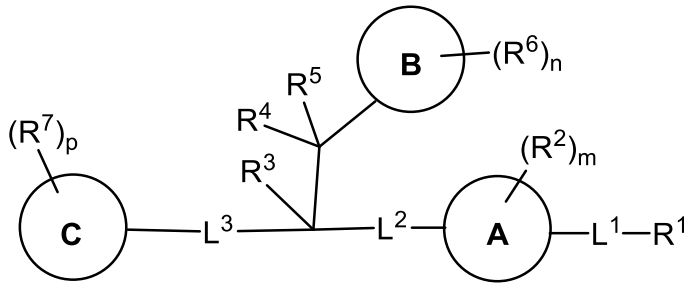
SUMMARY ~~OF THE INVENTION~~

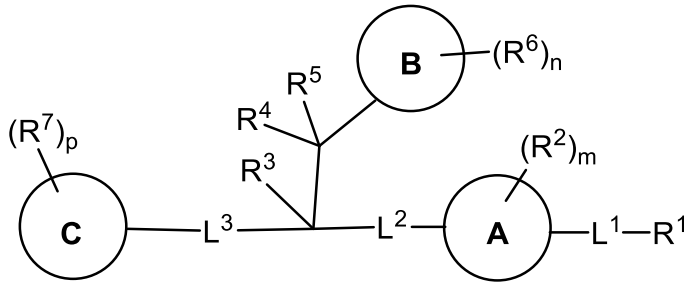
[0007] It has now been found that compounds of this ~~invention~~present disclosure, and pharmaceutically acceptable compositions thereof, are effective as inhibitors of USP30. Such compounds have the general formula **I**:



I

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

[0007a] In an aspect of the present disclosure, there is provided a compound of formula **I'**:



I'

or a pharmaceutically acