently halogen, $–R^\bullet$, -(halo$R^\bullet$), –OH, $–OR^\bullet$, –O(halo$R^\bullet$), –CN, –C(O)OH, $–C(O)OR^\bullet$, $–NH_2$, $–NHR^\bullet$, $–NR^\bullet_2$, or $-NO_2$, wherein each $R^\bullet$ is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently $C_{1–4}$ aliphatic, $–CH_2Ph$, $–O(CH_2)_{0–1}Ph$, or a 5–6–

membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

[0059] As used herein, the term "pharmaceutically acceptable salt" refers to those salts which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response and the like, and are commensurate with a reasonable benefit/risk ratio. Pharmaceutically acceptable salts are well known in the art. For example, S. M. Berge et al., describe pharmaceutically acceptable salts in detail in J. Pharmaceutical Sciences, 1977, 66, 1–19, incorporated herein by reference. Pharmaceutically acceptable salts of the compounds of this invention include those derived from suitable inorganic and organic acids and bases. Examples of pharmaceutically acceptable, nontoxic acid addition salts are salts of an amino group formed with inorganic acids such as hydrochloric acid, hydrobromic acid, phosphoric acid, sulfuric acid and perchloric acid or with organic acids such as acetic acid, oxalic acid, maleic acid, tartaric acid, citric acid, succinic acid or malonic acid or by using other methods used in the art such as ion exchange. Other pharmaceutically acceptable salts include adipate, alginate, ascorbate, aspartate, benzenesulfonate, benzoate, bisulfate, borate, butyrate, camphorate, camphorsulfonate, citrate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, formate, fumarate, glucoheptonate, glycerophosphate, gluconate, hemisulfate, heptanoate, hexanoate, hydroiodide, 2–hydroxy–ethanesulfonate, lactobionate, lactate, laurate, lauryl sulfate, malate, maleate, malonate, methanesulfonate, 2–naphthalenesulfonate, nicotinate, nitrate, oleate, oxalate, palmitate, pamoate, pectinate, persulfate, 3–phenylpropionate, phosphate, pivalate, propionate, stearate, succinate, sulfate, tartrate, thiocyanate, p–toluenesulfonate, undecanoate, valerate salts, and the like.

[0060] Salts derived from appropriate bases include alkali metal, alkaline earth metal, ammonium and $N^+(C_{1-4}alkyl)_4$ salts. Representative alkali or alkaline earth metal salts include sodium, lithium, potassium, calcium, magnesium, and the like. Further pharmaceutically acceptable salts include, when appropriate, nontoxic ammonium, quaternary ammonium, and amine cations formed using counterions such as halide, hydroxide, carboxylate, sulfate, phosphate, nitrate, loweralkyl sulfonate and aryl sulfonate.

[0061] Unless otherwise stated, structures depicted herein are also meant to include all isomeric (e.g., enantiomeric, diastereomeric, and geometric (or conformational)) forms of the

structure; for example, the R and S configurations for each asymmetric center, Z and E double bond isomers, and Z and E conformational isomers. Therefore, single stereochemical isomers as well as enantiomeric, diastereomeric, and geometric (or conformational) mixtures of the present compounds are within the scope of the invention. Unless otherwise stated, all tautomeric forms of the compounds of the invention are within the scope of the invention. Additionally, unless otherwise stated, structures depicted herein are also meant to include compounds that differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures including the replacement of hydrogen by deuterium or tritium, or the replacement of a carbon by a ^{13}C- or ^{14}C-enriched carbon are within the scope of this invention. Such compounds are useful, for example, as analytical tools, as probes in biological assays, or as therapeutic agents in accordance with the present invention. In certain embodiments, a provided compound may be substituted with one or more deuterium atoms.

[0062] As used herein, the term "binder" or "inhibitor" is defined as a compound that binds to CRBN and binds to or inhibits a targeted protein with measurable affinity. In certain embodiments, an inhibitor has an IC_{50} and/or binding constant of less than about 50 μM, less than about 1 μM, less than about 500 nM, less than about 100 nM, less than about 10 nM, or less than about 1 nM.

[0063] A compound of the present invention may be tethered to a detectable moiety. It will be appreciated that such compounds are useful as imaging agents. One of ordinary skill in the art will recognize that a detectable moiety may be attached to a provided compound *via* a suitable substituent. As used herein, the term "suitable substituent" refers to a moiety that is capable of covalent attachment to a detectable moiety. Such moieties are well known to one of ordinary skill in the art and include groups containing, e.g., a carboxylate moiety, an amino moiety, a thiol moiety, or a hydroxyl moiety, to name but a few. It will be appreciated that such moieties may be directly attached to a provided compound or *via* a tethering group, such as a bivalent saturated or unsaturated hydrocarbon chain. In some embodiments, such moieties may be attached via click chemistry. In some embodiments, such moieties may be attached via a 1,3-cycloaddition of an azide with an alkyne, optionally in the presence of a copper catalyst. Methods of using click chemistry are known in the art and include those described by Rostovtsev *et al.*, Angew. Chem. Int. Ed. 2002, 41, 2596-99 and Sun *et al.*, Bioconjugate Chem., 2006, 17, 52-57.

[0064] As used herein, the term "detectable moiety" is used interchangeably with the term "label" and relates to any moiety capable of being detected, e.g., primary labels and secondary labels. Primary labels, such as radioisotopes (e.g., tritium, ^{32}P, ^{33}P, ^{35}S, or ^{14}C), mass-tags, and fluorescent labels are signal generating reporter groups which can be detected without further modifications. Detectable moieties also include luminescent and phosphorescent groups.

[0065] The term "secondary label" as used herein refers to moieties such as biotin and various protein antigens that require the presence of a second intermediate for production of a detectable signal. For biotin, the secondary intermediate may include streptavidin-enzyme conjugates. For antigen labels, secondary intermediates may include antibody-enzyme conjugates. Some fluorescent groups act as secondary labels because they transfer energy to another group in the process of nonradiative fluorescent resonance energy transfer (FRET), and the second group produces the detected signal.

[0066] The terms "fluorescent label", "fluorescent dye", and "fluorophore" as used herein refer to moieties that absorb light energy at a defined excitation wavelength and emit light energy at a different wavelength. Examples of fluorescent labels include, but are not limited to: Alexa Fluor dyes (Alexa Fluor 350, Alexa Fluor 488, Alexa Fluor 532, Alexa Fluor 546, Alexa Fluor 568, Alexa Fluor 594, Alexa Fluor 633, Alexa Fluor 660 and Alexa Fluor 680), AMCA, AMCA-S, BODIPY dyes (BODIPY FL, BODIPY R6G, BODIPY TMR, BODIPY TR, BODIPY 530/550, BODIPY 558/568, BODIPY 564/570, BODIPY 576/589, BODIPY 581/591, BODIPY 630/650, BODIPY 650/665), Carboxyrhodamine 6G, carboxy-X-rhodamine (ROX), Cascade Blue, Cascade Yellow, Coumarin 343, Cyanine dyes (Cy3, Cy5, Cy3.5, Cy5.5), Dansyl, Dapoxyl, Dialkylaminocoumarin, 4',5'-Dichloro-2',7'-dimethoxy-fluorescein, DM-NERF, Eosin, Erythrosin, Fluorescein, FAM, Hydroxycoumarin, IRDyes (IRD40, IRD 700, IRD 800), JOE, Lissamine rhodamine B, Marina Blue, Methoxycoumarin, Naphthofluorescein, Oregon Green 488, Oregon Green 500, Oregon Green 514, Pacific Blue, PyMPO, Pyrene, Rhodamine B, Rhodamine 6G, Rhodamine Green, Rhodamine Red, Rhodol Green, 2',4',5',7'-Tetra-bromosulfone-fluorescein, Tetramethyl-rhodamine (TMR), Carboxytetramethylrhodamine (TAMRA), Texas Red, Texas Red-X.

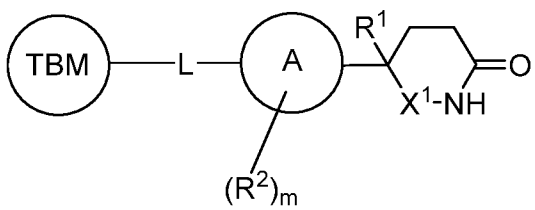
[0067] The term "mass-tag" as used herein refers to any moiety that is capable of being uniquely detected by virtue of its mass using mass spectrometry (MS) detection techniques.

Examples of mass-tags include electrophore release tags such as N-[3-[4'-[(p-Methoxytetrafluorobenzyl)oxy]phenyl]-3-methylglyceronyl]isonipecotic Acid, 4'-[2,3,5,6-Tetrafluoro-4-(pentafluorophenoxyl)]methyl acetophenone, and their derivatives. The synthesis and utility of these mass-tags is described in United States Patents 4,650,750, 4,709,016, 5,360,8191, 5,516,931, 5,602,273, 5,604,104, 5,610,020, and 5,650,270. Other examples of mass-tags include, but are not limited to, nucleotides, dideoxynucleotides, oligonucleotides of varying length and base composition, oligopeptides, oligosaccharides, and other synthetic polymers of varying length and monomer composition. A large variety of organic molecules, both neutral and charged (biomolecules or synthetic compounds) of an appropriate mass range (100-2000 Daltons) may also be used as mass-tags.

[0068] The terms "measurable affinity" and "measurably modulate," as used herein, means a measurable change in a CRBN activity between a sample comprising a compound of the present invention, or composition thereof, and CRBN, and an equivalent sample comprising CRBN, in the absence of said compound, or composition thereof.

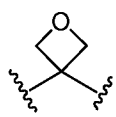
3. Description of Exemplary Embodiments:

[0069] As described above, in certain embodiments, the present invention provides a compound of formula **I**:



I

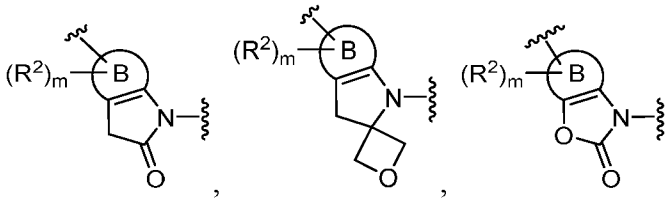
or a pharmaceutically acceptable salt thereof, wherein:

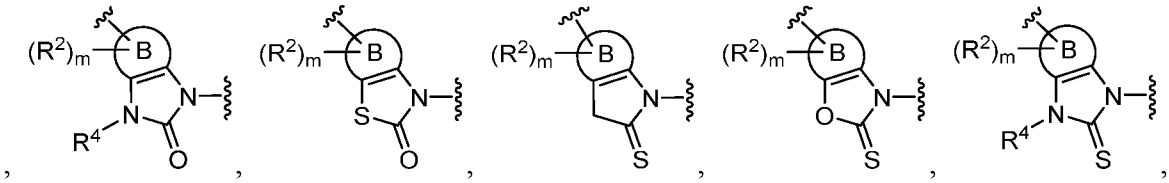
X^1 is a bivalent moiety selected from a covalent bond, $-CH_2-$, $-C(O)-$, $-C(S)-$, or  ;

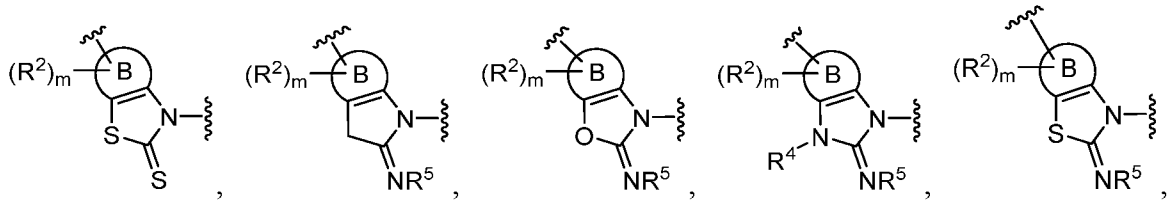
R^1 is hydrogen, deuterium, halogen, $-CN$, $-OR$, $-SR$, $-S(O)R$, $-S(O)_2R$, $-NR_2$, or an optionally substituted C_{1-4} aliphatic;

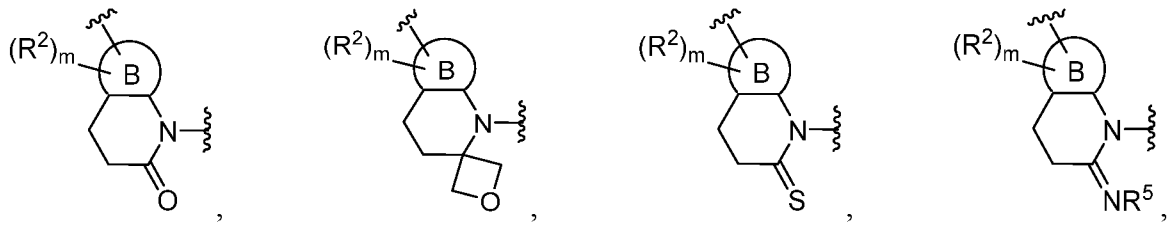
each R^2 is independently hydrogen, $-R^6$, halogen, $-CN$, $-NO_2$, $-OR$, $-SR$, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)N(R)OR$, $-OC(O)R$, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, or $-N(R)S(O)_2R$;

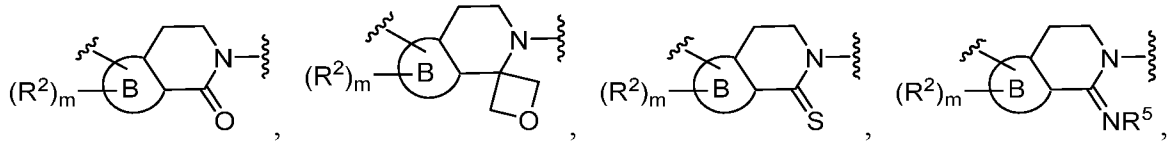
Ring A is a bi- or tricyclic ring selected from











wherein

Ring B is a fused ring selected from 6-membered aryl containing 0-2 nitrogen atoms, 5 to 7-membered partially saturated carbocyclyl, 5 to 7-membered partially saturated heterocyclyl with 1-2 heteroatoms independently selected from nitrogen, oxygen or sulfur, or 5-

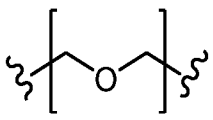
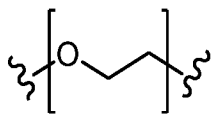
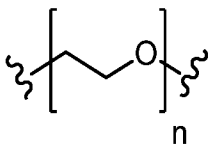
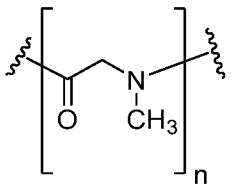
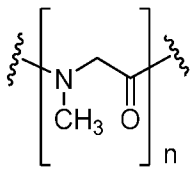
membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

R^3 is selected from hydrogen, halogen, –OR, $–N(R)_2$, or –SR;

each R^4 is independently hydrogen, $–R^6$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

R^5 is hydrogen, C_{1-4} aliphatic, or –CN;

each R^6 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -N(R)-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, $-S(O)_2-$, $-N(R)S(O)_2-$, $-S(O)_2N(R)-$, -N(R)C(O)-, -C(O)N(R)-, -OC(O)N(R)-, –N(R)C(O)O-,  ,  ,  ,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially

unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;;

TBM is a target binding moiety;

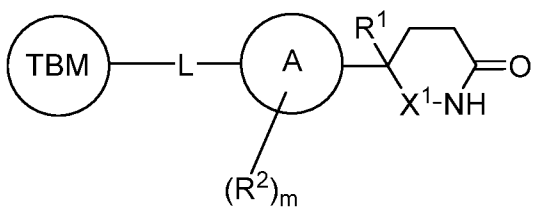
m is 0, 1, 2, 3 or 4;

each of n is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

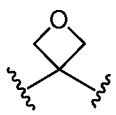
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0070] As described above, in certain embodiments, the present invention provides a compound of formula **I′**:



I′

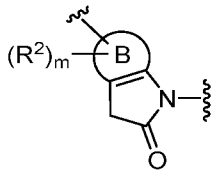
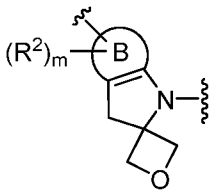
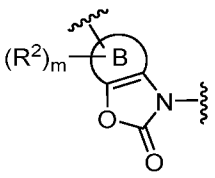
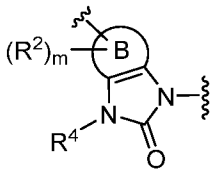
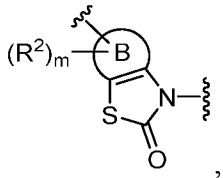
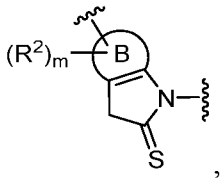
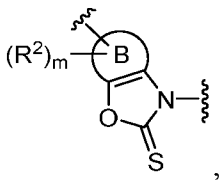
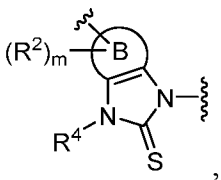
or a pharmaceutically acceptable salt thereof, wherein:

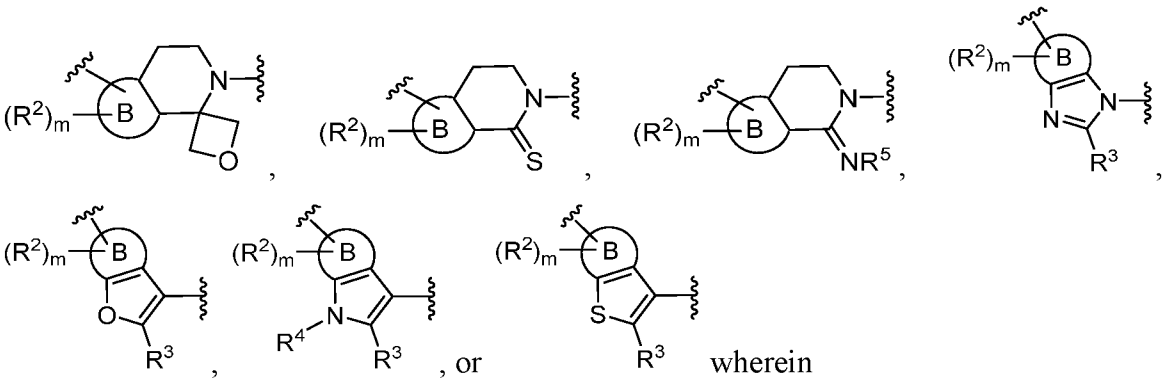
X^1 is a bivalent moiety selected from a covalent bond, $–CH_2–$, –C(O)–, –C(S)–, or  ;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, or an optionally substituted C_{1-4} aliphatic;

each R^2 is independently hydrogen, $–R^6$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$,

-C(O)N(R)OR, -OC(O)R, -OC(O)NR_2, -N(R)C(O)OR, -N(R)C(O)R, -N(R)C(O)NR_2, or –N(R)$S(O)_2$R;

Ring A is a bi- or tricyclic ring selected from  wherein Ring B is other than imidazo or benzo,   , wherein Ring B is other than benzo,  wherein Ring B is other than benzo,   ,  ,  ,



wherein

Ring B is a fused ring selected from 6-membered aryl containing 0-2 nitrogen atoms, 5 to 7-membered partially saturated carbocyclyl, 5 to 7-membered partially saturated heterocyclyl with 1-2 heteroatoms independently selected from nitrogen, oxygen or sulfur, or 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

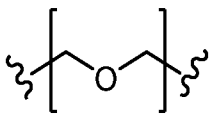
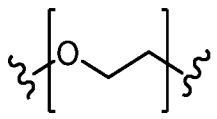
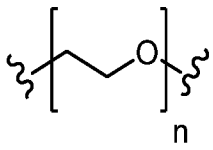
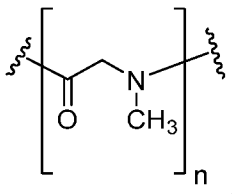
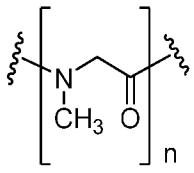
R^3 is selected from hydrogen, halogen, –OR, $–N(R)_2$, or –SR;

each R^4 is independently hydrogen, $–R^6$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

R^5 is hydrogen, C_{1-4} aliphatic, or –CN;

each R^6 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -N(R)-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, $-S(O)_2-$, $-N(R)S(O)_2-$, $-S(O)_2N(R)-$, -N(R)C(O)-, -

C(O)N(R)-, -OC(O)N(R)-, –N(R)C(O)O-,  ,  ,  ,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;;

TBM is a target binding moiety;

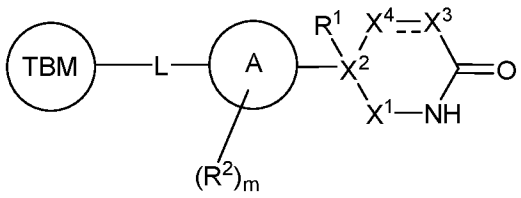
m is 0, 1, 2, 3 or 4;

each of n is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

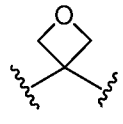
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0071] In certain embodiments, the present invention provides a compound of formula **I''**:



I″

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–C(R)_2–$, –C(O)–, –C(S)–, –P(O)(OR)–, –P(O)(R)–, $–P(O)(NR_2)–$, –S(O)–, $–S(O)_2–$, or  ;

X^2 is a carbon atom or silicon atom;

X^3 is a bivalent moiety selected from $–C(R)_2–$, –N(R)–, $–CF_2–$, –CHF–, –S–, or –O–;

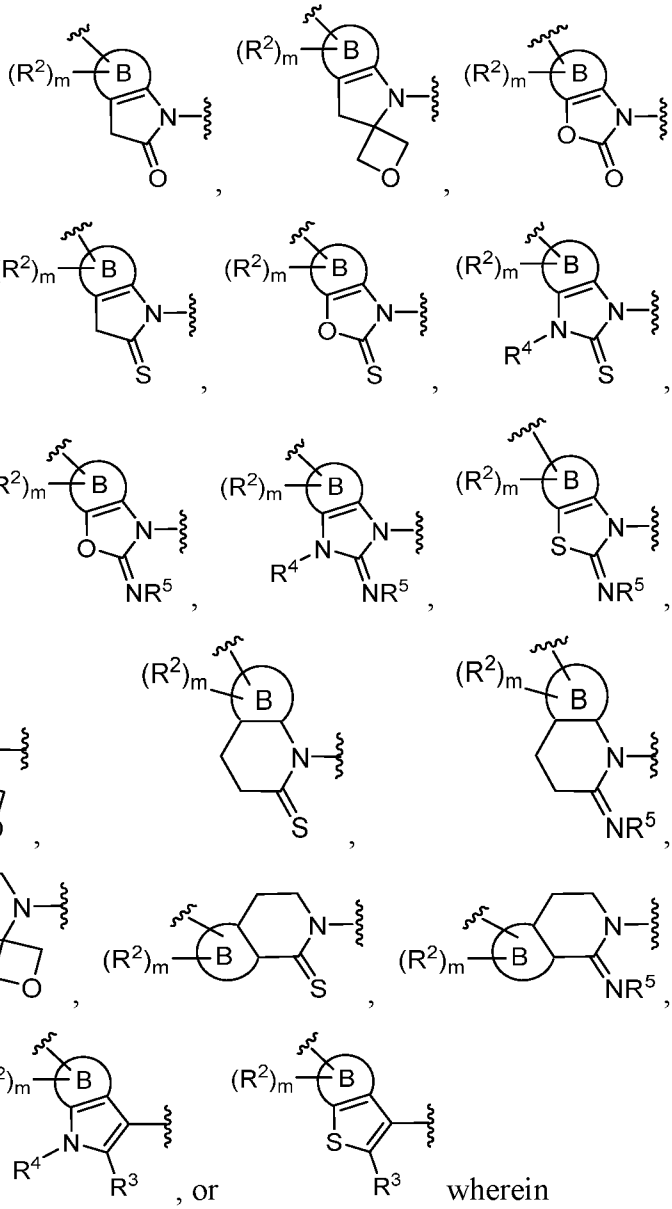
X^4 is a bivalent moiety selected from a covalent bond or $–C(R)_2–$;

--- is a single bond or double bond;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, $–P(O)(OR)_2$, $–P(O)(NR_2)OR$, $–P(O)(NR_2)_2$, $–Si(OH)_2R$, $–Si(OH)(R)_2$, $–Si(R)_3$, an optionally substituted C_{1-4} aliphatic, or:

R^1 and X^1 or X^4 are taken together with their intervening atoms to form a 5-7 membered saturated, partially unsaturated, carbocyclic ring or heterocyclic ring having 1-3 heteroatoms, independently selected from nitrogen, oxygen, or sulfur;

each R^2 is independently hydrogen, deuterium, $–R^6$, halogen, –CN, $–NO_2$, –OR, –SR, $–N(R)_2$, $–Si(OH)_2R$, $–Si(OH)(R)_2$, $–Si(R)_3$, $–S(O)_2R$, $–S(O)_2NR_2$, –S(O)R, –C(O)R, –C(O)OR, $–C(O)NR_2$, –C(O)N(R)OR, –OC(O)R, $–OC(O)NR_2$, –N(R)C(O)OR, –N(R)C(O)R, $–N(R)C(O)NR_2$, $–N(R)S(O)_2R$, $–N(R)S(O)_2NR_2$, $–P(O)(OR)_2$, $–P(O)(NR_2)OR$, or $–P(O)NR_2$;

Ring A is a bi- or tricyclic ring selected from  , wherein

Ring B is a fused ring selected from 6-membered aryl containing 0-3 nitrogen atoms, 5 to 7-membered partially saturated carbocyclyl, 5 to 7-membered partially saturated heterocyclyl with 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, or sulfur, or 5-membered heteroaryl with 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, or sulfur;

R^3 is selected from hydrogen, deuterium, halogen, –CN, $–NO_2$, –OR, $–NR_2$, –SR, $–S(O)_2R$, $–S(O)_2NR_2$, –S(O)R, –C(O)R, –C(O)OR, $–C(O)NR_2$, –C(O)NR(OR), –OC(O)R, $–OC(O)NR_2$, $–OP(O)(OR)_2$, $–OP(O)(NR_2)_2$, $–OP(O)(OR)NR_2$, –N(R)C(O)R,

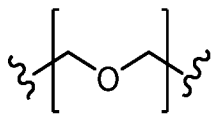
–N(R)C(O)OR, -N(R)C(O)NR_2, –N(R)S(O)$_2$R, –N(R)S(O)$_2NR_2$, –N(R)P(O)$(OR)_2$, –N(R)P(O)(OR)NR_2, –P(O)$(OR)_2$, –P(O)(NR_2)OR, –P(O)$(NR_2)_2$, –Si(OH)$_2$R, –Si(OH)$(R)_2$, or –Si$(R)_3$;

each R^4 is independently hydrogen, deuterium, –R^6, halogen, –S(O)$_2$R, –S(O)$_2NR_2$, –S(O)R, –C(O)R, –C(O)OR, –C(O)NR_2, –C(O)N(R)OR, –P(O)$(OR)_2$, –P(O)(NR_2)OR, or –P(O)$(NR_2)_2$;

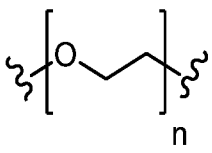
R^5 is hydrogen, deuterium, an optionally substituted C_{1-4} aliphatic, or –CN;

each R^6 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, or sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, or sulfur;

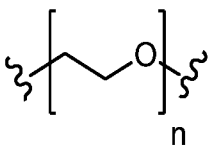
L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy–, –O–, –N(R)–, –Si$(R)_2$–, –Si(OH)(R)–, –Si$(OH)_2$–, –C(H)(CF_3)–, –P(O)(OR)–, –P(O)(R)–, –P(O)(NR_2)–, –S–, –OC(O)–, –C(O)O–, –C(O)–, –S(O)–, –S(O)$_2$–, –N(R)S(O)$_2$–, –S(O)$_2$N(R)–, –N(R)C(O)–, –C(O)N(R)–, –OC(O)N(R)–, –N(R)C(O)O–,



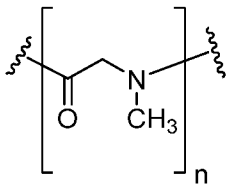
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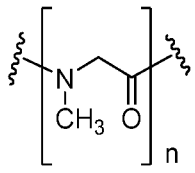
,



,



, or



, wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-8 membered saturated or partially unsaturated carbocyclylenyl, a 6-11 membered saturated or partially unsaturated spiro carbocyclylenyl, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-10 membered saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 6-11 membered saturated or partially unsaturated spiro

heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur;

TBM is a target binding moiety;

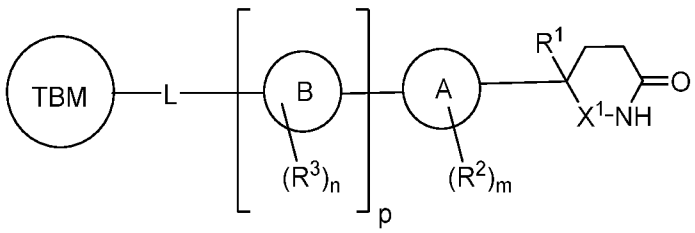
m is 0, 1, 2, 3 or 4;

each of n is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

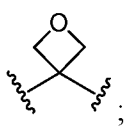
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0072] As described above, in certain embodiments, the present invention provides a compound of formula **II-A**:

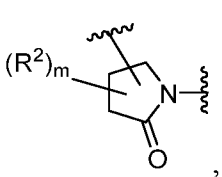
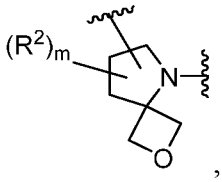
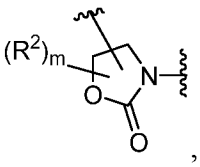
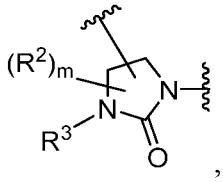
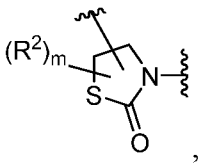
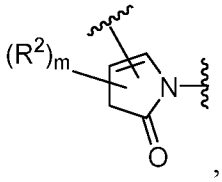
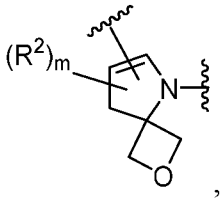
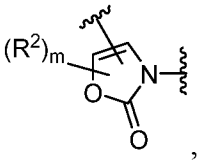
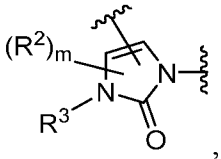
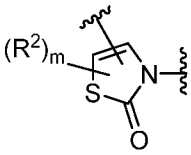
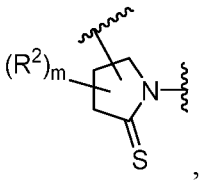
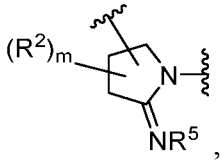
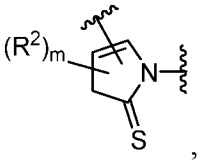
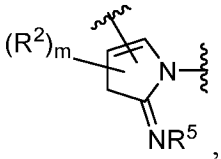
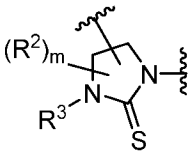
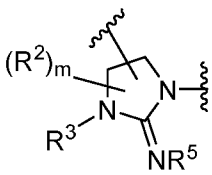
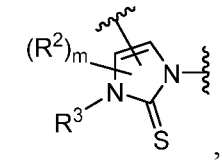
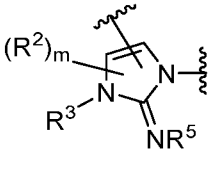
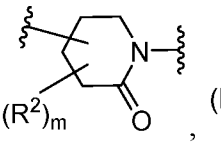
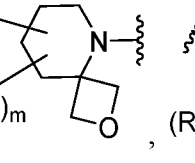
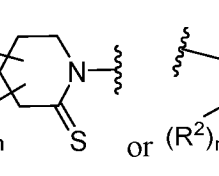
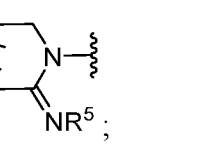
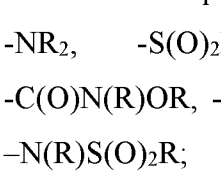
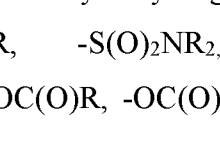
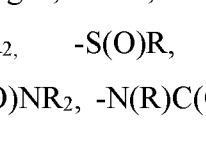
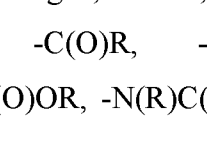
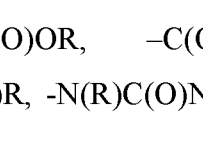


II-A

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–CH_2–$, –C(O)–, –C(S)–, or  ;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, or an optionally substituted C_{1-4} aliphatic;

Ring A is a mono- or bicyclic ring selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  or  ;

each R^2 is independently hydrogen, $–R^4$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

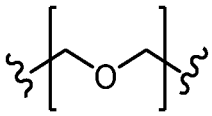
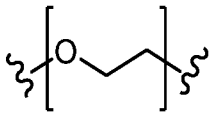
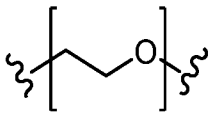
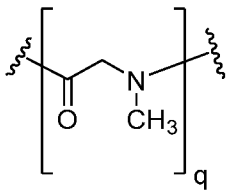
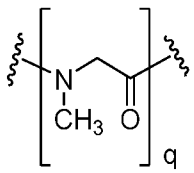
Ring B is selected from a 6-membered aryl containing 0-2 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each R^3 is independently hydrogen, $–R^4$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$,

-C(O)N(R)OR, -OC(O)R, -OC(O)NR_2, -N(R)C(O)OR, -N(R)C(O)R, -N(R)C(O)NR_2, or –N(R)$S(O)_2$R;

each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^5 is hydrogen, C_{1-4} aliphatic, or –CN;

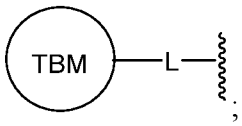
L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -N(R)-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, -$S(O)_2$-, -N(R)$S(O)_2$-, -$S(O)_2$N(R)-, -N(R)C(O)-, -C(O)N(R)-, -OC(O)N(R)-, –N(R)C(O)O-,  ,  ,  ,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

TBM is a target binding moiety;

m is 0, 1, or 2;

n is 0, 1, 2, 3, or 4;

p is 0 or 1, wherein when p is 0, the bond connecting Ring A and Ring B is connected to 

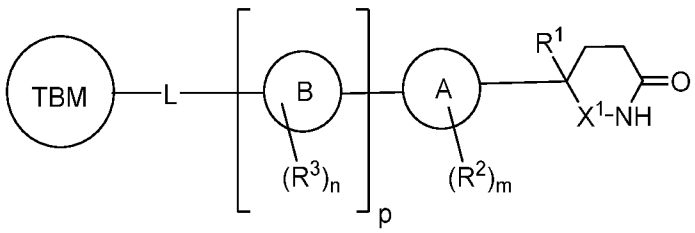
;

each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

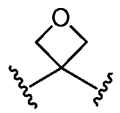
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0073] As described above, in certain embodiments, the present invention provides a compound of formula **II′-A**:



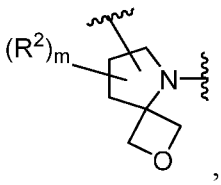
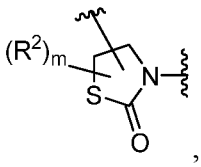
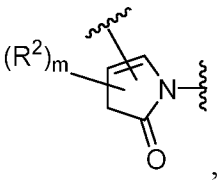
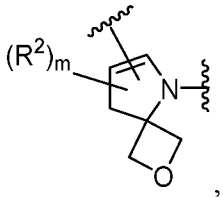
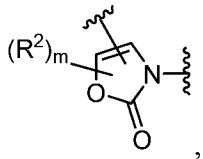
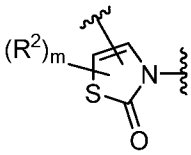
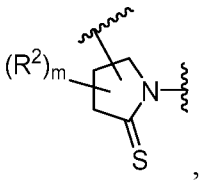
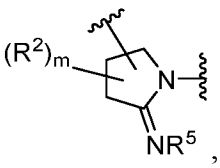
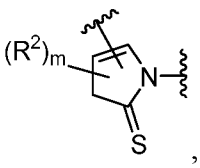
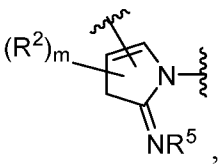
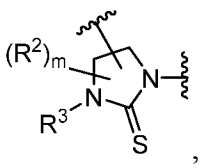
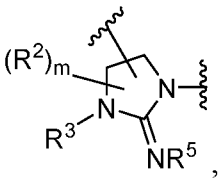
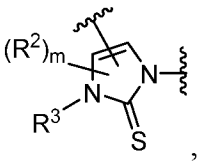
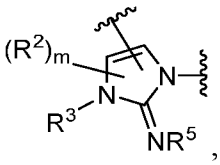
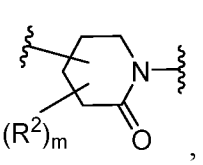
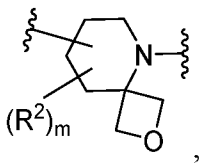
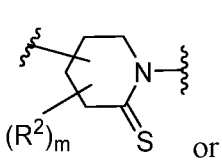
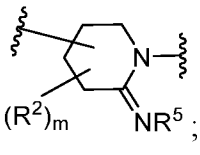
II′-A

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–CH_2–$, –C(O)–, –C(S)–, or 

;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, or an optionally substituted C_{1-4} aliphatic;

Ring A is a mono- or bicyclic ring selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , , , , , ,  ,  , , , , or ;

each R^2 is independently hydrogen, $-R^4$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

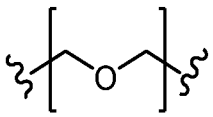
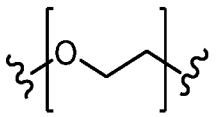
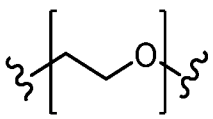
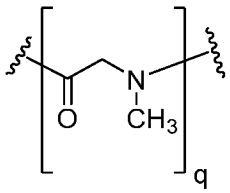
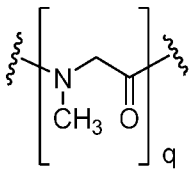
Ring B is selected from a 6-membered aryl containing 0-2 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each R^3 is independently hydrogen, $-R^4$, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms

independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^5 is hydrogen, C_{1-4} aliphatic, or –CN;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -N(R)-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, -$S(O)_2$-, -N(R)$S(O)_2$-, -$S(O)_2$N(R)-, -N(R)C(O)-, -C(O)N(R)-, -OC(O)N(R)-, –N(R)C(O)O-,  ,  ,  ,  , or  , wherein:

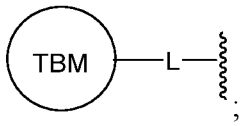
each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

TBM is a target binding moiety;

m is 0, 1, or 2;

n is 0, 1, 2, 3, or 4;

p is 0 or 1, wherein when p is 0, the bond connecting Ring A and Ring B is connected to



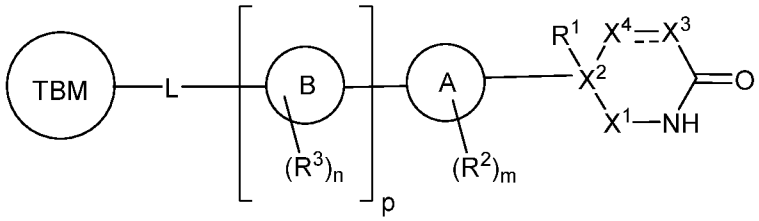
;

each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

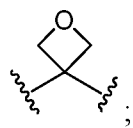
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0074] In certain embodiments, the present invention provides a compound of Formula **II″-A**:



II″-A

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–C(R)_2–$, –C(O)–, –C(S)–, –P(O)(OR)–, –P(O)(R)–, $–P(O)(NR_2)–$, $–S(O)–$, $–S(O)_2–$, or 

;

X^2 is a carbon atom or silicon atom;

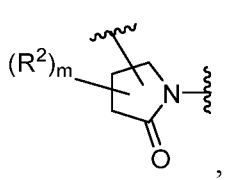
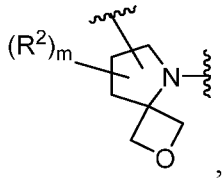
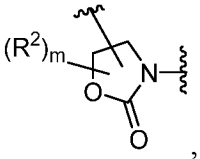
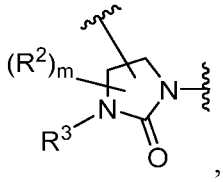
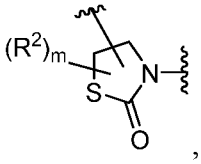
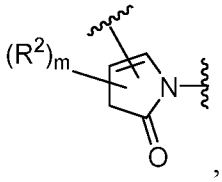
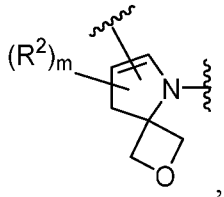
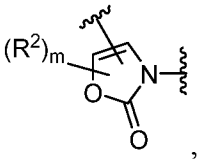
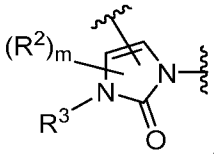
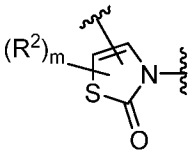
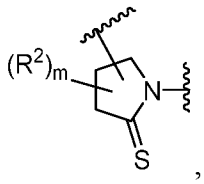
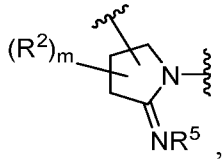
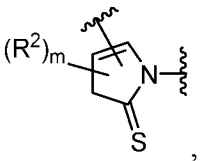
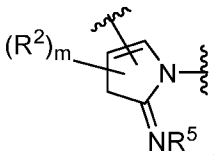
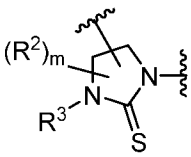
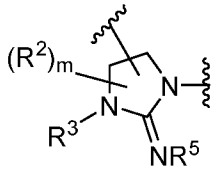
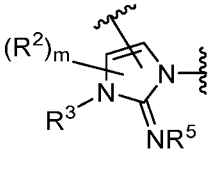
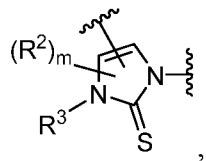
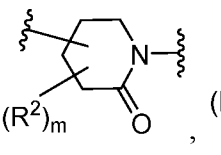
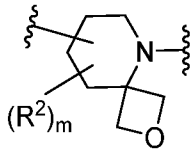
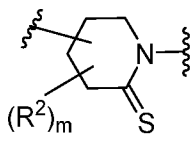
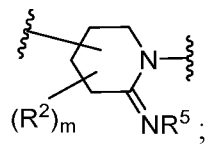
X^3 is a bivalent moiety selected from $–C(R)_2–$, $–N(R)–$, $–CF_2–$, –CHF–, –S–, or –O–;

X^4 is a bivalent moiety selected from a covalent bond or $–C(R)_2–$;

=== is a single bond or double bond;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, $–P(O)(OR)_2$, $–P(O)(NR_2)OR$, $–P(O)(NR_2)_2$, $–Si(OH)_2R$, $–Si(OH)(R)_2$, $–Si(R)_3$, an optionally substituted C_{1-4} aliphatic, or:

R^1 and X^1 or X^4 are taken together with their intervening atoms to form a 5-7 membered saturated, partially unsaturated, carbocyclic ring or heterocyclic ring having 1-3 heteroatoms, independently selected from nitrogen, oxygen, or sulfur;

Ring A is a mono- or bicyclic ring selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , ,  , , , ,  , ,  ,  ,  , or  ;

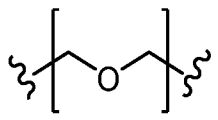
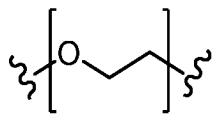
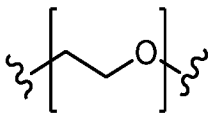
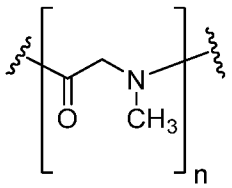
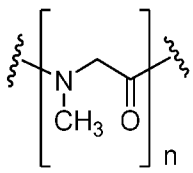
each R^2 is independently hydrogen, deuterium, $-R^4$, halogen, $-CN$, $-NO_2$, $-OR$, $-SR$, $-N(R)_2$, $-Si(OH)_2R$, $-Si(OH)(R)_2$, $-Si(R)_3$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)N(R)OR$, $-OC(O)R$, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, $-N(R)S(O)_2R$, $-N(R)S(O)_2NR_2$, $-P(O)(OR)_2$, $-P(O)(NR_2)OR$, or $-P(O)(NR_2)_2$;

Ring B is selected from a 6-membered aryl containing 0-3 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur;

each R^3 is selected from hydrogen, deuterium, $-R^4$, halogen, $-CN$, $-NO_2$, $-OR$, $-NR_2$, $-SR$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)NR(OR)$, $-OC(O)R$, $-OC(O)NR_2$, $-OP(O)(OR)_2$, $-OP(O)(NR_2)_2$, $-OP(O)(OR)NR_2$, $-N(R)C(O)R$, $-N(R)C(O)OR$, $-N(R)C(O)NR_2$, $-N(R)S(O)_2R$, $-N(R)S(O)_2NR_2$, $-N(R)P(O)(OR)_2$, $-N(R)P(O)(OR)NR_2$, $-P(O)(OR)_2$, $-P(O)(NR_2)OR$, $-P(O)(NR_2)_2$, $-Si(OH)_2R$, $-Si(OH)(R)_2$, or $-Si(R)_3$;

each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^5 is hydrogen, deuterium, an optionally substituted C_{1-4} aliphatic, or $-CN$;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by $-Cy-$, $-O-$, $-N(R)-$, $-Si(R)_2-$, $-Si(OH)(R)-$, $-Si(OH)_2-$, $-P(O)(OR)-$, $-P(O)(R)-$, $-P(O)(NR_2)-$, $-S-$, $-OC(O)-$, $-C(O)O-$, $-C(O)-$, $-S(O)-$, $-S(O)_2-$, $-N(R)S(O)_2-$, $-S(O)_2N(R)-$, $-N(R)C(O)-$, $-C(O)N(R)-$, $-OC(O)N(R)-$, $-N(R)C(O)O-$,  ,  ,  ,  , or  , wherein:

each $-Cy-$ is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 3-8 membered saturated or partially unsaturated carbocyclylenyl, a 6-11 membered saturated or partially unsaturated spiro carbocyclylenyl, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-10 membered saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 6-11 membered saturated or partially unsaturated spiro

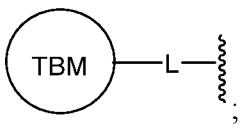
heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur;

TBM is a target binding moiety;

m is 0, 1, or 2;

n is 0, 1, 2, 3, or 4;

p is 0 or 1, wherein when p is 0, the bond connecting Ring A and Ring B is connected to



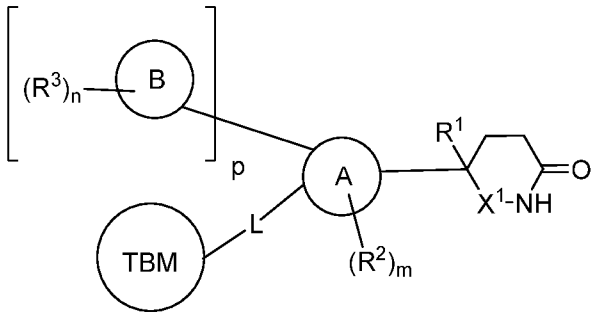
;

each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

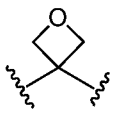
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0075] As described above, in certain embodiments, the present invention provides a compound of formula **II-B**:

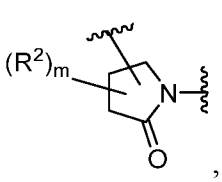
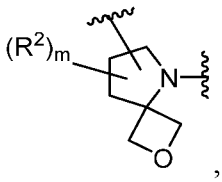
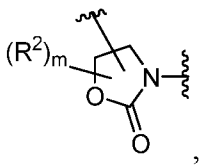
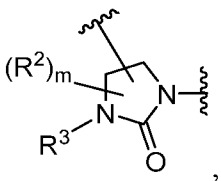
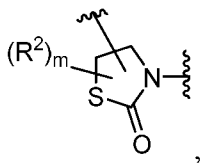
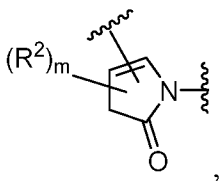
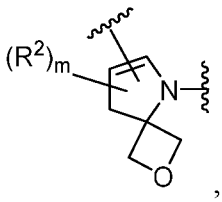
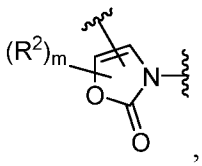
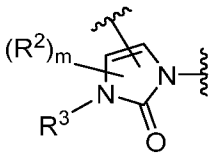
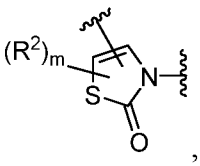
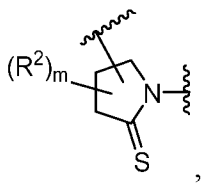
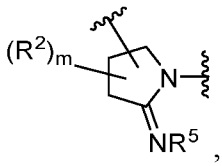


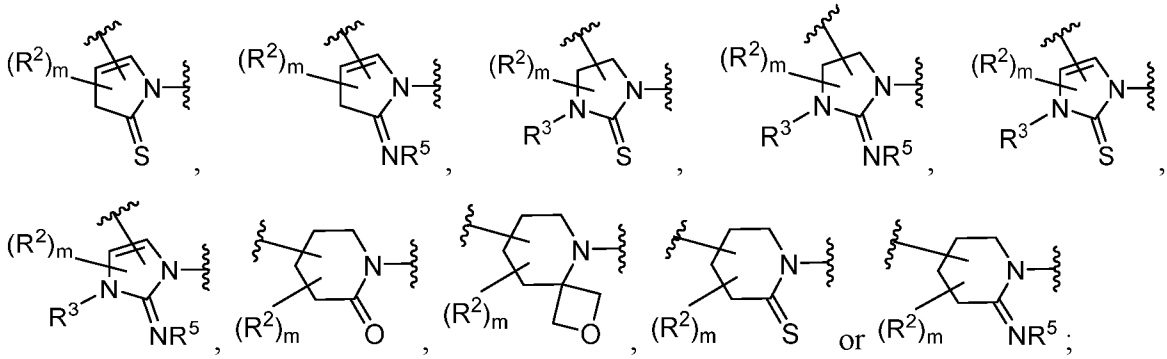
II-B

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–CH_2–$, –C(O)–, –C(S)–, or  ;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, $–S(O)R$, $–S(O)_2R$, $–NR_2$, or an optionally substituted C_{1-4} aliphatic;

Ring A is a mono- or bicyclic ring selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , 



each R^2 is independently hydrogen, $-R^4$, halogen, $-CN$, $-NO_2$, $-OR$, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $-C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $-N(R)S(O)_2R$;

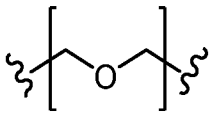
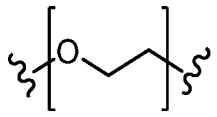
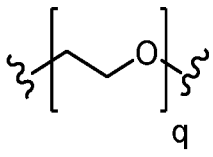
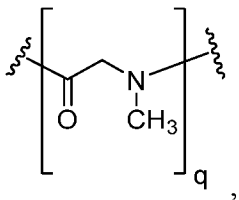
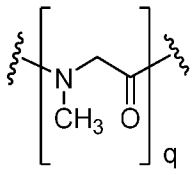
Ring B is selected from a 6-membered aryl containing 0-2 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each R^3 is independently hydrogen, $-R^4$, halogen, $-CN$, $-NO_2$, $-OR$, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $-C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $-N(R)S(O)_2R$;

each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^5 is hydrogen, C_{1-4} aliphatic, or $-CN$;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by $-Cy-$, -O-, -N(R)-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, $-S(O)_2-$, $-N(R)S(O)_2-$, $-S(O)_2N(R)-$, -N(R)C(O)-, -

C(O)N(R)-, -OC(O)N(R)-, –N(R)C(O)O-,  ,  ,  ,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

TBM is a target binding moiety;

m is 0, 1, or 2;

n is 0, 1, 2, 3, or 4;

p is 0 or 1;

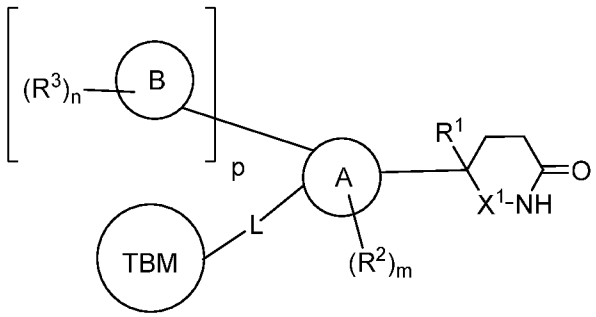
each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3

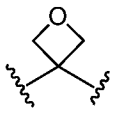
heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0076] As described above, in certain embodiments, the present invention provides a compound of formula **II′-B**:

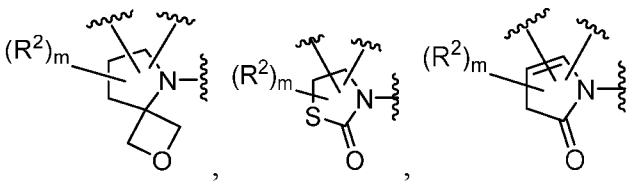


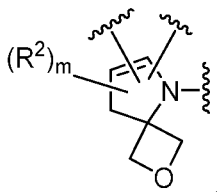
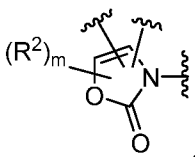
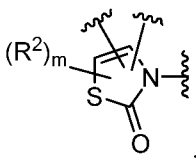
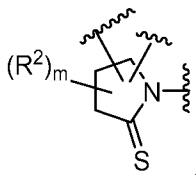
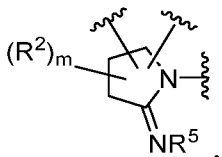
II′-B

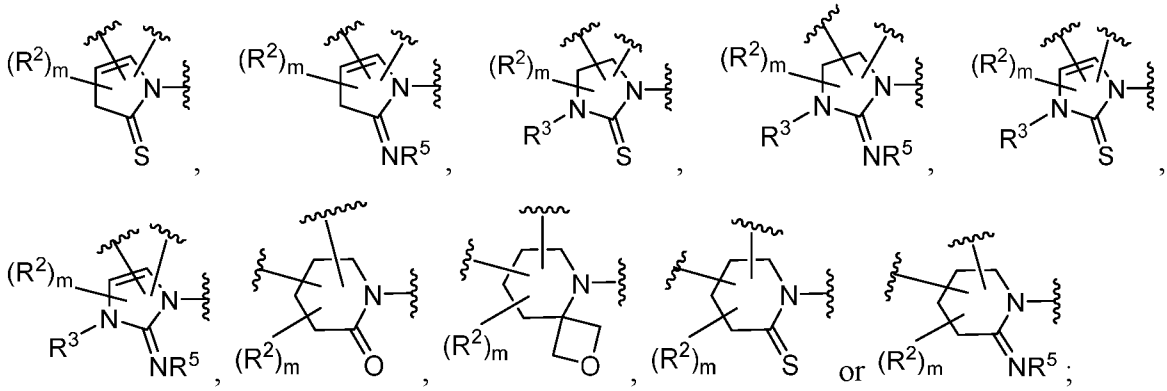
or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–CH_2–$, $–C(O)–$, $–C(S)–$, or  ;

R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, $–S(O)R$, $–S(O)_2R$, $–NR_2$, or an optionally substituted C_{1-4} aliphatic;

Ring A is a mono- or bicyclic ring selected from  , ,

 ,  ,  ,  ,  ,



each R^2 is independently hydrogen, $-R^4$, halogen, $-CN$, $-NO_2$, $-OR$, $-SR$, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)N(R)OR$, $-OC(O)R$, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, or $-N(R)S(O)_2R$;

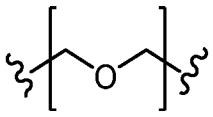
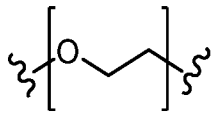
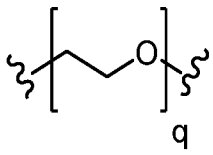
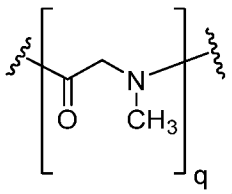
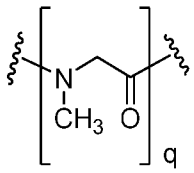
Ring B is selected from a 6-membered aryl containing 0-2 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each R^3 is independently hydrogen, $-R^4$, halogen, $-CN$, $-NO_2$, $-OR$, $-SR$, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)N(R)OR$, $-OC(O)R$, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, or $-N(R)S(O)_2R$;

each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^5 is hydrogen, C_{1-4} aliphatic, or $-CN$;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by $-Cy-$, $-O-$, $-N(R)-$, $-S-$, $-OC(O)-$, $-C(O)O-$, $-C(O)-$, $-S(O)-$, $-S(O)_2-$, $-N(R)S(O)_2-$, $-S(O)_2N(R)-$, $-N(R)C(O)-$, -

C(O)N(R)-, -OC(O)N(R)-, –N(R)C(O)O-,  ,  ,  ,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

TBM is a target binding moiety;

m is 0, 1, or 2;

n is 0, 1, 2, 3, or 4;

p is 0 or 1;

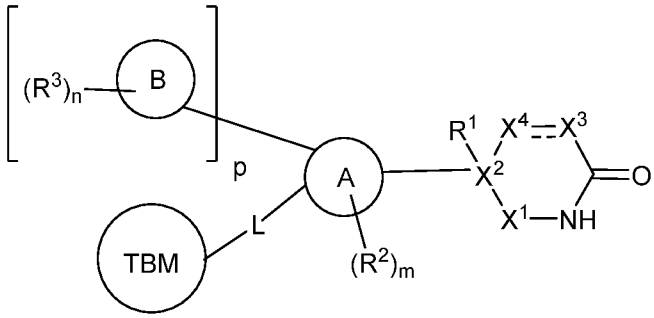
each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3

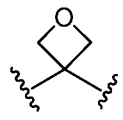
heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0077] In certain embodiments, the present invention provides a compound of Formula **II''-B**:



II''-B

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $-C(R)_2-$, $-C(O)-$, $-C(S)-$, $-P(O)(OR)-$, $-P(O)(R)-$, $-P(O)(NR_2)-$, $-S(O)-$, $-S(O)_2-$, or  ;

X^2 is a carbon atom or silicon atom;

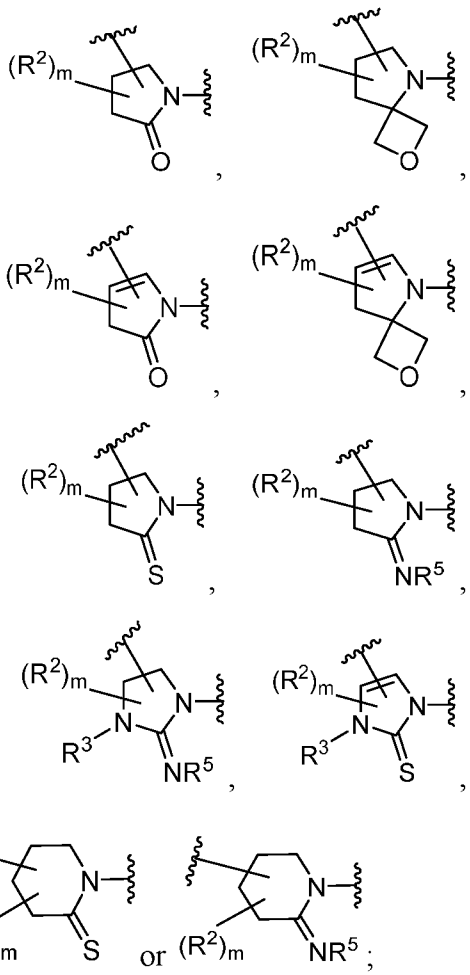
X^3 is a bivalent moiety selected from $-C(R)_2-$, $-N(R)-$, $-CF_2-$, $-CHF-$, $-S-$, or $-O-$;

X^4 is a bivalent moiety selected from a covalent bond or $-C(R)_2-$;

=== is a single bond or double bond;

R^1 is hydrogen, deuterium, halogen, $-CN$, $-OR$, $-SR$, $-S(O)R$, $-S(O)_2R$, $-NR_2$, $-P(O)(OR)_2$, $-P(O)(NR_2)OR$, $-P(O)(NR_2)_2$, $-Si(OH)_2R$, $-Si(OH)(R)_2$, $-Si(R)_3$, an optionally substituted C_{1-4} aliphatic, or:

R^1 and X^1 or X^4 are taken together with their intervening atoms to form a 5-7 membered saturated, partially unsaturated, carbocyclic ring or heterocyclic ring having 1-3 heteroatoms, independently selected from nitrogen, oxygen, or sulfur;

Ring A is a mono- or bicyclic ring selected from 

each R^2 is independently hydrogen, deuterium, $-R^6$, halogen, $-CN$, $-NO_2$, $-OR$, $-SR$, $-NR_2$, $-Si(OH)_2R$, $-Si(OH)(R)_2$, $-Si(R)_3$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)N(R)OR$, $-OC(O)R$, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, $-N(R)S(O)_2R$, $-N(R)S(O)_2NR_2$, $-P(O)(OR)_2$, $-P(O)(NR_2)OR$, or $-P(O)(NR_2)_2$;

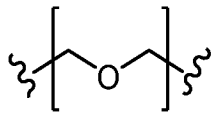
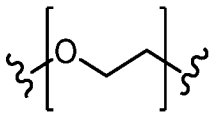
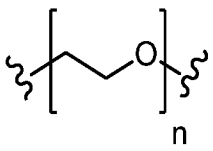
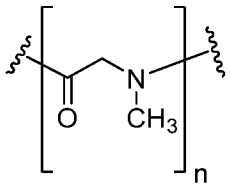
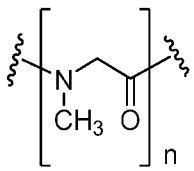
Ring B is selected from a 6-membered aryl containing 0-3 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur;

each R^3 is selected from hydrogen, deuterium, $-R^4$, halogen, $-CN$, $-NO_2$, $-OR$, $-NR_2$, $-SR$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)NR(OR)$, $-OC(O)R$, $-OC(O)NR_2$, $-OP(O)(OR)_2$, $-OP(O)(NR_2)_2$, $-OP(O)(OR)NR_2$, $-N(R)C(O)R$, $-N(R)C(O)OR$, $-N(R)C(O)NR_2$, $-N(R)S(O)_2R$, $-N(R)S(O)_2NR_2$, $-N(R)P(O)(OR)_2$,

–N(R)P(O)(OR)NR_2, –P(O)(OR)$_2$, –P(O)(NR_2)OR, –P(O)(NR_2)$_2$, –Si(OH)$_2$R, –Si(OH)(R)$_2$, or –Si(R)$_3$;

each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R^5 is hydrogen, deuterium, an optionally substituted C_{1-4} aliphatic, or –CN;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy–, –O–, –N(R)–, –Si(R)$_2$–, –Si(OH)(R)–, –Si(OH)$_2$–, –P(O)(OR)–, –P(O)(R)–, –P(O)(NR_2)–, –S–, –OC(O)–, –C(O)O–, –C(O)–, –S(O)–, –S(O)$_2$–, –N(R)S(O)$_2$–, –S(O)$_2$N(R)–, –N(R)C(O)–, –C(O)N(R)–, –OC(O)N(R)–, –N(R)C(O)O–,  ,  ,  ,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 3-8 membered saturated or partially unsaturated carbocyclylenyl, a 6-11 membered saturated or partially unsaturated spiro carbocyclylenyl, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-10 membered saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 6-11 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-6 membered

heteroarylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur;

TBM is a target binding moiety;

m is 0, 1, or 2;

n is 0, 1, 2, 3, or 4;

p is 0 or 1;

each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, deuterium, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur.

[0078] As defined above and described herein, X^1 is a bivalent moiety selected from a covalent bond, $–CH_2–$, $–C(R)_2–$, $–C(O)–$, $–C(S)–$, $–CH(R)–$, $–CH(CF_3)–$, $–P(O)(OR)–$, $–P(O)(R)–$, $–P(O)(NR_2)–$, $–S(O)–$, $–S(O)_2–$, or  .

[0079] In some embodiments, X^1 is a covalent bond. In some embodiments, X^1 is $–CH_2–$. In some embodiments, X^1 is $–C(R)_2–$. In some embodiments, X^1 is $–C(O)–$. In some embodiments, X^1 is $–C(S)–$. In some embodiments, X^1 is $–CH(R)–$. In some embodiments, X^1 is $–CH(CF_3)–$. In some embodiments, X^1 is $–P(O)(OR)–$. In some embodiments, X^1 is $–P(O)(R)–$. In some embodiments, X^1 is $–P(O)(NR_2)–$. In some embodiments, X^1 is $–S(O)–$. In some embodiments, X^1 is $–S(O)_2–$. In some embodiments, X^1 is  .

[0080] In some embodiments, X^1 is selected from those depicted in **Table 1**, below.

[0081] As defined above and described herein, X^2 is a carbon atom or silicon atom.

[0082] In some embodiments, X^2 is a carbon atom. In some embodiments, X^2 is a silicon atom.

[0083] In some embodiments, X^2 is selected from those depicted in **Table 1**, below.

[0084] As defined above and described herein, X^3 is a bivalent moiety selected from $–CH_2–$, $–C(R)_2–$, $–N(R)–$, $–CF_2–$, $–CHF–$, $–S–$, $–CH(R)–$, or $–O–$.

[0085] In some embodiments, X^3 is $–CH_2–$. In some embodiments, X^1 is $–C(R)_2–$. In some embodiments, X^3 is $–N(R)–$. In some embodiments, X^3 is $–CF_2–$. In some embodiments, X^3 is $–CHF–$. In some embodiments, X^3 is $–S–$. In some embodiments, X^3 is $–CH(R)–$. In some embodiments, X^3 is $–O–$.

[0086] In some embodiments, X^3 is selected from those depicted in **Table 1**, below.

[0087] As defined above and described herein, X^4 is a bivalent moiety selected from a covalent bond, $–CH_2–$, or $–C(R)_2–$.

[0088] In some embodiments, X^4 is a covalent bond. In some embodiments, X^4 is $–CH_2–$. In some embodiments, X^4 is $–C(R)_2–$.

[0089] In some embodiments, X^4 is selected from those depicted in **Table 1**, below.

[0090] As defined above and described herein, R^1 is hydrogen, deuterium, halogen, –CN, –OR, –SR, $–S(O)R$, $–S(O)_2R$, $–NR_2$, $–P(O)(OR)_2$, $–P(O)(NR_2)OR$, $–P(O)(NR_2)_2$, $–Si(OH)_2R$, $–Si(OH)(R)_2$, $–Si(R)_3$, an optionally substituted C_{1-4} aliphatic, or R^1 and X^1 or X^4 are taken together with their intervening atoms to form a 5-7 membered saturated, partially unsaturated, carbocyclic ring or heterocyclic ring having 1-3 heteroatoms, independently selected from nitrogen, oxygen, or sulfur.

[0091] In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is deuterium. In some embodiments, R^1 is halogen. In some embodiments, R^1 is –CN. In some embodiments, R^1 is –OR. In some embodiments, R^1 is –SR. In some embodiments, R^1 is $–S(O)R$. In some embodiments, R^1 is $–S(O)_2R$. In some embodiments, R^1 is $–NR_2$. In some embodiments, R^1 is $–P(O)(OR)_2$. In some embodiments, R^1 is $–P(O)(NR_2)OR$. In some embodiments, R^1 is $–P(O)(NR_2)_2$. In some embodiments, R^1 is $–Si(OH)_2R$. In some embodiments, R^1 is $–Si(OH)(R)_2$. In some embodiments, R^1 is $–Si(R)_3$. In some embodiments, R^1 is an optionally substituted C_{1-4} aliphatic. In some embodiments, R^1 and X^1 or

X^4 are taken together with their intervening atoms to form a 5-7 membered saturated, partially unsaturated, carbocyclic ring or heterocyclic ring having 1-3 heteroatoms, independently selected from nitrogen, oxygen, or sulfur.

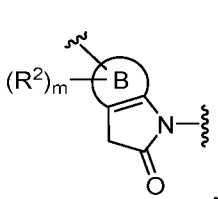
[0092] In some embodiments, R^1 is selected from those depicted in **Table 1**, below.

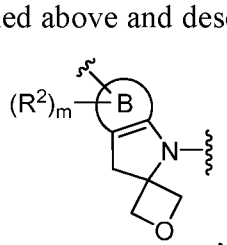
[0093] As defined above and described herein, each R^2 is independently hydrogen, deuterium, $-R^6$, halogen, $-CN$, $-NO_2$, $-OR$, $-SR$, $-N(R)_2$, $-Si(OH)_2R$, $-Si(OH)(R)_2$, $-Si(R)_3$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)N(R)OR$, $-OC(O)R$, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, $-N(R)S(O)_2R$, $-N(R)S(O)_2NR_2$, $-P(O)(OR)_2$, $-P(O)(NR_2)OR$, or $-P(O)(NR_2)_2$.

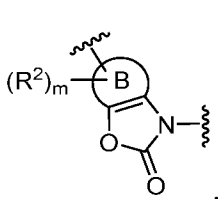
[0094] In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is deuterium. In some embodiments, R^2 is $-R^6$. In some embodiments, R^2 is halogen. In some embodiments, R^2 is $-CN$. In some embodiments, R^2 is $-NO_2$. In some embodiments, R^2 is $-OR$. In some embodiments, R^2 is $-Si(OH)_2R$. In some embodiments, R^2 is $-Si(OH)(R)_2$. In some embodiments, R^2 is $-SR$. In some embodiments, R^2 is $-NR_2$. In some embodiments, R^2 is $-Si(R)_3$. In some embodiments, R^2 is $-S(O)_2R$. In some embodiments, R^2 is $-S(O)_2NR_2$. In some embodiments, R^2 is $-S(O)R$. In some embodiments, R^2 is $-C(O)R$. In some embodiments, R^2 is $-C(O)OR$. In some embodiments, R^2 is $-C(O)NR_2$. In some embodiments, R^2 is $-C(O)N(R)OR$. In some embodiments, R^2 is $-OC(O)R$. In some embodiments, R^2 is $-OC(O)NR_2$. In some embodiments, R^2 is $-N(R)C(O)OR$. In some embodiments, R^2 is $-N(R)C(O)R$. In some embodiments, R^2 is $-N(R)C(O)NR_2$. In some embodiments, R^2 is $-N(R)S(O)_2R$. In some embodiments, R^2 is $-P(O)(OR)_2$. In some embodiments, R^2 is $-P(O)(NR_2)OR$. In some embodiments, R^2 is $-P(O)(NR_2)_2$.

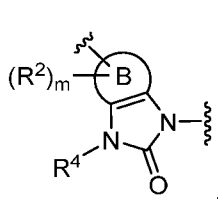
[0095] In some embodiments, R^2 is selected from those depicted in **Table 1**, below.

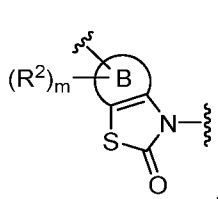
[0096] As defined above and described herein, Ring A is a bi- or tricyclic ring selected from



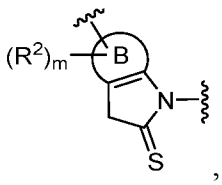
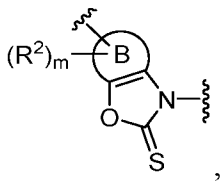
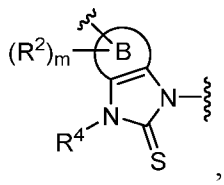
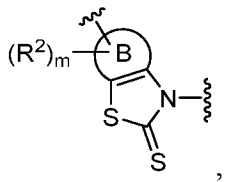
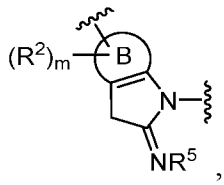
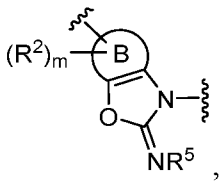
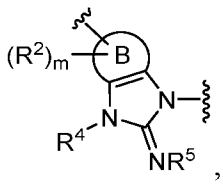
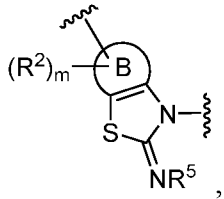
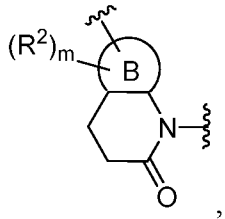
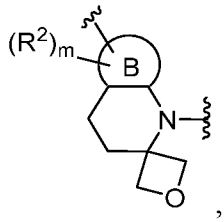
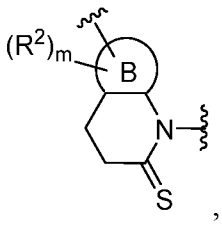
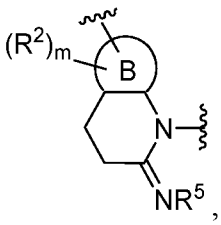
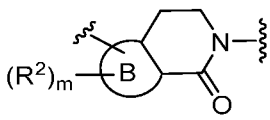
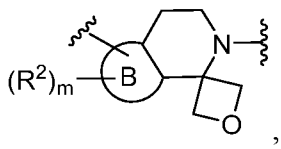
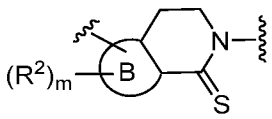
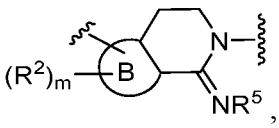
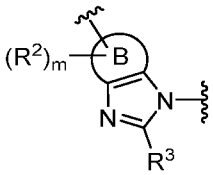
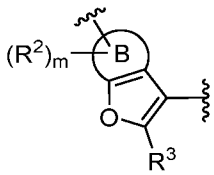
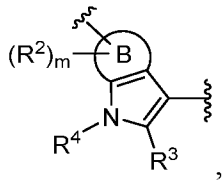
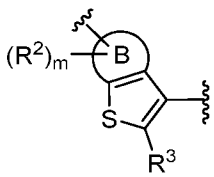
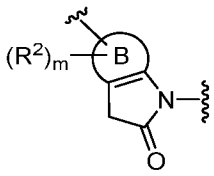
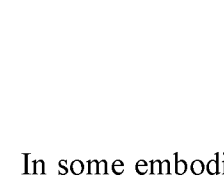
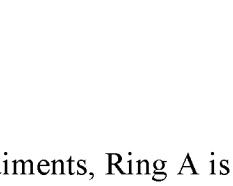
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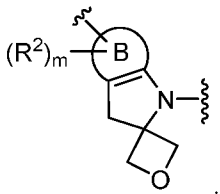
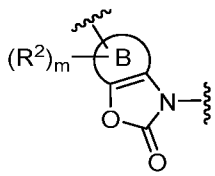
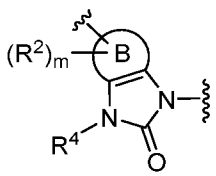
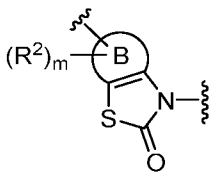
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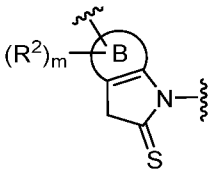
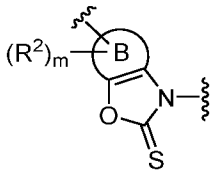
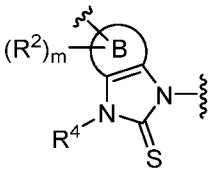
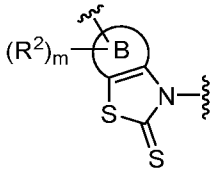
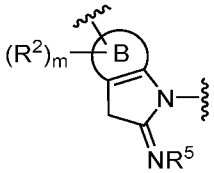
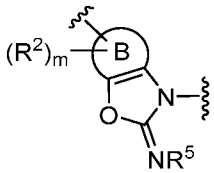
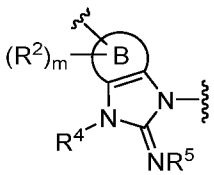
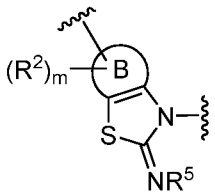
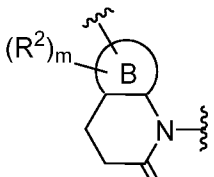
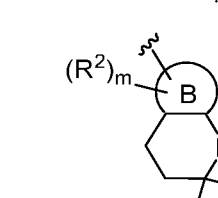
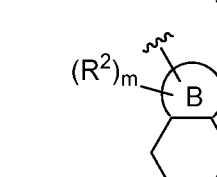
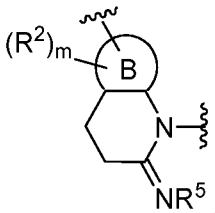
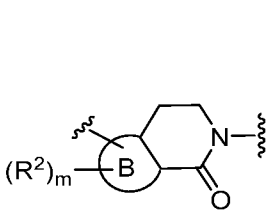
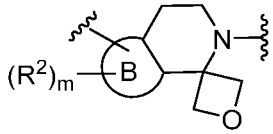
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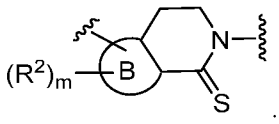
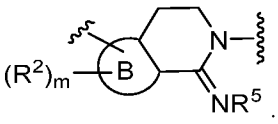
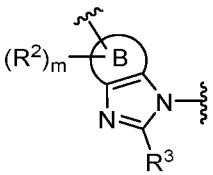
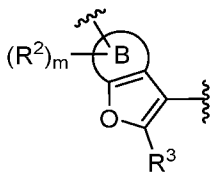
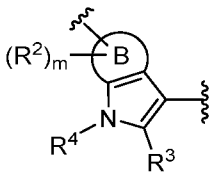
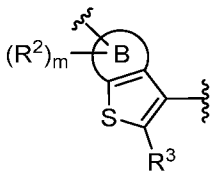
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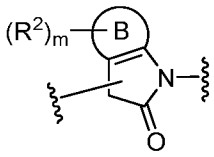
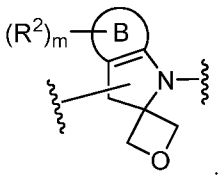
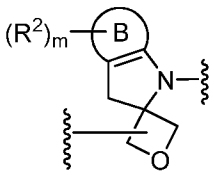
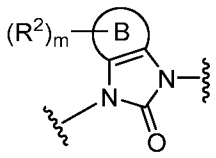
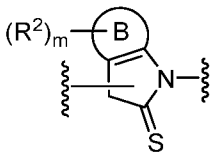
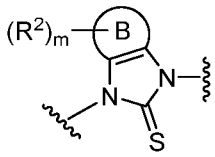
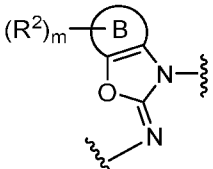
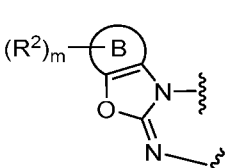
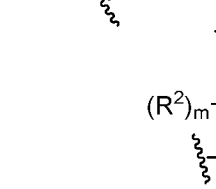
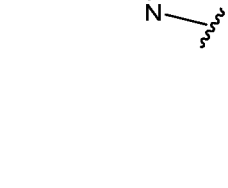
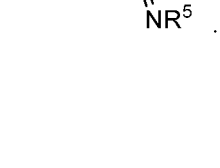
























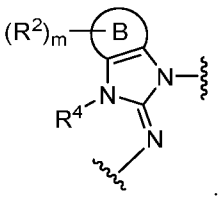
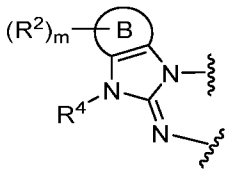
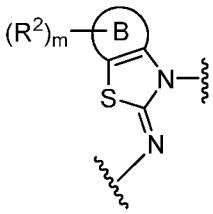
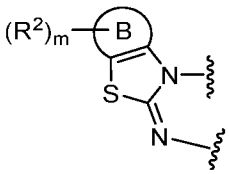
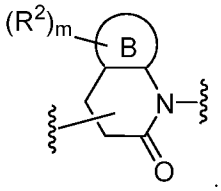
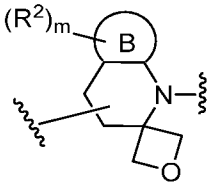
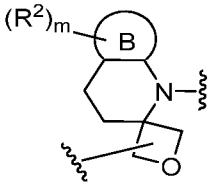
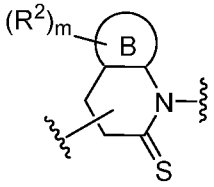
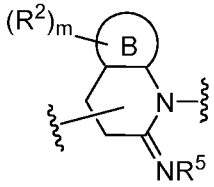
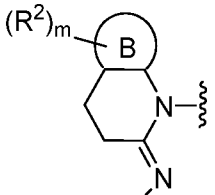
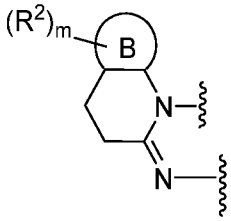
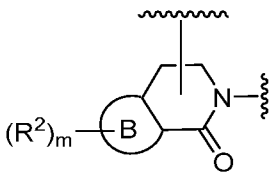
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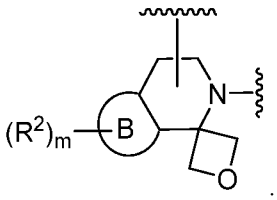
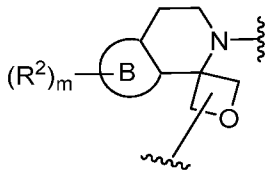
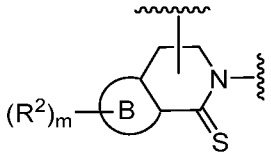
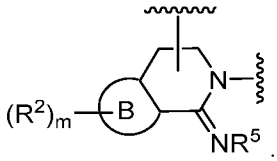
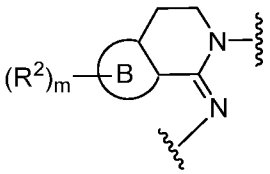
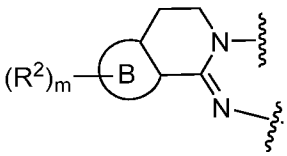
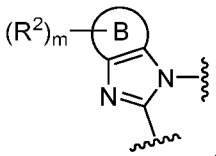
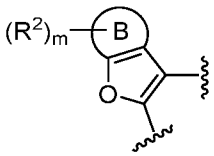
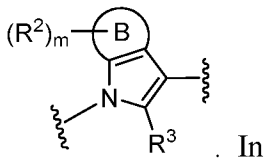
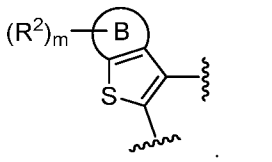
[0097] In some embodiments, Ring A is . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments,

Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is . In some embodiments, Ring A is . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  .


. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
.

[0098] In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
. In some embodiments, Ring A is 
.

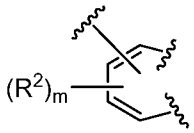
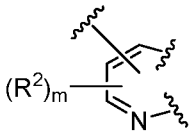
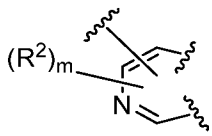
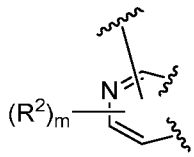
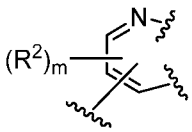
In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments,

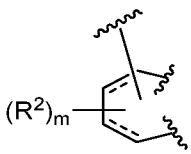
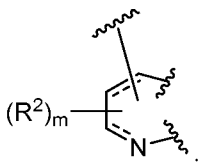
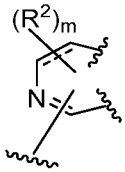
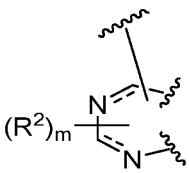
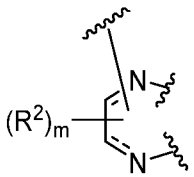
Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is .

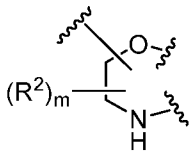
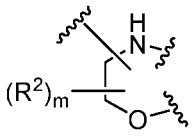
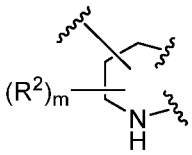
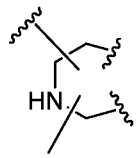
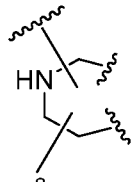
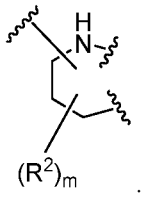
[0099] In some embodiments, Ring A is selected from those depicted in **Table 1**, below.

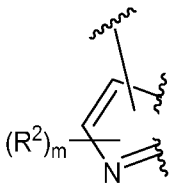
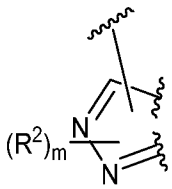
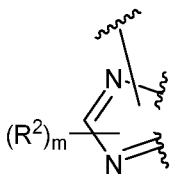
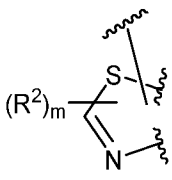
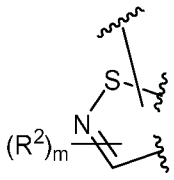
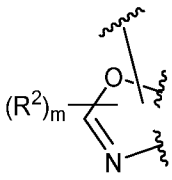
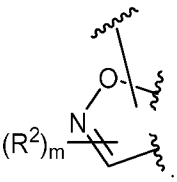
[00100] As defined above and described herein, Ring B is a fused ring selected from 6-membered aryl containing 0-3 nitrogen atoms, 5 to 7-membered partially saturated carbocyclyl, 5 to 7-membered partially saturated heterocyclyl with 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, or sulfur, or 5-membered heteroaryl with 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, or sulfur.

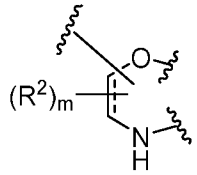
[00101] In some embodiments, Ring B is a 6-membered aryl containing 0-3 nitrogen atoms. In some embodiments, Ring B is a 5 to 7-membered partially saturated carbocyclyl. In some embodiments, Ring B is 5 to 7-membered partially saturated heterocyclyl with 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, or sulfur. In some embodiments, Ring B is 5-membered heteroaryl with 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, or sulfur.

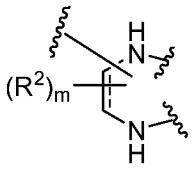
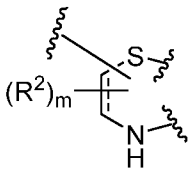
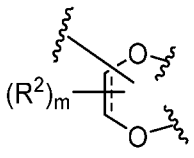
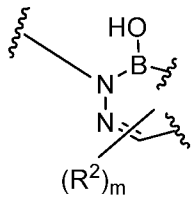
[00102] In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  .

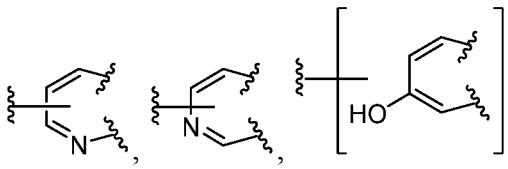
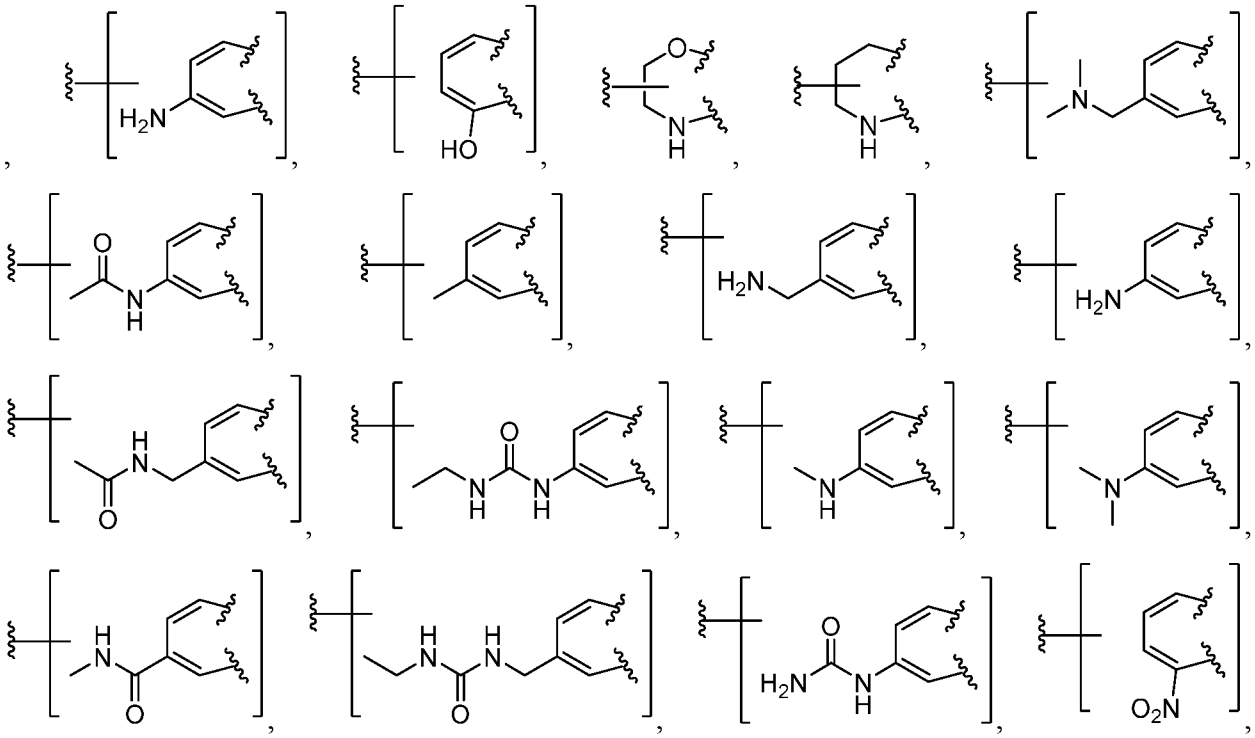
[00103] In some embodiments, each Ring B is  . In some embodiments, each Ring B is  . In some embodiments, each Ring B is  . In some embodiments, each Ring B is  . In some embodiments, Ring B is  .

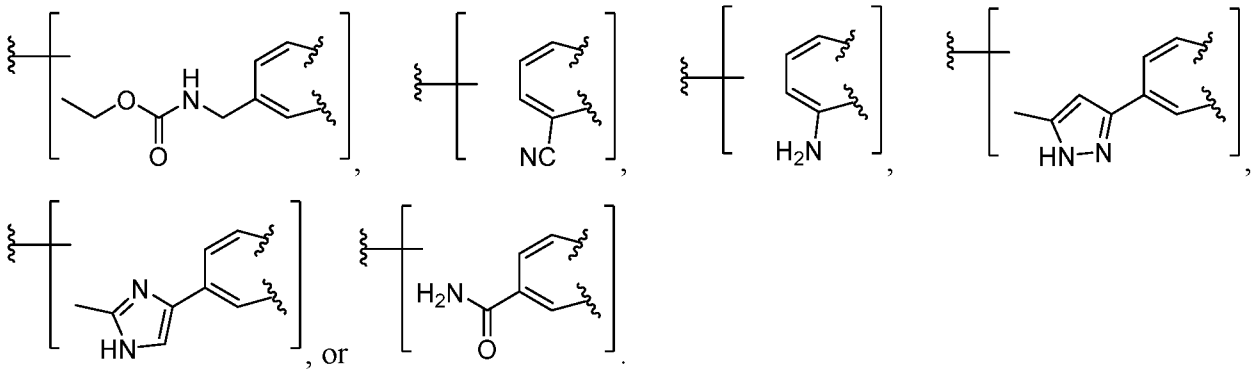
[00104] In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  .

[00105] In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  .



[00106] In some embodiments, Ring B is . In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  . In some embodiments, Ring B is  .

[00107] In some embodiments, Ring B is selected from  ,  .



[00108] In some embodiments, Ring B is selected from those depicted in **Table 1**, below.

[00109] As defined above and described herein, ⎓ is a single or double bond.

[00110] In some embodiments, ⎓ is a single bond. In some embodiments, ⎓ is a double bond.

[00111] In some embodiments, ⎓ is selected from those depicted in **Table 1**, below.

[00112] As defined above and described herein, R^3 is hydrogen, deuterium, halogen, –CN, –NO_2, –OR, –NR_2, –SR, –$S(O)_2R$, –$S(O)_2NR_2$, –S(O)R, –C(O)R, –C(O)OR, –$C(O)NR_2$, –C(O)NR(OR), –OC(O)R, –$OC(O)NR_2$, –$OP(O)(OR)_2$, –$OP(O)(NR_2)_2$, –$OP(O)(OR)NR_2$, –N(R)C(O)R, –N(R)C(O)OR, -$N(R)C(O)NR_2$, –$N(R)S(O)_2R$, –$N(R)S(O)_2NR_2$, –$N(R)P(O)(OR)_2$, –$N(R)P(O)(OR)NR_2$, –$P(O)(OR)_2$, –$P(O)(NR_2)OR$, –$P(O)(NR_2)_2$, –$Si(OH)_2R$, –$Si(OH)(R)_2$, or –$Si(R)_3$.

[00113] In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is deuterium. In some embodiments, R^3 is halogen. In some embodiments, R^3 is –CN. In some embodiments, R^3 is –NO_2. In some embodiments, R^3 is –OR. In some embodiments, R^3 is –NR_2. In some embodiments, R^3 is –SR. In some embodiments, R^3 is –$S(O)_2R$. In some embodiments, R^3 is –$S(O)_2NR_2$. In some embodiments, R^3 is –S(O)R. In some embodiments, R^3 is –C(O)R. In some embodiments, R^3 is –C(O)OR. In some embodiments, R^3 is –$C(O)NR_2$. In some embodiments, R^3 is –C(O)NR(OR). In some embodiments, R^3 is –OC(O)R. In some embodiments, R^3 is –$OC(O)NR_2$. In some embodiments, R^3 is –$OP(O)(OR)_2$. In some embodiments, R^3 is –$OP(O)(NR_2)_2$. In some embodiments, R^3 is –$OP(O)(OR)NR_2$. In some embodiments, R^3 is –N(R)C(O)R. In some embodiments, R^3 is –N(R)C(O)OR. In some embodiments, R^3 is –$N(R)C(O)NR_2$. In some embodiments, R^3 is –$N(R)S(O)_2R$. In some embodiments, R^3 is –$N(R)S(O)_2NR_2$. In some embodiments, R^3 is –$N(R)P(O)(OR)_2$. In some embodiments, R^3 is

–N(R)P(O)(OR)NR_2. In some embodiments, R^3 is –P(O)$(OR)_2$. In some embodiments, R^3 is –P(O)(NR_2)OR. In some embodiments, R^3 is –P(O)$(NR_2)_2$. In some embodiments, R^3 is –Si$(OH)_2$R. In some embodiments, R^3 is –Si(OH)$(R)_2$. In some embodiments, R^3 is –Si$(R)_3$.

[00114] In some embodiments, R^3 is methyl. In some embodiments, R^3 is –OCH_3. In some embodiments, R^3 is chloro.

[00115] In some embodiments, R^3 is selected from those depicted in **Table 1**, below.

[00116] As defined above and described herein, each R^4 is independently hydrogen, deuterium, –R^6, halogen, –CN, –NO_2, –OR, -SR, -NR_2, –S$(O)_2$R, –S$(O)_2NR_2$, –S(O)R, –C(O)R, –C(O)OR, –C(O)NR_2, –C(O)N(R)OR, –OC(O)R, –OC(O)NR_2, –N(R)C(O)OR, –N(R)C(O)R, –N(R)C(O)NR_2, –N(R)S$(O)_2$R, –P(O)$(OR)_2$, –P(O)(NR_2)OR, or –P(O)$(NR_2)_2$.

[00117] In some embodiments, R^4 is hydrogen. In some embodiments, R^4 is –R^6. In some embodiments, R^4 is halogen. In some embodiments, R^4 is –CN. In some embodiments, R^4 is –NO_2. In some embodiments, R^4 is –OR. In some embodiments, R^4 is –SR. In some embodiments, R^4 is –NR_2. In some embodiments, R^4 is –S$(O)_2$R. In some embodiments, R^4 is –S$(O)_2NR_2$. In some embodiments, R^4 is –S(O)R. In some embodiments, R^4 is –C(O)R. In some embodiments, R^4 is –C(O)OR. In some embodiments, R^4 is –C(O)NR_2. In some embodiments, R^4 is –C(O)N(R)OR. In some embodiments, R^4 is –OC(O)R. In some embodiments, R^4 is –OC(O)NR_2. In some embodiments, R^4 is –N(R)C(O)OR. In some embodiments, R^4 is –N(R)C(O)R. In some embodiments, R^4 is –N(R)C(O)NR_2. In some embodiments, R^4 is –N(R)S$(O)_2$R. In some embodiments, R^4 is –P(O)$(OR)_2$. In some embodiments, R^4 is –P(O)(NR_2)OR. In some embodiments, R^4 is –P(O)$(NR_2)_2$.

[00118] In some embodiments, R^4 is methyl. In some embodiments, R^4 is ethyl. In some embodiments, R^4 is cyclopropyl.

[00119] In some embodiments, R^4 is selected from those depicted in **Table 1**, below.

[00120] As defined above and described herein, R^5 is hydrogen, deuterium, an optionally substitute C_{1-4} aliphatic, or –CN.

[00121] In some embodiments, R^5 is hydrogen. In some embodiments, R^5 is deuterium. In some embodiments, R^5 is an optionally substituted C_{1-4} aliphatic. In some embodiments, R^5 is –CN.

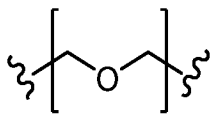
[00122] In some embodiments, R^5 is selected from those depicted in **Table 1**, below.

[00123] As defined above and described herein, each R^6 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur.

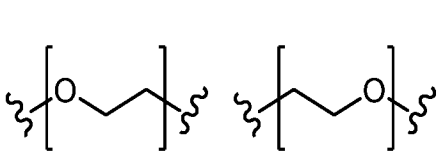
[00124] In some embodiments, R^6 is an optionally substituted C_{1-6} aliphatic. In some embodiments, R^6 is an optionally substituted phenyl. In some embodiments, R^6 is an optionally substituted 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur. In some embodiments, R^6 is an optionally substituted 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur.

[00125] In some embodiments, R^6 is selected from those depicted in **Table 1**, below.

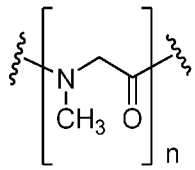
[00126] As defined above and described herein, L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy–, –O–, –N(R)–, –Si(R)$_2$–, –Si(OH)(R)–, –Si(OH)$_2$–, –P(O)(OR)–, –P(O)(R)–, –P(O)(NR$_2$)–, –S–, –OC(O)–, –C(O)O–, –C(O)–, –S(O)–, –S(O)$_2$–, –N(R)S(O)$_2$–, –S(O)$_2$N(R)–, –N(R)C(O)–, –C(O)N(R)–, –OC(O)N(R)–, –N(R)C(O)O–,



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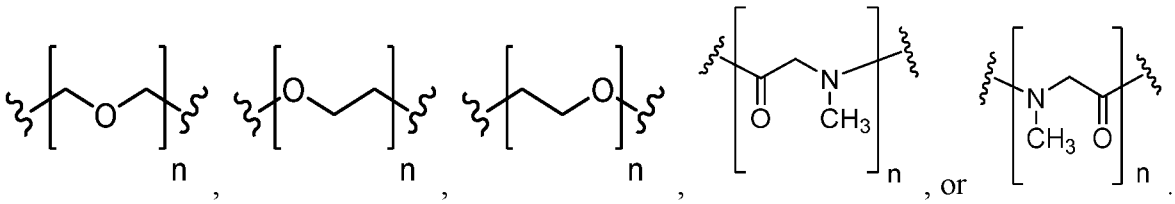
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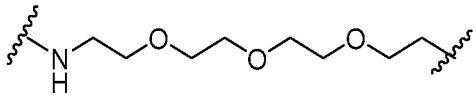
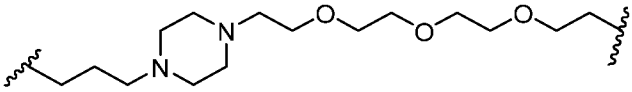
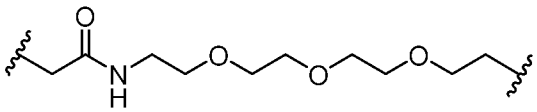
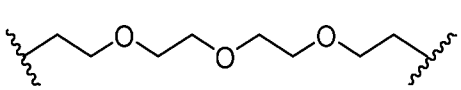
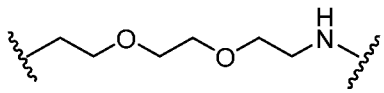
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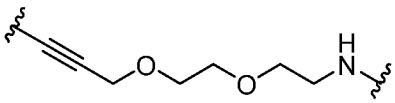
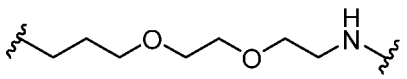
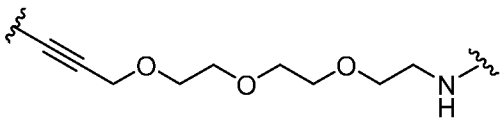
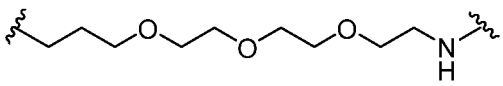
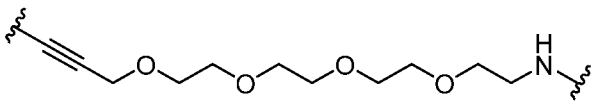
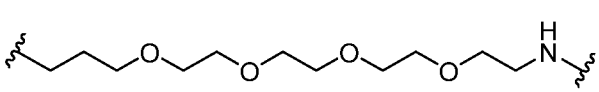
[00127] In some embodiments, L is a covalent bond. In some embodiments, L is a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy–, –O–, –N(R)–, –Si(R)$_2$–, –Si(OH)(R)–, –Si(OH)$_2$–, –P(O)(OR)–, –P(O)(R)–, –P(O)(NR$_2$)–, –S–, –OC(O)–, –C(O)O–, –C(O)–, –S(O)–, –S(O)$_2$–, –

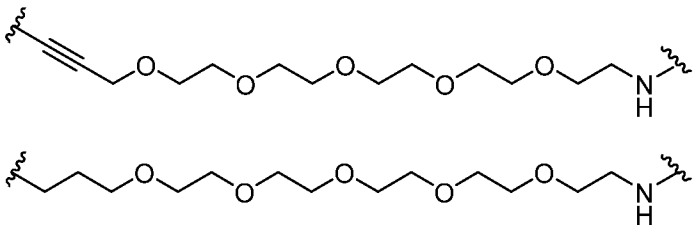
$N(R)S(O)_2$–, –$S(O)_2N(R)$–, –N(R)C(O)–, –C(O)N(R)–, –OC(O)N(R)–, –N(R)C(O)O–,



, , , , or .

[00128] In some embodiments, L is  . In some embodiments, L is  . In some embodiments, L is  . In some embodiments, L is  . some embodiments, L is  .

[00129] In some embodiments, L is  . In some embodiments, L is  . In some embodiments, L is  . In some embodiments, L is  . In some embodiments, L is  . In some embodiments, L is  .



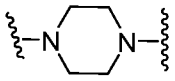
. In some embodiments, L is

[00130] In some embodiments, L is selected from those depicted in **Table 1**, below.

[00131] As defined above and described herein, each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 3-8 membered saturated or partially unsaturated carbocyclylenyl, a 6-11 membered saturated or partially unsaturated spiro carbocyclylenyl, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-10 membered saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 6-11 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur.

[00132] In some embodiments, –Cy– is an optionally substituted bivalent ring selected from phenylenyl. In some embodiments, –Cy– is an optionally substituted 8-10 membered bicyclic arylenyl. In some embodiments, –Cy– is an optionally substituted 3-8 membered saturated or partially unsaturated carbocyclylenyl. In some embodiments, –Cy– is an optionally substituted 6-11 membered saturated or partially unsaturated spiro carbocyclylenyl. In some embodiments, –Cy– is an optionally substituted 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated carbocyclylenyl. In some embodiments, –Cy– is an optionally substituted 4-10 membered saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur. In some embodiments, –Cy– is an optionally substituted 6-11 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen,

oxygen, silicon, phosphorus, or sulfur. In some embodiments, –Cy– is an optionally substituted 5-12 membered bridged or unbridged bicyclic saturated or partially unsaturated heterocyclylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur. In some embodiments, –Cy– is an optionally substituted 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, phosphorus, or sulfur.

[00133] In some embodiments, –Cy– is  .

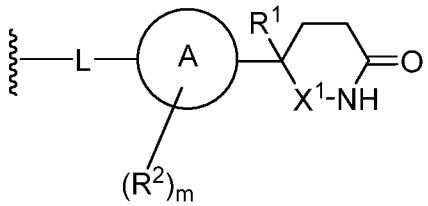
[00134] In some embodiments, –Cy– is selected from those depicted in **Table 1**, below.

[00135] As defined above and described herein, TBM is a target binding moiety.

[00136] In some embodiments, TBM is a target binding moiety.

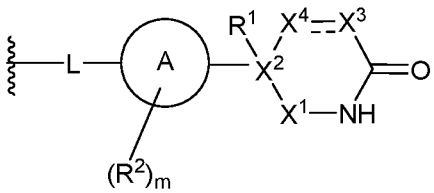
[00137] In some embodiments. TBM binds to a protein selected from those listed in paragraph [00181].

[00138] In some embodiments, TBM is selected from one of the drugs listed in **Table 2**, wherein



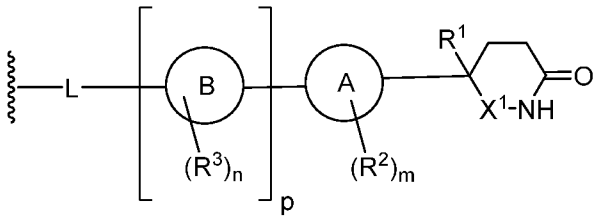
the drug is attached to at any modifiable carbon, oxygen, sulfur or nitrogen atom.

[00139] In some embodiments, TBM is selected from one of the drugs listed in **Table 2**, wherein



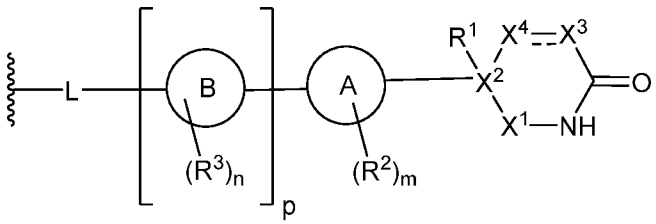
the drug is attached to at any modifiable carbon, oxygen, sulfur or nitrogen atom

[00140] In some embodiments, TBM is selected from one of the drugs listed in **Table 2**, wherein

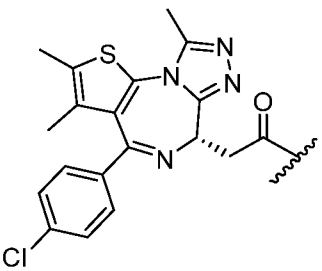
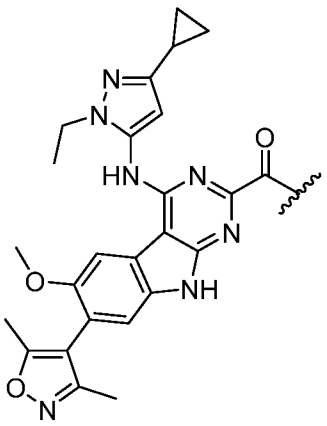
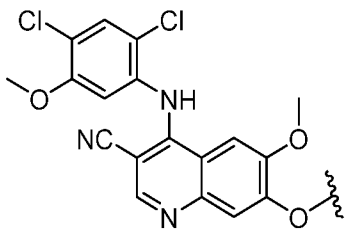


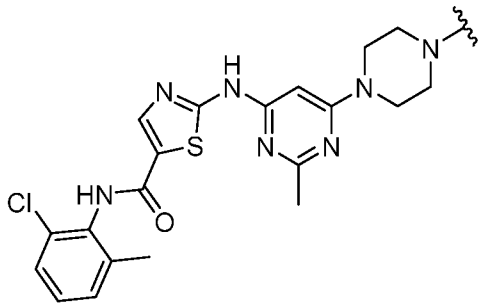
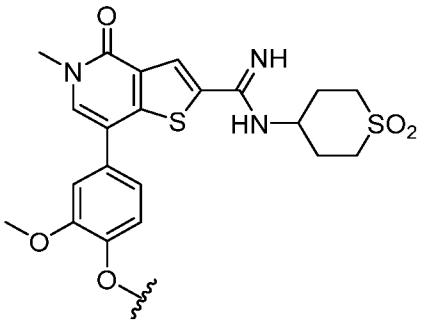
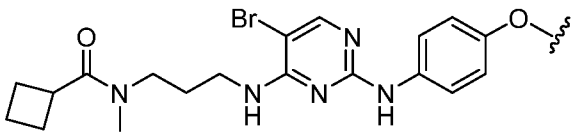
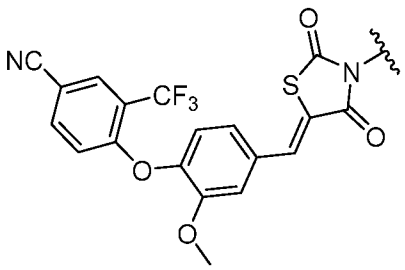
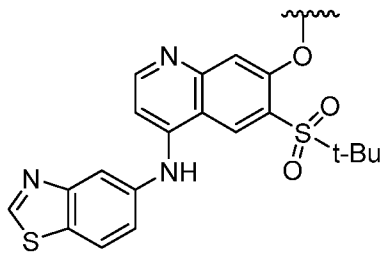
the drug is attached to at any modifiable carbon, oxygen, sulfur or nitrogen atom.

[00141] In some embodiments, TBM is selected from one of the drugs listed in **Table 2**, wherein



the drug is attached to at any modifiable carbon, oxygen, sulfur or nitrogen atom.

[00142] In some embodiments, TBM is  . In some embodiments, TBM is  . In some embodiments, TBM is  . In some

embodiments, TBM is  . In some embodiments, TBM is  . In some embodiments, TBM is  . In some embodiments, TBM is  . In some embodiments, TBM is  .

[00143] In some embodiments, TBM is selected from those depicted in **Table 1**, below.

[00144] As defined above and described herein, m is 0, 1, 2, 3 or 4.

[00145] In some embodiments, m is 0. In some embodiments, m is 1. In some embodiments, m is 2. In some embodiments, m is 3. In some embodiments, m is 4.

[00146] In some embodiments, m is selected from those depicted in **Table 1**, below.

[00147] As defined above and described herein, each n is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

[00148] In some embodiments, n is 0. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5.

In some embodiments, n is 6. In some embodiments, n is 7. In some embodiments, n is 8. In some embodiments, n is 9. In some embodiments, n is 10.

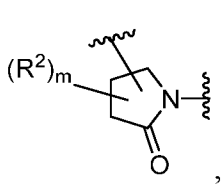
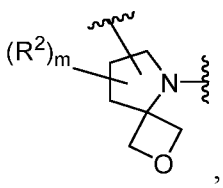
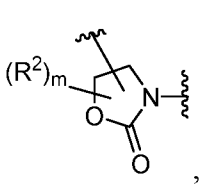
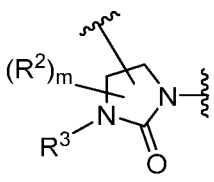
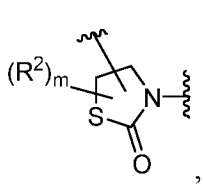
[00149] In some embodiments, n is selected from those depicted in **Table 1**, below.

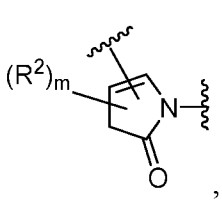
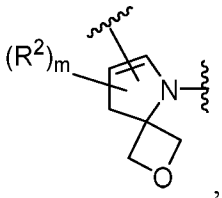
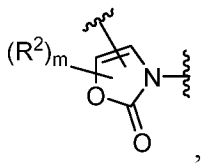
[00150] As defined above and described herein, each R is independently hydrogen, deuterium, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur, or two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from boron, nitrogen, oxygen, silicon, and sulfur.

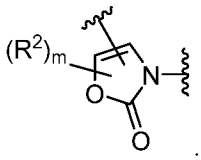
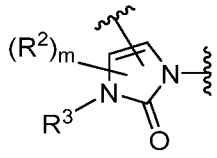
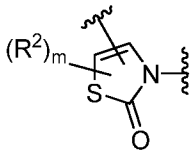
[00151] In some embodiments, R is hydrogen. In some embodiments, R is deuterium. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is optionally substituted phenyl. In some embodiments, R is optionally substituted 4-7 membered saturated or partially unsaturated heterocyclic having 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur. In some embodiments, R is optionally substituted 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur. In some embodiments, two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from boron, nitrogen, oxygen, silicon, and sulfur.

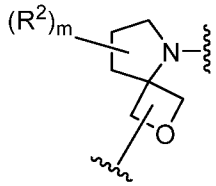
[00152] In some embodiments, R is selected from those depicted in **Table 1**, below.

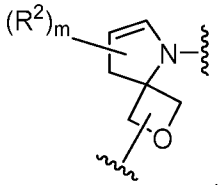
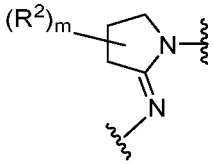
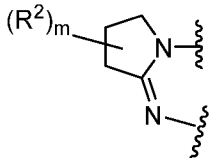
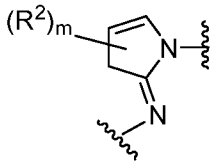
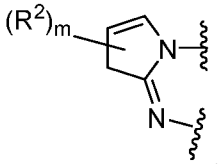
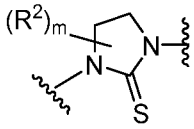
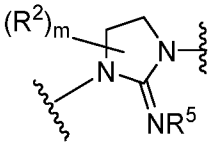
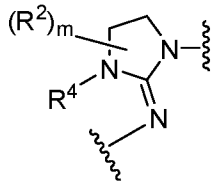
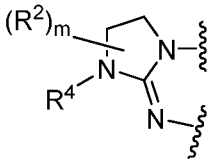
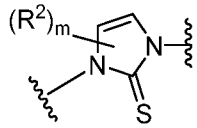
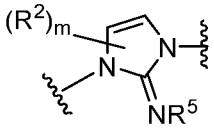
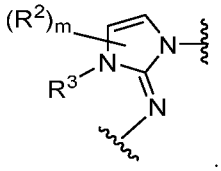
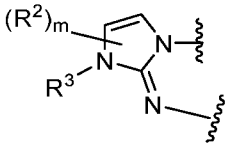
[00153] In some embodiments, the present invention provides a compound of formula **II-A** or **II-B**, wherein X^1, R^1, R^5, R, –Cy–, and TBM are recited as for formula **I** as above and herein, and Ring A, Ring B, R^2, R^3, R^4, L, m, n, p, and q are recited as for formula **II-A** and **II-B** as below and herein.

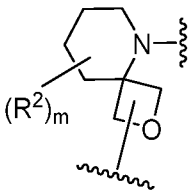
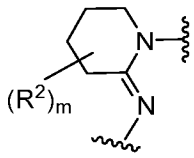
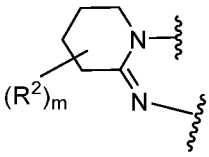
[00154] As defined above and described herein, Ring A is a mono- or bicyclic ring selected from  ,  ,  ,  ,  ,

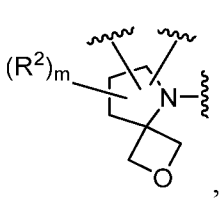
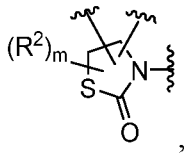
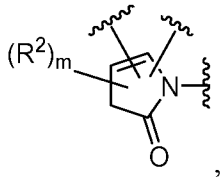
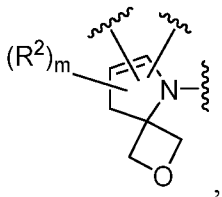
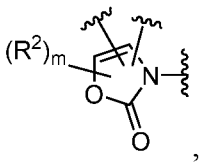
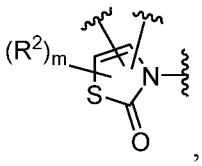
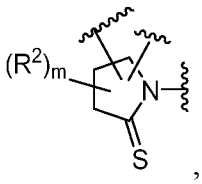
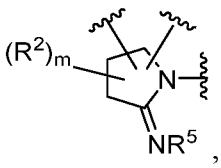
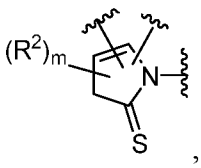
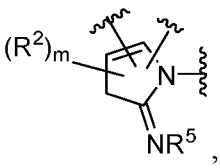
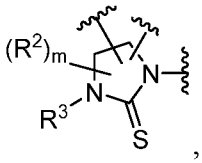
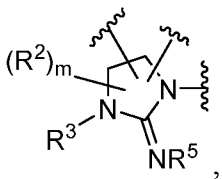
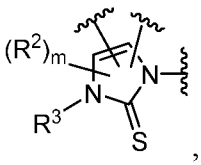
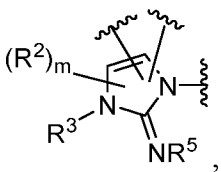
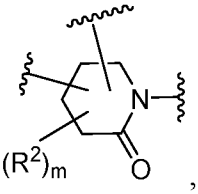
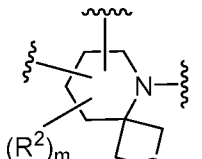
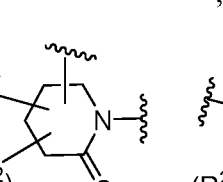
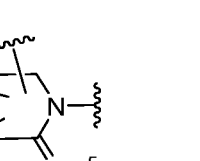
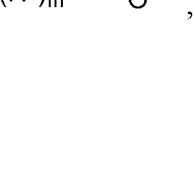




embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some

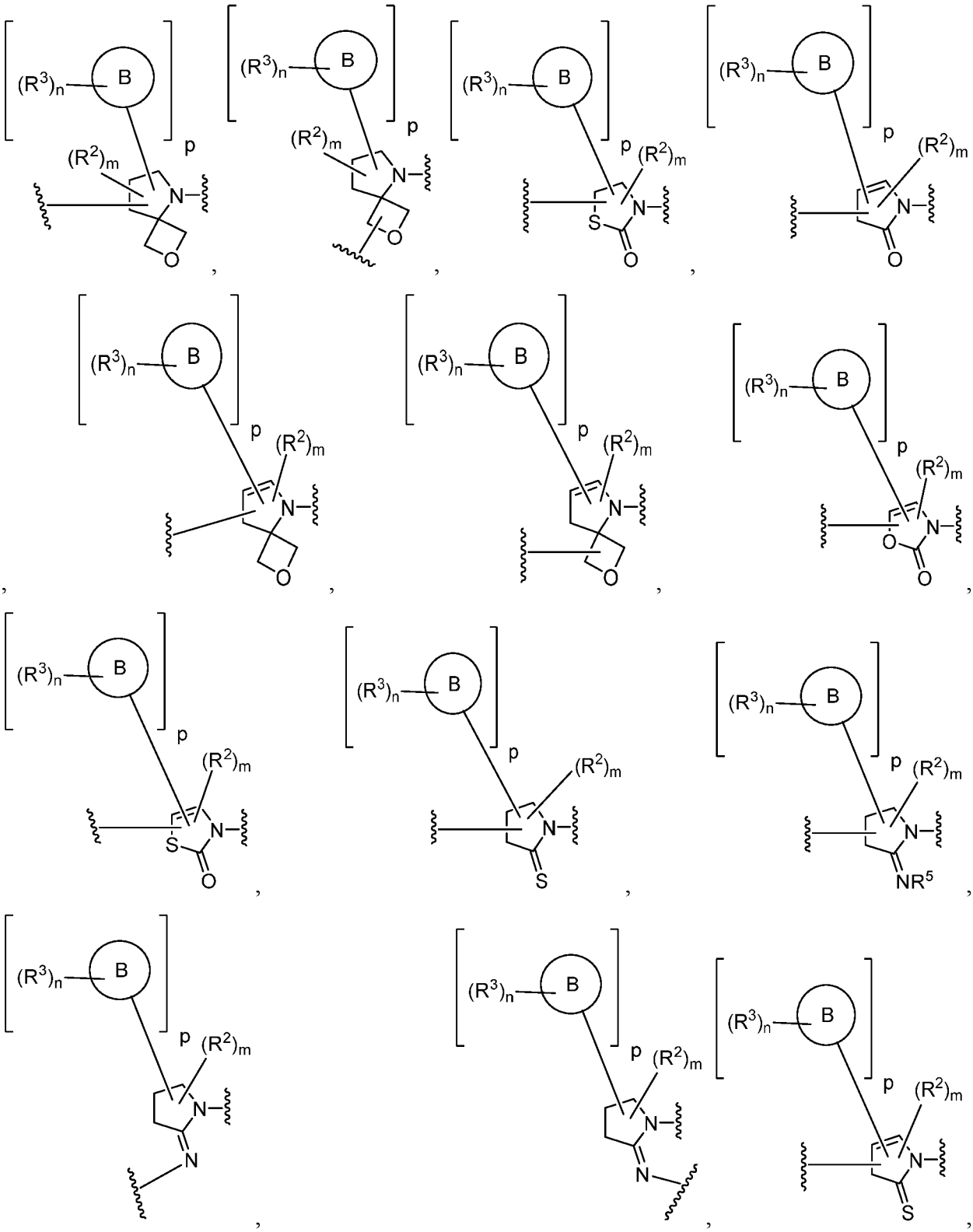


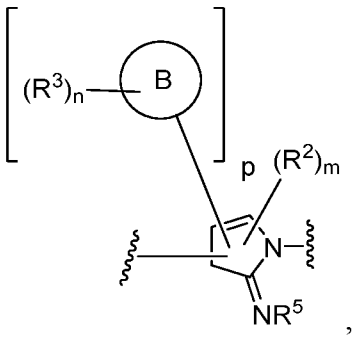
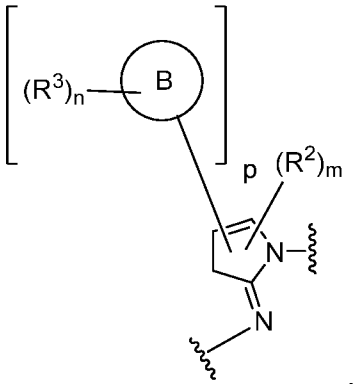
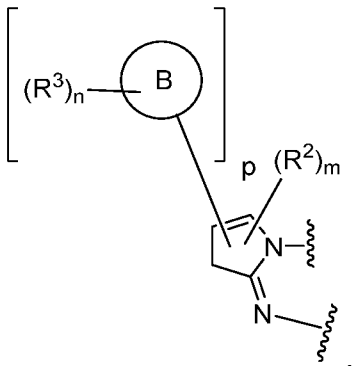
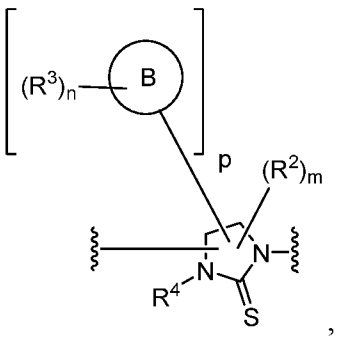
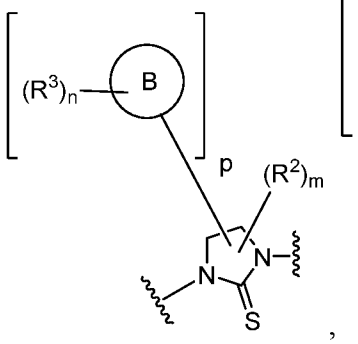
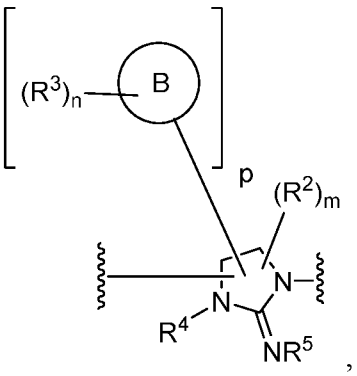
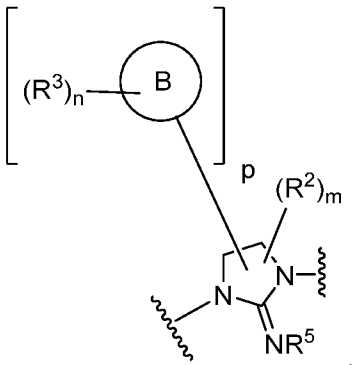
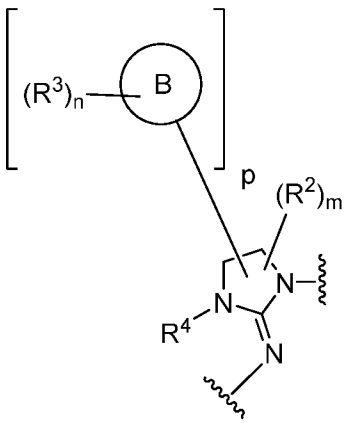
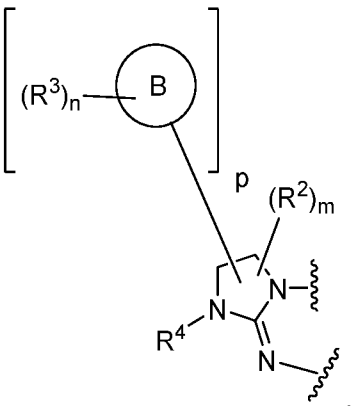
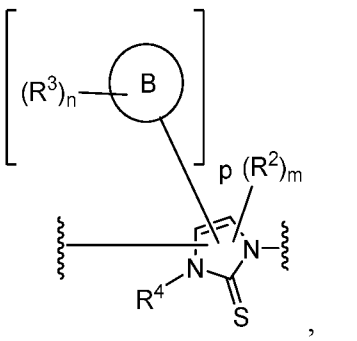
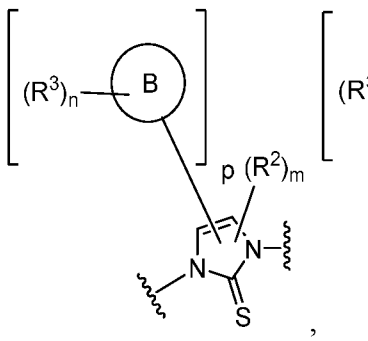
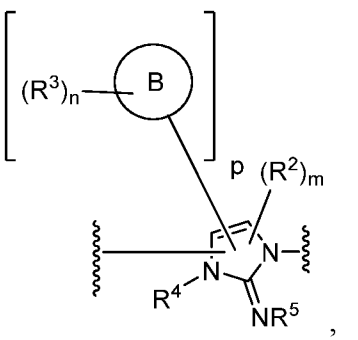
[00156] In some embodiments, Ring A is . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is . In some embodiments, Ring A is . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  . In some embodiments,

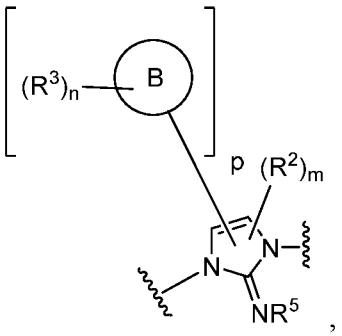
Ring A is  . In some embodiments, Ring A is  . In some embodiments, Ring A is  .

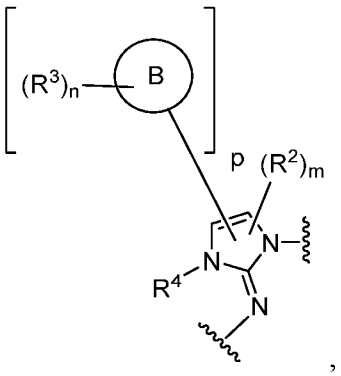
[00157] In some embodiments, Ring A is a mono- or bicyclic ring selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , , , , , ,  ,  , ,  , , , or .

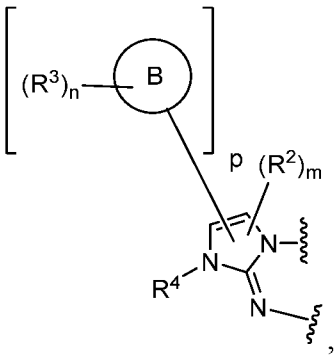
[00158] In some embodiments, Ring A is a mono- or bicyclic ring selected from

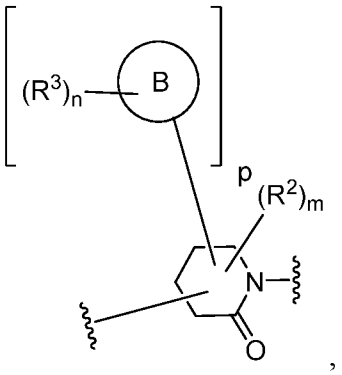


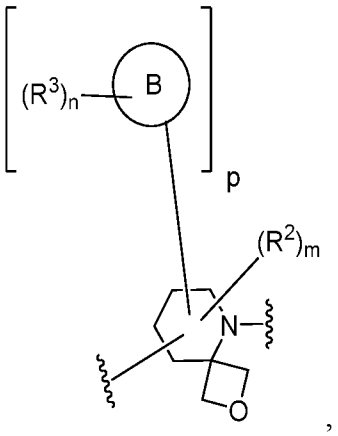

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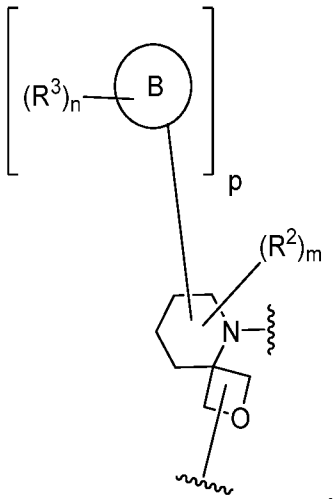


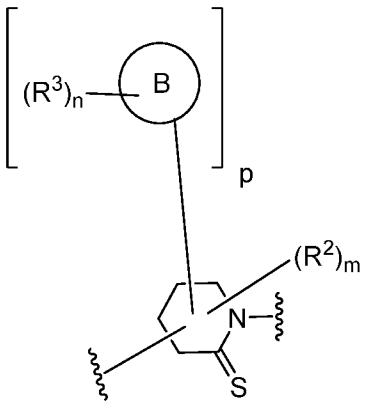


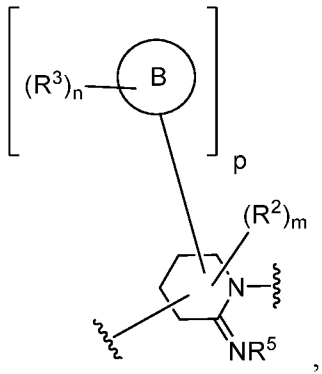


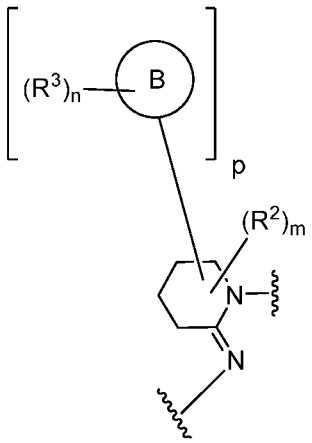


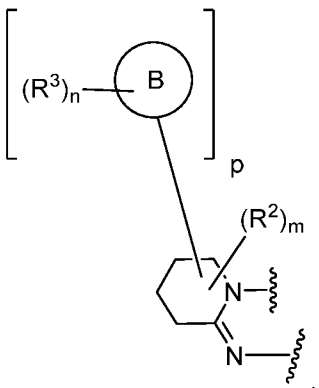




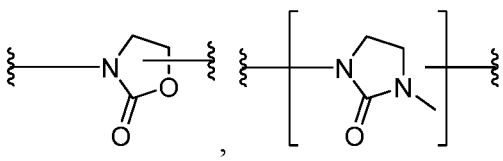


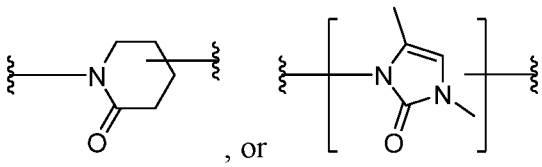
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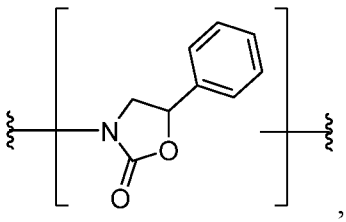
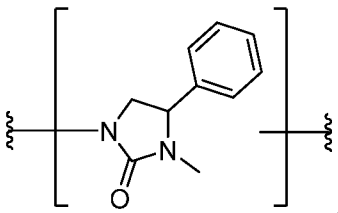
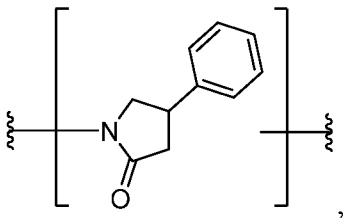
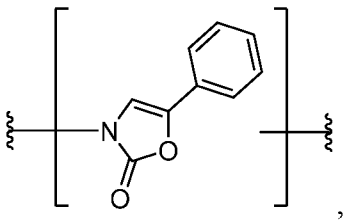
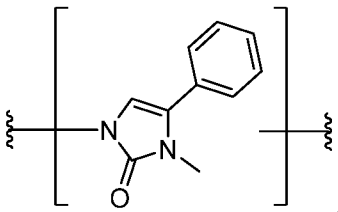
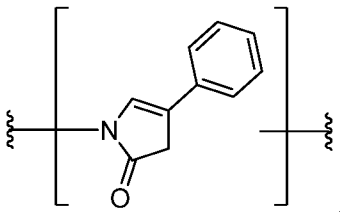
, or


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[00159] In some embodiments, Ring A is selected from


,


, , or .

[00160] In some embodiments, Ring A is selected from  ,  ,  ,  ,  , or  .

[00161] In some embodiments, Ring A is selected from those depicted in **Table 1**, below.

[00162] As defined above and described herein, each R^2 is independently hydrogen, deuterium, $-R^4$, halogen, $-CN$, $-NO_2$, $-OR$, $-SR$, $-NR_2$, $-Si(OH)_2R$, $-Si(OH)(R)_2$, $-Si(R)_3$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)N(R)OR$, $-OC(O)R$, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, $-N(R)S(O)_2R$, $-N(R)S(O)_2NR_2$, $-P(O)(OR)_2$, $-P(O)(NR_2)OR$, or $-P(O)(NR_2)_2$.

[00163] In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is deuterium. In some embodiments, R^2 is $-R^4$. In some embodiments, R^2 is halogen. In some embodiments, R^2 is $-CN$. In some embodiments, R^2 is $-NO_2$. In some embodiments, R^2 is $-OR$. In some embodiments, R^2 is $-Si(OH)_2R$. In some embodiments, R^2 is $-Si(OH)(R)_2$. In some embodiments, R^2 is $-SR$. In some embodiments, R^2 is $-NR_2$. In some embodiments, R^2 is $-Si(R)_3$. In some embodiments, R^2 is $-S(O)_2R$. In some embodiments, R^2 is $-S(O)_2NR_2$. In some embodiments, R^2 is $-S(O)R$. In some embodiments, R^2 is $-C(O)R$. In some embodiments, R^2 is $-C(O)OR$. In some embodiments, R^2 is $-C(O)NR_2$. In some embodiments, R^2 is $-C(O)N(R)OR$. In some embodiments, R^2 is $-OC(O)R$. In some embodiments, R^2 is $-OC(O)NR_2$. In some embodiments, R^2 is $-N(R)C(O)OR$. In some embodiments, R^2 is $-N(R)C(O)R$. In some embodiments, R^2 is $-N(R)C(O)NR_2$. In some embodiments, R^2 is $-N(R)S(O)_2R$. In some

embodiments, R^2 is $-P(O)(OR)_2$. In some embodiments, R^2 is $-P(O)(NR_2)OR$. In some embodiments, R^2 is $-P(O)(NR_2)_2$.

[00164] In some embodiments, R^2 is methyl.

[00165] In some embodiments, R^2 is selected from those depicted in **Table 1**, below.

[00166] As defined above and described herein, Ring B is selected from a 6-membered aryl containing 0-3 nitrogen atoms or a 5-membered heteroaryl with 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur.

[00167] In some embodiments, Ring B is a 6-membered aryl containing 0-3 nitrogen atoms. In some embodiments, Ring B is a 5-membered heteroaryl with 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur.

[00168] In some embodiments, Ring B is selected from those depicted in **Table 1**, below.

[00169] As defined above and described herein, each R^3 is independently hydrogen, deuterium, halogen, $-CN$, $-NO_2$, $-OR$, $-NR_2$, $-SR$, $-S(O)_2R$, $-S(O)_2NR_2$, $-S(O)R$, $-C(O)R$, $-C(O)OR$, $-C(O)NR_2$, $-C(O)NR(OR)$, $-OC(O)R$, $-OC(O)NR_2$, $-OP(O)(OR)_2$, $-OP(O)(NR_2)_2$, $-OP(O)(OR)NR_2$, $-N(R)C(O)R$, $-N(R)C(O)OR$, $-N(R)C(O)NR_2$, $-N(R)S(O)_2R$, $-N(R)S(O)_2NR_2$, $-N(R)P(O)(OR)_2$, $-N(R)P(O)(OR)NR_2$, $-P(O)(OR)_2$, $-P(O)(NR_2)OR$, $-P(O)(NR_2)_2$, $-Si(OH)_2R$, $-Si(OH)(R)_2$, or $-Si(R)_3$.

[00170] In some embodiments, R^3 is hydrogen. In some embodiments, R^3 is deuterium. In some embodiments, R^3 is halogen. In some embodiments, R^3 is $-CN$. In some embodiments, R^3 is $-NO_2$. In some embodiments, R^3 is $-OR$. In some embodiments, R^3 is $-NR_2$. In some embodiments, R^3 is $-SR$. In some embodiments, R^3 is $-S(O)_2R$. In some embodiments, R^3 is $-S(O)_2NR_2$. In some embodiments, R^3 is $-S(O)R$. In some embodiments, R^3 is $-C(O)R$. In some embodiments, R^3 is $-C(O)OR$. In some embodiments, R^3 is $-C(O)NR_2$. In some embodiments, R^3 is $-C(O)NR(OR)$. In some embodiments, R^3 is $-OC(O)R$. In some embodiments, R^3 is $-OC(O)NR_2$. In some embodiments, R^3 is $-OP(O)(OR)_2$. In some embodiments, R^3 is $-OP(O)(NR_2)_2$. In some embodiments, R^3 is $-OP(O)(OR)NR_2$. In some embodiments, R^3 is $-N(R)C(O)R$. In some embodiments, R^3 is $-N(R)C(O)OR$. In some embodiments, R^3 is $-N(R)C(O)NR_2$. In some embodiments, R^3 is $-N(R)S(O)_2R$. In some embodiments, R^3 is $-N(R)S(O)_2NR_2$. In some embodiments, R^3 is $-N(R)P(O)(OR)_2$. In some embodiments, R^3 is $-N(R)P(O)(OR)NR_2$. In some embodiments, R^3 is $-P(O)(OR)_2$. In some embodiments, R^3 is

–P(O)(NR_2)OR. In some embodiments, R^3 is –P(O)(NR_2)$_2$. In some embodiments, R^3 is –Si(OH)$_2$R. In some embodiments, R^3 is –Si(OH)(R)$_2$. In some embodiments, R^3 is –Si(R)$_3$.

[00171] In some embodiments, R^3 is selected from those depicted in **Table 1**, below.

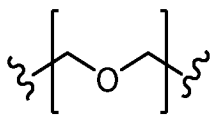
[00172] As defined above and described herein, each R^4 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur.

[00173] In some embodiments, R^4 is an optionally substituted C_{1-6} aliphatic. In some embodiments, R^4 is an optionally substituted phenyl. In some embodiments, R^4 is an optionally substituted 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur. In some embodiments, R^4 is an optionally substituted 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from boron, nitrogen, oxygen, silicon, and sulfur.

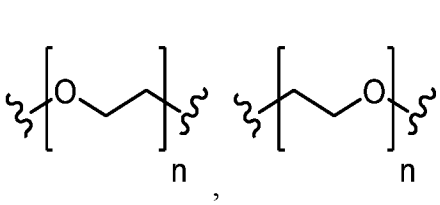
[00174] In some embodiments, R^4 is methyl.

[00175] In some embodiments, R^4 is selected from those depicted in **Table 1**, below.

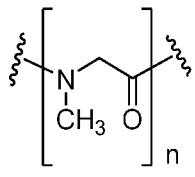
[00176] As defined above and described herein, L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy–, –O–, –N(R)–, –Si(R)$_2$–, –Si(OH)(R)–, –Si(OH)$_2$–, –P(O)(OR)–, –P(O)(R)–, –P(O)(NR_2)–, –S–, –OC(O)–, –C(O)O–, –C(O)–, –S(O)–, –S(O)$_2$–, –N(R)S(O)$_2$–, –S(O)$_2$N(R)–, –N(R)C(O)–, –C(O)N(R)–, –OC(O)N(R)–, –N(R)C(O)O–,



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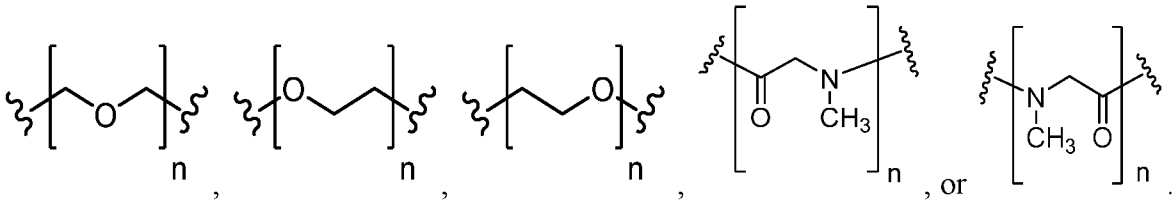
, or



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[00177] In some embodiments, L is a covalent bond. In some embodiments, L is a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy–, –O–, –N(R)–, –Si(R)$_2$–, –Si(OH)(R)–, –Si(OH)$_2$–

, –P(O)(OR)–, –P(O)(R)–, –P(O)(NR_2)–, –S–, –OC(O)–, –C(O)O–, –C(O)–, –S(O)–, –$S(O)_2$–, –N(R)$S(O)_2$–, –$S(O)_2$N(R)–, –N(R)C(O)–, –C(O)N(R)–, –OC(O)N(R)–, –N(R)C(O)O–,



, or .

[00178] In some embodiments, L is selected from those depicted in **Table 1**, below.

[00179] As defined above and described herein, m is 0, 1, or 2.

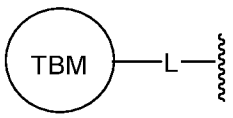
[00180] In some embodiments, m is 0. In some embodiments, m is 1. In some embodiments, m is 2.

[00181] In some embodiments, m is selected from those depicted in **Table 1**, below.

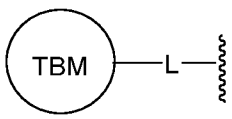
[00182] As defined above and described herein, n is 0, 1, 2, 3, or 4.

[00183] In some embodiments, n is 0. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4.

[00184] In some embodiments, n is selected from those depicted in **Table 1**, below.

[00185] As defined above and described herein, p is 0 or 1, wherein when p is 0, the bond connecting Ring A and Ring B is connected to 

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[00186] In some embodiments, p is 0. In some embodiments, p is 1. In some embodiments, p is 0 and the bond connecting Ring A and Ring B is connected to 

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[00187] In some embodiments, p is selected from those depicted in **Table 1**, below.

[00188] As defined above and described herein, each of q is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

[00189] In some embodiments, q is 0. In some embodiments, q is 1. In some embodiments, q is 2. In some embodiments, q is 3. In some embodiments, q is 4. In some embodiments, q is 5. In some embodiments, q is 6. In some embodiments, q is 7. In some embodiments, q is 8. In some embodiments, q is 9. In some embodiments, q is 10.

[00190] In some embodiments, q is selected from those depicted in **Table 1**, below.

[00191] In preferred aspects of the invention, the TBM group is a group, which binds to target proteins. Targets of the TBM group are numerous in kind and are selected from proteins that are expressed in a cell such that at least a portion of the sequences is found in the cell and may bind to a TBM group. The term"protein" includes oligopeptides and polypeptide sequences of sufficient length that they can bind to a TBM group according to the present invention. Any protein in a eukaryotic system, as described herein, are targets for ubiquitination mediated by the compounds according to the present invention.

[00192] TBM groups according to the present invention include, for example, include any moiety which binds to a protein specifically (binds to a target protein) and includes the following non-limiting examples of small molecule target protein moieties: Hsp90 inhibitors, kinase inhibitors, HDM2 & MDM2 inhibitors, compounds targeting Human BET Bromodomain-containing proteins, HDAC inhibitors, human lysine methyltransferase inhibitors, angiogenesis inhibitors, nuclear hormone receptor compounds, immunosuppressive compounds, and compounds targeting the aryl hydrocarbon receptor (AHR), among numerous others. The compositions described below exemplify some of the members of these nine types of small molecule target protein binding moieties. Such small molecule target protein binding moieties also include pharmaceutically acceptable salts, enantiomers, solvates and polymorphs of these compositions, as well as other small molecules that may target a protein of interest. These binding moieties are linked to the ubiquitin ligase binding moiety preferably through a linker in order to present a target protein (to which the protein target moiety is bound) in proximity to the ubiquitin ligase for ubiquitination and degradation.

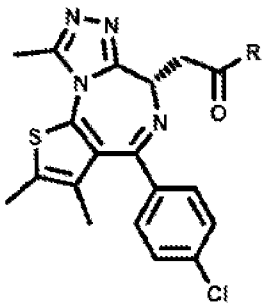
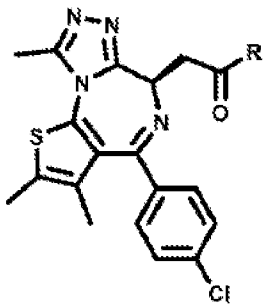
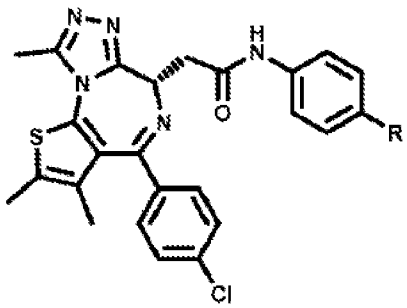
[00193] Any protein, which can bind to a target binding moiety or TBM group and acted on or degraded by an ubiquitin ligase is a target protein according to the present invention. In general, target proteins may include, for example, structural proteins, receptors, enzymes, cell surface proteins, proteins pertinent to the integrated function of a cell, including proteins involved in catalytic activity, aromatase activity, motor activity, helicase activity, metabolic processes (anabolism and catabolism), antioxidant activity, proteolysis, biosynthesis, proteins with kinase activity, oxidoreductase activity, transferase activity, hydrolase activity, lyase activity, isomerase activity, ligase activity, enzyme regulator activity, signal transducer activity, structural molecule activity, binding activity (protein, lipid carbohydrate), receptor activity, cell motility, membrane

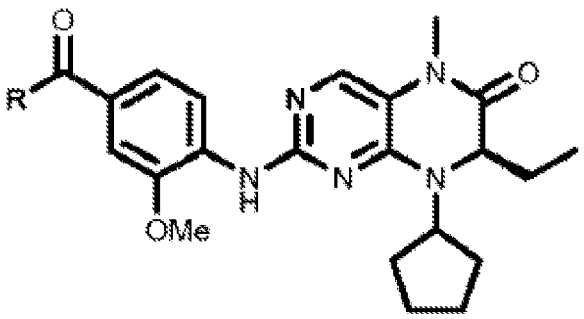
fusion, cell communication, regulation of biological processes, development, cell differentiation, response to stimulus, behavioral proteins, cell adhesion proteins, proteins involved in cell death, proteins involved in transport (including protein transporter activity, nuclear transport, ion transporter activity, channel transporter activity, carrier activity, permease activity, secretion activity, electron transporter activity, pathogenesis, chaperone regulator activity, nucleic acid binding activity, transcription regulator activity, extracellular organization and biogenesis activity, translation regulator activity. Proteins of interest can include proteins from eurkaryotes and prokaryotes including humans as targets for drug therapy, other animals, including domesticated animals, microbials for the determination of targets for antibiotics and other antimicrobials and plants, and even viruses, among numerous others.

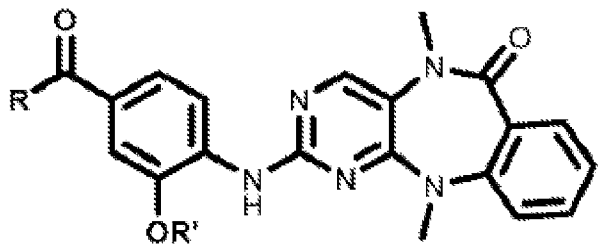
[00194] TBM (or target binding moiety) is a small molecule which is capable of binding to or binds to a target protein of interest.

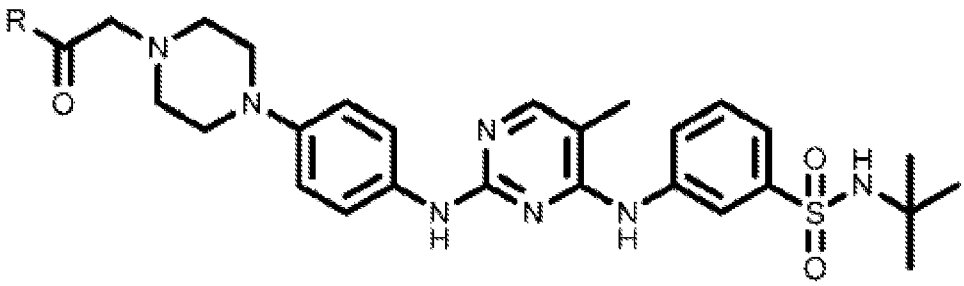
[00195] Some embodiments of the present application relate to TBMs which include but are not limited to Hsp90 inhibitors, kinase inhibitors, MDM2 inhibitors, compounds targeting Human BET Bromodomain-containing proteins, compounds targeting cytosolic signaling protein FKBP12, HDAC inhibitors, human lysine methyltransferase inhibitors, angiogenesis inhibitors, immunosuppressive compounds, and compounds targeting the aryl hydrocarbon receptor (AHR).

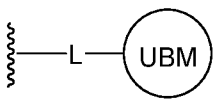
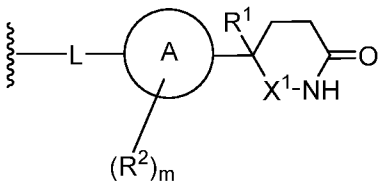
[00196] In some embodiments, TBM is a BRD ligand selected from

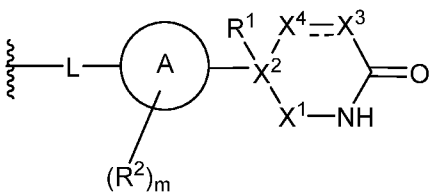
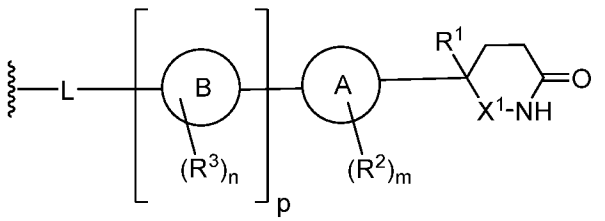




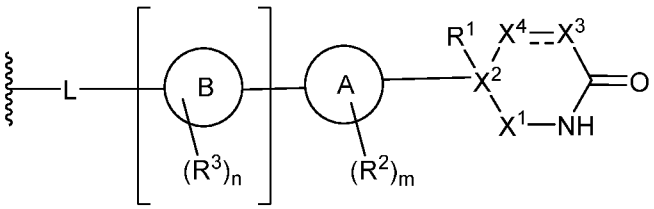




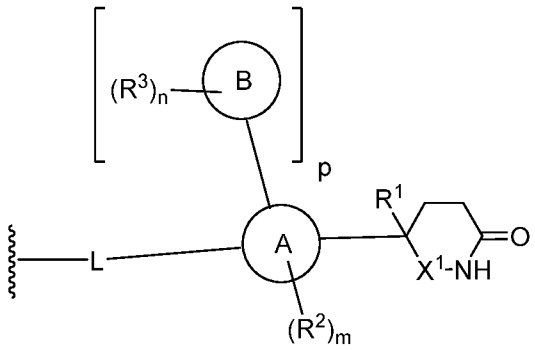


, wherein R denotes attachment to  ,  ,

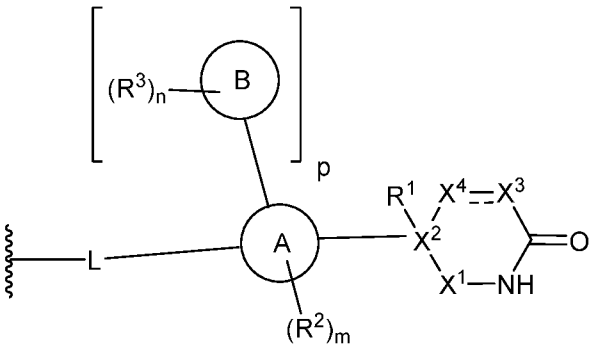
 ,  ,



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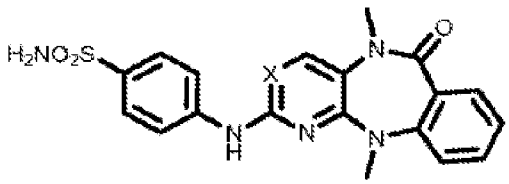


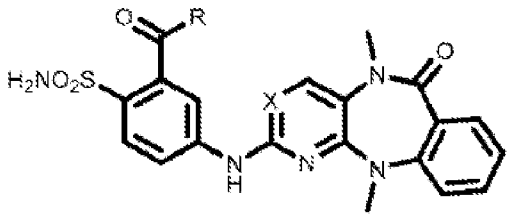
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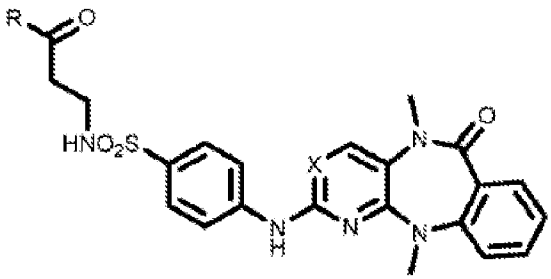


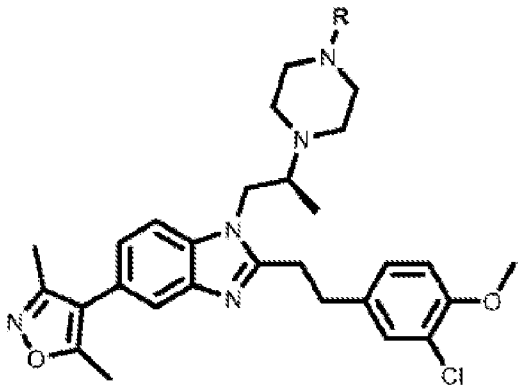
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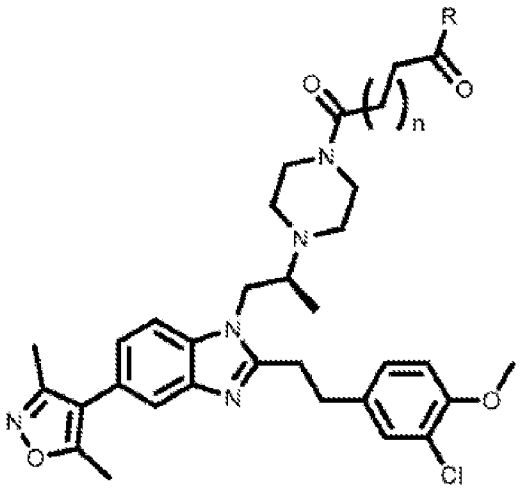
[00197] In some embodiments, TBM is a CREBBP ligand selected from

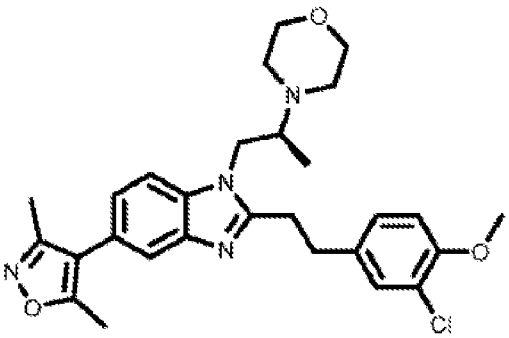


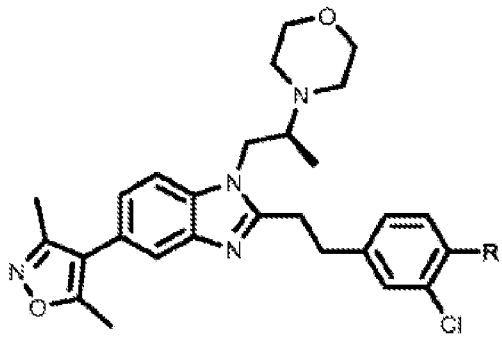


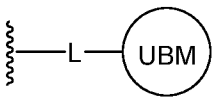
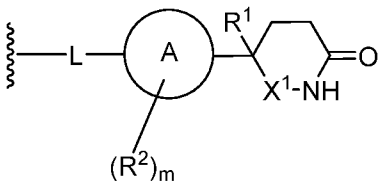
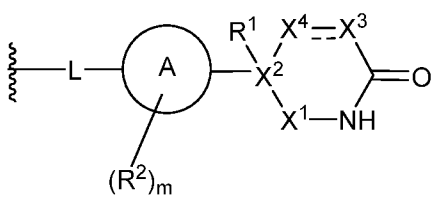
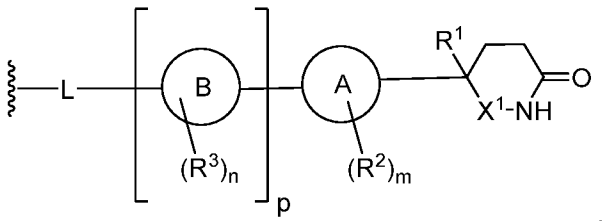


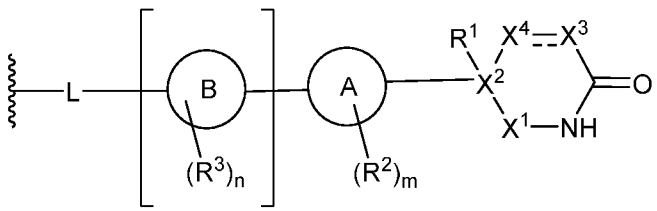




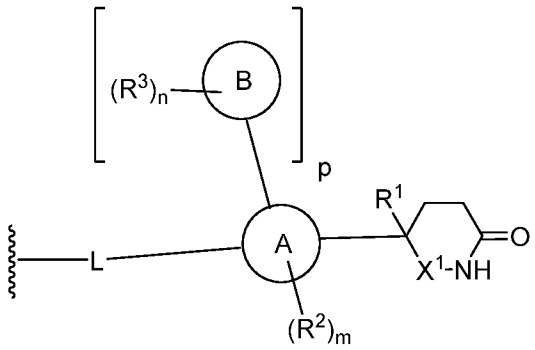




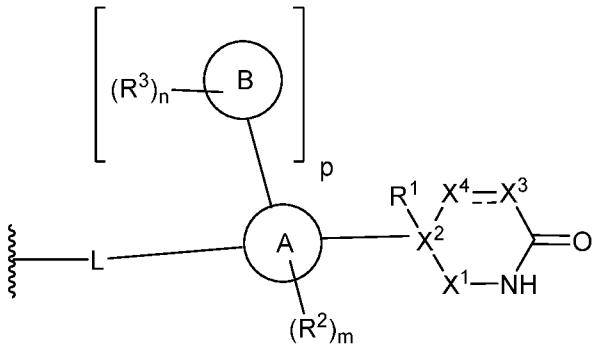
, wherein R denotes attachment to  ,  ,  ,  .



,

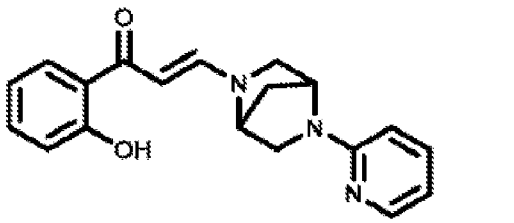


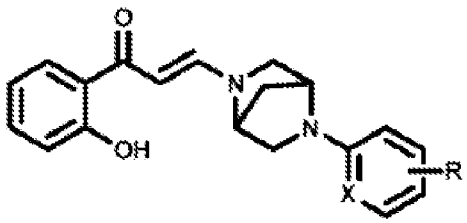
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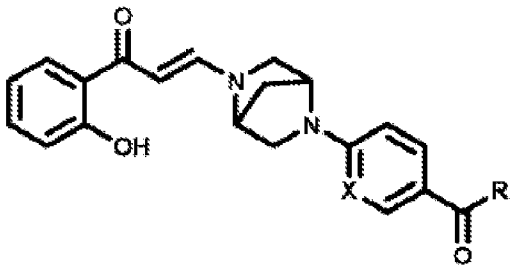


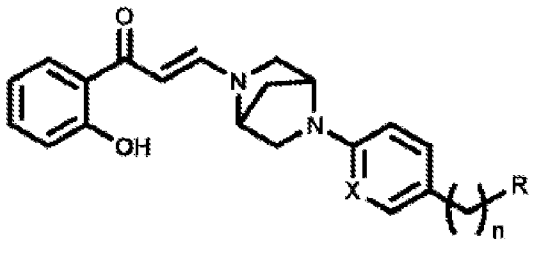
; X is N or C; and n is 0 to 8.

[00198] In some embodiments, TBM is a SMARCA4/PB1/SMARCA2 ligand selected from

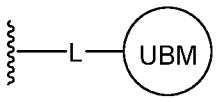




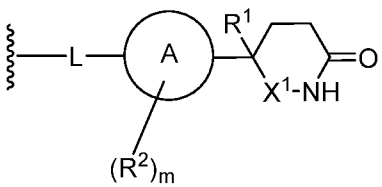




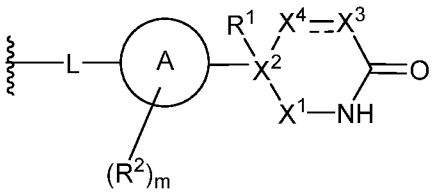
, wherein R denotes attachment to



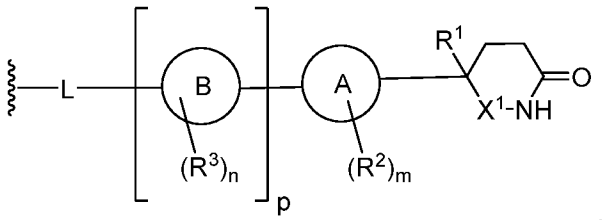
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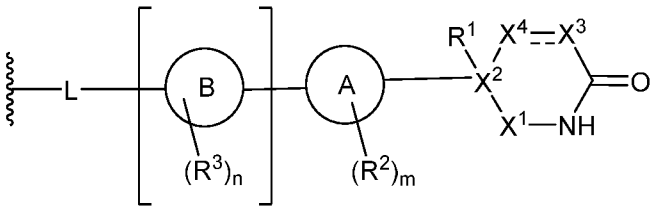
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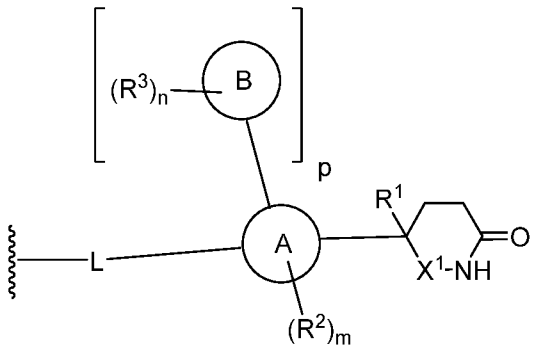
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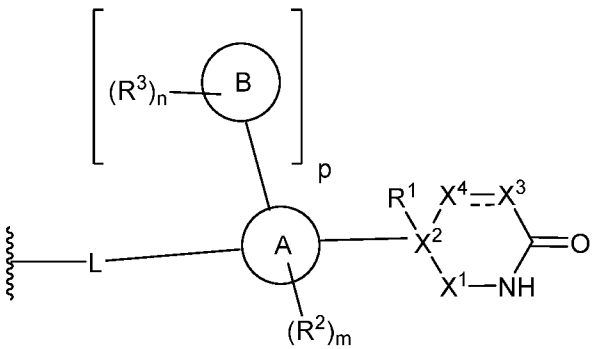
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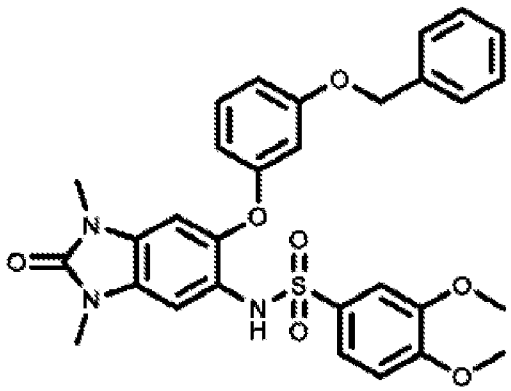


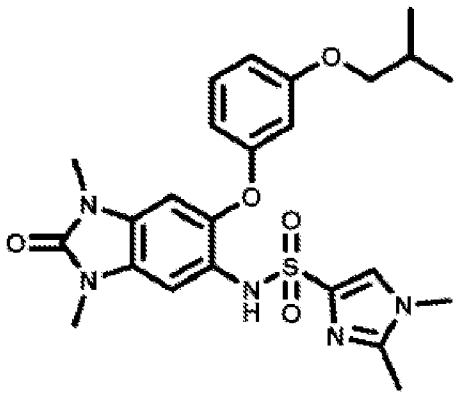
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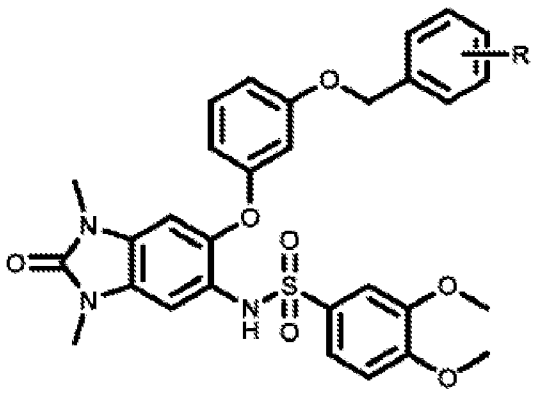


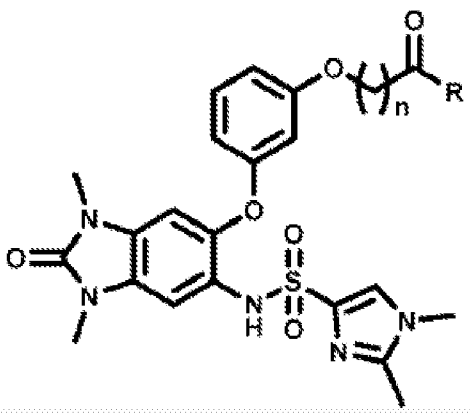
; X is N or C; and n is 0 to 8.

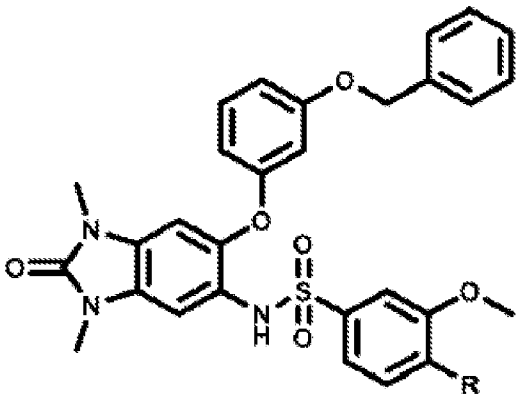
[00199] In some embodiments, TBM is a TRIM24/BRPF1 ligand selected from

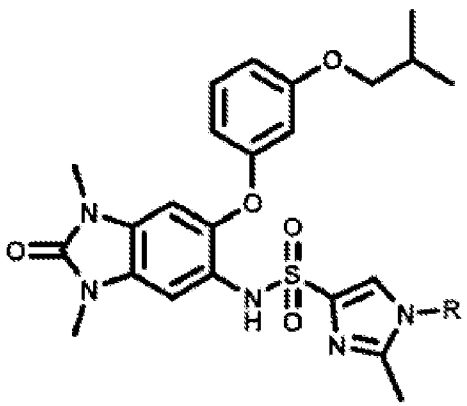


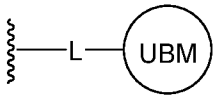
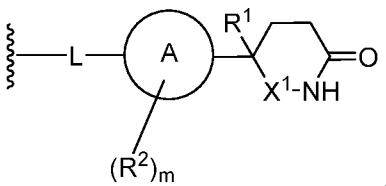


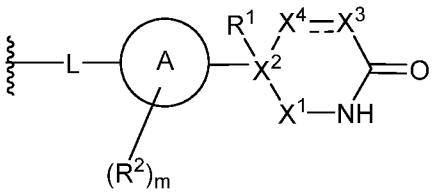




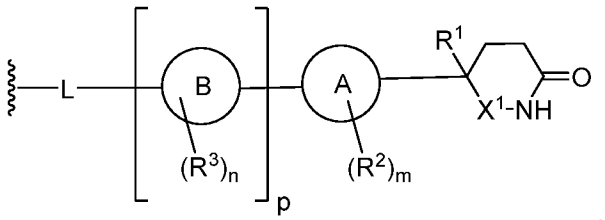




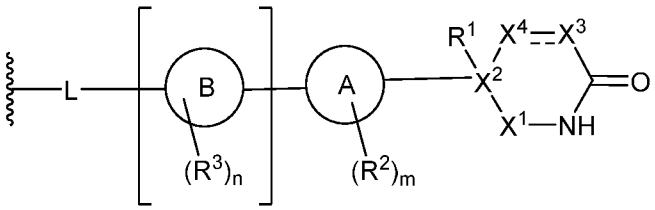
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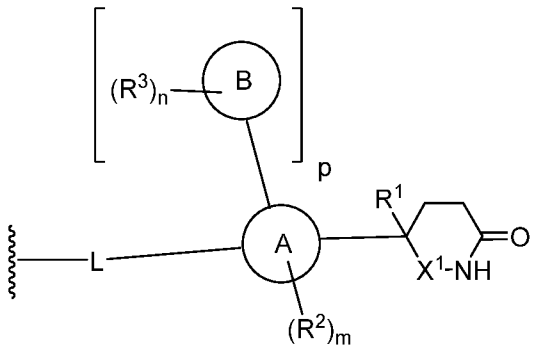
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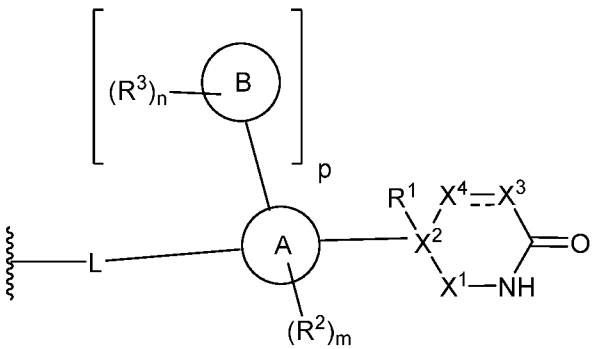
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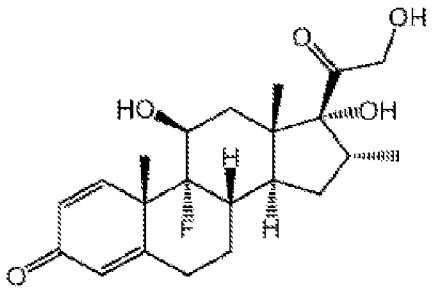
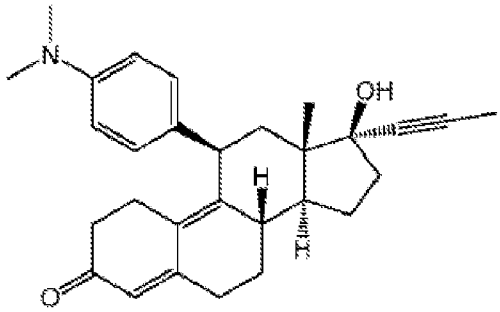
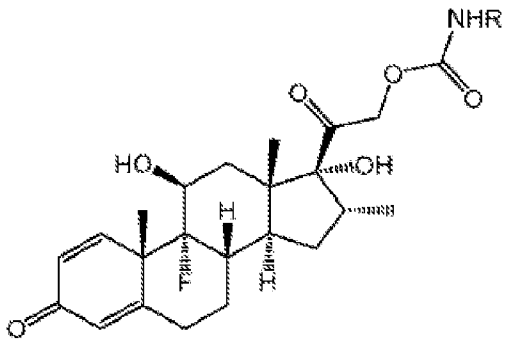
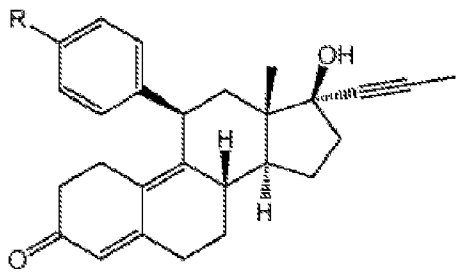
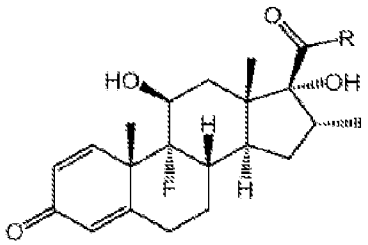
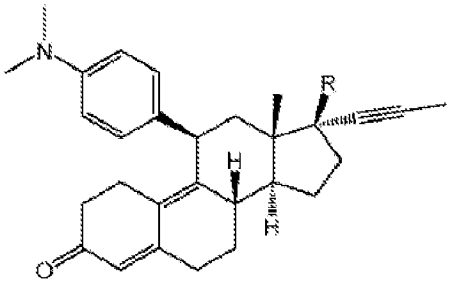
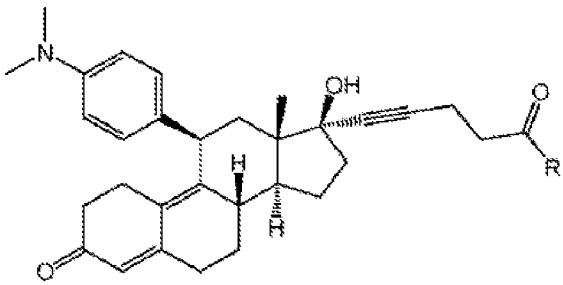


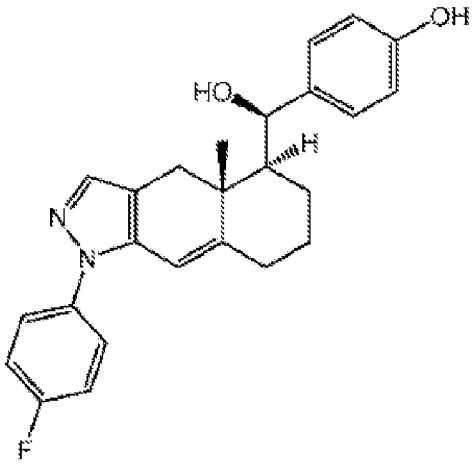
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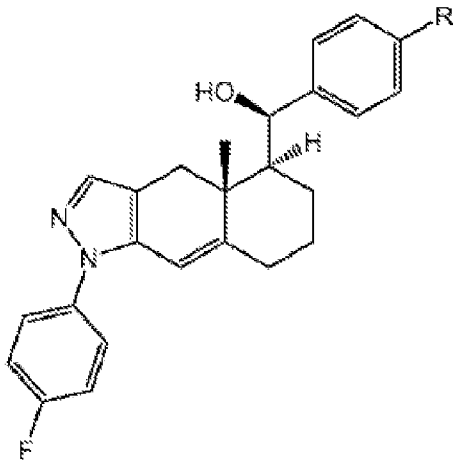


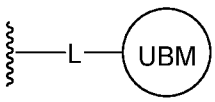
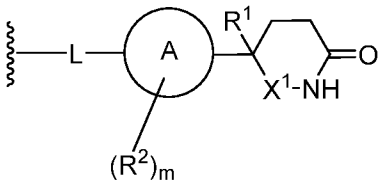
; and n is 0 to 8.

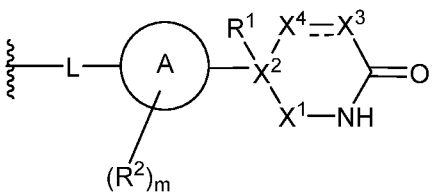
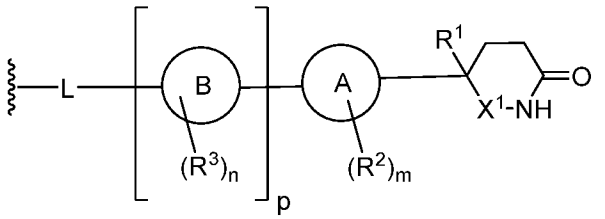
[00200] In some embodiments, TBM is a glucocorticoid receptor ligand selected from

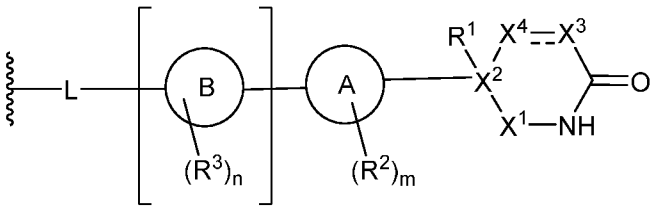










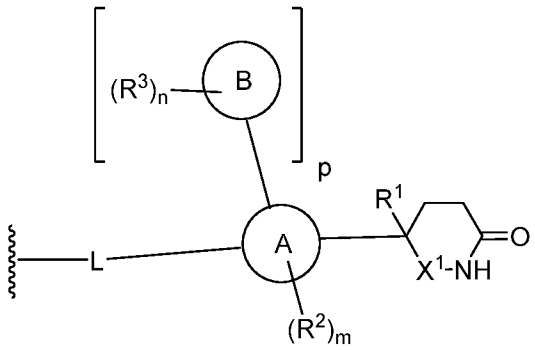


, wherein R denotes attachment to  ,  ,

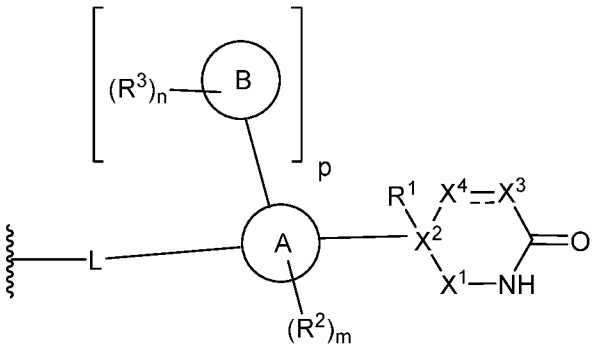
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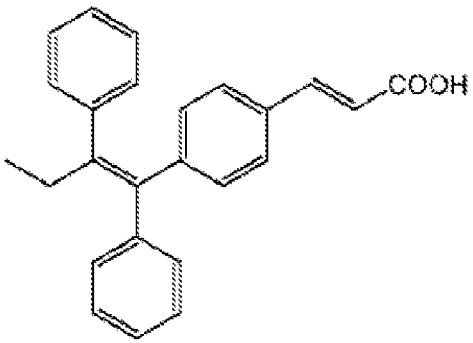


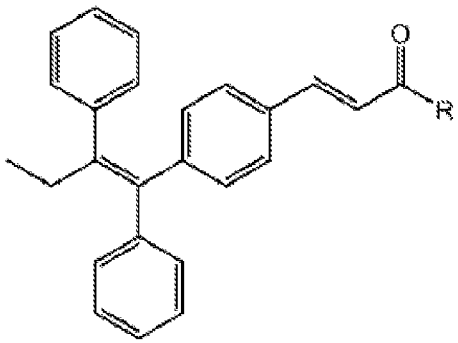
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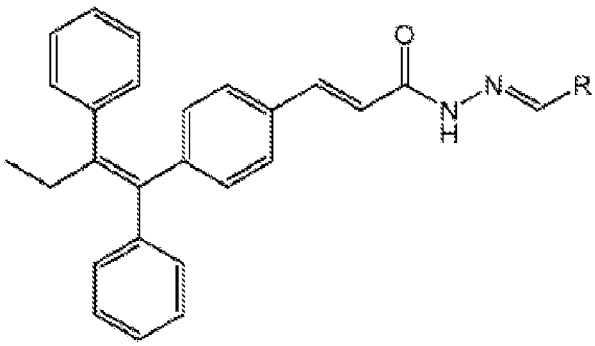


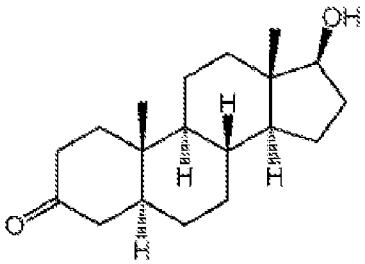
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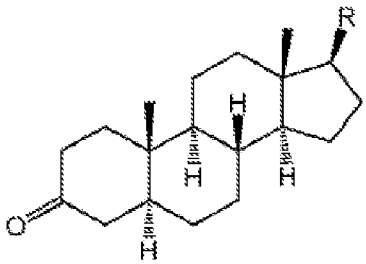
[00201] In some embodiments, TBM is a estrogen/androgen receptor ligand selected from

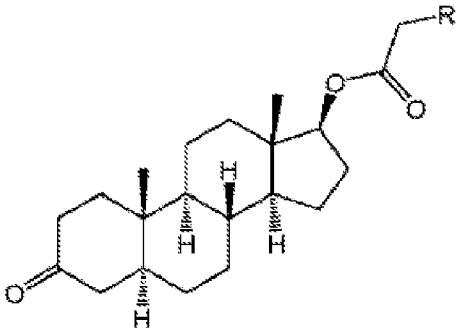


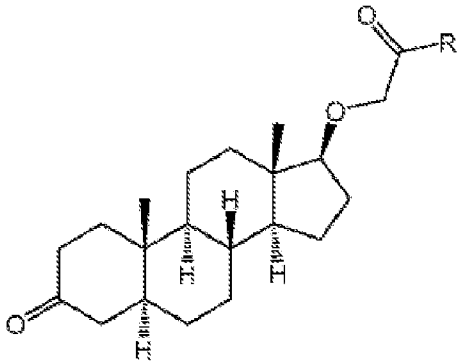


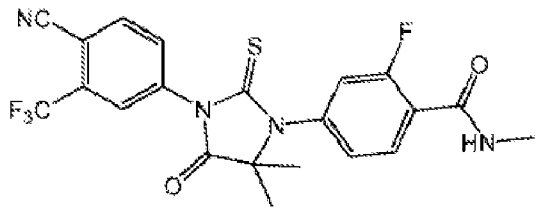


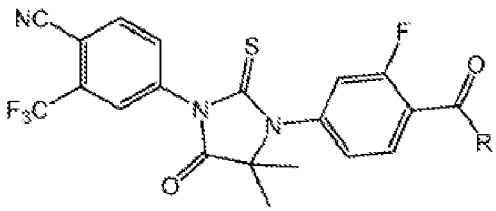


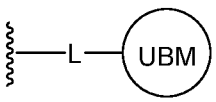
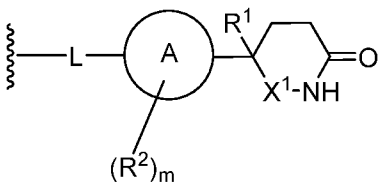


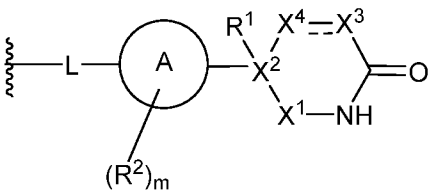


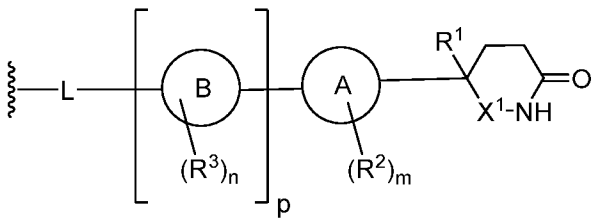


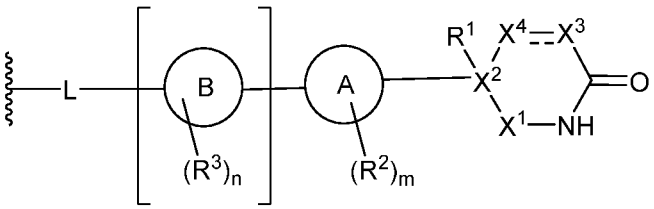




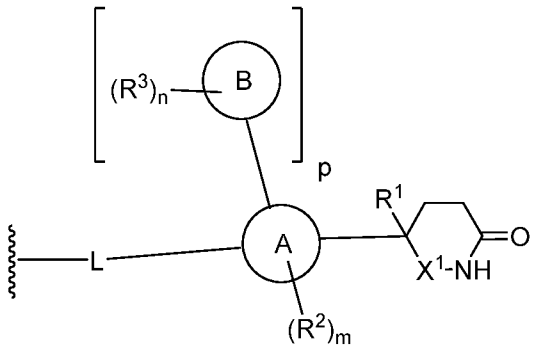
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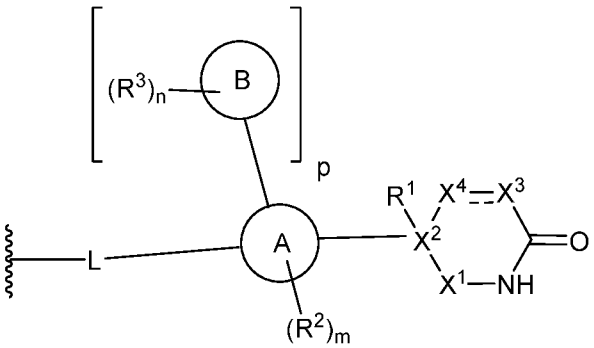
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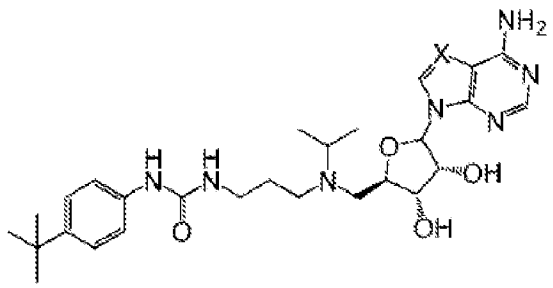


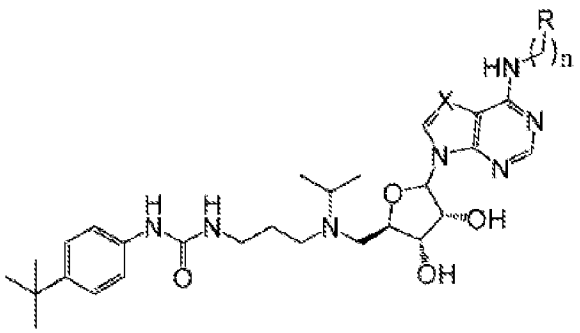
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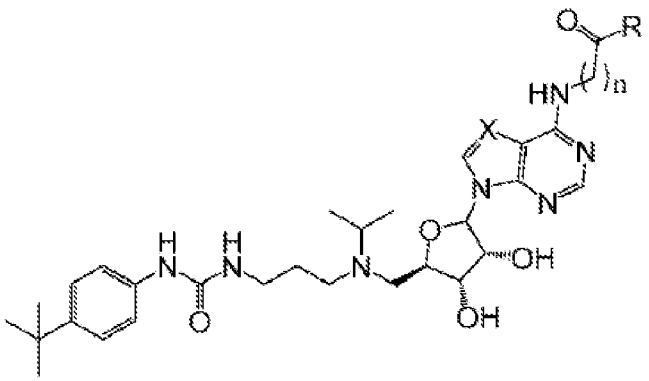


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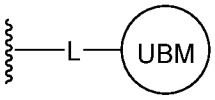
[00202] In some embodiments, TBM is a DOT1L ligand selected from

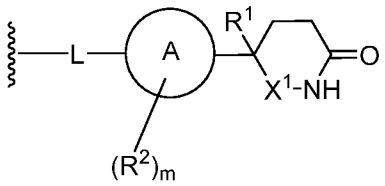


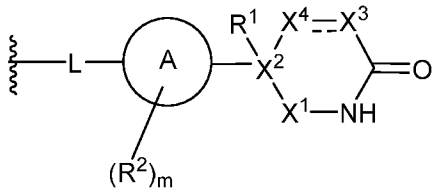


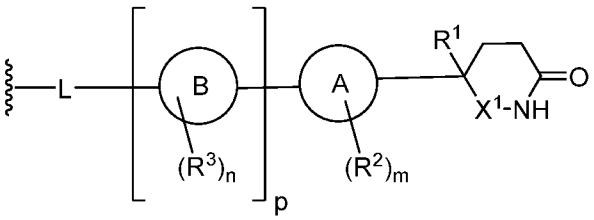


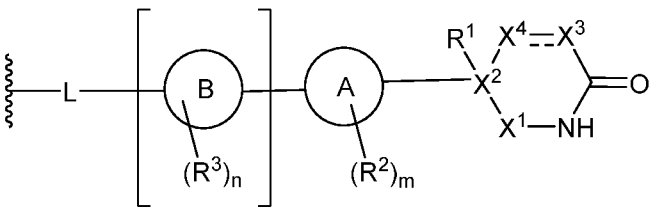
, wherein R denotes attachment to

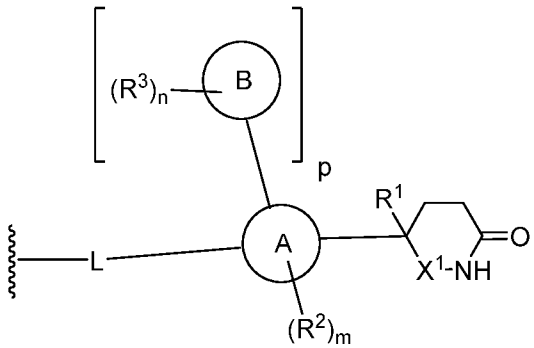


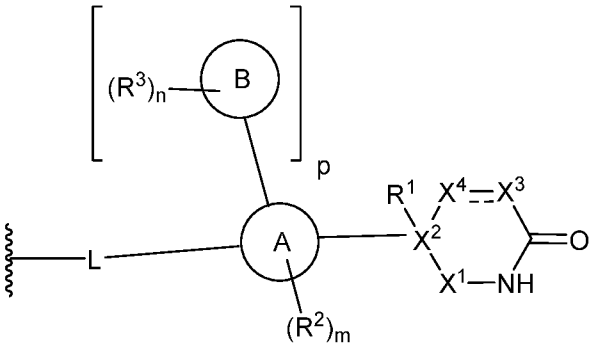
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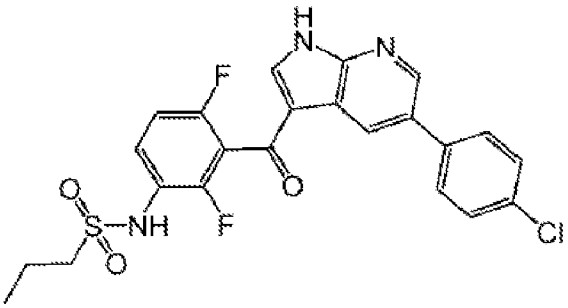
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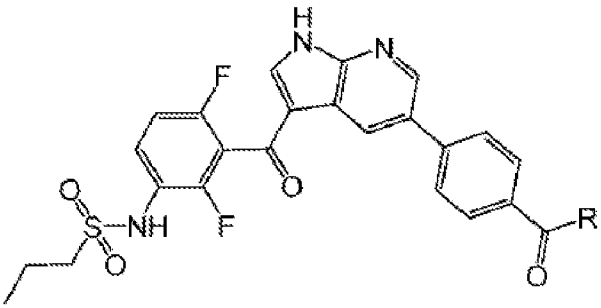
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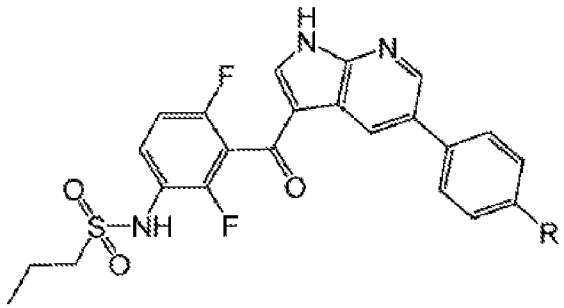
, or


; X is N or C; and n is 0 – 8.

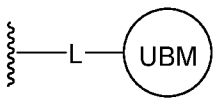
[00203] In some embodiments, TBM is a BRAF ligand selected from



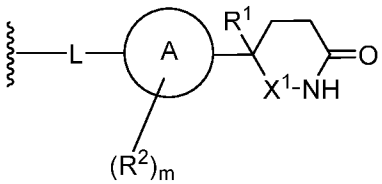




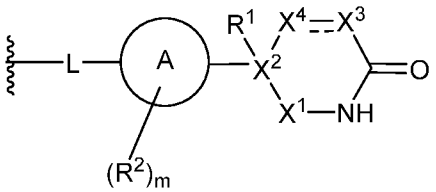
, wherein R denotes attachment to



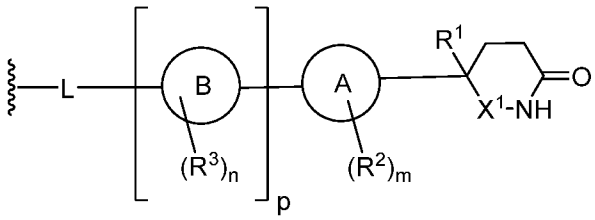
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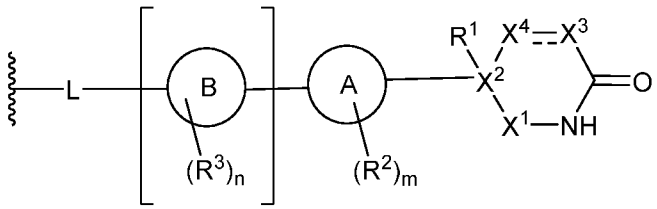
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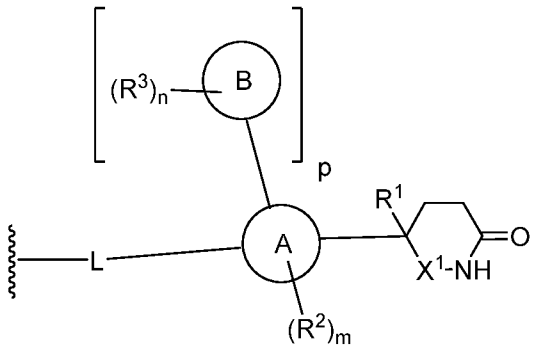
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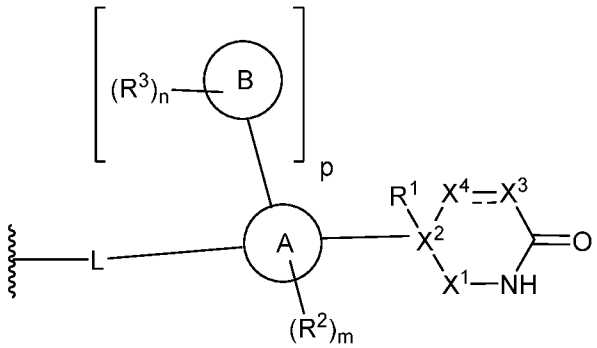
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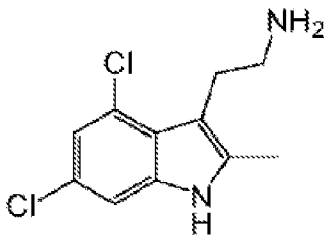


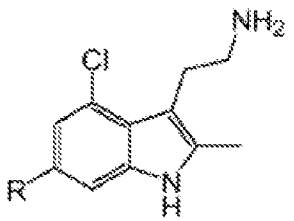
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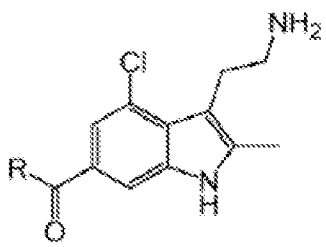


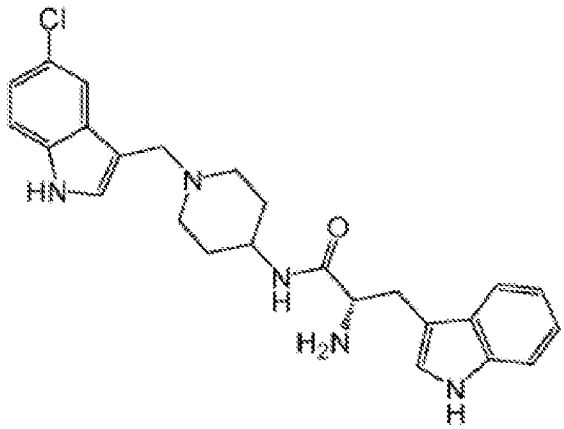
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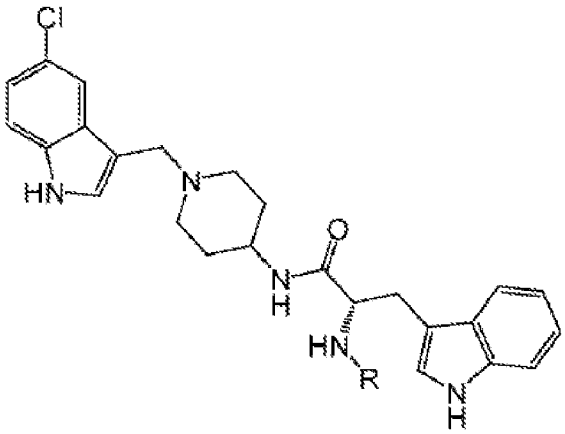
[00204] In some embodiments, TBM is a Ras ligand selected from

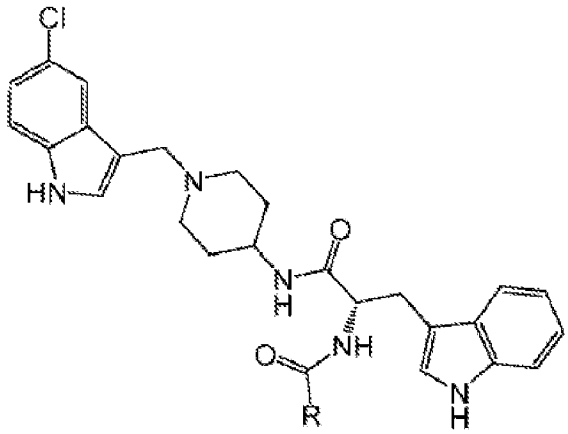


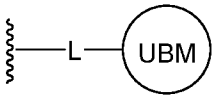
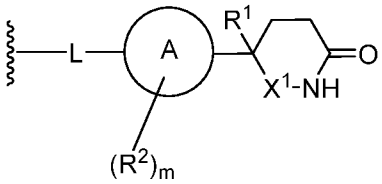


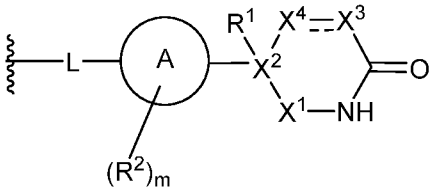
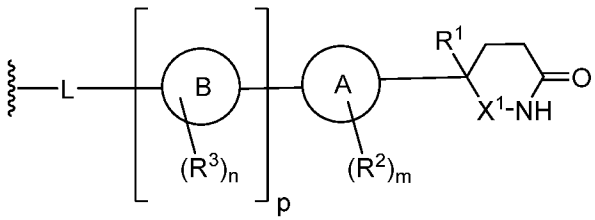


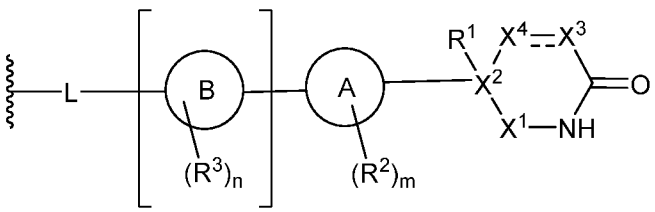
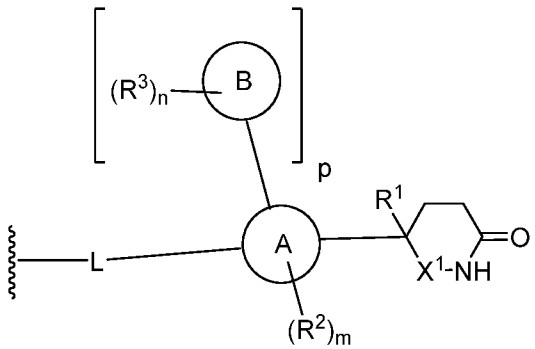


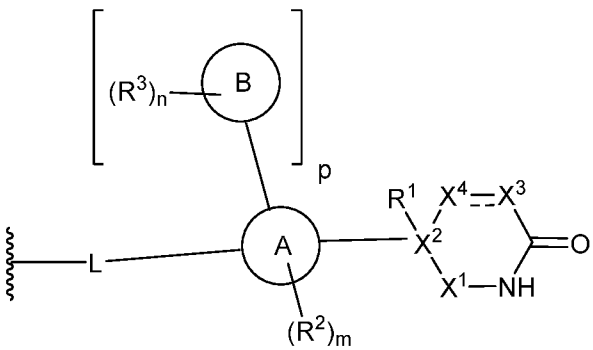




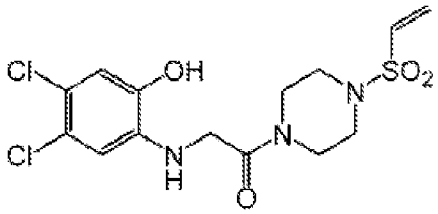
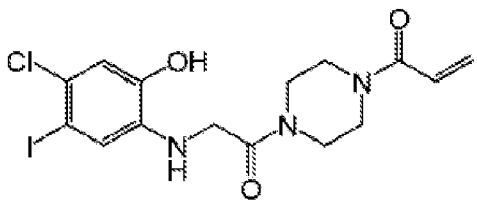
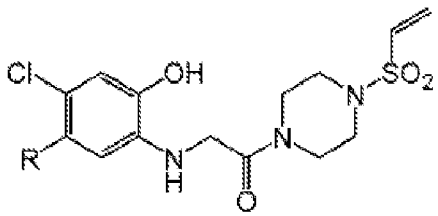
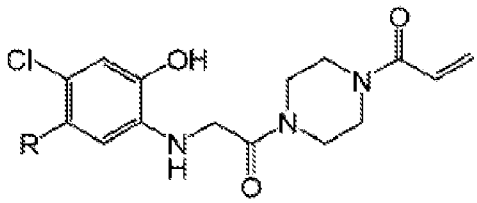
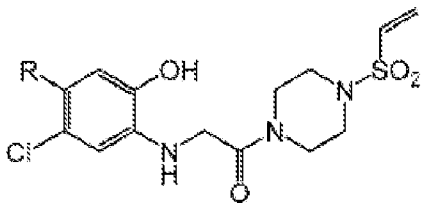
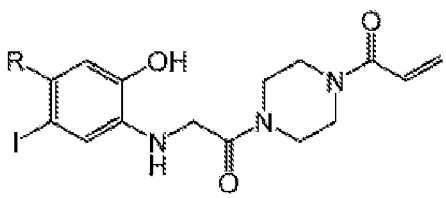
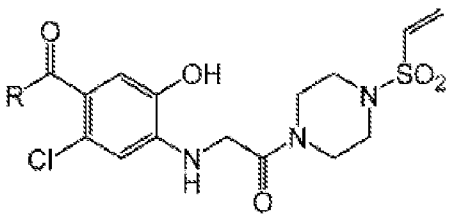
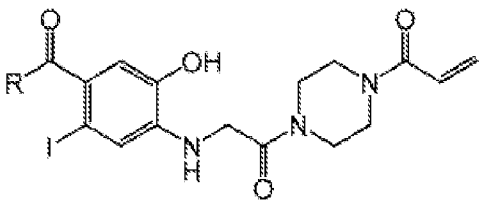
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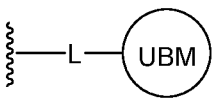
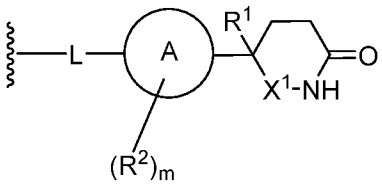
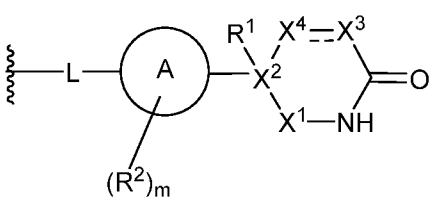
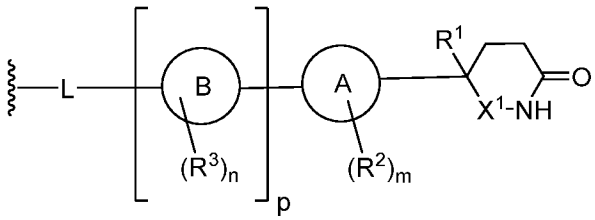
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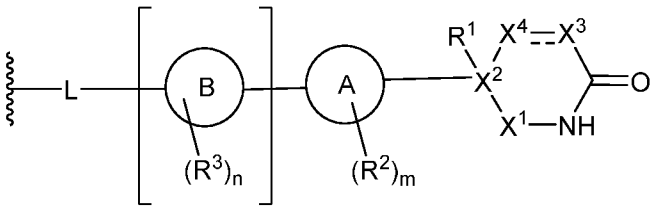
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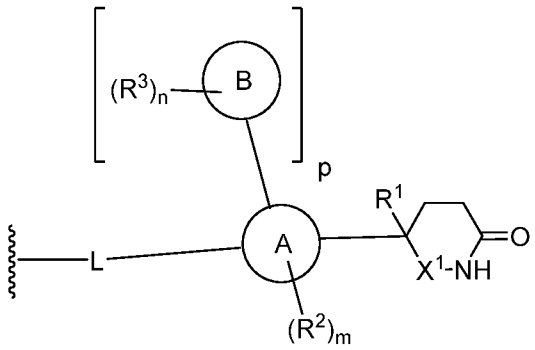
[00205] In some embodiments, TBM is a RasG12C ligand selected from

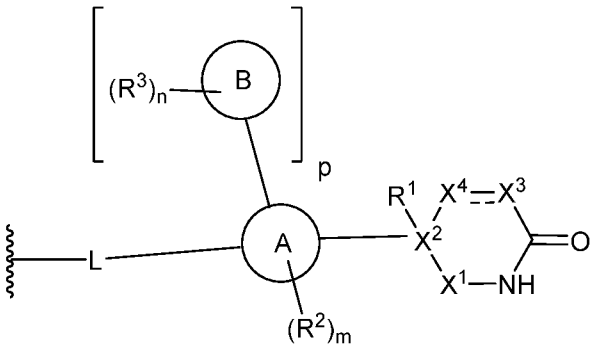
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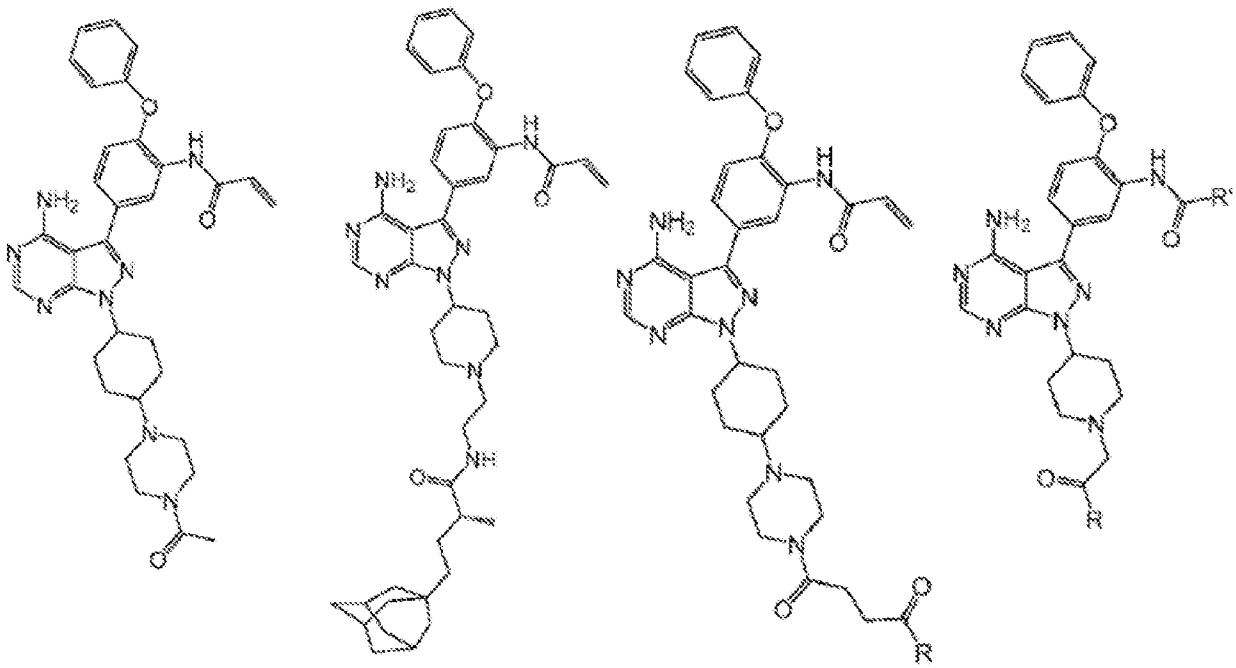


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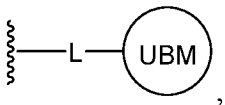
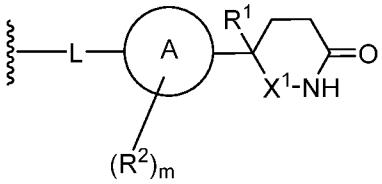
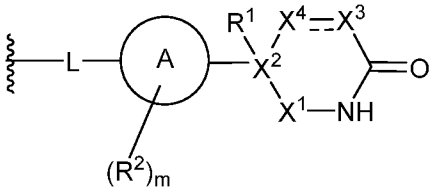
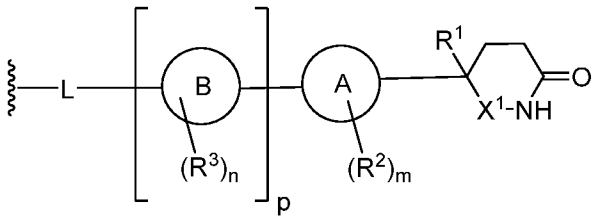
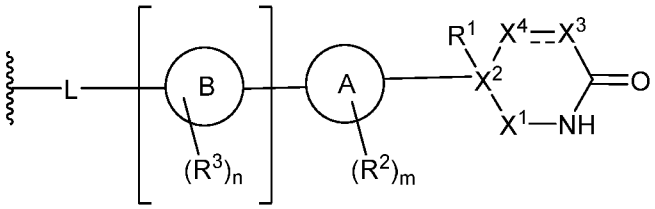
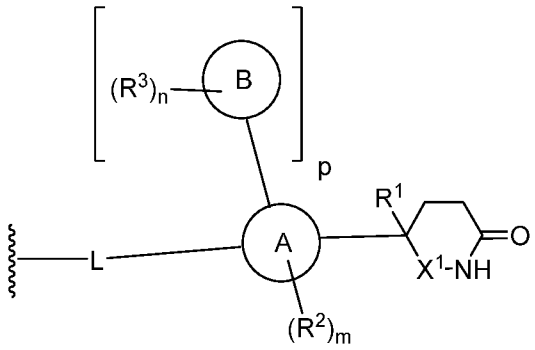
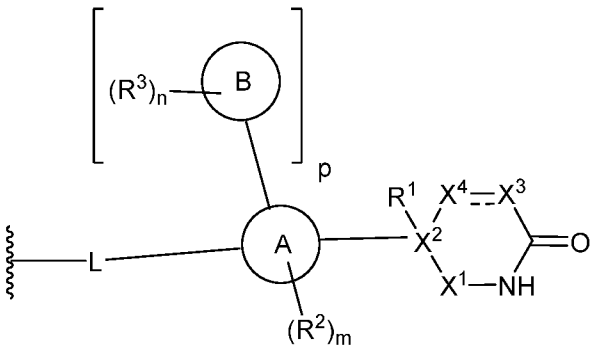


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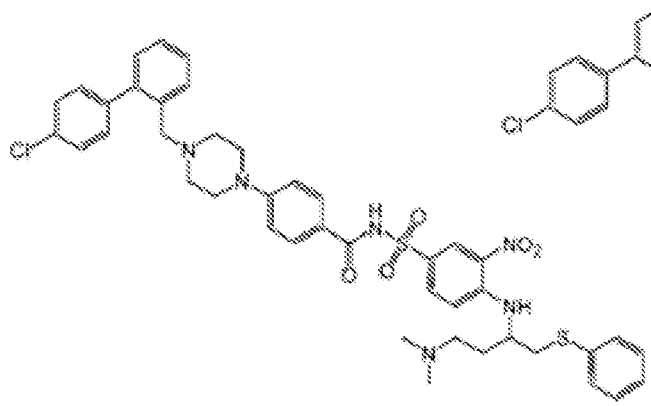
[00206] In some embodiments, TBM is a Her3 ligand selected from

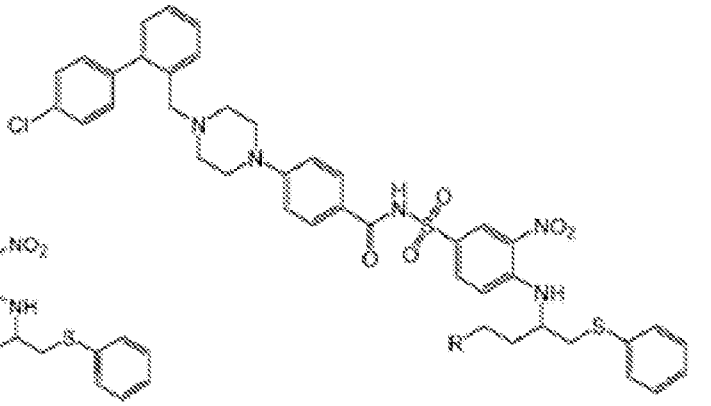


,

wherein R denotes attachment to  ,  ,  ,  ,  ,  ,  ; and R' is $-CH_2CH_3$ or $-CH=CH_2$.

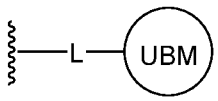
[00207] In some embodiments, TBM is a Bcl-2/Bcl-XL ligand selected from



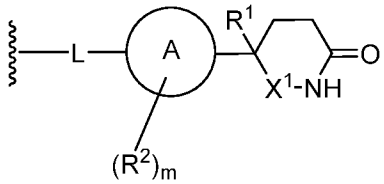


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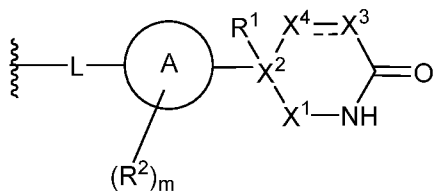
wherein R denotes attachment to



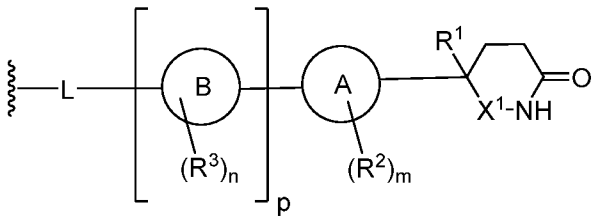
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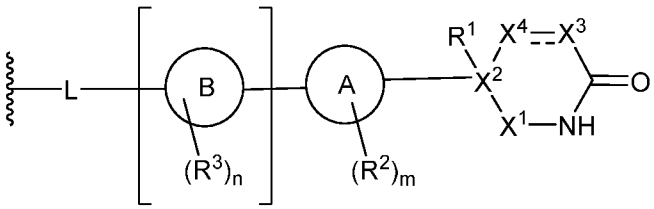
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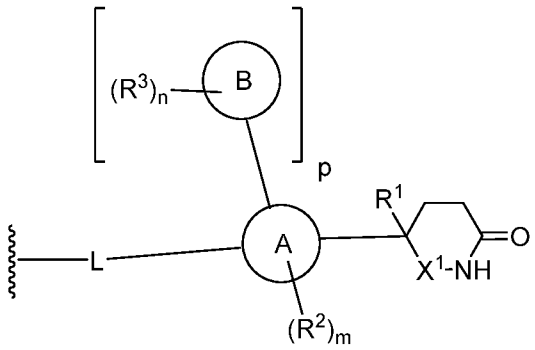
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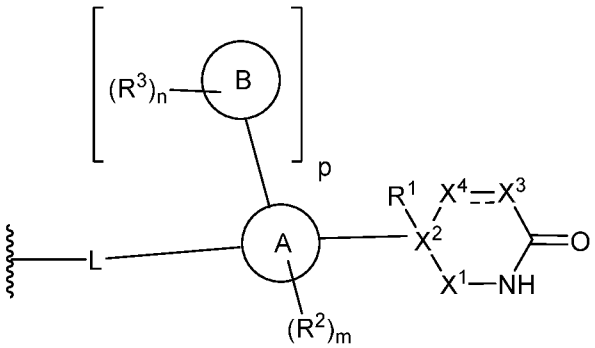
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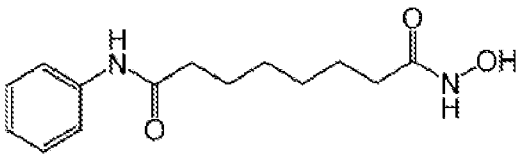


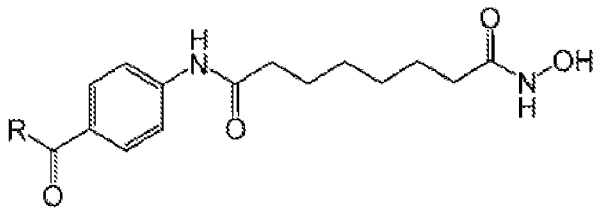
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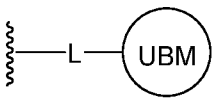
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[00208] In some embodiments, TBM is an HDAC ligand selected from

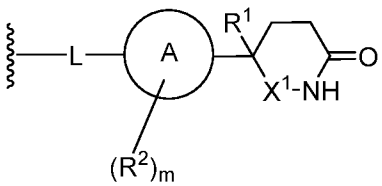




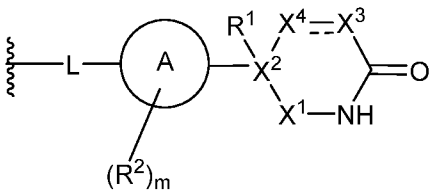
, wherein R denotes attachment to



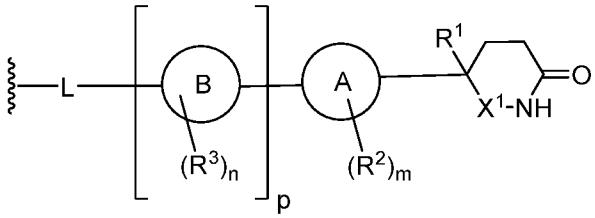
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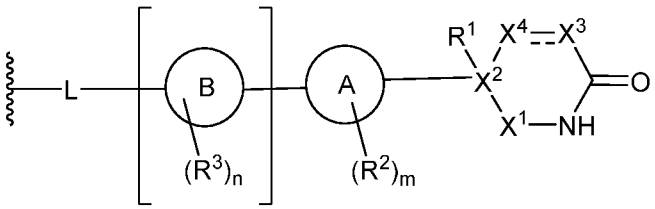
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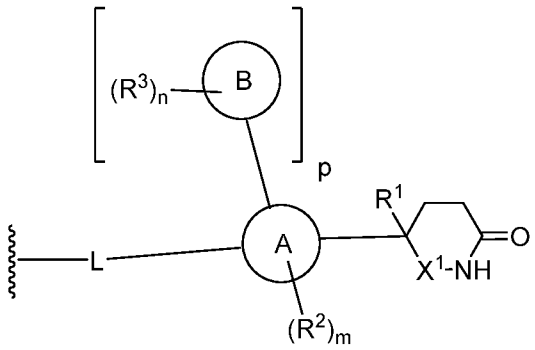
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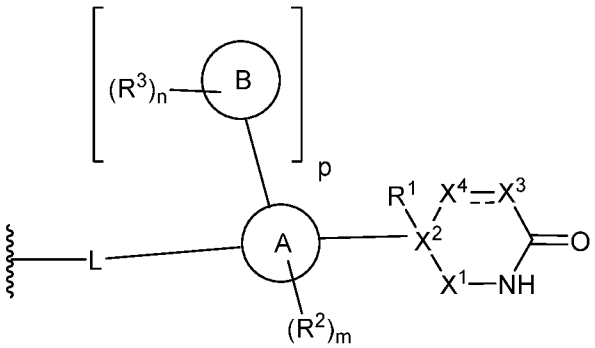
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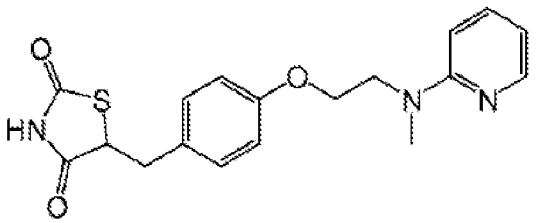


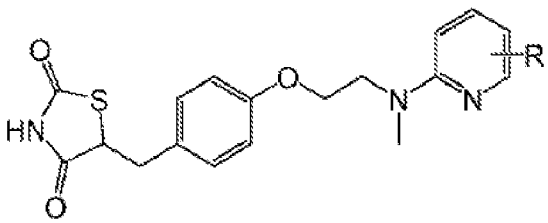
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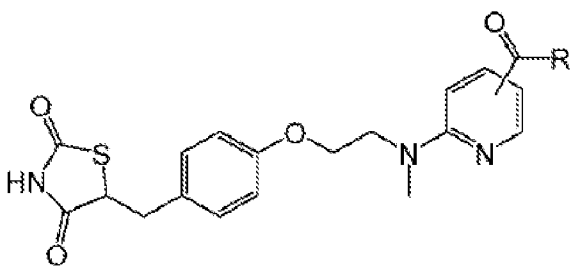


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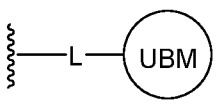
[00209] In some embodiments, TBM is a PPAR-gamma ligand selected from



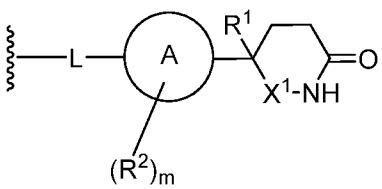




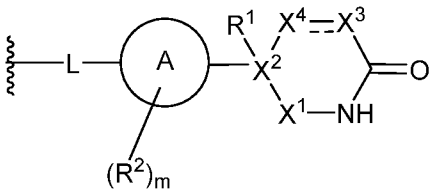
, wherein R denotes attachment to



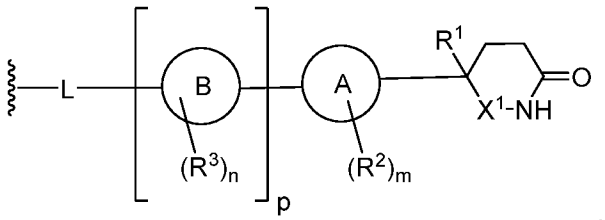
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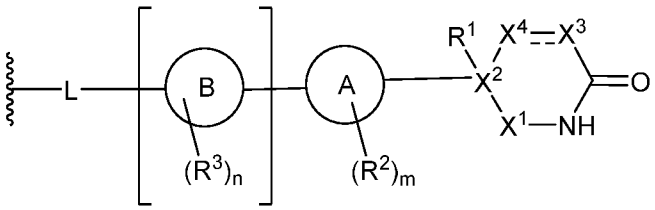
,


L
A
R1
X4=X3
X2
O
X1—NH
(R2)m

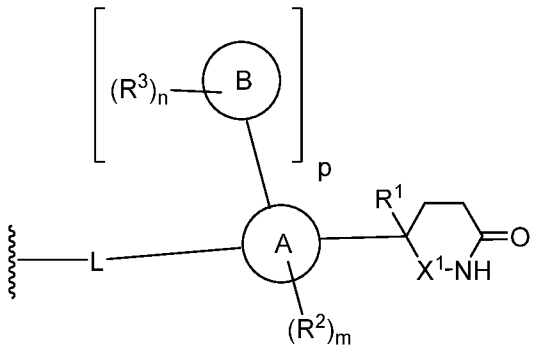
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L
B
A
R1
O
X1-NH
(R3)n
(R2)m
p

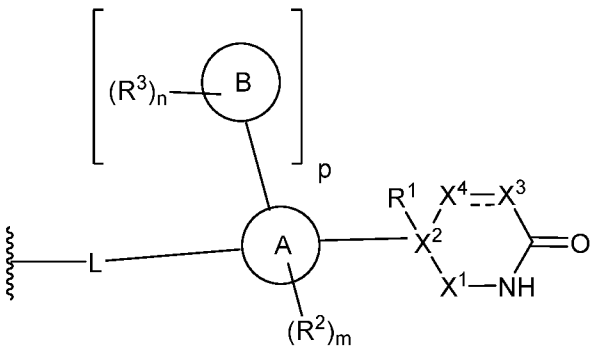
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L
B
A
R1
X4=X3
X2
O
X1—NH
(R3)n
(R2)m

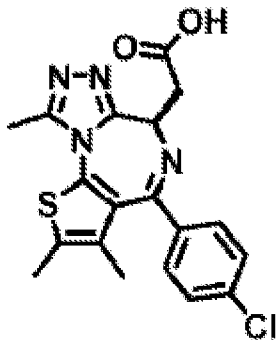
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(R3)n
B
p
L
A
R1
O
X1-NH
(R2)m

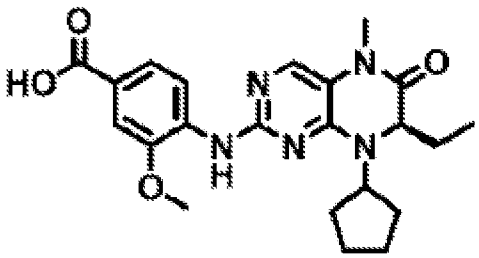
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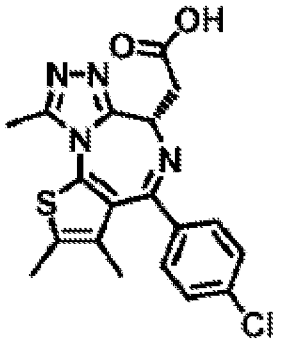

(R3)n
B
p
L
A
R1
X4=X3
X2
O
X1—NH
(R2)m

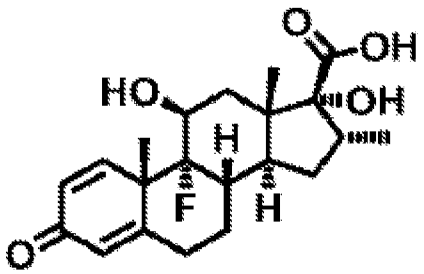
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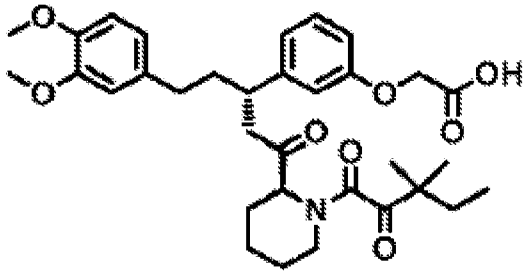


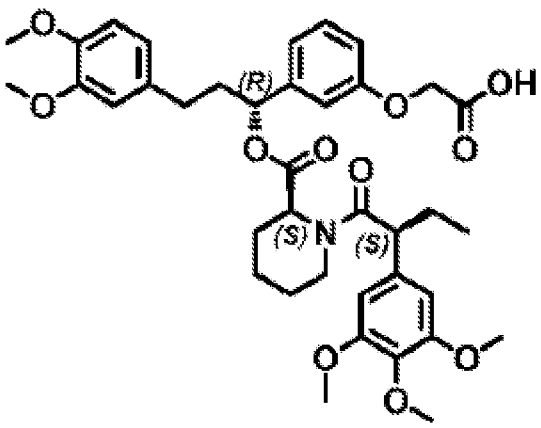
[00210] In some embodiments, TBM is selected from

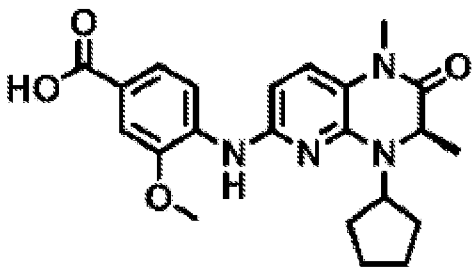




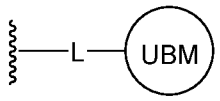
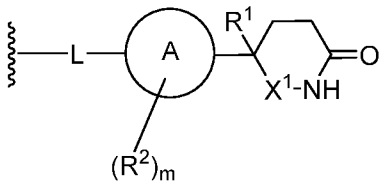
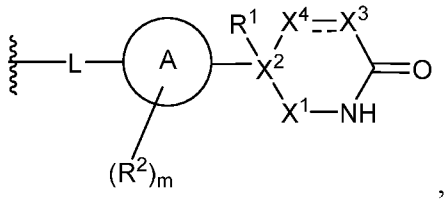
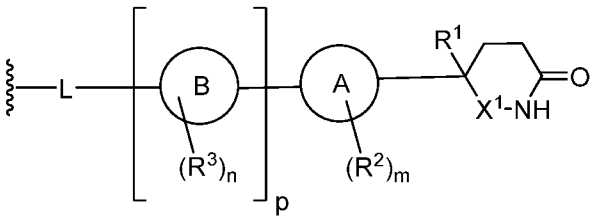
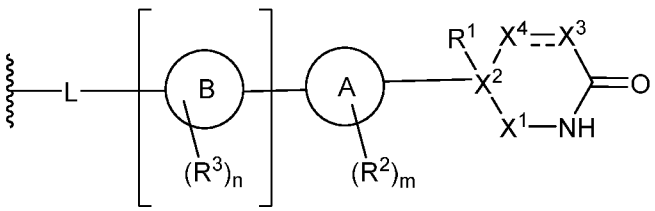
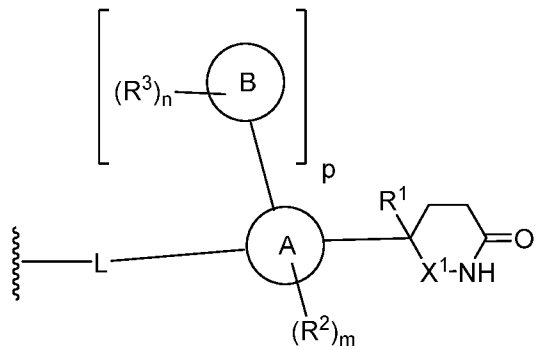
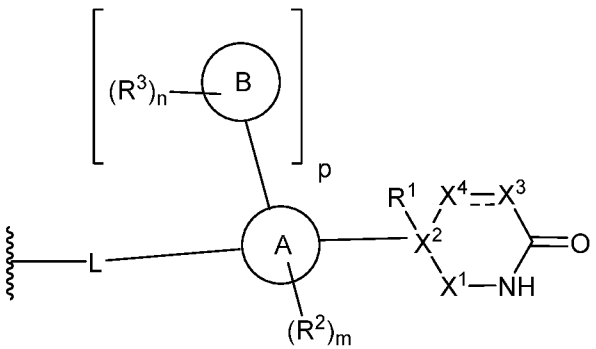






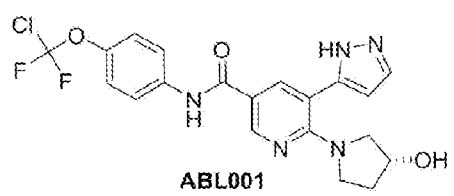


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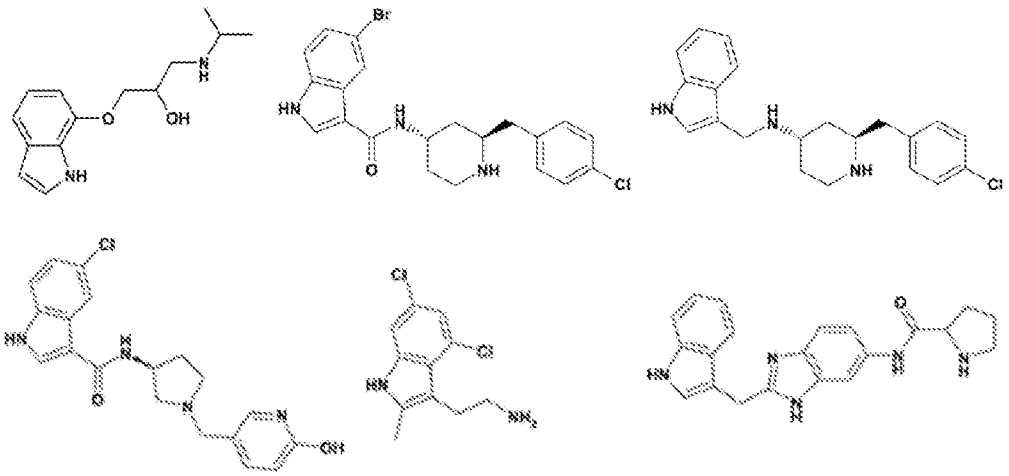
wherein  ,  ,  ,  ,  ,  , or  is attached to a modifiable carbon, oxygen, nitrogen or sulfur atom.

[00211] In some embodiments, TBM is an Abl, KRAS, SHP2, cRAF, MerTK or PRMT5 ligand that are selected from the following non-limiting examples:

Abl

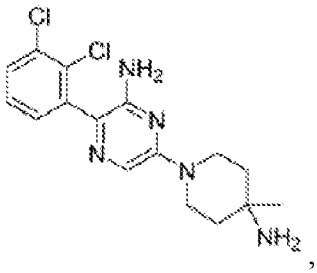

ABL001,

KRAS



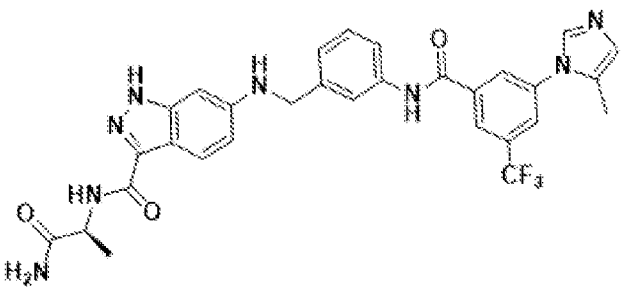
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SHP2



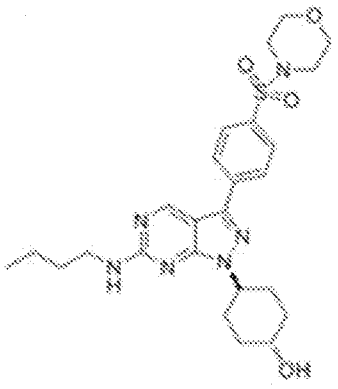
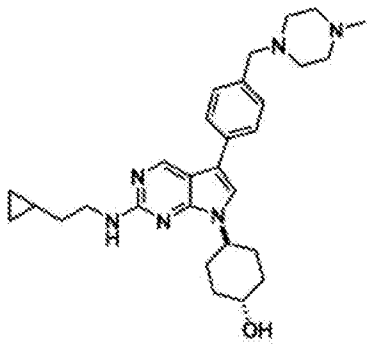
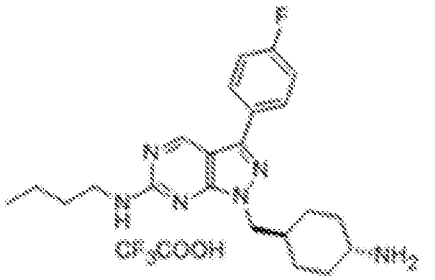
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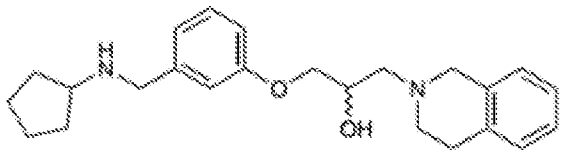
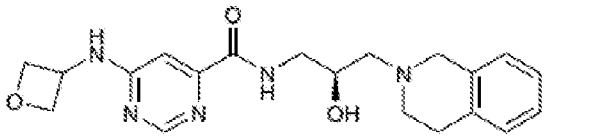


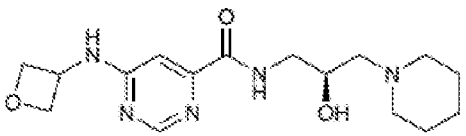
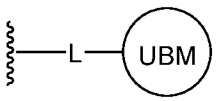
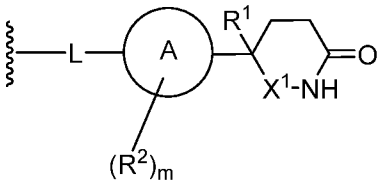
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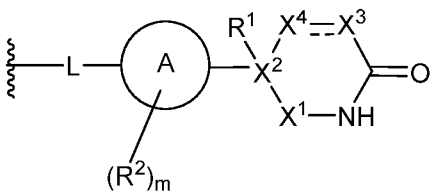
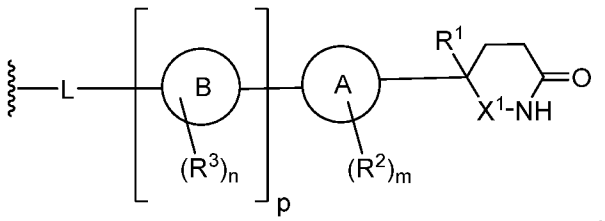
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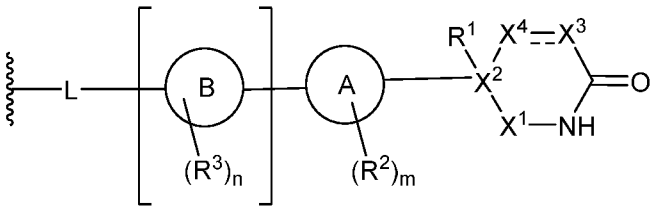
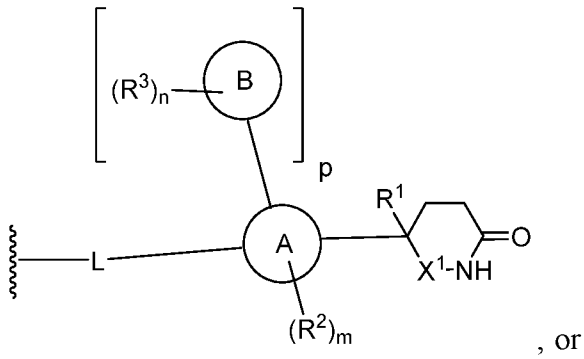

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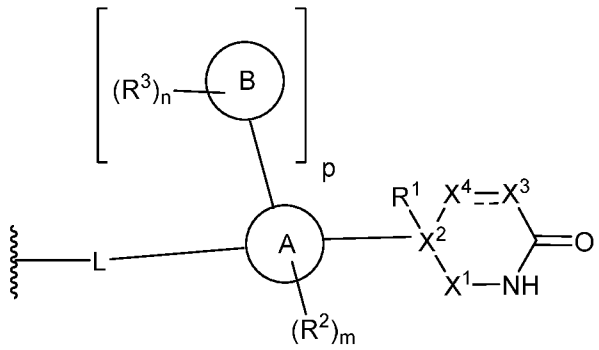
and PRMT5


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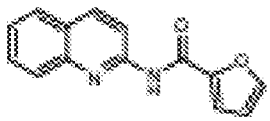
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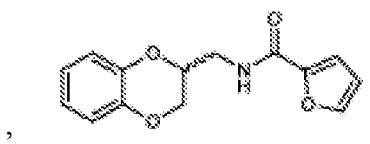
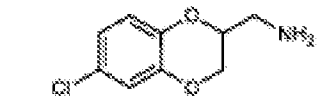
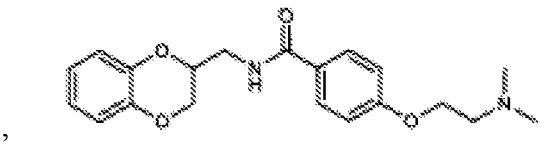
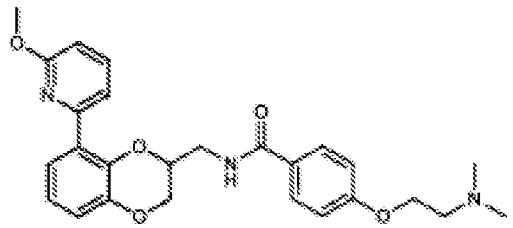
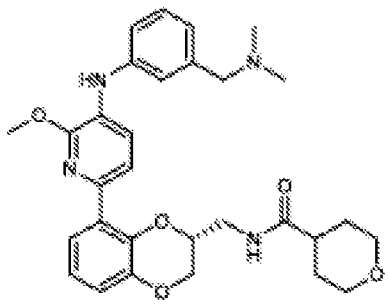


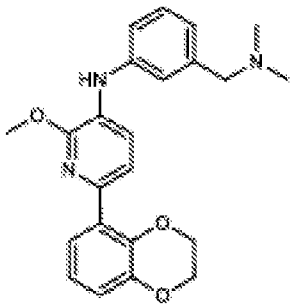
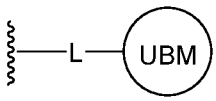
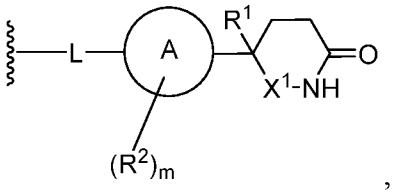
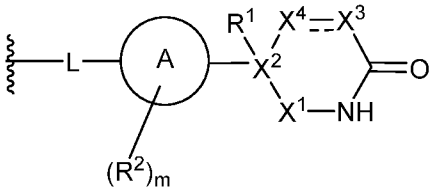
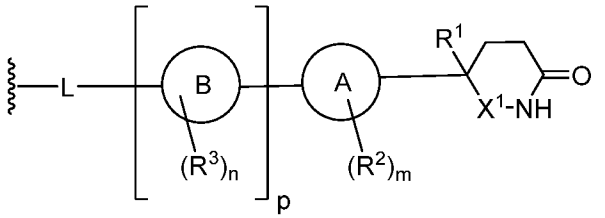
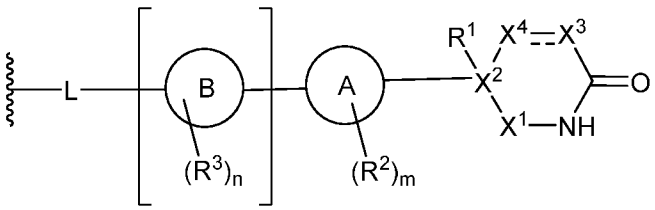
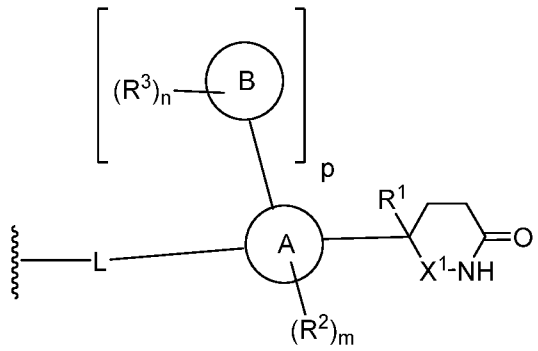
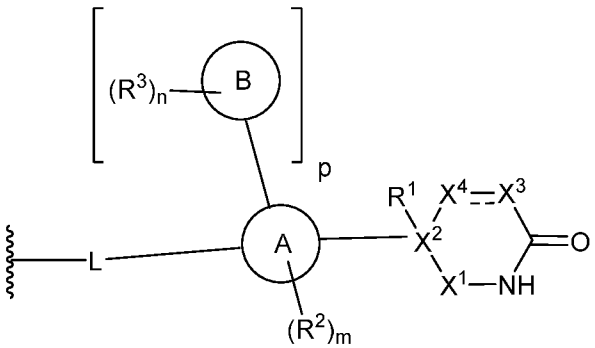
is attached to a modifiable carbon, oxygen, nitrogen or sulfur atom.

[00212] In some embodiments, a TBM moiety is selected from PTM moieties as recited in WO 2016/197032 the entirety of which is incorporated herein by reference. In some embodiments, a TBM moiety is selected from such inhibitors as described in WO 2016/197032 at paragraphs [00116] through [00173] wherein the recitation of a "Linker" moiety in WO 2016/197032 corresponds to the –L- group as defined and described herein.



[00213] In some embodiments, TBM is a KRAS ligand selected from

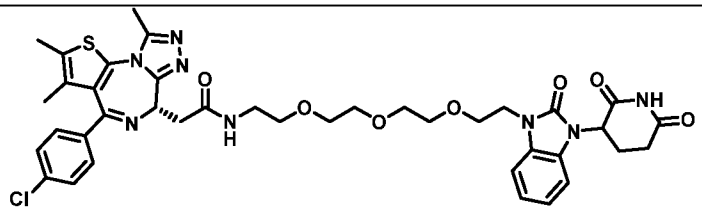
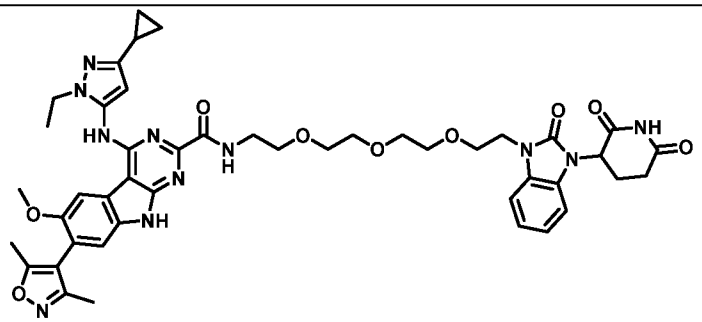
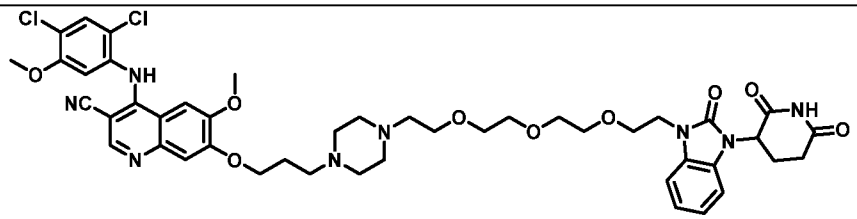
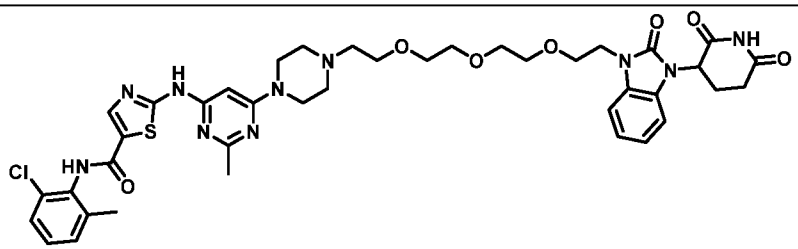
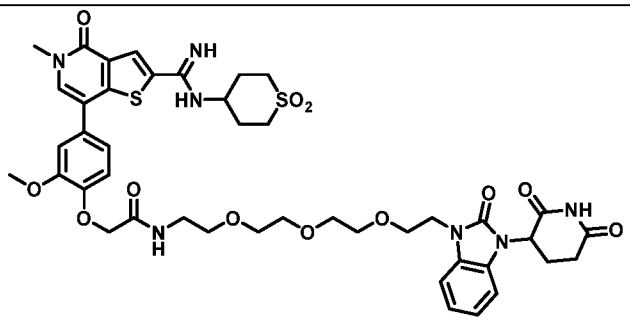
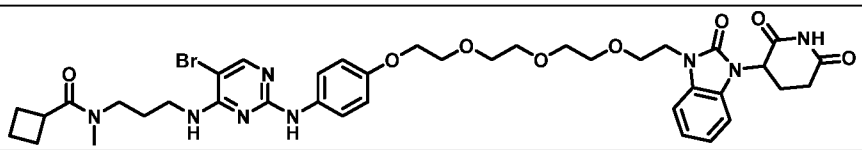
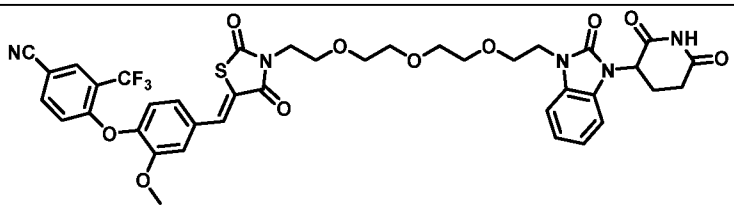

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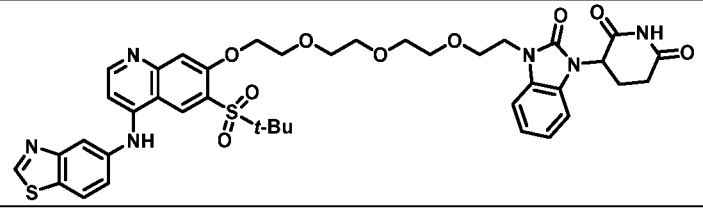
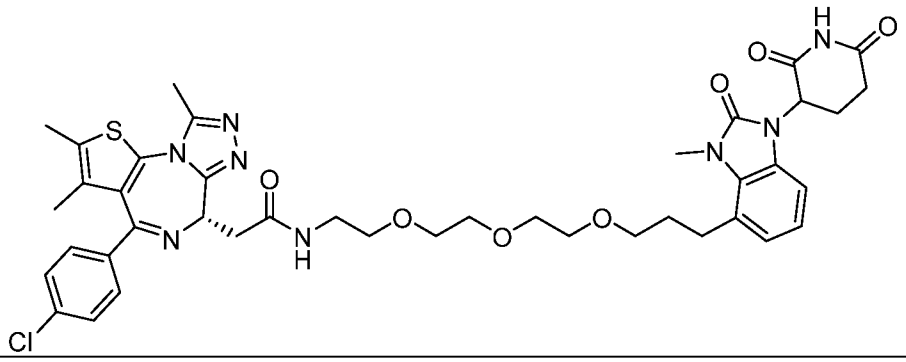
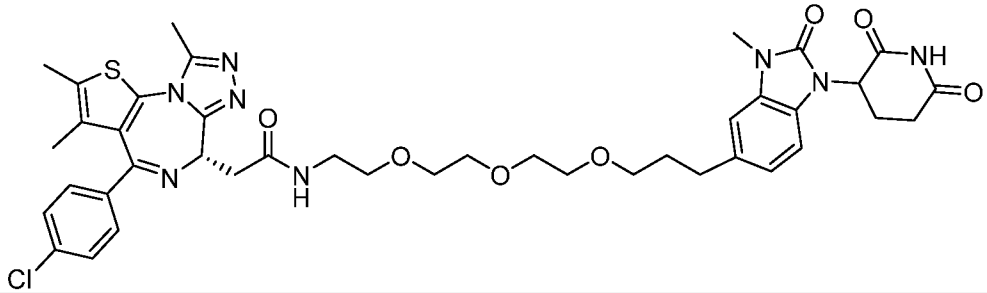
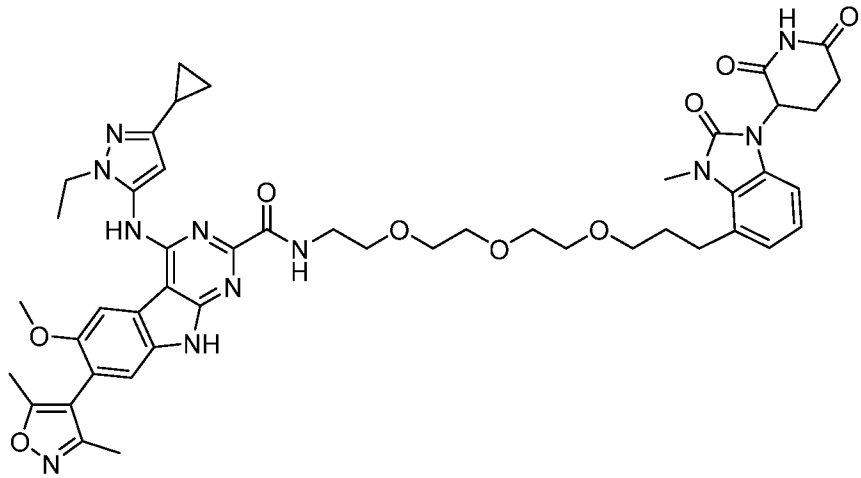

, wherein 
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, or 
is attached to a modifiable carbon, oxygen, nitrogen or sulfur atom.

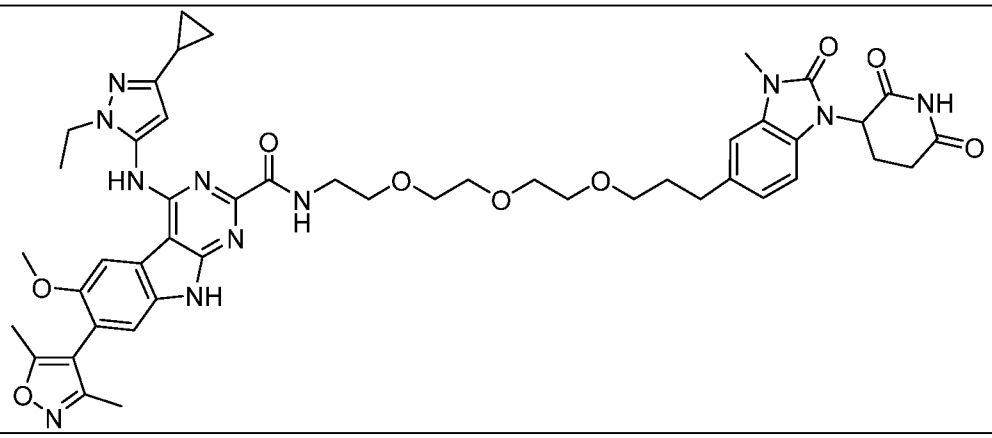
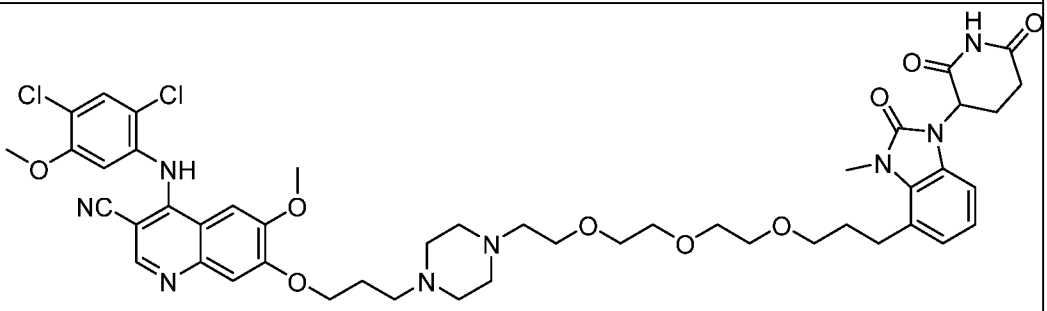
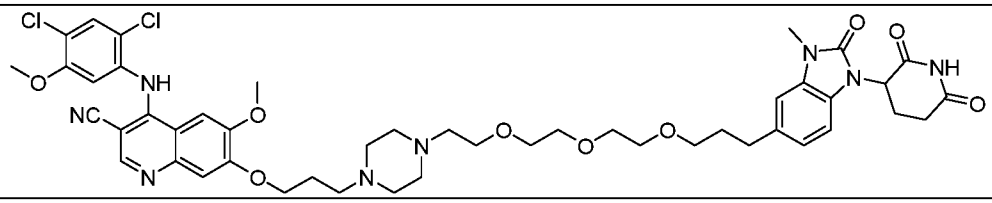
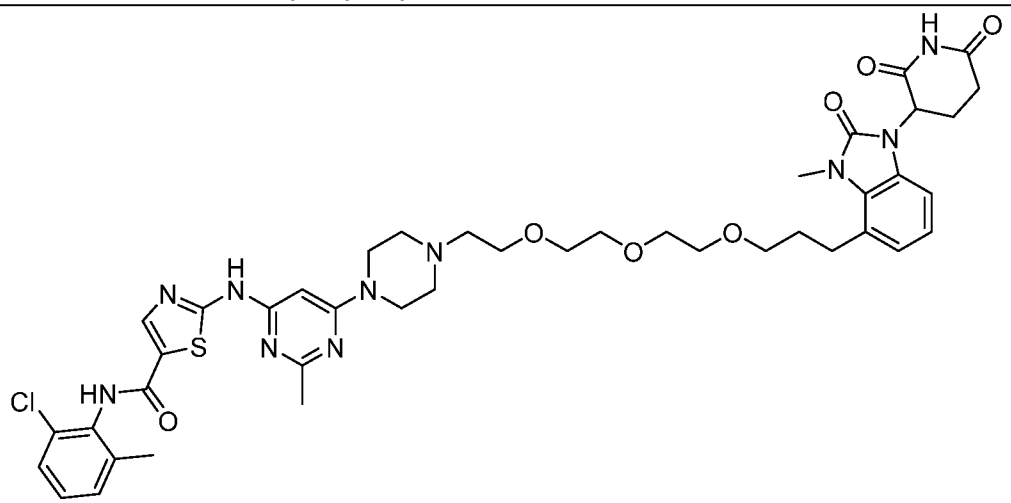
[00214] Exemplary compounds of the invention are set forth in **Table 1**, below.

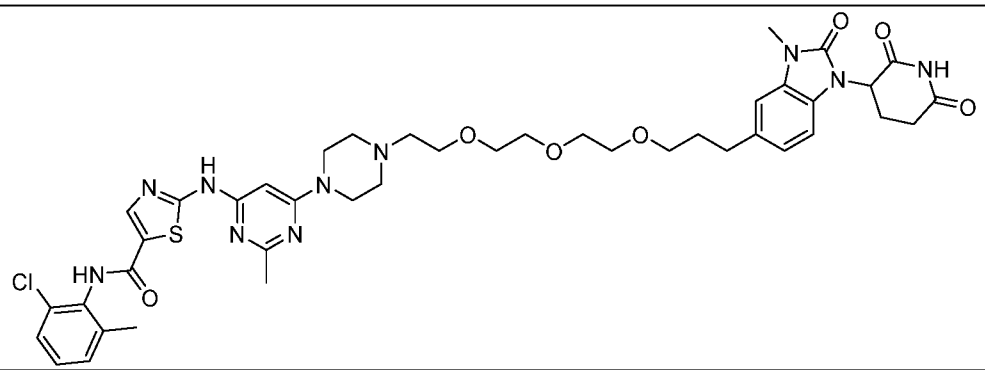
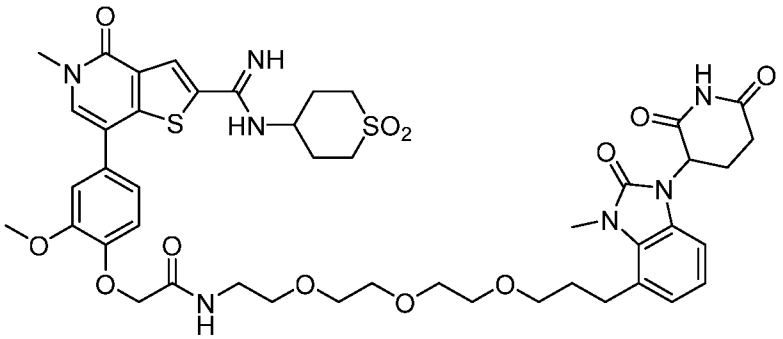
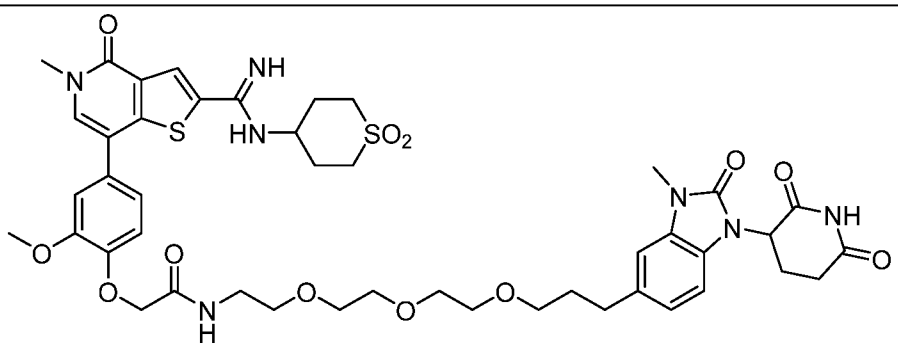
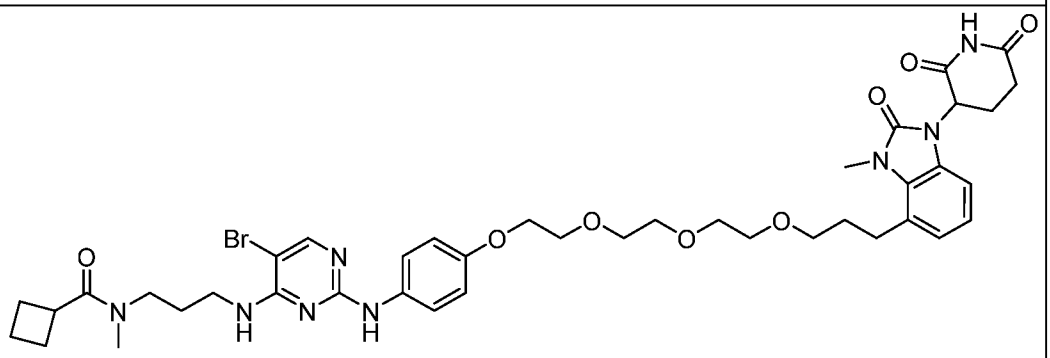
Table 1. Exemplary Compounds

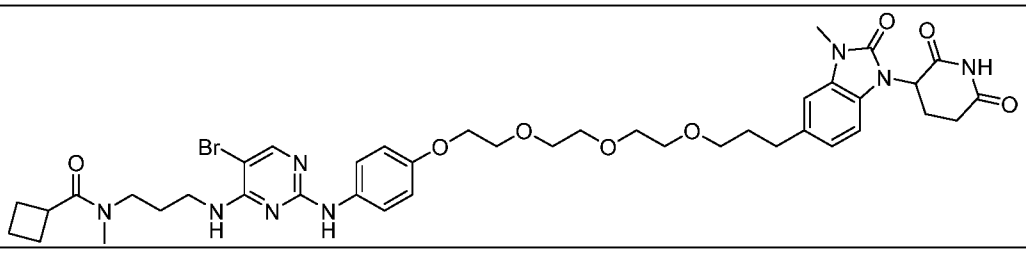
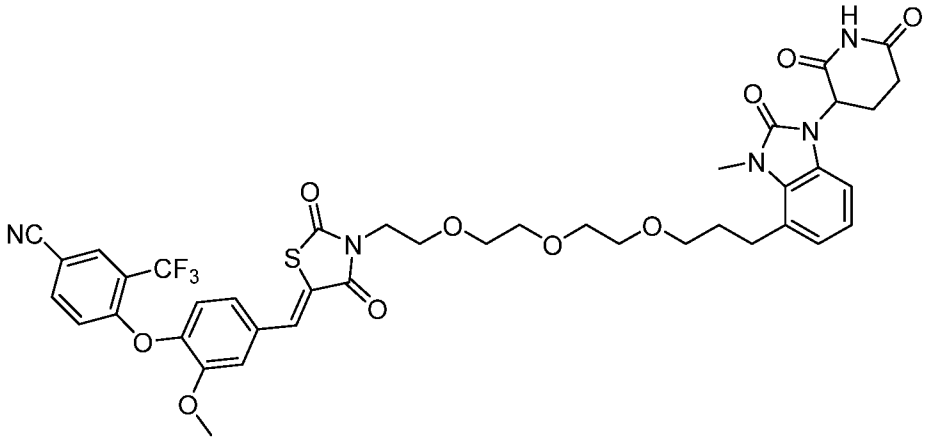
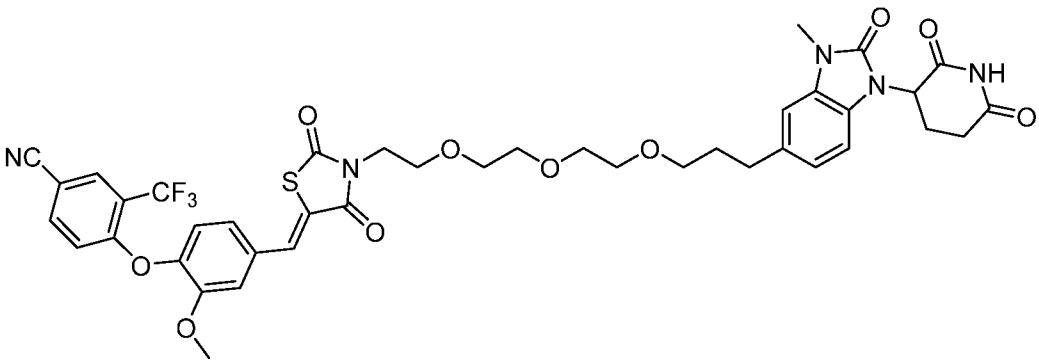
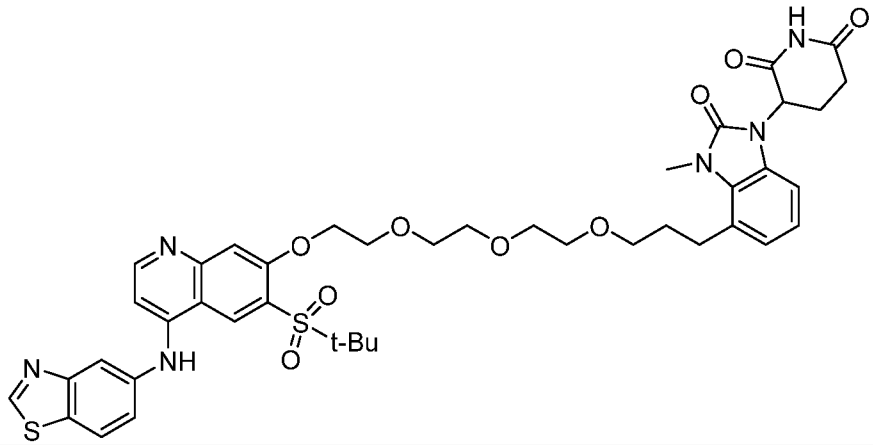
Compound Number	Structure

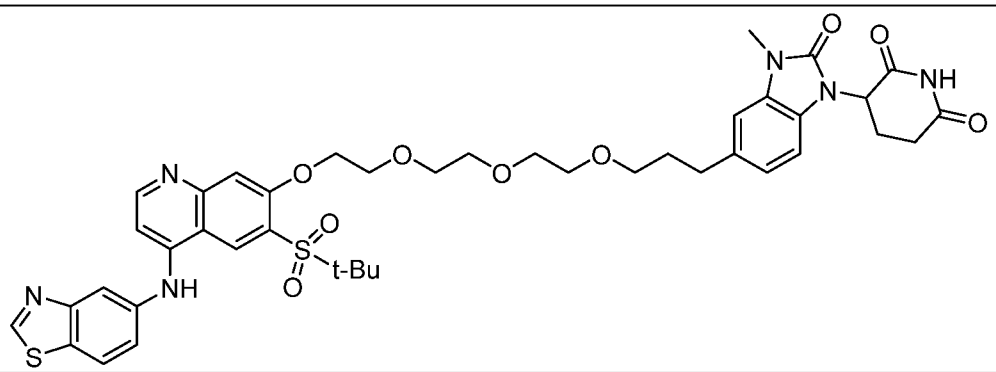
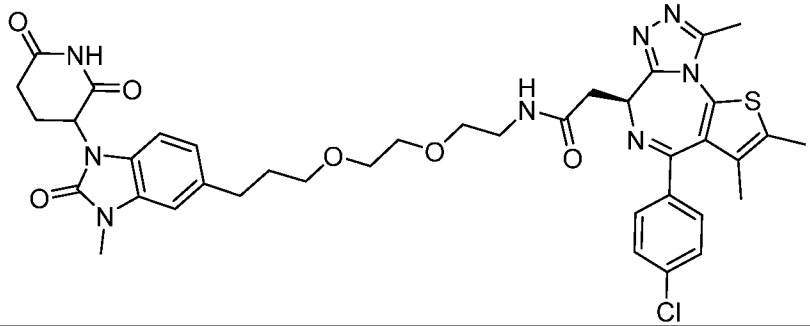
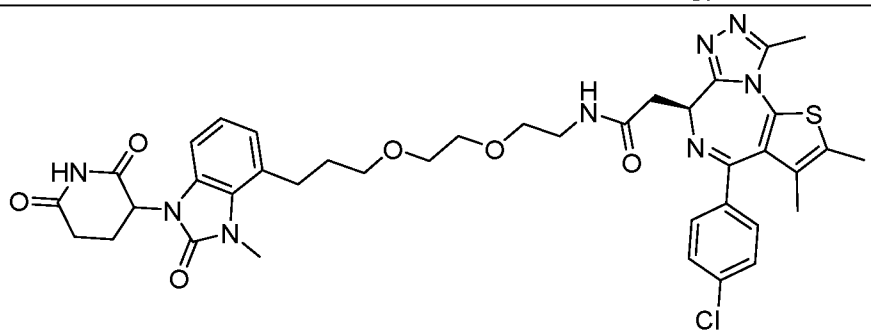
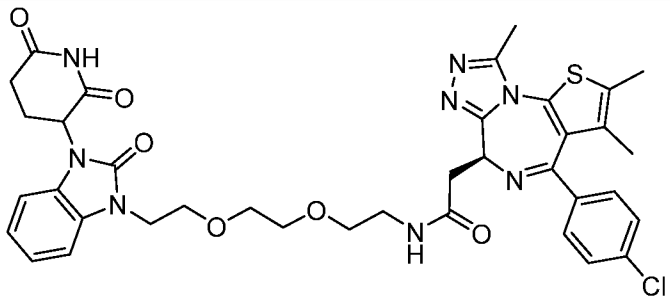
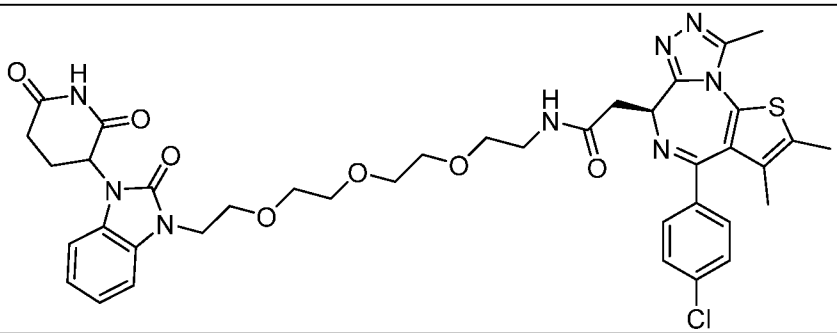
I-1	
I-2	
I-3	
I-4	
I-5	
I-6	
I-7	

I-8	
I-9	
I-10	
I-11	

I-12	
I-13	
I-14	
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I-16	
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I-19	

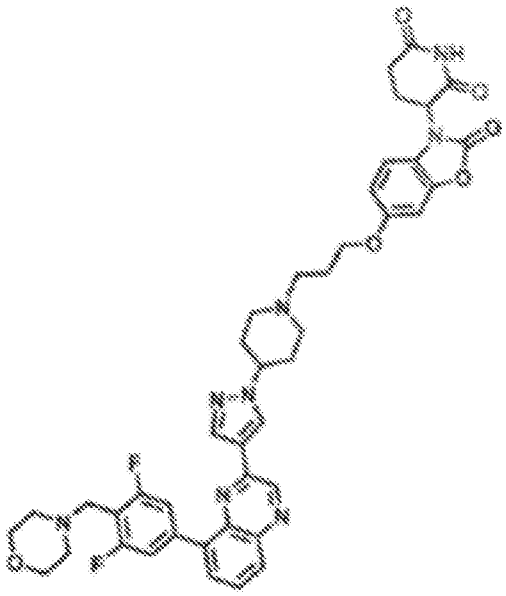
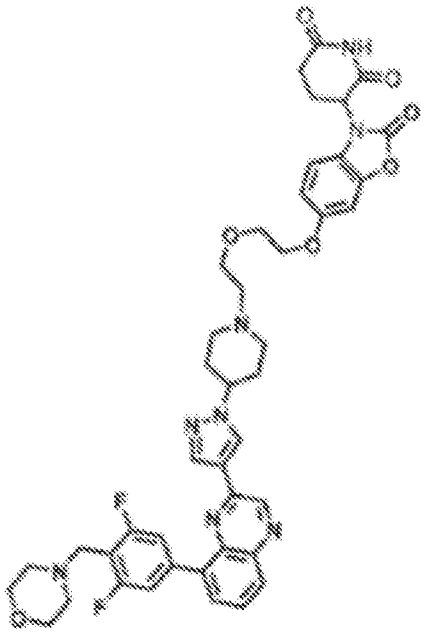
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I-22	
I-23	

I-24	
I-35	
I-36	
I-37	
I-38	

[00215] In some embodiments, the method employs a compound set forth in **Table 1**, above, or a pharmaceutically acceptable salt thereof.

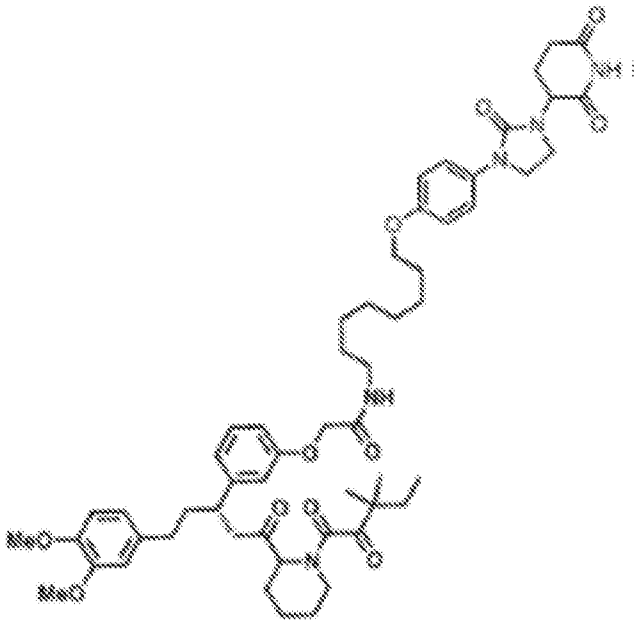
[00216] In some embodiments, the present invention provides a compound of formula **I**, wherein the compound is not any of compounds depicted in **Table A-1**, below.

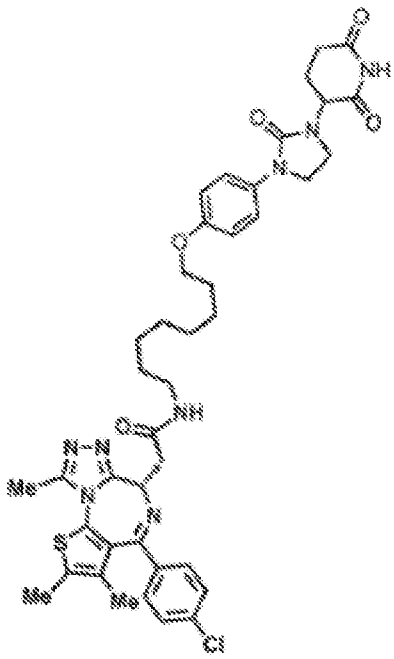
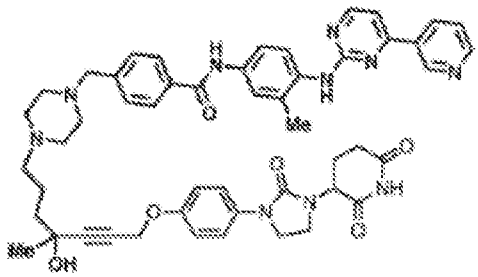
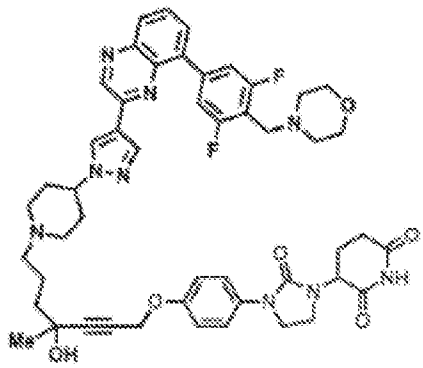
[00217] Table A-1.

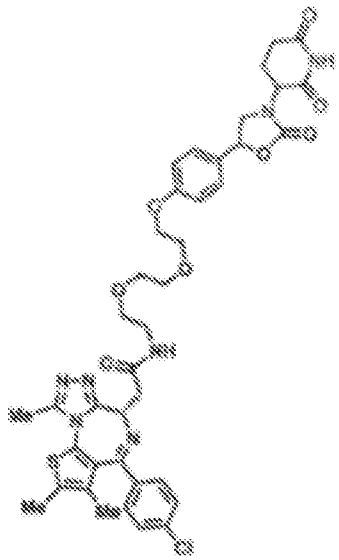
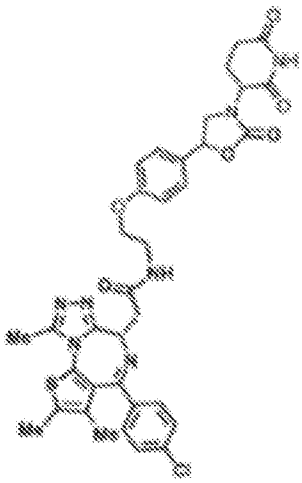
Compound Number	Structure
I-25	
I-26	

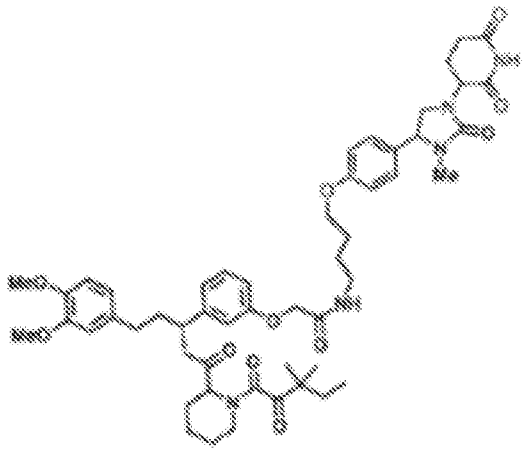
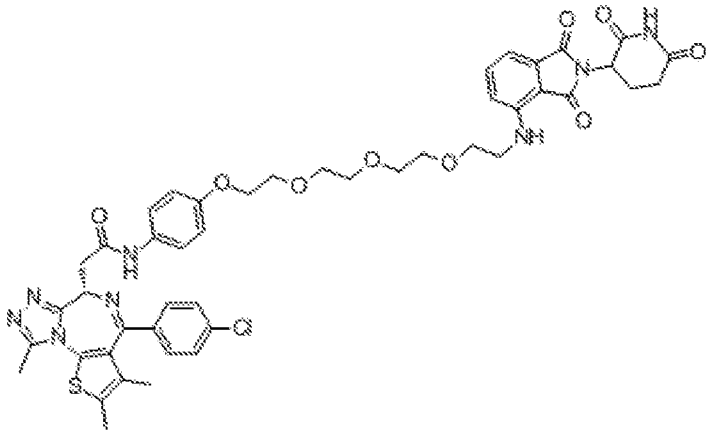
[00218] In some embodiments, the present invention provides a compound of formula **II-A**, wherein the compound is not any of compounds depicted in **Table A-2**, below.

[00219] **Table A-2**

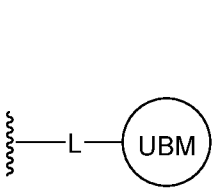
Compound Number	Structure
I-27	

I-28	
I-29	
I-30	

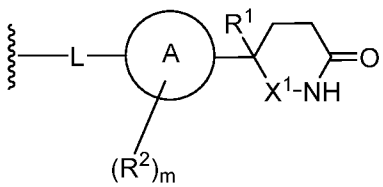
I-31	
I-32	

I-33	
I-34	

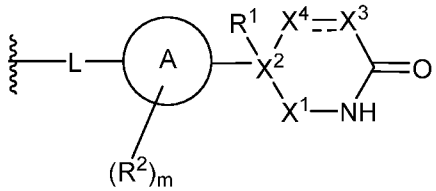
[00220] In some embodiments, TBM is one of the compounds in **Table 2**, below, wherein



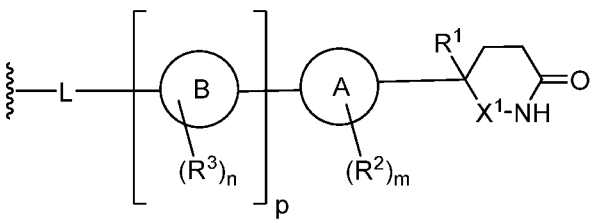
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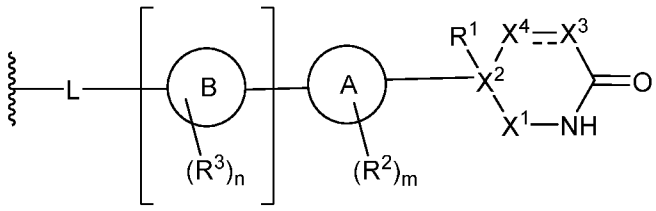
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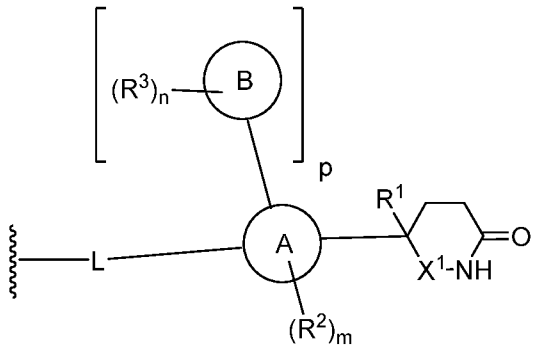
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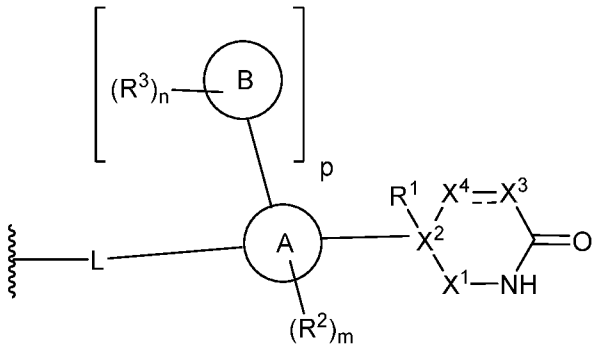
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, or



is attached to a modifiable carbon, oxygen, nitrogen or sulfur atom.

[00221] Table 2. Exemplary Drugs with Disease Indications and Gene Identifier for the Target Protein

Drug Name	Indication(s)	Gene
3196	anticholesterolaemic agent	THRB
Posiphen	for treatment of Alzheimer's disease	APP
Posiphen	for treatment of Alzheimer's disease	BACE1
MBO7133 (cytarabine prodrug)	antineoplastic agent	POLB
4SC-202	antineoplastic agent	HDAC1
4SC-202	antineoplastic agent	HDAC2
4SC-202	antineoplastic agent	HDAC3
4SC-202	antineoplastic agent	HDAC8
4SC-202	antineoplastic agent	FLT3
4SC-202	antineoplastic agent	VEGFA
4SC-205	antineoplastic agent	KIF11
768974	antiosteoporotic agent	PTH1R

Drug Name	Indication(s)	Gene
7a-methyl-19-nortestosterone,MENT	hormone replacement,male contraceptive	AR
A-007	antineoplastic agent	ESR1
A-007	antineoplastic agent	ESR2
oxybutynin	for treatment of incontinence	CHRM1
oxybutynin	for treatment of incontinence	CHRM2
oxybutynin	for treatment of incontinence	CHRM3
Testosterone	hormone replacement	AR
ABC294640	antineoplastic agent	SPHK1
ABC294640	antineoplastic agent	SPHK2
Aripiprazole	antipsychotic agent	DRD2
Aripiprazole	antipsychotic agent	HTR1A
Aripiprazole	antipsychotic agent	HTR2A
paclitaxel	antineoplastic agent	BCL2
paclitaxel	antineoplastic agent	TUBB1
navitoclax, ABT-263	antineoplastic agent	BCL2
navitoclax, ABT-263	antineoplastic agent	BCL2L1
navitoclax, ABT-263	antineoplastic agent	BCL2L2
fenofibrate	antidyslipidaemic agent	PPARA
Linifanib	antineoplastic agent	CSF1R
Linifanib	antineoplastic agent	FLT1
Linifanib	antineoplastic agent	FLT3
Linifanib	antineoplastic agent	FLT4
Linifanib	antineoplastic agent	KDR
Linifanib	antineoplastic agent	KIT
Linifanib	antineoplastic agent	PDGFRB
Linifanib	antineoplastic agent	RET
Linifanib	antineoplastic agent	TIE2

Drug Name	Indication(s)	Gene
AC-201	antidiabetic	IL1B
AC-201	antidiabetic	IL1RN
quizartinib	antineoplastic agent	FLT3
AC430	antiinflammatory agent,antineoplastic agent	JAK2
AC480	antineoplastic agent	EGFR
AC480	antineoplastic agent	ERBB2
AC480	antineoplastic agent	ERBB3
AC480	antineoplastic agent	ERBB4
acamprosate	for treatment of alcohol-dependance	GRIN3A
acamprosate	antineoplastic agent	GRM5
toremifene	antineoplastic agent,SERM	ESR1
acarbose	antidiabetic	AMY2A
acarbose	antidiabetic	GAA
acarbose	antidiabetic	MGAM
acarbose	antidiabetic	SI
organic nitrate + l-arginine	vasodilator	NOS3
Acccretropin	for treatment of turner´s syndrome	GHR
rabeprazole	Proton pump inhibitor	ATP4A
aclidinium	bronchodilator	CHRM1
aclidinium	bronchodilator	CHRM2
aclidinium	bronchodilator	CHRM3
aclidinium	bronchodilator	CHRM4
aclidinium	bronchodilator	CHRM5
acotiamide	for treatment of functional dyspepsia	ACHE
ACP-001	hormone replacement	GHR
ACP-104	antipsychotic agent	CHRM1
ACP-104	antipsychotic agent	DRD2

Drug Name	Indication(s)	Gene
ACP-104	antipsychotic agent	DRD3
ACP-104	antipsychotic agent	HTR2A
ACTB1003	antineoplastic agent	FGFR1
ACTB1003	antineoplastic agent	FGFR2
ACTB1003	antineoplastic agent	FGFR3
ACTB1003	antineoplastic agent	FGFR4
ACTB1003	antineoplastic agent	RPS6KB1
ACY-1215	antineoplastic agent	HDAC6
AD 337	analgesic,for treatment of fibromyalgia	SLC6A2
AD 337	analgesic,for treatment of fibromyalgia	SLC6A4
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
theophylline	bronchodilator	ADORA1
theophylline	bronchodilator	ADORA2A
theophylline	bronchodilator	ADORA2B
theophylline	bronchodilator	PDE3A
theophylline	bronchodilator	PDE4A
theophylline	bronchodilator	PDE4B
theophylline	bronchodilator	PDE5A
ADL5747	analgesic	OPRD1
ADL5859	analgesic	OPRD1
ADL5945	motilitant	OPRM1
ADL7445	motilitant	OPRM1
capsaicin	analgesic	TRPV1
fluticasone propionate	bronchodilator	NR3C1
salmeterol	bronchodilator	ADRB2

Drug Name	Indication(s)	Gene
ADX10059	antimigraine agent,for treatment of gastroesophageal reflux disease	GRM5
ADX415	antihypertensive agent	ADRA2A
ADX-71149	antipsychotic agent,antidepressant,anxiolytic	GRM2
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
AES-103	for treatment of sickle-cell disease	HBB
doxorubicin	antineoplastic agent	TOP2A
AEZS-112, ZEN-012	antineoplastic agent	TOP2A
AEZS-112, ZEN-012	antineoplastic agent	TUBB
AEZS-112, ZEN-012	antineoplastic agent	TUBB1
Afamelanotide	dermatological agent	MC1R
afatinib	antineoplastic agent	EGFR
afatinib	antineoplastic agent	ERBB2
ethinyl estradiol	contraceptive	ESR1
levonorgestrel	contraceptive	ESR1
levonorgestrel	contraceptive	PGR
levonorgestrel	contraceptive	SRD5A1
mecamylamine	motilitant	CHRNA2
AGI-1067, succinobucol	antiatherosclerosis agent	VCAM1
AGIX-4207	antiinflammatory agent,DMARD	unknown
AGN-214868	analgesic,neuralgia	ADRA1A
AGN-214868	analgesic,neuralgia	ADRA1B
AGN-214868	analgesic,neuralgia	ADRA1D
AGN-214868	analgesic,neuralgia	ADRA2A
AGN-214868	analgesic,neuralgia	ADRA2B
AGN-214868	analgesic,neuralgia	ADRA2C

Drug Name	Indication(s)	Gene
agomelatine	antidepressant	MTNR1B
agomelatine	antidepressant	HTR2B
agomelatine	antidepressant	HTR2C
agomelatine	antidepressant	MTNR1A
hydroxychloroquine	antirheumatic agent	TLR7
hydroxychloroquine	antirheumatic agent	TLR9
paclitaxel	antineoplastic agent	BCL2
paclitaxel	antineoplastic agent	TUBB1
AIKO-150	opioid antagonist	OPRM1
AIR645	antiasthmatic agent	IL4RA
AKB-6548	for treatment of anaemia	EGLN1
AKB-6548	for treatment of anaemia	EGLN2
AKL-0707	hormone replacement	GHRH
ALB109564(a)	antineoplastic agent	TUBB
ALB-127158(a)	antiobesity agent	MCHR1
salbutamol	bronchodilator	ADRB2
aleglitazar	cardiovascular agent	PPARA
aleglitazar	cardiovascular agent	PPARG
alfuzosin	for treatment of benign prostatic hyperplasia	ADRA1A
alfuzosin	for treatment of benign prostatic hyperplasia	ADRA1B
alfuzosin	for treatment of benign prostatic hyperplasia	ADRA1D
lidocaine	anesthetic	SCN10A
lidocaine	anesthetic	SCN5A
lidocaine	anesthetic	SCN9A
pemetrexed	antineoplastic agent	DHFR

Drug Name	Indication(s)	Gene
pemetrexed	antineoplastic agent	GART
pemetrexed	antineoplastic agent	TYMS
aliskiren	antihypertensive agent	REN
aliskiren	antihypertensive agent	REN
amlodipine	antihypertensive agent	CACNA1C
amlodipine	antihypertensive agent	CACNA1D
amlodipine	antihypertensive agent	CACNA1S
amlodipine	antihypertensive agent	CACNA2D1
amlodipine	antihypertensive agent	CACNB2
Alitretionine	antineoplastic agent	RARA
Alitretionine	antineoplastic agent	RARB
Alitretionine	antineoplastic agent	RARG
Alitretionine	antineoplastic agent	RXRA
Alitretionine	antineoplastic agent	RXRB
Alitretionine	antineoplastic agent	RXRG
Alitretionine	antineoplastic agent	RARA
Alitretionine	antineoplastic agent	RARB
Alitretionine	antineoplastic agent	RARG
Alitretionine	antineoplastic agent	RXRA
Alitretionine	antineoplastic agent	RXRB
Alitretionine	antineoplastic agent	RXRG
ALKS 33	for treatment of alcohol dependance,antidepressant	OPRD1
ALKS 33	for treatment of alcohol dependance,antidepressant	OPRK1
ALKS 33	for treatment of alcohol dependance,antidepressant	OPRM1
baclofen	for treatment of alcohol dependance	GABBR1

Drug Name	Indication(s)	Gene
baclofen	for treatment of alcohol dependance	GABBR2
ALKS 33	for treatment of alcohol dependance,antidepressant	OPRD1
ALKS 33	for treatment of alcohol dependance,antidepressant	OPRK1
ALKS 33	for treatment of alcohol dependance,antidepressant	OPRM1
ALKS 37	motilitant	OPRD1
ALKS 37	motilitant	OPRK1
ALKS 37	motilitant	OPRM1
ALKS 33	for treatment of alcohol dependance,antidepressant	OPRD1
ALKS 33	for treatment of alcohol dependance,antidepressant	OPRK1
ALKS 33	for treatment of alcohol dependance,antidepressant	OPRM1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRD1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRK1
almorexant	sleep disorder treatment	HCRTR1
almorexant	sleep disorder treatment	HCRTR2
almotriptan	antimigraine agent	HTR1B
almotriptan	antimigraine agent	HTR1D
morphine	analgesic	OPRD1
morphine	analgesic	OPRD1
morphine	analgesic	OPRK1
morphine	analgesic	OPRK1

Drug Name	Indication(s)	Gene
morphine	analgesic	OPRM1
morphine	analgesic	OPRM1
naltrexone	analgesic	OPRD1
naltrexone	analgesic	OPRD1
naltrexone	analgesic	OPRK1
naltrexone	analgesic	OPRK1
naltrexone	analgesic	OPRM1
naltrexone	analgesic	OPRM1
naltrexone	analgesic	SIGMAR1
alogliptin	antidiabetic	DPP4
alosetron	for treatment of irritable bowel syndrome	HTR3A
alprazolam	anxiolytic, sedative,hypnotic	GABRA1
alprazolam	anxiolytic, sedative,hypnotic	GABRA2
alprazolam	anxiolytic, sedative,hypnotic	GABRA3
alprazolam	anxiolytic, sedative,hypnotic	GABRA4
alprazolam	anxiolytic, sedative,hypnotic	GABRA5
alprazolam	anxiolytic, sedative,hypnotic	GABRA6
alprazolam	anxiolytic, sedative,hypnotic	GABRB1
alprazolam	anxiolytic, sedative,hypnotic	GABRB2
alprazolam	anxiolytic, sedative,hypnotic	GABRB3
alprazolam	anxiolytic, sedative,hypnotic	GABRD
alprazolam	anxiolytic, sedative,hypnotic	GABRE
alprazolam	anxiolytic, sedative,hypnotic	GABRG1
alprazolam	anxiolytic, sedative,hypnotic	GABRG2
alprazolam	anxiolytic, sedative,hypnotic	GABRG3
alprazolam	anxiolytic, sedative,hypnotic	GABRP
alprazolam	anxiolytic, sedative,hypnotic	GABRQ

Drug Name	Indication(s)	Gene
alprazolam	anxiolytic, sedative,hypnotic	GABRR2
alprazolam	anxiolytic, sedative,hypnotic	GABRR3
alprostadil	for treatment of erectile dysfunction,for treatment of sexual dysfunction in women	PTGER1
alprostadil	for treatment of erectile dysfunction,for treatment of sexual dysfunction in women	PTGER2
alprostadil	for treatment of erectile dysfunction,for treatment of sexual dysfunction in women	PTGER1
alprostadil	for treatment of erectile dysfunction,for treatment of sexual dysfunction in women	PTGER2
alprostadil	for treatment of erectile dysfunction,for treatment of sexual dysfunction in women	PTGER1
alprostadil	for treatment of erectile dysfunction,for treatment of sexual dysfunction in women	PTGER2
altropane	diagnostic agent for parkinson's disease and ADHD	SLC6A3
Alvespimycin	antineoplastic agent	HSP90AA1
Alvespimycin	antineoplastic agent	HSP90AB1
AM-101	for treatment of tinnitus	GRIN1
AM-101	for treatment of tinnitus	GRIN2A
AM-101	for treatment of tinnitus	GRIN2B
AM-101	for treatment of tinnitus	GRIN2C

Drug Name	Indication(s)	Gene
AM-101	for treatment of tinnitus	GRIN2D
AM-101	for treatment of tinnitus	GRIN3A
AM-101	for treatment of tinnitus	GRIN3B
AM-103	antiinflammatory agent	ALOX5AP
AM-152	antiinflammatory agent,antifibrotic agent	LPAR1
AM-211	antiinflammatory agent,antiallergy agent	GPR44
AM-461	antiinflammatory agent	PTGDR
AM-803	antiinflammatory agent	ALOX5AP
AMAP102	antiinflammatory agent,DMARD	HTR2B
AMAP102	antiinflammatory agent,DMARD	HTR2C
AMD-070	antiviral agent,HIV	CXCR4
ALS 2-0426	antidiabetic	DPP4
amibegron	antidepressant	ADRB3
amifostine	radiation-protective agent	ALPPL2
amiodarone	antiarrhytmic agent	ADRA1A
amiodarone	antiarrhytmic agent	ADRB1
amiodarone	antiarrhytmic agent	KCNH2
amisulpride	antipsychotic agent	DRD2
amisulpride	antipsychotic agent	DRD3
amitriptyline	analgesic	SLC6A2
amitriptyline	analgesic	SLC6A4
ketamine	analgesic	GRIN3A
amlodipine	antihypertensive agent, cardiovascular agent	CACNA1C
amlodipine	antihypertensive agent, cardiovascular agent	CACNA1D

Drug Name	Indication(s)	Gene
amlodipine	antihypertensive agent, cardiovascular agent	CACNA1S
amlodipine	antihypertensive agent, cardiovascular agent	CACNA2D1
amlodipine	antihypertensive agent, cardiovascular agent	CACNB2
amonafide	antineoplastic agent	TOP2A
amonafide	antineoplastic agent	TOP2B
aliskiren	antihypertensive agent	REN
amlodipine	antihypertensive agent	CACNA1C
amlodipine	antihypertensive agent	CACNA1D
amlodipine	antihypertensive agent	CACNA1S
amlodipine	antihypertensive agent	CACNA2D1
amlodipine	antihypertensive agent	CACNB2
hydrochlorothiazide	antihypertensive agent	SLC12A3
AN-2728	antiinflammatory agent, antipsoriatic	PDE4A
AN-2728	antiinflammatory agent, antipsoriatic	PDE4B
AN-2898	antiinflammatory agent, antipsoriatic	PDE4A
AN-2898	antiinflammatory agent, antipsoriatic	PDE4B
ANA773	antineoplastic agent	TLR7
Anacetrapib	for treatment of dyslipidemia	CETP
anamorelin	appetite stimulating agent	GHSR
anastrozole	antineoplastic agent	CYP19A1
anatibant	for treatment of traumatic brain injury	BDKRB2
ANAVEX 2-73	for treatment of Alzheimer's disease	SIGMAR1
clomifene	for treatment of testosterone deficiency	ESR1

Drug Name	Indication(s)	Gene
anhydrovinblastin	antineoplastic agent	TUBB
docetaxel	antineoplastic agent	TUBB1
AP1030	antiobesity agent	MC1R
AP1030	antiobesity agent	MC4R
oxybutynin	for treatment of overactive bladder	CHRM1
oxybutynin	for treatment of overactive bladder	CHRM2
oxybutynin	for treatment of overactive bladder	CHRM3
APC-100	antineoplastic agent	AR
APD125	for treatment of insomnia	HTR2A
APD421	antiemetic	DRD2
APD668	antidiabetic	GPR119
APD791	antithrombotic	HTR2A
APD916	for treatment of narcolepsy	HRH3
mepivacaine	anestethic	SCN10A
granisetron	antiemetic	HTR3A
apilimod	antiinflammatory agent, antipsoriatic	unknown
apixaban	antithrombotic	F10
misoprostol	labor-inducing agent	PTGIR
Aplindore	antiparkinson agent,for treatment of restlegs legs syndrome	DRD2
apomorphine	for treatment of sexual dysfunction in women,for treatment of erectile dysfunction,antiparkinson agent	DRD2
apomorphine	for treatment of sexual dysfunction in women,for treatment of erectile dysfunction,antiparkinson agent	DRD3

Drug Name	Indication(s)	Gene
apomorphine	for treatment of sexual dysfunction in women,for treatment of erectile dysfunction,antiparkinson agent	DRD4
apomorphine	for treatment of sexual dysfunction in women,for treatment of erectile dysfunction,antiparkinson agent	DRD2
apomorphine	for treatment of sexual dysfunction in women,for treatment of erectile dysfunction,antiparkinson agent	DRD3
apomorphine	for treatment of sexual dysfunction in women,for treatment of erectile dysfunction,antiparkinson agent	DRD4
apremilast	antiinflammatory agent, DMARD, antipsoriatic	PDE4A
apremilast	antiinflammatory agent, DMARD, antipsoriatic	PDE4B
aprepitant	antiemetic	TACR1
apricoxib	antineoplastic agent	PTGS2
AR-12	antineoplastic agent	PDK1
AR-12286	for treatment of glaucoma	ROCK1
AR-12286	for treatment of glaucoma	ROCK2
AR-42	antineoplastic agent	HDAC1
AR-42	antineoplastic agent	HDAC10
AR-42	antineoplastic agent	HDAC11
AR-42	antineoplastic agent	HDAC2
AR-42	antineoplastic agent	HDAC3
AR-42	antineoplastic agent	HDAC4
AR-42	antineoplastic agent	HDAC5

Drug Name	Indication(s)	Gene
AR-42	antineoplastic agent	HDAC6
AR-42	antineoplastic agent	HDAC7A
AR-42	antineoplastic agent	HDAC8
AR-42	antineoplastic agent	HDAC9
AR9281	antihypertensive agent	EPHX1
AR9281	antihypertensive agent	EPHX2
arbaclofen	symptomatic treatment for fragile X syndrome	GABBR1
arbaclofen	symptomatic treatment for fragile X syndrome	GABBR2
ARC100	antineoplastic agent	TUBB1
clonidine	for treatment of diabetic neuropathy,for treatment of ADHD,antimucositic	ADRA2A
clonidine	for treatment of diabetic neuropathy,for treatment of ADHD,antimucositic	ADRA2B
clonidine	for treatment of diabetic neuropathy,for treatment of ADHD,antimucositic	ADRA2C
ARD-07	for treatment of growth hormone deficiency	GHR
Argatroban	anticoagulant	F2
ARI-2243	antidiabetic	DPP4
ARI-3037MO	Vitamin B analog,for treatment for hyperlipidemia	GPR109A
ARI-3037MO	Vitamin B analog,for treatment for hyperlipidemia	GPR109B

Drug Name	Indication(s)	Gene
ARI-3037MO	Vitamin B analog,for treatment for hyperlipidemia	NNMT
ARI-3037MO	Vitamin B analog,for treatment for hyperlipidemia	QPRT
armodafinil	central nervous system stimulant	SLC6A3
ARN-509	antineoplastic agent	AR
ARQ-197	antineoplastic agent	MET
ARQ-501	antineoplastic agent	TOP1
ARQ-621	antineoplastic agent	KIF11
ARRY-162	antiinflammatory agent,DMARD,antineoplastic agent	MAP2K1
ARRY-162	antiinflammatory agent,DMARD,antineoplastic agent	MAP2K2
ARRY-300	antiinflammatory agent,DMARD,antineoplastic agent	MAP2K1
ARRY-300	antiinflammatory agent,DMARD,antineoplastic agent	MAP2K2
ARRY-334543	antineoplastic agent	EGFR
ARRY-334543	antineoplastic agent	ERBB2
ARRY-380	antineoplastic agent	ERBB2
ARRY-403	antidiabetic	GCK
ARRY-614	for treatment of myelodysplastic syndrome	ABL1
ARRY-614	for treatment of myelodysplastic syndrome	KDR
ARRY-614	for treatment of myelodysplastic syndrome	MAPK11

Drug Name	Indication(s)	Gene
ARRY-614	for treatment of myelodysplastic syndrome	MAPK12
ARRY-614	for treatment of myelodysplastic syndrome	MAPK13
ARRY-614	for treatment of myelodysplastic syndrome	MAPK14
ARRY-614	for treatment of myelodysplastic syndrome	TEK
ARRY-797	antineoplastic agent	MAPK11
ARRY-797	antineoplastic agent	MAPK12
ARRY-797	antineoplastic agent	MAPK13
ARRY-797	antineoplastic agent	MAPK14
arsenic trioxide	antineoplastic agent	CCND1
arsenic trioxide	antineoplastic agent	IKBKB
arsenic trioxide	antineoplastic agent	JUN
arsenic trioxide	antineoplastic agent	MAPK1
arsenic trioxide	antineoplastic agent	MAPK3
arsenic trioxide	antineoplastic agent	TXNRD1
arverapamil	for treatment of irritable bowel syndrome	CACNA1C
arverapamil	for treatment of irritable bowel syndrome	CACNA1D
arverapamil	for treatment of irritable bowel syndrome	CACNA1F
arverapamil	for treatment of irritable bowel syndrome	CACNA1G
arverapamil	for treatment of irritable bowel syndrome	CACNA1S

Drug Name	Indication(s)	Gene
arverapamil	for treatment of irritable bowel syndrome	CACNB1
arverapamil	for treatment of irritable bowel syndrome	CACNB2
arverapamil	for treatment of irritable bowel syndrome	CACNB3
arverapamil	for treatment of irritable bowel syndrome	CACNB4
sufentanil	adjuvant to anesthesia	OPRM1
sufentanil	adjuvant to anesthesia	OPRM1
sufentanil	analgesic,sedative	OPRM1
triazolam	analgesic,sedative	GABRA1
triazolam	analgesic,sedative	GABRA2
triazolam	analgesic,sedative	GABRA3
triazolam	analgesic,sedative	GABRA4
triazolam	analgesic,sedative	GABRA5
triazolam	analgesic,sedative	GABRA6
triazolam	analgesic,sedative	GABRB1
triazolam	analgesic,sedative	GABRB2
triazolam	analgesic,sedative	GABRB3
triazolam	analgesic,sedative	GABRD
triazolam	analgesic,sedative	GABRE
triazolam	analgesic,sedative	GABRG1
triazolam	analgesic,sedative	GABRG2
triazolam	analgesic,sedative	GABRG3
triazolam	analgesic,sedative	GABRP
triazolam	analgesic,sedative	GABRQ
triazolam	analgesic,sedative	GABRR1

Drug Name	Indication(s)	Gene
triazolam	analgesic,sedative	GABRR2
triazolam	analgesic,sedative	GABRR3
Arzoxifene	antineoplastic agent,antiosteoporotic agent	ESR1
ASC-J9	dermatological agent	AR
Asenapine	antipsychotic agent	ADRA1A
Asenapine	antipsychotic agent	ADRA2A
Asenapine	antipsychotic agent	ADRA2B
Asenapine	antipsychotic agent	ADRA2C
Asenapine	antipsychotic agent	DRD1
Asenapine	antipsychotic agent	DRD2
Asenapine	antipsychotic agent	DRD3
Asenapine	antipsychotic agent	DRD4
Asenapine	antipsychotic agent	HRH1
Asenapine	antipsychotic agent	HRH2
Asenapine	antipsychotic agent	HTR1A
Asenapine	antipsychotic agent	HTR1B
Asenapine	antipsychotic agent	HTR2A
Asenapine	antipsychotic agent	HTR2B
Asenapine	antipsychotic agent	HTR2C
Asenapine	antipsychotic agent	HTR5A
Asenapine	antipsychotic agent	HTR6
Asenapine	antipsychotic agent	HTR7
asimadoline	analgesic	OPRK1
ipragliflozin	antidiabetic	SLC5A2
AT-101	antineoplastic agent	BAD
AT-101	antineoplastic agent	BCL2
AT-101	antineoplastic agent	MCL1

Drug Name	Indication(s)	Gene
AT13387	antineoplastic agent	HSP90AA1
AT13387	antineoplastic agent	HSP90AB1
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
fentanyl	analgesic,opioid	OPRM1
AT7519	antineoplastic agent	CDK2
AT9283	antineoplastic agent	AURKA
AT9283	antineoplastic agent	AURKB
atamestane	antineoplastic agent	CYP19A1
toremifene	antineoplastic agent	ESR1
toremifene	antineoplastic agent	ESR2
ATHX-105	antiobesity agent	HTR2C
docetaxel	antineoplastic agent	TUBB1
ATI-7505	Parasympathomimetic	HTR4
prednisone	antiinflammatory agent,corticosteroid	NR3C1
atomoxetine	for treatment of ADHD	SLC6A2
atorvastatin	antihypecholesterolemic agent	HMGCR
atrasentan	antineoplastic agent	EDNRA
AUS-131	for treatment of menopausal symtpoms	ESR2
AV-412	antineoplastic agent	EGFR
AV-412	antineoplastic agent	ERBB2
AV608	antidepressant,for treatment of irritable bowel syndrome,antispasmodic	TACR1
tivozanib	antineoplastic agent	FLT1

Drug Name	Indication(s)	Gene
tivozanib	antineoplastic agent	FLT4
tivozanib	antineoplastic agent	KDR
Avanafil	for treatment of erectile dysfunction	PDE5A
AVE-1625	antiobesity agent,for treatment for Alzheimer's disease	CNR1
phentolamine	for treatment of erectile dysfunction	ADRA1A
phentolamine	for treatment of erectile dysfunction	ADRA2A
AVL-292	antineoplastic agent	BTK
AVN-101	for treatment of alzheimer's disease	HTR6
AVN-211	antipsychotic agent	HTR6
AVN-322	for treatment of alzheimer's disease	HTR6
AVN-944	antineoplastic agent	IMPDH1
AVN-944	antineoplastic agent	IMPDH2
avosentan	antihypertensive agent	EDNRA
dextromethorphan	antitussive agent	GRIN3A
dextromethorphan	antitussive agent	SIGMAR1
axitinib	antineoplastic agent	FLT1
axitinib	antineoplastic agent	FLT4
axitinib	antineoplastic agent	KDR
axitinib	antineoplastic agent	KIT
axitinib	antineoplastic agent	PDGFRA
axitinib	antineoplastic agent	PDGFRB
AXL1717	antineoplastic agent	IGF1R
prochlorperazine	antimigraine agent	DRD2
alprazolam	anxiolytic, sedative,hypnotic	GABRA1
alprazolam	anxiolytic, sedative,hypnotic	GABRA2
alprazolam	anxiolytic, sedative,hypnotic	GABRA3
alprazolam	anxiolytic, sedative,hypnotic	GABRA4

Drug Name	Indication(s)	Gene
alprazolam	anxiolytic, sedative,hypnotic	GABRA5
alprazolam	anxiolytic, sedative,hypnotic	GABRA6
alprazolam	anxiolytic, sedative,hypnotic	GABRB1
alprazolam	anxiolytic, sedative,hypnotic	GABRB2
alprazolam	anxiolytic, sedative,hypnotic	GABRB3
alprazolam	anxiolytic, sedative,hypnotic	GABRD
alprazolam	anxiolytic, sedative,hypnotic	GABRE
alprazolam	anxiolytic, sedative,hypnotic	GABRG1
alprazolam	anxiolytic, sedative,hypnotic	GABRG2
alprazolam	anxiolytic, sedative,hypnotic	GABRG3
alprazolam	anxiolytic, sedative,hypnotic	GABRP
alprazolam	anxiolytic, sedative,hypnotic	GABRQ
alprazolam	anxiolytic, sedative,hypnotic	GABRR1
alprazolam	anxiolytic, sedative,hypnotic	GABRR2
alprazolam	anxiolytic, sedative,hypnotic	GABRR3
fentanyl	adjuvant to anesthesia	OPRD1
fentanyl	adjuvant to anesthesia	OPRM1
loxapine	antipsychotic agent	DRD2
loxapine	antipsychotic agent	HTR2A
zaleplon	hypnotic	GABRA1
zaleplon	hypnotic	TSPO
azacitidine	antineoplastic agent	DNMT1
AZD-0837	anticoagulant	F2
AZD2066	analgesic,for treatment of gastroesophageal reflux disease	GRM5
AZD6244, ARRY-142886	antineoplastic agent	MAP2K1
AZD6244, ARRY-142886	antineoplastic agent	MAP2K2
AZD-8330	antineoplastic agent	MAP2K1

Drug Name	Indication(s)	Gene
AZD-8848	antiallergy agent	TLR7
azelastine	antiallergy agent	HRH1
azelastine	antiallergy agent	HRH1
azilsartan	antihypertensive agent	AGTR1
balsalazide	antiinflammatory agent	ALOX5
balsalazide	antiinflammatory agent	PPARG
balsalazide	antiinflammatory agent	PTGS1
balsalazide	antiinflammatory agent	PTGS2
bardoxolone	antineoplastic agent	NFKB1
bazedoxifene	antiosteoporotic agent	ESR1
bazedoxifene	antiosteoporotic agent	ESR2
ulodesine	antiinflammatory agent	PNP
becatecarin	antineoplastic agent	TOP2A
becatecarin	antineoplastic agent	TOP2B
beclomethasone	antiinflammatory agent,glucocorticoid	NR3C1
beclomethasone	antiinflammatory agent,glucocorticoid	NR3C1
beclomethasone	antiinflammatory agent,glucocorticoid	NR3C1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRK1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRM1
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
benazepril	antihypertensive agent	ACE
bepotastine	antiallergy agent	HRH1

Drug Name	Indication(s)	Gene
beraprost	antihypertensive agent	PTGIR
betamethasone	antiinflammatory agent,glucocorticoid	NR3C1
betamethasone	antiinflammatory agent,glucocorticoid	NR3C1
betrixaban	antithrombotic	F10
bexarotene	antineoplastic agent	RXRA
bexarotene	antineoplastic agent	RXRB
bexarotene	antineoplastic agent	RXRG
BF-1	antimigraine agent	HTR2B
BF-Derm1	antiallergy agent	HDC
BG-9928	for treatment of congestive heart failure	ADORA1
fluoxetine	for treatment of sleep apnea	SLC6A4
ondansetron	for treatment of sleep apnea	HTR3A
BGC20-1531	antimigraine agent	PTGER4
BGG-492	anticonvulsant,antimigraine agent	GRIA1
BGG-492	anticonvulsant,antimigraine agent	GRIA2
BGG-492	anticonvulsant,antimigraine agent	GRIA3
BGG-492	anticonvulsant,antimigraine agent	GRIA4
progesterone	neuroprotectant for stroke victims	ESR1
progesterone	neuroprotectant for stroke victims	NR3C2
progesterone	neuroprotectant for stroke victims	PGR
BI-10773	antidiabetic	SLC5A2
olodaterol	bronchodilator	ADRB2
Nintedanib	antineoplastic agent	FGFR1
Nintedanib	antineoplastic agent	FGFR2
Nintedanib	antineoplastic agent	FGFR3

Drug Name	Indication(s)	Gene
Nintedanib	antineoplastic agent	FLT1
Nintedanib	antineoplastic agent	FLT4
Nintedanib	antineoplastic agent	KDR
Nintedanib	antineoplastic agent	PDGFRA
Nintedanib	antineoplastic agent	PDGFRB
Bicalutamide	antineoplastic agent	AR
bifeprunox	antipsychotic agent,antiparkinson agent	DRD2
bifeprunox	antipsychotic agent,antiparkinson agent	DRD3
bifeprunox	antipsychotic agent,antiparkinson agent	HTR1A
bifeprunox	antipsychotic agent,antiparkinson agent	HTR2A
bifeprunox	antipsychotic agent,antiparkinson agent	HTR2C
bifeprunox	antipsychotic agent,antiparkinson agent	HTR7
BIM23A760	antineoplastic agent,treatment for acromegaly	DRD2
BIM23A760	antineoplastic agent,treatment for acromegaly	SSTR2
BIM23A760	antineoplastic agent,treatment for acromegaly	SSTR5
bimatoprost	antiglaucomic agent	PTGER1
bimatoprost	antiglaucomic agent	PTGER3
bimatoprost	antiglaucomic agent	PTGFR
bimoclomol	for treatment of diabetic neuropathy	HSF1

Drug Name	Indication(s)	Gene
bimosiamose	antiinflammatory agent,antipsoriatic	SELE
bimosiamose	antiinflammatory agent,antipsoriatic	SELL
bimosiamose	antiinflammatory agent,antipsoriatic	SELP
docetaxel	antineoplastic agent	BCL2
docetaxel	antineoplastic agent	TUBB1
binodenoson	diagnostic agent	ADORA2A
estradiol	hormone replacement,treatment for menopause	ESR1
estradiol	hormone replacement,treatment for menopause	ESR2
testosterone	hormone replacement	AR
dapagliflozin	antidiabetic	SLC5A2
BMS-582949	antiinflammatory agent,DMARD,antipsoriatic	MAPK11
BMS-582949	antiinflammatory agent,DMARD,antipsoriatic	MAPK12
BMS-582949	antiinflammatory agent,DMARD,antipsoriatic	MAPK13
BMS-582949	antiinflammatory agent,DMARD,antipsoriatic	MAPK14
BMS-299897	for treatment of alzheimer's disease	APH1A
BMS-299897	for treatment of alzheimer's disease	APH1B
BMS-299897	for treatment of alzheimer's disease	NCSTN
BMS-299897	for treatment of alzheimer's disease	PSEN1
BMS-299897	for treatment of alzheimer's disease	PSEN2
BMS-299897	for treatment of alzheimer's disease	PSENEN
BMS-708163	for treatment of alzheimer's disease	APH1A
BMS-708163	for treatment of alzheimer's disease	APH1B

Drug Name	Indication(s)	Gene
BMS-708163	for treatment of alzheimer's disease	NCSTN
BMS-708163	for treatment of alzheimer's disease	PSEN1
BMS-708163	for treatment of alzheimer's disease	PSEN2
BMS-708163	for treatment of alzheimer's disease	PSENEN
BMS-754807	antineoplastic agent	IGF1R
BMS-863233	antineoplastic agent	CDC7
calcitonin	antiosteoporotic agent	CALCR
NCX116	for treatment of glaucoma	PTGFR
bosutinib	antineoplastic agent	ABL1
bosutinib	antineoplastic agent	SRC
brimonidine	for treatment of glaucoma	ADRA2A
brimonidine	for treatment of glaucoma	ADRA2A
timolol	for treatment of glaucoma	ADRB1
timolol	for treatment of glaucoma	ADRB2
Brivaracetam	anticonvulsant	SV2A
bromfenac	opthalmological agent,NSAID	PTGS1
bromfenac	opthalmological agent,NSAID	PTGS2
bromocriptine	antidiabetic	DRD2
bromocriptine	antidiabetic	DRD3
Bryostatin	for treatment of alzheimer's disease	PRKCA
Bryostatin	for treatment of alzheimer's disease	PRKCB
Bryostatin	for treatment of alzheimer's disease	PRKCD
Bryostatin	for treatment of alzheimer's disease	PRKCE
Bryostatin	for treatment of alzheimer's disease	PRKCG
Bryostatin	for treatment of alzheimer's disease	PRKCH
Bryostatin	for treatment of alzheimer's disease	PRKCQ
Bryostatin	for treatment of alzheimer's disease	PRKD1
Bryostatin	for treatment of alzheimer's disease	PRKD2

Drug Name	Indication(s)	Gene
Bryostatin	for treatment of alzheimer's disease	PRKD3
Bryostatin-1	antineoplastic agent	PRKCA
Bryostatin-1	antineoplastic agent	PRKCB
Bryostatin-1	antineoplastic agent	PRKCD
Bryostatin-1	antineoplastic agent	PRKCE
Bryostatin-1	antineoplastic agent	PRKCG
Bryostatin-1	antineoplastic agent	PRKCH
Bryostatin-1	antineoplastic agent	PRKCQ
Bryostatin-1	antineoplastic agent	PRKD1
Bryostatin-1	antineoplastic agent	PRKD2
Bryostatin-1	antineoplastic agent	PRKD3
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
prochlorperazine	antiemetic	DRD2
bucindolol	for treatment of heart failure	ADRB1
bucindolol	for treatment of heart failure	ADRB2
budesonide	antiinflammatory agent,glucocorticoid	NR3C1
Formoterol	bronchodilator	ADRB2
budesonide	antiinflammatory agent,glucocorticoid	NR3C1
budesonide	antiinflammatory agent,glucocorticoid	NR3C1
budesonide	antiinflammatory agent,glucocorticoid	NR3C1
budesonide	antiinflammatory agent,glucocorticoid	NR3C1

Drug Name	Indication(s)	Gene
budesonide	antiinflammatory agent,glucocorticoid	NR3C1
budesonide	antiinflammatory agent,glucocorticoid	NR3C1
budiodarone	antiarrhytmic agent	ADRB1
budiodarone	antiarrhytmic agent	CACNA2D2
budiodarone	antiarrhytmic agent	KCNH2
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRK1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRM1
naloxone	analgesic	OPRK1
naloxone	analgesic	OPRM1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRK1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRM1
naloxone	for treatment of opioid addiction	OPRK1
naloxone	for treatment of opioid addiction	OPRM1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRK1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRM1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRK1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRM1

Drug Name	Indication(s)	Gene
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRK1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRM1
bupropion	antidepressant,appetite suppressant,smoking-cessation agent	SLC6A2
bupropion	antidepressant,appetite suppressant,smoking-cessation agent	SLC6A3
BVT.115959	analgesic	ADORA2A
BVT.28949	for treatment of glaucoma	HTR2A
amphetamine	for treatment of cognitive dysfunction,for treatment of ADHD	CARTPT
amphetamine	for treatment of cognitive dysfunction,for treatment of ADHD	SLC18A2
amphetamine	for treatment of cognitive dysfunction,for treatment of ADHD	SLC6A3
amphetamine	for treatment of cognitive dysfunction,for treatment of ADHD	TAAR1
C-1311	antineoplastic agent	TOP1
C-1311	antineoplastic agent	TOP2A
cabazitaxel	antineoplastic agent	TUBA4A
cabazitaxel	antineoplastic agent	TUBB1
amlodipine	antihypertensive agent, cardiovascular agent	CACNA1C
amlodipine	antihypertensive agent, cardiovascular agent	CACNA1D
amlodipine	antihypertensive agent, cardiovascular agent	CACNA1S

Drug Name	Indication(s)	Gene
amlodipine	antihypertensive agent, cardiovascular agent	CACNA2D1
amlodipine	antihypertensive agent, cardiovascular agent	CACNB2
atorvastatin	anticholesterolaemic agent	HMGCR
CAL-101	antineoplastic agent	PIK3CD
betamethasone	antiinflammatory agent,glucocorticoid	NR3C1
calcipotriene	antipsoriatic agent	VDR
calcitriol	antipsoriatic agent	VDR
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRK1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRM1
Canagliflozin	antidiabetic	SLC5A2
candesartan	antihypertensive agent	AGTR1
cangrelor	antithrombotic	P2RY12
PRS-211375	analgesic	CNR2
CAP7.1	antineoplastic agent	TOP2A
Caprospinol	for treatment of alzheimer's disease	APP
Carfilzomib	antineoplastic agent	PSMB1
Carfilzomib	antineoplastic agent	PSMB2
Carfilzomib	antineoplastic agent	PSMB5
cariprazine	antipsychotic agent	DRD2
cariprazine	antipsychotic agent	DRD3
carvedilol	for treatment of congestive heart failure	ADRA1A
carvedilol	cardiovascular agent	ADRB1

Drug Name	Indication(s)	Gene
carvedilol	cardiovascular agent	ADRB2
Casopitant	antiemetic	TACR1
dronabinol	analgesic	CNR1
dronabinol	analgesic	CNR2
CB-03-01	dermatological agent	AR
caricotamide	antineoplastic agent	NQO2
tretazicar	antineoplastic agent	DNA
abiraterone	antineoplastic agent	CYP17A1
JNK-401	antineoplastic agent	MAPK10
JNK-401	antineoplastic agent	MAPK8
JNK-401	antineoplastic agent	MAPK9
CCX025	antiinflammatory agent	CCR9
CCX140	antiinflammatory agent,antidiabetic	CCR2
CCX168	antiinflammatory agent,for treatment for autoimmune disease	C5AR1
CCX282	antiinflammatory agent,for treatment of Chron's disease,for treatment of ulceraite colitis	CCR9
CCX354	antiinflammatory agent,DMARD	CCR1
CCX832	antiinflammatory agent,for treatment for autoimmune disease	CMKLR1
fenofibrate	anticholesterolaemic agent	PPARA
azelastine	antiallergy agent	HRH1
budesonide	antiinflammatory agent,glucocorticoid	NR3C1
cediranib	antineoplastic agent	FLT1
cediranib	antineoplastic agent	FLT4
cediranib	antineoplastic agent	KDR

Drug Name	Indication(s)	Gene
celecoxib	NSAID	PTGS2
mycophenolate mofetil	immunosuppressant	IMPDH1
mycophenolate mofetil	immunosuppressant	IMPDH2
synthetic conjugated estrogens	for treatment of postmenopausal symptoms	ESR1
synthetic conjugated estrogens	for treatment of postmenopausal symptoms	ESR2
histamine	cytorprotective agent during cancer treatment	HRH2
CER-002	cardiovascular agent	PPARD
acetylsalicylic acid	NSAID	PTGS1
acetylsalicylic acid	NSAID	PTGS2
niacin	antidyslipidaemic agent	GPR109A
niacin	antidyslipidaemic agent	GPR109B
niacin	antidyslipidaemic agent	NNMT
niacin	antidyslipidaemic agent	QPRT
diclofenac	NSAID	PTGS1
diclofenac	NSAID	PTGS2
cetilistat	antiobesity agent	PNLIP
cetirizine	antiallergy agent	HRH1
CF-101	antiinflammatory agent,DMARD	ADORA3
CF-102	antineoplastic agent	ADORA3
CG100649	NSAID	CA1
CG100649	NSAID	PTGS2
clopidogrel	antiplatelet agent	P2RY12
omeprazol	antiulcer agent	ATP4A
CH-1504	antiinflammatory agent,DMARD	DHFR
CHF 4227	antiosteoporotic agent	ESR1

Drug Name	Indication(s)	Gene
CHF 4227	antiosteoporotic agent	ESR2
beclomethasone	antiinflammatory agent,glucocorticoid	NR3C1
formoterol	antiasthmatic agent	ADRB2
chidamide	antineoplastic agent	HDAC1
chidamide	antineoplastic agent	HDAC10
chidamide	antineoplastic agent	HDAC2
chidamide	antineoplastic agent	HDAC3
CHIR-265	antineoplastic agent	BRAF
CHIR-265	antineoplastic agent	KDR
CHIR-265	antineoplastic agent	RAF1
cyclosporine	immunosuppressant	CAMLG
cyclosporine	immunosuppressant	PPP3R2
tadalafil	for treatment of erectile dysfunction	PDE5A
cilansetron	for treatment of irritable bowel syndrome	HTR3A
cimicoxib	NSAID	PTGS2
isotretinoin	for treatment of acne	RARA
escitalopram	antidepressant	SLC6A4
tiramsetiv	for treatment of skeletal muscle disorders associated with aging and neuro-degenerative disorders.	TNNC1
tiramsetiv	for treatment of skeletal muscle disorders associated with aging and neuro-degenerative disorders.	TNNC2
tiramsetiv	for treatment of skeletal muscle disorders associated with aging and neuro-degenerative disorders.	TNNI1

Drug Name	Indication(s)	Gene
tiramsetiv	for treatment of skeletal muscle disorders associated with aging and neuro-degenerative disorders.	TNNI2
tiramsetiv	for treatment of skeletal muscle disorders associated with aging and neuro-degenerative disorders.	TNNT1
tiramsetiv	for treatment of skeletal muscle disorders associated with aging and neuro-degenerative disorders.	TNNT2
clazosentan	for treatment and prevention of vasospasm	EDNRA
clevidipine	antihypertensive agent	CACNA1C
clevidipine	antihypertensive agent	CACNA1D
clevidipine	antihypertensive agent	CACNA1F
clevidipine	antihypertensive agent	CACNA1S
clobazam	anxiolytic,anticonvulsant	GABRA1
clobazam	anxiolytic,anticonvulsant	GABRA2
clobazam	anxiolytic,anticonvulsant	GABRA3
clobazam	anxiolytic,anticonvulsant	GABRA4
clobazam	anxiolytic,anticonvulsant	GABRA5
clobazam	anxiolytic,anticonvulsant	GABRA6
clobazam	anxiolytic,anticonvulsant	GABRB1
clobazam	anxiolytic,anticonvulsant	GABRB2
clobazam	anxiolytic,anticonvulsant	GABRB3
clobazam	anxiolytic,anticonvulsant	GABRD
clobazam	anxiolytic,anticonvulsant	GABRE
clobazam	anxiolytic,anticonvulsant	GABRG1
clobazam	anxiolytic,anticonvulsant	GABRG2

Drug Name	Indication(s)	Gene
clobazam	anxiolytic,anticonvulsant	GABRG3
clobazam	anxiolytic,anticonvulsant	GABRP
clobazam	anxiolytic,anticonvulsant	GABRQ
clobazam	anxiolytic,anticonvulsant	GABRR1
clobazam	anxiolytic,anticonvulsant	GABRR2
clobazam	anxiolytic,anticonvulsant	GABRR3
clobetasol	antiinflammatory agent,corticosteroid	NR3C1
clodronate	antineoplastic agent	SLC25A4
clodronate	antineoplastic agent	SLC25A5
clodronate	antineoplastic agent	SLC25A6
Clofarabine	antineoplastic agent	POLA1
Clofarabine	antineoplastic agent	RRM1
clonidine	for treatment of diabetic neuropathy,for treatment of ADHD,antimucositic	ADRA2A
clonidine	for treatment of diabetic neuropathy,for treatment of ADHD,antimucositic	ADRA2B
clonidine	for treatment of diabetic neuropathy,for treatment of ADHD,antimucositic	ADRA2C
clonidine	for treatment of diabetic neuropathy,for treatment of ADHD,antimucositic	ADRA2A
clonidine	for treatment of diabetic neuropathy,for treatment of ADHD,antimucositic	ADRA2B

Drug Name	Indication(s)	Gene
clonidine	for treatment of diabetic neuropathy,for treatment of ADHD,antimucositic	ADRA2C
CLX-0921	antidiabetic	PPARG
CM2489	antiinflammatory agent,antipsoriatic	ORA1
CNDO101	antineoplastic agent	TOP2A
CNF1010	antineoplastic agent	HSP90AA1
CNF1010	antineoplastic agent	HSP90AB1
CNS-5161	analgesic	GRIN1
CNS-5161	analgesic	GRIN2A
CNS-5161	analgesic	GRIN2B
CNS-5161	analgesic	GRIN2C
CNS-5161	analgesic	GRIN2D
CNS-5161	analgesic	GRIN3A
CNS-5161	analgesic	GRIN3B
CNS-7056	sedative	GABRA2
CNS-7056	sedative	GABRA3
CNS-7056	sedative	GABRA5
CNS-7056	sedative	GABRA6
CNS-7056	sedative	GABRB1
CNS-7056	sedative	GABRB1
CNS-7056	sedative	GABRB2
CNS-7056	sedative	GABRB2
CNS-7056	sedative	GABRB3
CNS-7056	sedative	GABRD
CNS-7056	sedative	GABRD
CNS-7056	sedative	GABRE
CNS-7056	sedative	GABRG1

Drug Name	Indication(s)	Gene
CNS-7056	sedative	GABRG2
CNS-7056	sedative	GABRG3
CNS-7056	sedative	GABRG3
CNS-7056	sedative	GABRP
CNS-7056	sedative	GABRQ
CNS-7056	sedative	GABRR2
CNV2197944	analgesic	CACNA1B
oxycodone	analgesic	OPRD1
oxycodone	analgesic	OPRK1
oxycodone	analgesic	OPRM1
oxycodone	analgesic	OPRD1
oxycodone	analgesic	OPRK1
oxycodone	analgesic	OPRM1
COL-3	antineoplastic agent	MMP2
COL-3	antineoplastic agent	MMP9
colchicine	for treatment of gout	TUBB
bupivacaine	local anestethic,analgesic,neuralgia	SCN10A
conivaptan	for treatment of hyponatremia	AVPR1A
conivaptan	for treatment of hyponatremia	AVPR2
estrogen	for symptomatic treatment of menopausal symptoms	ESR1
estrogen	for symptomatic treatment of menopausal symptoms	ESR2
progesterone	for symptomatic treatment of menopausal symptoms	ESR1
progesterone	for symptomatic treatment of menopausal symptoms	NR3C2

Drug Name	Indication(s)	Gene
progesterone	for symptomatic treatment of menopausal symptoms	PGR
ethinyl estradiol	contraceptive	ESR1
gestodene	contraceptive	PGR
bupropion	antidepressant,appetite suppressant,smoking-cessation agent	SLC6A2
bupropion	antidepressant,appetite suppressant,smoking-cessation agent	SLC6A3
naltrexone	appetite suppressant	OPRD1
naltrexone	appetite suppressant	OPRK1
naltrexone	appetite suppressant	OPRM1
fomepizole	for treatment of ethanol intolerance	ADH1A
fomepizole	for treatment of ethanol intolerance	ADH1B
fomepizole	for treatment of ethanol intolerance	ADH1C
cordycepin	antineoplastic agent	DNTT
CORT 108297	for prevention of weight gain during antipsychotic treatment	NR3C1
CP-4126	antineoplastic agent	DNA
CP-609,754	antineoplastic agent	FNTA
CP-609,754	antineoplastic agent	FNTB
CPG 10101	immunostimulant	TLR9
CPG 52364	antiinflammatory agent	TLR7
CPG 52364	antiinflammatory agent	TLR8
CPG 52364	antiinflammatory agent	TLR9
CPI-613	antineoplastic agent	PDHA1
CPI-613	antineoplastic agent	PDHA2
CPI-613	antineoplastic agent	PDHB
CPI-613	antineoplastic agent	PDK1

Drug Name	Indication(s)	Gene
CPI-613	antineoplastic agent	PDK2
CPI-613	antineoplastic agent	PDK3
CPI-613	antineoplastic agent	PDK4
semapimod	antiinflammatory agent,for treatment of Chron's disease	MAPK11
semapimod	antiinflammatory agent,for treatment of Chron's disease	MAPK12
semapimod	antiinflammatory agent,for treatment of Chron's disease	MAPK13
semapimod	antiinflammatory agent,for treatment of Chron's disease	MAPK14
floxuridine	antineoplastic agent	TYMS
irinotecan	antineoplastic agent	TOP1
irinotecan	antineoplastic agent	TOP1MT
cytarabine	antineoplastic agent	POLB
daunorubicin	antineoplastic agent	TOP2A
daunorubicin	antineoplastic agent	TOP2B
CR665	analgesic	OPRK1
CR845	analgesic	OPRK1
pravastatin	antihypecholesterolemic agent	HMGCR
rosuvastatin	antihypecholesterolemic agent	HMGCR
561679	antidepressant	CRHR1
crizotinib	antineoplastic agent	ALK
crizotinib	antineoplastic agent	MET
CRTH2 receptor antagonist	antiallergy agent	GPR44
prednisolone	antiinflammatory agent,corticosteroid	NR3C1
dipyridamole	anticoagulant	ADA

Drug Name	Indication(s)	Gene
dipyridamole	anticoagulant	PDE10A
dipyridamole	anticoagulant	PDE4A
dipyridamole	anticoagulant	PDE5A
amoxapine	antidepressant	SLC6A2
amoxapine	antidepressant	SLC6A4
prednisolone	antiinflammatory agent,corticosteroid	NR3C1
paroxetine	antidepressant	SLC6A4
prednisolone	antiinflammatory agent,corticosteroid	NR3C1
amoxapine	antidepressant	SLC6A2
amoxapine	antidepressant	SLC6A4
dipyridamole	antithrombotic	ADA
dipyridamole	antithrombotic	PDE10A
dipyridamole	antithrombotic	PDE4A
dipyridamole	antithrombotic	PDE5A
budesonide	antiinflammatory agent,glucocorticoid	NR3C1
nortriptyline	antiasthmatic agent	SLC6A2
nortriptyline	antiasthmatic agent	SLC6A4
mometasone	antiinflammatory agent,glucocorticoid	NR3C1
nortriptyline	antidepressant	SLC6A2
nortriptyline	antidepressant	SLC6A4
bezafibrate	antidiabetic	PPARA
diflunisal	antidiabetic	PTGS1
diflunisal	antidiabetic	PTGS2
CS-3030	anticoagulant	F10

Drug Name	Indication(s)	Gene
CS-7017	antineoplastic agent	PPARG
amlodipine	antihypertensive agent	CACNA1C
amlodipine	antihypertensive agent	CACNA1D
amlodipine	antihypertensive agent	CACNA1S
amlodipine	antihypertensive agent	CACNA2D1
amlodipine	antihypertensive agent	CACNB2
olmesartan	antihypertensive agent	AGTR1
CTA018	antiinflammatory agent,antipsoriatic	CYP24A1
CTS-21166	for treatment of Alzheimer's disease	BACE1
CUDC-101	antineoplastic agent	EGFR
CUDC-101	antineoplastic agent	ERBB2
CUDC-101	antineoplastic agent	HDAC1
CUDC-101	antineoplastic agent	HDAC10
CUDC-101	antineoplastic agent	HDAC11
CUDC-101	antineoplastic agent	HDAC2
CUDC-101	antineoplastic agent	HDAC3
CUDC-101	antineoplastic agent	HDAC4
CUDC-101	antineoplastic agent	HDAC5
CUDC-101	antineoplastic agent	HDAC6
CUDC-101	antineoplastic agent	HDAC7
CUDC-101	antineoplastic agent	HDAC8
CUDC-101	antineoplastic agent	HDAC9
CVT-3619	antihyperlipidemic agent	ADORA1
CVT-6883	antiasthmatic agent	ADORA2B
CX157	antidepressant	MAOA
CX1632/S 47445	for treatment of Alzheimer's disease	GRIA1
CX1632/S 47445	for treatment of Alzheimer's disease	GRIA2
CX1632/S 47445	for treatment of Alzheimer's disease	GRIA3

Drug Name	Indication(s)	Gene
CX1632/S 47445	for treatment of Alzheimer's disease	GRIA4
CX-4945	antineoplastic agent	CSNK2A1
CX717	for treatment of Alzheimer's disease	GRIA1
CX717	for treatment of Alzheimer's disease	GRIA2
CX717	for treatment of Alzheimer's disease	GRIA3
CX717	for treatment of Alzheimer's disease	GRIA4
CXB909	for treatment of chemotherapy-induced peripheral neuropathy	LNGFR
CXB909	for treatment of chemotherapy-induced peripheral neuropathy	NTRK1
CYC116	antineoplastic agent	AURKA
CYC116	antineoplastic agent	AURKB
CYC116	antineoplastic agent	KDR
cyclosporine	immunosuppressant	CAMLG
cyclosporine	immunosuppressant	PPP3R2
duloxetine	antidepressant	SLC6A2
duloxetine	antidepressant	SLC6A4
cysteamine	for treatment of corneal cystine accumulation	cystine
cytarabine	antineoplastic agent	POLB
D3263	antineoplastic agent	TRPM8
Dabigatran	anticoagulant	F2
decitabine	antineoplastic agent	DNMT1
dapoxetine	for treatment of premature ejaculation	SLC6A4
darapladib	antiinflammatory agent,DMARD	PLA2G7
darifenacin	for treatment of overactive bladder	CHRM3
darusentan	antihypertensive agent	EDNRA

Drug Name	Indication(s)	Gene
dasatinib	antineoplastic agent	ABL1
dasatinib	antineoplastic agent	ABL2
dasatinib	antineoplastic agent	EPHA2
dasatinib	antineoplastic agent	FYN
dasatinib	antineoplastic agent	KIT
dasatinib	antineoplastic agent	LCK
dasatinib	antineoplastic agent	PDGFRB
dasatinib	antineoplastic agent	SRC
dasatinib	antineoplastic agent	STAT5B
dasatinib	antineoplastic agent	YES1
methylphenidate	for treatment of ADHD	SLC6A3
DB-959	antidiabetic	PPARD
DB-959	antidiabetic	PPARG
diazoxide choline	antidyslipidaemic agent	ABCC8
DDP225	for treatment of irritable bowel syndrome	HTR3A
DDP225	for treatment of irritable bowel syndrome	HTR3B
DDP225	for treatment of irritable bowel syndrome	HTR3C
DDP225	for treatment of irritable bowel syndrome	HTR3D
DDP225	for treatment of irritable bowel syndrome	HTR3E
DDP225	for treatment of irritable bowel syndrome	SLC6A2
Debio 0932	antineoplastic agent	HSP90AA1
Debio 0932	antineoplastic agent	HSP90AB1

Drug Name	Indication(s)	Gene
DEBIO-9902 SR	for treatment of Alzheimer's disease	ACHE
Degarelix	antineoplastic agent	GNRHR
Degarelix	antineoplastic agent	GNRHR2
denufosol	for treatment of cystic fibrosis	P2RY2
deoxynojirimycin	for treatment of Pompe disease	GAA
bupivacaine	local anestethic,analgesic,neuralgia	SCN10A
gabapentin	for treatment of neuropathic pain	CACNA1B
gabapentin	for treatment of neuropathic pain	CACNA2D1
gabapentin	for treatment of neuropathic pain	CACNA2D2
romidepsin	antineoplastic agent	HDAC1
romidepsin	antineoplastic agent	HDAC10
romidepsin	antineoplastic agent	HDAC11
romidepsin	antineoplastic agent	HDAC2
romidepsin	antineoplastic agent	HDAC3
romidepsin	antineoplastic agent	HDAC4
romidepsin	antineoplastic agent	HDAC5
romidepsin	antineoplastic agent	HDAC6
romidepsin	antineoplastic agent	HDAC7A
romidepsin	antineoplastic agent	HDAC8
romidepsin	antineoplastic agent	HDAC9
dersalazine	antiinflammatory agent,for treatment of ulcerative colitis	PTGS1
dersalazine	antiinflammatory agent,for treatment of ulcerative colitis	PTGS2
dersalazine	antiinflammatory agent,for treatment of ulcerative colitis	TNF
desloratadine	antiallergy agent	HRH1

Drug Name	Indication(s)	Gene
desonide	antiinflammatory agent,corticosteroid	NR3C1
dexamethasone	antiinflammatory agent,glucocorticoid,for treatment of Meniere's disease	NR3C1
Dexanabinol	neuroprotectant	GRIN1
Dexanabinol	neuroprotectant	GRIN2A
Dexanabinol	neuroprotectant	GRIN2B
Dexanabinol	neuroprotectant	GRIN2D
Dexanabinol	neuroprotectant	GRIN3A
Dexanabinol	neuroprotectant	GRIN3B
dexlipotam	for treatment of diabetic neuropathy	PDHB
dexloxiglumide	motilitant	CCKAR
dexpramipexole	for treatment of amyotrophic lateral sclerosis (ALS)	DRD2
dexpramipexole	for treatment of amyotrophic lateral sclerosis (ALS)	DRD3
dexpramipexole	for treatment of amyotrophic lateral sclerosis (ALS)	DRD4
DG031	antiinflammatory agent,myocardial infarction prophylaxis	ALOX5AP
DG041	Platelet Aggregation Inhibitor	PTGER3
DG051	antiinflammatory agent,myocardial infarction prophylaxis	LTA4H
DG071	for treatment of alzheimer's disease	PDE4A
DG071	for treatment of alzheimer's disease	PDE4B
DG3173	hormone replacement	SSTR1
DG3173	hormone replacement	SSTR2

Drug Name	Indication(s)	Gene
DG3173	hormone replacement	SSTR4
DG3173	hormone replacement	SSTR5
diazepam	anticonvulsant	GABRA1
diazepam	anticonvulsant	GABRA2
diazepam	anticonvulsant	GABRA3
diazepam	anticonvulsant	GABRA5
diazepam	anticonvulsant	GABRB1
diazepam	anticonvulsant	GABRB2
diazepam	anticonvulsant	GABRB3
diazepam	anticonvulsant	GABRD
diazepam	anticonvulsant	GABRE
diazepam	anticonvulsant	GABRG1
diazepam	anticonvulsant	GABRG2
diazepam	anticonvulsant	GABRG3
diazepam	anticonvulsant	GABRP
diazepam	anticonvulsant	GABRQ
diazepam	anticonvulsant	GABRR1
diazepam	anticonvulsant	GABRR2
diazepam	anticonvulsant	GABRR3
diclofenac	analgesic	PTGS1
diclofenac	analgesic	PTGS2
Diclofenac	analgesic	PTGS1
Diclofenac	analgesic	PTGS2
Diclofenac	analgesic	PTGS1
Diclofenac	analgesic	PTGS2
Diclofenac	NSAID	PTGS1
Diclofenac	NSAID	PTGS2
Diclofenac	for treatment of glaucoma	PTGS1

Drug Name	Indication(s)	Gene
Diclofenac	for treatment of glaucoma	PTGS2
difluprednate	antiinflammatory agent,corticosteroid	NR3C1
diltiazem	antihypertensive agent	CACNG1
latrepirdine	neuroprotectant	ACHE
latrepirdine	neuroprotectant	GRIN1
latrepirdine	neuroprotectant	GRIN2A
latrepirdine	neuroprotectant	GRIN2B
latrepirdine	neuroprotectant	GRIN2C
latrepirdine	neuroprotectant	GRIN2D
latrepirdine	neuroprotectant	GRIN3A
latrepirdine	neuroprotectant	GRIN3B
dimiracetam	nootropic	GRIN1
dimiracetam	nootropic	GRIN2A
dimiracetam	nootropic	GRIN2B
dimiracetam	nootropic	GRIN2C
dimiracetam	nootropic	GRIN2D
DIO-902	antidiabetic	ERG11
diquafosol	opthalmological agent	P2RY2
carbidopa	antiparkinson agent	DDC
levodopa	antiparkinson agent	DRD1
levodopa	antiparkinson agent	DRD2
omeprazole	antiulcer agent	ATP4A
betanechol	antidiabetic	CHRM2
calcitriol	antineoplastic agent	VDR
Docetaxel	antineoplastic agent	BCL2
Docetaxel	antineoplastic agent	TBB1
dolasetron	antiemetic	HTR3A

Drug Name	Indication(s)	Gene
dolasetron	antiemetic	HTR3B
dolasetron	antiemetic	HTR3C
dolasetron	antiemetic	HTR3D
dolasetron	antiemetic	HTR3E
donepezil	for treatment of alzheimer's disease	ACHE
beclomethasone dipropionate	antiinflammatory agent,glucocorticoid	NR3C1
DOV 102,677	antidepressant	SLC6A2
DOV 102,677	antidepressant	SLC6A3
DOV 102,677	antidepressant	SLC6A4
DOV 216,303	antidepressant	SLC6A2
DOV 216,303	antidepressant	SLC6A3
DOV 216,303	antidepressant	SLC6A4
DOV 21947	antidepressant	SLC6A2
DOV 21947	antidepressant	SLC6A3
DOV 21947	antidepressant	SLC6A4
dovitinib	antineoplastic agent	FGFR1
dovitinib	antineoplastic agent	FGFR2
dovitinib	antineoplastic agent	FGFR3
dovitinib	antineoplastic agent	FLT1
dovitinib	antineoplastic agent	FLT1
dovitinib	antineoplastic agent	FLT1
dovitinib	antineoplastic agent	FLT4
dovitinib	antineoplastic agent	KDR
dovitinib	antineoplastic agent	PDGFRB
doxepin	antimigraine agent	SLC6A2
doxepin	antimigraine agent	SLC6A4

Drug Name	Indication(s)	Gene
doxercalciferol	for treatment of secondary hyperparathyroidism	VDR
doxorubicin	antineoplastic agent	TOP2A
doxorubicin	antineoplastic agent	TOP2A
doxorubicin	antineoplastic agent	TOP2A
doxorubicin	antineoplastic agent	TOP2A
DP-VPA	anticonvulsant	ABAT
DRF 10945	antidyslipidaemic agent	PPARA
dronabinol	appetite stimulant	CNR1
drospirenone	hormone replacement	PGR
estradiol	hormone replacement	ESR1
estradiol	hormone replacement	ESR2
DSC-103	antiosteoporotic agent	VDR
DTS-201	antineoplastic agent	TOP2A
bupivacaine	local anestethic,analgesic,neuralgia	SCN10A
bupivacaine	local anestethic,analgesic,neuralgia	SCN10A
sildenafil	for treatment of erectile dysfunction	PDE5A
dutasteride	for treatment of benign prostate hyperplasia	SRD5A1
dutasteride	for treatment of benign prostate hyperplasia	SRD5A2
tamsulosin	for treatment of benign prostatic hyperplasia	ADRA1A
dutasteride	for treatment of benign prostate hyperplasia	SRD5A1
dutogliptin	antidiabetic	DPP4
azelastine	antiallergy agent	HRH1

Drug Name	Indication(s)	Gene
fluticasone	antiinflammatory agent,glucocorticoid	NR3C1
perampanel	anticonvulsant	GRIA1
perampanel	anticonvulsant	GRIA2
perampanel	anticonvulsant	GRIA3
perampanel	anticonvulsant	GRIA4
E2012	for treatment of Alzheimer's disease	PSEN1
lenvatinib	antineoplastic agent	FGFR1
lenvatinib	antineoplastic agent	FLT1
lenvatinib	antineoplastic agent	FLT4
lenvatinib	antineoplastic agent	KDR
lenvatinib	antineoplastic agent	KIT
lenvatinib	antineoplastic agent	PDGFRA
lenvatinib	antineoplastic agent	PDGFRB
ecabet	antiulcer agent	PGA3
ecabet	antiulcer agent	PGC
ecopipam	for treatment of tourettes syndrome,for treatment of pathological gambling	DRD1
edoxaban	antithrombotic	F10
venlafaxine	antidepressant	SLC6A2
venlafaxine	antidepressant	SLC6A4
eflornithine	for treatment of unwanted facial hair in women	ODC1
dexamethasone	antiinflammatory agent,glucocorticoid,for treatment of Meniere's disease	NR3C1
Etazolate	for treatment of alzheimer's disease	GABRA2

Drug Name	Indication(s)	Gene
Etazolate	for treatment of alzheimer's disease	GABRA3
Etazolate	for treatment of alzheimer's disease	GABRB1
Etazolate	for treatment of alzheimer's disease	GABRB2
Etazolate	for treatment of alzheimer's disease	GABRE
Etazolate	for treatment of alzheimer's disease	GABRG1
Etazolate	for treatment of alzheimer's disease	PDE4A
Etazolate	for treatment of alzheimer's disease	PDE4B
Etazolate	for treatment of alzheimer's disease	PDE4C
Etazolate	for treatment of alzheimer's disease	PDE4D
ronomilast	antiinflammatory agent	PDE4A
ronomilast	antiinflammatory agent	PDE4B
ED-71	antiosteoporotic agent	VDR
oxycodone	analgesic	OPRD1
oxycodone	analgesic	OPRK1
oxycodone	analgesic	OPRM1
eliglustat	for treatment of Gaucher's disease	UGCG
elinogrel	antiplatelet agent	P2RY12
Elocalcitol	for treatment of benign prostatic hyperplasia	VDR
bupropion	antidepressant,appetite suppressant,smoking-cessation agent	SLC6A2
bupropion	antidepressant,appetite suppressant,smoking-cessation agent	SLC6A3
zonisamide	appetite suppressant	CACNA1G
zonisamide	appetite suppressant	CACNA1H
zonisamide	appetite suppressant	CACNA1I
zonisamide	appetite suppressant	SCN11A
zonisamide	appetite suppressant	SCN1A

Drug Name	Indication(s)	Gene
zonisamide	appetite suppressant	SCN1B
zonisamide	appetite suppressant	SCN2A
zonisamide	appetite suppressant	SCN2B
zonisamide	appetite suppressant	SCN3A
zonisamide	appetite suppressant	SCN3B
zonisamide	appetite suppressant	SCN4A
zonisamide	appetite suppressant	SCN4B
zonisamide	appetite suppressant	SCN5A
zonisamide	appetite suppressant	SCN9A
enalapril	antihypertensive agent	ACE
felodipine	antihypertensive agent	CACNA1C
felodipine	antihypertensive agent	CACNA1D
felodipine	antihypertensive agent	CACNA1S
felodipine	antihypertensive agent	CACNA2D1
felodipine	antihypertensive agent	CACNANB2
paclitaxel	antineoplastic agent	BCL2
paclitaxel	antineoplastic agent	TUBB1
eniluracil	antineoplastic agent	DPYD
ENMD-1198	antineoplastic agent	HIF1A
ENMD-2076	antineoplastic agent	ABL1
ENMD-2076	antineoplastic agent	AURKA
ENMD-2076	antineoplastic agent	BLK
ENMD-2076	antineoplastic agent	CSF1R
ENMD-2076	antineoplastic agent	FGFR1
ENMD-2076	antineoplastic agent	FGFR2
ENMD-2076	antineoplastic agent	FLT3
ENMD-2076	antineoplastic agent	FLT4
ENMD-2076	antineoplastic agent	FYN

Drug Name	Indication(s)	Gene
ENMD-2076	antineoplastic agent	JAK2
ENMD-2076	antineoplastic agent	KDR
ENMD-2076	antineoplastic agent	KIT
ENMD-2076	antineoplastic agent	LCK
ENMD-2076	antineoplastic agent	NTRK1
ENMD-2076	antineoplastic agent	PDGFRA
ENMD-2076	antineoplastic agent	PTK2
ENMD-2076	antineoplastic agent	RET
ENMD-2076	antineoplastic agent	SRC
ENMD-2076	antineoplastic agent	YES1
entacapone	antiparkinson agent	COMT
carbidopa	antiparkinson agent	DDC
entacapone	antiparkinson agent	COMT
levodopa	antiparkinson agent	DRD1
levodopa	antiparkinson agent	DRD2
levodopa	antiparkinson agent	DRD3
levodopa	antiparkinson agent	DRD4
levodopa	antiparkinson agent	DRD5
entinostat	antineoplastic agent	HDAC1
entinostat	antineoplastic agent	HDAC3
Enzastaurin	antineoplastic agent	PRKCB
EP217609	anticoagulant	F10
EP217609	anticoagulant	F2
EP42675	anticoagulant	F10
EP42675	anticoagulant	F2
EPI-743	for treatment of Chron's disease,for treatment of ulcerative colitis	NQO1
epinastine	antiallergy agent	HRH1

Drug Name	Indication(s)	Gene
epinastine	antiallergy agent	HRH2
eplerenone	antihypertensive agent	NR3C2
eplivanserine	for treatment of insomnia	HTR2A
eplivanserine	for treatment of insomnia	HTR2C
Epothilone D	antineoplastic agent	TUBB1
eprotirome	antidyslipidaemic agent	THRB
erdosteine	for treatment of chronic obstructive pulmonary disorder (COPD)	ELANE
eritoran	for treatment of sepsis	TLR4
Eslicarbazepine	anticonvulsant	SCN5A
esmirtazapine	for treatment of insomnia,for treatment of menopausal symptoms	ADRA2A
esmirtazapine	for treatment of insomnia,for treatment of menopausal symptoms	HTR2A
esmirtazapine	for treatment of insomnia,for treatment of menopausal symptoms	HTR3A
esomeprazole	Proton pump inhibitor	ATP4A
estradiol	contraceptive	ESR1
estradiol	contraceptive	ESR1
estradiol	contraceptive	ESR2
norethisterone	contraceptive	PGR
estradiol	for treatment of menopausal symptoms	ESR1
estradiol	for treatment of menopausal symptoms	ESR2
estradiol	for treatment of menopausal symptoms	ESR1

Drug Name	Indication(s)	Gene
estradiol	for treatment of menopausal symptoms	ESR2
estradiol	contraceptive	ESR1
dienogest	contraceptive	ESR1
dienogest	contraceptive	PGR
estradiol	contraceptive	ESR2
estradiol	contraceptive	ESR2
estradiol	for treatment of menopausal symptoms	ESR1
estradiol	for treatment of menopausal symptoms	ESR2
levonorgestrel	for treatment of menopausal symptoms	ESR1
levonorgestrel	for treatment of menopausal symptoms	PGR
levonorgestrel	for treatment of menopausal symptoms	SRD5A1
estradiol	for treatment of menopausal symptoms	ESR1
estradiol	for treatment of menopausal symptoms	ESR2
estradiol	for treatment of menopausal symptoms	ESR1
estradiol	for treatment of menopausal symptoms	ESR2
drospirenone	contraceptive	AR
drospirenone	contraceptive	NR3C2
drospirenone	contraceptive	PGR

Drug Name	Indication(s)	Gene
estradiol	contraceptive	ESR1
estradiol	contraceptive	ESR2
ethinyl estradiol	contraceptive	ESR1
levonorgestrel	contraceptive	ESR1
levonorgestrel	contraceptive	PGR
etilevodopa	antiparkinson agent	DRD1
etilevodopa	antiparkinson agent	DRD2
etilevodopa	antiparkinson agent	DRD3
etilevodopa	antiparkinson agent	DRD4
etilevodopa	antiparkinson agent	DRD5
etodolac	NSAID	PTGS2
etonogestrel	contraceptive	ESR1
etonogestrel	contraceptive	PGR
ethinyl estradiol	contraceptive	ESR1
etonogestrel	contraceptive	ESR1
etonogestrel	contraceptive	PGR
etoricoxib	NSAID	PTGS2
EV-077-3201-2TBS	antidiabetic	PPARG
everolimus	immunosuppressant	MTOR
raloxifen	for treatment of menopausal symptoms	ESR1
raloxifen	for treatment of menopausal symptoms	ESR2
metoclopramide	for treatment of diabetic gastroparesis	CHRM1
metoclopramide	for treatment of diabetic gastroparesis	DRD2
EVP-6124	nootropic	CHRNA7

Drug Name	Indication(s)	Gene
EVT-101	antidepressant	GRIN2B
EVT-103	antidepressant	GRIN2B
EVT-201	hypnotic	GABRA2
EVT-201	hypnotic	GABRA3
EVT-201	hypnotic	GABRA5
EVT-201	hypnotic	GABRA6
EVT-201	hypnotic	GABRB1
EVT-201	hypnotic	GABRB1
EVT-201	hypnotic	GABRB2
EVT-201	hypnotic	GABRB2
EVT-201	hypnotic	GABRB3
EVT-201	hypnotic	GABRD
EVT-201	hypnotic	GABRD
EVT-201	hypnotic	GABRE
EVT-201	hypnotic	GABRG1
EVT-201	hypnotic	GABRG2
EVT-201	hypnotic	GABRG3
EVT-201	hypnotic	GABRG3
EVT-201	hypnotic	GABRP
EVT-201	hypnotic	GABRQ
EVT-201	hypnotic	GABRR2
EVT-302	smoking-cessation agent	MA0B
EVT-401	antiinflammatory agent	P2RX7
Exebryl-1	for treatment of alzheimer's disease	APP
Exebryl-1	for treatment of alzheimer's disease	MAPT
exemestane	antineoplastic agent	CYP19A1
ezatiostat	for treatment of Myelodysplastic Syndrome	GSTP1

Drug Name	Indication(s)	Gene
PEG-SN38	antineoplastic agent	TOP1MT
PEG-SN38	antineoplastic agent	TOP1
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
febuxostat	for treatment of gout	XDH
felodipine	antihypertensive agent	CACNA1C
felodipine	antihypertensive agent	CACNA1D
felodipine	antihypertensive agent	CACNA1S
felodipine	antihypertensive agent	CACNA2D1
felodipine	antihypertensive agent	CACNB2
fenoldopam	antihypertensive agent	DRD1
fenoldopam	antihypertensive agent	DRD5
fenretinide	antineoplastic agent	RARA
fenretinide	antineoplastic agent	RARB
fenretinide	antineoplastic agent	RARG
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
fentanyl	analgesic	OPRD1

Drug Name	Indication(s)	Gene
fentanyl	analgesic	OPRM1
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
fesoterodine	for treatment of overactive bladder syndrome	CHRM3
fexofenadine	antiallergy agent	HRH1
pseudoephedrine	antiallergy agent	ADRA1A
pseudoephedrine	antiallergy agent	ADRA2A
pseudoephedrine	antiallergy agent	SLC6A2
pseudoephedrine	antiallergy agent	SLC6A3
pseudoephedrine	antiallergy agent	SLC6A4
FG-2216	for treatment of anemia	EGLN1
FG-2216	for treatment of anemia	EGLN2
FG-2216	for treatment of anemia	EGLN3
FG-4592	for treatment of anemia	EGLN1
FG-4592	for treatment of anemia	EGLN2
FG-4592	for treatment of anemia	EGLN3
fingolimod	for treatment of multiple sclerosis	S1PR1
fipamezole	antiparkinson agent	ADRA2A
fipamezole	antiparkinson agent	ADRA2B
fipamezole	antiparkinson agent	ADRA2C
icatibant	for treatment of hereditary angioedema	BDKRB2
fispemifene	hormone replacement	ESR1
fispemifene	hormone replacement	ESR2
FK352B	antihypertensive agent	ADORA1
alvocidib	antineoplastic agent	CDC2
alvocidib	antineoplastic agent	CDK10

Drug Name	Indication(s)	Gene
alvocidib	antineoplastic agent	CDK2
alvocidib	antineoplastic agent	CDK3
alvocidib	antineoplastic agent	CDK4
alvocidib	antineoplastic agent	CDK5
alvocidib	antineoplastic agent	CDK6
alvocidib	antineoplastic agent	CDK7
alvocidib	antineoplastic agent	CDK8
alvocidib	antineoplastic agent	CDK9
flibanserin	for treatment of female sexual dysfunction	HTR1A
flibanserin	for treatment of female sexual dysfunction	HTR2A
flovagatran	anticoagulant	F2
fludarabine	antineoplastic agent	DCK
fludarabine	antineoplastic agent	POLA1
fludarabine	antineoplastic agent	RRM1
flunisolide	antiinflammatory agent,glucocorticoid	NR3C1
flunisolide	antiinflammatory agent,glucocorticoid	NR3C1
fluocinonide	antiinflammatory agent,glucocorticoid	NR3C1
fluoxetine	antidepressant	SLC6A4
flupirtine	analgesic	KCNJ3
flupirtine	analgesic	KCNJ5
flupirtine	analgesic	KCNJ6
flupirtine	analgesic	KCNJ9

Drug Name	Indication(s)	Gene
fluticasone	antiinflammatory agent,glucocorticoid	NR3C1
fluvastatin	antihypecholesterolemic agent	HMGCR
fluvoxamine	antidepressant	SLC6A4
dexmethylphenidate	for treatment of ADHD	SLC6A3
dexmethylphenidate	for treatment of ADHD	SLCA2
forodesine	antineoplastic agent	PNP
formoterol	bronchodilator	ADRB2
formoterol	for treatment of chronic obstructive pulmonary disorder (COPD)	ADRB2
fosphenytoin	anticonvulsant	SCN5A
fospropofol	hypnotic and sedative	GABRB2
fospropofol	hypnotic and sedative	GABRB3
fostamatinib	antiinflammatory agent,DMARD	SYK
cyclosporine	immunosuppressant	CAMLG
cyclosporine	immunosuppressant	PPP3R2
prednisolone	antiinflammatory agent,corticosteroid	NR3C1
frovatriptan	antimigraine agent	HTR1B
frovatriptan	antimigraine agent	HTR1D
fruquintinib	antineoplastic agent	FLT1
fruquintinib	antineoplastic agent	FLT4
fruquintinib	antineoplastic agent	KDR
dexamethasone	antiinflammatory agent,glucocorticoid,for treatment of Meniere's disease	NR3C1
fulvestrant	antineoplastic agent	ESR1
leucovorin	adjuvant to chemotherapy	TYMS

Drug Name	Indication(s)	Gene
FX125L	antiasthmatic agent	CCR1
FX125L	antiasthmatic agent	CXCR1
FX125L	antiasthmatic agent	CXCR2
FX125L	antiasthmatic agent	CXCR4
gabapentin	analgesic	CACNA1B
gabapentin	analgesic	CACNA2D1
gabapentin	analgesic	CACNA2D2
gaboxadol	hypnotic	GABRA2
gaboxadol	hypnotic	GABRA3
gaboxadol	hypnotic	GABRA5
gaboxadol	hypnotic	GABRA6
gaboxadol	hypnotic	GABRB1
gaboxadol	hypnotic	GABRB1
gaboxadol	hypnotic	GABRB2
gaboxadol	hypnotic	GABRB2
gaboxadol	hypnotic	GABRB3
gaboxadol	hypnotic	GABRD
gaboxadol	hypnotic	GABRE
gaboxadol	hypnotic	GABRG1
gaboxadol	hypnotic	GABRP
galantamine	for treatment of alzheimer's disease	ACHE
ganaxolone	anticonvulsant	GABRA1
ganaxolone	anticonvulsant	GABRA2
ganaxolone	anticonvulsant	GABRA3
ganaxolone	anticonvulsant	GABRA4
ganaxolone	anticonvulsant	GABRA5
ganaxolone	anticonvulsant	GABRA6

Drug Name	Indication(s)	Gene
gantacurium	muscle relaxant,neuromuscular blocking agent	CHRNA2
GDC-0068	antineoplastic agent	AKT1
GDC-0068	antineoplastic agent	AKT2
GDC-0068	antineoplastic agent	AKT3
GDC-0973	antineoplastic agent	MAP2K1
gemcitabine	antineoplastic agent	RRM1
gepirone	antidepressant	HTR1A
progesterone	for prevention of preterm delivery	PGR
GGTI-2418	antineoplastic agent	FNTA
GGTI-2418	antineoplastic agent	PGGT1B
GL1001	for treatment of Chron's disease,for treatment of ulcerative colitis	ACE2
glimepiride	antidiabetic	KCNJ1
glimepiride	antidiabetic	ABCC8
glimepiride	antidiabetic	KCNJ11
GLPG0187	antineoplastic agent	ITGA5
GLPG0187	antineoplastic agent	ITGAV
GLPG0187	antineoplastic agent	ITGB1
GLPG0187	antineoplastic agent	ITGB3
GLPG0187	antineoplastic agent	ITGB5
GLPG0187	antineoplastic agent	ITGB6
GLPG0259	antiinflammatory agent,DMARD	MAPKAPK5
GLPG0492	for treatment of cachexia	AR
GLPG0634	antiinflammatory agent,DMARD	JAK1
GLPG0634	antiinflammatory agent,DMARD	JAK2
Glufosfamide	antineoplastic agent	SLC2A1
Glufosfamide	antineoplastic agent	SLC2A2

Drug Name	Indication(s)	Gene
Glufosfamide	antineoplastic agent	SLC2A3
Glufosfamide	antineoplastic agent	SLC2A4
Glufosfamide	antineoplastic agent	SLC2A5
Glufosfamide	antineoplastic agent	SLC5A1
Glufosfamide	antineoplastic agent	SLC5A2
Glufosfamide	antineoplastic agent	SLC5A4
glyburide	antidiabetic	ABCC8
metformin	antidiabetic	PRKAB1
glycopyrrolate	antineoplastic agent	CHRM1
GMI-1070	for treatment of sickle-cell disease	SELE
GMI-1070	for treatment of sickle-cell disease	SELL
GMI-1070	for treatment of sickle-cell disease	SELP
GMX1777	antineoplastic agent	NAMPT
NBI-42902	for treatment of postmenopausal symptoms,antineoplastic agent	GNRHR
NBI-42902	for treatment of postmenopausal symptoms,antineoplastic agent	GNRHR2
GPI-1485	antiparkinson agent	FKBP1A
GPX-100	antineoplastic agent	TOP2A
granisetron	antiemetic	HTR3A
granisetron	antiemetic	HTR3B
granisetron	antiemetic	HTR3C
granisetron	antiemetic	HTR3D
granisetron	antiemetic	HTR3E
granisetron	antiemetic	HTR3A
granisetron	antiemetic	HTR3B
granisetron	antiemetic	HTR3C
granisetron	antiemetic	HTR3D

Drug Name	Indication(s)	Gene
granisetron	antiemetic	HTR3E
GS-9411	for treatment of pulmonary disease	SCNN1A
GS-9411	for treatment of pulmonary disease	SCNN1B
GS-9411	for treatment of pulmonary disease	SCNN1D
GS-9411	for treatment of pulmonary disease	SCNN1G
GSI-136	for treatment of Alzheimer's disease	APH1A
GSI-136	for treatment of Alzheimer's disease	APH1B
GSI-136	for treatment of Alzheimer's disease	NCSTN
GSI-136	for treatment of Alzheimer's disease	PSEN1
GSI-136	for treatment of Alzheimer's disease	PSEN2
GSI-136	for treatment of Alzheimer's disease	PSENEN
GSK-1004723	antiallergy agent	HRH1
GSK-1004723	antiallergy agent	HRH3
trametinib	antineoplastic agent	MAP2K1
GSK2118436	antineoplastic agent	BRAF
GSK-961081	bronchodilator	ADRB2
GSK-961081	bronchodilator	CHRM3
GTS-21	for treatment of schizophrenia	CHRNA7
GTx-758	antineoplastic agent	LHCGR
guanfacine	for treatment of ADHD	ADRA2A
GW501516	antidyslipidaemic agent	PPARA
GW501516	antidyslipidaemic agent	PPARD
GW501516	antidyslipidaemic agent	PPARG
GW642444	bronchodilator	ADRB2
halofuginone	antineoplastic agent	EPRS
flurbiprofen	antiinflammatory agent,NSAID	PTGS2
nitric oxide	antiinflammatory agent	GUCY1A2
HE3235	antineoplastic agent	AR

Drug Name	Indication(s)	Gene
doxorubicin	antineoplastic agent	TOP2A
heparin	anticoagulant	F10
heparin	anticoagulant	SERPINC1
heparin	anticoagulant	F10
heparin	anticoagulant	SERPINC1
HF0220	for treatment of alzheimer's disease	unknown
HGS1029	antineoplastic agent	BIRC2
HGS1029	antineoplastic agent	BIRC3
HGS1029	antineoplastic agent	BIRC5
HGS1029	antineoplastic agent	XIAP
amlodipine	antihypertensive agent	CACNA1C
amlodipine	antihypertensive agent	CACNA1D
amlodipine	antihypertensive agent	CACNA1S
amlodipine	antihypertensive agent	CACNA2D1
amlodipine	antihypertensive agent	CACNAB2
simvastatin	antihypertensive agent	HMGCR
amiloride	antihypertensive agent	SCNN1A
amiloride	antihypertensive agent	SCNN1B
amiloride	antihypertensive agent	SCNN1D
amiloride	antihypertensive agent	SCNN1G
spironolactone	antihypertensive agent	NR3C2
huperzine-A	for treatment of Alzheimer's disease	ACHE
hydralazine	antihypertensive agent	AOC3
isosorbide dinitrate	antihypertensive agent	NPR1
hydroxytamoxifen	for treatment of cyclic mastalgia	ESR1
hydroxytamoxifen	for treatment of cyclic mastalgia	ESR2
famotidine	acid reducer	HRH2

Drug Name	Indication(s)	Gene
famotidine	for treatment of gastric ulcer and gastroesophageal reflux	HRH2
ibuprofen	NSAID	PTGS1
ibuprofen	NSAID	PTGS2
ibandronate	antiosteoporotic agent	FDPS
dexamethasone	antiinflammatory agent,glucocorticoid,for treatment of Meniere's disease	NR3C1
ibudilast	neuroprotectant	PDE4A
ibudilast	neuroprotectant	PDE4B
ibudilast	neuroprotectant	PDE4C
ICA-105665	anticonvulsant	KCNQ1
ICA-105665	anticonvulsant	KCNQ2
ICA-105665	anticonvulsant	KCNQ3
ICA-105665	anticonvulsant	KCNQ4
ICA-105665	anticonvulsant	KCNQ5
idrabiotaparinux	antithrombotic	F10
idraparinux	antithrombotic	F10
iferanserin	antihemorrhoidal agent	HTR2A
iloperidone	antipsychotic agent,atypical	ADRA1A
iloperidone	antipsychotic agent,atypical	ADRA2C
iloperidone	antipsychotic agent,atypical	DRD1
iloperidone	antipsychotic agent,atypical	DRD2
iloperidone	antipsychotic agent,atypical	DRD3
iloperidone	antipsychotic agent,atypical	HRH1
iloperidone	antipsychotic agent,atypical	HTR1A
iloperidone	antipsychotic agent,atypical	HTR2A
iloperidone	antipsychotic agent,atypical	HTR6

Drug Name	Indication(s)	Gene
iloperidone	antipsychotic agent,atypical	HTR7
iloprost	antihypertensive agent	PTGER1
iloprost	antihypertensive agent	PTGIR
fluocinolone acetonide	antiinflammatory agent,glucocorticoid	NR3C1
imatinib	antineoplastic agent	ABL1
imatinib	antineoplastic agent	CSF1R
imatinib	antineoplastic agent	DDR1
imatinib	antineoplastic agent	KIT
imatinib	antineoplastic agent	NTRK1
imatinib	antineoplastic agent	PDGFRA
imatinib	antineoplastic agent	PDGFRB
imatinib	antineoplastic agent	RET
Imiquimod	anti wart agent,antineoplastic agent	TLR7
implitapide	antiatherosclerotic agent	MTTP
INCB13739	antidiabetic	HSD11B1
INCB18424	antineoplastic agent,antiinflammatory agent	JAK1
INCB18424	antineoplastic agent,antiinflammatory agent	JAK2
INCB3284	antiinflammatory agent,DMARD	CCR2
INCB7839	antineoplastic agent	ADAM10
INCB7839	antineoplastic agent	ADAM17
indacaterol	bronchodilator	ADRB2
indomethacin	NSAID	KCNE1
indomethacin	NSAID	KCNQ1
Indiplon	hypnotic	GABRA1
inecalcitol	antineoplastic agent,prostate cancer	VDR

Drug Name	Indication(s)	Gene
apomorphine	for treatment of sexual dysfunction in women,for treatment of erectile dysfunction,antiparkinson agent	DRD2
apomorphine	for treatment of sexual dysfunction in women,for treatment of erectile dysfunction,antiparkinson agent	DRD3
apomorphine	for treatment of sexual dysfunction in women,for treatment of erectile dysfunction,antiparkinson agent	DRD4
atropine	nerve agent antidote	CHRM1
atropine	nerve agent antidote	CHRM2
atropine	nerve agent antidote	CHRM3
atropine	nerve agent antidote	CHRM4
atropine	nerve agent antidote	CHRM5
iniparib	antineoplastic agent	PARP1
INK128	antineoplastic agent	CRTC1
INK128	antineoplastic agent	CRTC2
INNO-206	antineoplastic agent	TOP2A
INO-8875	for treatment of glaucoma	ADORA1
INS37217	for treatment of rhegmatogenous retinal detachment	P2RY2
INS37217	for treatment of cystic fibrosis,for treatment of perennial allergic rhinitis	P2RY2
INSM-18	antineoplastic agent,prostate cancer	ERBB2
INSM-18	antineoplastic agent,prostate cancer	IGF1R
AMG-131	antidiabetic	PPARG

Drug Name	Indication(s)	Gene
apomorphine	for treatment of sexual dysfunction in women,for treatment of erectile dysfunction,antiparkinson agent	DRD2
apomorphine	for treatment of sexual dysfunction in women,for treatment of erectile dysfunction,antiparkinson agent	DRD3
apomorphine	for treatment of sexual dysfunction in women,for treatment of erectile dysfunction,antiparkinson agent	DRD4
ketorolac	NSAID	PTGS2
morphine	analgesic	OPRD1
morphine	analgesic	OPRK1
morphine	analgesic	OPRM1
retaspimycin	antineoplastic agent	HSP90AA1
retaspimycin	antineoplastic agent	HSP90AA2
retaspimycin	antineoplastic agent	HSP90AB1
IPI-504	antineoplastic agent	HSP90AA1
IPI-504	antineoplastic agent	HSP90AA2
IPI-504	antineoplastic agent	HSP90AB1
IPI-940	analgesic	FAAH
ipratropium	for treatment of chronic obstructive pulmonary disorder (COPD)	CHRM1
ipratropium	for treatment of chronic obstructive pulmonary disorder (COPD)	CHRM2
salbutamol	for treatment of chronic obstructive pulmonary disorder (COPD)	ADRB2
IPX066	antiparkinson agent	DDC
irbesartan	antihypertensive agent	AGTR1

Drug Name	Indication(s)	Gene
gefitinib	antineoplastic agent	EGFR
irinotecan	antineoplastic agent	TOP1
isofagomine	for treatment of Gaucher's disease	GBA
ispinesib	antineoplastic agent	KIF11
istaroxime	for treatment of heart failure	ATP1A1
istaroxime	for treatment of heart failure	ATP2A2
istradefylline	antiparkinson agent	ADORA2A
bromfenac	opthalmological agent,NSAID	PTGS1
bromfenac	opthalmological agent,NSAID	PTGS2
bromfenac	opthalmological agent,NSAID	PTGS1
bromfenac	opthalmological agent,NSAID	PTGS2
Givinostat	antineoplastic agent,antiinflammatory agent	HDAC1
Givinostat	antineoplastic agent,antiinflammatory agent	HDAC10
Givinostat	antineoplastic agent,antiinflammatory agent	HDAC2
Givinostat	antineoplastic agent,antiinflammatory agent	HDAC3
Givinostat	antineoplastic agent,antiinflammatory agent	HDAC4
Givinostat	antineoplastic agent,antiinflammatory agent	HDAC5
Givinostat	antineoplastic agent,antiinflammatory agent	HDAC6
Givinostat	antineoplastic agent,antiinflammatory agent	HDAC7

Drug Name	Indication(s)	Gene
Givinostat	antineoplastic agent,antiinflammatory agent	HDAC8
Givinostat	antineoplastic agent,antiinflammatory agent	HDAC9
ITI-007	antipsychotic agent	DRD2
ITI-007	antipsychotic agent	HTR2A
ITI-007	antipsychotic agent	PPP1R1B
ITI-007	antipsychotic agent	SLC6A4
itopride	motilitant	ACHE
itopride	motilitant	DRD2
IW-6118	analgesic	FAAH
ixabepilone	antineoplastic agent	TUBB3
JB991	antiinflammatory agent,dermatologic agent	PPARG
JNJ-37822681	antipsychotic agent	DRD2
JSM 6427	for treatment of age-related macular degeneration	ITGA5
JSM 6427	for treatment of age-related macular degeneration	ITGB1
ropinirole	for treatment of restlegs legs syndrome	DRD2
ropinirole	for treatment of restlegs legs syndrome	DRD3
ropinirole	for treatment of restlegs legs syndrome	DRD4
clonazepam	anticonvulsant	GABRA2
clonazepam	anticonvulsant	GABRA3
clonazepam	anticonvulsant	GABRA5

Drug Name	Indication(s)	Gene
clonazepam	anticonvulsant	GABRA6
clonazepam	anticonvulsant	GABRB1
clonazepam	anticonvulsant	GABRB1
clonazepam	anticonvulsant	GABRB2
clonazepam	anticonvulsant	GABRB2
clonazepam	anticonvulsant	GABRB3
clonazepam	anticonvulsant	GABRD
clonazepam	anticonvulsant	GABRD
clonazepam	anticonvulsant	GABRE
clonazepam	anticonvulsant	GABRG2
clonazepam	anticonvulsant	GABRG3
clonazepam	anticonvulsant	GABRG3
clonazepam	anticonvulsant	GABRP
clonazepam	anticonvulsant	GABRQ
clonazepam	anticonvulsant	GABRR2
Karenitecin	antineoplastic agent	TOP1
KC706	antiinflammatory agent,DMARD	MAPK11
KC706	antiinflammatory agent,DMARD	MAPK12
KC706	antiinflammatory agent,DMARD	MAPK13
KC706	antiinflammatory agent,DMARD	MAPK14
KD3010	antiobesity agent,for treatment of metabolic disorders	PPARD
ketoprofen	NSAID	PTGS1
ketoprofen	NSAID	PTGS2
ketoprofen	NSAID	PTGS1
ketoprofen	NSAID	PTGS1
ketoprofen	NSAID	PTGS2
ketoprofen	NSAID	PTGS2

Drug Name	Indication(s)	Gene
ketorolac	NSAID	PTGS1
ketorolac	NSAID	PTGS2
ketotifen	antiallergy agent	HRH1
ketoprofen	NSAID	PTGS1
ketoprofen	NSAID	PTGS1
ketoprofen	NSAID	PTGS2
ketoprofen	NSAID	PTGS2
KN38-7271	neuroprotectant	CNR1
KN38-7271	neuroprotectant	CNR2
KOS-2187	for treatment of gastrointestinal motility disorders	MLNR
kp201	analgesic	OPRD1
kp201	analgesic	OPRK1
kp201	analgesic	OPRM1
KRP-104	antidiabetic	DPP4
KUC-7483	for treatment of overactive bladder	ADRB3
KX2-391	antineoplastic agent	SRC
granisetron	antiemetic	HTR3A
Lacosamide	anticonvulsant,analgesic,neuropathic pain	DPYSL2
lamotrigine	anticonvulsant	SCN2A
lanreotide	for treatment of acromegaly	SSTR1
lanreotide	for treatment of acromegaly	SSTR5
lansoprazole	antiulcer agent	ATP4A
lansoprazole	antiulcer agent	ATP4A
LAS-100977	bronchodilator	ADRB2
lasmiditan	antimigraine agent	HTR1F

Drug Name	Indication(s)	Gene
lasofoxifene	antiosteoporotic agent,hormone replacement therapy	ESR1
latanoprost	for treatment of glaucoma	PTGFR
timolol	for treatment of glaucoma	ADRB1
timolol	for treatment of glaucoma	ADRB2
latanoprost	for treatment of glaucoma	PTGFR
latanoprost	for treatment of glaucoma	PTGFR
atorvastatin	anticholesterolaemic agent	HMGCR
fenofibrate	anticholesterolaemic agent	PPARA
fenofibrate	anticholesterolaemic agent	PPARA
sirolimus	immunosuppressant	FGF2
sirolimus	immunosuppressant	FKBP1A
sirolimus	immunosuppressant	FRAP1
Erismodegib	antineoplastic agent	SMO
LEE011	antineoplastic agent	CDK4
LEE011	antineoplastic agent	CDK6
lercanidipine	antihypertensive agent	CACNG1
LE-SN38	antineoplastic agent	TOP1
LE-SN38	antineoplastic agent	TOP1MT
lesogaberan	for treatment of gastrointestinal reflux disease	GABBR1
lesogaberan	for treatment of gastrointestinal reflux disease	GABBR2
lestaurtinib	antineoplastic agent	FLT3
lestaurtinib	antineoplastic agent	NTRK1
lestaurtinib	antineoplastic agent	NTRK2
lestaurtinib	antineoplastic agent	NTRK3
lestaurtinib	antineoplastic agent	JAK2

Drug Name	Indication(s)	Gene
ambrisentan	antihypertensive agent	EDNRA
ambrisentan	antihypertensive agent	EDNRB
letrozole	antineoplastic agent	CYP19A1
salbutamol	bronchodilator	ADRB2
levetiracetam	anticonvulsant	CACNA1B
levetiracetam	anticonvulsant	SV2A
levocetirizine	antiallergy agent	HRH1
levodopa	antiparkinson agent	DRD1
levodopa	antiparkinson agent	DRD2
levodopa	antiparkinson agent	DRD3
levodopa	antiparkinson agent	DRD4
levodopa	antiparkinson agent	DRD5
levomilnacipran	antidepressant	SLC6A2
levomilnacipran	antidepressant	SLC6A4
ethinyl estradiol	contraceptive	ESR1
levonorgestrel	contraceptive	ESR1
levonorgestrel	contraceptive	PGR
levonorgestrel	contraceptive	SRD5A1
Levosimendan	for treatment of heart failure	KCNJ11
Levosimendan	for treatment of heart failure	TNNC1
levothyroxine	hormone replacement	THRA
levothyroxine	hormone replacement	THRB
levothyroxine	hormone replacement	THRA
levothyroxine	hormone replacement	THRB
LGD-1550	antineoplastic agent	RARA
LGD-1550	antineoplastic agent	RARB
LGD-1550	antineoplastic agent	RARG
LGD-2941	antiosteoporotic agent	AR

Drug Name	Indication(s)	Gene
LGD-4033	hormone replacement	AR
LGD-4665	thrombopoietic agent	MPL
Liarozole	dermatological agent,for treatment of ichtyosis	CYP26A1
licarbazepine	for treatment of bipolar disorder	SCN5A
licofelone	antiinflammatory agent	ALOX5
licofelone	antiinflammatory agent	PTGS2
lidocaine	anestethic	SCN9A
lidocaine	anestethic	SCN10A
lidocaine	anestethic	SCN5A
piroxicam	antiinflammatory agent,NSAID	PTGS2
lidocaine	anestethic	SCN10A
lidocaine	anestethic	SCN5A
lidocaine	anestethic	SCN9A
lidocaine	anestethic	SCN10A
lidocaine	anestethic	SCN5A
lidocaine	anestethic	SCN9A
lidocaine	anestethic	SCN10A
lidocaine	anestethic	SCN5A
lidocaine	anestethic	SCN9A
LIM-0705	for improving pharmacokinetics of tacrolimus	ABCA5
LIM-0705	for improving pharmacokinetics of tacrolimus	ABCB1
Linaglipton	antidiabetic	DPP4
fluticasone propionate	for treatment of symptomatic exophthalmos associated with thyroid-related eye disease	NR3C1

Drug Name	Indication(s)	Gene
salbutamol	for treatment of symptomatic exophthalmos associated with thyroid-related eye disease	ADRB2
docetaxel	antineoplastic agent	BCL2
docetaxel	antineoplastic agent	TUBB1
doxorubicin	antineoplastic agent	TOP2A
paclitaxel	antineoplastic agent	TOP2A
lurtotecan	antineoplastic agent	TOP1
mitoxantrone	antineoplastic agent	TOP2A
prednisolone	antiinflammatory agent,corticosteroid	NR3C1
Lipotecan	antineoplastic agent	TOP1
lisinopril	antihypertensive agent	ACE
Lisofylline	antidiabetic	STAT4
lixivaptan	for treatment of hyponatremia	AVPR2
Lobeline	for treatment of metamphetamine addicton	SLC18A2
lofexidine	for treatment of opiate withdrawal	ADRA2A
lofexidine	for treatment of opiate withdrawal	ADRA2B
lofexidine	for treatment of opiate withdrawal	ADRA2C
lomitapide	anticholesterolaemic agent	MTTP
LOR-253	antineoplastic agent	MTF1
loratadine	antiasthmatic agent	HRH1
montelukast	antiasthmatic agent	CYSLTR1
Lorcaserin	antiobesity agent	HTR2C
loteprednol etabonate	antiinflammatory agent,corticosteroid	NR3C1
methamphetamine	neuroprotectant	ADRA2A

Drug Name	Indication(s)	Gene
methamphetamine	neuroprotectant	ADRA2B
methamphetamine	neuroprotectant	ADRA2C
methamphetamine	neuroprotectant	MAOA
methamphetamine	neuroprotectant	MAOB
methamphetamine	neuroprotectant	SLC18A1
methamphetamine	neuroprotectant	SLC18A2
methamphetamine	neuroprotectant	SLC6A2
methamphetamine	neuroprotectant	SLC6A3
methamphetamine	neuroprotectant	SLC6A4
methamphetamine	neuroprotectant	TAAR1
lovastatin	anticholesterolaemic agent	HMGCR
enoxaparin	anticoagulant	F2
vortioxetine	antidepressant	HTR1A
vortioxetine	antidepressant	HTR1B
vortioxetine	antidepressant	HTR3A
vortioxetine	antidepressant	HTR7
vortioxetine	antidepressant	SLC6A4
Tedatioxetine	antidepressant	ADRA1A
Tedatioxetine	antidepressant	HTR2C
Tedatioxetine	antidepressant	HTR2C
Tedatioxetine	antidepressant	HTR3A
Tedatioxetine	antidepressant	SLC6A2
Tedatioxetine	antidepressant	SLC6A3
Tedatioxetine	antidepressant	SLC6A4
zicronapine	antipsychotic agent	DRD4
Lu-AE58054	antipsychotic agent	HTR6
Lubiprostone	motilitant,for treatment of irritable bowel disorder	CLCN2

Drug Name	Indication(s)	Gene
lumiracoxib	NSAID	PTGS2
eszopiclone	hypnotic	GABRA1
eszopiclone	hypnotic	GABRA2
eszopiclone	hypnotic	GABRA3
eszopiclone	hypnotic	GABRA5
eszopiclone	hypnotic	TSPO
lurasidone	antipsychotic agent	ADRA2C
lurasidone	antipsychotic agent	DRD2
lurasidone	antipsychotic agent	HTR1A
lurasidone	antipsychotic agent	HTR2A
lurasidone	antipsychotic agent	HTR7
LX1031	for treatment of irritable bowel syndrome	TPH1
LX1032	for treatment of carcinoid syndrome	TPH1
cyclosporine A	immunosuppressant,opthalmological agent	CAMLG
cyclosporine A	immunosuppressant,opthalmological agent	PPP3R2
LX4211	antidiabetic	SLC5A1
LX4211	antidiabetic	SLC5A2
LY2140023	antipsychotic agent	GRM2
LY2140023	antipsychotic agent	GRM3
LY3009104	antiinflammatory agent,DMARD	JAK1
LY3009104	antiinflammatory agent,DMARD	JAK2
semagacestat	for treatment of Alzheimer's disease	PSEN1
semagacestat	for treatment of Alzheimer's disease	PSEN2
LY-517717	anticoagulant	F10
naveglitazar	antidiabetic	PPARA

Drug Name	Indication(s)	Gene
naveglitazar	antidiabetic	PPARG
LY-674	anticholesterolaemic agent	PPARA
M0002	for treatemnt of ascites	AVPR2
heparin	anticoagulant	F10
heparin	anticoagulant	HPSE
heparin	anticoagulant	SERPINC1
morphine	analgesic	OPRD1
morphine	analgesic	OPRK1
morphine	analgesic	OPRM1
macitentan	cardiovascular agent	EDNRA
macitentan	cardiovascular agent	EDNRB
dihydroergotamine	antimigraine agent	HTR1B
dihydroergotamine	antimigraine agent	HTR1D
budesonide	antiinflammatory agent,glucocorticoid	NR3C1
formoterol	bronchodilator	ADRB2
budesonide	antiinflammatory agent,glucocorticoid	NR3C1
masitinib	antiinflammatory agent,DMARD,antineoplastic agent	ABL1
masitinib	antiinflammatory agent,DMARD,antineoplastic agent	CSF1R
masitinib	antiinflammatory agent,DMARD,antineoplastic agent	HCK
masitinib	antiinflammatory agent,DMARD,antineoplastic agent	KIT
masitinib	antiinflammatory agent,DMARD,antineoplastic agent	LYN

Drug Name	Indication(s)	Gene
masitinib	antiinflammatory agent,DMARD,antineoplastic agent	PDGFRA
masitinib	antiinflammatory agent,DMARD,antineoplastic agent	PDGFRB
masitinib	antiinflammatory agent,DMARD,antineoplastic agent	SRC
mesalazine	for treatment of ulcerative proctitis	ALOX5
mesalazine	for treatment of ulcerative proctitis	PPARG
mesalazine	for treatment of ulcerative proctitis	PTGS1
mesalazine	for treatment of ulcerative proctitis	PTGS2
MB07811	antidyslipidaemic agent	THRB
MBX-2044	antidiabetic	PPARG
MBX-2982	antidiabetic	GPR119
MBX-8025	antidyslipidaemic agent	PPARD
lisinopril	antihypertensive agent	ACE
lisinopril	antihypertensive agent	ACE2
MC-1	cardioprotectant	LPAR4
MC-1	cardioprotectant	LPAR6
MC-1	cardioprotectant	P2RY1
MC-1	cardioprotectant	P2RY10
MC-1	cardioprotectant	P2RY11
MC-1	cardioprotectant	P2RY12
MC-1	cardioprotectant	P2RY13
MC-1	cardioprotectant	P2RY14
MC-1	cardioprotectant	P2RY2
MC-1	cardioprotectant	P2RY4
MC-1	cardioprotectant	P2RY6
MC-1	cardioprotectant	P2RY8

Drug Name	Indication(s)	Gene
MCD-386	for treatment of Alzheimer's disease	CHRM1
MDAM	antineoplastic agent	DHFR
MDV3100	antineoplastic agent	AR
Mebendazole	antineoplastic agent	TUBA1A
Mebendazole	antineoplastic agent	TUBB2C
mecamylamine	for treatment of ADHD	CHRNA2
melogliptin	antidiabetic	DPP4
MEM 1003	for treatment of Alzheimer's disease	CACNA1C
MEM 1003	for treatment of Alzheimer's disease	CACNA1D
MEM 1003	for treatment of Alzheimer's disease	CACNA1F
MEM 1003	for treatment of Alzheimer's disease	CACNA1S
MEM 1414	for treatment of Alzheimer's disease	PDE4A
MEM 1414	for treatment of Alzheimer's disease	PDE4B
MEM 63908	for treatment of Alzheimer's disease	CHRNA7
MEM3454	for treatment of Alzheimer's disease	CHRNA7
memantine	for treatment of glaucoma	GRIN2A
memantine	for treatment of glaucoma	GRIN2B
memantine	for treatment of glaucoma	GRIN3A
vorinostat	antineoplastic agent	HDAC1
vorinostat	antineoplastic agent	HDAC2
vorinostat	antineoplastic agent	HDAC3
vorinostat	antineoplastic agent	HDAC6
mesalamine	antiinflammatory agent	ALOX5
mesalamine	antiinflammatory agent	PPARG
mesalamine	antiinflammatory agent	PTGS1
mesalamine	antiinflammatory agent	PTGS2
WX-671	antineoplastic agent	PLAU

Drug Name	Indication(s)	Gene
Oxypurinol	for treatment of heart failure,for treatment of gout	XDH
metaglidasen	antidiabetic	PPARG
metformin	antidiabetic	PRKAB1
metformin	antidiabetic	PRKAB1
metformin	antidiabetic	PRKAB1
Methylnaltrexone	for treatment of opioid-induced constipation	OPRM1
methylphenidate	for treatment of ADHD	SLC6A2
methylphenidate	for treatment of ADHD	SLC6A3
methylphenidate	for treatment of ADHD	SLC6A4
methylphenidate	for treatment of ADHD	SLC6A2
methylphenidate	for treatment of ADHD	SLC6A3
methylphenidate	for treatment of ADHD	SLC6A4
methylphenidate	for treatment of ADHD	SLC6A2
methylphenidate	for treatment of ADHD	SLC6A3
methylphenidate	for treatment of ADHD	SLC6A4
methyltestosterone	for treatment of dysfunctional libido in women	AR
metoclopramide	motilitant,for treatment of gastroesophageal reflux disease	CHRM1
metoclopramide	motilitant,for treatment of gastroesophageal reflux disease	DRD2
metoclopramide	antiemetic	CHRM1
metoclopramide	antiemetic	DRD2
metoprolol	antihypertensive agent	ADRB1
MF101	for treatment of menopausal symptoms	ESR2

Drug Name	Indication(s)	Gene
MGCD-0103	antineoplastic agent	HDAC1
MGCD-0103	antineoplastic agent	HDAC10
MGCD-0103	antineoplastic agent	HDAC11
MGCD-0103	antineoplastic agent	HDAC2
MGCD-0103	antineoplastic agent	HDAC3
MGCD-0103	antineoplastic agent	HDAC4
MGCD-0103	antineoplastic agent	HDAC5
MGCD-0103	antineoplastic agent	HDAC6
MGCD-0103	antineoplastic agent	HDAC7A
MGCD-0103	antineoplastic agent	HDAC8
MGCD-0103	antineoplastic agent	HDAC9
MGCD265	antineoplastic agent	FLT1
MGCD265	antineoplastic agent	FLT4
MGCD265	antineoplastic agent	KDR
MGCD265	antineoplastic agent	MET
MGCD265	antineoplastic agent	MST1R
MGCD265	antineoplastic agent	TEK
morphine	analgesic	OPRD1
morphine	analgesic	OPRK1
morphine	analgesic	OPRM1
paclitaxel	antiinflammatory agent,DMARD	BCL2
paclitaxel	antiinflammatory agent,DMARD	TUBB1
Midostaurin	antineoplastic agent	FLT3
Mifepristone	opthalmological agent,for lowering intraocular pressure	NR3C1
Mifepristone	opthalmological agent,for lowering intraocular pressure	PGR
Mifepristone	antipsychotic,antidepressant	NR3C1

Drug Name	Indication(s)	Gene
Mifepristone	antipsychotic,antidepressant	PGR
migalastat	enzyme replacement therapy,for treatment of Fabry disease	GLA
miglustat	for treatment of Gaucher's disease	UGCG
milataxel	antineoplastic agent	BCL2
milataxel	antineoplastic agent	TUBB1
Milnacipran	for treatment of fibromyalgia syndrome	SLC6A2
Milnacipran	for treatment of fibromyalgia syndrome	SLC6A4
milveterol	bronchodilator	ADRB2
MIM-D3	opthalmological agent	NTRK1
minodronate	antineoplastic agent	FDPS
pramipexole	antiparkinson agent	DRD2
pramipexole	antiparkinson agent	DRD3
pramipexole	antiparkinson agent	DRD4
mirtazapine	antidepressant	ADRA2A
mirtazapine	antidepressant	HTR2A
mirtazapine	antidepressant	HTR3A
mitemcinal	for treatment of gastroparesis	MLNR
mitiglinide	antidiabetic	ABCC8
mitoxantrone	antineoplastic agent	TOP2A
MIV-701	for treatment of osteoporosis	CTSK
laropiprant	for counteracting niacin-induced flushing	PTGDR
niacin	antidyslipidaemic agent	GPR109A
niacin	antidyslipidaemic agent	GPR109B
niacin	antidyslipidaemic agent	NNMT

Drug Name	Indication(s)	Gene
niacin	antidyslipidaemic agent	QPRT
laropiprant	for counteracting niacin-induced flushing	PTGDR
niacin	antidyslipidaemic agent	GPR109A
niacin	antidyslipidaemic agent	GPR109B
niacin	antidyslipidaemic agent	NNMT
niacin	antidyslipidaemic agent	QPRT
simvastatin	anticholesterolaemic agent	HMGCR
MK-1775	antineoplastic agent	WEE1
MK-2206	antineoplastic agent	AKT1
MK-2206	antineoplastic agent	AKT2
MK-2206	antineoplastic agent	AKT3
suvorexant	hypnotic	HCRTR1
suvorexant	hypnotic	HCRTR2
MK-4827	antineoplastic agent	PARP1
MK-4827	antineoplastic agent	PARP2
MKC-1	antineoplastic agent	IPO11
MKC-1	antineoplastic agent	IPO13
MKC-1	antineoplastic agent	IPO4
MKC-1	antineoplastic agent	IPO7
MKC-1	antineoplastic agent	IPO8
MKC-1	antineoplastic agent	IPO9
MKC-1	antineoplastic agent	TUBB
MKC-1	antineoplastic agent	TUBB1
MLN-0415	antiinflammatory agent	IKBKB
MLN-4924	antineoplastic agent	UBA3
MLN-8054	antineoplastic agent	AUR2
MLN-8237	antineoplastic agent	AURKA

Drug Name	Indication(s)	Gene
MLN-9708	antineoplastic agent	PSMB1
MLN-9708	antineoplastic agent	PSMB2
MLN-9708	antineoplastic agent	PSMB5
MLN-9708	antineoplastic agent	PSMD1
MLN-9708	antineoplastic agent	PSMD2
MN-201	antineoplastic agent	VDR
MN-246	for treatment of overactive bladder	ADRB3
MN-305	antidepressant,hypnotic	HTR1A
moclobemide	antidepressant	MAOA
modafinil	central nervous system stimulant	SLC6A3
Modufolin	antineoplastic agent	TYMS
formoterol	antiasthmatic agent	ADRB2
mometasone	antiinflammatory agent,glucocorticoid	NR3C1
montelukast	antiasthmatic agent	CYSLTR1
morphine	analgesic	OPRD1
morphine	analgesic	OPRK1
morphine	analgesic	OPRM1
morphine	analgesic	OPRK1
morphine	analgesic	OPRK1
morphine	analgesic	OPRK1
dextromethorphan	analgesic	GRIN3A
dextromethorphan	analgesic	SIGMAR1
morphine	analgesic	OPRD1
morphine	analgesic	OPRK1
morphine	analgesic	OPRM1
morphine	analgesic	OPRD1
morphine	analgesic	OPRK1

Drug Name	Indication(s)	Gene
morphine	analgesic	OPRM1
naltrexone	analgesic	OPRD1
naltrexone	analgesic	OPRK1
naltrexone	analgesic	OPRM1
naltrexone	analgesic	SIGMAR1
mosapride	for treatment of Gastrointestinal reflux disease (GERD)	HTR4
motesanib	antineoplastic agent	FLT1
motesanib	antineoplastic agent	FLT4
motesanib	antineoplastic agent	KDR
motesanib	antineoplastic agent	KIT
motesanib	antineoplastic agent	PDGFRA
motesanib	antineoplastic agent	PDGFRB
motexafin gadolinium	antineoplastic agent	RRM1
motexafin gadolinium	antineoplastic agent	RRM2
motexafin gadolinium	antineoplastic agent	RRM2B
motexafin gadolinium	antineoplastic agent	TXNRD1
motexafin gadolinium	antineoplastic agent	TXNRD2
motexafin gadolinium	antineoplastic agent	TXNRD3
morphine	analgesic	OPRD1
morphine	analgesic	OPRK1
morphine	analgesic	OPRM1
oxycodone	analgesic	OPRM1
oxycodone	analgesic	OPRM1
oxycodone	analgesic	OPRM1
plerixafor	antineoplastic agent	CXCR4
MP0112	for treatment of diabetic retinopathy	FLT1
MP0112	for treatment of diabetic retinopathy	KDR

Drug Name	Indication(s)	Gene
amuvatinib	antineoplastic agent	FLT3
amuvatinib	antineoplastic agent	KIT
amuvatinib	antineoplastic agent	MET
amuvatinib	antineoplastic agent	PDGFRA
amuvatinib	antineoplastic agent	PDGFRB
amuvatinib	antineoplastic agent	RAD51
amuvatinib	antineoplastic agent	RET
MPC-0920	antithrombotic	F2
MPI-674	for treatment of abnormal uterine bleeding (AUB)	CYP19A1
MPI-676	for treatment of endometriosis	CYP19A1
nitroglycerin	for treatment of Raynaud's disease	NPR1
MRX-4	antiinflammatory agent	PLA2G3
MRX-6	antiinflammatory agent	PLA2G3
mitoglitazone	antidiabetic	PPARG
talniflumate	for treatment of cystic fibrosis	CLCA1
MSX-122	antineoplastic agent	CXCR4
metoclopramide	antimigraine agent	CHRM1
metoclopramide	antimigraine agent	DRD2
naproxen	antimigraine agent	PTGS1
naproxen	antimigraine agent	PTGS2
dihydroergotamine	antimigraine agent	HTR1B
dihydroergotamine	antimigraine agent	HTR1D
naproxen	antimigraine agent	PTGS1
naproxen	antimigraine agent	PTGS2
sumatriptan	antimigraine agent	HTR1A
sumatriptan	antimigraine agent	HTR1B
sumatriptan	antimigraine agent	HTR1D

Drug Name	Indication(s)	Gene
sumatriptan	antimigraine agent	HTR1F
doxorubicin	antineoplastic agent	TOP2A
isothiourea	antihypertensive agent	NOS1
isothiourea	antihypertensive agent	NOS2
isothiourea	antihypertensive agent	NOS3
muraglitazar	antidiabetic	PPARA
muraglitazar	antidiabetic	PPARG
mycophenolic acid	immunosuppressant	IMPDH1
mycophenolic acid	immunosuppressant	IMPDH2
MPC-3100	antineoplastic agent	HSP90AA1
MPC-3100	antineoplastic agent	HSP90AB1
docetaxel	antineoplastic agent	BCL2
docetaxel	antineoplastic agent	TUBB1
nabilone	antiemetic	CNR1
nabilone	antiemetic	CNR2
nalbuphine	analgesic	OPRD1
nalbuphine	analgesic	OPRK1
nalbuphine	analgesic	OPRM1
nalmefene	smoking-cessation agent,for treatment of addiction	OPRD1
nalmefene	smoking-cessation agent,for treatment of addiction	OPRK1
nalmefene	smoking-cessation agent,for treatment of addiction	OPRM1
memantine	for treatment of Alzheimer's disease	GRIN2A
memantine	for treatment of Alzheimer's disease	GRIN2B
memantine	for treatment of Alzheimer's disease	GRIN3A
diclofenac	NSAID	PTGS1

Drug Name	Indication(s)	Gene
diclofenac	NSAID	PTGS2
Naproxcinod	NSAID	GUCY1A2
Naproxcinod	NSAID	PTGS1
Naproxcinod	NSAID	PTGS2
esomeprazole	Proton pump inhibitor	ATP4A
naproxen	NSAID	PTGS1
naproxen	NSAID	PTGS2
naproxen etemesil	NSAID	PTGS1
naproxen etemesil	NSAID	PTGS2
naratriptan	antimigraine agent	HTR1A
naratriptan	antimigraine agent	HTR1B
naratriptan	antimigraine agent	HTR1D
naratriptan	antimigraine agent	HTR1F
ketamine	analgesic	GRIN3A
ketamine	analgesic	GRIN3A
Nav 1.7 blocker	analgesic	SCN9A
NB-1011	antineoplastic agent	TYMS
NBI-56418	antineoplastic agent	GNRHR
NBI-98854	antipsychotic agent	SLC18A2
NCX 1510	antiallergy agent	GUCY1A2
NCX 1510	antiallergy agent	HRH1
NCX 4016	antithrombotic	GUCY1A2
NCX 4016	antithrombotic	PTGS1
NCX 4016	antithrombotic	PTGS2
carbidopa	antiparkinson agent	DDC
nebivolol	antihypertensive agent	ADRB1
nelarabine	antineoplastic agent	POLA1

Drug Name	Indication(s)	Gene
nepicastat	for treatment of addiction,for treatment of post-traumatic stress disorder	DBH
neramexane	for treatment of Alzheimer's disease	GRIN2A
neramexane	for treatment of Alzheimer's disease	GRIN2B
neramexane	for treatment of Alzheimer's disease	GRIN3A
neratinib	antineoplastic agent	EGFR
neratinib	antineoplastic agent	ERBB2
ethinyl estradiol	contraceptive	ESR1
progestin	contraceptive	PGR
Neu-2000	cardioprotectant	GRIN1
Neu-2000	cardioprotectant	GRIN2A
Neu-2000	cardioprotectant	GRIN2B
Neu-2000	cardioprotectant	GRIN2C
Neu-2000	cardioprotectant	GRIN2D
Neu-2000	cardioprotectant	GRIN3A
Neu-2000	cardioprotectant	GRIN3B
rotigotine	antiparkinson agent	DRD2
rotigotine	antiparkinson agent	DRD3
rotigotine	antiparkinson agent	DRD4
sorafenib	antineoplastic agent	BRAF
sorafenib	antineoplastic agent	FLT3
sorafenib	antineoplastic agent	FLT4
sorafenib	antineoplastic agent	KDR
sorafenib	antineoplastic agent	KIT
sorafenib	antineoplastic agent	PDGFRB
sorafenib	antineoplastic agent	RAF1
NG2-73	hypnotic	GABRA2

Drug Name	Indication(s)	Gene
NG2-73	hypnotic	GABRA3
NG2-73	hypnotic	GABRA5
NG2-73	hypnotic	GABRA6
NG2-73	hypnotic	GABRB1
NG2-73	hypnotic	GABRB1
NG2-73	hypnotic	GABRB2
NG2-73	hypnotic	GABRB2
NG2-73	hypnotic	GABRB3
NG2-73	hypnotic	GABRD
NG2-73	hypnotic	GABRD
NG2-73	hypnotic	GABRE
NG2-73	hypnotic	GABRG1
NG2-73	hypnotic	GABRG2
NG2-73	hypnotic	GABRG3
NG2-73	hypnotic	GABRG3
NG2-73	hypnotic	GABRP
NG2-73	hypnotic	GABRQ
NG2-73	hypnotic	GABRR2
NGD-4715	appetite suppressant	MCHR1
NGD-8243	analgesic	TRPV1
NGX267	for treatment of dry mouth	CHRM1
niacin receptor agonist	antiatherosclerotic agent	HCAR2
niacin receptor agonist	antiatherosclerotic agent	HCAR3
NIC5-15	for treatment of Alzheimer's disease	APH1A
NIC5-15	for treatment of Alzheimer's disease	PSENEN
nilotinib	antineoplastic agent	ABL1

Drug Name	Indication(s)	Gene
nitisinone	for treatment of restlegs legs syndrome,for treatment of hereditary tyrosinemia type 1 (HT-1)	HPD
PEG-irinotecan	antineoplastic agent	TOP1
PEG-irinotecan	antineoplastic agent	TOP1MT
PEG-docetaxel	antineoplastic agent	BCL2
PEG-docetaxel	antineoplastic agent	TUBB1
PEG-naloxol	for treatment of opioid-induced constipation	OPRM1
NM-702	for treatment of intermittent claudication	PDE3A
NM-702	for treatment of intermittent claudication	PDE3B
hydromorphone	analgesic	OPRD1
hydromorphone	analgesic	OPRK1
hydromorphone	analgesic	OPRM1
NMS-1116354	antineoplastic agent	CDC7
NNZ-2566	neuroprotectant	IGF1
ethinyl estradiol	contraceptive	ESR1
norelgestromin	contraceptive	ESR1
norelgestromin	contraceptive	PGR
noscapine	antineoplastic agent	HIF1A
latanoprost	for treatment of glaucoma	PTGFR
Cyclosporine A	immunosuppressant,opthalmological agent	CAMLG
Cyclosporine A	immunosuppressant,opthalmological agent	PPP3R2
sumatriptan	antimigraine agent	HTR1A

Drug Name	Indication(s)	Gene
sumatriptan	antimigraine agent	HTR1B
sumatriptan	antimigraine agent	HTR1D
sumatriptan	antimigraine agent	HTR1F
17-beta estradiol	opthalmological agent	ESR1
17-beta estradiol	opthalmological agent	ESR2
Fluoxetine	for treatment of autism	HTR2A
Fluoxetine	for treatment of autism	SLC6A4
NPS-2143	antiosteoporotic agent	CASR
diazepam	anticonvulsant	GABRA1
diazepam	anticonvulsant	GABRA2
diazepam	anticonvulsant	GABRA3
diazepam	anticonvulsant	GABRA5
diazepam	anticonvulsant	GABRB1
diazepam	anticonvulsant	GABRB2
diazepam	anticonvulsant	GABRB3
diazepam	anticonvulsant	GABRD
diazepam	anticonvulsant	GABRE
diazepam	anticonvulsant	GABRG1
diazepam	anticonvulsant	GABRG2
diazepam	anticonvulsant	GABRG3
diazepam	anticonvulsant	GABRP
diazepam	anticonvulsant	GABRQ
diazepam	anticonvulsant	GABRR1
diazepam	anticonvulsant	GABRR2
diazepam	anticonvulsant	GABRR3
NRM8499	for treatment of Alzheimer's disease	APP
NRP290	analgesic	OPRD1
NRP290	analgesic	OPRK1

Drug Name	Indication(s)	Gene
NRP290	analgesic	OPRM1
triiodothyronine (T3)	hormone replacement	THRA
triiodothyronine (T3)	hormone replacement	THRB
NRX-5183	hematopoietic agent	RARA
NS-304	antihypertensive agent	PTGIR
NSD-644	analgesic,antidepressant	SLC6A2
NSD-644	analgesic,antidepressant	SLC6A3
NSD-644	analgesic,antidepressant	SLC6A4
NSD-788	antidepressant	SLC6A2
NSD-788	antidepressant	SLC6A4
allopurinol	for treatment of gout	XDH
NV-52	antiinflammatory agent	TBXAS1
glycopyrronium	for treatment of chronic obstructive pulmonary disease (COPD)	CHRM1
tizanidine	for treatment of skeletal muscular spasticity	ADRA2A
tizanidine	for treatment of skeletal muscular spasticity	ADRA2B
tizanidine	for treatment of skeletal muscular spasticity	ADRA2C
NXN-188	antimigraine agent	HTR1B
NXN-188	antimigraine agent	HTR1D
NXN-188	antimigraine agent	NOS1
ondansetron	antiemetic	HTR3A
paclitaxel	antineoplastic agent	BCL2
paclitaxel	antineoplastic agent	TUBB1
obatoclax	antineoplastic agent	BCL2
betahistine	antiobesity agent	HRH1

Drug Name	Indication(s)	Gene
betahistine	antiobesity agent	HRH3
obeticholic acid	for treatment of non-alcoholic fatty liver disease (NAFLD),for treatment of Primary Biliary Cirrhosis (PBC)	NR1H4
OC000459	antiallergy agent	PD2R2
ocinaplon	anxiolytic	GABRA2
ocinaplon	anxiolytic	GABRA3
ocinaplon	anxiolytic	GABRA5
ocinaplon	anxiolytic	GABRA6
ocinaplon	anxiolytic	GABRB1
ocinaplon	anxiolytic	GABRB1
ocinaplon	anxiolytic	GABRB2
ocinaplon	anxiolytic	GABRB2
ocinaplon	anxiolytic	GABRB3
ocinaplon	anxiolytic	GABRD
ocinaplon	anxiolytic	GABRD
ocinaplon	anxiolytic	GABRE
ocinaplon	anxiolytic	GABRG1
ocinaplon	anxiolytic	GABRG2
ocinaplon	anxiolytic	GABRG3
ocinaplon	anxiolytic	GABRG3
ocinaplon	anxiolytic	GABRP
ocinaplon	anxiolytic	GABRQ
ocinaplon	anxiolytic	GABRR2
heparin	antithrombotic	F10
heparin	antithrombotic	F2
odanacatib	antiosteoporotic agent	CTSK
Oglemilast	antiasthmatic agent	PDE4A

Drug Name	Indication(s)	Gene
Oglemilast	antiasthmatic agent	PDE4B
olanzapine	antipsychotic agent	ADRA1A
olanzapine	antipsychotic agent	ADRA1B
olanzapine	antipsychotic agent	ADRA2A
olanzapine	antipsychotic agent	ADRA2B
olanzapine	antipsychotic agent	ADRA2C
olanzapine	antipsychotic agent	CHRM1
olanzapine	antipsychotic agent	CHRM2
olanzapine	antipsychotic agent	CHRM3
olanzapine	antipsychotic agent	CHRM4
olanzapine	antipsychotic agent	CHRM5
olanzapine	antipsychotic agent	DRD1
olanzapine	antipsychotic agent	DRD2
olanzapine	antipsychotic agent	DRD3
olanzapine	antipsychotic agent	DRD4
olanzapine	antipsychotic agent	DRD5
olanzapine	antipsychotic agent	HRH1
olanzapine	antipsychotic agent	HTR1A
olanzapine	antipsychotic agent	HTR1B
olanzapine	antipsychotic agent	HTR1D
olanzapine	antipsychotic agent	HTR1E
olanzapine	antipsychotic agent	HTR2A
olanzapine	antipsychotic agent	HTR2C
olanzapine	antipsychotic agent	HTR3A
olanzapine	antipsychotic agent	HTR6
olanzapine	antipsychotic agent	HTR7
fluoxetine	antidepressant,for treatment of bipolar disorder	SLC6A4

Drug Name	Indication(s)	Gene
olanzapine	antidepressant,for treatment of bipolar disorder	ADRA1A
olanzapine	antidepressant,for treatment of bipolar disorder	ADRA1B
olanzapine	antidepressant,for treatment of bipolar disorder	ADRA2A
olanzapine	antidepressant,for treatment of bipolar disorder	ADRA2B
olanzapine	antidepressant,for treatment of bipolar disorder	ADRA2C
olanzapine	antidepressant,for treatment of bipolar disorder	CHRM1
olanzapine	antidepressant,for treatment of bipolar disorder	CHRM2
olanzapine	antidepressant,for treatment of bipolar disorder	CHRM3
olanzapine	antidepressant,for treatment of bipolar disorder	CHRM4
olanzapine	antidepressant,for treatment of bipolar disorder	CHRM5
olanzapine	antidepressant,for treatment of bipolar disorder	DRD1
olanzapine	antidepressant,for treatment of bipolar disorder	DRD2
olanzapine	antidepressant,for treatment of bipolar disorder	DRD3
olanzapine	antidepressant,for treatment of bipolar disorder	DRD4

Drug Name	Indication(s)	Gene
olanzapine	antidepressant,for treatment of bipolar disorder	DRD5
olanzapine	antidepressant,for treatment of bipolar disorder	HRH1
olanzapine	antidepressant,for treatment of bipolar disorder	HTR1A
olanzapine	antidepressant,for treatment of bipolar disorder	HTR1B
olanzapine	antidepressant,for treatment of bipolar disorder	HTR1D
olanzapine	antidepressant,for treatment of bipolar disorder	HTR1E
olanzapine	antidepressant,for treatment of bipolar disorder	HTR2A
olanzapine	antidepressant,for treatment of bipolar disorder	HTR2C
olanzapine	antidepressant,for treatment of bipolar disorder	HTR3A
olanzapine	antidepressant,for treatment of bipolar disorder	HTR6
olanzapine	antidepressant,for treatment of bipolar disorder	HTR7
olesoxime	for treatment of motor neuron disease	TSPO
olesoxime	for treatment of motor neuron disease	VDAC1
olesoxime	for treatment of motor neuron disease	VDAC2
olesoxime	for treatment of motor neuron disease	VDAC3
olmesartan	antihypertensive agent	AGTR1
olmesartan	for treatment of glaucoma	AGTR1

Drug Name	Indication(s)	Gene
olopatadine	antiallergy agent	HRH1
omacetaxine mepesuccinate	antineoplastic agent	Ribosome A-site
ombrabulin	antineoplastic agent	TUBB1
omecamtiv mecarbil	for treatment of heart failure	Cardiac Mysoin
omeprazole	Proton pump inhibitor	ATP4A
omeprazole	Proton pump inhibitor	ATP4A
omeprazole	Proton pump inhibitor	ATP4A
omigapil	antiparkinson agent,for treatment of amyotrophic lateral sclerosis (ALS)	GAPDA
omigapil	antiparkinson agent,for treatment of amyotrophic lateral sclerosis (ALS)	SIAH1
amitriptyline	analgesic	HTR2A
amitriptyline	analgesic	HTR2A
amitriptyline	analgesic	SLC6A2
amitriptyline	analgesic	SLC6A2
amitriptyline	analgesic	SLC6A4
amitriptyline	analgesic	SLC6A4
ketoprofen	NSAID	PTGS1
ketoprofen	NSAID	PTGS1
ketoprofen	NSAID	PTGS2
ketoprofen	NSAID	PTGS2
oxymetazoline	analgesic	ADRA1A
oxymetazoline	analgesic	ADRA1A
oxymetazoline	analgesic	ADRA2A
oxymetazoline	analgesic	ADRA2A
rigosertib	antineoplastic agent	PIK3CA
rigosertib	antineoplastic agent	PIK3CB
rigosertib	antineoplastic agent	PIK3CD

Drug Name	Indication(s)	Gene
rigosertib	antineoplastic agent	PLK1
paclitaxel	antineoplastic agent	BCL2
paclitaxel	antineoplastic agent	TUBB1
ondansetron	antiemetic	HTR3A
oprozomib	antineoplastic agent	PSMB1
oprozomib	antineoplastic agent	PSMB2
oprozomib	antineoplastic agent	PSMB5
oprozomib	antineoplastic agent	PSMD1
oprozomib	antineoplastic agent	PSMD2
paclitaxel	antineoplastic agent	BCL2
paclitaxel	antineoplastic agent	TUBB1
OPB-51602	antineoplastic agent	STAT3
OPC-28326	vasodilator	ADRA2B
OPC-28326	vasodilator	ADRA2C
OPC-34712	antidepressant	DRD2
OPC-34712	antidepressant	HTR1A
OPC-34712	antidepressant	HTR2A
OPC-34712	antidepressant	HTR7
OPC-51803	for treatment of incontinence	AVPR2
doxycyklin	for treatment of dental disease	MMP8
estrogen	contraceptive,for treatment of female sexual dysfunction	ESR1
estrogen	contraceptive,for treatment of female sexual dysfunction	ESR2
progestogen	contraceptive,for treatment of female sexual dysfunction	PGR
estriol E3	for treatment of multiple sclerosis	ESR1
estriol E3	for treatment of multiple sclerosis	ESR2

Drug Name	Indication(s)	Gene
paclitaxel	antineoplastic agent	BCL2
paclitaxel	antineoplastic agent	TUBB1
lidocaine	anesthetic	SCN10A
lidocaine	anesthetic	SCN5A
lidocaine	anesthetic	SCN9A
prilocaine	anesthetic	SCN5A
olanzapine	antipsychotic agent	ADRA1A
olanzapine	antipsychotic agent	ADRA1B
olanzapine	antipsychotic agent	ADRA2A
olanzapine	antipsychotic agent	ADRA2B
olanzapine	antipsychotic agent	ADRA2C
olanzapine	antipsychotic agent	CHRM1
olanzapine	antipsychotic agent	CHRM2
olanzapine	antipsychotic agent	CHRM3
olanzapine	antipsychotic agent	CHRM4
olanzapine	antipsychotic agent	CHRM5
olanzapine	antipsychotic agent	DRD1
olanzapine	antipsychotic agent	DRD2
olanzapine	antipsychotic agent	DRD3
olanzapine	antipsychotic agent	DRD4
olanzapine	antipsychotic agent	DRD5
olanzapine	antipsychotic agent	HRH1
olanzapine	antipsychotic agent	HTR1A
olanzapine	antipsychotic agent	HTR1B
olanzapine	antipsychotic agent	HTR1D
olanzapine	antipsychotic agent	HTR1E
olanzapine	antipsychotic agent	HTR2A
olanzapine	antipsychotic agent	HTR2C

Drug Name	Indication(s)	Gene
olanzapine	antipsychotic agent	HTR3A
olanzapine	antipsychotic agent	HTR6
olanzapine	antipsychotic agent	HTR7
zonisamide	antipsychotic agent	CACNA1G
zonisamide	antipsychotic agent	CACNA1H
zonisamide	antipsychotic agent	CACNA1I
zonisamide	antipsychotic agent	SCN11A
zonisamide	antipsychotic agent	SCN1A
zonisamide	antipsychotic agent	SCN1B
zonisamide	antipsychotic agent	SCN2A
zonisamide	antipsychotic agent	SCN2B
zonisamide	antipsychotic agent	SCN3A
zonisamide	antipsychotic agent	SCN3B
zonisamide	antipsychotic agent	SCN4A
zonisamide	antipsychotic agent	SCN4B
zonisamide	antipsychotic agent	SCN5A
zonisamide	antipsychotic agent	SCN9A
orlistat	antiobesity agent	FASN
orlistat	antiobesity agent	LPL
orlistat	antiobesity agent	PNLIP
ortataxel	antineoplastic agent	BCL2
ortataxel	antineoplastic agent	TUBB1
orteronel	antineoplastic agent	CYP17A1
OSI-027	antineoplastic agent	MTOR
OSI-461	antineoplastic agent	PDE5A
OSI-7904L	antineoplastic agent	TYMS
OSI-906	antineoplastic agent	IGF1R
OSI-930	antineoplastic agent	KDR

Drug Name	Indication(s)	Gene
ospemifene	for treatment of postmenopausal vaginal atrophy	ESR1
ospemifene	for treatment of postmenopausal vaginal atrophy	ESR2
enobosarm	hormone replacement	AR
OT-730	for treatment of glaucoma	ADRB1
OT-730	for treatment of glaucoma	ADRB2
otamixaban	antithrombotic	F10
dexamethasone	antiinflammatory agent,glucocorticoid,for treatment of Meniere's disease	NR3C1
famotidine	acid reducer	HRH2
omeprazole	Proton pump inhibitor	ATP4A
zolpidem	hypnotic	GABRA1
zolpidem	hypnotic	GABRA2
zolpidem	hypnotic	GABRA3
OX914	antiallergy agent	PDE4A
OX914	antiallergy agent	PDE4B
oxandrolone	anabolic agent	AR
oxcarbazepine	anticonvulsant	SCN5A
combretastatin A1 di-phosphate	antineoplastic agent	TUBB1
oxycodone	analgesic	OPRD1
oxycodone	analgesic	OPRK1
oxycodone	analgesic	OPRM1
niacin	substance abuse deterrant	GPR109A
niacin	substance abuse deterrant	GPR109B
niacin	substance abuse deterrant	NNMT
niacin	substance abuse deterrant	QPRT

Drug Name	Indication(s)	Gene
oxycodone	analgesic	OPRD1
oxycodone	analgesic	OPRK1
oxycodone	analgesic	OPRM1
oxycodone	analgesic	OPRD1
oxycodone	analgesic	OPRK1
oxycodone	analgesic	OPRM1
oxymorphone	analgesic	OPRD1
oxymorphone	analgesic	OPRM1
P-552	for treatment of dry mouth	ACCN2
P-552	for treatment of dry mouth	ACCN3
P-552	for treatment of dry mouth	ACCN4
P-552	for treatment of dry mouth	ASIC2
P-552	for treatment of dry mouth	SCNN1A
P-552	for treatment of dry mouth	SCNN1B
P-552	for treatment of dry mouth	SCNN1D
P-552	for treatment of dry mouth	SCNN1G
acetylsalicylic acid	NSAID	PTGS1
acetylsalicylic acid	NSAID	PTGS2
omeprazole	Proton pump inhibitor	ATP4A
paclitaxel	antineoplastic agent	BCL2
paclitaxel	antineoplastic agent	TUBB1
paclitaxel	antineoplastic agent	BCL2
paclitaxel	antineoplastic agent	TUBB1
paclitaxel	for treatment of peripheral arterial disease (PAD)	BCL2
paclitaxel	for treatment of peripheral arterial disease (PAD)	TUBB1

Drug Name	Indication(s)	Gene
pagoclone	for treatment of premature ejaculation,for treatment of persistant stuttering	GABRA2
pagoclone	for treatment of premature ejaculation,for treatment of persistant stuttering	GABRB2
paliperidone	antipsychotic agent	DRD2
paliperidone	antipsychotic agent	HTR2A
Palomid 529	for treatment of age-related macular degeneration	MTOR
Palonosetron	antiemetic	HTR3A
Panobinostat	antineoplastic agent	HDAC1
Panobinostat	antineoplastic agent	HDAC10
Panobinostat	antineoplastic agent	HDAC11
Panobinostat	antineoplastic agent	HDAC2
Panobinostat	antineoplastic agent	HDAC3
Panobinostat	antineoplastic agent	HDAC4
Panobinostat	antineoplastic agent	HDAC5
Panobinostat	antineoplastic agent	HDAC6
Panobinostat	antineoplastic agent	HDAC7A
Panobinostat	antineoplastic agent	HDAC8
Panobinostat	antineoplastic agent	HDAC9
pantoprazole	Proton pump inhibitor	ATP4A
pardoprunox	antiparkinson agent	ADRA1A
pardoprunox	antiparkinson agent	ADRA2A
pardoprunox	antiparkinson agent	DRD2
pardoprunox	antiparkinson agent	DRD3
pardoprunox	antiparkinson agent	DRD4

Drug Name	Indication(s)	Gene
pardoprunox	antiparkinson agent	HTR1A
pardoprunox	antiparkinson agent	HTR7
parecoxib	antiinflammatory agent,NSAID	PTGS2
paricalcitol	for treatment of hyperparathyroidism	VDR
paroxetine	antidepressant	SLC6A4
Pazopanib	antineoplastic agent	FLT1
Pazopanib	antineoplastic agent	FLT4
Pazopanib	antineoplastic agent	KDR
bleomycin	antineoplastic agent	LIG1
CRA-024781	antineoplastic agent	HDAC1
CRA-024781	antineoplastic agent	HDAC10
CRA-024781	antineoplastic agent	HDAC2
CRA-024781	antineoplastic agent	HDAC3
CRA-024781	antineoplastic agent	HDAC6
ibrutinib	antineoplastic agent	BTK
PD-6735	hypnotic	MTNR1A
PD-6735	hypnotic	MTNR1B
10-propargyl-10-deazaaminopterin	antineoplastic agent	DHFR
PEG-camptothecin	antineoplastic agent	TOP1
pentosan polysulfate	for symptomatic treatment of bladder pain or discomfort associated with interstitial cystitis	FGF1
pentosan polysulfate	for symptomatic treatment of bladder pain or discomfort associated with interstitial cystitis	FGF2

Drug Name	Indication(s)	Gene
pentosan polysulfate	for symptomatic treatment of bladder pain or discomfort associated with interstitial cystitis	FGF4
pentostatin	antineoplastic agent	ADA
pentoxifylline	for treatment of amyotrophic lateral sclerosis (ALS)	ADORA1
pentoxifylline	for treatment of amyotrophic lateral sclerosis (ALS)	ADORA2B
pentoxifylline	for treatment of amyotrophic lateral sclerosis (ALS)	PDE4A
pentoxifylline	for treatment of amyotrophic lateral sclerosis (ALS)	PDE4B
pentoxifylline	for treatment of amyotrophic lateral sclerosis (ALS)	PDE5A
ingenol Mebutate	for treatment of actinic keratosis,antineoplastic agent	PKN1
ingenol Mebutate	for treatment of actinic keratosis,antineoplastic agent	PKN2
ingenol Mebutate	for treatment of actinic keratosis,antineoplastic agent	PRKCA
ingenol Mebutate	for treatment of actinic keratosis,antineoplastic agent	PRKCB1
ingenol Mebutate	for treatment of actinic keratosis,antineoplastic agent	PRKCD
ingenol Mebutate	for treatment of actinic keratosis,antineoplastic agent	PRKCE
ingenol Mebutate	for treatment of actinic keratosis,antineoplastic agent	PRKCG

Drug Name	Indication(s)	Gene
ingenol Mebutate	for treatment of actinic keratosis,antineoplastic agent	PRKCH
ingenol Mebutate	for treatment of actinic keratosis,antineoplastic agent	PRKCI
ingenol Mebutate	for treatment of actinic keratosis,antineoplastic agent	PRKCQ
ingenol Mebutate	for treatment of actinic keratosis,antineoplastic agent	PRKCZ
irinotecan	antineoplastic agent	TOP1
irinotecan	antineoplastic agent	TOP1MT
perifosine	antineoplastic agent	AKT1
perifosine	antineoplastic agent	AKT2
perifosine	antineoplastic agent	AKT3
PF-00610355	bronchodilator	ADRB2
PF-04554878	antineoplastic agent	PTK2
Dacomitinib	antineoplastic agent	EGFR
Dacomitinib	antineoplastic agent	ERBB2
Dacomitinib	antineoplastic agent	ERBB4
PG-490-88	antineoplastic agent	NFKB1
PG-490-88	antineoplastic agent	NFKB2
PG545	antineoplastic agent	HPSE
PH-797804	antiinflammatory agent,DMARD	MAPK11
PH-797804	antiinflammatory agent,DMARD	MAPK12
PH-797804	antiinflammatory agent,DMARD	MAPK13
PH-797804	antiinflammatory agent,DMARD	MAPK14
phenoxodiol	antineoplastic agent	SPHK1
phenoxodiol	antineoplastic agent	SPHK2
phenserine	for treatment of Alzheimer's disease	ACHE

Drug Name	Indication(s)	Gene
physostigmine	for treatment of dry mouth	ACHE
Pimavanserin	antiparkinson agent	HTR2A
pimecrolimus	antiinflammatory agent	MTOR
pioglitazone	antidiabetic	PPARG
metformin	antidiabetic	PRKAB1
pioglitazone	antidiabetic	PPARG
pirfenidone	for treatment of fibrotic conditions	MAPK11
pirfenidone	for treatment of fibrotic conditions	MAPK12
pirfenidone	for treatment of fibrotic conditions	MAPK13
pirfenidone	for treatment of fibrotic conditions	MAPK14
pitavastatin	anticholesterolaemic agent	HMGCR
PL37	analgesic,neuropathic pain	ANPEP
PL37	analgesic,neuropathic pain	MME
clopidogrel	antithrombotic	P2RY12
PLK-1 inhibitor	antineoplastic agent	PLK1
vemurafenib	antineoplastic agent	BRAF
PMI-001	antiinflammatory agent,DMARD	NR3C1
naproxen	NSAID	PTGS1
naproxen	NSAID	PTGS2
omeprazole	Proton pump inhibitor	ATP4A
carmustine	antineoplastic agent	GSR
ponatinib	antineoplastic agent	ABL1
ponatinib	antineoplastic agent	SRC
ponesimod	antiinflammatory agent,for treatment of multiple sclerosis	S1PR1
Posiphen	for treatment of Alzheimer's disease	APP
Posiphen	for treatment of Alzheimer's disease	BACE1
Posiphen	for treatment of Alzheimer's disease	BACE2

Drug Name	Indication(s)	Gene
pozanicline	for treatment of Alzheimer's disease	CHRNA4
pozanicline	for treatment of Alzheimer's disease	CHRNB2
PPC-5650	analgesic	ACCN2
PPI-2458	antineoplastic agent	METAP2
PR-15	antithrombotic	GP6
prasterone	hormone supplement for increasing bone mineral density in patients with systemic lupus erythematosus	AR
prasugrel	antithrombotic	P2RY12
fenofibrate	anticholesterolaemic agent	PPARA
pravastatin	anticholesterolaemic agent	HMGCR
prednisolone	antiinflammatory agent,corticosteroid	NR3C1
prednisolone	antiinflammatory agent,corticosteroid	NR3C1
pregabalin	analgesic,neuropathic pain,for treatment of restlegs legs syndrome	CACNA1A
preladenant	antiparkinson agent	ADORA2A
pridopidine	for treatment of Huntington's disease	DRD2
desvenlafaxine	for treatment of menopausal symptoms,antidepressant	SLC6A2
desvenlafaxine	for treatment of menopausal symptoms,antidepressant	SLC6A4
diclofenac	NSAID	PTGS1
diclofenac	NSAID	PTGS2
telapristone	for treatment of uterin fibroids and endometriosis	PGR

Drug Name	Indication(s)	Gene
progesterone	for reducing the risk of pre-term birth for women with short cervix a mid-pregnancy	PGR
testosterone	hormone replacement	AR
eltrombopag	thrombopoietic	MPL
propafenone	antiarrythmic agent	KCNH2
propafenone	antiarrythmic agent	SCN5A
propionyl-L-carnitine	for treatment of intermittent claudication	CPT1A
propionyl-L-carnitine	for treatment of intermittent claudication	CPT2
propionyl-L-carnitine	for treatment of intermittent claudication	CRAT
propionyl-L-carnitine	for treatment of intermittent claudication	CROT
propionyl-L-carnitine	for treatment of intermittent claudication	SLC22A4
propionyl-L-carnitine	for treatment of intermittent claudication	SLC22A5
propionyl-L-carnitine	for treatment of intermittent claudication	SLC25A20
propionyl-L-carnitine	for treatment of intermittent claudication	SLC25A29
propofol	sedative	GABRB2
propofol	sedative	GABRB3
propofol	sedative	SCN2A
propofol	sedative	SCN4A
propofol	sedative	GABRB2

Drug Name	Indication(s)	Gene
propofol	sedative	GABRB3
propofol	sedative	SCN2A
propofol	sedative	SCN4A
OPC-14523	antidepressant	HTR1A
OPC-14523	antidepressant	PGRMC1
OPC-14523	antidepressant	SIGMAR1
OPC-14523	antidepressant	SLC6A4
PRT062607	antiinflammatory agent	SYK
prucalopride	motilitant	HTR4
PRX-00023	antidepressant,anxiolytic	HTR1A
PRX-07034	antiobesity agent,nootropic	HTR6
PRX-08066	antihypertensive agent	HTR2B
PRX-3140	for treatment of Alzheimer's disease	HTR4
PS433540	antihypertensive agent	AGTR1
PS433540	antihypertensive agent	AGTR2
PS433540	antihypertensive agent	EDNRA
lidocaine	for treatment of premature ejaculation	EGFR
lidocaine	for treatment of premature ejaculation	SCN10A
lidocaine	for treatment of premature ejaculation	SCN5A
prilocaine	for treatment of premature ejaculation	SCN5A
phenylephrine	for treatment of incontinence	ADRA1A
phenylephrine	for treatment of incontinence	ADRA1B
phenylephrine	for treatment of incontinence	ADRA1D
PSD-506	for treatment of overactive bladder	CHRM2

Drug Name	Indication(s)	Gene
PSD-506	for treatment of overactive bladder	CHRM3
PSN357	antidiabetic	PYGB
PSN357	antidiabetic	PYGL
PSN357	antidiabetic	PYGM
PSN602	antiobesity agent	HTR1A
PSN602	antiobesity agent	SLC6A2
PSN602	antiobesity agent	SLC6A3
PSN602	antiobesity agent	SLC6A4
PSN821	antidiabetic	GPR119
glycopyrrolate	for treatment of chronic obstructive pulmonary disorder (COPD)	CHRM1
formoterol	for treatment of chronic obstructive pulmonary disorder (COPD)	ADRB2
glycopyrrolate	for treatment of chronic obstructive pulmonary disorder (COPD)	CHRM1
formoterol	for treatment of chronic obstructive pulmonary disorder (COPD)	ADRB2
PTC299	antineoplastic agent	FLT1
PTC299	antineoplastic agent	FLT4
PTC299	antineoplastic agent	KDR
naltrexone	analgesic	OPRD1
naltrexone	analgesic	OPRD1
naltrexone	analgesic	OPRK1
naltrexone	analgesic	OPRK1
naltrexone	analgesic	OPRM1
naltrexone	analgesic	OPRM1
naltrexone	analgesic	SIGMAR1
tramadol	analgesic	HTR2C

Drug Name	Indication(s)	Gene
tramadol	analgesic	OPRK1
tramadol	analgesic	OPRK1
tramadol	analgesic	OPRM1
tramadol	analgesic	OPRM1
tramadol	analgesic	SLC6A2
tramadol	analgesic	SLC6A2
tramadol	analgesic	SLC6A4
acetaminophen	analgesic	PTGS1
acetaminophen	analgesic	PTGS1
acetaminophen	analgesic	PTGS2
acetaminophen	analgesic	PTGS2
hydrocodone	analgesic	OPRD1
hydrocodone	analgesic	OPRD1
hydrocodone	analgesic	OPRM1
hydrocodone	analgesic	OPRM1
naltrexone	analgesic	OPRD1
naltrexone	analgesic	OPRD1
naltrexone	analgesic	OPRK1
naltrexone	analgesic	OPRK1
naltrexone	analgesic	OPRM1
naltrexone	analgesic	OPRM1
naltrexone	analgesic	SIGMAR1
naltrexone	analgesic	SIGMAR1
naltrexone	analgesic	OPRD1
naltrexone	analgesic	OPRK1
naltrexone	analgesic	OPRM1
oxycodone	analgesic	OPRD1
oxycodone	analgesic	OPRK1

Drug Name	Indication(s)	Gene
oxycodone	analgesic	OPRM1
naltrexone	analgesic	OPRD1
naltrexone	analgesic	OPRK1
naltrexone	analgesic	OPRM1
Pumosetrag	motilitant	HTR3A
Pumosetrag	motilitant	HTR3B
Pumosetrag	motilitant	HTR3C
Pumosetrag	motilitant	HTR3D
Pumosetrag	motilitant	HTR3E
PW2101	antihypertensive agent	ADRB2
PX-12	antineoplastic agent	TXN
PX-478	antineoplastic agent	HIF1A
belinostat	antineoplastic agent	HDAC1
belinostat	antineoplastic agent	HDAC10
belinostat	antineoplastic agent	HDAC11
belinostat	antineoplastic agent	HDAC2
belinostat	antineoplastic agent	HDAC3
belinostat	antineoplastic agent	HDAC4
belinostat	antineoplastic agent	HDAC5
belinostat	antineoplastic agent	HDAC6
belinostat	antineoplastic agent	HDAC7A
belinostat	antineoplastic agent	HDAC8
belinostat	antineoplastic agent	HDAC9
PYM50028	antiparkinson agent	GFRA1
PYM50028	antiparkinson agent	NGFR
PYM50028	antiparkinson agent	NTRK1
PYM50028	antiparkinson agent	NTRK2
quinapril	antihypertensive agent	ACE

Drug Name	Indication(s)	Gene
glycopyrronium bromide	for treatment of chronic obstructive pulmonary disorder (COPD)	ADRB2
indacaterol	for treatment of chronic obstructive pulmonary disorder (COPD)	CHRM1
R112	antiallergy agent	FCER1A
R112	antiallergy agent	FCER1G
R112	antiallergy agent	MS4A2
R343	antiallergy agent	SYK
R348	antiinflammatory agent	JAK3
R667	for treatment of emphysema	RARA
R667	for treatment of emphysema	RARB
R667	for treatment of emphysema	RARG
R763	antineoplastic agent	AURKA
R763	antineoplastic agent	AURKB
R763	antineoplastic agent	AURKC
RAD1901	for treatment of postmenopausal symptoms	ESR1
raltitrexed	antineoplastic agent	TYMS
ramelteon	for treatment of insomnia	MTNR1A
ramelteon	for treatment of insomnia	MTNR1B
ranolazine	antiallergy agent	SCN5A
ranolazine	antiallergy agent	SCN9A
ranirestat	for treatment of diabetic neuropathy	AKR1B1
ranitidine	antiulcer agent	HRH2
rasagiline	antiparkinson agent	MAOB
RC-8800	for improving the antiproliferative and apoptotic properties of vitamin D3	CYP46A1

Drug Name	Indication(s)	Gene
RDEA119	antineoplastic agent	MAPK1
RDEA119	antineoplastic agent	MAPK3
regadenoson	diagnostic agent	ADORA2A
regorafenib	antineoplastic agent	KDR
regorafenib	antineoplastic agent	TEK
relacatib	antiosteoporotic agent	CTSK
eletriptan	antimigraine agent	HTR1D
remifentanil	analgesic	OPRM1
Nalbuphine	analgesic	OPRD1
Nalbuphine	analgesic	OPRK1
Nalbuphine	analgesic	OPRM1
naloxone	analgesic	OPRD1
naloxone	analgesic	OPRK1
naloxone	analgesic	OPRM1
renzapride	for treatment of irritable bowel syndrome	HTR2A
renzapride	for treatment of irritable bowel syndrome	HTR2B
renzapride	for treatment of irritable bowel syndrome	HTR2C
renzapride	for treatment of irritable bowel syndrome	HTR3A
renzapride	for treatment of irritable bowel syndrome	HTR4
repaglinide	antidiabetic	ABCC8
ropinirol	antiparkinson agent	DRD2
ropinirol	antiparkinson agent	DRD3

Drug Name	Indication(s)	Gene
resiniferatoxin	for treatment of interstitial cystitis,antiincontinence agent	TRPV1
Resminostat	antineoplastic agent	HDAC1
Resminostat	antineoplastic agent	HDAC10
Resminostat	antineoplastic agent	HDAC11
Resminostat	antineoplastic agent	HDAC2
Resminostat	antineoplastic agent	HDAC3
Resminostat	antineoplastic agent	HDAC4
Resminostat	antineoplastic agent	HDAC5
Resminostat	antineoplastic agent	HDAC6
Resminostat	antineoplastic agent	HDAC7A
Resminostat	antineoplastic agent	HDAC8
Resminostat	antineoplastic agent	HDAC9
Resveratrol	for treatment of herpes simplex virus 1	PDE4B
Resveratrol	for treatment of herpes simplex virus 1	PDE4D
retigabine	anticonvulsant	KCNQ1
retigabine	anticonvulsant	KCNQ2
retigabine	anticonvulsant	KCNQ3
retigabine	anticonvulsant	KCNQ4
retigabine	anticonvulsant	KCNQ5
rEV131	antiallergy agent	HRH4
lenalidomide	antineoplastic agent	TNFSF11
RG2833	for treatment of Friedrich's ataxia	HDAC3
RG3039	for treatment of spinal muscular atrophy	DCPS
Ridaforolimus	antineoplastic agent	MTOR

Drug Name	Indication(s)	Gene
riluzole	for treatment of ALS	SCN5A
riluzole	for treatment of ALS	SLC7A11
rimcazole	antineoplastic agent	SIGMAR1
Rimonabant	antiobesity agent	CNR1
riociguat	antihypertensive agent	GUCY1A2
riociguat	antihypertensive agent	GUCY1A3
riociguat	antihypertensive agent	GUCY1B2
riociguat	antihypertensive agent	GUCY1B3
risedronate	antiosteoporotic agent	FDPS
Risperdal	antipsychotic agent	DRD2
Risperdal	antipsychotic agent	HTR2A
rivaroxaban	antithrombotic	F10
rivastigmine	for treatment of Alzheimer's disease	ACHE
rivastigmine	for treatment of Alzheimer's disease	BCHE
Rob 803	antiinflammatory agent,DMARD	unknown
rocuronium	muscle relaxant	CHRM2
rocuronium	muscle relaxant	CHRNA2
rocuronium	muscle relaxant	HTR3A
rofecoxib	NSAID	PTGS2
roflumilast	for treatment of chronic obstructive pulmonary disorder (COPD)	PDE4A
roflumilast	for treatment of chronic obstructive pulmonary disorder (COPD)	PDE4B
rolofylline	for treatment of congestive heart failure	ADORA1
ronacaleret	antiiosteoporotic agent	CASR
ropivacaine	anestethic	SCN10A
glimepiride	antidiabetic	ABCC8

Drug Name	Indication(s)	Gene
glimepiride	antidiabetic	KCNJ1
glimepiride	antidiabetic	KCNJ11
rosiglitazone	antidiabetic	PPARG
metformin	antidiabetic	PRKAB1
rosiglitazone	antidiabetic	PPARG
rosiglitazone	for treatment of Alzheimer's disease,antidiabetic	PPARG
ketorolac	antimigraine agent	PTGS1
ketorolac	antimigraine agent	PTGS2
bromovinyl deoxyuridine	antineoplastic agent	POLA1
RPC1063	for treatment of multiple sclerosis	S1PR1
RPL-554	bronchodilator	PDE3A
RPL-554	bronchodilator	PDE3B
RPL-554	bronchodilator	PDE4A
RPL-554	bronchodilator	PDE4B
RTA 744	antineoplastic agent	TOP2A
RTA 744	antineoplastic agent	TOP2B
rubitecan	antineoplastic agent	TOP1
ruboxistaurin	for treatment of diabetic neuropathy	PRKCB1
RVX-208	antiatherosclerotic agent	APOA1
gimestat	antineoplastic agent	DPYD
tegafur	antineoplastic agent	TYMS
paclitaxel	antineoplastic agent	BCL2
paclitaxel	antineoplastic agent	TUBB1
SA4503	antidepressant,neuroprotectant	SIGMAR1
Safinamide	antiparkinson agent	CACNA1B
Safinamide	antiparkinson agent	CACNA2D1
Safinamide	antiparkinson agent	CACNA2D2

Drug Name	Indication(s)	Gene
Safinamide	antiparkinson agent	CACNB3
Safinamide	antiparkinson agent	CACNB4
Safinamide	antiparkinson agent	MAOB
Safinamide	antiparkinson agent	SCN11A
Safinamide	antiparkinson agent	SCN11A
Safinamide	antiparkinson agent	SCN1A
Safinamide	antiparkinson agent	SCN2A
Safinamide	antiparkinson agent	SCN3A
Safinamide	antiparkinson agent	SCN4A
Safinamide	antiparkinson agent	SCN5A
Safinamide	antiparkinson agent	SCN7A
Safinamide	antiparkinson agent	SCN8A
Safinamide	antiparkinson agent	SCN9A
tetrahydrobiopterin	for treatment of phenolketonuria (PKU)	NOS3
tetrahydrobiopterin	for treatment of phenolketonuria (PKU)	PAH
tetrahydrobiopterin	for treatment of phenolketonuria (PKU)	TH
tetrahydrobiopterin	for treatment of phenolketonuria (PKU)	TPH1
SAR 1118	antiinflammatory agent	ICAM1
SAR 1118	antiinflammatory agent	ITGAL
SAR 1118	antiinflammatory agent	ITGB2
saredutant	antidepressant,anxiolytic	TACR2
nabilone	analgesic,neuropathic pain,for treatment of restlegs legs syndrome	CNR2

Drug Name	Indication(s)	Gene
nabilone	analgesic,neuropathic pain,for treatment of restlegs legs syndrome	CNR2
Saxagliptin	antidiabetic	DPP4
SB1518	antineoplastic agent	JAK2
SB-559448	thrombopoietic agent	MPL
SB-681323	antiinflammatory agent,DMARD	MAPK14
firategrast	antiinflammatory agent	ITGA4
firategrast	antiinflammatory agent	ITGB1
pracinostat	antineoplastic agent	HDAC1
pracinostat	antineoplastic agent	HDAC10
pracinostat	antineoplastic agent	HDAC11
pracinostat	antineoplastic agent	HDAC2
pracinostat	antineoplastic agent	HDAC3
pracinostat	antineoplastic agent	HDAC4
pracinostat	antineoplastic agent	HDAC5
pracinostat	antineoplastic agent	HDAC6
pracinostat	antineoplastic agent	HDAC7A
pracinostat	antineoplastic agent	HDAC8
pracinostat	antineoplastic agent	HDAC9
SCH-527123	for treatment of chronic obstructive pulmonary disorder (COPD)	CXCR1
SCH-527123	for treatment of chronic obstructive pulmonary disorder (COPD)	CXCR2
talmapimod	antiinflammatory agent,DMARD	MAPK14
SCY-635	for treatment of hepatitis C	PP1A
SCY-635	for treatment of hepatitis C	PP1D
scyllo-inositol	for treatment of Alzheimer's disease	APP
R-etodolac	antineoplastic agent	RXRA

Drug Name	Indication(s)	Gene
selegiline	antidepressant	MAOB
selegiline	antiparkinson agent	MAOB
seletracetam	anticonvulsant	SV2A
selexipag	antihypertensive agent	PTGIR
seliciclib	antineoplastic agent	CDK2
seliciclib	antineoplastic agent	CDK7
seliciclib	antineoplastic agent	CDK9
maraviroc	antiviral agent,HIV	CCR5
eszopiclone	anxiolytic	GABRA1
clavulanic acid	antidepressant	FOLH1
SERTINDOLE	antipsychotic agent	ADRA1A
SERTINDOLE	antipsychotic agent	ADRA1B
SERTINDOLE	antipsychotic agent	ADRA1D
SERTINDOLE	antipsychotic agent	DRD2
SERTINDOLE	antipsychotic agent	HTR2A
SERTINDOLE	antipsychotic agent	HTR2C
SERTINDOLE	antipsychotic agent	HTR6
SERTINDOLE	antipsychotic agent	KCNH2
salmeterol	bronchodilator	ADRB2
Quetiapine	antipsychotic agent,antidepressant	DRD2
Quetiapine	antipsychotic agent,antidepressant	HTR2A
Quetiapine	antipsychotic agent,antidepressant	HTR2B
Quetiapine	antipsychotic agent,antidepressant	HTR2C
Quetiapine	antipsychotic agent,antidepressant	HTR2C
SF1126	antineoplastic agent	MTOR
SF1126	antineoplastic agent	PIK3C3
SF1126	antineoplastic agent	PIK3CA
SF1126	antineoplastic agent	PIK3CA

Drug Name	Indication(s)	Gene
SF1126	antineoplastic agent	PIK3CB
SF1126	antineoplastic agent	PIK3CD
SF1126	antineoplastic agent	PIK3CD
SF1126	antineoplastic agent	PIK3CG
SF1126	antineoplastic agent	PIK3CG
SF1126	antineoplastic agent	PRKDC
SGI-1776	antineoplastic agent	PIM1
SGI-1776	antineoplastic agent	PIM2
SGI-1776	antineoplastic agent	PIM3
beclomethasone	antiinflammatory agent,glucocorticoid	NR3C1
SGX523	antineoplastic agent	MET
sibutramine	appetite suppressant	SLC6A2
sibutramine	appetite suppressant	SLC6A3
sibutramine	appetite suppressant	SLC6A4
sildenafil	for treatment of erectile dysfucntion,antihypertensive agent	PDE5A
doxepin	hypnotic	CHRM1
doxepin	hypnotic	CHRM2
doxepin	hypnotic	CHRM3
doxepin	hypnotic	CHRM4
doxepin	hypnotic	CHRM5
doxepin	hypnotic	HRH1
doxepin	hypnotic	HRH2
doxepin	hypnotic	HTR2A
doxepin	hypnotic	HTR2B
doxepin	hypnotic	HTR2C
doxepin	hypnotic	SLC6A2

Drug Name	Indication(s)	Gene
doxepin	hypnotic	SLC6A4
Silodosin	for treatment of BPH-related urinary symptoms	ADRA1A
sirolimus	for treatment of wet age-related macular degeneration	FKBP1A
sirolimus	for treatment of wet age-related macular degeneration	MTOR
sirolimus	immunosuppressant	FKBP1A
sirolimus	immunosuppressant	MTOR
Sitagliptin	antidiabetic	DPP4
sivelestat	for treatment of acute lung injury associated with systemic inflammatory response syndrome (SIRS)	ELA2
zaleplon	hypnotic	GABRA1
zaleplon	hypnotic	TSPO
fluticasone	antiinflammatory agent,glucocorticoid	NR3C1
formoterol	bronchodilator	ADRB2
amphetamine	for treatment of cognitive dysfunction,for treatment of ADHD	SLC18A2
amphetamine	for treatment of cognitive dysfunction,for treatment of ADHD	SLC6A3
amphetamine	for treatment of cognitive dysfunction,for treatment of ADHD	TAAR1
dextroamphetamine	for treatment of ADHD	SLC18A2
dextroamphetamine	for treatment of ADHD	SLC6A2
dextroamphetamine	for treatment of ADHD	SLC6A3

Drug Name	Indication(s)	Gene
SLx-2101	antihypertensive agent,for treatment of erectile dysfunction	PDE5A
SLx-4090	antidyslipidaemic agent	MTTP
SNS-032	antineoplastic agent	CDK2
SNS-032	antineoplastic agent	CDK7
SNS-032	antineoplastic agent	CDK9
SNS-314	antineoplastic agent	AURKA
SNS-314	antineoplastic agent	AURKB
SNX-5422	antineoplastic agent	HSP90AA1
SNX-5422	antineoplastic agent	HSP90AB1
sobetirome	antihypecholesterolemic agent	THRB
gamma hydroxybutyric acid	hypnotic	GABBR1
gamma hydroxybutyric acid	hypnotic	GABBR2
gamma hydroxybutyric acid	hypnotic	SLC5A2
stibogluconate	antineoplastic agent	PTPN11
levonorgestrel	contraceptive	ESR1
levonorgestrel	contraceptive	PGR
levonorgestrel	contraceptive	SRD5A1
solabegron	antidiabetic,for treatment of irritable bowel syndrome,antiincontinence agent	ADRB3
Solifenacin	for treatment of incontinence	CHRM1
Solifenacin	for treatment of incontinence	CHRM2
Solifenacin	for treatment of incontinence	CHRM3
Solifenacin	for treatment of incontinence	CHRM4
Solifenacin	for treatment of incontinence	CHRM5
SOU-001	for treatment of incontinence	ADRA1A
SOU-001	for treatment of incontinence	ADRA1B

Drug Name	Indication(s)	Gene
SOU-001	for treatment of incontinence	ADRA1D
SOU-003	for treatment of incontinence	AVPR2
doxorubicin	antineoplastic agent	TOP2A
carbamazepine	for treatment of bipolar disorder	SCN5A
mesalamine	for treatment of ulcerative colitis	ALOX5
mesalamine	for treatment of ulcerative colitis	CHUK
mesalamine	for treatment of ulcerative colitis	IKBKB
mesalamine	for treatment of ulcerative colitis	PPARG
mesalamine	for treatment of ulcerative colitis	PTGS1
mesalamine	for treatment of ulcerative colitis	PTGS2
allopurinol	antiuricemic agent	XDH
SPP676	antihypertensive agent	REN
Resveratrol	antidiabetic,antineoplastic agent	PDE4B
Resveratrol	antidiabetic,antineoplastic agent	PDE4D
ganetespib	antineoplastic agent	HSP90AA1
ganetespib	antineoplastic agent	HSP90AB1
stannsoporfin	for prevention of hyperbilirubinemia	HMOX1
stannsoporfin	for prevention of hyperbilirubinemia	HMOX2
nateglinide	antidiabetic	ABCC8
morphine	analgesic	OPRK1
morphine	analgesic	OPRK1
morphine	analgesic	OPRK1
strontium ranelate	antiosteoporotic agent	CASR
STX107	for treatment of Fragile X symptoms	GRM5
sucralfate	antiulcer agent	PGA3
sufentanil	analgesic	OPRD1
sufentanil	analgesic	OPRK1
sufentanil	analgesic	OPRM1

Drug Name	Indication(s)	Gene
sufentanil	analgesic	OPRD1
sufentanil	analgesic	OPRK1
sufentanil	analgesic	OPRM1
sulfasalazine	antiinflammatory agent,DMARD	ACAT1
sulfasalazine	antiinflammatory agent,DMARD	PPARG
sulfasalazine	antiinflammatory agent,DMARD	PTGS1
sulfasalazine	antiinflammatory agent,DMARD	PTGS2
sulodexide	for treatment of diabetic nephropathy	SERPINC1
sulodexide	for treatment of diabetic nephropathy	SERPIND1
Sumatriptan	antimigraine agent	HTR1A
Sumatriptan	antimigraine agent	HTR1B
Sumatriptan	antimigraine agent	HTR1D
Sumatriptan	antimigraine agent	HTR1F
Sumatriptan	antimigraine agent	HTR1A
Sumatriptan	antimigraine agent	HTR1B
Sumatriptan	antimigraine agent	HTR1D
Sumatriptan	antimigraine agent	HTR1F
Sumatriptan	antimigraine agent	HTR1A
Sumatriptan	antimigraine agent	HTR1B
Sumatriptan	antimigraine agent	HTR1D
Sumatriptan	antimigraine agent	HTR1F
surinabant	smoking-cessation agent	CNR1
latanoprost	for treatment of glaucoma	PTGFR
sunitinib	antineoplastic agent	FLT1
sunitinib	antineoplastic agent	FLT3
sunitinib	antineoplastic agent	FLT4
sunitinib	antineoplastic agent	KDR
sunitinib	antineoplastic agent	KIT

Drug Name	Indication(s)	Gene
sunitinib	antineoplastic agent	PDGFRA
sunitinib	antineoplastic agent	PDGFRB
sunitinib	antineoplastic agent	RET
SUVN-502	for treatment of Alzheimer's disease	HTR6
SVT-40776	for treatment of incontinence	CHRM3
tozadenant	antiparkinson agent	ADORA2A
nitisinone	antiparkinson agent	HPD
T-5224	antiinflammatory agent,DMARD	JUN
T-62	analgesic	ADORA1
tacrolimus	immunosuppressant	FKBP1A
tacrolimus	immunosuppressant	FKBP1A
TAFA-93	immunosuppressant	FRAP1
TAK-242	for treatment of sepsis	TLR4
dexlansoprazole	Proton pump inhibitor	ATP4A
TAK-442	antithrombotic	F10
Talabostat	for treatment of neutropenia	CSF3
talampanel	antiparkinson agent,antineoplastic agent	GRIA1
talampanel	antiparkinson agent,antineoplastic agent	GRIA2
talampanel	antiparkinson agent,antineoplastic agent	GRIA3
talampanel	antiparkinson agent,antineoplastic agent	GRIA4
talarozole	antipsoriatic agent,for treatment of acne	CYP26A1
talarozole	antipsoriatic agent,for treatment of acne	CYP26B1

Drug Name	Indication(s)	Gene
talarozole	antipsoriatic agent,for treatment of acne	CYP26C1
talnetant	antipsychotic agent	TACR3
talotrexin	antineoplastic agent	DHFR
Tamibarotene	antineoplastic agent	RARA
Tamibarotene	antineoplastic agent	RARB
tamsulosin	for treatment of urinary symptoms associated with BPH	ADRA1A
tamsulosin	for treatment of urinary symptoms associated with BPH	ADRA1B
tamsulosin	for treatment of urinary symptoms associated with BPH	ADRA1D
tandutinib	antineoplastic agent	FLT3
Tanespimycin	antineoplastic agent	HSP90AA1
Tanespimycin	antineoplastic agent	HSP90AB1
tapentadol	analgesic	OPRM1
tapentadol	analgesic	SLC6A2
tapentadol	analgesic,opioid	MOR
Taranabant	antiobesity agent,smoking-cessation agent	CNR1
erlotinib	antineoplastic agent	EGFR
tariquidar	adjuvant to chemotherapy	ABCB1
TAS-108	antineoplastic agent	ESR1
TAS-108	antineoplastic agent	ESR2
tasimelteon	hypnotic	MTNR1A
tasimelteon	hypnotic	MTNR1B
Tasocitinib	antiinflammatory agent,DMARD	JAK3

Drug Name	Indication(s)	Gene
tazarotene	antipsoriatic agent,for treatment of acne	RARA
tazarotene	antipsoriatic agent,for treatment of acne	RARB
tazarotene	antipsoriatic agent,for treatment of acne	RARG
tazarotene	antipsoriatic agent,for treatment of acne	RXRB
TBR-652	antiviral agent,HIV	CCR5
ispronicline	nootropic	CHRNA4
ispronicline	nootropic	CHRNB2
TC-2403-12	for treatment of ulcerative colitis	CHRNA4
TC-2403-12	for treatment of ulcerative colitis	CHRNB2
TC-2696	analgesic	CHRNA4
TC-2696	analgesic	CHRNB2
TC-5214	antidepressant	CHRNA4
TC-5214	antidepressant	CHRNB2
TC-5619	neuroprotectant	CHRNA7
TC-6499	analgesic,neuropathic pain	CHRNA4
TC-6499	analgesic,neuropathic pain	CHRNB2
TC-6987	antiasthmatic agent,antidiabetic	CHRNA7
TD-1211	for treatment of opioid-induced gastrointestinal side-effects	OPRM1
tecadenoson	antiarrhytmic agent	ADORA1
tecarfarin	antithrombotic	VKORC1
tegaserod	motilitant	HTR4
telatinib	antineoplastic agent	FLT1
telatinib	antineoplastic agent	FLT4

Drug Name	Indication(s)	Gene
telatinib	antineoplastic agent	KDR
telatinib	antineoplastic agent	PDGFRA
telatinib	antineoplastic agent	PDGFRB
telmisartan	antihypertensive agent	AGTR1
temsirolimus	antineoplastic agent	FRAP1
terguride	for treatment of pulmonary arterial hypertension	HTR2A
terguride	for treatment of pulmonary arterial hypertension	HTR2B
teriflunomide	for treatment of multiple sclerosis	DHODH
terlipressin	for treatment of hepatorenal syndrome	AVPR1A
terlipressin	for treatment of hepatorenal syndrome	AVPR1B
terlipressin	for treatment of hepatorenal syndrome	AVPR2
tesetaxel	antineoplastic agent	BCL2
tesetaxel	antineoplastic agent	TUBB1
tesmilifene	adjuvant to chemotherapy	ABCB1
tesmilifene	adjuvant to chemotherapy	CYP3A4
tesmilifene	adjuvant to chemotherapy	CYP3A5
tesmilifene	adjuvant to chemotherapy	CYP3A7
tesofensine	antiobesity agent	SLC6A2
tesofensine	antiobesity agent	SLC6A4
testosterone	hormone replacement,for treatment of female sexual dysfunction	AR
testosterone	for treatment of female sexual dysfunction	AR

Drug Name	Indication(s)	Gene
testosterone	hormone replacement	AR
testosterone	for treatment of female sexual dysfunction	AR
testosterone	hormone replacement	AR
testosterone	hormone replacement	AR
testosterone	for treatment of female sexual dysfunction	AR
tetrabenazine	for treatment of Huntington's disease	SLC18A2
tetrodotoxin	analgesic	SCN10A
tetrodotoxin	analgesic	SCN11A
tetrodotoxin	analgesic	SCN1A
tetrodotoxin	analgesic	SCN2A
tetrodotoxin	analgesic	SCN3A
tetrodotoxin	analgesic	SCN4A
tetrodotoxin	analgesic	SCN5A
tetrodotoxin	analgesic	SCN8A
tetrodotoxin	analgesic	SCN9A
tezampanel	antimigraine agent,analgesic	GRIA1
tezampanel	antimigraine agent,analgesic	GRIA2
tezampanel	antimigraine agent,analgesic	GRIA3
tezampanel	antimigraine agent,analgesic	GRIA4
tezampanel	antimigraine agent,analgesic	GRIK1
tezampanel	antimigraine agent,analgesic	GRIK2
tezampanel	antimigraine agent,analgesic	GRIK3
tezampanel	antimigraine agent,analgesic	GRIK4
tezampanel	antimigraine agent,analgesic	GRIK5
TG-0054	adjuvant to stem cell transplantation	CXCR4
TG02, SB1317	antineoplastic agent	CDK2

Drug Name	Indication(s)	Gene
TG02, SB1317	antineoplastic agent	ERK5
TG02, SB1317	antineoplastic agent	FLT3
TG02, SB1317	antineoplastic agent	JAK2
TG101348	antineoplastic agent	JAK2
thalidomide	antineoplastic agent	FGFR2
thalidomide	antineoplastic agent	NFKB1
thalidomide	antineoplastic agent	PTGS2
thalidomide	antineoplastic agent	TNF
sitaxsentan	for treatment of pulmonary arterial hypertension	EDNRA
ketoprofen	NSAID	PTGS1
ketoprofen	NSAID	PTGS1
ketoprofen	NSAID	PTGS2
ketoprofen	NSAID	PTGS2
pilocarpine	for treatment of incontinence	CHRM1
pilocarpine	for treatment of incontinence	CHRM2
pilocarpine	for treatment of incontinence	CHRM3
tolterodine	for treatment of incontinence	CHRM1
tolterodine	for treatment of incontinence	CHRM2
tolterodine	for treatment of incontinence	CHRM3
tolterodine	for treatment of incontinence	CHRM4
tolterodine	for treatment of incontinence	CHRM5
Ticagrelor	antithrombotic	P2RY12
tideglusib	for treatment of Alzheimer's disease	GSK3A
tideglusib	for treatment of Alzheimer's disease	GSK3B
tilarginine	for treatment of cardiogenic shock	NOS2

Drug Name	Indication(s)	Gene
tiotropium	for treatment of cystic fibrosis,for treatment of chronic obstructive pulmonary disorder (COPD)	CHRM1
tiotropium	for treatment of cystic fibrosis,for treatment of chronic obstructive pulmonary disorder (COPD)	CHRM2
tiotropium	for treatment of cystic fibrosis,for treatment of chronic obstructive pulmonary disorder (COPD)	CHRM3
tipifarnib	antineoplastic agent	FNTA
tipifarnib	antineoplastic agent	FNTB
tizanidine	muscle relaxant	ADRA2A
tizanidine	muscle relaxant	ADRA2B
tizanidine	muscle relaxant	ADRA2C
canfosfamide	antineoplastic agent	GSTP1
TLN-4601	antineoplastic agent	TSPO
obinepitide	antiobesity agent	NPY2R
obinepitide	antiobesity agent	PPYR1
TM30339	antiobesity agent	PPYR1
TM38837	antiobesity agent	CNR1
ondansetron	for treatment of obsessive compulsive disorder (OCD)	HTR3A
galeterone	antineoplastic agent	AR
galeterone	antineoplastic agent	CYP17A1
tolterodine	for treatment of incontinence	CHRM1
tolterodine	for treatment of incontinence	CHRM2
tolterodine	for treatment of incontinence	CHRM3
tolterodine	for treatment of incontinence	CHRM4

Drug Name	Indication(s)	Gene
tolterodine	for treatment of incontinence	CHRM5
tolvaptan	antihypertensive agent	AVPR2
Tonabersat	antimigraine agent	HTR1D
alprostadil	for treatment of erectile dysfunction,for treatment of sexual dysfunction in women	PTGER1
alprostadil	for treatment of erectile dysfunction,for treatment of sexual dysfunction in women	PTGER2
menadione	for reducing EGFR-inhibitor-induced dermatological side effects	GGCX
menadione	for reducing EGFR-inhibitor-induced dermatological side effects	VKORC1
menadione	for reducing EGFR-inhibitor-induced dermatological side effects	VKORC1L1
testosterone	hormone replacement	AR
topiramate	anticonvulsant	CA2
topiramate	anticonvulsant	CA4
topiramate	anticonvulsant	GABRA1
topiramate	anticonvulsant	GRIK1
topiramate	anticonvulsant	SCN1A
topiramate	anticonvulsant,antimigraine agent	CA2
topiramate	anticonvulsant,antimigraine agent	CA4
topiramate	anticonvulsant,antimigraine agent	GABRA1
topiramate	anticonvulsant,antimigraine agent	GRIK1
topiramate	anticonvulsant,antimigraine agent	SCN1A
topotecan	antineoplastic agent	TOP1
Torcetrapib	antidyslipidaemic agent	CETP

Drug Name	Indication(s)	Gene
morphine	analgesic	OPRD1
morphine	analgesic	OPRK1
morphine	analgesic	OPRM1
bosentan	for treatment of pulmonary arterial hypertension	EDNRA
bosentan	for treatment of pulmonary arterial hypertension	EDNRB
tramadol	analgesic	HTR2C
tramadol	analgesic	OPRK1
tramadol	analgesic	OPRM1
tramadol	analgesic	OPRM1
tramadol	analgesic	SLC6A2
tramadol	analgesic	SLC6A2
tramadol	analgesic	SLC6A4
tramadol	analgesic	SLC6A4
tramadol	analgesic	HTR2C
tramadol	analgesic	OPRK1
tramadol	analgesic	OPRM1
tramadol	analgesic	OPRM1
tramadol	analgesic	SLC6A2
tramadol	analgesic	SLC6A2
tramadol	analgesic	SLC6A4
tramadol	analgesic	SLC6A4
tramadol	analgesic	HTR2C
tramadol	analgesic	OPRK1
tramadol	analgesic	OPRM1
tramadol	analgesic	OPRM1
tramadol	analgesic	SLC6A2

Drug Name	Indication(s)	Gene
tramadol	analgesic	SLC6A2
tramadol	analgesic	SLC6A4
tramadol	analgesic	SLC6A4
homotaurine	for treatment of Alzheimer's disease	APP
trandolapril	antihypertensive agent	ACE
tranexamic acid	antimenorrhagic agent	PLAT
capsaicin	analgesic	TRPV1
diclofenac	NSAID	PTGS1
diclofenac	NSAID	PTGS2
estradiol	hormone replacement	ESR1
estradiol	hormone replacement	ESR2
granisetron	antiemetic	HTR3A
lidocaine	anestethic	SCN10A
lidocaine	anestethic	SCN5A
lidocaine	anestethic	SCN9A
epinephrine	anestethic	ADRA1A
epinephrine	anestethic	ADRA1B
epinephrine	anestethic	ADRA1D
epinephrine	anestethic	ADRA2A
epinephrine	anestethic	ADRA2B
epinephrine	anestethic	ADRB1
epinephrine	anestethic	ADRB2
lidocaine	anestethic	SCN10A
lidocaine	anestethic	SCN5A
lidocaine	anestethic	SCN9A
oxybutynin	for treatment of incontinence	CHRM1
oxybutynin	for treatment of incontinence	CHRM2
oxybutynin	for treatment of incontinence	CHRM3

Drug Name	Indication(s)	Gene
oxycodone	analgesic	OPRD1
oxycodone	analgesic	OPRK1
oxycodone	analgesic	OPRM1
fentanyl	analgesic	OPRD1
fentanyl	analgesic	OPRM1
timolol	for treatment of glaucoma	ADRB1
timolol	for treatment of glaucoma	ADRB2
travoprost	for treatment of glaucoma	PTGFR
trazodone	antidepressant	HTR1A
trazodone	antidepressant	HTR2A
trazodone	antidepressant	HTR2C
trazodone	antidepressant	SLC6A4
trelanserin	for treatment of intermittent claudication	HTR1B
trelanserin	for treatment of intermittent claudication	HTR2A
tretinoin	for treatment of acne	RARG
tretinoin	for treatment of acne	RXRB
tretinoin	for treatment of acne	RXRG
triamcinolone	for treatment of diabetic macular edema	NR3C1
Triapine	antineoplastic agent	RRM2
amlodipine	antihypertensive agent	CACNA1C
amlodipine	antihypertensive agent	CACNA1D
amlodipine	antihypertensive agent	CACNA1S
amlodipine	antihypertensive agent	CACNA2D1
amlodipine	antihypertensive agent	CACNB2
hydrochlorothiazide	antihypertensive agent	SLC12A3

Drug Name	Indication(s)	Gene
olmesartan	antihypertensive agent	AGTR1
triciribine	antineoplastic agent	AKT1
triciribine	antineoplastic agent	AKT2
triciribine	antineoplastic agent	AKT3
HE3286	antiinflammatory agent,DMARD	NR3C1
trodusquemine	antiobesity agent	PTPN1
trospium	for treatment of incontinence	CHRM1
TTP889	anticoagulant	F9
lapatinib	antineoplastic agent	EGFR
lapatinib	antineoplastic agent	ERBB2
TZP-101	for treatment of gastroparesis	GHSR
TZP-102	for treatment of gastroparesis	GHSR
heparin	for treatment of pelvic pain of bladder origin and interstitital cystitis	F10
heparin	for treatment of pelvic pain of bladder origin and interstitital cystitis	SERPINC1
lidocaine	for treatment of pelvic pain of bladder origin and interstitital cystitis	SCN10A
lidocaine	for treatment of pelvic pain of bladder origin and interstitital cystitis	SCN5A
lidocaine	for treatment of pelvic pain of bladder origin and interstitital cystitis	SCN9A
udenafil	for treatment of erectile dysfunction	PDE5A
tegafur	antineoplastic agent	TYMS
Ulipristal	contraceptive	PGR
heparin	antithrombotic	F10
heparin	antithrombotic	SERPINC1

Drug Name	Indication(s)	Gene
ursodeoxycholic acid	for prevention of recurrence of colorectal polyps	AKR1C2
topiramate	anticonvulsant	CA2
topiramate	anticonvulsant	CA4
topiramate	anticonvulsant	GABRA1
topiramate	anticonvulsant	GRIK1
topiramate	anticonvulsant	SCN1A
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRD1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRK1
buprenorphine	antidepressant,analgesic,for treatment of opioid addiction	OPRM1
carbidopa	antiparkinson agent	DDC
melevodopa	antiparkinson agent	DRD1
melevodopa	antiparkinson agent	DRD2
melevodopa	antiparkinson agent	DRD3
melevodopa	antiparkinson agent	DRD4
melevodopa	antiparkinson agent	DRD5
V158866	analgesic	FAAH
V24343	antiobesity agent	CNR1
V3381	analgesic,neuropathic pain	GRIN1
V3381	analgesic,neuropathic pain	GRIN2A
V3381	analgesic,neuropathic pain	GRIN2B
V3381	analgesic,neuropathic pain	GRIN2C
V3381	analgesic,neuropathic pain	GRIN2D
V3381	analgesic,neuropathic pain	GRIN3A
V3381	analgesic,neuropathic pain	GRIN3B

Drug Name	Indication(s)	Gene
V3381	analgesic,neuropathic pain	MAOA
V3381	analgesic,neuropathic pain	MAOB
VA106483	for treatment of BPH-related urinary symptoms	AVPR2
VA111913	for treatment of dysmenorrhea	AVPR1A
VA111913	for treatment of dysmenorrhea	AVPR1B
VA111913	for treatment of dysmenorrhea	AVPR2
Vadimezan	antineoplastic agent	HIPK2
Vadimezan	antineoplastic agent	KDR
Vadimezan	antineoplastic agent	PIM3
valproic acid	anticonvulsant	ABAT
valproic acid	anticonvulsant	ACADSB
valproic acid	anticonvulsant	HDAC9
valproic acid	for treatment of basal cell carcinoma	ABAT
valproic acid	for treatment of basal cell carcinoma	ACADSB
valproic acid	for treatment of basal cell carcinoma	HDAC9
valsartan	antihypertensive agent	AGTR1
vapitadine	antiallergy agent	HRH1
vapreotide	for treatment of liver cirrhosis-related variceal bleeding	SSTR2
vapreotide	for treatment of liver cirrhosis-related variceal bleeding	SSTR5
vardenafil	for treatment of erectile dysfunction	PDE5A
varenicline	smoking-cessation agent	CHRNA3
varenicline	smoking-cessation agent	CHRNA4
varenicline	smoking-cessation agent	CHRNA7
varenicline	smoking-cessation agent	CHRNB2
varenicline	smoking-cessation agent	CHRNB4

Drug Name	Indication(s)	Gene
varespladib	antiinflammatory agent	PLA2G10
varespladib	antiinflammatory agent	PLA2G2A
varespladib	antiinflammatory agent	PLA2G5
varespladib	antiinflammatory agent	PLA2G10
varespladib	antiinflammatory agent	PLA2G2A
varespladib	antiinflammatory agent	PLA2G5
ethinyl estradiol	contraceptive	ESR1
norethindrone	contraceptive	PGR
Vatalanib	antineoplastic agent	FLT1
Vatalanib	antineoplastic agent	FLT4
Vatalanib	antineoplastic agent	KDR
Vatalanib	antineoplastic agent	KIT
Vatalanib	antineoplastic agent	PDGFRA
Vatalanib	antineoplastic agent	PDGFRB
Vatalanib	antineoplastic agent	FLT1
Vatalanib	antineoplastic agent	FLT4
Vatalanib	antineoplastic agent	KDR
Vatalanib	antineoplastic agent	KIT
Vatalanib	antineoplastic agent	PDGFRA
Vatalanib	antineoplastic agent	PDGFRB
VEL-0230	antirheumatic agent	CTSK
bortezomib	antineoplastic agent	PSMB1
bortezomib	antineoplastic agent	PSMB2
bortezomib	antineoplastic agent	PSMB5
bortezomib	antineoplastic agent	PSMD1
bortezomib	antineoplastic agent	PSMD2
bupropion	antidepressant,appetite suppressant,smoking-cessation agent	SLC6A2

Drug Name	Indication(s)	Gene
bupropion	antidepressant,appetite suppressant,smoking-cessation agent	SLC6A3
velneperit	antiobesity agent	NPY5R
velusetrag	motilitant	HTR4
fluticasone furoate	antiinflammatory agent,glucocorticoid	NR3C1
verapamil	antihypertensive agent	CACNA1C
verapamil	antihypertensive agent	CACNA1D
verapamil	antihypertensive agent	CACNA1F
verapamil	antihypertensive agent	CACNA1S
verapamil	antihypertensive agent	CACNB1
verapamil	antihypertensive agent	CACNB2
verapamil	antihypertensive agent	CACNB3
verapamil	antihypertensive agent	CACNB4
vestipitant	for treatment of tinnitus,hypnotic	TACR1
VGX-1027	antiinflammatory agent,DMARD	unknown
VIA-2291	antiatherosclerotic agent	ALOX5
VIA-3196	antidyslipidaemic agent	THRB
Calcitonin	antiosteoporotic agent	CALCR
methotrexate	DMARD	DHFR
vicriviroc	antiviral agent,HIV	CCR5
vidofludimus	antiinflammatory agent,DMARD	DHODH
vidofludimus	antiinflammatory agent,DMARD	IL17A
vidofludimus	antiinflammatory agent,DMARD	IL17B
vidofludimus	antiinflammatory agent,DMARD	IL17C
vidofludimus	antiinflammatory agent,DMARD	IL17D
vidofludimus	antiinflammatory agent,DMARD	IL17E
Vigabatrin	for treatment of addiction	ABAT

Drug Name	Indication(s)	Gene
Vigabatrin	for treatment of addiction	GABBR1
vilazodone	antidepressant	HTR1A
vildagliptin	antidiabetic	DPP4
vincristine	antineoplastic agent	TUBA4A
vincristine	antineoplastic agent	TUBB
vinorelbine	antineoplastic agent	TUBB
BIIB014	antiparkinson agent	ADORA2A
Virulizin	antineoplastic agent	IL12A
Virulizin	antineoplastic agent	IL12B
naltrexone	for treatment of substance abuse	OPRD1
naltrexone	for treatment of substance abuse	OPRK1
naltrexone	for treatment of substance abuse	OPRM1
Voclosporin	antiinflammatory agent,DMARD,immunosuppressant	PPIA
Voclosporin	antiinflammatory agent,DMARD,immunosuppressant	PPP3CA
Voclosporin	antiinflammatory agent,DMARD,immunosuppressant	PPP3CB
Voclosporin	antiinflammatory agent,DMARD,immunosuppressant	PPP3CC
vofopitant	for treatment of post-traumatic stress disorder,hypnotic	TACR1
voglibose	antidiabetic	MGAM
volinanserin	hypnotic	HTR2A
vorapaxar	cardiovascular agent	F2R
vorapaxar	cardiovascular agent	F2RL2
vorapaxar	cardiovascular agent	F2RL3
Voreloxin	antineoplastic agent	TOP2A

Drug Name	Indication(s)	Gene
Voreloxin	antineoplastic agent	TOP2B
Histrelin	antineoplastic agent	GNRHR
Histrelin	antineoplastic agent	GNRHR2
TRPV1 antagonist	analgesic	TRPV1
VR-147	antimigraine agent	HTR1B
VR-147	antimigraine agent	HTR1D
heparin	for treatment of cystic fibrosis	F10
heparin	for treatment of cystic fibrosis	SERPINC1
etodolac	for treatment of cancer cachexia	PTGS1
etodolac	NSAID	PTGS2
propranolol	for treatment of cancer cachexia	ADRB1
VTP-27999	antihypertensive agent	REN
VTX-1463	antiallergy agent	TLR8
VTX-2337	antineoplastic agent	TLR8
VX-509	antiinflammatory agent,DMARD	JAK3
WX-554	antineoplastic agent	MAP2K1
WX-554	antineoplastic agent	MAP2K2
WX-554	antineoplastic agent	MAP2K3
WX-554	antineoplastic agent	MAP2K4
WX-554	antineoplastic agent	MAP2K5
WX-554	antineoplastic agent	MAP2K6
WX-554	antineoplastic agent	MAP2K7
tozasertib	antineoplastic agent	AURKA
tozasertib	antineoplastic agent	AURKB
tozasertib	antineoplastic agent	AURKC
VX-702	antiinflammatory agent,cardiovascular agent	MAPK11

Drug Name	Indication(s)	Gene
VX-702	antiinflammatory agent,cardiovascular agent	MAPK12
VX-702	antiinflammatory agent,cardiovascular agent	MAPK13
VX-702	antiinflammatory agent,cardiovascular agent	MAPK14
VX-765	antipsoriatic agent,anticonvulsant	CASP1
ivacaftor	for treatment of cystic fibrosis	CFTR
VX-809	for treatment of cystic fibrosis	CFTR
ivacaftor	for treatment of cystic fibrosis	CFTR
VX-809	for treatment of cystic fibrosis	CFTR
WX-UK1	antineoplastic agent	PLAU
emzetibe	antidyslipidaemic agent	NPC1L1
emzetibe	antidyslipidaemic agent	SOAT1
simvastatin	antidyslipidaemic agent	HMGCR
NRP104	for treatment of ADHD	ADRA1B
NRP104	for treatment of ADHD	SLC18A2
NRP104	for treatment of ADHD	SLC6A3
xaliproden	neuroprotectant	HTR1A
XL019	antineoplastic agent	JAK2
cabozantinib	antineoplastic agent	KDR
cabozantinib	antineoplastic agent	MET
XL228	antineoplastic agent	ABL1
XL228	antineoplastic agent	AURKA
XL228	antineoplastic agent	IGF1R
XL228	antineoplastic agent	SRC
XL281	antineoplastic agent	ARAF
XL281	antineoplastic agent	BRAF

Drug Name	Indication(s)	Gene
XL281	antineoplastic agent	RAF1
XL418	antineoplastic agent	AKT1
XL418	antineoplastic agent	AKT2
XL418	antineoplastic agent	AKT3
XL418	antineoplastic agent	RPS6KB1
XL647	antineoplastic agent	EGFR
XL647	antineoplastic agent	EPHB4
XL647	antineoplastic agent	ERBB2
XL647	antineoplastic agent	FLT1
XL647	antineoplastic agent	FLT4
XL647	antineoplastic agent	KDR
XL765	antineoplastic agent	MTOR
XL765	antineoplastic agent	PIK3CA
XL765	antineoplastic agent	PIK3CD
XL765	antineoplastic agent	PIK3CG
XL820	antineoplastic agent	FLT1
XL820	antineoplastic agent	FLT4
XL820	antineoplastic agent	KDR
XL820	antineoplastic agent	KIT
XL820	antineoplastic agent	PDGFRA
XL820	antineoplastic agent	PDGFRB
XL844	antineoplastic agent	CHEK1
XL844	antineoplastic agent	CHEK2
XL880	antineoplastic agent	KDR
XL880	antineoplastic agent	MET
XL888	antineoplastic agent	HSP90AA1
XL888	antineoplastic agent	HSP90AB1
XL999	antineoplastic agent	AXL

Drug Name	Indication(s)	Gene
XL999	antineoplastic agent	FGFR1
XL999	antineoplastic agent	FLT1
XL999	antineoplastic agent	FLT3
XL999	antineoplastic agent	FLT4
XL999	antineoplastic agent	KDR
XL999	antineoplastic agent	KIT
XL999	antineoplastic agent	PDGFRB
camptothecin	antineoplastic agent	TOP1
XMT-1107	antineoplastic agent	METAP2
tranexamic acid	for treatment of menorrhagia	PLG
XP13512	for treatment of restless legs syndrome	CACNA1B
XP13512	for treatment of restless legs syndrome	CACNA2D1
XP13512	for treatment of restless legs syndrome	CACNA2D2
R-baclofen	for treatment of gastrointestinal reflux disease	GABBR1
R-baclofen	for treatment of gastrointestinal reflux disease	GABBR2
XP21279	antiparkinson agent	DRD1
XP21279	antiparkinson agent	DRD2
XP21279	antiparkinson agent	DRD3
XP21279	antiparkinson agent	DRD4
XP21279	antiparkinson agent	DRD5
gantofiban	antithrombotic,antiatherosclerotic agent	ITGA2B

Drug Name	Indication(s)	Gene
gantofiban	antithrombotic,antiatherosclerotic agent	ITGB3
finasteride	antineoplastic agent	AKR1D1
finasteride	antineoplastic agent	SRD5A1
finasteride	antineoplastic agent	SRD5A2
YM-178	for treatment of overactive bladder	ADRB3
YM-598	antineoplastic agent	EDNRA
vandetanib	antineoplastic agent	EGFR
vandetanib	antineoplastic agent	FLT1
vandetanib	antineoplastic agent	FLT4
vandetanib	antineoplastic agent	KDR
vandetanib	antineoplastic agent	RET
zafirlukast	antiasthmatic agent	CYSLTR1
zaleplon	hypnotic	GABRA1
zaleplon	hypnotic	TSPO
ranitidine	antiulcer agent	HRH2
beloranib	antiobesity agent	METAP2
zibotentan	antineoplastic agent	EDNRA
ziconotide	analgesic	CACNA1B
ziprasidone	antipsychotic agent	DRD2
ziprasidone	antipsychotic agent	HTR2A
ondansetron	antiemetic	HTR3A
zoledronate	antiosteoporotic agent	FDPS
zoledronate	antiosteoporotic agent	GGPS1
zolmitriptan	antimigraine agent	HTR1A
zolmitriptan	antimigraine agent	HTR1B
zolmitriptan	antimigraine agent	HTR1D
zolmitriptan	antimigraine agent	HTR1F

Drug Name	Indication(s)	Gene
sertraline	antidepressant,for treatment of obsessive compulsive disorder (OCD)	SLC6A3
sertraline	antidepressant,for treatment of obsessive compulsive disorder (OCD)	SLC6A4
zolpidem	hypnotic	GABRA1
zonisamide	anticonvulsant	CACNA1G
zonisamide	anticonvulsant	CACNA1H
zonisamide	anticonvulsant	CACNA1I
zonisamide	anticonvulsant	SCN11A
zonisamide	anticonvulsant	SCN1A
zonisamide	anticonvulsant	SCN1B
zonisamide	anticonvulsant	SCN2A
zonisamide	anticonvulsant	SCN2B
zonisamide	anticonvulsant	SCN3A
zonisamide	anticonvulsant	SCN3B
zonisamide	anticonvulsant	SCN4A
zonisamide	anticonvulsant	SCN4B
zonisamide	anticonvulsant	SCN5A
zonisamide	anticonvulsant	SCN9A
zosuquidar	adjuvant to chemotherapy	ABCB1
zucapsaicin	analgesic	TRPV1
hydrocodone	analgesic	OPRD1
hydrocodone	analgesic	OPRM1
zileuton	antiinflammatory agent	ALOX5
ASP015K	for treatment of rheumatoid arthritis	JAK1
ASP015K	for treatment of rheumatoid arthritis	JAK3

Drug Name	Indication(s)	Gene
CHF 6001	antiasthmatic; for treatment of chronic obstructive pulmonary disease	PDE4A
CHF 6001	antiasthmatic; for treatment of chronic obstructive pulmonary disease	PDE4B
CUDC-427	antineoplastic agent	XIAP
ARQ 087	antineoplastic agent	FGFR1
ARQ 087	antineoplastic agent	FGFR2
ARQ 087	antineoplastic agent	FGFR3
deuterated dextromethorphan	for treatment of neurologic and psychiatric disorders	GRIN3A
deuterated dextromethorphan	for treatment of neurologic and psychiatric disorders	OPRS1
olanzapine	antipsychotic agent	ADRA1A
olanzapine	antipsychotic agent	ADRA1B
olanzapine	antipsychotic agent	ADRA2A
olanzapine	antipsychotic agent	ADRA2B
olanzapine	antipsychotic agent	ADRA2C
olanzapine	antipsychotic agent	CHRM1
olanzapine	antipsychotic agent	CHRM2
olanzapine	antipsychotic agent	CHRM3
olanzapine	antipsychotic agent	CHRM4
olanzapine	antipsychotic agent	CHRM5
olanzapine	antipsychotic agent	DRD1
olanzapine	antipsychotic agent	DRD2
olanzapine	antipsychotic agent	DRD3
olanzapine	antipsychotic agent	DRD4

Drug Name	Indication(s)	Gene
olanzapine	antipsychotic agent	DRD5
olanzapine	antipsychotic agent	HRH1
olanzapine	antipsychotic agent	HTR1A
olanzapine	antipsychotic agent	HTR1B
olanzapine	antipsychotic agent	HTR1D
olanzapine	antipsychotic agent	HTR1E
olanzapine	antipsychotic agent	HTR2A
olanzapine	antipsychotic agent	HTR2C
olanzapine	antipsychotic agent	HTR3A
olanzapine	antipsychotic agent	HTR6
olanzapine	antipsychotic agent	HTR7
samidoprhan	for treatment of addiction	MOR
Ethyl eicosapentaenoic acid	for treatment of cardiovascular disorders	PPARD
Ethyl eicosapentaenoic acid	for treatment of cardiovascular disorders	PPARG
Ethyl eicosapentaenoic acid	for treatment of cardiovascular disorders	PTGS1
Ethyl eicosapentaenoic acid	for treatment of cardiovascular disorders	PTGS2
BCX4161	for treatment of hereditary angioedema	KLKB1
ACEBUTOLOL	Antihypertensive Agents	ADRB1
ACENOCOUMAROL	Anticoagulants	VKORC1
ACEPROMETAZINE	Hypnotics and Sedatives	HRH1
ACETAZOLAMIDE	Anticonvulsants; Diuretics; antiglaucomic agent	CA1

Drug Name	Indication(s)	Gene
ACETAZOLAMIDE	Anticonvulsants; Diuretics; antiglaucomic agent	CA12
ACETAZOLAMIDE	Anticonvulsants; Diuretics; antiglaucomic agent	CA2
ACETOHEXAMIDE	Hypoglycemic Agents	KCNJ1
ACETOPHENAZINE	Antipsychotic Agents	DRD1
ACETOPHENAZINE	Antipsychotic Agents	DRD2
ACETYLDIGITOXIN	Anti-Arrhythmia Agents	ATP1A1
ACITRETIN	Keratolytic Agents	RARA
ADAPALENE	Dermatologic Agents	RARA
ADAPALENE	Dermatologic Agents	RARB
ADAPALENE	Dermatologic Agents	RARG
ADAPALENE	Dermatologic Agents	RXRA
ADAPALENE	Dermatologic Agents	RXRB
ADAPALENE	Dermatologic Agents	RXRG
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRA1
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRA2
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRA3
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRA5
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRB1
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRB2
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRB3
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRD
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRE
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRG1
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRG2
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRG3
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRP

Drug Name	Indication(s)	Gene
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRR1
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRR2
ADINAZOLAM	Anti-anxiety Agents; anticonvulsant	GABRR3
ALCAFTADINE	Anti-Allergic Agents	HRH1
ALCLOMETASONE	Anti-Inflammatory Agents; Anti-pruritics; Corticosteroids, topical	NR3C1
ALENDRONATE	Bisphosphonates	FDPS
ALFENTANIL	Analgesics, Opioid	OPRM1
Alitretionine	Antineoplastic Agents	RARA
Alitretionine	Antineoplastic Agents	RARB
Alitretionine	Antineoplastic Agents	RARG
Alitretionine	Antineoplastic Agents	RXRA
Alitretionine	Antineoplastic Agents	RXRB
Alitretionine	Antineoplastic Agents	RXRG
ALMITRINE	Respiratory Stimulant Agents	ATP1A1
ALPRENOLOL	Anti-Arrhythmia Agents; Antihypertensive Agents	ADRB1
ALPRENOLOL	Anti-Arrhythmia Agents; Antihypertensive Agents	ADRB2
ALSEROXYLON	Antipsychotic Agents; Antihypertensive Agents	SLC18A2
ALVIMOPAN	Opiate Antagonists	OPRM1
AMBENONIUM	Antimyasthenics	ACHE
AMCINONIDE	Anti-Inflammatory Agents; Anti-pruritics; Corticosteroids, topical	NR3C1
AMINOCAPROIC ACID	Antifibrinolytic Agents	PLG
AMINOGLUTETHIMIDE	Antineoplastic agents	CYP19A1

Drug Name	Indication(s)	Gene
AMRINONE	Cardiotonic Agents; Phosphodiesterase Inhibitors	PDE3A
AMRINONE	Cardiotonic Agents; Phosphodiesterase Inhibitors	PDE4B
ANILERIDINE	Analgesics; Narcotics	OPRM1
ANISINDIONE	Anticoagulants	GGCX
ANISOTROPINE METHYLBROMIDE	Antispasmodics; Anti-ulcer Agents	CHRM1
ANISOTROPINE METHYLBROMIDE	Antispasmodics; Anti-ulcer Agents	CHRM2
ANISOTROPINE METHYLBROMIDE	Antispasmodics; Anti-ulcer Agents	CHRM3
APRACLONIDINE	Antiglaucomic Agents	ADRA2A
APRINDINE	Anti-Arrhythmia Agents	SCN5A
ARBUTAMINE	Cardiotonic Agents	ADRB1
ARDEPARIN	Anticoagulants	SERPINC1
ARDEPARIN	Anticoagulants	SERPIND1
ARFORMOTEROL	Bronchodilator Agents	ADRB2
ASTEMIZOLE	Anti-Allergic Agents	HRH1
ATENOLOL	Anti-Arrhythmia Agents; Antihypertensive Agents	ADRB1
ATRACURIUM	Muscle Relaxants	CHRNA2
AURANOFIN	Antirheumatic Agents	IKBKB
AZATADINE	Anti-Allergic Agents	HRH1
BENDROFLUMETHIAZIDE	Antihypertensive Agents; Diuretics	SLC12A3
BENTIROMIDE	Diagnostic Agents	HPN
BENTIROMIDE	Diagnostic Agents	HPN
BENZOCAINE	Anesthetics, Local	SCN10A

Drug Name	Indication(s)	Gene
BENZONATATE	Antitussive Agents	SCN5A
BENZPHETAMINE	Central Nervous System Stimulants	ADRA1A
BENZPHETAMINE	Central Nervous System Stimulants	ADRA2A
BENZQUINAMIDE	Antiemetics; Antipsychotic Agents	CHRM1
BENZQUINAMIDE	Antiemetics; Antipsychotic Agents	CHRM2
BENZQUINAMIDE	Antiemetics; Antipsychotic Agents	CHRM3
BENZQUINAMIDE	Antiemetics; Antipsychotic Agents	CHRM4
BENZQUINAMIDE	Antiemetics; Antipsychotic Agents	CHRM5
BENZQUINAMIDE	Antiemetics; Antipsychotic Agents	HRH1
BENZTHIAZIDE	Antihypertensive Agents; Diuretics	SLC12A3
BENZTROPINE	Antiparkinson Agents	CHRM1
BENZTROPINE	Antiparkinson Agents	SLC6A3
BENZYLPENICILLOYL POLYLYSINE	Diagnostic Agents	FCER1A
BENZYLPENICILLOYL POLYLYSINE	Diagnostic Agents	FCER1G
BEPRIDIL	Anti-Arrhythmia Agents; Antihypertensive Agents	ATP1A1
BEPRIDIL	Anti-Arrhythmia Agents; Antihypertensive Agents	CACNA1A
BEPRIDIL	Anti-Arrhythmia Agents; Antihypertensive Agents	KCNQ1
BEPRIDIL	Anti-Arrhythmia Agents; Antihypertensive Agents	SCN5A
BEPRIDIL	Anti-Arrhythmia Agents; Antihypertensive Agents	TNNC1
BETAXOLOL	Antihypertensive Agents	ADRB1
BETAZOLE	Diagnostic Agents	HRH2

Drug Name	Indication(s)	Gene
BETHANECHOL	Parasympathomimetics	CHRM1
BETHANIDINE	Antihypertensive Agents	ADRA1A
BETHANIDINE	Antihypertensive Agents	ADRA1B
BETHANIDINE	Antihypertensive Agents	ADRA1D
BETHANIDINE	Antihypertensive Agents	ADRA2A
BETHANIDINE	Antihypertensive Agents	ADRA2B
BETHANIDINE	Antihypertensive Agents	ADRA2C
BETHANIDINE	Antihypertensive Agents	SLC6A2
BEVANTOLOL	Antihypertensive Agents	ADRB1
BIPERIDEN	Antidyskinetics	CHRM1
BIPERIDEN	Antidyskinetics	CHRNA2
BISOPROLOL	Antihypertensive Agents	ADRB1
BRINZOLAMIDE	Antiglaucomic Agents	CA2
BROMAZEPAM	Hypnotics and Sedatives	GABRA1
BROMAZEPAM	Hypnotics and Sedatives	GABRA2
BROMAZEPAM	Hypnotics and Sedatives	GABRA3
BROMAZEPAM	Hypnotics and Sedatives	GABRA4
BROMAZEPAM	Hypnotics and Sedatives	GABRA5
BROMAZEPAM	Hypnotics and Sedatives	GABRA6
BROMAZEPAM	Hypnotics and Sedatives	GABRB1
BROMAZEPAM	Hypnotics and Sedatives	GABRB2
BROMAZEPAM	Hypnotics and Sedatives	GABRB3
BROMAZEPAM	Hypnotics and Sedatives	GABRD
BROMAZEPAM	Hypnotics and Sedatives	GABRE
BROMAZEPAM	Hypnotics and Sedatives	GABRG1
BROMAZEPAM	Hypnotics and Sedatives	GABRG2
BROMAZEPAM	Hypnotics and Sedatives	GABRG3
BROMAZEPAM	Hypnotics and Sedatives	GABRP

Drug Name	Indication(s)	Gene
BROMAZEPAM	Hypnotics and Sedatives	GABRQ
BROMAZEPAM	Hypnotics and Sedatives	GABRR1
BROMAZEPAM	Hypnotics and Sedatives	GABRR2
BROMAZEPAM	Hypnotics and Sedatives	GABRR3
BROMODIPHENHYDRAMINE	Anti-Allergic Agents	HRH1
BROMPHENIRAMINE	Anti-Allergic Agents	HRH1
BUCLIZINE	Antiemetics	CHRM1
BUCLIZINE	Antiemetics	HRH1
BUMETANIDE	Antihypertensive Agents; Diuretics	SLC12A1
BUMETANIDE	Antihypertensive Agents; Diuretics	SLC12A2
BUMETANIDE	Antihypertensive Agents; Diuretics	SLC12A4
BUMETANIDE	Antihypertensive Agents; Diuretics	SLC12A5
BUSPIRONE	Anti-anxiety Agents	DRD2
BUSPIRONE	Anti-anxiety Agents	HTR1A
BUTABARBITAL	Hypnotics and Sedatives	CHRNA4
BUTABARBITAL	Hypnotics and Sedatives	CHRNA7
BUTABARBITAL	Hypnotics and Sedatives	GABRA1
BUTABARBITAL	Hypnotics and Sedatives	GABRA2
BUTABARBITAL	Hypnotics and Sedatives	GABRA3
BUTABARBITAL	Hypnotics and Sedatives	GABRA4
BUTABARBITAL	Hypnotics and Sedatives	GABRA5
BUTABARBITAL	Hypnotics and Sedatives	GABRA6
BUTABARBITAL	Hypnotics and Sedatives	GRIA2
BUTABARBITAL	Hypnotics and Sedatives	GRIK2
BUTALBITAL	Analgesics	CHRNA4
BUTALBITAL	Analgesics	CHRNA7
BUTALBITAL	Analgesics	GABRA1
BUTALBITAL	Analgesics	GABRA2

Drug Name	Indication(s)	Gene
BUTALBITAL	Analgesics	GABRA3
BUTALBITAL	Analgesics	GABRA4
BUTALBITAL	Analgesics	GABRA5
BUTALBITAL	Analgesics	GABRA6
BUTALBITAL	Analgesics	GRIA2
BUTALBITAL	Analgesics	GRIK2
BUTETHAL	Hypnotics and Sedatives	CHRNA4
BUTETHAL	Hypnotics and Sedatives	CHRNA7
BUTETHAL	Hypnotics and Sedatives	GABRA1
BUTETHAL	Hypnotics and Sedatives	GABRA2
BUTETHAL	Hypnotics and Sedatives	GABRA3
BUTETHAL	Hypnotics and Sedatives	GABRA4
BUTETHAL	Hypnotics and Sedatives	GABRA5
BUTETHAL	Hypnotics and Sedatives	GABRA6
BUTETHAL	Hypnotics and Sedatives	GRIA2
BUTETHAL	Hypnotics and Sedatives	GRIK2
BUTORPHANOL	Analgesics, Opioid	OPRD1
BUTORPHANOL	Analgesics, Opioid	OPRK1
BUTORPHANOL	Analgesics, Opioid	OPRM1
CABERGOLINE	Antiparkinson Agents	DRD2
CAFFEINE	Central Nervous System Stimulants	ADORA1
CAFFEINE	Central Nervous System Stimulants	ADORA2A
CAFFEINE	Central Nervous System Stimulants	PDE4B
CALCIPOTRIOL	Dermatologic Agents	VDR
CANDOXATRIL	Antihypertensive Agents	ACE
CANDOXATRIL	Antihypertensive Agents	MME
CAPTOPRIL	Antihypertensive Agents	ACE
CARBACHOL	Antiglaucomic Agents	CHRM1

Drug Name	Indication(s)	Gene
CARBACHOL	Antiglaucomic Agents	CHRM2
CARBACHOL	Antiglaucomic Agents	CHRNA2
CARBETOCIN	Labor Inducing Agents	OXTR
CARBIMAZOLE	Antithyroid Agents	TPO
CARBINOXAMINE	Anti-Allergic Agents	CHRM1
CARBINOXAMINE	Anti-Allergic Agents	HRH1
CARBOPROST TROMETHAMINE	Abortifacient Agents	PTGER1
CARPHENAZINE	Antipsychotic Agents	DRD1
CARPHENAZINE	Antipsychotic Agents	DRD2
CARPHENAZINE	Antipsychotic Agents	DRD5
CARPROFEN	Anti-Inflammatory Agents, Non-Steroidal	PTGS2
CARTEOLOL	Antiglaucomic Agents	ADRB1
CARTEOLOL	Antiglaucomic Agents	ADRB2
CERULETIDE	Diagnostic Agents	CCKAR
CEVIMELINE	Parasympathomimetics	CHRM1
CEVIMELINE	Parasympathomimetics	CHRM3
CHLOPHEDIANOL	Antitussive Agents	HRH1
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRA1
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRA2
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRA3
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRA4
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRA5
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRA6
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRB1
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRB2
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRB3

Drug Name	Indication(s)	Gene
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRD
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRE
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRG1
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRG2
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRG3
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRP
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRQ
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRR1
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRR2
CHLORDIAZEPOXIDE	Hypnotics and Sedatives	GABRR3
CHLORMERODRIN	Antihypertensive Agents; Diuretics	SLC12A1
CHLORMEZANONE	Anti-anxiety Agents; Muscle Relaxants	BZRP
CHLOROPROCAINE	Anesthetics, Local	SCN10A
CHLOROTHIAZIDE	Antihypertensive Agents; Diuretics	CA1
CHLOROTHIAZIDE	Antihypertensive Agents; Diuretics	CA2
CHLOROTHIAZIDE	Antihypertensive Agents; Diuretics	CA4
CHLOROTHIAZIDE	Antihypertensive Agents; Diuretics	SLC12A3
CHLOROTRIANISENE	Hormone Replacement Agents	ESR1
CHLORPHENIRAMINE	Anti-Allergic Agents	HRH1
CHLORPROPAMIDE	Hypoglycemic Agents	KCNJ1
CHLORPROTHIXENE	Antipsychotic Agents	DRD1
CHLORPROTHIXENE	Antipsychotic Agents	DRD2
CHLORPROTHIXENE	Antipsychotic Agents	DRD3
CHLORPROTHIXENE	Antipsychotic Agents	HRH1
CHLORPROTHIXENE	Antipsychotic Agents	HTR2A
CHLORPROTHIXENE	Antipsychotic Agents	HTR2B
CHLORPROTHIXENE	Antipsychotic Agents	HTR2C

Drug Name	Indication(s)	Gene
CHLORTHALIDONE	Antihypertensive Agents; Diuretics	SLC12A1
CHLORZOXAZONE	Muscle Relaxants	KCNMA1
CICLESONIDE	Anti-Inflammatory Agents; Anti-allergic agents; Glucocorticoids	NR3C1
CILASTATIN	Adjuvants, enzyme inhibitors	DPEP1
CILAZAPRIL	Antihypertensive Agents	ACE
CILOSTAZOL	Platelet Aggregation Inhibitors	PDE3A
CIMETIDINE	GI Anti-Ulcer Agents, antihistamines	HRH2
CINACALCET	Calcimimetics	CASR
CINALUKAST	Anti-Asthmatic Agents	CYSLTR1
CINNARIZINE	Anti-Allergic Agents	HRH1
CINOLAZEPAM	Hypnotics and Sedatives	GABRA1
CINOLAZEPAM	Hypnotics and Sedatives	GABRA2
CINOLAZEPAM	Hypnotics and Sedatives	GABRA3
CINOLAZEPAM	Hypnotics and Sedatives	GABRA5
CINOLAZEPAM	Hypnotics and Sedatives	GABRB1
CINOLAZEPAM	Hypnotics and Sedatives	GABRB2
CINOLAZEPAM	Hypnotics and Sedatives	GABRB3
CINOLAZEPAM	Hypnotics and Sedatives	GABRD
CINOLAZEPAM	Hypnotics and Sedatives	GABRE
CINOLAZEPAM	Hypnotics and Sedatives	GABRG1
CINOLAZEPAM	Hypnotics and Sedatives	GABRG2
CINOLAZEPAM	Hypnotics and Sedatives	GABRG3
CINOLAZEPAM	Hypnotics and Sedatives	GABRP
CINOLAZEPAM	Hypnotics and Sedatives	GABRR1
CINOLAZEPAM	Hypnotics and Sedatives	GABRR2
CINOLAZEPAM	Hypnotics and Sedatives	GABRR3

Drug Name	Indication(s)	Gene
CISAPRIDE	Parasympathomimetics	HTR4
CISATRACURIUM BESYLATE	Neuromuscular Blocking Agents	CHRNA2
CITALOPRAM	Antidepressive Agents, Second-Generation	SLC6A4
CLEMASTINE	Anti-Allergic Agents	HRH1
CLENBUTEROL	Bronchodilator Agents	ADRB2
CLIDINIUM	GI Anti-Ulcer Agents, anticholinergic; Antispasmodics	CHRM1
CLOCORTOLONE	Anti-Inflammatory Agents; Anti-pruritics; Corticosteroids, topical	NR3C1
CLOFIBRATE	Anticholesteremic Agents	PPARA
CLOMIPRAMINE	Antidepressive Agents, Tricyclic	SLC6A2
CLOMIPRAMINE	Antidepressive Agents, Tricyclic	SLC6A4
CLORAZEPATE	Hypnotics and Sedatives	BZRP
CLORAZEPATE	Hypnotics and Sedatives	GABRA1
CLORAZEPATE	Hypnotics and Sedatives	GABRA2
CLORAZEPATE	Hypnotics and Sedatives	GABRA3
CLORAZEPATE	Hypnotics and Sedatives	GABRA4
CLORAZEPATE	Hypnotics and Sedatives	GABRA5
CLORAZEPATE	Hypnotics and Sedatives	GABRA6
CLORAZEPATE	Hypnotics and Sedatives	GABRB1
CLORAZEPATE	Hypnotics and Sedatives	GABRB2
CLORAZEPATE	Hypnotics and Sedatives	GABRB3
CLORAZEPATE	Hypnotics and Sedatives	GABRD
CLORAZEPATE	Hypnotics and Sedatives	GABRE
CLORAZEPATE	Hypnotics and Sedatives	GABRG1
CLORAZEPATE	Hypnotics and Sedatives	GABRG2

Drug Name	Indication(s)	Gene
CLORAZEPATE	Hypnotics and Sedatives	GABRG3
CLORAZEPATE	Hypnotics and Sedatives	GABRP
CLORAZEPATE	Hypnotics and Sedatives	GABRQ
CLORAZEPATE	Hypnotics and Sedatives	GABRR1
CLORAZEPATE	Hypnotics and Sedatives	GABRR2
CLORAZEPATE	Hypnotics and Sedatives	GABRR3
CLOTIAZEPAM	Hypnotics and Sedatives	GABRA1
CLOTIAZEPAM	Hypnotics and Sedatives	GABRA2
CLOTIAZEPAM	Hypnotics and Sedatives	GABRA3
CLOTIAZEPAM	Hypnotics and Sedatives	GABRA5
CLOTIAZEPAM	Hypnotics and Sedatives	GABRB1
CLOTIAZEPAM	Hypnotics and Sedatives	GABRB2
CLOTIAZEPAM	Hypnotics and Sedatives	GABRB3
CLOTIAZEPAM	Hypnotics and Sedatives	GABRD
CLOTIAZEPAM	Hypnotics and Sedatives	GABRE
CLOTIAZEPAM	Hypnotics and Sedatives	GABRG1
CLOTIAZEPAM	Hypnotics and Sedatives	GABRG2
CLOTIAZEPAM	Hypnotics and Sedatives	GABRG3
CLOTIAZEPAM	Hypnotics and Sedatives	GABRP
CLOTIAZEPAM	Hypnotics and Sedatives	GABRR1
CLOTIAZEPAM	Hypnotics and Sedatives	GABRR2
CLOTIAZEPAM	Hypnotics and Sedatives	GABRR3
CLOZAPINE	Antipsychotic Agents	DRD1
CLOZAPINE	Antipsychotic Agents	DRD2
CLOZAPINE	Antipsychotic Agents	DRD4
CLOZAPINE	Antipsychotic Agents	HRH1
CLOZAPINE	Antipsychotic Agents	HRH4
CLOZAPINE	Antipsychotic Agents	HTR1A

Drug Name	Indication(s)	Gene
CLOZAPINE	Antipsychotic Agents	HTR2A
CLOZAPINE	Antipsychotic Agents	HTR2C
COCAINE	local anesthetic	DRD3
COCAINE	local anesthetic	OPRK1
COCAINE	local anesthetic	SCN10A
COCAINE	local anesthetic	SCN11A
COCAINE	local anesthetic	SCN5A
COCAINE	local anesthetic	SLC6A2
COCAINE	local anesthetic	SLC6A3
COCAINE	local anesthetic	SLC6A4
CODEINE	Analgesics, Opioid; Antitussive Agents	OPRD1
CODEINE	Analgesics, Opioid; Antitussive Agents	OPRK1
CODEINE	Analgesics, Opioid; Antitussive Agents	OPRM1
CONJUGATED ESTROGENS	Hormone Replacement Agents	ESR1
CROMOGLICATE	Anti-Asthmatic Agents	KCNMA1
CYCLIZINE	Antiemetics	HRH1
CYCLOBENZAPRINE	Antidepressive Agents, Tricyclic	HTR2A
CYCLOPENTOLATE	Mydriatics	CHRM1
CYCLOTHIAZIDE	Antihypertensive Agents; Diuretics	FXYD2
CYCRIMINE	Antiparkinson Agents	CHRM1
CYPROHEPTADINE	Anti-Allergic Agents; Appetite Stimulant	HRH1
CYPROHEPTADINE	Anti-Allergic Agents; Appetite Stimulant	HTR2A

Drug Name	Indication(s)	Gene
CYPROTERONE	Hypersexuality-inhibiting agents; Antihirsutism agents	AR
DACARBAZINE	Antineoplastic Agents	POLA2
DALFAMPRIDINE	MS-treatment	KCNA1
DANAZOL	Antiendometriosis Agent, Antineoplastic Agent	ESR1
DANAZOL	Antiendometriosis Agent, Antineoplastic Agent	GNRHR
DANAZOL	Antiendometriosis Agent, Antineoplastic Agent	GNRHR2
DANTROLENE	Muscle Relaxants	RYR1
DAPIPRAZOLE	ophthalmological agent	ADRA1A
DAPIPRAZOLE	ophthalmological agent	ADRA1B
DAPIPRAZOLE	ophthalmological agent	ADRA1D
DEBRISOQUIN	Antihypertensive Agents	ADRA1A
DEBRISOQUIN	Antihypertensive Agents	ADRA1B
DEBRISOQUIN	Antihypertensive Agents	ADRA1D
DEBRISOQUIN	Antihypertensive Agents	ADRA2A
DEBRISOQUIN	Antihypertensive Agents	ADRA2B
DEBRISOQUIN	Antihypertensive Agents	ADRA2C
DECAMETHONIUM	Muscle Relaxants	CHRNA2
DEMECARIUM BROMIDE	Antiglaucomic Agents	ACHE
DEMECARIUM BROMIDE	Antiglaucomic Agents	BCHE
DESERPIDINE	Antihypertensive Agents	ACE
DESFLURANE	inhalation anesthetics	ATP2C1
DESFLURANE	inhalation anesthetics	ATP5D
DESFLURANE	inhalation anesthetics	GABRA1
DESFLURANE	inhalation anesthetics	GLRA1

Drug Name	Indication(s)	Gene
DESFLURANE	inhalation anesthetics	GRIA1
DESFLURANE	inhalation anesthetics	KCNA1
DESFLURANE	inhalation anesthetics	MT-ND1
DESIPRAMINE	Antidepressive Agents, Tricyclic	ADRB1
DESIPRAMINE	Antidepressive Agents, Tricyclic	ADRB2
DESIPRAMINE	Antidepressive Agents, Tricyclic	CHRM1
DESIPRAMINE	Antidepressive Agents, Tricyclic	CHRM2
DESIPRAMINE	Antidepressive Agents, Tricyclic	HRH1
DESIPRAMINE	Antidepressive Agents, Tricyclic	SLC6A2
DESIPRAMINE	Antidepressive Agents, Tricyclic	SLC6A4
DESLANOSIDE	Antiarrhythmia Agents; Cardiotonic Agents	ATP1A1
DESOGESTREL	Contraceptives, Oral	ESR1
DESOGESTREL	Contraceptives, Oral	PGR
DESOXIMETASONE	Anti-Inflammatory Agents; Glucocorticoids	NR3C1
DESOXYCORTICOSTERONE PIVALATE	Hormone Replacement Agents, anti-addison agent	NR3C2
DEXBROMPHENIRAMINE	Anti-Allergic Agents	HRH1
DEXFENFLURAMINE	Appetite Depressants	SLC6A4
DEXMEDETOMIDINE	Analgesics; Hypnotics and Sedatives	ADRA2A
DEXTROMETHORPHAN	Antitussive Agents	GRIN3A
DEXTROMETHORPHAN	Antitussive Agents	OPRS1
DEZOCINE	Analgesics, Opioid	OPRK1
DEZOCINE	Analgesics, Opioid	OPRM1
DIAZOXIDE	Antihypertensive Agents; Vasodilator Agents	SLC12A3
DIBUCAINE	Anesthetics, Local	SCN10A

Drug Name	Indication(s)	Gene
DIBUCAINE	Anesthetics, Local	SCN5A
DICHLORPHENAMIDE	Antiglaucomic Agents	CA1
DICUMAROL	Anticoagulants	VKORC1
DICYCLOMINE	Antispasmodics	CHRM1
DIENESTROL	Hormone Replacement Agents	ESR1
DIETHYLPROPION	Appetite Depressants	SLC6A2
DIETHYLPROPION	Appetite Depressants	SLC6A3
DIETHYLSTILBESTROL	Hormone Replacement Agents	ESR1
DIFLORASONE	Anti-Inflammatory Agents; Glucocorticoids	NR3C1
DIGITOXIN	Anti-Arrhythmia Agents; Cardiotonic Agents	ATP1A1
DIGOXIN	Anti-Arrhythmia Agents; Cardiotonic Agents	ATP1A1
DIHYDROTACHYSTEROL	Anti-migraine Agents	VDR
DIMENHYDRINATE	Antiemetics	HRH1
DINOPROST TROMETHAMINE	Abortifacient Agents	PTGIR
DINOPROSTONE	Abortifacient Agents	PTGER1
DINOPROSTONE	Abortifacient Agents	PTGER2
DINOPROSTONE	Abortifacient Agents	PTGER3
DINOPROSTONE	Abortifacient Agents	PTGER4
DIPHEMANIL METHYLSULFATE	Bronchodilator Agents	CHRM3
DIPHENHYDRAMINE	Anti-Allergic Agents; Hypnotics and sedatives; Antiemetics; Antipruritics; Antitussives	HRH1
DIPHENIDOL	Antiemetics	CHRM1

Drug Name	Indication(s)	Gene
DIPHENIDOL	Antiemetics	CHRM2
DIPHENIDOL	Antiemetics	CHRM3
DIPHENOXYLATE	Antidiarrheals	OPRM1
DIPHENYLPYRALINE	Anti-Allergic Agents	HRH1
DIPIVEFRIN	Ophthalmologicals	ADRA2A
DISOPYRAMIDE	Anti-Arrhythmia Agents	SCN5A
DISULFIRAM	Alcohol Deterrents	ALDH2
DIVALPROEX SODIUM	Anticonvulsants; Antimanic Agents	ABAT
DOBUTAMINE	Cardiotonic Agents	ADRB1
DOFETILIDE	Anti-Arrhythmia Agents	KCNH2
DOFETILIDE	Anti-Arrhythmia Agents	KCNJ12
DOFETILIDE	Anti-Arrhythmia Agents	KCNK2
DOMPERIDONE	Antiemetics	DRD2
DOXACURIUM	Muscle Relaxants	CHRM2
DOXACURIUM	Muscle Relaxants	CHRNA2
DOXACURIUM CHLORIDE	Muscle Relaxants	CHRM2
DOXACURIUM CHLORIDE	Muscle Relaxants	CHRNA2
DOXAZOSIN	Anticholesteremic Agents; Antihypertensive Agents; Vasodilator Agents	ADRA1A
DOXAZOSIN	Anticholesteremic Agents; Antihypertensive Agents; Vasodilator Agents	ADRA1B
DOXAZOSIN	Anticholesteremic Agents; Antihypertensive Agents; Vasodilator Agents	ADRA1D

Drug Name	Indication(s)	Gene
DOXYLAMINE	Anti-Allergic Agents; Antiemetics; Antitussive Agents; Hypnotics and Sedatives	HRH1
DROMOSTANOLONE	Antineoplastic Agents, Hormonal	AR
DRONEDARONE	Anti-Arrhythmia Agents	ADRA1A
DRONEDARONE	Anti-Arrhythmia Agents	ADRB1
DRONEDARONE	Anti-Arrhythmia Agents	KCNH2
DROPERIDOL	Adjuvants, Anesthesia	DRD2
DUTASTERIDE	Anti-baldness Agents, Antihyperplasia Agents	SRD5A1
DUTASTERIDE	Anti-baldness Agents, Antihyperplasia Agents	SRD5A2
DYCLONINE	Anesthetics, Local	SCN10A
DYDROGESTERONE	Antidysmennorheal Agents	PGR
DYPHYLLINE	Bronchodilator Agents; Vasodilator Agents	PDE4A
DYPHYLLINE	Bronchodilator Agents; Vasodilator Agents	PDE4B
DYPHYLLINE	Bronchodilator Agents; Vasodilator Agents	PDE4C
DYPHYLLINE	Bronchodilator Agents; Vasodilator Agents	PDE4D
DYPHYLLINE	Bronchodilator Agents; Vasodilator Agents	PDE7A
DYPHYLLINE	Bronchodilator Agents; Vasodilator Agents	PDE7B
ECHOTHIOPHATE IODIDE	Miotics	BCHE
EDROPHONIUM	Anti-Arrhythmia Agents; Antidotes	ACHE

Drug Name	Indication(s)	Gene
EMEDASTINE	Anti-Allergic Agents	HRH1
ENCAINIDE	Anti-Arrhythmia Agents	SCN5A
ENFLURANE	Anesthetics, Inhalation	ATP2C1
ENFLURANE	Anesthetics, Inhalation	ATP5D
ENFLURANE	Anesthetics, Inhalation	GABRA1
ENFLURANE	Anesthetics, Inhalation	GLRA1
ENFLURANE	Anesthetics, Inhalation	GRIA1
ENFLURANE	Anesthetics, Inhalation	KCNA1
ENFLURANE	Anesthetics, Inhalation	KCNMA1
ENFLURANE	Anesthetics, Inhalation	MT-ND1
ENOXIMONE	Cardiotonic Agents; Vasodilator Agents	PDE3A
ENPROFYLLINE	Anti-Asthmatic Agents; Antiarrhythmic Agents; Bronchodilator Agents	PDE4A
ENPROFYLLINE	Anti-Asthmatic Agents; Antiarrhythmic Agents; Bronchodilator Agents	PDE4B
EPHEDRINE	Central Nervous System Stimulants	ADRA1A
EPIRUBICIN	Antineoplastic Agents	CHD1
EPIRUBICIN	Antineoplastic Agents	TOP2A
EPOPROSTENOL	Antihypertensive Agents; Platelet Aggregation Inhibitors	PTGIR
EPROSARTAN	Antihypertensive Agents	AGTR1
ERGOCALCIFEROL	Antihypocalcemic Agents	VDR
ERGOLOID MESYLATE	Nootropic Agents; Vasodilator Agents	ADRA1A

Drug Name	Indication(s)	Gene
ERGOLOID MESYLATE	Nootropic Agents; Vasodilator Agents	ADRA2A
ERGOTAMINE	Anti-migraine Agents	HTR1B
ERGOTAMINE	Anti-migraine Agents	HTR1D
ERYTHRITYL TETRANITRATE	Antianginal Agents; Vasodilator Agents	NPR1
ERYTHRITYL TETRANITRATE	Antianginal Agents; Vasodilator Agents	NPR2
ESMOLOL	Anti-Arrhythmia Agents	ADRB1
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRA1
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRA2
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRA3
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRA5
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRB1
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRB2
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRB3
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRD
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRE

Drug Name	Indication(s)	Gene
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRG1
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRG2
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRG3
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRP
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRR1
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRR2
ESTAZOLAM	Anti-anxiety Agents; Anticonvulsants	GABRR3
ESTRIOL	Hormone Replacement Agents	ESR1
ESTRONE	Hormone Replacement Agents	ESR1
ETHACRYNIC ACID	Antihypertensive Agents; Diuretics	SLC12A1
ETHOPROPAZINE	Antidyskinetics	CHRM1
ETHOSUXIMIDE	Anticonvulsants	CACNA1G
ETHOTOIN	Anticonvulsants	SCN5A
ETHOXZOLAMIDE	Antihypertensive Agents, Diuretics; Antiglaucoma agents	CA1
ETHYNODIOL DIACETATE	Contraceptives, Oral, Synthetic	ESR1
ETHYNODIOL DIACETATE	Contraceptives, Oral, Synthetic	PGR
ETOMIDATE	Anesthetics, Intravenous	ADRA2B
ETOMIDATE	Anesthetics, Intravenous	GABRA1
ETOPOSIDE	Antineoplastic Agents	TOP2A
EZETIMIBE	Anticholesteremic Agents	NPC1L1

Drug Name	Indication(s)	Gene
FELBAMATE	Anticonvulsants; Antiepileptics	GRIN2A
FELBAMATE	Anticonvulsants; Antiepileptics	GRIN2B
FELBAMATE	Anticonvulsants; Antiepileptics	GRIN3A
FENCAMFAMINE	Central Nervous System Stimulants	SLC6A3
FENOPROFEN	NSAID	PTGS1
FENOPROFEN	NSAID	PTGS2
FENOTEROL	Bronchodilator Agents; Tocolytic Agents	ADRB2
FLAVOXATE	Antispasmodics	CHRM1
FLAVOXATE	Antispasmodics	CHRM2
FLECAINIDE	Anti-Arrhythmia Agents	SCN5A
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRA1
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRA2
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRA3
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRA5
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRB1
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRB2
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRB3
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRD

Drug Name	Indication(s)	Gene
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRE
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRG1
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRG2
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRG3
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRP
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRR1
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRR2
FLUDIAZEPAM	Anti-anxiety Agents; Anticonvulsants	GABRR3
FLUDROCORTISONE	Anti-Inflammatory Agents; corticosteroid	NR3C2
FLUMAZENIL	Antidotes, Benzodoazepine Overdose	GABRA1
FLUMAZENIL	Antidotes, Benzodoazepine Overdose	GABRA2
FLUMAZENIL	Antidotes, Benzodoazepine Overdose	GABRA3
FLUMAZENIL	Antidotes, Benzodoazepine Overdose	GABRA5
FLUMETHASONE PIVALATE	Anti-Inflammatory Agents; corticosteroid	NR3C1

Drug Name	Indication(s)	Gene
FLUNARIZINE	Anticonvulsants; Vasodilator Agents	CACNA1G
FLUNARIZINE	Anticonvulsants; Vasodilator Agents	CACNA1H
FLUNARIZINE	Anticonvulsants; Vasodilator Agents	CACNA1I
FLUNARIZINE	Anticonvulsants; Vasodilator Agents	HRH1
FLUNITRAZEPAM	Hypnotics and Sedatives	BZRP
FLUNITRAZEPAM	Hypnotics and Sedatives	GABRA2
FLUNITRAZEPAM	Hypnotics and Sedatives	GABRA3
FLUNITRAZEPAM	Hypnotics and Sedatives	GABRA4
FLUNITRAZEPAM	Hypnotics and Sedatives	GABRA5
FLUNITRAZEPAM	Hypnotics and Sedatives	GABRA6
FLUOROMETHOLONE	Anti-Inflammatory Agents; Anti-allergic agents; Glucocorticoids	NR3C1
FLUOXYMESTERONE	Anabolic Agents; Antineoplastic Agents	AR
FLUPENTHIXOL	Antipsychotic Agents	DRD1
FLUPENTHIXOL	Antipsychotic Agents	DRD2
FLUPHENAZINE	Antipsychotic Agents	DRD1
FLUPHENAZINE	Antipsychotic Agents	DRD2
FLURANDRENOLIDE	Anti-Inflammatory Agents; Glucocorticoids	NR3C1
FLURAZEPAM	Hypnotics and Sedatives	GABRA1
FLURAZEPAM	Hypnotics and Sedatives	GABRA2
FLURAZEPAM	Hypnotics and Sedatives	GABRA3
FLURAZEPAM	Hypnotics and Sedatives	GABRA4
FLURAZEPAM	Hypnotics and Sedatives	GABRA5
FLURAZEPAM	Hypnotics and Sedatives	GABRA6
FLURAZEPAM	Hypnotics and Sedatives	GABRB1
FLURAZEPAM	Hypnotics and Sedatives	GABRB2

Drug Name	Indication(s)	Gene
FLURAZEPAM	Hypnotics and Sedatives	GABRB3
FLURAZEPAM	Hypnotics and Sedatives	GABRD
FLURAZEPAM	Hypnotics and Sedatives	GABRE
FLURAZEPAM	Hypnotics and Sedatives	GABRG1
FLURAZEPAM	Hypnotics and Sedatives	GABRG2
FLURAZEPAM	Hypnotics and Sedatives	GABRG3
FLURAZEPAM	Hypnotics and Sedatives	GABRP
FLURAZEPAM	Hypnotics and Sedatives	GABRQ
FLURAZEPAM	Hypnotics and Sedatives	GABRR1
FLURAZEPAM	Hypnotics and Sedatives	GABRR2
FLURAZEPAM	Hypnotics and Sedatives	GABRR3
FLUSPIRILENE	Antipsychotic Agents	DRD2
FLUTAMIDE	Antineoplastic Agents, Hormonal	AR
FONDAPARINUX	Antithrombotic Agents	SERPINC1
FORASARTAN	Antihypertensive Agents	AGTR1
FOSINOPRIL	Antihypertensive Agents	ACE
FUROSEMIDE	Antihypertensive Agents; Diuretics	SLC12A1
GALLAMINE TRIETHIODIDE	Muscle Relaxants, Skeletal	CHRNA2
GEMFIBROZIL	Antilipemic Agents	PPARA
GLIBENCLAMIDE	Hypoglycemic Agents	KCNJ1
GLIBENCLAMIDE	Hypoglycemic Agents	KCNJ11
GLICLAZIDE	Hypoglycemic Agents	KCNJ1
GLIPIZIDE	Hypoglycemic Agents	KCNJ1
GLYCODIAZINE	Hypoglycemic Agents	KCNJ1
GONADORELIN	Fertility Agents	GNRHR
GONADORELIN	Fertility Agents	GNRHR2
GUANABENZ	Antihypertensive Agents	ADRA2A
GUANADREL SULFATE	Antihypertensive Agents	SLC6A2

Drug Name	Indication(s)	Gene
GUANETHIDINE	Antihypertensive Agents	SLC6A2
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRA1
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRA2
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRA3
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRA5
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRB1
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRB2
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRB3
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRD
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRE
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRG1
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRG2
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRG3
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRP

Drug Name	Indication(s)	Gene
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRR1
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRR2
HALAZEPAM	Anti-anxiety Agents; Muscle Relaxants; Sedative	GABRR3
HALOBETASOL PROPIONATE	Anti-inflammatory Agents	NR3C1
HALOPERIDOL	Antipsychotic Agents	DRD2
HALOTHANE	Anesthetics, Inhalation	ATP5D
HEXAFLURONIUM BROMIDE	Muscle Relaxants	BCHE
HEXOBARBITAL	Hypnotics and Sedatives	CHRNA4
HEXOBARBITAL	Hypnotics and Sedatives	CHRNA7
HEXOBARBITAL	Hypnotics and Sedatives	GABRA1
HEXOBARBITAL	Hypnotics and Sedatives	GABRA2
HEXOBARBITAL	Hypnotics and Sedatives	GABRA3
HEXOBARBITAL	Hypnotics and Sedatives	GABRA4
HEXOBARBITAL	Hypnotics and Sedatives	GABRA5
HEXOBARBITAL	Hypnotics and Sedatives	GABRA6
HEXOBARBITAL	Hypnotics and Sedatives	GRIA2
HEXOBARBITAL	Hypnotics and Sedatives	GRIK2
HEXYLCAINE	Anesthetics, Local	SCN10A
HEXYLCAINE	Anesthetics, Local	SCN5A
HOMATROPINE METHYLBROMIDE	GI Anti-Ulcer Agents, Antimuscarinics	CHRM1
HOMATROPINE METHYLBROMIDE	GI Anti-Ulcer Agents, Antimuscarinics	CHRM2

Drug Name	Indication(s)	Gene
HOMATROPINE METHYLBROMIDE	GI Anti-Ulcer Agents, Antimuscarinics	CHRM3
HOMATROPINE METHYLBROMIDE	GI Anti-Ulcer Agents, Antimuscarinics	CHRM4
HOMATROPINE METHYLBROMIDE	GI Anti-Ulcer Agents, Antimuscarinics	CHRM5
HYDROCORTAMATE	Anti-Inflammatory Agents; Glucocorticoids	NR3C1
HYDROCORTAMATE	Anti-Inflammatory Agents; Glucocorticoids	NR3C1
HYDROFLUMETHIAZIDE	Antihypertensive Agents; Diuretics	SLC12A1
HYDROXYUREA	Antineoplastic Agents	RRM1
HYDROXYZINE	Antipruritics; Anxiolytics sedatives and hypnotics	HRH1
IBUTILIDE	Anti-Arrhythmia Agents	CACNA1C
IBUTILIDE	Anti-Arrhythmia Agents	CACNA2D1
IBUTILIDE	Anti-Arrhythmia Agents	CACNB1
IBUTILIDE	Anti-Arrhythmia Agents	KCNH2
IDARUBICIN	Antineoplastic Agents	TOP2A
IFOSFAMIDE	Antineoplastic Agents	DNMT1
IMIPRAMINE	Antidepressive Agents, Tricyclic	SLC6A2
IMIPRAMINE	Antidepressive Agents, Tricyclic	SLC6A4
INDAPAMIDE	Antihypertensive Agents; Diuretics	KCNE1
INDAPAMIDE	Antihypertensive Agents; Diuretics	KCNQ1
INDECAINIDE	Anti-Arrhythmia Agents	SCN5A
ISOCARBOXAZID	Antidepressive Agents	MAOA
ISOCARBOXAZID	Antidepressive Agents	MAOB
ISOETHARINE	Bronchodilator Agents	ADRB1

Drug Name	Indication(s)	Gene
ISOFLURANE	Anesthetics, Inhalation	ATP2C1
ISOFLURANE	Anesthetics, Inhalation	GABRA1
ISOFLURANE	Anesthetics, Inhalation	GLRA1
ISOFLURANE	Anesthetics, Inhalation	GRIA1
ISOFLURANE	Anesthetics, Inhalation	KCNA1
ISOFLUROPHATE	Antiglaucomic Agents	BCHE
ISOPROTERENOL	Bronchodilator Agents; Cardiotonic Agents	ADRB1
ISOPROTERENOL	Bronchodilator Agents; Cardiotonic Agents	ADRB2
ISOSORBIDE-5-MONONITRATE	Antianginal Agents; Vasodilator Agents	NPR1
ISRADIPINE	Antihypertensive Agents; Vasodilator Agents	CACNA1C
ISRADIPINE	Antihypertensive Agents; Vasodilator Agents	CACNA2D1
LABETALOL	Antihypertensive Agents	ADRA1A
LABETALOL	Antihypertensive Agents	ADRA1B
LABETALOL	Antihypertensive Agents	ADRB1
LABETALOL	Antihypertensive Agents	ADRB2
LEFLUNOMIDE	Antirheumatic Agents	DHODH
LEVALLORPHAN	Opiate Antagonists	OPRM1
LEVOBUNOLOL	Antiglaucomic Agents	ADRB1
LEVOBUNOLOL	Antiglaucomic Agents	ADRB2
LEVOBUPIVACAINE	Anesthetics, Local	SCN10A
LEVOCABASTINE	Anti-Allergic Agents	HRH1
LEVOMETHADYL ACETATE	Analgesics, Opioid	OPRM1
LEVORPHANOL	Analgesics, Opioid	OPRM1

Drug Name	Indication(s)	Gene
LIOTHYRONINE	Hormone Replacement Agents	THRA
LIOTHYRONINE	Hormone Replacement Agents	THRB
LISDEXAMFETAMINE	Central Nervous System Stimulants	ADRA1A
LISDEXAMFETAMINE	Central Nervous System Stimulants	ADRA1B
LISDEXAMFETAMINE	Central Nervous System Stimulants	SLC6A3
LISURIDE	Antiparkinson Agents	DRD1
LISURIDE	Antiparkinson Agents	DRD2
LISURIDE	Antiparkinson Agents	HTR1A
LOPERAMIDE	Antidiarrheals	OPRM1
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	BZRP
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRA1
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRA2
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRA3
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRA4
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRA5

Drug Name	Indication(s)	Gene
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRA6
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRB1
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRB2
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRB3
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRD
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRE
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRG1
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRG2
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRG3

Drug Name	Indication(s)	Gene
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRP
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRQ
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRR1
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRR2
LORAZEPAM	Anti-anxiety Agents; Anticonvulsants; Hypnotics and Sedatives	GABRR3
LOSARTAN	Antihypertensive Agents	AGTR1
MAPROTILINE	Antidepressive Agents, Second-Generation	SLC6A2
MARIMASTAT	Antineoplastic Agents	MMP2
MARIMASTAT	Antineoplastic Agents	MMP3
MARIMASTAT	Antineoplastic Agents	MMP9
MARINOL	Antiemetics	CNR1
MECLIZINE	Antiemetics	HRH1
MECLOFENAMIC ACID	NSAID	ALOX5
MECLOFENAMIC ACID	NSAID	PTGS1
MECLOFENAMIC ACID	NSAID	PTGS2
MEDRYSONE	Anti-Inflammatory Agents, Topical	NR3C1
MEFENAMIC ACID	NSAID	PTGS1

Drug Name	Indication(s)	Gene
MEFENAMIC ACID	NSAID	PTGS2
MEGESTROL	Antineoplastic Agents, Hormonal; Contraceptives	ESR1
MEGESTROL	Antineoplastic Agents, Hormonal; Contraceptives	PGR
MELATONIN	Hypnotics and Sedatives	MTNR1A
MELATONIN	Hypnotics and Sedatives	MTNR1B
MELOXICAM	NSAID	PTGS2
MENTHOL	Antipruritics	TRPA1
MENTHOL	Antipruritics	TRPM8
MENTHOL	Antipruritics	TRPV3
MEPENZOLATE	Antispasmodics	GPR109A
MEPENZOLATE	Antispasmodics	GPR109B
MEPERIDINE	Analgesics, Opioid	OPRK1
MEPHENTERMINE	Antihypotensive Agents; Vasoconstrictor Agents	ADRA1A
MEPHENYTOIN	Anticonvulsants	SCN5A
MEPROBAMATE	Anticonvulsants; Hypnotics and Sedatives	GABRA1
MEPROBAMATE	Anticonvulsants; Hypnotics and Sedatives	GABRA2
MEPROBAMATE	Anticonvulsants; Hypnotics and Sedatives	GABRA3
MEPROBAMATE	Anticonvulsants; Hypnotics and Sedatives	GABRA4
MEPROBAMATE	Anticonvulsants; Hypnotics and Sedatives	GABRA5

Drug Name	Indication(s)	Gene
MEPROBAMATE	Anticonvulsants; Hypnotics and Sedatives	GABRA6
MEQUITAZINE	Anti-Allergic Agents	HRH1
MERCAPTOPURINE	Antineoplastic Agents	HPRT1
MESORIDAZINE	Antipsychotic Agents	DRD2
MESORIDAZINE	Antipsychotic Agents	HTR2A
MESTRANOL	Contraceptives, Oral	ESR1
METARAMINOL	Antihypotensive Agents; Vasoconstrictor Agents	ADRA1A
METHADONE	Analgesics, Opioid; Antitussive Agents	OPRM1
METHADYL ACETATE	Analgesics, Opioid	OPRM1
METHANTHELINE	GI Anti-Ulcer Agents, anticholinergic; Antispasmodics	CHRM1
METHARBITAL	Anticonvulsants	CHRNA4
METHARBITAL	Anticonvulsants	CHRNA7
METHARBITAL	Anticonvulsants	GABRA1
METHARBITAL	Anticonvulsants	GABRA2
METHARBITAL	Anticonvulsants	GABRA3
METHARBITAL	Anticonvulsants	GABRA4
METHARBITAL	Anticonvulsants	GABRA5
METHARBITAL	Anticonvulsants	GABRA6
METHARBITAL	Anticonvulsants	GRIA2
METHARBITAL	Anticonvulsants	GRIK2
METHAZOLAMIDE	Antihypertensive Agents, Diuretics; Antiglaucoma agents	CA1
METHDILAZINE	Anti-Allergic Agents	HRH1
METHIMAZOLE	Antithyroid Agents	TPO

Drug Name	Indication(s)	Gene
METHOHEXITAL	Anesthetics, Intravenous	GABRA1
METHOTRIMEPRAZINE	Antipsychotic Agents	ADRA1A
METHOTRIMEPRAZINE	Antipsychotic Agents	ADRA1B
METHOTRIMEPRAZINE	Antipsychotic Agents	ADRA1D
METHOTRIMEPRAZINE	Antipsychotic Agents	CHRM1
METHOTRIMEPRAZINE	Antipsychotic Agents	CHRM2
METHOTRIMEPRAZINE	Antipsychotic Agents	CHRM3
METHOTRIMEPRAZINE	Antipsychotic Agents	CHRM4
METHOTRIMEPRAZINE	Antipsychotic Agents	CHRM5
METHOTRIMEPRAZINE	Antipsychotic Agents	DRD3
METHOTRIMEPRAZINE	Antipsychotic Agents	HRH1
METHOTRIMEPRAZINE	Antipsychotic Agents	HTR2B
METHOXAMINE	Antihypotensive Agents; Vasoconstrictor Agents	ADRA1A
METHOXAMINE	Antihypotensive Agents; Vasoconstrictor Agents	ADRA1B
METHOXYFLURANE	Anesthetics, Inhalation	ATP5D
METHYCLOTHIAZIDE	Antihypertensive Agents; Diuretics	SLC12A1
METHYLDOPA	Antihypertensive Agents	ADRA2A
METHYLERGONOVINE	Abortifacient Agents	DRD1
METHYLNALTREXONE BROMIDE	OIC treatment	OPRM1
METHYLPHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	CHRNA4
METHYLPHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	CHRNA7
METHYLPHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GABRA1

Drug Name	Indication(s)	Gene
METHYLPHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GABRA2
METHYLPHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GABRA3
METHYLPHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GABRA4
METHYLPHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GABRA5
METHYLPHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GABRA6
METHYLPHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GRIA2
METHYLPHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GRIK2
METHYLPREDNISOLONE	Anti-Inflammatory Agents; Glucocorticoids	NR3C1
METHYLPREDNISOLONE	Anti-Inflammatory Agents; Glucocorticoids	NR3C1
METHYLSCOPOLAMINE	Antispasmodics	CHRM1
METHYPRYLON	Hypnotics and Sedatives	GABRA1
METHYSERGIDE	Anti-migraine agents; Vasoconstrictor Agents	HTR1A
METHYSERGIDE	Anti-migraine agents; Vasoconstrictor Agents	HTR2A
METHYSERGIDE	Anti-migraine agents; Vasoconstrictor Agents	HTR2C
METHYSERGIDE	Anti-migraine agents; Vasoconstrictor Agents	HTR7

Drug Name	Indication(s)	Gene
METIPRANOLOL	Anti-Arrhythmia Agents; Antihypertensive Agents; Anti-glaucoma agent	ADRB1
METIPRANOLOL	Anti-Arrhythmia Agents; Antihypertensive Agents; Anti-glaucoma agent	ADRB2
METIXENE	Antiparkinson Agents	CHRM1
METIXENE	Antiparkinson Agents	CHRM2
METIXENE	Antiparkinson Agents	CHRM3
METIXENE	Antiparkinson Agents	CHRM4
METIXENE	Antiparkinson Agents	CHRM5
METOCURINE	Muscle Relaxants	CHRNA2
METOCURINE IODIDE	Muscle Relaxants	CHRNA2
METOLAZONE	Antihypertensive Agents; Diuretics	SLC12A1
METOLAZONE	Antihypertensive Agents; Diuretics	SLC12A3
METOPROLOL	Anti-Arrhythmia Agents; Antihypertensive Agents	ADRB1
METYRAPONE	Diagnostic Agents	CYP11B1
METYROSINE	Catecholamine synthesis inhibitors	TH
MEXILETINE	Anti-Arrhythmia Agents	SCN5A
MIANSERIN	Antidepressive Agents, Second-Generation	ADRA2A
MIANSERIN	Antidepressive Agents, Second-Generation	HRH1
MIANSERIN	Antidepressive Agents, Second-Generation	HTR2A
MIANSERIN	Antidepressive Agents, Second-Generation	HTR2C

Drug Name	Indication(s)	Gene
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRA1
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRA2
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRA3
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRA4
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRA5
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRA6
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRB1
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRB2
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRB3
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRD
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRE
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRG1
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRG2
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRG3

Drug Name	Indication(s)	Gene
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRP
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRQ
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRR1
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRR2
MIDAZOLAM	Adjuvants, Anesthesia; Hypnotics and Sedatives	GABRR3
MIDODRINE	Antihypotensive Agents; Vasoconstrictor Agents	ADRA1A
MIDODRINE	Antihypotensive Agents; Vasoconstrictor Agents	ADRA1B
MIGLITOL	Hypoglycemic Agents	MGAM
MILRINONE	Cardiotonic Agents; Vasodilator Agents	PDE3A
MILRINONE	Cardiotonic Agents; Vasodilator Agents	PDE4A
MINAPRINE	Antidepressive Agents	DRD1
MINAPRINE	Antidepressive Agents	DRD2
MINAPRINE	Antidepressive Agents	HTR2A
MINAPRINE	Antidepressive Agents	HTR2B
MINAPRINE	Antidepressive Agents	HTR2C
MINAPRINE	Antidepressive Agents	SLC6A4
MINOXIDIL	Antihypertensive Agents; Vasodilator Agents	KCNJ1
MIVACURIUM	Muscle Relaxants	CHRM2

Drug Name	Indication(s)	Gene
MIVACURIUM	Muscle Relaxants	CHRNA2
MOEXIPRIL	Antihypertensive Agents	ACE
MOLINDONE	Antipsychotic Agents	DRD2
MORICIZINE	Anti-Arrhythmia Agents	SCN5A
NABUMETONE	Anti-Inflammatory Agents, Non-Steroidal	PTGS1
NABUMETONE	Anti-Inflammatory Agents, Non-Steroidal	PTGS2
NADOLOL	Anti-Arrhythmia Agents; Antihypertensive Agents	ADRB1
NADOLOL	Anti-Arrhythmia Agents; Antihypertensive Agents	ADRB2
NAFARELIN	Antiendometriosis Agent	GNRHR
NAFARELIN	Antiendometriosis Agent	GNRHR2
NANDROLONE	Antianemic Agents; anti-osteoporosis agents	AR
NEDOCROMIL	Anti-Allergic Agents; Anti-Asthmatic Agents	CYSLTR1
NEFAZODONE	Antidepressive Agents, Second-Generation	ADRA1A
NEFAZODONE	Antidepressive Agents, Second-Generation	ADRA1B
NEFAZODONE	Antidepressive Agents, Second-Generation	HTR2A
NEFAZODONE	Antidepressive Agents, Second-Generation	SLC6A2
NEFAZODONE	Antidepressive Agents, Second-Generation	SLC6A4

Drug Name	Indication(s)	Gene
NEOSTIGMINE	Parasympathomimetics	ACHE
NEPAFENAC	NSAID	PTGS1
NEPAFENAC	NSAID	PTGS2
NICARDIPINE	Anti-Arrhythmia Agents; Antihypertensive Agents	CACNA1C
NICERGOLINE	Nootropic Agents; Vasodilator Agents	ADRA1A
NICOTINE	Central Nervous System Stimulants	CHRNA10
NICOTINE	Central Nervous System Stimulants	CHRNA2
NICOTINE	Central Nervous System Stimulants	CHRNA4
NICOTINE	Central Nervous System Stimulants	CHRNA7
NICOTINE	Central Nervous System Stimulants	CHRNA9
NICOTINE	Central Nervous System Stimulants	CHRNB2
NIFEDIPINE	Antianginal Agents; Vasodilator Agents	CACNA2D1
NIFLUMIC ACID	NSAID	PLA2G1B
NIFLUMIC ACID	NSAID	PTGS2
NILUTAMIDE	Antineoplastic Agents	AR
NIMODIPINE	Antihypertensive Agents; Vasodilator Agents	CACNG1
NISOLDIPINE	Antihypertensive Agents; Vasodilator Agents	CACNA1A
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRA1
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRA2
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRA3

Drug Name	Indication(s)	Gene
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRA4
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRA5
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRA6
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRB1
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRB2
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRB3
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRD
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRE
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRG1
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRG2
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRG3
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRP
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRQ
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRR1

Drug Name	Indication(s)	Gene
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRR2
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	GABRR3
NITRAZEPAM	Anticonvulsants; Hypnotics and Sedatives	SCN1A
NITRENDIPINE	Antihypertensive Agents; Vasodilator Agents	CACNG1
NITROPRUSSIDE	Antihypertensive Agents; Vasodilator Agents	NPR1
NIZATIDINE	GI Anti-Ulcer Agents, antihistamines	HRH2
NOREPINEPHRINE	Antihypotensive Agents; Vasoconstrictor Agents	ADRA1A
NOREPINEPHRINE	Antihypotensive Agents; Vasoconstrictor Agents	ADRA1B
NOREPINEPHRINE	Antihypotensive Agents; Vasoconstrictor Agents	ADRA1D
NOREPINEPHRINE	Antihypotensive Agents; Vasoconstrictor Agents	ADRA2A
NOREPINEPHRINE	Antihypotensive Agents; Vasoconstrictor Agents	ADRA2B
NOREPINEPHRINE	Antihypotensive Agents; Vasoconstrictor Agents	ADRA2C
NORETHINDRONE	Contraceptives, Oral, Synthetic	PGR
NORGESTIMATE	Contraceptives, Oral, Synthetic	ESR1
NORGESTIMATE	Contraceptives, Oral, Synthetic	PGR
NORGESTREL	Contraceptives, Oral, Synthetic	ESR1

Drug Name	Indication(s)	Gene
NORGESTREL	Contraceptives, Oral, Synthetic	PGR
ORCIPRENALINE	Bronchodilator Agents	ADRB2
ORPHENADRINE	Antiparkinson Agents; Muscle Relaxants, Central	GRIN1
ORPHENADRINE	Antiparkinson Agents; Muscle Relaxants, Central	GRIN2D
ORPHENADRINE	Antiparkinson Agents; Muscle Relaxants, Central	GRIN3A
ORPHENADRINE	Antiparkinson Agents; Muscle Relaxants, Central	GRIN3B
ORPHENADRINE	Antiparkinson Agents; Muscle Relaxants, Central	HRH1
OUABAIN	Cardiotonic Agents	ATP1A1
OXAPROZIN	NSAID	PTGS2
OXAZEPAM	Hypnotics and Sedatives	GABRA1
OXAZEPAM	Hypnotics and Sedatives	GABRA2
OXAZEPAM	Hypnotics and Sedatives	GABRA3
OXAZEPAM	Hypnotics and Sedatives	GABRA4
OXAZEPAM	Hypnotics and Sedatives	GABRA5
OXAZEPAM	Hypnotics and Sedatives	GABRA6
OXAZEPAM	Hypnotics and Sedatives	GABRB1
OXAZEPAM	Hypnotics and Sedatives	GABRB2
OXAZEPAM	Hypnotics and Sedatives	GABRB3
OXAZEPAM	Hypnotics and Sedatives	GABRD
OXAZEPAM	Hypnotics and Sedatives	GABRE
OXAZEPAM	Hypnotics and Sedatives	GABRG1
OXAZEPAM	Hypnotics and Sedatives	GABRG2
OXAZEPAM	Hypnotics and Sedatives	GABRG3

Drug Name	Indication(s)	Gene
OXAZEPAM	Hypnotics and Sedatives	GABRP
OXAZEPAM	Hypnotics and Sedatives	GABRQ
OXAZEPAM	Hypnotics and Sedatives	GABRR1
OXAZEPAM	Hypnotics and Sedatives	GABRR2
OXAZEPAM	Hypnotics and Sedatives	GABRR3
OXPRENOLOL	Antihypertensive Agents; Anti-Arrhythmia Agents	ADRB1
OXPRENOLOL	Antihypertensive Agents; Anti-Arrhythmia Agents	ADRB2
OXYBUPROCAINE	Anesthetics, Local	SCN10A
OXYPHENCYCLIMINE	GI Anti-Ulcer Agents, anticholinergic; Antispasmodics	CHRM1
OXYPHENCYCLIMINE	GI Anti-Ulcer Agents, anticholinergic; Antispasmodics	CHRM2
OXYPHENCYCLIMINE	GI Anti-Ulcer Agents, anticholinergic; Antispasmodics	CHRM3
OXYPHENONIUM	Mydriatics	CHRM1
PAMIDRONATE	Bisphosphonates	FDPS
PANCURONIUM	Muscle Relaxants	CHRNA2
PAPAVERINE	Antispasmodics; Anti-impotence Agents; Vasodilator Agents	PDE4B
PARAMETHADIONE	Anticonvulsants	CACNA1I
PARAMETHASONE	Anti-Inflammatory Agents; Glucocorticoids	NR3C1
PEMETREXED	Antineoplastic Agents	DHFR
PEMETREXED	Antineoplastic Agents	GART
PEMETREXED	Antineoplastic Agents	TYMS
PEMIROLAST	Anti-Allergic Agents	HRH1

Drug Name	Indication(s)	Gene
PENBUTOLOL	Antihypertensive Agents	ADRB1
PENBUTOLOL	Antihypertensive Agents	ADRB2
PENTAGASTRIN	Diagnostic Agents	CCKBR
PENTAZOCINE	Analgesics, Opioid	OPRK1
PENTAZOCINE	Analgesics, Opioid	OPRM1
PENTOBARBITAL	Hypnotics and Sedatives	CHRNA4
PENTOBARBITAL	Hypnotics and Sedatives	CHRNA7
PENTOBARBITAL	Hypnotics and Sedatives	GABRA1
PENTOBARBITAL	Hypnotics and Sedatives	GABRA2
PENTOBARBITAL	Hypnotics and Sedatives	GABRA3
PENTOBARBITAL	Hypnotics and Sedatives	GABRA4
PENTOBARBITAL	Hypnotics and Sedatives	GABRA5
PENTOBARBITAL	Hypnotics and Sedatives	GABRA6
PENTOBARBITAL	Hypnotics and Sedatives	GRIA2
PENTOBARBITAL	Hypnotics and Sedatives	GRIK2
PENTOLINIUM	Antihypertensive Agents	CHRNA10
PERGOLIDE	Antiparkinson Agents	DRD1
PERGOLIDE	Antiparkinson Agents	DRD2
PERHEXILINE	Antianginal Agents; Vasodilator Agents	CPT1A
PERHEXILINE	Antianginal Agents; Vasodilator Agents	CPT2
PERINDOPRIL	Antihypertensive Agents	ACE
PERPHENAZINE	Antipsychotic Agents	DRD1
PERPHENAZINE	Antipsychotic Agents	DRD2
PHENACEMIDE	Anticonvulsants	SCN1A
PHENDIMETRAZINE	Appetite Depressants	ADRA1A
PHENDIMETRAZINE	Appetite Depressants	ADRA1B

Drug Name	Indication(s)	Gene
PHENELZINE	Antidepressive Agents	MAOA
PHENELZINE	Antidepressive Agents	MAOB
PHENFORMIN	Hypoglycemic Agents	PRKAA1
PHENINDIONE	Anticoagulants	VKORC1
PHENIRAMINE	Anti-Allergic Agents	HRH1
PHENMETRAZINE	Appetite Depressants	SLC6A2
PHENMETRAZINE	Appetite Depressants	SLC6A3
PHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	CHRNA4
PHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	CHRNA7
PHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GABRA1
PHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GABRA2
PHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GABRA3
PHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GABRA4
PHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GABRA5
PHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GABRA6
PHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GRIA1
PHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GRIA2

Drug Name	Indication(s)	Gene
PHENOBARBITAL	Anticonvulsants; Hypnotics and Sedatives	GRIK2
PHENOXYBENZAMINE	Anticonvulsants; Hypnotics and Sedatives	ADRA1A
PHENPROCOUMON	Anticoagulants	VKORC1
PHENTERMINE	Appetite Depressants	SLC6A2
PHENTERMINE	Appetite Depressants	SLC6A3
PHENTERMINE	Appetite Depressants	SLC6A4
PHENTOLAMINE	Antihypertensive Agents	ADRA2A
PHENYLBUTAZONE	NSAID	PTGIS
PHENYLBUTAZONE	NSAID	PTGS2
PHENYLPROPANOLAMINE	Appetite Depressants; Nasal Decongestants	ADRA1A
PHENYLPROPANOLAMINE	Appetite Depressants; Nasal Decongestants	ADRA2A
PHENYTOIN	Anticonvulsants	SCN1A
PHENYTOIN	Anticonvulsants	SCN5A
PHYTONADIONE	Antifibrinolytic Agents	GGCX
PICROTOXIN	Central Nervous System Stimulants; Convulsants	GABRA1
PICROTOXIN	Central Nervous System Stimulants; Convulsants	GABRR1
PIMOZIDE	Antidyskinetics; Antipsychotic Agents	DRD2
PINDOLOL	Antihypertensive Agents	ADRB1
PINDOLOL	Antihypertensive Agents	ADRB2
PIPECURONIUM	Muscle Relaxants	CHRNA2

Drug Name	Indication(s)	Gene
PIRENZEPINE	GI Anti-Ulcer Agents, anticholinergic; Antispasmodics	CHRM1
PODOFILOX	Antineoplastic Agents, Phytogenic; Keratolytic Agents	TOP2A
POLYTHIAZIDE	Antihypertensive Agents; Diuretics	SLC12A3
PRACTOLOL	Anti-Arrhythmia Agents	ADRB1
PRALATREXATE	Antineoplastic Agents	DHFR
PRANLUKAST	Anti-Asthmatic Agents	CYSLTR1
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRA1
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRA2
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRA3
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRA5
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRB1
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRB2
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRB3
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRD
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRE
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRG1

Drug Name	Indication(s)	Gene
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRG2
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRG3
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRP
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRR1
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRR2
PRAZEPAM	Anti-anxiety Agents; Hypnotics and Sedatives	GABRR3
PRAZOSIN	Antihypertensive Agents; antispasmodics	ADRA1A
PRAZOSIN	Antihypertensive Agents; antispasmodics	ADRA1B
PRAZOSIN	Antihypertensive Agents; antispasmodics	ADRA1D
PREDNICARBATE	Anti-Inflammatory Agents; Corticosteroids	NR3C1
PRIMIDONE	Anticonvulsants	CHRNA4
PRIMIDONE	Anticonvulsants	CHRNA7
PRIMIDONE	Anticonvulsants	GABRA1
PRIMIDONE	Anticonvulsants	GABRA2
PRIMIDONE	Anticonvulsants	GABRA3
PRIMIDONE	Anticonvulsants	GABRA4
PRIMIDONE	Anticonvulsants	GABRA5
PRIMIDONE	Anticonvulsants	GABRA6

Drug Name	Indication(s)	Gene
PRIMIDONE	Anticonvulsants	GRIA2
PRIMIDONE	Anticonvulsants	GRIK2
PROBENECID	Uricosuric Agents	SLC22A11
PROBENECID	Uricosuric Agents	SLC22A8
PROCAINAMIDE	Anti-Arrhythmia Agents	SCN5A
PROCAINE	Anesthetics, Local	SCN10A
PROCATEROL	Bronchodilator Agents	ADRB2
PROCYCLIDINE	Antidyskinetics; Antiparkinson Agents	CHRM1
PROCYCLIDINE	Antidyskinetics; Antiparkinson Agents	CHRM2
PROCYCLIDINE	Antidyskinetics; Antiparkinson Agents	CHRM4
PROGABIDE	Anticonvulsants	GABBR1
PROGABIDE	Anticonvulsants	GABRA1
PROMAZINE	Antiemetics; Antipsychotic Agents	ADRA1A
PROMAZINE	Antiemetics; Antipsychotic Agents	ADRA1B
PROMAZINE	Antiemetics; Antipsychotic Agents	ADRA1D
PROMAZINE	Antiemetics; Antipsychotic Agents	CHRM1
PROMAZINE	Antiemetics; Antipsychotic Agents	CHRM2
PROMAZINE	Antiemetics; Antipsychotic Agents	CHRM3
PROMAZINE	Antiemetics; Antipsychotic Agents	CHRM4
PROMAZINE	Antiemetics; Antipsychotic Agents	CHRM5
PROMAZINE	Antiemetics; Antipsychotic Agents	DRD1
PROMAZINE	Antiemetics; Antipsychotic Agents	DRD2
PROMAZINE	Antiemetics; Antipsychotic Agents	DRD4
PROMAZINE	Antiemetics; Antipsychotic Agents	HRH1
PROMAZINE	Antiemetics; Antipsychotic Agents	HTR2A

Drug Name	Indication(s)	Gene
PROMAZINE	Antiemetics; Antipsychotic Agents	HTR2C
PROMETHAZINE	Hypnotics and Sedatives; Anti-anxiety agents; Anti-allergic Agents	CHRM1
PROMETHAZINE	Hypnotics and Sedatives; Anti-anxiety agents; Anti-allergic Agents	CHRM2
PROMETHAZINE	Hypnotics and Sedatives; Anti-anxiety agents; Anti-allergic Agents	CHRM3
PROMETHAZINE	Hypnotics and Sedatives; Anti-anxiety agents; Anti-allergic Agents	CHRM4
PROMETHAZINE	Hypnotics and Sedatives; Anti-anxiety agents; Anti-allergic Agents	CHRM5
PROMETHAZINE	Hypnotics and Sedatives; Anti-anxiety agents; Anti-allergic Agents	HRH1
PROPANTHELINE	GI Anti-Ulcer Agents, anticholinergic; Antispasmodics	CHRM1
PROPARACAINE	Anesthetics, Local	SCN10A
PROPERICIAZINE	Antipsychotic Agents	ADRA1A
PROPERICIAZINE	Antipsychotic Agents	ADRA1B
PROPERICIAZINE	Antipsychotic Agents	ADRA1D
PROPIOMAZINE	Hypnotics and Sedatives	ADRA1A
PROPIOMAZINE	Hypnotics and Sedatives	ADRA1B
PROPIOMAZINE	Hypnotics and Sedatives	ADRA1D
PROPIOMAZINE	Hypnotics and Sedatives	CHRM1
PROPIOMAZINE	Hypnotics and Sedatives	CHRM2
PROPIOMAZINE	Hypnotics and Sedatives	CHRM3
PROPIOMAZINE	Hypnotics and Sedatives	CHRM4
PROPIOMAZINE	Hypnotics and Sedatives	CHRM5
PROPIOMAZINE	Hypnotics and Sedatives	DRD1

Drug Name	Indication(s)	Gene
PROPIOMAZINE	Hypnotics and Sedatives	DRD2
PROPIOMAZINE	Hypnotics and Sedatives	DRD4
PROPIOMAZINE	Hypnotics and Sedatives	HRH1
PROPIOMAZINE	Hypnotics and Sedatives	HTR2A
PROPIOMAZINE	Hypnotics and Sedatives	HTR2C
PROPOXYPHENE	Analgesics, Opioid; Antitussive Agents	OPRD1
PROPOXYPHENE	Analgesics, Opioid; Antitussive Agents	OPRK1
PROPOXYPHENE	Analgesics, Opioid; Antitussive Agents	OPRM1
PROPYLTHIOURACIL	Antithyroid Agents	TPO
PROTRIPTYLINE	Antidepressive Agents, Tricyclic	SLC6A2
PROTRIPTYLINE	Antidepressive Agents, Tricyclic	SLC6A4
PYRIDOSTIGMINE	Antimyasthenics	ACHE
QUAZEPAM	Hypnotics and Sedatives	GABRA1
QUAZEPAM	Hypnotics and Sedatives	GABRA2
QUAZEPAM	Hypnotics and Sedatives	GABRA3
QUAZEPAM	Hypnotics and Sedatives	GABRA5
QUAZEPAM	Hypnotics and Sedatives	GABRB1
QUAZEPAM	Hypnotics and Sedatives	GABRB3
QUAZEPAM	Hypnotics and Sedatives	GABRD
QUAZEPAM	Hypnotics and Sedatives	GABRE
QUAZEPAM	Hypnotics and Sedatives	GABRG1
QUAZEPAM	Hypnotics and Sedatives	GABRG2
QUAZEPAM	Hypnotics and Sedatives	GABRG3
QUAZEPAM	Hypnotics and Sedatives	GABRP
QUAZEPAM	Hypnotics and Sedatives	GABRR1

Drug Name	Indication(s)	Gene
QUAZEPAM	Hypnotics and Sedatives	GABRR2
QUAZEPAM	Hypnotics and Sedatives	GABRR3
QUINESTROL	Hormone Replacement Agents	ESR1
QUINETHAZONE	Antihypertensive Agents; Diuretics	SLC12A3
QUINIDINE	Anti-Arrhythmia Agents	SCN5A
RALOXIFENE	Hormone Replacement Agents	ESR1
RALOXIFENE	Hormone Replacement Agents	ESR2
RAMIPRIL	Antihypertensive Agents	ACE
REMIKIREN	Antihypertensive Agents	REN
REMOXIPRIDE	Antipsychotic Agents	DRD2
RESCINNAMINE	Antihypertensive Agents	ACE
RESERPINE	Antihypertensive Agents; Antipsychotic Agents	SLC18A2
RIMEXOLONE	Anti-Inflammatory Agents; Corticosteroids	NR3C1
RIMEXOLONE	Anti-Inflammatory Agents; Corticosteroids	NR3C1
RISEDRONATE	Bisphosphonates	FDPS
RISPERIDONE	Antipsychotic Agents	DRD2
RISPERIDONE	Antipsychotic Agents	HTR2A
RITODRINE	Tocolytic Agents	ADRB2
RIZATRIPTAN	Anti-migraine Agents	HTR1B
RIZATRIPTAN	Anti-migraine Agents	HTR1D
SALICYLIC ACID	Keratolytic Agents	PTGS1
SALICYLIC ACID	Keratolytic Agents	PTGS2
SALSALATE	Anti-Inflammatory Agents, Non-Steroidal	PTGS1

Drug Name	Indication(s)	Gene
SALSALATE	Anti-Inflammatory Agents, Non-Steroidal	PTGS2
SAPRISARTAN	Antihypertensive Agents	AGTR1
SAPROPTERIN	PKU-treatment	PAH
SCOPOLAMINE	Adjuvants, Anesthesia; Antispasmodics; Mydriatics	CHRM1
SECOBARBITAL	Adjuvants, anesthesia; Hypnotics and Sedatives	CHRNA4
SECOBARBITAL	Adjuvants, anesthesia; Hypnotics and Sedatives	CHRNA7
SECOBARBITAL	Adjuvants, anesthesia; Hypnotics and Sedatives	GABRA1
SECOBARBITAL	Adjuvants, anesthesia; Hypnotics and Sedatives	GABRA2
SECOBARBITAL	Adjuvants, anesthesia; Hypnotics and Sedatives	GABRA3
SECOBARBITAL	Adjuvants, anesthesia; Hypnotics and Sedatives	GABRA4
SECOBARBITAL	Adjuvants, anesthesia; Hypnotics and Sedatives	GABRA5
SECOBARBITAL	Adjuvants, anesthesia; Hypnotics and Sedatives	GABRA6
SECOBARBITAL	Adjuvants, anesthesia; Hypnotics and Sedatives	GRIA2
SECOBARBITAL	Adjuvants, anesthesia; Hypnotics and Sedatives	GRIK2
SEVOFLURANE	Anesthetics, Inhalation	ATP2C1
SEVOFLURANE	Anesthetics, Inhalation	ATP5D

Drug Name	Indication(s)	Gene
SEVOFLURANE	Anesthetics, Inhalation	GABRA1
SEVOFLURANE	Anesthetics, Inhalation	GLRA1
SEVOFLURANE	Anesthetics, Inhalation	GRIA1
SEVOFLURANE	Anesthetics, Inhalation	KCNA1
SEVOFLURANE	Anesthetics, Inhalation	MT-ND1
SODIUM TETRADECYL SULFATE	Sclerosing Agents	PROC
SOTALOL	Anti-Arrhythmia Agents	KCNH2
SPIRAPRIL	Antihypertensive Agents	ACE
SUCCINYLCHOLINE	Muscle Relaxants, Skeletal	CHRM1
SULFINPYRAZONE	Uricosuric Agents	ABCC1
SULFINPYRAZONE	Uricosuric Agents	ABCC2
SULINDAC	NSAID	PTGS1
SULINDAC	NSAID	PTGS2
SULPIRIDE	Antidepressive Agents, Second-Generation; Antipsychotic Agents	DRD2
SUPROFEN	NSAID	PTGS1
SUPROFEN	NSAID	PTGS2
TACRINE	Nootropic Agents	ACHE
TALBUTAL	Analgesics	CHRNA4
TALBUTAL	Analgesics	CHRNA7
TALBUTAL	Analgesics	GABRA1
TALBUTAL	Analgesics	GABRA2
TALBUTAL	Analgesics	GABRA3
TALBUTAL	Analgesics	GABRA4
TALBUTAL	Analgesics	GABRA5
TALBUTAL	Analgesics	GABRA6
TALBUTAL	Analgesics	GRIA2

Drug Name	Indication(s)	Gene
TALBUTAL	Analgesics	GRIK2
TAMOXIFEN	Antineoplastic Agents, Hormonal	ESR1
TAMOXIFEN	Antineoplastic Agents, Hormonal	ESR2
TASOSARTAN	Antihypertensive Agents	AGTR1
TEMAZEPAM	Hypnotics and Sedatives	BZRP
TEMAZEPAM	Hypnotics and Sedatives	GABRA1
TEMAZEPAM	Hypnotics and Sedatives	GABRA2
TEMAZEPAM	Hypnotics and Sedatives	GABRA3
TEMAZEPAM	Hypnotics and Sedatives	GABRA4
TEMAZEPAM	Hypnotics and Sedatives	GABRA5
TEMAZEPAM	Hypnotics and Sedatives	GABRA6
TEMAZEPAM	Hypnotics and Sedatives	GABRB1
TEMAZEPAM	Hypnotics and Sedatives	GABRB2
TEMAZEPAM	Hypnotics and Sedatives	GABRB3
TEMAZEPAM	Hypnotics and Sedatives	GABRD
TEMAZEPAM	Hypnotics and Sedatives	GABRE
TEMAZEPAM	Hypnotics and Sedatives	GABRG1
TEMAZEPAM	Hypnotics and Sedatives	GABRG2
TEMAZEPAM	Hypnotics and Sedatives	GABRG3
TEMAZEPAM	Hypnotics and Sedatives	GABRP
TEMAZEPAM	Hypnotics and Sedatives	GABRQ
TEMAZEPAM	Hypnotics and Sedatives	GABRR1
TEMAZEPAM	Hypnotics and Sedatives	GABRR2
TEMAZEPAM	Hypnotics and Sedatives	GABRR3
TENIPOSIDE	Antineoplastic Agents	TOP2A
TENOXICAM	NSAID	PTGS1
TENOXICAM	NSAID	PTGS2

Drug Name	Indication(s)	Gene
TERAZOSIN	Antineoplastic Agents; antihypertensive agents	ADRA1A
TERAZOSIN	Antineoplastic Agents; antihypertensive agents	ADRA1B
TERAZOSIN	Antineoplastic Agents; antihypertensive agents	ADRA1D
TERBUTALINE	Bronchodilator Agents; Tocolytic Agents	ADRB2
TERFENADINE	Anti-Allergic Agents	HRH1
TESTOLACTONE	Antineoplastic Agents, Hormonal	CYP19A1
THIAMYLAL	Anesthetics, Intravenous	GABRA1
THIAMYLAL	Anesthetics, Intravenous	KCNJ11
THIAMYLAL	Anesthetics, Intravenous	KCNJ8
THIETHYLPERAZINE	Antiemetics	CHRM1
THIETHYLPERAZINE	Antiemetics	CHRM2
THIETHYLPERAZINE	Antiemetics	CHRM3
THIETHYLPERAZINE	Antiemetics	CHRM4
THIETHYLPERAZINE	Antiemetics	CHRM5
THIETHYLPERAZINE	Antiemetics	DRD1
THIETHYLPERAZINE	Antiemetics	DRD2
THIETHYLPERAZINE	Antiemetics	DRD4
THIETHYLPERAZINE	Antiemetics	HRH1
THIETHYLPERAZINE	Antiemetics	HTR2A
THIETHYLPERAZINE	Antiemetics	HTR2C
THIOPENTAL	Anesthetics, Intravenous	CHRNA4
THIOPENTAL	Anesthetics, Intravenous	CHRNA7
THIOPENTAL	Anesthetics, Intravenous	GABRA1
THIOPENTAL	Anesthetics, Intravenous	GABRA2

Drug Name	Indication(s)	Gene
THIOPENTAL	Anesthetics, Intravenous	GABRA3
THIOPENTAL	Anesthetics, Intravenous	GABRA4
THIOPENTAL	Anesthetics, Intravenous	GABRA5
THIOPENTAL	Anesthetics, Intravenous	GABRA6
THIOPENTAL	Anesthetics, Intravenous	GRIA2
THIOPENTAL	Anesthetics, Intravenous	GRIK2
THIORIDAZINE	Antipsychotic Agents	ADRA1A
THIORIDAZINE	Antipsychotic Agents	DRD1
THIORIDAZINE	Antipsychotic Agents	DRD2
THIORIDAZINE	Antipsychotic Agents	HTR2A
TIAGABINE	Anticonvulsants	ABAT
TIAGABINE	Anticonvulsants	SLC6A1
TIAPROFENIC ACID	NSAID	PTGS2
TICLOPIDINE	Platelet Aggregation Inhibitors	P2RY12
TILUDRONATE	Bisphosphonates	PTPN1
TIROFIBAN	Platelet Aggregation Inhibitors	ITGA2B
TIROFIBAN	Platelet Aggregation Inhibitors	ITGB3
TOCAINIDE	Anti-Arrhythmia Agents	SCN5A
TOLAZAMIDE	Hypoglycemic Agents	KCNJ1
TOLAZOLINE	Antihypertensive Agents	ADRA1A
TOLBUTAMIDE	Hypoglycemic Agents	KCNJ1
TOLCAPONE	Antiparkinson Agents	COMT
TOLMETIN	NSAID	PTGS1
TOLMETIN	NSAID	PTGS2
TOPIRAMATE	Anticonvulsants; anti-migraine agents	CA2
TOPIRAMATE	Anticonvulsants; anti-migraine agents	CA4

Drug Name	Indication(s)	Gene
TOPIRAMATE	Anticonvulsants; anti-migraine agents	GABRA1
TOPIRAMATE	Anticonvulsants; anti-migraine agents	GRIK1
TOPIRAMATE	Anticonvulsants; anti-migraine agents	SCN1A
TORASEMIDE	Antihypertensive Agents; Diuretics	SLC12A1
TRANYLCYPROMINE	Antidepressive Agents	MAOA
TRANYLCYPROMINE	Antidepressive Agents	MAOB
TREPROSTINIL	Antihypertensive Agents; Antithrombotic Agents	P2RY12
TREPROSTINIL	Antihypertensive Agents; Antithrombotic Agents	PPARG
TRIAMTERENE	Antihypertensive Agents; Diuretics	SCNN1A
TRIAMTERENE	Antihypertensive Agents; Diuretics	SCNN1B
TRIAMTERENE	Antihypertensive Agents; Diuretics	SCNN1D
TRIAMTERENE	Antihypertensive Agents; Diuretics	SCNN1G
TRICHLORMETHIAZIDE	Antihypertensive Agents; Diuretics	CA1
TRICHLORMETHIAZIDE	Antihypertensive Agents; Diuretics	CA2
TRICHLORMETHIAZIDE	Antihypertensive Agents; Diuretics	CA4
TRICHLORMETHIAZIDE	Antihypertensive Agents; Diuretics	KCNMA1
TRICHLORMETHIAZIDE	Antihypertensive Agents; Diuretics	SLC12A1
TRIDIHEXETHYL	GI Anti-Ulcer Agents, anticholinergic; Antispasmodics	CHRM1
TRIDIHEXETHYL	GI Anti-Ulcer Agents, anticholinergic; Antispasmodics	CHRM2
TRIDIHEXETHYL	GI Anti-Ulcer Agents, anticholinergic; Antispasmodics	CHRM3

Drug Name	Indication(s)	Gene
TRIFLUOPERAZINE	Antiemetics; Antipsychotic Agents	ADRA1A
TRIFLUOPERAZINE	Antiemetics; Antipsychotic Agents	DRD1IP
TRIFLUOPERAZINE	Antiemetics; Antipsychotic Agents	DRD2
TRIFLUPROMAZINE	Antiemetics; Antipsychotic Agents	CHRM1
TRIFLUPROMAZINE	Antiemetics; Antipsychotic Agents	CHRM2
TRIFLUPROMAZINE	Antiemetics; Antipsychotic Agents	DRD1
TRIFLUPROMAZINE	Antiemetics; Antipsychotic Agents	DRD2
TRIFLUPROMAZINE	Antiemetics; Antipsychotic Agents	HTR2B
TRIHEXYPHENIDYL	Antiparkinson Agents	CHRM1
TRILOSTANE	Antiadrenal	HSD3B1
TRILOSTANE	Antiadrenal	HSD3B2
TRIMEPRAZINE	Antipruritics	HRH1
TRIMETHADIONE	Anticonvulsants	CACNA1G
TRIMETHAPHAN	Antihypertensive Agents; Vasodilator Agents	CHRNA10
TRIMETREXATE	Antineoplastic Agents	DHFR
TRIMIPRAMINE	Antidepressive Agents, Tricyclic	SLC6A2
TRIMIPRAMINE	Antidepressive Agents, Tricyclic	SLC6A4
TRIPELENNAMINE	Anti-Allergic Agents	HRH1
TRIPROLIDINE	Anti-Allergic Agents	HRH1
TROPICAMIDE	Diagnostic Agents; Mydriatics	CHRM4
TUBOCURARINE	Muscle Relaxants, Skeletal	CHRNA2
VALPROIC ACID	Anticonvulsants	ABAT
VALRUBICIN	Antineoplastic Agents	TOP2A
WARFARIN	Anticoagulants	VKORC1
WARFARIN	Anticoagulants	VKORC1L1
VINBLASTINE	Antineoplastic Agents	TUBB2A
VINDESINE	Antineoplastic Agents	TUBB1

Drug Name	Indication(s)	Gene
XIMELAGATRAN	Anticoagulants	F2
YOHIMBINE	Mydriatics; Anti-impotence Agents	ADRA2A
YOHIMBINE	Mydriatics; Anti-impotence Agents	ADRA2B
YOHIMBINE	Mydriatics; Anti-impotence Agents	ADRA2C
ZOPICLONE	Hypnotics and Sedatives	BZRP
ZOPICLONE	Hypnotics and Sedatives	GABRA1
ZOPICLONE	Hypnotics and Sedatives	GABRA2
ZOPICLONE	Hypnotics and Sedatives	GABRA3
ZOPICLONE	Hypnotics and Sedatives	GABRA5
ZUCLOPENTHIXOL	Antipsychotic Agents	DRD1
ZUCLOPENTHIXOL	Antipsychotic Agents	DRD2
ZUCLOPENTHIXOL	Antipsychotic Agents	DRD5

5. Uses, Formulation and Administration

Pharmaceutically acceptable compositions

[00222] According to another embodiment, the invention provides a composition comprising a compound of this invention or a pharmaceutically acceptable derivative thereof and a pharmaceutically acceptable carrier, adjuvant, or vehicle. The amount of compound in compositions of this invention is such that is effective to measurably bind CRBN, or a mutant thereof, and a targeted protein, or a mutant thereof, in a biological sample or in a patient. In certain embodiments, a composition of this invention is formulated for administration to a patient in need of such composition. In some embodiments, a composition of this invention is formulated for oral administration to a patient.

[00223] The term "patient," as used herein, means an animal, preferably a mammal, and most preferably a human.

[00224] The term "pharmaceutically acceptable carrier, adjuvant, or vehicle" refers to a non-toxic carrier, adjuvant, or vehicle that does not destroy the pharmacological activity of the compound with which it is formulated. Pharmaceutically acceptable carriers, adjuvants or vehicles

that may be used in the compositions of this invention include, but are not limited to, ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances such as phosphates, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, water, salts or electrolytes, such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, zinc salts, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sodium carboxymethylcellulose, polyacrylates, waxes, polyethylene-polyoxypropylene-block polymers, polyethylene glycol and wool fat.

[00225] A "pharmaceutically acceptable derivative" means any non-toxic salt, ester, salt of an ester or other derivative of a compound of this invention that, upon administration to a recipient, is capable of providing, either directly or indirectly, a compound of this invention or an inhibitorily active metabolite or residue thereof.

[00226] As used herein, the term "active metabolite or residue thereof" means that a metabolite or residue thereof is also a binder of CRBN, or a mutant thereof, or a targeted protein, or a mutant thereof.

[00227] Compositions of the present invention may be administered orally, parenterally, by inhalation spray, topically, rectally, nasally, buccally, vaginally or via an implanted reservoir. The term "parenteral" as used herein includes subcutaneous, intravenous, intramuscular, intra-articular, intra-synovial, intrasternal, intrathecal, intrahepatic, intralesional and intracranial injection or infusion techniques. Preferably, the compositions are administered orally, intraperitoneally or intravenously. Sterile injectable forms of the compositions of this invention may be aqueous or oleaginous suspension. These suspensions may be formulated according to techniques known in the art using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally acceptable diluent or solvent, for example as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium.

[00228] For this purpose, any bland fixed oil may be employed including synthetic mono- or di-glycerides. Fatty acids, such as oleic acid and its glyceride derivatives are useful in the

preparation of injectables, as are natural pharmaceutically-acceptable oils, such as olive oil or castor oil, especially in their polyoxyethylated versions. These oil solutions or suspensions may also contain a long-chain alcohol diluent or dispersant, such as carboxymethyl cellulose or similar dispersing agents that are commonly used in the formulation of pharmaceutically acceptable dosage forms including emulsions and suspensions. Other commonly used surfactants, such as Tweens, Spans and other emulsifying agents or bioavailability enhancers which are commonly used in the manufacture of pharmaceutically acceptable solid, liquid, or other dosage forms may also be used for the purposes of formulation.

[00229] Pharmaceutically acceptable compositions of this invention may be orally administered in any orally acceptable dosage form including, but not limited to, capsules, tablets, aqueous suspensions or solutions. In the case of tablets for oral use, carriers commonly used include lactose and corn starch. Lubricating agents, such as magnesium stearate, are also typically added. For oral administration in a capsule form, useful diluents include lactose and dried cornstarch. When aqueous suspensions are required for oral use, the active ingredient is combined with emulsifying and suspending agents. If desired, certain sweetening, flavoring or coloring agents may also be added.

[00230] Alternatively, pharmaceutically acceptable compositions of this invention may be administered in the form of suppositories for rectal administration. These can be prepared by mixing the agent with a suitable non-irritating excipient that is solid at room temperature but liquid at rectal temperature and therefore will melt in the rectum to release the drug. Such materials include cocoa butter, beeswax and polyethylene glycols.

[00231] Pharmaceutically acceptable compositions of this invention may also be administered topically, especially when the target of treatment includes areas or organs readily accessible by topical application, including diseases of the eye, the skin, or the lower intestinal tract. Suitable topical formulations are readily prepared for each of these areas or organs.

[00232] Topical application for the lower intestinal tract can be effected in a rectal suppository formulation (see above) or in a suitable enema formulation. Topically-transdermal patches may also be used.

[00233] For topical applications, provided pharmaceutically acceptable compositions may be formulated in a suitable ointment containing the active component suspended or dissolved in one

or more carriers. Carriers for topical administration of compounds of this invention include, but are not limited to, mineral oil, liquid petrolatum, white petrolatum, propylene glycol, polyoxyethylene, polyoxypropylene compound, emulsifying wax and water. Alternatively, provided pharmaceutically acceptable compositions can be formulated in a suitable lotion or cream containing the active components suspended or dissolved in one or more pharmaceutically acceptable carriers. Suitable carriers include, but are not limited to, mineral oil, sorbitan monostearate, polysorbate 60, cetyl esters wax, cetearyl alcohol, 2-octyldodecanol, benzyl alcohol and water.

[00234] For ophthalmic use, provided pharmaceutically acceptable compositions may be formulated as micronized suspensions in isotonic, pH adjusted sterile saline, or, preferably, as solutions in isotonic, pH adjusted sterile saline, either with or without a preservative such as benzylalkonium chloride. Alternatively, for ophthalmic uses, the pharmaceutically acceptable compositions may be formulated in an ointment such as petrolatum.

[00235] Pharmaceutically acceptable compositions of this invention may also be administered by nasal aerosol or inhalation. Such compositions are prepared according to techniques well-known in the art of pharmaceutical formulation and may be prepared as solutions in saline, employing benzyl alcohol or other suitable preservatives, absorption promoters to enhance bioavailability, fluorocarbons, and/or other conventional solubilizing or dispersing agents.

[00236] Most preferably, pharmaceutically acceptable compositions of this invention are formulated for oral administration. Such formulations may be administered with or without food. In some embodiments, pharmaceutically acceptable compositions of this invention are administered without food. In other embodiments, pharmaceutically acceptable compositions of this invention are administered with food.

[00237] The amount of compounds of the present invention that may be combined with the carrier materials to produce a composition in a single dosage form will vary depending upon the host treated, the particular mode of administration. Preferably, provided compositions should be formulated so that a dosage of between 0.01 - 100 mg/kg body weight/day of the compound can be administered to a patient receiving these compositions.

[00238] It should also be understood that a specific dosage and treatment regimen for any particular patient will depend upon a variety of factors, including the activity of the specific

compound employed, the age, body weight, general health, sex, diet, time of administration, rate of excretion, drug combination, and the judgment of the treating physician and the severity of the particular disease being treated. The amount of a compound of the present invention in the composition will also depend upon the particular compound in the composition.

Uses of Compounds and Pharmaceutically Acceptable Compositions

[00239] Presently described are compositions and methods that relate to the surprising and unexpected discovery that an E3 Ubiquitin Ligase protein, e.g., cereblon, ubiquitinates a target protein once it and the target protein are placed in proximity by a bifunctional or chimeric construct that binds the E3 Ubiquitin Ligase protein and the target protein. Accordingly the present invention provides such compounds and compositions comprising an E3 Ubiquintin Ligase binding moiety ("UBM") coupled to a protein target binding moiety ("TBM"), which result in the ubiquitination of a chosen target protein, which leads to degradation of the target protein by the proteasome .

[00240] Compounds and compositions described herein are generally useful for the modulation of targeted ubiquitination, especially with respect to a variety of polypeptides and other proteins, which are degraded and/or otherwise inhibited. In some embodiments the protein inhibited by the compounds and methods of the invention comprises those proteins listed in paragraph [00181].

[00241] Compounds and compositions described herein exhibit a broad range of pharmacological activities, consistent with the degradation/inhibition of targeted polypeptides.

[00242] Accordingly, compounds that bind CRBN are beneficial, especially those with selectivity over E3 ligases. Such compounds should deliver a pharmacological response that favorably treats one or more of the conditions described herein without the side-effects associated with the binding of E3 ligases.

[00243] Even though CRBN binders are known in the art, there is a continuing need to provide novel binders having more effective or advantageous pharmaceutically relevant properties. For example, compounds with increased activity, selectivity over other E3 ligases, and ADMET (absorption, distribution, metabolism, excretion, and/or toxicity) properties. Thus, in some embodiments, the present invention provides binders of CRBN which show selectivity over other E3 ligases.

[00244] The activity of a compound utilized in this invention as an binder of CRBN, or a mutant thereof, may be assayed *in vitro*, *in vivo* or in a cell line. *In vitro* assays include assays that determine the subsequent functional consequences, or activity of activated CRBN, or a mutant thereof. Alternate *in vitro* assays quantitate the ability of the compound to bind to CRBN. Binding may be measured by radiolabeling the compound prior to binding, isolating the compound/CRBN complex and determining the amount of radiolabel bound. Alternatively, compound binding may be determined by running a competition experiment where new compounds are incubated with CRBN bound to known radioligands. Representative *in vitro* and *in vivo* assays useful in assaying a CRBN binder include those described and disclosed in, Boichenko et al. J. Med. Chem. (2016) 59, 770-774 and Iconomou and Saunders Biochemical Journal (2016) 473, 4083-4101, each of which is herein incorporated by reference in its entirety. Detailed conditions for assaying a compound utilized in this invention as an binder of CRBN, or a mutant thereof, are set forth in the Examples below.

[00245] The term"Ubiquitin Ligase" refers to a family of proteins that facilitate the transfer of ubiquitin to a specific substrate protein, targeting the substrate protein for degradation. For example, cereblon is an E3 Ubiquitin Ligase protein that alone or in combination with an E2 ubiquitin-conjugating enzyme causes the attachment of ubiquitin to a lysine on a target protein, and subsequently targets the specific protein substrates for degradation by the proteasome. Thus, E3 ubiquitin ligase alone or in complex with an E2 ubiquitin conjugating enzyme is responsible for the transfer of ubiquitin to targeted proteins. In general, the ubiquitin ligase is involved in polyubiquitination such that a second ubiquitin is attached to the first; a third is attached to the second, and so forth. Polyubiquitination marks proteins for degradation by the proteasome. However, there are some ubiquitination events that are limited to mono- ubiquitination, in which only a single ubiquitin is added by the ubiquitin ligase to a substrate molecule. Mono-ubiquitinated proteins are not targeted to the proteasome for degradation, but may instead be altered in their cellular location or function, for example, via binding other proteins that have domains capable of binding ubiquitin. Further complicating matters, different lysines on ubiquitin can be targeted by an E3 to make chains. The most common lysine is Lys48 on the ubiquitin chain. This is the lysine used to make polyubiquitin, which is recognized by the proteasome.

[00246] As used herein, the terms "treatment," "treat," and "treating" refer to reversing, alleviating, delaying the onset of, or inhibiting the progress of a disease or disorder, or one or more symptoms thereof, as described herein. In some embodiments, treatment may be administered after one or more symptoms have developed. In other embodiments, treatment may be administered in the absence of symptoms. For example, treatment may be administered to a susceptible individual prior to the onset of symptoms (e.g., in light of a history of symptoms and/or in light of genetic or other susceptibility factors). Treatment may also be continued after symptoms have resolved, for example to prevent or delay their recurrence.

[00247] The description provides therapeutic compositions as described herein for effectuating the degradation of proteins of interest for the treatment or amelioration of a disease, e.g., cancer. In certain additional embodiments, the disease is multiple myeloma. As such, in another aspect, the description provides a method of ubiquitinating/ degrading a target protein in a cell. In certain embodiments, the method comprises administering a bifunctional compound as described herein comprising, e.g., a UBM and a TBM, linked through a linker moiety, as otherwise described herein, wherein the UBM is coupled to the TBM and wherein the UBM recognizes a ubiquitin pathway protein (e.g., an ubiquitin ligase, preferably an E3 ubiquitin ligase such as, e.g., cereblon) and the TBM recognizes the target protein such that degradation of the target protein will occur when the target protein is placed in proximity to the ubiquitin ligase, thus resulting in degradation/inhibition of the effects of the target protein and the control of protein levels. The control of protein levels afforded by the present invention provides treatment of a disease state or condition, which is modulated through the target protein by lowering the level of that protein in the cell, e.g., cell of a patient. In certain embodiments, the method comprises administering an effective amount of a compound as described herein, optionally including a pharamaceutically acceptable excipient, carrier, adjuvant, another bioactive agent or combination thereof.

[00248] In additional embodiments, the description provides methods for treating or emeliorating a disease, disorder or symptom thereof in a subject or a patient, comprising administering to a subject in need thereof a composition comprising an effective amount, e.g., a therapeutically effective amount, of a compound as described herein or salt form thereof, and a pharmaceutically acceptable excipient, carrier, adjuvant, another bioactive agent or combination

thereof, wherein the composition is effective for treating or ameliorating the disease or disorder or symptom thereof in the subject.

[00249] In another aspect, the description provides methods for identifying the effects of the degradation of proteins of interest in a biological system using compounds according to the present invention.

[00250] In another embodiment, the present invention is directed to a method of treating a human patient in need for a disease state or condition modulated through a protein where the degradation of that protein will produce a therapeutic effect in that patient, the method comprising administering to a patient in need an effective amount of a compound according to the present invention, optionally in combination with another bioactive agent. The disease state or condition may be a disease caused by a microbial agent or other exogenous agent such as a virus, bacteria, fungus, protozoa or other microbe or may be a disease state, which is caused by overexpression of a protein, which leads to a disease state and/or condition.

[00251] Disease states of conditions which may be treated using compounds according to the present invention include, for example, asthma, autoimmune diseases such as multiple sclerosis, various cancers, ciliopathies, cleft palate, diabetes, heart disease, hypertension, inflammatory bowel disease, mental retardation, mood disorder, obesity, refractive error, infertility, Angelman syndrome, Canavan disease, Coeliac disease, Charcot–Marie–Tooth disease, Cystic fibrosis, Duchenne muscular dystrophy, Haemochromatosis, Haemophilia, Klinefelter's syndrome, Neurofibromatosis, Phenylketonuria, Polycystic kidney disease, (PKD1) or 4 (PKD2) Prader–Willi syndrome, Sickle-cell disease, Tay–Sachs disease, Turner syndrome.

[00252] Further disease states or conditions which may be treated by compounds according to the present invention include Alzheimer's disease, Amyotrophic lateral sclerosis (Lou Gehrig's disease), Anorexia nervosa, Anxiety disorder, Atherosclerosis, Attention deficit hyperactivity disorder, Autism, Bipolar disorder, Chronic fatigue syndrome, Chronic obstructive pulmonary disease, Crohn's disease, Coronary heart disease, Dementia, Depression, Diabetes mellitus type 1, Diabetes mellitus type 2, Epilepsy, Guillain–Barré syndrome, Irritable bowel syndrome, Lupus, Metabolic syndrome, Multiple sclerosis, Myocardial infarction, Obesity, Obsessive–compulsive disorder, Panic disorder, Parkinson's disease, Psoriasis, Rheumatoid arthritis, Sarcoidosis, Schizophrenia, Stroke, Thromboangiitis obliterans, Tourette syndrome, Vasculitis.

[00253] Still additional disease states or conditions which can be treated by compounds according to the present invention include aceruloplasminemia, Achondrogenesis type II, achondroplasia, Acrocephaly, Gaucher disease type 2, acute intermittent porphyria, Canavan disease, Adenomatous Polyposis Coli, ALA dehydratase deficiency, adenylosuccinate lyase deficiency, Adrenogenital syndrome, Adrenoleukodystrophy, ALA-D porphyria, ALA dehydratase deficiency, Alkaptonuria, Alexander disease, Alkaptonuric ochronosis, alpha 1-antitrypsin deficiency, alpha-1 proteinase inhibitor, emphysema, amyotrophic lateral sclerosis Alström syndrome, Alexander disease, Amelogenesis imperfecta, ALA dehydratase deficiency, Anderson-Fabry disease, androgen insensitivity syndrome, Anemia Angiokeratoma Corporis Diffusum, Angiomatosis retinae (von Hippel–Lindau disease) Apert syndrome, Arachnodactyly (Marfan syndrome), Stickler syndrome, Arthrochalasis multiplex congenital (Ehlers–Danlos syndrome#arthrochalasia type) ataxia telangiectasia, Rett syndrome, primary pulmonary hypertension, Sandhoff disease, neurofibromatosis type II, Beare-Stevenson cutis gyrata syndrome, Mediterranean fever, familial, Benjamin syndrome, beta-thalassemia, Bilateral Acoustic Neurofibromatosis (neurofibromatosis type II), factor V Leiden thrombophilia, Bloch-Sulzberger syndrome (incontinentia pigmenti), Bloom syndrome, X- linked sideroblastic anemia, Bonnevie-Ullrich syndrome (Turner syndrome), Bourneville disease (tuberous sclerosis), prion disease, Birt–Hogg–Dubé syndrome, Brittle bone disease (osteogenesis imperfecta), Broad Thumb-Hallux syndrome (Rubinstein-Taybi syndrome), Bronze Diabetes/Bronzed Cirrhosis (hemochromatosis), Bulbospinal muscular atrophy (Kennedy's disease), Burger-Grutz syndrome (lipoprotein lipase deficiency), CGD Chronic granulomatous disorder, Campomelic dysplasia, biotinidase deficiency, Cardiomyopathy (Noonan syndrome), Cri du chat, CAVD (congenital absence of the vas deferens), Caylor cardiofacial syndrome (CBAVD), CEP (congenital erythropoietic porphyria), cystic fibrosis, congenital hypothyroidism, Chondrodystrophy syndrome (achondroplasia), otospondylomegaepiphyseal dysplasia, Lesch-Nyhan syndrome, galactosemia, Ehlers–Danlos syndrome, Thanatophoric dysplasia, Coffin-Lowry syndrome, Cockayne syndrome, (familial adenomatous polyposis), Congenital erythropoietic porphyria, Congenital heart disease, Methemoglobinemia/Congenital methaemoglobinaemia, achondroplasia, X-linked sideroblastic anemia, Connective tissue disease, Conotruncal anomaly face syndrome, Cooley's Anemia (beta-thalassemia), Copper storage disease (Wilson's disease),

Copper transport disease (Menkes disease), hereditary coproporphyria, Cowden syndrome, Craniofacial dysarthrosis (Crouzon syndrome), Creutzfeldt-Jakob disease (prion disease), Cockayne syndrome, Cowden syndrome, Curschmann-Batten-Steinert syndrome (myotonic dystrophy), Beare-Stevenson cutis gyrata syndrome, primary hyperoxaluria, spondyloepimetaphyseal dysplasia (Strudwick type), muscular dystrophy, Duchenne and Becker types (DBMD), Usher syndrome, Degenerative nerve diseases including de Grouchy syndrome and Dejerine-Sottas syndrome, developmental disabilities, distal spinal muscular atrophy, type V, androgen insensitivity syndrome, Diffuse Globoid Body Sclerosis (Krabbe disease), Di George's syndrome, Dihydrotestosterone receptor deficiency, androgen insensitivity syndrome, Down syndrome, Dwarfism, erythropoietic protoporphyria Erythroid 5-aminolevulinate synthetase deficiency, Erythropoietic porphyria, erythropoietic protoporphyria, erythropoietic uroporphyria, Friedreich's ataxia,, familial paroxysmal polyserositis, porphyria cutanea tarda, familial pressure sensitive neuropathy, primary pulmonary hypertension (PPH), Fibrocystic disease of the pancreas, fragile X syndrome, galactosemia, genetic brain disorders, Giant cell hepatitis (Neonatal hemochromatosis), Gronblad-Strandberg syndrome (pseudoxanthoma elasticum), Gunther disease (congenital erythropoietic porphyria), haemochromatosis, Hallgren syndrome, sickle cell anemia, hemophilia, hepatoerythropoietic porphyria (HEP), Hippel- Lindau disease (von Hippel-Lindau disease), Huntington's disease, Hutchinson-Gilford progeria syndrome (progeria), Hyperandrogenism, Hypochondroplasia, Hypochromic anemia, Immune system disorders, including X-linked severe combined immunodeficiency, Insley- Astley syndrome, Jackson-Weiss syndrome, Joubert syndrome, Lesch-Nyhan syndrome, Jackson-Weiss syndrome, Kidney diseases, including hyperoxaluria, Klinefelter's syndrome, Kniest dysplasia, Lacunar dementia,Langer-Saldino achondrogenesis, ataxia telangiectasia, Lynch syndrome, Lysyl-hydroxylase deficiency, Machado-Joseph disease, Metabolic disorders, including Kniest dysplasia, Marfan syndrome, Movement disorders, Mowat-Wilson syndrome, cystic fibrosis, Muenke syndrome, Multiple neurofibromatosis, Nance-Insley syndrome, Nance-Sweeney chondrodysplasia, Niemann–Pick disease, Noack syndrome (Pfeiffer syndrome), Osler-Weber-Rendu disease, Peutz-Jeghers syndrome, Polycystic kidney disease, polyostotic fibrous dysplasia (McCune–Albright syndrome), Peutz-Jeghers syndrome, Prader- Labhart-Willi syndrome, hemochromatosis, primary hyperuricemia syndrome (Lesch-Nyhan syndrome), primary

pulmonary hypertension, primary senile degenerative dementia, prion disease, progeria (Hutchinson Gilford Progeria Syndrome), progressive chorea, chronic hereditary (Huntington) (Huntington's disease), progressive muscular atrophy, spinal muscular atrophy, propionic acidemia, protoporphyria, proximal myotonic dystrophy, pulmonary arterial hypertension, PXE (pseudoxanthoma elasticum), Rb (retinoblastoma), Recklinghausen disease (neurofibromatosis type I), Recurrent polyserositis, Retinal disorders, Retinoblastoma, Rett syndrome, RFALS type 3, Ricker syndrome, Riley-Day syndrome, Roussy-Levy syndrome, severe achondroplasia with developmental delay and acanthosis nigricans (SADDAN), Li- Fraumeni syndrome, sarcoma, breast, leukemia, and adrenal gland (SBLA) syndrome, sclerosis tuberose (tuberous sclerosis), SDAT, SED congenital (spondyloepiphyseal dysplasia congenita), SED Strudwick (spondyloepimetaphyseal dysplasia, Strudwick type), SEDc (spondyloepiphyseal dysplasia congenita) SEMD, Strudwick type (spondyloepimetaphyseal dysplasia, Strudwick type), Shprintzen syndrome, Skin pigmentation disorders, Smith-Lemli- Opitz syndrome, South-African genetic porphyria (variegate porphyria), infantile-onset ascending hereditary spastic paralysis, Speech and communication disorders, sphingolipidosis, Tay-Sachs disease, spinocerebellar ataxia, Stickler syndrome, stroke, androgen insensitivity syndrome, tetrahydrobiopterin deficiency, beta-thalassemia, Thyroid disease, Tomaculous neuropathy (hereditary neuropathy with liability to pressure palsies), Treacher Collins syndrome, Triplo X syndrome (triple X syndrome), Trisomy 21 (Down syndrome), Trisomy X, VHL syndrome (von Hippel-Lindau disease), Vision impairment and blindness (Alström syndrome), Vrolik disease, Waardenburg syndrome, Warburg Sjo Fledelius Syndrome, Weissenbacher-Zweymüller syndrome, Wolf–Hirschhorn syndrome, Wolff Periodic disease, Weissenbacher-Zweymüller syndrome and Xeroderma pigmentosum, among others.

[00254] The term "neoplasia" or“cancer” is used throughout the specification to refer to the pathological process that results in the formation and growth of a cancerous or malignant neoplasm, i.e., abnormal tissue that grows by cellular proliferation, often more rapidly than normal and continues to grow after the stimuli that initiated the new growth cease. Malignant neoplasms show partial or complete lack of structural organization and functional coordination with the normal tissue and most invade surrounding tissues, metastasize to several sites, and are likely to recur after attempted removal and to cause the death of the patient unless adequately treated. As

used herein, the term neoplasia is used to describe all cancerous disease states and embraces or encompasses the pathological process associated with malignant hematogenous, ascitic and solid tumors. Exemplary cancers which may be treated by the present compounds either alone or in combination with at least one additional anti-cancer agent include squamous-cell carcinoma, basal cell carcinoma, adenocarcinoma, hepatocellular carcinomas, and renal cell carcinomas, cancer of the bladder, bowel, breast, cervix, colon, esophagus, head, kidney, liver, lung, neck, ovary, pancreas, prostate, and stomach; leukemias; benign and malignant lymphomas, particularly Burkitt's lymphoma and Non-Hodgkin's lymphoma; benign and malignant melanomas; myeloproliferative diseases; sarcomas, including Ewing's sarcoma, hemangiosarcoma, Kaposi's sarcoma, liposarcoma, myosarcomas, peripheral neuroepithelioma, synovial sarcoma, gliomas, astrocytomas, oligodendrogliomas, ependymomas, gliobastomas, neuroblastomas, ganglioneuromas, gangliogliomas, medulloblastomas, pineal cell tumors, meningiomas, meningeal sarcomas, neurofibromas, and Schwannomas; bowel cancer, breast cancer, prostate cancer, cervical cancer, uterine cancer, lung cancer, ovarian cancer, testicular cancer, thyroid cancer, astrocytoma, esophageal cancer, pancreatic cancer, stomach cancer, liver cancer, colon cancer, melanoma; carcinosarcoma, Hodgkin's disease, Wilms' tumor and teratocarcinomas. Additional cancers which may be treated using compounds according to the present invention include, for example, T-lineage Acute lymphoblastic Leukemia (T-ALL), T-lineage lymphoblastic Lymphoma (T-LL), Peripheral T-cell lymphoma, Adult T-cell Leukemia, Pre-B ALL, Pre-B Lymphomas, Large B- cell Lymphoma, Burkitts Lymphoma, B-cell ALL, Philadelphia chromosome positive ALL and Philadelphia chromosome positive CML.

[00255] In some embodiments, the present invention provides a method for treating one or more disorders, wherein the disorders are selected from autoimmune disorders, inflammatory disorders, proliferative disorders, endocrine disorders, neurological disorders, and disorders associated with transplantation, said method comprising administering to a patient in need thereof, a pharmaceutical composition comprising an effective amount of a compound of the present invention, or a pharmaceutically acceptable salt thereof.

[00256] In some embodiments, compounds of the present invention induce the ubiquitination and degradation of a target protein selected from the group consisting of A1BG, A1CF, A2M, A2ML1, A3GALT2, A4GALT, A4GNT, AAAS, AACS, AADAC, AADACL2, AADACL3,

AADACL4, AADAT, AAED1, AAGAB, AAK1, AAMDC, AAMP, AANAT, AAR2, AARD, AARS, AARS2, AARSD1, AASDH, AASDHPPT, AASS, AATF, AATK, AATK-AS1, ABAT, ABCA1, ABCA10, ABCA12, ABCA13, ABCA2, ABCA3, ABCA4, ABCA5, ABCA6, ABCA7, ABCA8, ABCA9, ABCB1, ABCB10, ABCB11, ABCB4, ABCB5, ABCB6, ABCB7, ABCB8, ABCB9, ABCC1, ABCC10, ABCC11, ABCC12, ABCC2, ABCC3, ABCC4, ABCC5, ABCC6, ABCC8, ABCC9, ABCD1, ABCD2, ABCD3, ABCD4, ABCE1, ABCF1, ABCF2, ABCF3, ABCG1, ABCG2, ABCG4, ABCG5, ABCG8, ABHD1, ABHD10, ABHD11, ABHD12, ABHD12B, ABHD13, ABHD14A, ABHD14A-ACY1, ABHD14B, ABHD15, ABHD16A, ABHD16B, ABHD17A, ABHD17B, ABHD17C, ABHD18, ABHD2, ABHD3, ABHD4, ABHD5, ABHD6, ABHD8, ABI1, ABI2, ABI3, ABI3BP, ABL1, ABL2, ABLIM1, ABLIM2, ABLIM3, ABO, ABR, ABRA, ABRACL, ABRAXAS1, ABRAXAS2, ABT1, ABTB1, ABTB2, AC001226.2, AC002094.3, AC002115.2, AC002310.4, AC002310.5, AC002429.2, AC002985.1, AC002996.1, AC003002.1, AC003002.2, AC003002.3, AC003002.4, AC003005.1, AC003006.1, AC003688.1, AC004076.1, AC004080.3, AC004223.3, AC004233.2, AC004556.1, AC004691.2, AC004706.4, AC004754.1, AC004805.1, AC004832.3, AC004922.1, AC004997.1, AC005020.2, AC005041.1, AC005154.6, AC005258.1, AC005324.3, AC005324.4, AC005520.1, AC005551.1, AC005670.2, AC005697.1, AC005702.2, AC005726.2, AC005779.2, AC005832.4, AC005833.1, AC005833.3, AC005837.2, AC005841.2, AC005885.1, AC005943.1, AC006030.1, AC006254.1, AC006269.1, AC006449.4, AC006486.1, AC006538.2, AC006978.2, AC007040.2, AC007192.1, AC007240.1, AC007325.1, AC007325.2, AC007325.4, AC007326.4, AC007375.2, AC007383.6, AC007537.5, AC007731.5, AC007906.2, AC007998.2, AC008073.3, AC008162.2, AC008393.2, AC008403.1, AC008481.3, AC008537.1, AC008560.1, AC008575.1, AC008575.2, AC008687.1, AC008687.4, AC008687.8, AC008695.1, AC008735.6, AC008750.8, AC008758.1, AC008758.4, AC008758.5, AC008758.6, AC008763.2, AC008763.3, AC008764.1, AC008764.4, AC008770.2, AC008770.3, AC008878.1, AC008878.2, AC008878.3, AC008982.1, AC008982.3, AC009014.1, AC009086.2, AC009119.2, AC009122.1, AC009133.6, AC009163.2, AC009163.4, AC009286.3, AC009336.2, AC009477.2, AC009690.1, AC009690.3, AC009779.3, AC010132.3, AC010255.3, AC010319.2, AC010323.1, AC010325.1, AC010326.2, AC010327.1, AC010422.3, AC010422.5, AC010422.6, AC010463.1, AC010487.3, AC010522.1, AC010531.1, AC010542.3, AC010547.4, AC010547.5, AC010615.4, AC010616.1, AC010619.1, AC010646.1, AC010724.2, AC011005.1,

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Protein Level Control

[00257] This description also provides methods for the control of protein levels with a cell. This is based on the use of compounds as described herein, which are known to interact with a specific target protein such that degradation of a target protein in vivo will result in the control of the amount of protein in a biological system, prerferably to a particular therapeutic benefit.

[00258] Furthermore, the invention provides the use of a compound according to the definitions herein, or a pharmaceutically acceptable salt, or a hydrate or solvate thereof for the preparation of a medicament for the treatment of an autoimmune disorder, an inflammatory disorder, or a proliferative disorder, or a disorder commonly occurring in connection with transplantation.

Combination Therapies

[00259] Depending upon the particular condition, or disease, to be treated, additional therapeutic agents, which are normally administered to treat that condition, may be administered in combination with compounds and compositions of this invention. As used herein, additional therapeutic agents that are normally administered to treat a particular disease, or condition, are known as "appropriate for the disease, or condition, being treated."

[00260] In certain embodiments, a provided combination, or composition thereof, is administered in combination with another therapeutic agent.

[00261] Examples of agents the combinations of this invention may also be combined with include, without limitation: treatments for Alzheimer's Disease such as Aricept® and Excelon®; treatments for HIV such as ritonavir; treatments for Parkinson's Disease such as L-DOPA/carbidopa, entacapone, ropinrole, pramipexole, bromocriptine, pergolide, trihexephendyl, and amantadine; agents for treating Multiple Sclerosis (MS) such as beta interferon (e.g., Avonex® and Rebif®), Copaxone®, and mitoxantrone; treatments for asthma such as albuterol and Singulair®; agents for treating schizophrenia such as zyprexa, risperdal, seroquel, and haloperidol; anti-inflammatory agents such as corticosteroids, TNF blockers, IL-1 RA, azathioprine, cyclophosphamide, and sulfasalazine; immunomodulatory and immunosuppressive agents such as cyclosporin, tacrolimus, rapamycin, mycophenolate mofetil, interferons, corticosteroids, cyclophophamide, azathioprine, and sulfasalazine; neurotrophic factors such as acetylcholinesterase inhibitors, MAO inhibitors, interferons, anti-convulsants, ion channel blockers, riluzole, and anti-Parkinsonian agents; agents for treating cardiovascular disease such as beta-blockers, ACE inhibitors, diuretics, nitrates, calcium channel blockers, and statins; agents for treating liver disease such as corticosteroids, cholestyramine, interferons, and anti-viral agents; agents for treating blood disorders such as corticosteroids, anti-leukemic agents, and growth factors; agents that prolong or improve pharmacokinetics such as cytochrome P450 inhibitors (i.e., inhibitors of metabolic breakdown) and CYP3A4 inhibitors (e.g., ketokenozole and ritonavir), and agents for treating immunodeficiency disorders such as gamma globulin.

[00262] In certain embodiments, combination therapies of the present invention, or a pharmaceutically acceptable composition thereof, are administered in combination with a monoclonal antibody or an siRNA therapeutic.

[00263] Those additional agents may be administered separately from a provided combination therapy, as part of a multiple dosage regimen. Alternatively, those agents may be part of a single dosage form, mixed together with a compound of this invention in a single composition. If administered as part of a multiple dosage regime, the two active agents may be submitted simultaneously, sequentially or within a period of time from one another normally within five hours from one another.

[00264] As used herein, the term "combination," "combined," and related terms refers to the simultaneous or sequential administration of therapeutic agents in accordance with this invention. For example, a combination of the present invention may be administered with another therapeutic agent simultaneously or sequentially in separate unit dosage forms or together in a single unit dosage form.

[00265] The amount of additional therapeutic agent present in the compositions of this invention will be no more than the amount that would normally be administered in a composition comprising that therapeutic agent as the only active agent. Preferably the amount of additional therapeutic agent in the presently disclosed compositions will range from about 50% to 100% of the amount normally present in a composition comprising that agent as the only therapeutically active agent.

[00266] In one embodiment, the present invention provides a composition comprising a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and one or more additional therapeutic agents. The therapeutic agent may be administered together with a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B**, or may be administered prior to or following administration of a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B**. Suitable therapeutic agents are described in further detail below. In certain embodiments, a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** may be administered up to 5 minutes, 10 minutes, 15 minutes, 30 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 5, hours, 6 hours, 7 hours, 8 hours, 9 hours, 10 hours, 11 hours, 12 hours, 13 hours, 14 hours, 15 hours, 16 hours, 17 hours, or 18 hours before the therapeutic agent. In other embodiments, a compound of formula **I**,

formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** may be administered up to 5 minutes, 10 minutes, 15 minutes, 30 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 5, hours, 6 hours, 7 hours, 8 hours, 9 hours, 10 hours, 11 hours, 12 hours, 13 hours, 14 hours, 15 hours, 16 hours, 17 hours, or 18 hours following the therapeutic agent.

[00267] In another embodiment, the present invention provides a method of treating an inflammatory disease, disorder or condition by administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and one or more additional therapeutic agents. Such additional therapeutic agents may be small molecules or recombinant biologic agents and include, for example, acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDS) such as aspirin, ibuprofen, naproxen, etodolac (Lodine®) and celecoxib, colchicine (Colcrys®), corticosteroids such as prednisone, prednisolone, methylprednisolone, hydrocortisone, and the like, probenecid, allopurinol, febuxostat (Uloric®), sulfasalazine (Azulfidine®), antimalarials such as hydroxychloroquine (Plaquenil®) and chloroquine (Aralen®), methotrexate (Rheumatrex®), gold salts such as gold thioglucose (Solganal®), gold thiomalate (Myochrysine®) and auranofin (Ridaura®), D-penicillamine (Depen® or Cuprimine®), azathioprine (Imuran®), cyclophosphamide (Cytoxan®), chlorambucil (Leukeran®), cyclosporine (Sandimmune®), leflunomide (Arava®) and "anti-TNF" agents such as etanercept (Enbrel®), infliximab (Remicade®), golimumab (Simponi®), certolizumab pegol (Cimzia®) and adalimumab (Humira®), "anti-IL-1" agents such as anakinra (Kineret®) and rilonacept (Arcalyst®), canakinumab (Ilaris®), anti-Jak inhibitors such as tofacitinib, antibodies such as rituximab (Rituxan®), "anti-T-cell" agents such as abatacept (Orencia®), "anti-IL-6" agents such as tocilizumab (Actemra®), diclofenac, cortisone, hyaluronic acid (Synvisc® or Hyalgan®), monoclonal antibodies such as tanezumab, anticoagulants such as heparin (Calcinparine® or Liquaemin®) and warfarin (Coumadin®), antidiarrheals such as diphenoxylate (Lomotil®) and loperamide (Imodium®), bile acid binding agents such as cholestyramine, alosetron (Lotronex®), lubiprostone (Amitiza®), laxatives such as Milk of Magnesia, polyethylene glycol (MiraLax®), Dulcolax®, Correctol® and Senokot®, anticholinergics or antispasmodics such as dicyclomine (Bentyl®), Singulair®, beta-2 agonists such as albuterol (Ventolin® HFA, Proventil® HFA),

levalbuterol (Xopenex®), metaproterenol (Alupent®), pirbuterol acetate (Maxair®), terbutaline sulfate (Brethaire®), salmeterol xinafoate (Serevent®) and formoterol (Foradil®), anticholinergic agents such as ipratropium bromide (Atrovent®) and tiotropium (Spiriva®), inhaled corticosteroids such as beclomethasone dipropionate (Beclovent®, Qvar®, and Vanceril®), triamcinolone acetonide (Azmacort®), mometasone (Asthmanex®), budesonide (Pulmocort®), and flunisolide (Aerobid®), Afviar®, Symbicort®, Dulera®, cromolyn sodium (Intal®), methylxanthines such as theophylline (Theo-Dur®, Theolair®, Slo-bid®, Uniphyl®, Theo-24®) and aminophylline, IgE antibodies such as omalizumab (Xolair®), nucleoside reverse transcriptase inhibitors such as zidovudine (Retrovir®), abacavir (Ziagen®), abacavir/lamivudine (Epzicom®), abacavir/lamivudine/zidovudine (Trizivir®), didanosine (Videx®), emtricitabine (Emtriva®), lamivudine (Epivir®), lamivudine/zidovudine (Combivir®), stavudine (Zerit®), and zalcitabine (Hivid®), non-nucleoside reverse transcriptase inhibitors such as delavirdine (Rescriptor®), efavirenz (Sustiva®), nevairapine (Viramune®) and etravirine (Intelence®), nucleotide reverse transcriptase inhibitors such as tenofovir (Viread®), protease inhibitors such as amprenavir (Agenerase®), atazanavir (Reyataz®), darunavir (Prezista®), fosamprenavir (Lexiva®), indinavir (Crixivan®), lopinavir and ritonavir (Kaletra®), nelfinavir (Viracept®), ritonavir (Norvir®), saquinavir (Fortovase® or Invirase®), and tipranavir (Aptivus®), entry inhibitors such as enfuvirtide (Fuzeon®) and maraviroc (Selzentry®), integrase inhibitors such as raltegravir (Isentress®), doxorubicin (Hydrodaunorubicin®), vincristine (Oncovin®), bortezomib (Velcade®), and dexamethasone (Decadron ®) in combination with lenalidomide (Revlimid ®), or any combination(s) thereof.

[00268] In another embodiment, the present invention provides a method of treating rheumatoid arthritis comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and one or more additional therapeutic agents selected from non-steroidal anti-inflammatory drugs (NSAIDS) such as aspirin, ibuprofen, naproxen, etodolac (Lodine®) and celecoxib, corticosteroids such as prednisone, prednisolone, methylprednisolone, hydrocortisone, and the like, sulfasalazine (Azulfidine®), antimalarials such as hydroxychloroquine (Plaquenil®) and chloroquine (Aralen®), methotrexate (Rheumatrex®), gold salts such as gold thioglucose (Solganal®), gold thiomalate (Myochrysine®) and auranofin (Ridaura®), D-penicillamine

(Depen® or Cuprimine®), azathioprine (Imuran®), cyclophosphamide (Cytoxan®), chlorambucil (Leukeran®), cyclosporine (Sandimmune®), leflunomide (Arava®) and "anti-TNF" agents such as etanercept (Enbrel®), infliximab (Remicade®), golimumab (Simponi®), certolizumab pegol (Cimzia®) and adalimumab (Humira®), "anti-IL-1" agents such as anakinra (Kineret®) and rilonacept (Arcalyst®), antibodies such as rituximab (Rituxan®), "anti-T-cell" agents such as abatacept (Orencia®) and "anti-IL-6" agents such as tocilizumab (Actemra®).

[00269] In some embodiments, the present invention provides a method of treating osteoarthritis comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and one or more additional therapeutic agents selected from acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDS) such as aspirin, ibuprofen, naproxen, etodolac (Lodine®) and celecoxib, diclofenac, cortisone, hyaluronic acid (Synvisc® or Hyalgan®) and monoclonal antibodies such as tanezumab.

[00270] In some embodiments, the present invention provides a method of treating systemic lupus erythematosus comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and one or more additional therapeutic agents selected from acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDS) such as aspirin, ibuprofen, naproxen, etodolac (Lodine®) and celecoxib, corticosteroids such as prednisone, prednisolone, methylprednisolone, hydrocortisone, and the like, antimalarials such as hydroxychloroquine (Plaquenil®) and chloroquine (Aralen®), cyclophosphamide (Cytoxan®), methotrexate (Rheumatrex®), azathioprine (Imuran®) and anticoagulants such as heparin (Calcinparine® or Liquaemin®) and warfarin (Coumadin®).

[00271] In some embodiments, the present invention provides a method of treating Crohn's disesase, ulcerative colitis, or inflammatory bowel disease comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and one or more additional therapeutic agents selected from mesalamine (Asacol®) sulfasalazine (Azulfidine®), antidiarrheals such as diphenoxylate (Lomotil®) and loperamide (Imodium®), bile acid binding agents such as cholestyramine, alosetron (Lotronex®), lubiprostone (Amitiza®), laxatives such as

Milk of Magnesia, polyethylene glycol (MiraLax®), Dulcolax®, Correctol® and Senokot® and anticholinergics or antispasmodics such as dicyclomine (Bentyl®), anti-TNF therapies, steroids, and antibiotics such as Flagyl or ciprofloxacin.

[00272] In some embodiments, the present invention provides a method of treating asthma comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and one or more additional therapeutic agents selected from Singulair®, beta-2 agonists such as albuterol (Ventolin® HFA, Proventil® HFA), levalbuterol (Xopenex®), metaproterenol (Alupent®), pirbuterol acetate (Maxair®), terbutaline sulfate (Brethaire®), salmeterol xinafoate (Serevent®) and formoterol (Foradil®), anticholinergic agents such as ipratropium bromide (Atrovent®) and tiotropium (Spiriva®), inhaled corticosteroids such as prednisone, prednisolone, beclomethasone dipropionate (Beclovent®, Qvar®, and Vanceril®), triamcinolone acetonide (Azmacort®), mometasone (Asthmanex®), budesonide (Pulmocort®), flunisolide (Aerobid®), Afviar®, Symbicort®, and Dulera®, cromolyn sodium (Intal®), methylxanthines such as theophylline (Theo-Dur®, Theolair®, Slo-bid®, Uniphyl®, Theo-24®) and aminophylline, and IgE antibodies such as omalizumab (Xolair®).

[00273] In some embodiments, the present invention provides a method of treating COPD comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and one or more additional therapeutic agents selected from beta-2 agonists such as albuterol (Ventolin® HFA, Proventil® HFA), levalbuterol (Xopenex®), metaproterenol (Alupent®), pirbuterol acetate (Maxair®), terbutaline sulfate (Brethaire®), salmeterol xinafoate (Serevent®) and formoterol (Foradil®), anticholinergic agents such as ipratropium bromide (Atrovent®) and tiotropium (Spiriva®), methylxanthines such as theophylline (Theo-Dur®, Theolair®, Slo-bid®, Uniphyl®, Theo-24®) and aminophylline, inhaled corticosteroids such as prednisone, prednisolone, beclomethasone dipropionate (Beclovent®, Qvar®, and Vanceril®), triamcinolone acetonide (Azmacort®), mometasone (Asthmanex®), budesonide (Pulmocort®), flunisolide (Aerobid®), Afviar®, Symbicort®, and Dulera®,

[00274] In another embodiment, the present invention provides a method of treating a hematological malignancy comprising administering to a patient in need thereof a compound of

formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and one or more additional therapeutic agents selected from rituximab (Rituxan®), cyclophosphamide (Cytoxan®), doxorubicin (Hydrodaunorubicin®), vincristine (Oncovin®), prednisone, a hedgehog signaling inhibitor, a BTK inhibitor, a JAK/pan-JAK inhibitor, a PI3K inhibitor, a SYK inhibitor, and combinations thereof.

[00275] In another embodiment, the present invention provides a method of treating a solid tumor comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and one or more additional therapeutic agents selected from rituximab (Rituxan®), cyclophosphamide (Cytoxan®), doxorubicin (Hydrodaunorubicin®), vincristine (Oncovin®), prednisone, a hedgehog signaling inhibitor, a BTK inhibitor, a JAK/pan-JAK inhibitor, a PI3K inhibitor, a SYK inhibitor, and combinations thereof.

[00276] In another embodiment, the present invention provides a method of treating a hematological malignancy comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and a Hedgehog (Hh) signaling pathway inhibitor. In some embodiments, the hematological malignancy is DLBCL (Ramirez *et al* "Defining causative factors contributing in the activation of hedgehog signaling in diffuse large B-cell lymphoma" Leuk. Res. (2012), published online July 17, and incorporated herein by reference in its entirety).

[00277] In another embodiment, the present invention provides a method of treating diffuse large B-cell lymphoma (DLBCL) comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and one or more additional therapeutic agents selected from rituximab (Rituxan®), cyclophosphamide (Cytoxan®), doxorubicin (Hydrodaunorubicin®), vincristine (Oncovin®), prednisone, a hedgehog signaling inhibitor, and combinations thereof.

[00278] In another embodiment, the present invention provides a method of treating multiple myeloma comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and one or more additional therapeutic agents selected from bortezomib

(Velcade®), and dexamethasone (Decadron®), a hedgehog signaling inhibitor, a BTK inhibitor, a JAK/pan-JAK inhibitor, a TYK2 inhibitor, a PI3K inhibitor, a SYK inhibitor in combination with lenalidomide (Revlimid®).

[00279] In another embodiment, the present invention provides a method of treating or lessening the severity of a disease comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and a BTK inhibitor, wherein the disease is selected from inflammatory bowel disease, arthritis, systemic lupus erythematosus (SLE), vasculitis, idiopathic thrombocytopenic purpura (ITP), rheumatoid arthritis, psoriatic arthritis, osteoarthritis, Still's disease, juvenile arthritis, diabetes, myasthenia gravis, Hashimoto's thyroiditis, Ord's thyroiditis, Graves' disease, autoimmune thyroiditis, Sjogren's syndrome, multiple sclerosis, systemic sclerosis, Lyme neuroborreliosis, Guillain-Barre syndrome, acute disseminated encephalomyelitis, Addison's disease, opsoclonus-myoclonus syndrome, ankylosing spondylosis, antiphospholipid antibody syndrome, aplastic anemia, autoimmune hepatitis, autoimmune gastritis, pernicious anemia, celiac disease, Goodpasture's syndrome, idiopathic thrombocytopenic purpura, optic neuritis, scleroderma, primary biliary cirrhosis, Reiter's syndrome, Takayasu's arteritis, temporal arteritis, warm autoimmune hemolytic anemia, Wegener's granulomatosis, psoriasis, alopecia universalis, Behcet's disease, chronic fatigue, dysautonomia, membranous glomerulonephropathy, endometriosis, interstitial cystitis, pemphigus vulgaris, bullous pemphigoid, neuromyotonia, scleroderma, vulvodynia, a hyperproliferative disease, rejection of transplanted organs or tissues, Acquired Immunodeficiency Syndrome (AIDS, also known as HIV), type 1 diabetes, graft versus host disease, transplantation, transfusion, anaphylaxis, allergies (e.g., allergies to plant pollens, latex, drugs, foods, insect poisons, animal hair, animal dander, dust mites, or cockroach calyx), type I hypersensitivity, allergic conjunctivitis, allergic rhinitis, and atopic dermatitis, asthma, appendicitis, atopic dermatitis, asthma, allergy, blepharitis, bronchiolitis, bronchitis, bursitis, cervicitis, cholangitis, cholecystitis, chronic graft rejection, colitis, conjunctivitis, Crohn's disease, cystitis, dacryoadenitis, dermatitis, dermatomyositis, encephalitis, endocarditis, endometritis, enteritis, enterocolitis, epicondylitis, epididymitis, fasciitis, fibrositis, gastritis, gastroenteritis, Henoch-Schonlein purpura, hepatitis, hidradenitis suppurativa, immunoglobulin A nephropathy, interstitial lung disease, laryngitis, mastitis,

meningitis, myelitis myocarditis, myositis, nephritis, oophoritis, orchitis, osteitis, otitis, pancreatitis, parotitis, pericarditis, peritonitis, pharyngitis, pleuritis, phlebitis, pneumonitis, pneumonia, polymyositis, proctitis, prostatitis, pyelonephritis, rhinitis, salpingitis, sinusitis, stomatitis, synovitis, tendonitis, tonsillitis, ulcerative colitis, uveitis, vaginitis, vasculitis, or vulvitis, B-cell proliferative disorder, e.g., diffuse large B cell lymphoma, follicular lymphoma, chronic lymphocytic lymphoma, chronic lymphocytic leukemia, acute lymphocytic leukemia, B-cell prolymphocytic leukemia, lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia, splenic marginal zone lymphoma, multiple myeloma (also known as plasma cell myeloma), non-Hodgkin's lymphoma, Hodgkin's lymphoma, plasmacytoma, extranodal marginal zone B cell lymphoma, nodal marginal zone B cell lymphoma, mantle cell lymphoma, mediastinal (thymic) large B cell lymphoma, intravascular large B cell lymphoma, primary effusion lymphoma, Burkitt lymphoma/leukemia, or lymphomatoid granulomatosis, breast cancer, prostate cancer, or cancer of the mast cells (e.g., mastocytoma, mast cell leukemia, mast cell sarcoma, systemic mastocytosis), bone cancer, colorectal cancer, pancreatic cancer, diseases of the bone and joints including, without limitation, rheumatoid arthritis, seronegative spondyloarthropathies (including ankylosing spondylitis, psoriatic arthritis and Reiter's disease), Behcet's disease, Sjogren's syndrome, systemic sclerosis, osteoporosis, bone cancer, bone metastasis, a thromboembolic disorder, (e.g., myocardial infarct, angina pectoris, reocclusion after angioplasty, restenosis after angioplasty, reocclusion after aortocoronary bypass, restenosis after aortocoronary bypass, stroke, transitory ischemia, a peripheral arterial occlusive disorder, pulmonary embolism, deep venous thrombosis), inflammatory pelvic disease, urethritis, skin sunburn, sinusitis, pneumonitis, encephalitis, meningitis, myocarditis, nephritis, osteomyelitis, myositis, hepatitis, gastritis, enteritis, dermatitis, gingivitis, appendicitis, pancreatitis, cholocystitus, agammaglobulinemia, psoriasis, allergy, Crohn's disease, irritable bowel syndrome, ulcerative colitis, Sjogren's disease, tissue graft rejection, hyperacute rejection of transplanted organs, asthma, allergic rhinitis, chronic obstructive pulmonary disease (COPD), autoimmune polyglandular disease (also known as autoimmune polyglandular syndrome), autoimmune alopecia, pernicious anemia, glomerulonephritis, dermatomyositis, multiple sclerosis, scleroderma, vasculitis, autoimmune hemolytic and thrombocytopenic states, Goodpasture's syndrome, atherosclerosis, Addison's disease, Parkinson's disease, Alzheimer's disease, diabetes, septic shock, systemic lupus

erythematosus (SLE), rheumatoid arthritis, psoriatic arthritis, juvenile arthritis, osteoarthritis, chronic idiopathic thrombocytopenic purpura, Waldenstrom macroglobulinemia, myasthenia gravis, Hashimoto's thyroiditis, atopic dermatitis, degenerative joint disease, vitiligo, autoimmune hypopituitarism, Guillain-Barre syndrome, Behcet's disease, scleraderma, mycosis fungoides, acute inflammatory responses (such as acute respiratory distress syndrome and ischemia/reperfusion injury), and Graves' disease.

[00280] In another embodiment, the present invention provides a method of treating or lessening the severity of a disease comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and a PI3K inhibitor, wherein the disease is selected from a cancer, a neurodegenative disorder, an angiogenic disorder, a viral disease, an autoimmune disease, an inflammatory disorder, a hormone-related disease, conditions associated with organ transplantation, immunodeficiency disorders, a destructive bone disorder, a proliferative disorder, an infectious disease, a condition associated with cell death, thrombin-induced platelet aggregation, chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL), liver disease, pathologic immune conditions involving T cell activation, a cardiovascular disorder, and a CNS disorder.

[00281] In another embodiment, the present invention provides a method of treating or lessening the severity of a disease comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and a PI3K inhibitor, wherein the disease is selected from benign or malignant tumor, carcinoma or solid tumor of the brain, kidney (e.g., renal cell carcinoma (RCC)), liver, adrenal gland, bladder, breast, stomach, gastric tumors, ovaries, colon, rectum, prostate, pancreas, lung, vagina, endometrium, cervix, testis, genitourinary tract, esophagus, larynx, skin, bone or thyroid, sarcoma, glioblastomas, neuroblastomas, multiple myeloma or gastrointestinal cancer, especially colon carcinoma or colorectal adenoma or a tumor of the neck and head, an epidermal hyperproliferation, psoriasis, prostate hyperplasia, a neoplasia, a neoplasia of epithelial character, adenoma, adenocarcinoma, keratoacanthoma, epidermoid carcinoma, large cell carcinoma, non-small-cell lung carcinoma, lymphomas, (including, for example, non-Hodgkin's Lymphoma (NHL) and Hodgkin's lymphoma (also termed Hodgkin's or

Hodgkin's disease)), a mammary carcinoma, follicular carcinoma, undifferentiated carcinoma, papillary carcinoma, seminoma, melanoma, or a leukemia, diseases include Cowden syndrome, Lhermitte-Dudos disease and Bannayan-Zonana syndrome, or diseases in which the PI3K/PKB pathway is aberrantly activated, asthma of whatever type or genesis including both intrinsic (non-allergic) asthma and extrinsic (allergic) asthma, mild asthma, moderate asthma, severe asthma, bronchitic asthma, exercise-induced asthma, occupational asthma and asthma induced following bacterial infection, acute lung injury (ALI), adult/acute respiratory distress syndrome (ARDS), chronic obstructive pulmonary, airways or lung disease (COPD, COAD or COLD), including chronic bronchitis or dyspnea associated therewith, emphysema, as well as exacerbation of airways hyperreactivity consequent to other drug therapy, in particular other inhaled drug therapy, bronchitis of whatever type or genesis including, but not limited to, acute, arachidic, catarrhal, croupus, chronic or phthinoid bronchitis, pneumoconiosis (an inflammatory, commonly occupational, disease of the lungs, frequently accompanied by airways obstruction, whether chronic or acute, and occasioned by repeated inhalation of dusts) of whatever type or genesis, including, for example, aluminosis, anthracosis, asbestosis, chalicosis, ptilosis, siderosis, silicosis, tabacosis and byssinosis, Loffler's syndrome, eosinophilic, pneumonia, parasitic (in particular metazoan) infestation (including tropical eosinophilia), bronchopulmonary aspergillosis, polyarteritis nodosa (including Churg-Strauss syndrome), eosinophilic granuloma and eosinophil-related disorders affecting the airways occasioned by drug-reaction, psoriasis, contact dermatitis, atopic dermatitis, alopecia areata, erythema multiforma, dermatitis herpetiformis, scleroderma, vitiligo, hypersensitivity angiitis, urticaria, bullous pemphigoid, lupus erythematosus, pemphisus, epidermolysis bullosa acquisita, conjunctivitis, keratoconjunctivitis sicca, and vernal conjunctivitis, diseases affecting the nose including allergic rhinitis, and inflammatory disease in which autoimmune reactions are implicated or having an autoimmune component or etiology, including autoimmune hematological disorders (e.g. hemolytic anemia, aplastic anemia, pure red cell anemia and idiopathic thrombocytopenia), systemic lupus erythematosus, rheumatoid arthritis, polychondritis, sclerodoma, Wegener granulamatosis, dermatomyositis, chronic active hepatitis, myasthenia gravis, Steven-Johnson syndrome, idiopathic sprue, autoimmune inflammatory bowel disease (e.g. ulcerative colitis and Crohn's disease), endocrine opthalmopathy, Grave's disease, sarcoidosis, alveolitis, chronic hypersensitivity pneumonitis, multiple sclerosis, primary biliary

cirrhosis, uveitis (anterior and posterior), keratoconjunctivitis sicca and vernal keratoconjunctivitis, interstitial lung fibrosis, psoriatic arthritis and glomerulonephritis (with and without nephrotic syndrome, e.g. including idiopathic nephrotic syndrome or minal change nephropathy, restenosis, cardiomegaly, atherosclerosis, myocardial infarction, ischemic stroke and congestive heart failure, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Huntington's disease, and cerebral ischemia, and neurodegenerative disease caused by traumatic injury, glutamate neurotoxicity and hypoxia.

[00282] In some embodiments the present invention provides a method of treating or lessening the severity of a disease comprising administering to a patient in need thereof a compound of formula **I**, formula **I′**, formula **I″**, formula **II-A**, formula **II′-A**, formula **II″-A**, formula **II-B**, formula **II′-B**, or formula **II″-B** and a Bcl-2 inhibitor, wherein the disease is an inflammatory disorder, an autoimmune disorder, a proliferative disorder, an endocrine disorder, a neurological disorder, or a disorder associated with transplantation. In some embodiments, the disorder is a proliferative disorder, lupus, or lupus nephritis. In some embodiments, the proliferative disorder is chronic lymphocytic leukemia, diffuse large B-cell lymphoma, Hodgkin's disease, small-cell lung cancer, non-small-cell lung cancer, myelodysplastic syndrome, lymphoma, a hematological neoplasm, or solid tumor.

[00283] The compounds and compositions, according to the method of the present invention, may be administered using any amount and any route of administration effective for treating or lessening the severity of an autoimmune disorder, an inflammatory disorder, a proliferative disorder, an endocrine disorder, a neurological disorder, or a disorder associated with transplantation. The exact amount required will vary from subject to subject, depending on the species, age, and general condition of the subject, the severity of the infection, the particular agent, its mode of administration, and the like. Compounds of the invention are preferably formulated in dosage unit form for ease of administration and uniformity of dosage. The expression "dosage unit form" as used herein refers to a physically discrete unit of agent appropriate for the patient to be treated. It will be understood, however, that the total daily usage of the compounds and compositions of the present invention will be decided by the attending physician within the scope of sound medical judgment. The specific effective dose level for any particular patient or organism will depend upon a variety of factors including the disorder being treated and the severity of the

disorder; the activity of the specific compound employed; the specific composition employed; the age, body weight, general health, sex and diet of the patient; the time of administration, route of administration, and rate of excretion of the specific compound employed; the duration of the treatment; drugs used in combination or coincidental with the specific compound employed, and like factors well known in the medical arts. The term "patient", as used herein, means an animal, preferably a mammal, and most preferably a human.

[00284] Pharmaceutically acceptable compositions of this invention can be administered to humans and other animals orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments, or drops), bucally, as an oral or nasal spray, or the like, depending on the severity of the infection being treated. In certain embodiments, the compounds of the invention may be administered orally or parenterally at dosage levels of about 0.01 mg/kg to about 50 mg/kg and preferably from about 1 mg/kg to about 25 mg/kg, of subject body weight per day, one or more times a day, to obtain the desired therapeutic effect.

[00285] Liquid dosage forms for oral administration include, but are not limited to, pharmaceutically acceptable emulsions, microemulsions, solutions, suspensions, syrups and elixirs. In addition to the active compounds, the liquid dosage forms may contain inert diluents commonly used in the art such as, for example, water or other solvents, solubilizing agents and emulsifiers such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethylformamide, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor, and sesame oils), glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan, and mixtures thereof. Besides inert diluents, the oral compositions can also include adjuvants such as wetting agents, emulsifying and suspending agents, sweetening, flavoring, and perfuming agents.

[00286] Injectable preparations, for example, sterile injectable aqueous or oleaginous suspensions may be formulated according to the known art using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation may also be a sterile injectable solution, suspension or emulsion in a nontoxic parenterally acceptable diluent or solvent, for example, as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, U.S.P. and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose

any bland fixed oil can be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid are used in the preparation of injectables.

[00287] Injectable formulations can be sterilized, for example, by filtration through a bacterial-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions which can be dissolved or dispersed in sterile water or other sterile injectable medium prior to use.

[00288] In order to prolong the effect of a compound of the present invention, it is often desirable to slow the absorption of the compound from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material with poor water solubility. The rate of absorption of the compound then depends upon its rate of dissolution that, in turn, may depend upon crystal size and crystalline form. Alternatively, delayed absorption of a parenterally administered compound form is accomplished by dissolving or suspending the compound in an oil vehicle. Injectable depot forms are made by forming microencapsule matrices of the compound in biodegradable polymers such as polylactide-polyglycolide. Depending upon the ratio of compound to polymer and the nature of the particular polymer employed, the rate of compound release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the compound in liposomes or microemulsions that are compatible with body tissues.

[00289] Compositions for rectal or vaginal administration are preferably suppositories which can be prepared by mixing the compounds of this invention with suitable non-irritating excipients or carriers such as cocoa butter, polyethylene glycol or a suppository wax which are solid at ambient temperature but liquid at body temperature and therefore melt in the rectum or vaginal cavity and release the active compound.

[00290] Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound is mixed with at least one inert, pharmaceutically acceptable excipient or carrier such as sodium citrate or dicalcium phosphate and/or a) fillers or extenders such as starches, lactose, sucrose, glucose, mannitol, and silicic acid, b) binders such as, for example, carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidinone, sucrose, and acacia, c) humectants such as glycerol, d) disintegrating agents such as agar--agar, calcium carbonate, potato or tapioca starch, alginic acid, certain

silicates, and sodium carbonate, e) solution retarding agents such as paraffin, f) absorption accelerators such as quaternary ammonium compounds, g) wetting agents such as, for example, cetyl alcohol and glycerol monostearate, h) absorbents such as kaolin and bentonite clay, and i) lubricants such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof. In the case of capsules, tablets and pills, the dosage form may also comprise buffering agents.

[00291] Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugar as well as high molecular weight polyethylene glycols and the like. The solid dosage forms of tablets, dragees, capsules, pills, and granules can be prepared with coatings and shells such as enteric coatings and other coatings well known in the pharmaceutical formulating art. They may optionally contain opacifying agents and can also be of a composition that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally, in a delayed manner. Examples of embedding compositions that can be used include polymeric substances and waxes. Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugar as well as high molecular weight polethylene glycols and the like.

[00292] The active compounds can also be in micro-encapsulated form with one or more excipients as noted above. The solid dosage forms of tablets, dragees, capsules, pills, and granules can be prepared with coatings and shells such as enteric coatings, release controlling coatings and other coatings well known in the pharmaceutical formulating art. In such solid dosage forms the active compound may be admixed with at least one inert diluent such as sucrose, lactose or starch. Such dosage forms may also comprise, as is normal practice, additional substances other than inert diluents, e.g., tableting lubricants and other tableting aids such a magnesium stearate and microcrystalline cellulose. In the case of capsules, tablets and pills, the dosage forms may also comprise buffering agents. They may optionally contain opacifying agents and can also be of a composition that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally, in a delayed manner. Examples of embedding compositions that can be used include polymeric substances and waxes.

[00293] Dosage forms for topical or transdermal administration of a compound of this invention include ointments, pastes, creams, lotions, gels, powders, solutions, sprays, inhalants or patches. The active component is admixed under sterile conditions with a pharmaceutically acceptable carrier and any needed preservatives or buffers as may be required. Ophthalmic formulation, ear drops, and eye drops are also contemplated as being within the scope of this invention. Additionally, the present invention contemplates the use of transdermal patches, which have the added advantage of providing controlled delivery of a compound to the body. Such dosage forms can be made by dissolving or dispensing the compound in the proper medium. Absorption enhancers can also be used to increase the flux of the compound across the skin. The rate can be controlled by either providing a rate controlling membrane or by dispersing the compound in a polymer matrix or gel.

[00294] According to one embodiment, the invention relates to a method of modulating CRBN activity in a biological sample comprising the step of contacting said biological sample with a compound of this invention, or a composition comprising said compound.

[00295] According to another embodiment, the invention relates to a method of binding CRBN, or a mutant thereof, activity in a biological sample comprising the step of contacting said biological sample with a compound of this invention, or a composition comprising said compound.

[00296] The term "biological sample", as used herein, includes, without limitation, cell cultures or extracts thereof; biopsied material obtained from a mammal or extracts thereof; and blood, saliva, urine, feces, semen, tears, or other body fluids or extracts thereof.

[00297] Binding CRBN (or a mutant thereof) activity in a biological sample is useful for a variety of purposes that are known to one of skill in the art. Examples of such purposes include, but are not limited to, biological specimen storage and biological assays.

[00298] Another embodiment of the present invention relates to a method of modulating CRBN activity in a patient comprising the step of administering to said patient a compound of the present invention, or a composition comprising said compound.

[00299] According to another embodiment, the invention relates to a method of modulating the activity of CRBN, or a mutant thereof, in a patient comprising the step of administering to said patient a compound of the present invention, or a composition comprising said compound. According to certain embodiments, the invention relates to a method of reversibly or irreversibly

modulating one or more of CRBN, or a mutant thereof, activity in a patient comprising the step of administering to said patient a compound of the present invention, or a composition comprising said compound. In other embodiments, the present invention provides a method for treating a disorder mediated by CRBN, or a mutant thereof, in a patient in need thereof, comprising the step of administering to said patient a compound according to the present invention or pharmaceutically acceptable composition thereof. Such disorders are described in detail herein.

[00300] Depending upon the particular condition, or disease, to be treated, additional therapeutic agents that are normally administered to treat that condition, may also be present in the compositions of this invention. As used herein, additional therapeutic agents that are normally administered to treat a particular disease, or condition, are known as "appropriate for the disease, or condition, being treated."

[00301] A compound of the current invention may also be used to advantage in combination with other therapeutic compounds. In some embodiments, the other therapeutic compounds are antiproliferative compounds. Such antiproliferative compounds include, but are not limited to aromatase inhibitors; antiestrogens; topoisomerase I inhibitors; topoisomerase II inhibitors; microtubule active compounds; alkylating compounds; histone deacetylase inhibitors; compounds which induce cell differentiation processes; cyclooxygenase inhibitors; MMP inhibitors; mTOR inhibitors; antineoplastic antimetabolites; platin compounds; compounds targeting/decreasing a protein or lipid kinase activity and further anti-angiogenic compounds; compounds which target, decrease or inhibit the activity of a protein or lipid phosphatase; gonadorelin agonists; anti-androgens; methionine aminopeptidase inhibitors; matrix metalloproteinase inhibitors; bisphosphonates; biological response modifiers; antiproliferative antibodies; heparanase inhibitors; inhibitors of Ras oncogenic isoforms; telomerase inhibitors; proteasome inhibitors; compounds used in the treatment of hematologic malignancies; compounds which target, decrease or inhibit the activity of Flt-3; Hsp90 inhibitors such as 17-AAG (17-allylaminogeldanamycin, NSC330507), 17-DMAG (17-dimethylaminoethylamino-17-demethoxy-geldanamycin, NSC707545), IPI-504, CNF1010, CNF2024, CNF1010 from Conforma Therapeutics; temozolomide (Temodal®); kinesin spindle protein inhibitors, such as SB715992 or SB743921 from GlaxoSmithKline, or pentamidine/chlorpromazine from CombinatoRx; MEK inhibitors such as ARRY142886 from Array BioPharma, AZD6244 from AstraZeneca, PD181461 from Pfizer

and leucovorin. The term "aromatase inhibitor" as used herein relates to a compound which inhibits estrogen production, for instance, the conversion of the substrates androstenedione and testosterone to estrone and estradiol, respectively. The term includes, but is not limited to steroids, especially atamestane, exemestane and formestane and, in particular, non-steroids, especially aminoglutethimide, roglethimide, pyridoglutethimide, trilostane, testolactone, ketokonazole, vorozole, fadrozole, anastrozole and letrozole. Exemestane is marketed under the trade name Aromasin™. Formestane is marketed under the trade name Lentaron™. Fadrozole is marketed under the trade name Afema™. Anastrozole is marketed under the trade name Arimidex™. Letrozole is marketed under the trade names Femara™ or Femar™. Aminoglutethimide is marketed under the trade name Orimeten™. A combination of the invention comprising a chemotherapeutic agent which is an aromatase inhibitor is particularly useful for the treatment of hormone receptor positive tumors, such as breast tumors.

[00302] The term "antiestrogen" as used herein relates to a compound which antagonizes the effect of estrogens at the estrogen receptor level. The term includes, but is not limited to tamoxifen, fulvestrant, raloxifene and raloxifene hydrochloride. Tamoxifen is marketed under the trade name Nolvadex™. Raloxifene hydrochloride is marketed under the trade name Evista™. Fulvestrant can be administered under the trade name Faslodex™. A combination of the invention comprising a chemotherapeutic agent which is an antiestrogen is particularly useful for the treatment of estrogen receptor positive tumors, such as breast tumors.

[00303] The term "anti-androgen" as used herein relates to any substance which is capable of inhibiting the biological effects of androgenic hormones and includes, but is not limited to, bicalutamide (Casodex™). The term "gonadorelin agonist" as used herein includes, but is not limited to abarelix, goserelin and goserelin acetate. Goserelin can be administered under the trade name Zoladex™.

[00304] The term "topoisomerase I inhibitor" as used herein includes, but is not limited to topotecan, gimatecan, irinotecan, camptothecian and its analogues, 9-nitrocamptothecin and the macromolecular camptothecin conjugate PNU-166148. Irinotecan can be administered, e.g. in the form as it is marketed, e.g. under the trademark Camptosar™. Topotecan is marketed under the trade name Hycamptin™.

[00305] The term "topoisomerase II inhibitor" as used herein includes, but is not limited to the anthracyclines such as doxorubicin (including liposomal formulation, such as Caelyx™), daunorubicin, epirubicin, idarubicin and nemorubicin, the anthraquinones mitoxantrone and losoxantrone, and the podophillotoxines etoposide and teniposide. Etoposide is marketed under the trade name Etopophos™. Teniposide is marketed under the trade name VM 26-Bristol Doxorubicin is marketed under the trade name Acriblastin ™ or Adriamycin™. Epirubicin is marketed under the trade name Farmorubicin™. Idarubicin is marketed. under the trade name Zavedos™. Mitoxantrone is marketed under the trade name Novantron.

[00306] The term "microtubule active agent" relates to microtubule stabilizing, microtubule destabilizing compounds and microtublin polymerization inhibitors including, but not limited to taxanes, such as paclitaxel and docetaxel; vinca alkaloids, such as vinblastine or vinblastine sulfate, vincristine or vincristine sulfate, and vinorelbine; discodermolides; cochicine and epothilones and derivatives thereof. Paclitaxel is marketed under the trade name Taxol™. Docetaxel is marketed under the trade name Taxotere™. Vinblastine sulfate is marketed under the trade name Vinblastin R.P™. Vincristine sulfate is marketed under the trade name Farmistin™.

[00307] The term "alkylating agent" as used herein includes, but is not limited to, cyclophosphamide, ifosfamide, melphalan or nitrosourea (BCNU or Gliadel). Cyclophosphamide is marketed under the trade name Cyclostin™. Ifosfamide is marketed under the trade name Holoxan™.

[00308] The term "histone deacetylase inhibitors" or "HDAC inhibitors" relates to compounds which inhibit the histone deacetylase and which possess antiproliferative activity. This includes, but is not limited to, suberoylanilide hydroxamic acid (SAHA).

[00309] The term "antineoplastic antimetabolite" includes, but is not limited to, 5-fluorouracil or 5-FU, capecitabine, gemcitabine, DNA demethylating compounds, such as 5-azacytidine and decitabine, methotrexate and edatrexate, and folic acid antagonists such as pemetrexed. Capecitabine is marketed under the trade name Xeloda™. Gemcitabine is marketed under the trade name Gemzar™.

[00310] The term "platin compound" as used herein includes, but is not limited to, carboplatin, cis-platin, cisplatinum and oxaliplatin. Carboplatin can be administered, e.g., in the form as it is

marketed, e.g. under the trademark Carboplat™. Oxaliplatin can be administered, e.g., in the form as it is marketed, e.g. under the trademark Eloxatin™.

[00311] The term "compounds targeting/decreasing a protein or lipid kinase activity; or a protein or lipid phosphatase activity; or further anti-angiogenic compounds" as used herein includes, but is not limited to, protein tyrosine kinase and/or serine and/or threonine kinase inhibitors or lipid kinase inhibitors, such as a) compounds targeting, decreasing or inhibiting the activity of the platelet-derived growth factor-receptors (PDGFR), such as compounds which target, decrease or inhibit the activity of PDGFR, especially compounds which inhibit the PDGF receptor, such as an N-phenyl-2-pyrimidine-amine derivative, such as imatinib, SU101, SU6668 and GFB-111; b) compounds targeting, decreasing or inhibiting the activity of the fibroblast growth factor-receptors (FGFR); c) compounds targeting, decreasing or inhibiting the activity of the insulin-like growth factor receptor I (IGF-IR), such as compounds which target, decrease or inhibit the activity of IGF-IR, especially compounds which inhibit the kinase activity of IGF-I receptor, or antibodies that target the extracellular domain of IGF-I receptor or its growth factors; d) compounds targeting, decreasing or inhibiting the activity of the Trk receptor tyrosine kinase family, or ephrin B4 inhibitors; e) compounds targeting, decreasing or inhibiting the activity of the AxI receptor tyrosine kinase family; f) compounds targeting, decreasing or inhibiting the activity of the Ret receptor tyrosine kinase; g) compounds targeting, decreasing or inhibiting the activity of the Kit/SCFR receptor tyrosine kinase, such as imatinib; h) compounds targeting, decreasing or inhibiting the activity of the C-kit receptor tyrosine kinases, which are part of the PDGFR family, such as compounds which target, decrease or inhibit the activity of the c-Kit receptor tyrosine kinase family, especially compounds which inhibit the c-Kit receptor, such as imatinib; i) compounds targeting, decreasing or inhibiting the activity of members of the c-Abl family, their gene-fusion products (e.g. BCR-Abl kinase) and mutants, such as compounds which target decrease or inhibit the activity of c-Abl family members and their gene fusion products, such as an N-phenyl-2-pyrimidine-amine derivative, such as imatinib or nilotinib (AMN107); PD180970; AG957; NSC 680410; PD173955 from ParkeDavis; or dasatinib (BMS-354825); j) compounds targeting, decreasing or inhibiting the activity of members of the protein kinase C (PKC) and Raf family of serine/threonine kinases, members of the MEK, SRC, JAK/pan-JAK, FAK, PDK1, PKB/Akt, Ras/MAPK, PI3K, SYK, BTK and TEC family, and/or members of the cyclin-

dependent kinase family (CDK) including staurosporine derivatives, such as midostaurin; examples of further compounds include UCN-01, safingol, BAY 43-9006, Bryostatin 1, Perifosine; llmofosine; RO 318220 and RO 320432; GO 6976; lsis 3521; LY333531/LY379196; isochinoline compounds; FTIs; PD184352 or QAN697 (a P13K inhibitor) or AT7519 (CDK inhibitor); k) compounds targeting, decreasing or inhibiting the activity of protein-tyrosine kinase inhibitors, such as compounds which target, decrease or inhibit the activity of protein-tyrosine kinase inhibitors include imatinib mesylate (Gleevec™) or tyrphostin such as Tyrphostin A23/RG-50810; AG 99; Tyrphostin AG 213; Tyrphostin AG 1748; Tyrphostin AG 490; Tyrphostin B44; Tyrphostin B44 (+) enantiomer; Tyrphostin AG 555; AG 494; Tyrphostin AG 556, AG957 and adaphostin (4-{[(2,5- dihydroxyphenyl)methyl]amino}-benzoic acid adamantyl ester; NSC 680410, adaphostin); l) compounds targeting, decreasing or inhibiting the activity of the epidermal growth factor family of receptor tyrosine kinases ($EGFR_1$ ErbB2, ErbB3, ErbB4 as homo- or heterodimers) and their mutants, such as compounds which target, decrease or inhibit the activity of the epidermal growth factor receptor family are especially compounds, proteins or antibodies which inhibit members of the EGF receptor tyrosine kinase family, such as EGF receptor, ErbB2, ErbB3 and ErbB4 or bind to EGF or EGF related ligands, CP 358774, ZD 1839, ZM 105180; trastuzumab (Herceptin™), cetuximab (Erbitux™), Iressa, Tarceva, OSI-774, Cl-1033, EKB-569, GW-2016, E1.1, E2.4, E2.5, E6.2, E6.4, E2.11, E6.3 or E7.6.3, and 7H-pyrrolo-[2,3-d]pyrimidine derivatives; m) compounds targeting, decreasing or inhibiting the activity of the c-Met receptor, such as compounds which target, decrease or inhibit the activity of c-Met, especially compounds which inhibit the kinase activity of c-Met receptor, or antibodies that target the extracellular domain of c-Met or bind to HGF, n) compounds targeting, decreasing or inhibiting the kinase activity of one or more JAK family members (JAK1/JAK2/JAK3/TYK2 and/or pan-JAK), including but not limited to PRT-062070, SB-1578, baricitinib, pacritinib, momelotinib, VX-509, AZD-1480, TG-101348, tofacitinib, and ruxolitinib; o) compounds targeting, decreasing or inhibiting the kinase activity of PI3 kinase (PI3K) including but not limited to ATU-027, SF-1126, DS-7423, PBI-05204, GSK-2126458, ZSTK-474, buparlisib, pictrelisib, PF-4691502, BYL-719, dactolisib, XL-147, XL-765, and idelalisib; and; and q) compounds targeting, decreasing or inhibiting the signaling effects of hedgehog protein (Hh) or smoothened receptor (SMO) pathways,

including but not limited to cyclopamine, vismodegib, itraconazole, erismodegib, and IPI-926 (saridegib).

[00312] The term "PI3K inhibitor" as used herein includes, but is not limited to compounds having inhibitory activity against one or more enzymes in the phosphatidylinositol-3-kinase family, including, but not limited to PI3Kα, PI3Kγ, PI3Kδ, PI3Kβ, PI3K-C2α, PI3K-C2β, PI3K-C2γ, Vps34, p110-α, p110-β, p110-γ, p110-δ, p85-α, p85-β, p55-γ, p150, p101, and p87. Examples of PI3K inhibitors useful in this invention include but are not limited to ATU-027, SF-1126, DS-7423, PBI-05204, GSK-2126458, ZSTK-474, buparlisib, pictrelisib, PF-4691502, BYL-719, dactolisib, XL-147, XL-765, and idelalisib.

[00313] The term "BTK inhibitor" as used herein includes, but is not limited to compounds having inhibitory activity against Bruton's Tyrosine Kinase (BTK), including, but not limited to AVL-292 and ibrutinib.

[00314] The term "SYK inhibitor" as used herein includes, but is not limited to compounds having inhibitory activity against spleen tyrosine kinase (SYK), including but not limited to PRT-062070, R-343, R-333, Excellair, PRT-062607, and fostamatinib.

[00315] The term "Bcl-2 inhibitor" as used herein includes, but is not limited to compounds having inhibitory activity against B-cell lymphoma 2 protein (Bcl-2), including but not limited to ABT-199, ABT-731, ABT-737, apogossypol, Ascenta's pan-Bcl-2 inhibitors, curcumin (and analogs thereof), dual Bcl-2/Bcl-xL inhibitors (Infinity Pharmaceuticals/Novartis Pharmaceuticals), Genasense (G3139), HA14-1 (and analogs thereof; see WO2008118802), navitoclax (and analogs thereof, see US7390799), NH-1 (Shenayng Pharmaceutical University), obatoclax (and analogs thereof, see WO2004106328), S-001 (Gloria Pharmaceuticals), TW series compounds (Univ. of Michigan), and venetoclax. In some embodiments the Bcl-2 inhibitor is a small molecule therapeutic. In some embodiments the Bcl-2 inhibitor is a peptidomimetic.

[00316] Further examples of BTK inhibitory compounds, and conditions treatable by such compounds in combination with compounds of this invention can be found in WO2008039218 and WO2011090760, the entirety of which are incorporated herein by reference.

[00317] Further examples of SYK inhibitory compounds, and conditions treatable by such compounds in combination with compounds of this invention can be found in WO2003063794, WO2005007623, and WO2006078846, the entirety of which are incorporated herein by reference.

[00318] Further examples of PI3K inhibitory compounds, and conditions treatable by such compounds in combination with compounds of this invention can be found in WO2004019973, WO2004089925, WO2007016176, US8138347, WO2002088112, WO2007084786, WO2007129161, WO2006122806, WO2005113554, and WO2007044729 the entirety of which are incorporated herein by reference.

[00319] Further examples of JAK inhibitory compounds, and conditions treatable by such compounds in combination with compounds of this invention can be found in WO2009114512, WO2008109943, WO2007053452, WO2000142246, and WO2007070514, the entirety of which are incorporated herein by reference.

[00320] Further anti-angiogenic compounds include compounds having another mechanism for their activity, e.g. unrelated to protein or lipid kinase inhibition e.g. thalidomide (Thalomid™) and TNP-470.

[00321] Examples of proteasome inhibitors useful for use in combination with compounds of the invention include, but are not limited to bortezomib, disulfiram, epigallocatechin-3-gallate (EGCG), salinosporamide A, carfilzomib, ONX-0912, CEP-18770, and MLN9708.

[00322] Compounds which target, decrease or inhibit the activity of a protein or lipid phosphatase are e.g. inhibitors of phosphatase 1, phosphatase 2A, or CDC25, such as okadaic acid or a derivative thereof.

[00323] Compounds which induce cell differentiation processes include, but are not limited to, retinoic acid, α- γ- or δ- tocopherol or α- γ- or δ-tocotrienol.

[00324] The term cyclooxygenase inhibitor as used herein includes, but is not limited to, Cox-2 inhibitors, 5-alkyl substituted 2-arylaminophenylacetic acid and derivatives, such as celecoxib (Celebrex™), rofecoxib (Vioxx™), etoricoxib, valdecoxib or a 5-alkyl-2- arylaminophenylacetic acid, such as 5-methyl-2-(2'-chloro-6'-fluoroanilino)phenyl acetic acid, lumiracoxib.

[00325] The term "bisphosphonates" as used herein includes, but is not limited to, etridonic, clodronic, tiludronic, pamidronic, alendronic, ibandronic, risedronic and zoledronic acid. Etridonic acid is marketed under the trade name Didronel™. Clodronic acid is marketed under the trade name Bonefos™. Tiludronic acid is marketed under the trade name Skelid™. Pamidronic acid is marketed under the trade name Aredia™. Alendronic acid is marketed under the trade name Fosamax™. Ibandronic acid is marketed under the trade name Bondranat™. Risedronic acid is

marketed under the trade name Actonel™. Zoledronic acid is marketed under the trade name Zometa™. The term "mTOR inhibitors" relates to compounds which inhibit the mammalian target of rapamycin (mTOR) and which possess antiproliferative activity such as sirolimus (Rapamune®), everolimus (Certican™), CCI-779 and ABT578.

[00326] The term "heparanase inhibitor" as used herein refers to compounds which target, decrease or inhibit heparin sulfate degradation. The term includes, but is not limited to, PI-88. The term "biological response modifier" as used herein refers to a lymphokine or interferons.

[00327] The term "inhibitor of Ras oncogenic isoforms", such as H-Ras, K-Ras, or N-Ras, as used herein refers to compounds which target, decrease or inhibit the oncogenic activity of Ras; for example, a "farnesyl transferase inhibitor" such as L-744832, DK8G557 or R115777 (Zarnestra™). The term "telomerase inhibitor" as used herein refers to compounds which target, decrease or inhibit the activity of telomerase. Compounds which target, decrease or inhibit the activity of telomerase are especially compounds which inhibit the telomerase receptor, such as telomestatin.

[00328] The term "methionine aminopeptidase inhibitor" as used herein refers to compounds which target, decrease or inhibit the activity of methionine aminopeptidase. Compounds which target, decrease or inhibit the activity of methionine aminopeptidase include, but are not limited to, bengamide or a derivative thereof.

[00329] The term "proteasome inhibitor" as used herein refers to compounds which target, decrease or inhibit the activity of the proteasome. Compounds which target, decrease or inhibit the activity of the proteasome include, but are not limited to, Bortezomib (Velcade™) and MLN 341.

[00330] The term "matrix metalloproteinase inhibitor" or ("MMP" inhibitor) as used herein includes, but is not limited to, collagen peptidomimetic and nonpeptidomimetic inhibitors, tetracycline derivatives, e.g. hydroxamate peptidomimetic inhibitor batimastat and its orally bioavailable analogue marimastat (BB-2516), prinomastat (AG3340), metastat (NSC 683551) BMS-279251, BAY 12-9566, TAA211, MMI270B or AAJ996.

[00331] The term "compounds used in the treatment of hematologic malignancies" as used herein includes, but is not limited to, FMS-like tyrosine kinase inhibitors, which are compounds targeting, decreasing or inhibiting the activity of FMS-like tyrosine kinase receptors (Flt-3R);

interferon, 1-β-D-arabinofuransylcytosine (ara-c) and bisulfan; ALK inhibitors, which are compounds which target, decrease or inhibit anaplastic lymphoma kinase, and Bcl-2 inhibitors.

[00332] Compounds which target, decrease or inhibit the activity of FMS-like tyrosine kinase receptors (Flt-3R) are especially compounds, proteins or antibodies which inhibit members of the Flt-3R receptor kinase family, such as PKC412, midostaurin, a staurosporine derivative, SU11248 and MLN518.

[00333] The term "HSP90 inhibitors" as used herein includes, but is not limited to, compounds targeting, decreasing or inhibiting the intrinsic ATPase activity of HSP90; degrading, targeting, decreasing or inhibiting the HSP90 client proteins via the ubiquitin proteosome pathway. Compounds targeting, decreasing or inhibiting the intrinsic ATPase activity of HSP90 are especially compounds, proteins or antibodies which inhibit the ATPase activity of HSP90, such as 17-allylamino,17-demethoxygeldanamycin (17AAG), a geldanamycin derivative; other geldanamycin related compounds; radicicol and HDAC inhibitors.

[00334] The term "antiproliferative antibodies" as used herein includes, but is not limited to, trastuzumab (Herceptin™), Trastuzumab-DM1, erbitux, bevacizumab (Avastin™), rituximab (Rituxan®), PRO64553 (anti-CD40) and 2C4 Antibody. By antibodies is meant intact monoclonal antibodies, polyclonal antibodies, multispecific antibodies formed from at least 2 intact antibodies, and antibodies fragments so long as they exhibit the desired biological activity.

[00335] For the treatment of acute myeloid leukemia (AML), compounds of the current invention can be used in combination with standard leukemia therapies, especially in combination with therapies used for the treatment of AML. In particular, compounds of the current invention can be administered in combination with, for example, farnesyl transferase inhibitors and/or other drugs useful for the treatment of AML, such as Daunorubicin, Adriamycin, Ara-C, VP-16, Teniposide, Mitoxantrone, Idarubicin, Carboplatinum and PKC412. In some embodiments, the present invention provides a method of treating AML associated with an ITD and/or D835Y mutation, comprising administering a compound of the present invention together with a one or more FLT3 inhibitors. In some embodiments, the FLT3 inhibitors are selected from quizartinib (AC220), a staurosporine derivative (*e.g.* midostaurin or lestaurtinib), sorafenib, tandutinib, LY-2401401, LS-104, EB-10, famitinib, NOV-110302, NMS-P948, AST-487, G-749, SB-1317,

S-209, SC-110219, AKN-028, fedratinib, tozasertib, and sunitinib. In some embodiments, the FLT3 inhibitors are selected from quizartinib, midostaurin, lestaurtinib, sorafenib, and sunitinib.

[00336] Other anti-leukemic compounds include, for example, Ara-C, a pyrimidine analog, which is the 2'-alpha-hydroxy ribose (arabinoside) derivative of deoxycytidine. Also included is the purine analog of hypoxanthine, 6-mercaptopurine (6-MP) and fludarabine phosphate. Compounds which target, decrease or inhibit activity of histone deacetylase (HDAC) inhibitors such as sodium butyrate and suberoylanilide hydroxamic acid (SAHA) inhibit the activity of the enzymes known as histone deacetylases. Specific HDAC inhibitors include MS275, SAHA, FK228 (formerly FR901228), Trichostatin A and compounds disclosed in US 6,552,065 including, but not limited to, N-hydroxy-3-[4-[[[2-(2-methyl-1H-indol-3-yl)-ethyl]- amino]methyl]phenyl]-2E-2-propenamide, or a pharmaceutically acceptable salt thereof and N-hydroxy-3-[4-[(2-hydroxyethyl){2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2- propenamide, or a pharmaceutically acceptable salt thereof, especially the lactate salt. Somatostatin receptor antagonists as used herein refer to compounds which target, treat or inhibit the somatostatin receptor such as octreotide, and SOM230. Tumor cell damaging approaches refer to approaches such as ionizing radiation. The term "ionizing radiation" referred to above and hereinafter means ionizing radiation that occurs as either electromagnetic rays (such as X-rays and gamma rays) or particles (such as alpha and beta particles). Ionizing radiation is provided in, but not limited to, radiation therapy and is known in the art. See Hellman, Principles of Radiation Therapy, Cancer, in Principles and Practice of Oncology, Devita et al., Eds., 4th Edition, Vol. 1, pp. 248-275 (1993).

[00337] Also included are EDG binders and ribonucleotide reductase inhibitors. The term "EDG binders" as used herein refers to a class of immunosuppressants that modulates lymphocyte recirculation, such as FTY720. The term "ribonucleotide reductase inhibitors" refers to pyrimidine or purine nucleoside analogs including, but not limited to, fludarabine and/or cytosine arabinoside (ara-C), 6-thioguanine, 5-fluorouracil, cladribine, 6-mercaptopurine (especially in combination with ara-C against ALL) and/or pentostatin. Ribonucleotide reductase inhibitors are especially hydroxyurea or 2-hydroxy-1H-isoindole-1,3-dione derivatives.

[00338] Also included are in particular those compounds, proteins or monoclonal antibodies of VEGF such as 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine or a pharmaceutically acceptable salt thereof, 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine succinate;

Angiostatin™; Endostatin™; anthranilic acid amides; ZD4190; ZD6474; SU5416; SU6668; bevacizumab; or anti-VEGF antibodies or anti-VEGF receptor antibodies, such as rhuMAb and RHUFab, VEGF aptamer such as Macugon; FLT-4 inhibitors, FLT-3 inhibitors, VEGFR-2 IgGI antibody, Angiozyme (RPI 4610) and Bevacizumab (Avastin™).

[00339] Photodynamic therapy as used herein refers to therapy which uses certain chemicals known as photosensitizing compounds to treat or prevent cancers. Examples of photodynamic therapy include treatment with compounds, such as Visudyne™ and porfimer sodium.

[00340] Angiostatic steroids as used herein refers to compounds which block or inhibit angiogenesis, such as, e.g., anecortave, triamcinolone, hydrocortisone, 11-α-epihydrocotisol, cortexolone, 17α-hydroxyprogesterone, corticosterone, desoxycorticosterone, testosterone, estrone and dexamethasone.

[00341] Implants containing corticosteroids refers to compounds, such as fluocinolone and dexamethasone.

[00342] Other chemotherapeutic compounds include, but are not limited to, plant alkaloids, hormonal compounds and antagonists; biological response modifiers, preferably lymphokines or interferons; antisense oligonucleotides or oligonucleotide derivatives; shRNA or siRNA; or miscellaneous compounds or compounds with other or unknown mechanism of action.

[00343] The compounds of the invention are also useful as co-therapeutic compounds for use in combination with other drug substances such as anti-inflammatory, bronchodilatory or antihistamine drug substances, particularly in the treatment of obstructive or inflammatory airways diseases such as those mentioned hereinbefore, for example as potentiators of therapeutic activity of such drugs or as a means of reducing required dosaging or potential side effects of such drugs. A compound of the invention may be mixed with the other drug substance in a fixed pharmaceutical composition or it may be administered separately, before, simultaneously with or after the other drug substance. Accordingly the invention includes a combination of a compound of the invention as hereinbefore described with an anti-inflammatory, bronchodilatory, antihistamine or anti-tussive drug substance, said compound of the invention and said drug substance being in the same or different pharmaceutical composition.

[00344] Suitable anti-inflammatory drugs include steroids, in particular glucocorticosteroids such as budesonide, beclamethasone dipropionate, fluticasone propionate, ciclesonide or

mometasone furoate; non-steroidal glucocorticoid receptor agonists; LTB4 antagonists such LY293111, CGS025019C, CP-195543, SC-53228, BIIL 284, ONO 4057, SB 209247; LTD4 antagonists such as montelukast and zafirlukast; PDE4 inhibitors such cilomilast (Ariflo® GlaxoSmithKline), Roflumilast (Byk Gulden),V-11294A (Napp), BAY19-8004 (Bayer), SCH-351591 (Schering- Plough), Arofylline (Almirall Prodesfarma), PD189659 / PD168787 (Parke-Davis), AWD-12- 281 (Asta Medica), CDC-801 (Celgene), SeICID(TM) CC-10004 (Celgene), VM554/UM565 (Vernalis), T-440 (Tanabe), KW-4490 (Kyowa Hakko Kogyo); A2a agonists; A2b antagonists; and beta-2 adrenoceptor agonists such as albuterol (salbutamol), metaproterenol, terbutaline, salmeterol fenoterol, procaterol, and especially, formoterol and pharmaceutically acceptable salts thereof. Suitable bronchodilatory drugs include anticholinergic or antimuscarinic compounds, in particular ipratropium bromide, oxitropium bromide, tiotropium salts and CHF 4226 (Chiesi), and glycopyrrolate.

[00345] Suitable antihistamine drug substances include cetirizine hydrochloride, acetaminophen, clemastine fumarate, promethazine, loratidine, desloratidine, diphenhydramine and fexofenadine hydrochloride, activastine, astemizole, azelastine, ebastine, epinastine, mizolastine and tefenadine.

[00346] Other useful combinations of compounds of the invention with anti-inflammatory drugs are those with antagonists of chemokine receptors, e.g. CCR-1, CCR-2, CCR-3, CCR-4, CCR-5, CCR-6, CCR-7, CCR-8, CCR-9 and CCR10, CXCR1, CXCR2, CXCR3, CXCR4, CXCR5, particularly CCR-5 antagonists such as Schering-Plough antagonists SC-351125, SCH-55700 and SCH-D, and Takeda antagonists such as N-[[4-[[[6,7-dihydro-2-(4-methylphenyl)-5H-benzo-cyclohepten-8-yl]carbonyl]amino]phenyl]-methyl]tetrahydro-N,N-dimethyl-2H-pyran-4-aminium chloride (TAK-770).

[00347] The structure of the active compounds identified by code numbers, generic or trade names may be taken from the actual edition of the standard compendium "The Merck Index" or from databases, e.g. Patents International (e.g. IMS World Publications).

[00348] A compound of the current invention may also be used in combination with known therapeutic processes, for example, the administration of hormones or radiation. In certain embodiments, a provided compound is used as a radiosensitizer, especially for the treatment of tumors which exhibit poor sensitivity to radiotherapy.

[00349] A compound of the current invention can be administered alone or in combination with one or more other therapeutic compounds, possible combination therapy taking the form of fixed combinations or the administration of a compound of the invention and one or more other therapeutic compounds being staggered or given independently of one another, or the combined administration of fixed combinations and one or more other therapeutic compounds. A compound of the current invention can besides or in addition be administered especially for tumor therapy in combination with chemotherapy, radiotherapy, immunotherapy, phototherapy, surgical intervention, or a combination of these. Long-term therapy is equally possible as is adjuvant therapy in the context of other treatment strategies, as described above. Other possible treatments are therapy to maintain the patient's status after tumor regression, or even chemopreventive therapy, for example in patients at risk.

[00350] Those additional agents may be administered separately from an inventive compound-containing composition, as part of a multiple dosage regimen. Alternatively, those agents may be part of a single dosage form, mixed together with a compound of this invention in a single composition. If administered as part of a multiple dosage regime, the two active agents may be submitted simultaneously, sequentially or within a period of time from one another normally within five hours from one another.

[00351] As used herein, the term “combination,” “combined,” and related terms refers to the simultaneous or sequential administration of therapeutic agents in accordance with this invention. For example, a compound of the present invention may be administered with another therapeutic agent simultaneously or sequentially in separate unit dosage forms or together in a single unit dosage form. Accordingly, the present invention provides a single unit dosage form comprising a compound of the current invention, an additional therapeutic agent, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

[00352] The amount of both an inventive compound and additional therapeutic agent (in those compositions which comprise an additional therapeutic agent as described above) that may be combined with the carrier materials to produce a single dosage form will vary depending upon the host treated and the particular mode of administration. Preferably, compositions of this invention should be formulated so that a dosage of between 0.01 - 100 mg/kg body weight/day of an inventive compound can be administered.

[00353] In those compositions which comprise an additional therapeutic agent, that additional therapeutic agent and the compound of this invention may act synergistically. Therefore, the amount of additional therapeutic agent in such compositions will be less than that required in a monotherapy utilizing only that therapeutic agent. In such compositions a dosage of between 0.01 – 1,000 μg/kg body weight/day of the additional therapeutic agent can be administered.

[00354] The amount of additional therapeutic agent present in the compositions of this invention will be no more than the amount that would normally be administered in a composition comprising that therapeutic agent as the only active agent. Preferably the amount of additional therapeutic agent in the presently disclosed compositions will range from about 50% to 100% of the amount normally present in a composition comprising that agent as the only therapeutically active agent.

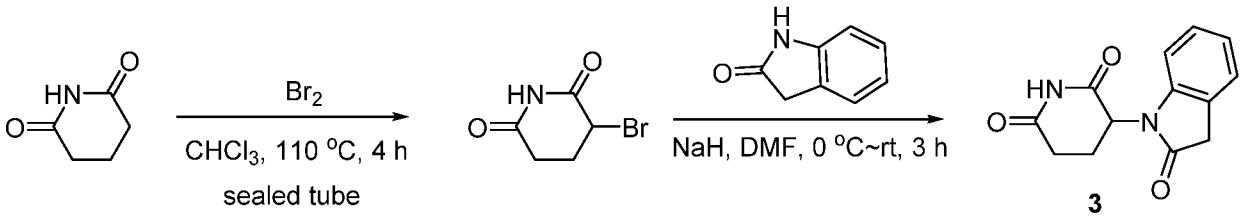
[00355] The compounds of this invention, or pharmaceutical compositions thereof, may also be incorporated into compositions for coating an implantable medical device, such as prostheses, artificial valves, vascular grafts, stents and catheters. Implantable devices coated with a compound of this invention are another embodiment of the present invention.

EXEMPLIFICATION

[00356] As depicted in the Examples below, in certain exemplary embodiments, compounds are prepared according to the following general procedures. It will be appreciated that, although the general methods depict the synthesis of certain compounds of the present invention, the following general methods, and other methods known to one of ordinary skill in the art, can be applied to all compounds and subclasses and species of each of these compounds, as described herein.

[00357] Example 1. Synthesis of 3-(2-Oxo-2,3-dihydro-1H-indol-1-yl)piperidine-2,6-dione, compound 3

Scheme 1

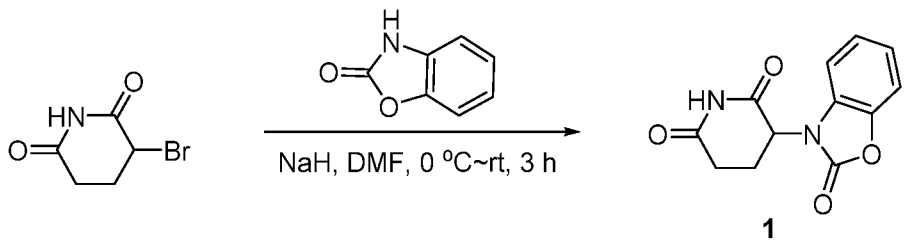


[00358] 3-Bromopiperidine-2,6-dione. To a stirred solution of piperidine-2,6-dione (5 g, 44.20 mmol) in $CHCl_3$ (10 mL) was added Br_2 (2.25 mL) in one portion at room temperature under nitrogen atmosphere. The reaction mixture was sealed in a tube and stirred for 4 hours at 110 °C. The resulting mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with 50% ethyl acetate in petroleum ether to afford 3-bromopiperidine-2,6-dione as a pink solid (3.2 g, 38%): ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.05 (br s, 1H), 4.89 (dd, J = 5.2, 3.9 Hz, 1H), 2.60 (dt, J = 9.8, 4.7 Hz, 2H), 2.46 (ddd, J = 9.6, 5.1, 3.9 Hz, 1H), 2.15 (dq, J = 14.9, 4.9 Hz, 1H); LC/MS (ESI, *m/z*): $[(M + 1)]^+$ = 192.1, 194. 1.

[00359] 3-(2-Oxo-2,3-dihydro-1*H*-indol-1-yl)piperidine-2,6-dione**.** To a stirred solution of 2,3-dihydro-1*H*-indol-2-one (228 mg, 1.71 mmol) in DMF (2 mL) was added NaH (75.3 mg, 1.88 mmol, 60% w/w dispersed into mineral oil) at 0 °C under nitrogen atmosphere. The reaction mixture was stirred for 20 min at 0 °C. To the above mixture was added dropwise a solution of 3-bromopiperidine-2,6-dione (164.4 mg, 0.86 mmol) in DMF (0.5 mL) at 0 °C. The resulting mixture was stirred for additional 3 hours at room temperature. The resulting mixture was quenched with AcOH (0.5 mL) and was concentrated under reduced pressure. The residue was purified by prep-TLC, eluted with 50% ethyl acetate in petroleum ether to afford 3-(2-oxo-2,3-dihydro-1*H*-indol-1-yl)piperidine-2,6-dione, **3**, as a light yellow solid (14.2 mg, 4%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.55 – 10.43 (m, 1H), 7.33 – 7.11 (m, 1H), 7.01 – 6.90 (m, 2H), 6.84 (t, J = 9.0 Hz, 1H), 4.09 – 3.94 (m, 1H), 2.67 – 2.59 (m, 1H), 2.47 – 2.36 (m, 1H), 2.02 – 1.72 (m, 1H), 1.62 – 1.35 (m, 1H); .LC/MS (ESI, *m/z*): $[(M + 1)]^+$ = 245.2.

[00360] **Example 2. Synthesis of 3-(2-oxobenzo[d]oxazol-3(2H)-yl)piperidine-2,6-dione, 1**

Scheme 2



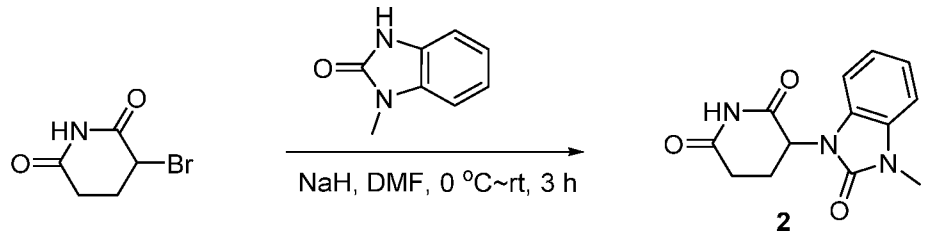
1

[00361] 3-(2-oxobenzo[d]oxazol-3(2H)-yl)piperidine-2,6-dione. To a stirred solution of 2,3-

dihydro-1,3-benzoxazol-2-one (210 mg, 1.55 mmol) in DMF (3 mL) was added NaH (68.3 mg, 1.71 mmol, 60% w/w dispersed into mineral oil) at 0 °C under nitrogen atmosphere. The reaction mixture was stirred for 20 min at 0 °C. To the above mixture was added dropwise a solution of 3-bromopiperidine-2,6-dione (149.2 mg, 0.78 mmol) in DMF (0.5 mL) at 0 °C. The resulting mixture was stirred for additional 3 hours at room temperature. The resulting mixture was quenched with AcOH (0.2 mL) and was concentrated under reduced pressure. The residue was purified by prep-TLC, eluted with 50% ethyl acetate in petroleum ether to afford 3-(2-oxo-2,3-dihydro-1,3-benzoxazol-3-yl)piperidine-2,6-dione, **1**, as a light yellow solid (30.2 mg, 8%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.23 (br s, 1H), 7.42 – 7.38 (m, 1H), 7.32 – 7.14 (m, 3H), 5.39 (dd, J = 12.8, 5.2 Hz, 1H), 2.98 – 2.80 (m, 1H), 2.78 – 2.60 (m, 2H), 2.24 – 2.11 (m, 1H); LC/MS (ESI, *m/z*): $[(M + 1)]^+ = 247.1$.

[00362] Example 3. Synthesis of 3-(3-Methyl-2-oxo-2,3-dihydro-1H-1,3-benzodiazol-1-yl)piperidine-2,6-dione, 2

Scheme 3



2

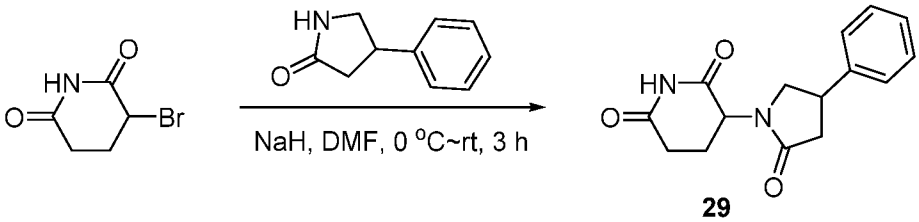
[00363] 3-(3-Methyl-2-oxo-2,3-dihydro-1*H*-1,3-benzodiazol-1-yl)piperidine-2,6-dione.

To a stirred solution of 1-methyl-2,3-dihydro-1*H*-1,3-benzodiazol-2-one (217 mg, 1.46 mmol) in DMF (2 mL) was added NaH (64.5 mg, 1.61 mmol, 60% w/w dispersed into mineral oil) at 0 °C under nitrogen atmosphere. The reaction mixture was stirred for 20 min at 0 °C. To the above mixture was added dropwise a solution of 3-bromopiperidine-2,6-dione(140.6 mg, 0.73 mmol) in DMF (0.5 mL) at 0 °C. The resulting mixture was stirred for additional 3 hours at room temperature. The resulting mixture was quenched with AcOH (0.5 mL) and was concentrated under reduced pressure. The crude product was purified by prep-HPLC with the following conditions: Column: XBridge Shield RP18 EVO Column, 5 um, 19 x 150 mm; Mobile Phase A: water (plus 0.05% FA), Mobile Phase B: ACN; Flow rate: 20 mL/min; Gradient: 10% B to 35% B in 7 min; Detector: UV 220 nm; Rt: 6.30 min. Desired fractions were collected and concentrated

under reduced pressure. The residue was lyophilized to afford 3-(3-methyl-2-oxo-2,3-dihydro-1*H*-1,3-benzodiazol-1-yl)piperidine-2,6-dione, **2**, as a white solid (30.4 mg, 21%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.03 (br s, 1H), 7.13 – 6.97 (m, 4H), 5.30 (dd, J = 12.7, 5.4 Hz, 1H), 3.35 (s, 3H), 2.90 – 2.78 (m, 1H), 2.73 – 2.49 (m, 2H), 2.03 – 1.90 (m, 1H); LC/MS (ESI, *m/z*): $[(M + 1)]^+$ = 260.2.

[00364] Example 4. Synthesis of 3-(2-Oxo-4-phenylpyrrolidin-1-yl)piperidine-2,6-dione, 29

Scheme 4



29

[00365] 3-(2-Oxo-4-phenylpyrrolidin-1-yl)piperidine-2,6-dione. To a stirred solution of 4-phenylpyrrolidin-2-one (211 mg, 1.31 mmol) in DMF (2 mL) was added NaH (57.6 mg, 1.44 mmol, 60% w/w dispersed into mineral oil) at 0 °C under nitrogen atmosphere. The reaction mixture was stirred for 20 min at 0 °C. To the above mixture was added dropwise a solution of 3-bromopiperidine-2,6-dione (125.7 mg, 0.65 mmol) in DMF (0.5 mL) at 0 °C. The resulting mixture was stirred for additional 3 hours at room temperature. The resulting mixture was quenched with AcOH (0.5 mL) and concentrated under reduced pressure. The crude product was purified by prep-HPLC with the following conditions: Column: XBridge Shield RP18 EVO Column, 5 um, 19 x 150 mm; Mobile Phase A: water (plus 0.05% FA), Mobile Phase B: ACN; Flow rate: 20 mL/min; Gradient: 15% B to 45% B in 7 min; Detector: UV 220 nm; Rt: 5.72 min). Desired fractions were collected and concentrated under reduced pressure. The residue was lyophilized to afford 3-(2-oxo-4-phenylpyrrolidin-1-yl)piperidine-2,6-dione, **29**, as a white solid (29.4 mg, 9%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.94 (br s, 1H), 7.40 – 7.31 (m, 4H), 7.27 (dt, J = 5.9, 2.8 Hz, 1H), 4.93 – 4.86 (m, 1H), 3.79 – 3.56 (m, 2H), 3.33 – 3.15 (m, 1H), 2.90 – 2.69 (m, 2H), 2.60 – 2.50 (m, 1H), 2.48 – 2.36 (m, 1H), 2.35 – 2.16 (m, 1H), 1.92 – 1.80 (m, 1H); LC/MS (ESI, *m/z*): $[(M + 1)]^+$ = 273.2.

[00366] Example 5. Time-Resolved Fluorescence Resonance Energy Transfer (TR-FRET) Assay.

[00367] Equal volumes of His-tagged CRBN-DDB1 complex (56nM) was mixed with Eu-cryptate labeled Anti-6HIS-monoclonal antibody (50x dilution from the commercial stock solution, Vender: Cisbio, Cat. #61HI2KLA) in a final buffer containing 20 mM HEPES pH 7.0, 150 mM NaCl, 0.005% Tween-20. The solution was then mixed with Cy5-labeled thalidomide (final 8nM) and various concentrations of compounds (a serial 3-fold dilution with the top concentration 200 uM). The mixture were incubated at room temperature for 1 hour. FRET signals were measured on an EnVision plate reader (Perkin Elmer) by exciting at 340 nm and recording emission at both 615 nm as no FRET control and 665 nm as the FRET signals with a 60 microsecond delay. FRET efficiency was calculated as the ratio of fluorescent signals at 665nM/615nM. Quantitative loss of FRET efficiency as a function of compound concentrations was fitted by a four-parameter Logistic Function using GraphPad Prism 7.0 and the IC50 values were reported for each compound.

[00368] **Table 2** shows the results for selected compounds in the time-resolved fluorescence resonance energy transfer (TR-FRET) assay. The compound numbers correspond to the compound numbers in the examples. Compounds having an activity designated as "A" provided an IC_{50} of <1 μM; compounds having an activity designated as "B" provided an IC_{50} of 1 -10 μM; compounds having an activity designated as "C" provided an IC_{50} of 10 -100 μM; and compounds having an activity designated as "D" provided an IC_{50} of >100 μM. For reference, the known CRBN binders provided the following IC_{50} values in the TR-FRET assay: thalidomide (IC_{50} = 2.9 μM), lenalidomide (IC_{50} = 1.17 μM) and pomalidomide (IC_{50} = 1.28 μM).

[00369] Table 2. TR-FRET Assay Results

Compound #	CRBN HTRF IC_{50} (μM)
1	A
2	A
3	C
29	B

[00370] Example 6. Fluorescence Polarization (FP) Assay.

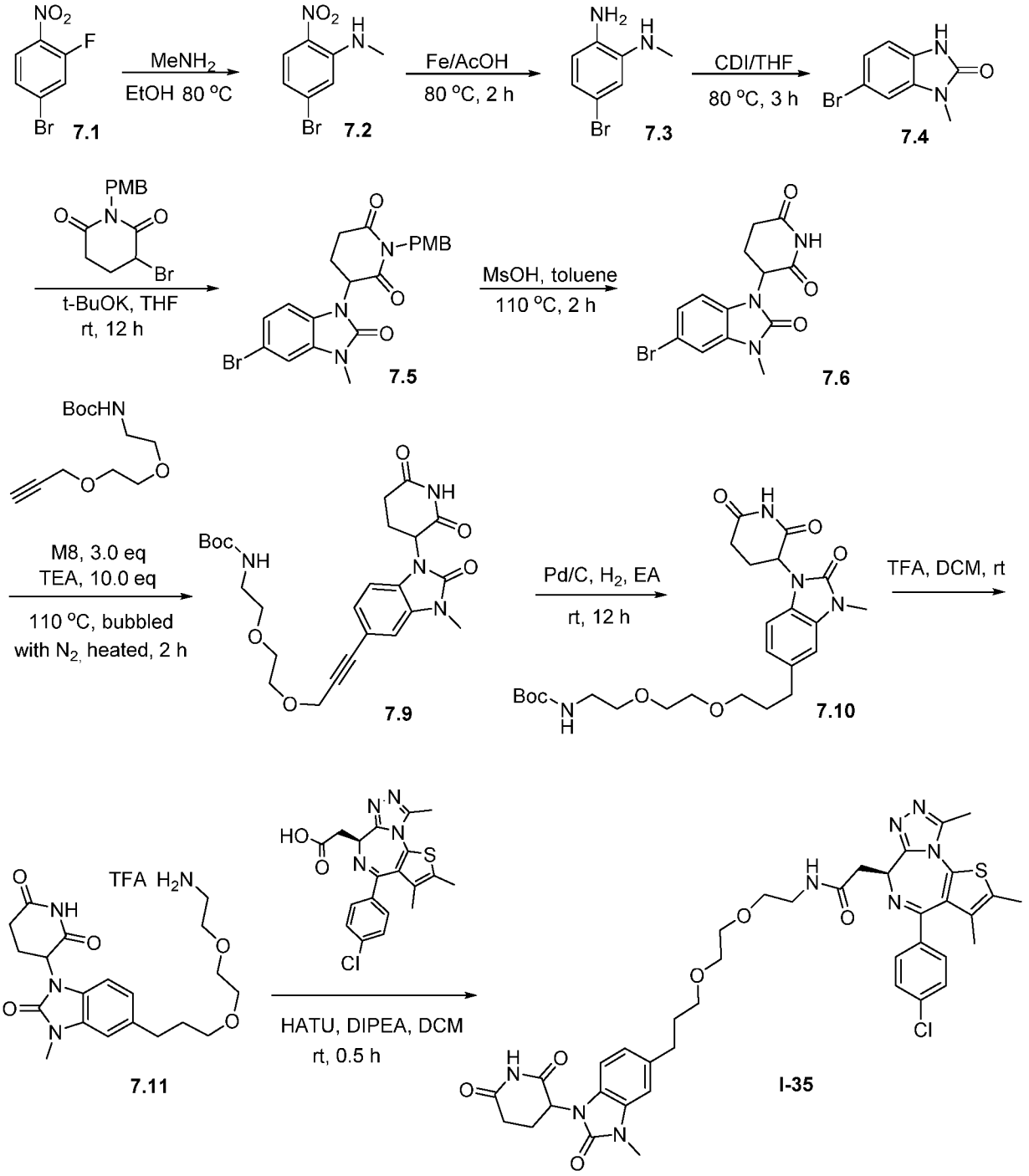
[00371] Untagged CRBN-DDB1 complex (final 50nM) was mixed with Cy5-labeled thalidomide (final 20nM) and various concentrations of compounds (a serial 3-fold dilution with the top concentration of 200uM). The final solution contained 50 mM HEPES, 200 mM NaCl and 2mM DTT, pH 7.5. The mixtures were incubated at room temperature for 10min. The FP signals were recorded on an EnVision plate reader (Perkin Elmer) using the following settings: Excitation Light (%): 100; Measurement Height: 12; G-Factor: 1; Detector Gain 1: 500; Detector Gain 2: 500; Flash Number: 100. Dose-dependent loss of FP signals was fitted by four-parameter Logistic Function using GraphPad Prism 7.0 and the IC50 values were reported for each compound.

[00372] **Table 3** shows the results for selected compounds in the fluorescence polarization (FP) assay. The compound numbers correspond to the compound numbers in the examples. Compounds having an activity designated as "A" provided an IC_{50} of <1 μM; compounds having an activity designated as "B" provided an IC_{50} of 1 -10 μM; compounds having an activity designated as "C" provided an IC_{50} of 10 -100 μM; and compounds having an activity designated as "D" provided an IC_{50} of >100 μM. For reference, the known CRBN binders provided the following IC_{50} values in the FP assay: thalidomide (IC_{50} = 2.4 μM) and pomalidomide (IC_{50} = 1.15 μM).

[00373] Table 3. Fluorescence Polarization (FP) Assay Results

CMPD #	CRBN FP IC_{50} (μM)
1	A
2	A
3	D
29	C

[00374] Example 7. Synthesis of 2-((S)-4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)-N-(2-(2-(3-(1-(2,6-dioxopiperidin-3-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)propoxy)ethoxy)ethyl)acetamide (I-35)



[00375] 5-Bromo-N-methyl-2-nitroaniline (**7.2**)

[00376] 4-Bromo-2-fluoro-1-nitrobenzene (23 g, 105 mmol) was dissolved in EtOH (20 mL), $MeNH_2$ (250 mL, 33% in EtOH) was added, the mixture was stirred at R.T overnight. When LC-MS showed the starting material was consumed, the solvent was evaporated and the resulting

crude was dissolved in EtOAc (300 mL) and washed with water (200 mL x 2) and brine (200 mL), dried over anhydrous Na_2SO_4. The solid was filtered and the filtrate was concentrated to give the crude product 5-bromo-N-methyl-2-nitroaniline as yellow solid (23 g, 95 % yield). ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 9.2 Hz, 2H), 7.01 (s, 1H), 6.76 (d, J = 9.2 Hz, 1H), 3.02 (s, 3H). LC-MS (ESI^+): m/z 232.1 $(M+H)^+$.

[00377] 5-Bromo-N1-methylbenzene-1,2-diamine (**7.3**)

[00378] 5-Bromo-N-methyl-2-nitroaniline (23.0 g, 0.100 mol) was dissolved in AcOH (230 mL), then EtOAc (230 mL) and H_2O (50 mL) were added. The mixture was warmed to 50 °C, then Fe powder (20 g, 0.36 mol) was added and the mixture was heated to 80 °C about 30 min. TLC the starting material was consumed, the mixture was cooled to R.T. EtOAc (300 mL) and H_2O (300 mL) were added, the organic phase was washed with H_2O (500 mL x 2) and brine (300 mL), the organic phase was dried over anhydrous Na_2SO_4. The solid was filtered and the filtrate was concentrated, the residue was purified by column chromatography on silica gel (EA: PE = 1:2) to give the product 5-bromo-N1-methylbenzene-1,2-diamine (14 g, yield 70 %). LC-MS (ESI^+): m/z 202.1 $(M+H)^+$.

[00379] 6-Bromo-1-methyl-1H-benzo[d]imidazol-2(3H)-one (**7.4**)

[00380] 5-Bromo-N1-methylbenzene-1,2-diamine (14 g, 69.3 mmol) was dissolved in THF (200 mL), CDI (13.4 g, 83.2 mmol) was added. The mixture was reflux about 2 hours under N_2. When LCMS showed the staring material was consumed, the solvent was evaporated and the resulting crude was purified by column chromatography on silica gel (EA : PE = 1 : 2) to give the product 6-bromo-1-methyl-1H-benzo[d]imidazol-2(3H)-one (10 g, yield 63 %). ^1H NMR (400 MHz, DMSO -d_6) δ 11.0 (s, 1H), 7.33 (s, 1H), 7.13 (t, J = 8.0 Hz, 1H), 6.92 (d, J = 8.0 Hz, 1H), 3.26 (s, 3H). LC-MS (ESI^+): m/z 228.1 $(M+H)^+$.

[00381] 3-(5-Bromo-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-(4-methoxybenzyl)piperidine-2,6-dione (**7.5**)

[00382] To a solution of 6-bromo-1-methyl-1H-benzo[d]imidazol-2(3H)-one (5.0 g, 22.1 mmol) in THF was added t-BuOK (2.48 g, 22.1 mmol) at 0 °C. The mixture was stirred at at 0 °C for 30 min, then 3-bromo-1-(4-methoxybenzyl) piperidine-2,6-dione(6.9 g, 22.1 mmol) was added and the reaction mixture was stirred at room temperature overnight. Then the mixture was concentrated and the residue was purified by column chromatography on silica gel (EtOAc : DCM

= 1 : 1) to give the product 3-(5-bromo-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-(4-methoxybenzyl)piperidine-2,6-dione (3.7 g, yield 37 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.48-7.47 (d, J = 2.0 Hz, 1H), 7.21-7.16 (m, 3H), 7.02-6.99 (d, J = 8.4 Hz, 1H), 6.87-6.84 (m, 2H), 5.55-5.51 (dd, J_1 = 6.4 Hz, J_2 = 14.2 Hz, 1H), 4.84-4.73 (q, J = 14.4 Hz, 2H), 3.72 (s, 3H), 3.34 (s, 3H), 3.08-3.00 (m, 1H), 2.84-2.67 (m, 2H), 2.09-2.04 (m ,1H). LC-MS (ESI$^+$): m/z 459.4 $(M+H)^+$.

[00383] 3-(5-Bromo-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidine-2,6-dione (**7.6**)

[00384] To a solution of 3-(5-bromo-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-(4-methoxybenzyl) piperidine-2,6-dione (1.5 g, 3.28 mmol) in toluene (30 mL) was added Methanesulfonic acid (10 mL). The reaction mixture was heated to 110 °C about 2 hours under N_2. The reaction mixture was cooled to room temperature then the solvent was removed by reduced pressure. The residue was dissolved in EtOAc (20 mL) and washed with H_2O (10 mL) and brine (10 mL). The organic phase was dried over anhydrous Na_2SO_4. The solid was filtered and the filtrate was concentrated, the residue was purified by column chromatography on silica gel (EtOAc : DCM = 1 : 1) to give the product 3-(5-bromo-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidine-2,6-dione (0.8 g, yield 72%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.13 (s, 1H), 7.47 (d, J = 1.6 Hz, 1H), 7.22 (dd, J = 10.4, 2.0 Hz, 1H) ,7.11 (d, J = 8.4 Hz ,1H), 5.41-5.36 (m , 1H), 3.34 (s, 3H), 2.92-2.85 (m, 1H), 2.74-2.60 (m, 2H), 2.05-1.99 (m, 1H). LC-MS (ESI$^+$): m/z 339.2 $(M+H)^+$.

[00385] Tert-butyl (2-(2-((3-(1-(2,6-dioxopiperidin-3-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)prop-2-yn-1-yl)oxy)ethoxy)ethyl)carbamate (**7.9**)

[00386] A mixture of 3-(5-bromo-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidine-2,6-dione (200 mg, 0.592 mmol), tert-butyl (2-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethoxy)ethyl)carbamate (430 mg, 1.78 mmol), $Pd(PPh_3)_2Cl_2$ (34 mg, 0.0474 mmol), CuI (18 mg, 0.0947 mmol) and DMF (15 mL) was bubbled with N_2 for 10 min. Then to the mixture was added TEA (598 mg, 5.92 mmol) under N_2. The mixture was heated to 110 °C under N_2 and stirred for 3 h. To the mixture was added H_2O (50 mL) and the mixture was extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4. The solid was filtered and the filtrate was concentrated, the residue was purified by

column chromatography on silica gel (DCM/EA = 1/1 +1% THF) to give tert-butyl (2-(2-((3-(1-(2,6-dioxopiperidin-3-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)prop-2-yn-1-yl)oxy)ethoxy)ethyl)carbamate (100 mg, 34 % yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.20 (d, J = 8.3 Hz, 1H), 7.13 (s, 1H), 6.75 (d, J = 8.2 Hz, 1H), 5.20 (dd, J = 12.6, 5.4 Hz, 1H), 4.44 (s, 2H), 3.77-3.75 (m, 2H), 3.69-3.67 (m, 2H), 3.57 (t, J = 5.2 Hz, 2H), 3.43 (s, 3H), 3.34 (d, J = 5.2 Hz, 2 H), 2.88-2.70 (m, 2H), 2.27-2.22 (m, 2H), 1.44 (s, 9H). LC-MS (ESI$^+$): m/z 401.1 $(M\text{-}Boc+H)^+$

[00387] Tert-butyl (2-(2-(3-(1-(2,6-dioxopiperidin-3-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)propoxy)ethoxy)ethyl)carbamate (**7.10**)

[00388] A solution of tert-butyl (2-(2-((3-(1-(2,6-dioxopiperidin-3-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)prop-2-yn-1-yl)oxy)ethoxy)ethyl)carbamate (40 mg, 0.0800 mmol), Pd/C (10 %, 4 mg) in EtOAc (10 mL) was stirred for overnight at rt under H_2. The mixture was filtered, concentrated and purified by prep-HPLC to give tert-butyl (2-(2-(3-(1-(2,6-dioxopiperidin-3-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)propoxy)ethoxy)ethyl)carbamate (10 mg, 25 % yield) as a white solid.

[00389] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 6.91 (d, J = 8.5 Hz, 1H), 6.88 (s, 1H), 6.72 (d, J = 8.0 Hz, 1H), 5.20 (dd, J = 12.6, 5.3 Hz, 1H), 3.63-3.55 (m, 6H), 3.49 (t, J = 6.4 Hz, 2H), 3.43 (s, 3H), 3.33 (d, J = 5.3 Hz, 2 H), 3.00-2.78 (m, 4H), 2.27-2.22 (m, 2H), 2.03-1.98 (m, 2 H), 1.44 (s, 9H). LC-MS (ESI$^+$): m/z 405.2 $(M\text{-}Boc+H)^+$

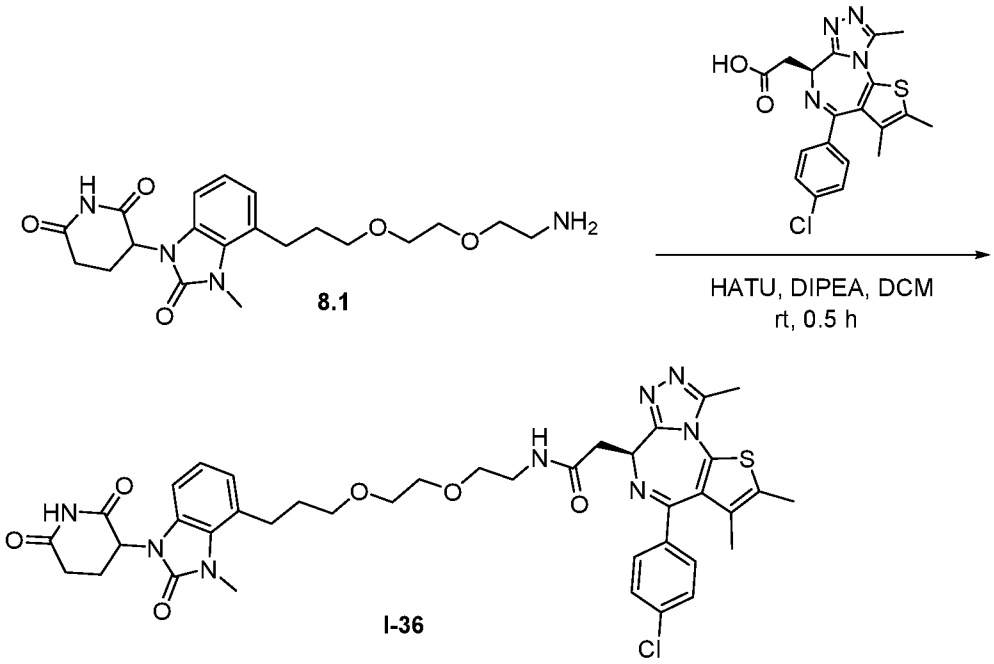
[00390] 3-(5-(3-(2-(2-Aminoethoxy)ethoxy)propyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidine-2,6-dione (**7.11**)

[00391] To a solution of tert-butyl (2-(2-(3-(1-(2,6-dioxopiperidin-3-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)propoxy)ethoxy)ethyl)carbamate (100 mg, 0.248 mmol) in DCM (10 mL) was added TFA (5 mL). The mixture was stirred for 2 h at rt. The mixture was concentrated to give TFA salt of 3-(5-(3-(2-(2-aminoethoxy)ethoxy)propyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidine-2,6-dione (100 mg, 100 % yield) as a yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.10 (s, 1H), 7.77 (br s, 3H), 7.03-7.00 (m, 2H), 6.88-6.86 (m, 1H), 5.35 (dd, J = 12.8, 5.4 Hz, 1H), 3.61-3.56 (m, 4 H), 3.54-3.52 (m, 2H), 3.41 (t, J = 6.5 Hz, 2H), 3.33 (s, 3H), 3.00-2.86 (m, 3H), 2.74-2.60 (m, 4H), 2.02-1.97 (m, 1H), 1.86-1.79 (m, 2H). LC-MS (ESI$^+$): m/z 405.1$(M+H)^+$

[00392] 2-((S)-4-(4-Chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)-N-(2-(2-(3-(1-(2,6-dioxopiperidin-3-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)propoxy)ethoxy)ethyl)acetamide (**I-35**)

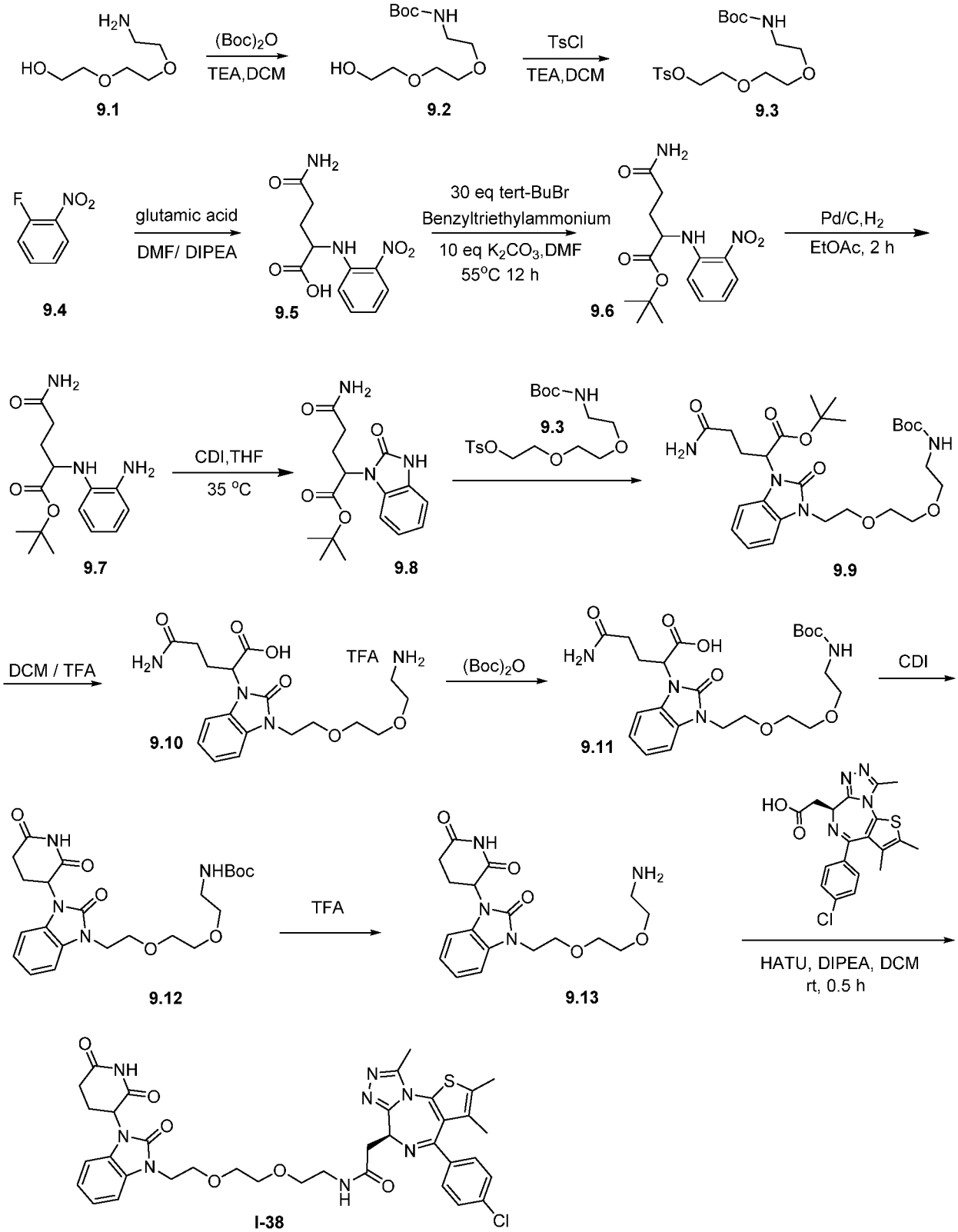
[00393] A mixture of TFA salt of 3-(5-(3-(2-(2-aminoethoxy)ethoxy)propyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidine-2,6-dione (20 mg, 0.0495 mmol), HATU (28 mg, 0.0743 mmol), (S)-2-(4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)acetic acid (22 mg, 0.0545 mmol), DIPEA (19 mg, 0.149 mmol) in DCM (15 mL) was stirred at rt. for 1 h. Then H_2O (10 mL) was added to the mixture, the mixture was extracted with DCM (10 mL x 3). The organic layers were dried over anhydrous Na_2SO_4. The solid was filtered and the filtrate was concentrated. Then the resulting residue was purified by column chromatography on silica gel (DCM/MeOH = 10/1) and prep-HPLC to give 2-((S)-4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)-N-(2-(2-(3-(1-(2,6-dioxopiperidin-3-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)propoxy)ethoxy)ethyl)acetamide (10 mg, 26 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.07 (s, 1H), 8.28 (t, J = 5.7 Hz, 1H), 7.49-7.41 (dd, J = 24.0, 8.6 Hz, 4H), 7.03 (s, 1H), 7.00 (d, J = 8.0 Hz, 1 H), 6.86 (d, J = 7.9 Hz, 1H), 5.33 (dd, J = 12.6, 5.2 Hz, 1H), 4.50 (dd, J = 8.0, 6.0 Hz, 1H), 3.56-3.46 (m, 6 H), 3.40 (t, J = 6.4 Hz, 2H), 3.30 (s, 3 H), 3.30-3.17 (m, 4H), 2.90-2.85 (m, 1H), 2.71-2.63 (m, 4H), 2.59 (s, 3H), 2.40 (s, 3H), 2.00-1.98 (m, 1H), 1.85-1.78 (m, 2H), 1.61 (s, 3H). LC-MS (ESI$^+$): m/z 787.2$(M+H)^+$.

[00394] Example 8. 2-((S)-4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)-N-(2-(2-(3-(1-(2,6-dioxopiperidin-3-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)propoxy)ethoxy)ethyl)acetamide (I-36)



[00395] A mixture of TFA salt of 3-(4-(3-(2-(2-aminoethoxy)ethoxy)propyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidine-2,6-dione (20 mg, 0.0495 mmol), HATU (28 mg, 0.0743 mmol), (S)-2-(4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)acetic acid (22 mg, 0.0545 mmol), DIPEA (19 mg, 0.149 mmol) and DCM (15 mL) was stirred for 1 h at rt. Then H_2O (10 mL) was added to the mixture, the mixture was extracted with DCM (10 mL x 3). The organic layers were dried over anhydrous Na_2SO_4. The solid was filtered and the filtrate was concentrated. Then the resulting residue was purified by column chromatography on silica gel (DCM/MeOH = 10/1) and prep-HPLC to give 2-((S)-4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)-N-(2-(2-(3-(1-(2,6-dioxopiperidin-3-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)propoxy)ethoxy)ethyl)acetamide (8 mg, 21 % yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.09 (s, 1H), 8.28 (t, J = 5.4 Hz, 1H), 7.48 (d, J = 8.7 Hz, 2 H), 7.42 (d, J = 8.7 Hz, 2 H), 6.96-6.92 (m, 2H), 6.87-6.85 (m, 1 H), 5.36 (dd, J = 12.5, 5.3 Hz, 1H), 4.50 (dd, J = 8.0, 6.1 Hz, 1H), 3.57-3.54 (m, 7 H), 3.50-3.45 (m, 4H), 3.29-3.17 (m, 4H), 2.96-2.84 (m, 3H), 2.71-2.63 (m, 2H), 2.59 (s, 3H), 2.40 (s, 3H), 2.00-1.97 (m, 1H), 1.96-1.79 (m, 2H), 1.61 (s, 3H). LC-MS (ESI$^+$): m/z 787.2(M+H)$^+$.

[00396] Example 9. Synthesis of 2-((S)-4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)-N-(2-(2-(2-(3-(2,6-dioxopiperidin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)ethoxy)ethoxy)ethyl)acetamide (I-38)



[00397] tert-Butyl (2-(2-(2-hydroxyethoxy)ethoxy)ethyl)carbamate (**9.2**)

[00398] To a stirred solution of 2-(2-(2-aminoethoxy)ethoxy)ethan-1-ol (1.0 g, 6.72 mmol) in DCM (25 mL) was added $(Boc)_2O$ (1.92 g, 13.5 mmol), TEA (1.36 g, 13.5 mmol) at r.t. The reaction mixture was stirred at r.t. for 2 h. TLC (10% MeOH / 90% DCM, silica gel plate) showed complete consumption of the starting material after this time. The mixture was concentrated in vacuo to give tert-butyl (2-(2-(2-hydroxyethoxy)ethoxy)ethyl)carbamate (1.7 g, crude) as a yellow oil, the crude product was used directly with further purification.

[00399] 2,2-Dimethyl-4-oxo-3,8,11-trioxa-5-azatridecan-13-yl 4-methylbenzenesulfonate (**9.3**)

[00400] To a stirred solution of tert-butyl (2-(2-(2-hydroxyethoxy)ethoxy)ethyl)carbamate (1.7 g, 6.82 mmol) in DCM (10 mL) was added TEA (1.7 g, 16.83 mmol) at r.t. To the above reaction mixture was added dropwise TsCl (1.9 g, 9.97 mmol) in DCM (5 mL) at 0 °C. After the addition the reaction was stirred at r.t. overnight. TLC (10% MeOH / 90% DCM, silica gel plate) showed the starting material was consumed. The mixture was concentrated in vacuo. The residure was purified via column chromatography on silica gel (Petroleum ether / EtOAc =5% - 80%) to give 2,2-dimethyl-4-oxo-3,8,11-trioxa-5-azatridecan-13-yl 4-methylbenzenesulfonate (2.4 g, 87.3 %) as a yellow oil. LC-MS (ESI^+): m/z 404.2 $(M+H)^+$.

[00401] (2-Nitrophenyl)glutamine (**9.5**)

[00402] To a stirred solution of 1-fluoro-2-nitrobenzene (10 g, 0.069 mol) in EtOH (150 mL) was added glutamine (14.7 g, 0.104 mol), K_2CO_3 (33.4 g, 0.242 mol) at r.t.. The reaction mixture was heated at 95 °C overnight. The reaction mixture was cooled to r.t.. The reaction mixture was adjusted to PH = 3~4. Then a yellow solid was formed. The solid was collected by filtration, dried in vacuo to give the product (2-nitrophenyl)glutamine (4.5 g, yield 25%) as a yellow solid.

[00403] ^1H NMR (400 MHz, DMSO-d_6) δ 13.30 (s, 1H), 8.34 (d, J = 7.4 Hz, 1H), 8.10 (dd, J = 8.6, 1.5 Hz, 1H), 7.65 – 7.46 (m, 1H), 7.33 (s, 1H), 7.05 (d, J = 8.5 Hz, 1H), 6.86 – 6.67 (m, 2H), 4.49 (dd, J = 12.7, 5.7 Hz, 1H), 2.26 – 2.01 (m, 4H).

[00404] tert-Butyl (2-nitrophenyl)glutaminate (**9.6**)

[00405] To a stirred solution of (2-nitrophenyl)glutamine (2.72 g, 10.2 mmol) in DMF (100 mL) was added 2-bromo-2-methylpropane (41.87 g, 305.6 mol), Benzyltriethylammonium (3.49 g, 15.3 mol), K_2CO_3 (28.2 mg, 204 mmol) at r.t. in a sealed glass tube. Then the reaction mixture was heated to 52 °C for 12 h. TLC (50% EtOAc / 50% DCM, silica gel plate) showed the starting

material was consumed. H_2O (500 mL) was added, the mixture was cooled to r.t. and extracted with EtOAc (250 mL x 3). The combined organic layer was washed with brine, dried and concentrated in vacuo. The residue was purified via column chromatography (DCM / EtOAc = 5%-80%) to give the desired compound tert-butyl (2-nitrophenyl)glutaminate (1.95 g, yield 59.1 %) as a yellow solid. LC-MS (ESI^+): m/z 324.1 $(M+H)^+$.

[00406] tert-Butyl (2-aminophenyl)glutaminate (**9.7**)

[00407] To a stirred solution of tert-butyl (2-nitrophenyl)glutaminate (1.89 g, 5.85 mmol) in EtOAc (40 mL) was added Pd/C (200 mg) at r.t.. The reaction mixture was degassed and purged with hydrogen several times. Then the reaction mixture was stirred at r.t. for 1 h under H_2. TLC (50% EtOAc / 50% DCM, silica gel plate) showed the starting material was consumed. The mixture was filtered and concentrated in vacuo. The residue was purified via column chromatography (DCM / EtOAc = 5% - 80%) to give the desired compound tert-butyl (2-aminophenyl)glutaminate (1.8 g, 100 %) as a yellow oil. LC-MS (ESI^+): m/z 294.2 $(M+H)^+$.

[00408] tert-Butyl 5-amino-5-oxo-2-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pentanoate (**9.8**)

[00409] To a stirred solution of tert-butyl (2-aminophenyl)glutaminate (1.7 g, 5.8 mmol) in THF (60 mL) was added CDI (1.88 g, 11.6 mol) at r.t. The reaction mixture was stirred at r.t. for 12 h. TLC (50% EtOAc / 50% DCM, silica gel plate) showed the starting material was consumed. H_2O (50 mL) was added and the mixture was extracted with EtOAc (50 mL x 3). The combined organic layer was washed with brine, dried and concentrated in vacuo. The mixture was purified via column chromatography (DCM / EtOAc = 5% - 80%) to give the desired compound tert-butyl 5-amino-5-oxo-2-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pentanoate (1.31 g, yield 70.8 %) as a yellow solid. ^1H NMR (400 MHz, DMSO-d_6) δ 10.92 (s, 1H), 7.22 (s, 1H), 7.06 – 6.94 (m, 4H), 6.73 (s, 1H), 4.94 (dd, J = 10.8, 4.9 Hz, 1H), 2.40 – 2.30 (m, 1H), 2.24 (ddd, J = 19.5, 9.0, 5.3 Hz, 1H), 2.03 (td, J = 8.7, 4.5 Hz, 1H), 1.90 (ddd, J = 15.2, 9.5, 5.4 Hz, 1H), 1.35 (s, 9H). LC-MS (ESI^+): m/z 320.1 $(M+H)^+$.

[00410] tert-Butyl 5-amino-2-(3-(2,2-dimethyl-4-oxo-3,8,11-trioxa-5-azatridecan-13-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-5-oxopentanoate (**9.9**)

[00411] To a stirred solution of tert-butyl 5-amino-5-oxo-2-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)pentanoate (300 mg, 0.940 mmol) in DMF (30 mL) was added 2,2-

dimethyl-4-oxo-3,8,11-trioxa-5-azatridecan-13-yl 4-methylbenzenesulfonate (9.3, 530.6 mg, 1.32 mmol), K_2CO_3 (181.7 mg, 1.32 mmol) at r.t.. The reaction mixture was heated to 69 °C for 12 h. TLC (10% MeOH / 90% DCM, silica gel plate) showed the starting material was consumed. H_2O (50 mL) was added and the mixture was extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine, dried and concentrated in vacuo. The mixture was purified via reverse phase column chromatography (MeOH / H_2O = 5% - 80%) to give tert-butyl 5-amino-2-(3-(2,2-dimethyl-4-oxo-3,8,11-trioxa-5-azatridecan-13-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-5-oxopentanoate (298 mg, 57.6 %) as a yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.25 (d, J = 7.6 Hz, 1H), 7.21 (s, 1H), 7.05 (qd, J = 9.1, 4.4 Hz, 3H), 6.73 (s, 2H), 5.00 (dd, J = 10.6, 5.0 Hz, 1H), 4.00 (t, J = 5.6 Hz, 2H), 3.67 (t, J = 5.6 Hz, 2H), 3.51 (dd, J = 5.8, 3.6 Hz, 2H), 3.43 (dd, J = 5.7, 3.6 Hz, 2H), 3.34 (s, 1H), 3.30 (d, J = 5.2 Hz, 1H), 3.02 (dd, J = 11.9, 6.0 Hz, 2H), 2.42 – 2.18 (m, 2H), 2.03 (ddd, J = 15.8, 11.3, 4.4 Hz, 1H), 1.91 (ddd, J = 15.2, 9.4, 5.5 Hz, 1H), 1.47 (s, 9 H), 1.23 (s, 9 H). LC-MS (ESI$^+$): m/z 551.3 $(M+H)^+$.

[00412] 5-Amino-2-(3-(2-(2-(2-aminoethoxy)ethoxy)ethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-5-oxopentanoic acid (**9.10**)

[00413] To a stirred solution of tert-butyl 5-amino-2-(3-(2,2-dimethyl-4-oxo-3,8,11-trioxa-5-azatridecan-13-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-5-oxopentanoate (395 mg, 0.536 mmol) in DCM (5 mL) was added TFA (5 mL) at r.t. The reaction mixture was stirred at r.t. for 1 h. TLC (10% MeOH / 90% DCM, silica gel plate) showed the starting material was consumed. The mixture was concentrated in vacuo. The mixture was purified via reverse phase HPLC (MeOH / H_2O =5% - 80%) to give 5-amino-2-(3-(2-(2-(2-aminoethoxy)ethoxy)ethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-5-oxopentanoic acid (215.1 mg, 89.2 %) as a colorless oil. LC-MS (ESI$^+$): m/z 396.2 $(M+H)^+$.

[00414] 5-Amino-2-(3-(2,2-dimethyl-4-oxo-3,8,11-trioxa-5-azatridecan-13-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-5-oxopentanoic acid (**9.11**)

[00415] To a stirred solution of 5-amino-2-(3-(2-(2-(2-aminoethoxy)ethoxy)ethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-5-oxopentanoic acid (650 mg, 1.646 mmol) in DCM (20 mL) was added $(Boc)_2O$ (533.2 mg, 2.468 mmol), TEA (249.3 mg, 2.468 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 0.5 h. TLC (10% MeOH / 90% DCM, silica gel plate) showed the starting material was consumed. The mixture was concentrated in vacuo. The mixture was purified

via reverse phase HPLC (MeOH / H_2O = 5% - 80%) to give 5-amino-2-(3-(2,2-dimethyl-4-oxo-3,8,11-trioxa-5-azatridecan-13-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-5-oxopentanoic acid (435.1 mg, 53.5 %) as a colorless oil. LC-MS (ESI^+): m/z 495.2 $(M+H)^+$.

[00416] tert-Butyl (2-(2-(2-(3-(2,6-dioxopiperidin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)ethoxy)ethoxy)ethyl)carbamate (**9.12**)

[00417] To a stirred solution of 5-amino-2-(3-(2,2-dimethyl-4-oxo-3,8,11-trioxa-5-azatridecan-13-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-5-oxopentanoic acid (500 mg, 1.01 mmol) in dioxane (10 mL) was added CDI (245.9 mg, 1.518 mol) and DMAP (2 mg, 0.016 mol) at r.t. under nitrogen. Then the reaction mixture was heated at 100 °C for 5 hs. TLC (10% MeOH / 90% DCM, silica gel plate) showed complete consumption of the starting material after this time. The mixture was concentrated in vacuo. The mixture was purified via reverse phase column chromatography (CH_3CN / H_2O =5% - 80%) to give tert-butyl (2-(2-(2-(3-(2,6-dioxopiperidin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)ethoxy)ethoxy)ethyl)carbamate (297.1 mg, 61.7 %) as a white solid. ^1H NMR (400 MHz, DMSO-d_6) δ 11.09 (s, 1H), 7.26 (d, J = 7.3 Hz, 1H), 7.06 (ddt, J = 15.3, 7.5, 7.0 Hz, 3H), 6.72 (s, 1H), 5.37 (dd, J = 12.7, 5.3 Hz, 1H), 4.00 (t, J = 5.6 Hz, 2H), 3.68 (t, J = 5.6 Hz, 2H), 3.52 (dd, J = 5.8, 3.5 Hz, 2H), 3.44 (dd, J = 5.7, 3.6 Hz, 2H), 3.35 – 3.26 (m, 2H), 3.06 – 2.99 (m, 2H), 2.97 – 2.85 (m, 1H), 2.78 – 2.58 (m, 2H), 2.01 (dd, J = 11.3, 6.1 Hz, 1H), 1.36 (s, 9H). LC-MS (ESI^+): m/z 477.2 $(M+H)^+$.

[00418] 3-(3-(2-(2-(2-Aminoethoxy)ethoxy)ethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidine-2,6-dione (**9.13**)

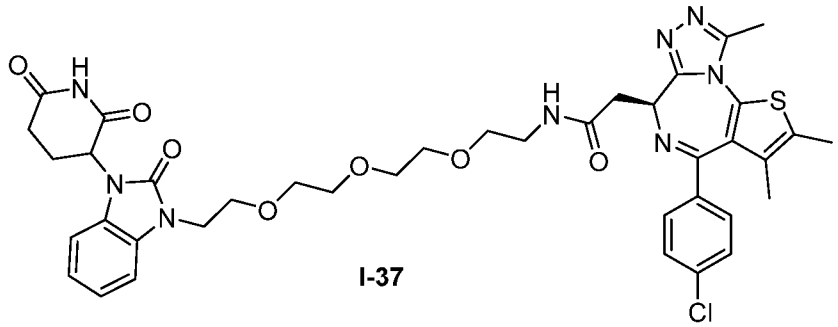
[00419] To a stirred solution of tert-butyl (2-(2-(2-(3-(2,6-dioxopiperidin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)ethoxy)ethoxy)ethyl)carbamate (330 mg, 0.693 mmol) in DCM (5 mL) was added TFA (5 mL) at r.t. The reaction mixture was stirred at r.t. for 1 h. TLC (10% MeOH / 90% DCM, silica gel plate) showed complete consumption of the starting material after this time. The mixture was concentrated in vacuo. The residue was dissolved in deionized water and cooled to 0 °C. The mixture was freeze-drying to give 3-(3-(2-(2-(2-aminoethoxy)ethoxy)ethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidine-2,6-dione (305.1 mg, 89.8 %) as a pale yellow solid. ^1H NMR (400 MHz, DMSO-d_6) δ 11.11 (s, 1H), 7.76 (s, 3H), 7.34 – 7.22 (m, 1H), 7.18 – 6.97 (m, 3H), 5.38 (dd, J = 12.6, 5.4 Hz, 1H), 4.02 (t, J = 5.5 Hz, 2H), 3.70 (t, J = 5.5 Hz, 2H), 3.64 – 3.46 (m, 6H), 2.91 (tt, J = 11.3, 5.8 Hz, 3H), 2.71 (ddd, J

= 36.9, 22.7, 11.0 Hz, 2H), 2.02 (dd, *J* = 8.8, 3.5 Hz, 1H). LC-MS (ESI^+): m/z 377.1 $(M+H)^+$.

[00420] 2-((S)-4-(4-Chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)-N-(2-(2-(2-(3-(2,6-dioxopiperidin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)ethoxy)ethoxy)ethyl)acetamide (**I-38**)

[00421] To a stirred solution of 3-(3-(2-(2-(2-aminoethoxy)ethoxy)ethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidine-2,6-dione (38.5 mg, 0.0786 mol) in DCM (5 mL) were added (S)-2-(4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)acetic acid (40.8 mg, 0.102 mol), HATU (38.8 mg, 0.102 mol) and DIPEA (13.2 mg, 0.102 mmol) at r.t.. The reaction mixture was stirred at r.t. for 3 h. TLC (10% MeOH / 90% DCM, silica gel plate) showed the starting material was consumed. The mixture was concentrated in vacuo. H_2O (5 mL) and the mixture was extracted with EtOAc (10 mL x 3). The combined organic layer was washed with brine, dried and concentrated in vacuo. The mixture was purified via reverse phase HPLC (MeOH / H_2O = 5% - 80%) to give 2-((S)-4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)-N-(2-(2-(2-(3-(2,6-dioxopiperidin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)ethoxy)ethoxy)ethyl)acetamide (35.7 mg, 59.9 %) as a yellow solid. ^1H NMR (400 MHz, DMSO-d_6) δ 11.09 (s, 1H), 8.24 (t, *J* = 5.6 Hz, 1H), 7.48 (d, *J* = 8.7 Hz, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.25 (d, *J* = 7.3 Hz, 1H), 7.15 – 6.97 (m, 3H), 5.37 (dd, *J* = 12.9, 5.5 Hz, 1H), 4.51 (t, *J* = 7.0 Hz, 1H), 4.00 (t, *J* = 5.6 Hz, 2H), 3.69 (t, *J* = 5.6 Hz, 2H), 3.59 – 3.52 (m, 2H), 3.52 – 3.45 (m, 2H), 3.40 (t, *J* = 5.9 Hz, 2H), 3.32 – 3.13 (m, 4H), 2.96 – 2.81 (m, 1H), 2.78 – 2.62 (m, 2H), 2.59 (s, 3H), 2.41 (s, 3H), 2.06 – 1.97 (m, 1H), 1.61 (s, 3H). LC-MS (ESI^+): m/z 759.1 $(M+H)^+$.

[00422] Example 10. 2-((S)-4-(4-Chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)-N-(2-(2-(2-(2-(3-(2,6-dioxopiperidin-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)ethoxy)ethoxy)ethoxy)ethyl)acetamide (I-37)



I-37

[00423] **I-37** was prepared according to Example 9 substituting starting material **9.1** with 2-(2-(2-(2-aminoethoxy)ethoxy)ethoxy)ethan-1-ol. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.09 (s, 1H), 8.26 (t, J = 5.6 Hz, 1H), 7.48 (d, J = 8.7 Hz, 2H), 7.42 (d, J = 8.6 Hz, 2H), 7.30 – 7.21 (m, 1H), 7.13 – 6.97 (m, 3H), 5.37 (dd, J = 12.8, 5.4 Hz, 1H), 4.51 (dd, J = 7.9, 6.2 Hz, 1H), 3.99 (t, J = 5.6 Hz, 2H), 3.68 (t, J = 5.5 Hz, 2H), 3.56 – 3.50 (m, 2H), 3.50 – 3.40 (m, 8H), 3.33 – 3.16 (m, 4H), 2.96 – 2.85 (m, 1H), 2.79 – 2.63 (m, 2H), 2.59 (s, 3H), 2.41 (s, 3H), 2.05 – 1.98 (m, 1H), 1.62 (s, 3H).LC-MS (ESI$^+$): m/z 803.3 $(M+H)^+$.

[00424] **Example 11. BRD4 Degradation in NAMALWA Cells**

[00425] **Materials and Cell Lines**

[00426] Cell information: NAMALWA cultured in RPMI-1640 containing 10% FBS, 2mM L-Glutamine. Cell lysis buffer: RIPA buffer with protease/phosphatase inhibitor cocktail. Primary antibodies: BRD4, CST, #13440S (1:1,000) and beta-Actin mouse mAb, sigma, A5441 (1:10000). Secondary antibodies: Goat anti-mouse(700) Licor, #926-68070 (1:10,000) and goat anti-rabbit (800) Licor #926-32211 (1:10,000)

[00427] **Western Blot Protocol**

- 2.5E06 NAMALWA cells, 0.9 mL cell suspension were seeded into each well of a 12-well plate.
- Compounds were diluted in DMSO and 0.1mL was added to the assay plate to final concentrations of 1 uM, 0.3 uM, 0.1 uM, 0.03 uM, 0.01 uM, 0.003 uM, 0.001 uM, 0.0003 uM, DMSO (negative control) incubated for 2 h, n=2.
- Cell were centrifuged the cell precipitates was washed with cold DPBS and lysed in 30 uL RIPA buffer on ice for 30 min without sonication.
- After centrifugation at 14,000 rpm for 10 min, the supernatant was collected, and diluted 1/5 for protein concentration determination (cell experiment) using the bicinchoninic acid method.
- 3X loading buffer was added to the samples followed by incubation in boiling water for 5 min.
- Samples and protein marker were loaded into lanes in 10% Midi gel (140 V, 5.5 - 6 h), following Semi-wet (25 V, ,2.5A, 13min) with Trans-blot Turbo.
- Membranes were blocked with Odyssey blocking buffer for 1 h at RT.

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- Membranes were incubated with IRAK4 Abs and beta-Actin Abs overnight.
- Goat anti-rabbit 800 and goat anti-mouse 700 secondary antibodies were diluted in 1:10 000 ratio with Odyssey buffer containing 0.1% Tween 20. Membranes were incubated for 1 h at RT.
- Membranes were scanned with Odyssey imaging system.

[00428] **Table 4** shows % BRD4 degradation induced by select compounds in NAMALWA cells using Western Blot analysis. The protocol was run at 8 different inhibitor concentrations: 1 uM, 0.3 uM, 0.1 uM, 0.03 uM, 0.01 uM, 0.003 uM, 0.001 uM, and 0.0003 uM, using neat DMSO as the negative control. The compound numbers correspond to the compound numbers in Table 1 and the examples. Compounds having an inhibitory activity designated as "A" provided greater than 80 precent protein degradation; compounds having an inhibitory activity designated as "B" provided 60 to 80 precent protein degradation; compounds having an inhibitory activity designated as "C" provided 40 to 60 precent protein degradation; compounds having an inhibitory activity designated as "D" provided less than 40 percent protein degradation.

[00429] **Table 4. BRD4 Degradation Results**

Cpnd #	1 uM	0.3 uM	0.1 uM	0.03 uM	0.01 uM	0.003 uM	0.001 uM	0.0003 uM
I-35	A	A	A	A	A	A	A	B
I-36	B	B	B	B	C	C	C	C
I-37	A	A	A	A	A	A	B	B
I-38	A	A	A	A	A	A	B	D

[00430] While we have described a number of embodiments of this invention, it is apparent that our basic examples may be altered to provide other embodiments that utilize the compounds and methods of this invention. Therefore, it will be appreciated that the scope of this invention is to be defined by the appended claims rather than by the specific embodiments that have been represented by way of example.

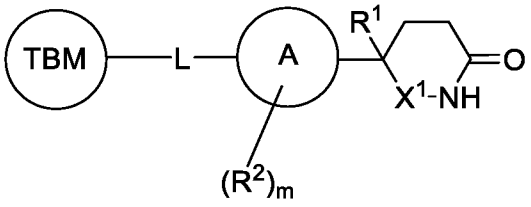
[00431] Any reference to publications cited in this specification is not an admission that the disclosures constitute common general knowledge in Australia.

[00432] The term "comprise" and variants of the term such as "comprises" or "comprising" are used herein to denote the inclusion of a stated integer or stated integers but not to exclude any other integer or any other integers, unless in the context or usage an exclusive interpretation of the term is required.

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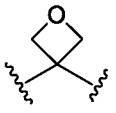
[00433] Definitions of specific embodiments of the invention as claimed herein follows.

[00434] In a first aspect, the present invention relates to a compound of formula **I**:



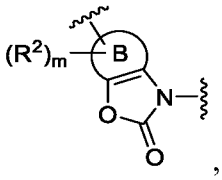
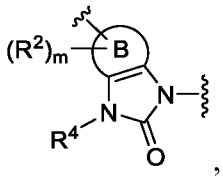
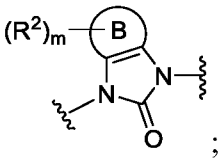
I

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–CH_2–$, –C(O)–, –C(S)–, or  ;

R^1 is hydrogen, halogen, –CN, –OR, –SR, $–S(O)R$, $–S(O)_2R$, $–NR_2$, or an optionally substituted C_{1-4} aliphatic;

each R^2 is independently hydrogen, R^6, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

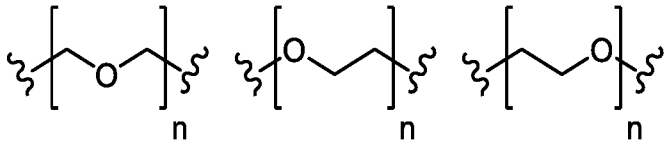
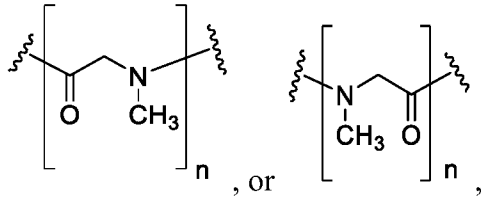
Ring A is a bicyclic ring selected from  ,  , or  ;

Ring B is a fused ring selected from 6-membered aryl containing 0-2 nitrogen atoms, 5 to 7-membered partially saturated carbocyclyl, 5 to 7-membered partially saturated heterocyclyl with 1-2 heteroatoms independently selected from nitrogen, oxygen or sulfur, or 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

R^4 is independently hydrogen, R^6, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, $-N(R)C(O)OR$, $-N(R)C(O)R$, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

each R^6 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

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L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -NR-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, -$S(O)_2$-, -$NRS(O)_2$-, -$S(O)_2NR$-, -NRC(O)-, -C(O)NR-, -OC(O)NR-, –NRC(O)O-,  ,  , or , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

TBM is a target binding moiety, wherein the target binding moiety is a BET binding moiety;

m is 0, 1, 2, 3 or 4;

each of n is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

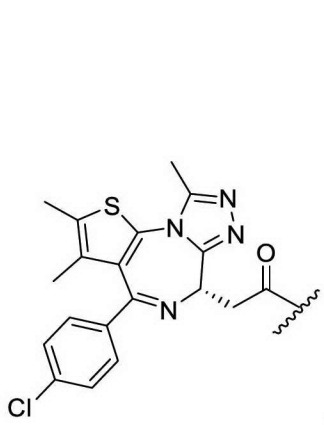
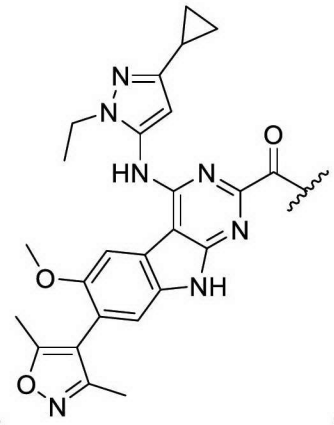
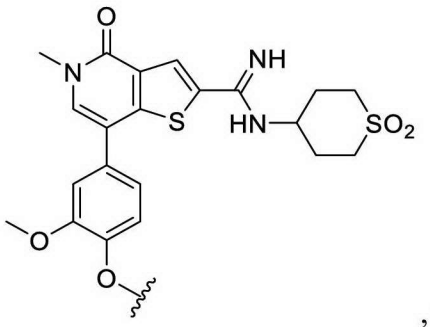
each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3

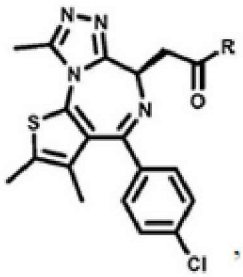
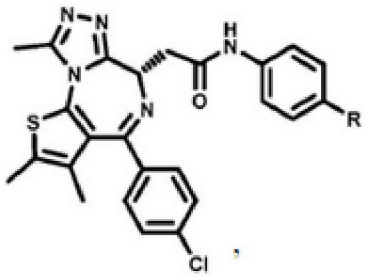
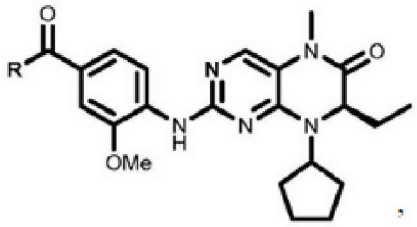
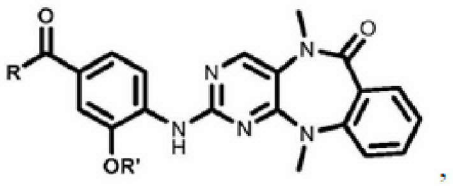
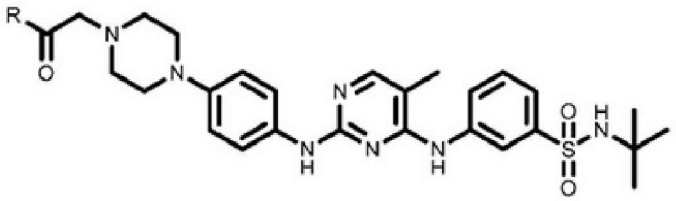
heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur;

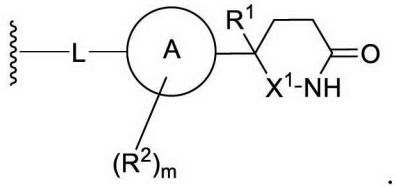
wherein the BET binding moiety is:

(a)



, or

, or

(b)


,

,

,

,

or ,


wherein R denotes attachment to .

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[00435] In a second aspect, the present invention relates to a pharmaceutical composition comprising a compound according to the first aspect, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

[00436] In a third aspect, the present invention relates to a method of degrading a target protein in a biological sample comprising contacting the sample with the compound of the first aspect, or a pharmaceutically acceptable salt thereof.

[00437] In a fourth aspect, the present invention relates to a method of treating a target protein-mediated disorder, disease, or condition in a patient comprising administering to said patient the compound of the first aspect or the pharmaceutical composition of the second aspect.

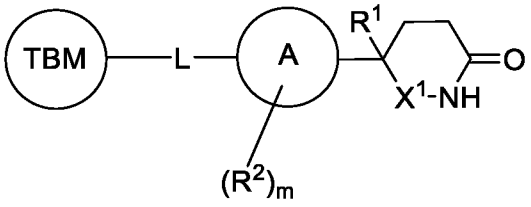
[00438] In a fifth aspect, the present invention relates to a use of a compound of the first aspect or the pharmaceutical composition of the second aspect in the manufacture of a medicament for treating a target protein-mediated disorder, disease, or condition.

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CLAIMS

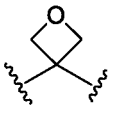
We claim:

1. A compound of formula **I**:



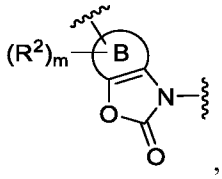
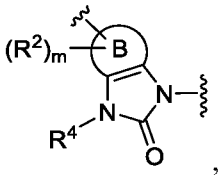
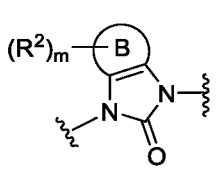
I

or a pharmaceutically acceptable salt thereof, wherein:

X^1 is a bivalent moiety selected from a covalent bond, $–CH_2–$, –C(O)–, –C(S)–, or  ;

R^1 is hydrogen, halogen, –CN, –OR, –SR, –S(O)R, $–S(O)_2R$, $–NR_2$, or an optionally substituted C_{1-4} aliphatic;

each R^2 is independently hydrogen, R^6, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

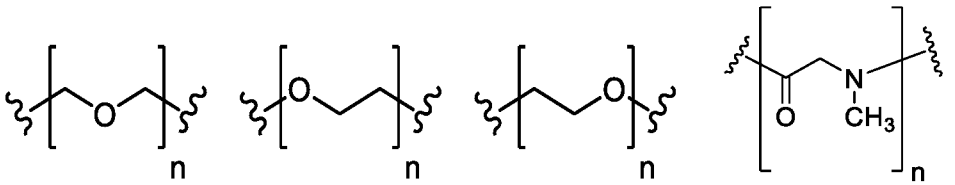
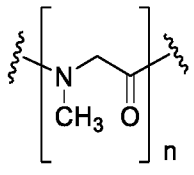
Ring A is a bicyclic ring selected from  ,  , or  ;

Ring B is a fused ring selected from 6-membered aryl containing 0-2 nitrogen atoms, 5 to 7-membered partially saturated carbocyclyl, 5 to 7-membered partially saturated heterocyclyl with 1-2 heteroatoms independently selected from nitrogen, oxygen or sulfur, or 5-membered heteroaryl with 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

R^4 is independently hydrogen, R^6, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $–C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$;

each R^6 is independently an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-50} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -NR-, -S-, -OC(O)-, -

C(O)O-, -C(O)-, -S(O)-, -$S(O)_2$-, -$NRS(O)_2$-, -$S(O)_2NR$-, -NRC(O)-, -C(O)NR-, -OC(O)NR-, –NRC(O)O-,  , or  , wherein:

each –Cy– is independently an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-7 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

TBM is a target binding moiety, wherein the target binding moiety is a BET binding moiety;

m is 0, 1, 2, 3 or 4;

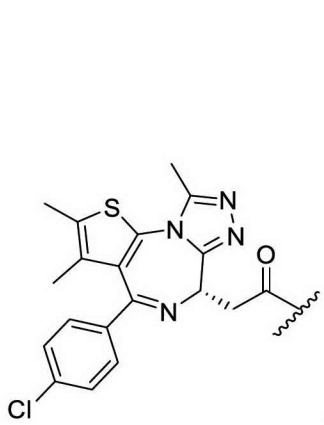
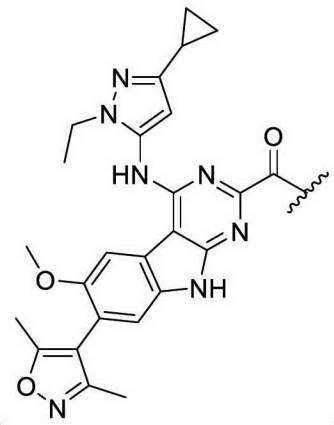
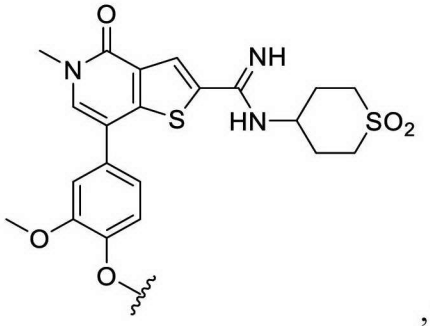
each of n is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each R is independently hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

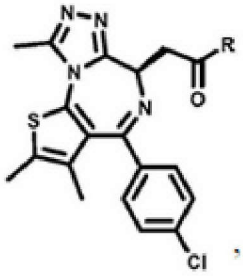
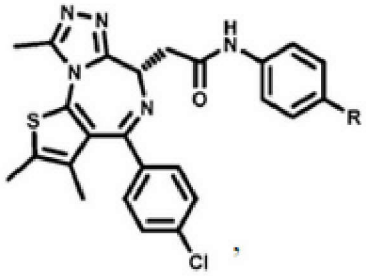
two R groups on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen, and sulfur;

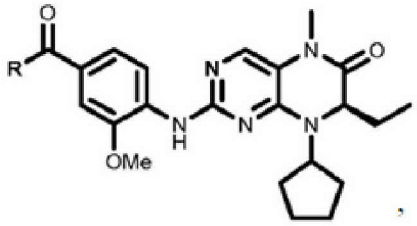
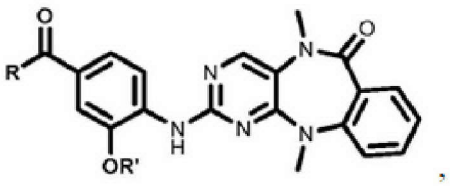
wherein the BET binding moiety is:

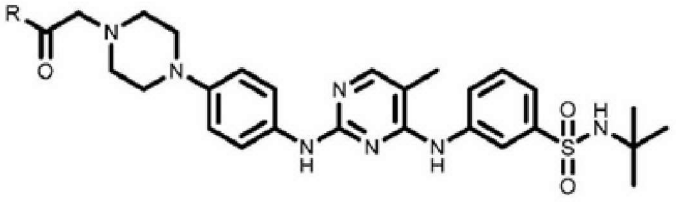
(a)


, 
, or 
, or

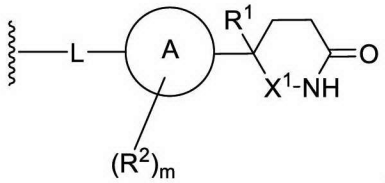
(b)


, 
,


, 
,


,

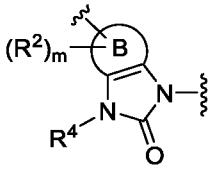
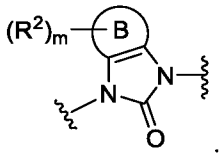
or



wherein R denotes attachment to .

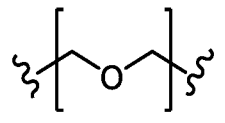
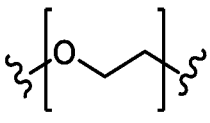
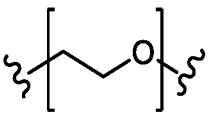
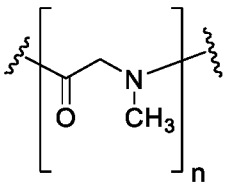
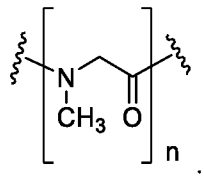
2. The compound of claim 1, wherein X^1 is –C(O)–.

3. The compound of claim 1, wherein R^1 is hydrogen, halogen, –OR, –SR, –S(O)R, –$S(O)_2$R, –NR_2, or an optionally substituted C_{1-4} aliphatic.

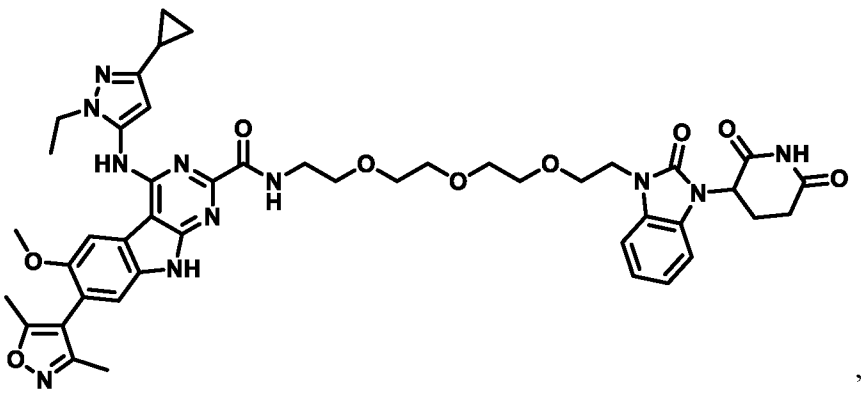
4. The compound of claim 1, wherein Ring A is  or  .

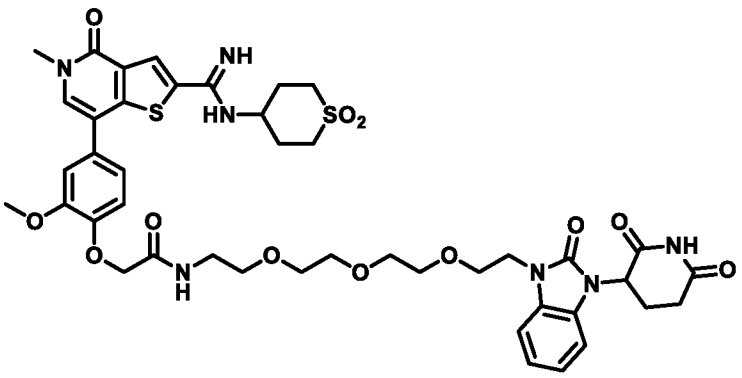
5. The compound of claim 1, wherein Ring B is selected from 6-membered aryl containing 0-2 nitrogen atoms, 6-membered partially saturated carbocyclyl, or 6-membered partially saturated heterocyclyl with 1-2 heteroatoms independently selected from nitrogen, oxygen or sulfur.

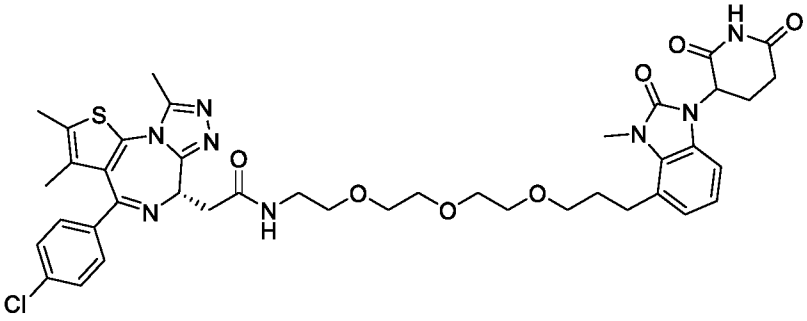
6. The compound of claim 1, wherein R^4 is hydrogen, R^6, halogen, –CN, $–NO_2$, –OR, -SR, $-NR_2$, $-S(O)_2R$, $-S(O)_2NR_2$, -S(O)R, -C(O)R, -C(O)OR, $-C(O)NR_2$, -C(O)N(R)OR, -OC(O)R, $-OC(O)NR_2$, -N(R)C(O)OR, -N(R)C(O)R, $-N(R)C(O)NR_2$, or $–N(R)S(O)_2R$.

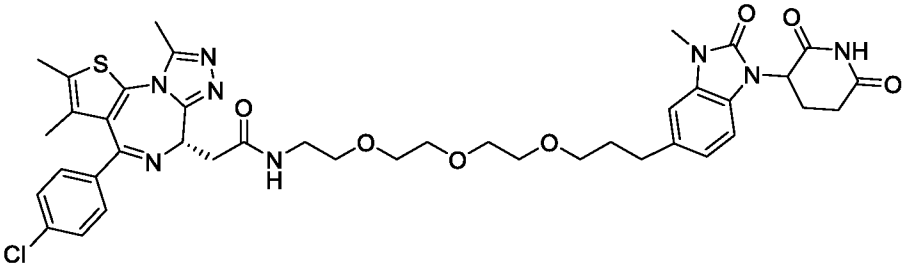
7. The compound of claim 1, wherein L is a bivalent, saturated or unsaturated, straight or branched C_{1-20} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by –Cy-, -O-, -NR-, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, $-S(O)_2-$, $-NRS(O)_2-$, $-S(O)_2NR-$, -NRC(O)-, -C(O)NR-, -OC(O)NR-, –NRC(O)O-,  ,  ,  ,  ,  , or .

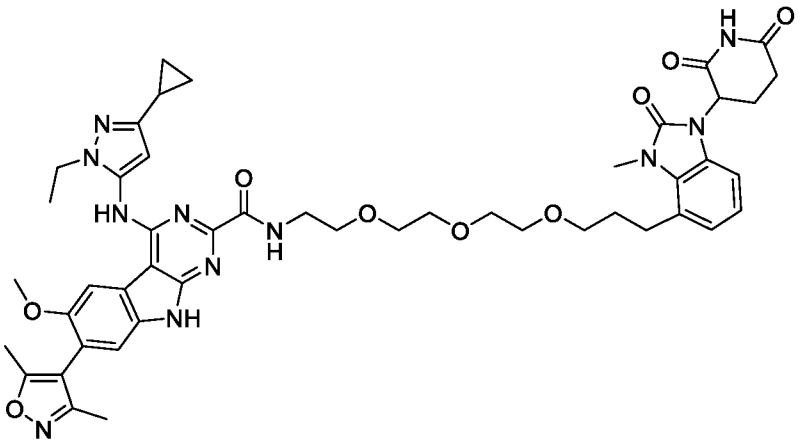
8. The compound of claim 1, wherein said compound is selected from

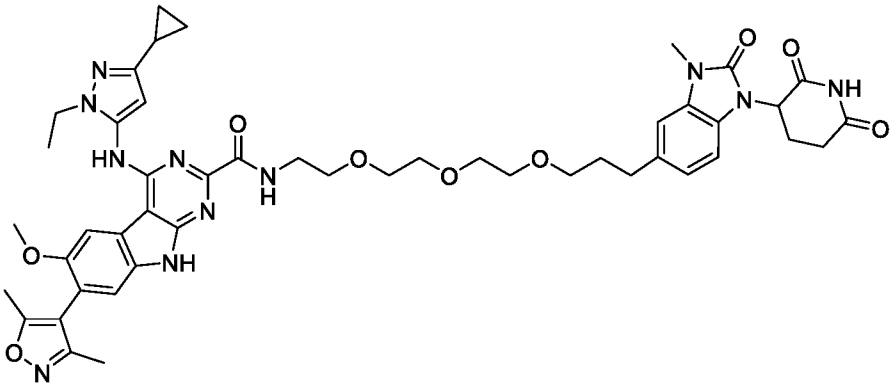
I-2  ,

I-5  ,

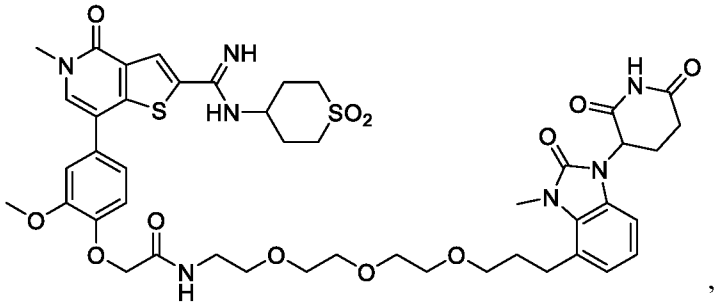
I-9  ,

I-10  ,

I-11  ,

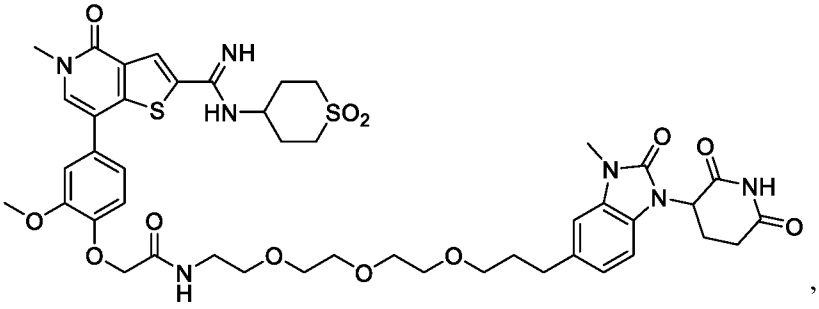
I-12  ,

I-17



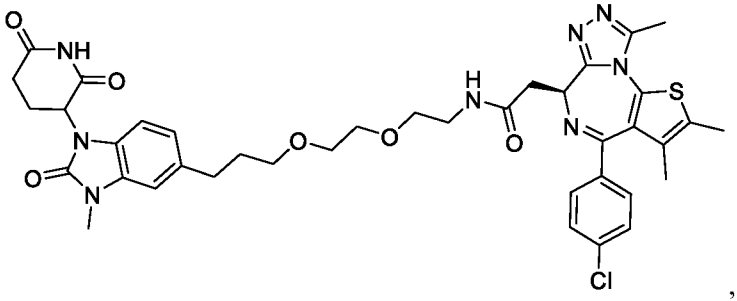
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I-18



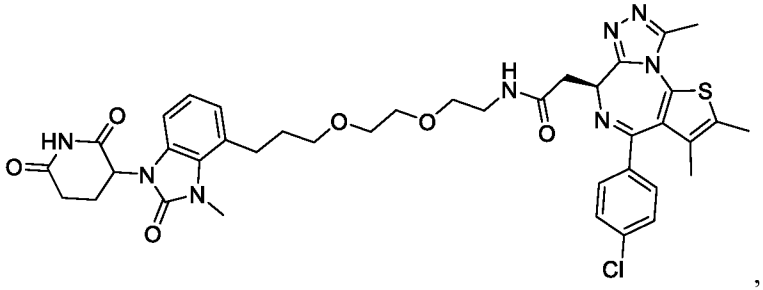
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I-35



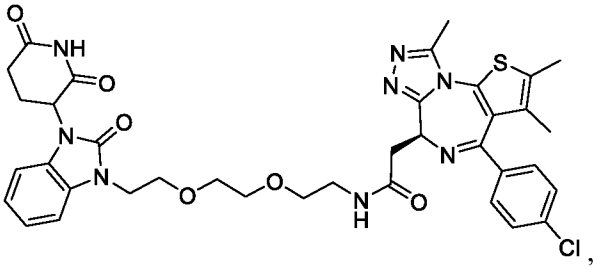
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I-36



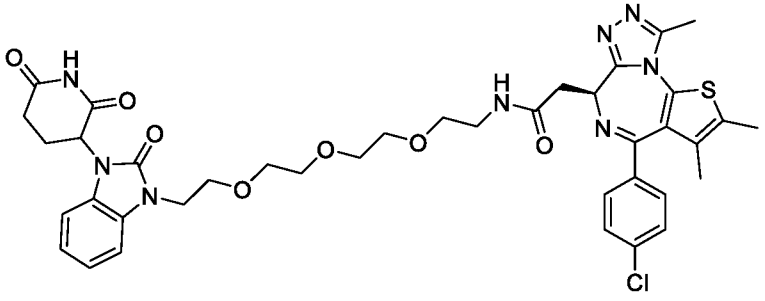
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or a pharmaceutically acceptable salt thereof.

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9. A pharmaceutical composition comprising a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

10. A method of degrading a target protein in a biological sample comprising contacting the sample with the compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof.

11. A method of treating a target protein-mediated disorder, disease, or condition in a patient comprising administering to said patient the compound of any one of claims 1-8 or the pharmaceutical composition of claim 9.

12. Use of a compound of any one of claims 1-8 or the pharmaceutical composition of claim 9 in the manufacture of a medicament for treating a target protein-mediated disorder, disease, or condition.

13. The method of claim 11 or the use of claim 12, wherein the disorder is selected from an autoimmune disorder, an inflammatory disorder, a proliferative disorder, an endocrine disorder, a neurological disorder, or a disorder associated with transplantation.

14. The method or use of claim 13, wherein the disorder is a proliferative disorder.

15. The method or use of claim 14, wherein the proliferative disorder is a cancer.

16. The method or use of claim 15, wherein the cancer is squamous-cell carcinoma, basal cell carcinoma, adenocarcinoma, hepatocellular carcinomas, and renal cell carcinomas, cancer of the bladder, bowel, breast, cervix, colon, esophagus, head, kidney, liver, lung, neck, ovary, pancreas, prostate, and stomach; leukemias; benign and malignant lymphomas, particularly Burkitt's lymphoma and Non-Hodgkin's lymphoma; benign and malignant melanomas; myeloproliferative diseases; multiple myeloma, sarcomas, including Ewing's sarcoma, hemangiosarcoma, Kaposi's sarcoma, liposarcoma, myosarcomas, peripheral neuroepithelioma, synovial sarcoma, gliomas, astrocytomas, oligodendrogliomas, ependymomas, gliobastomas, neuroblastomas, ganglioneuromas, gangliogliomas, medulloblastomas, pineal cell tumors, meningiomas, meningeal sarcomas, neurofibromas, and Schwannomas; bowel cancer, breast cancer, prostate cancer, cervical cancer, uterine cancer, lung cancer, ovarian cancer, testicular cancer, thyroid cancer, astrocytoma, esophageal cancer, pancreatic cancer, stomach cancer, liver cancer, colon cancer, melanoma; carcinosarcoma, Hodgkin's disease, Wilms' tumor or teratocarcinomas, T-lineage Acute lymphoblastic Leukemia (T-ALL), T-lineage lymphoblastic Lymphoma (T-LL), Peripheral T-cell lymphoma, Adult T-cell Leukemia, Pre-B ALL, Pre-B Lymphomas, Large B-cell Lymphoma,

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Burkitts Lymphoma, B-cell ALL, Philadelphia chromosome positive ALL and Philadelphia chromosome positive CML.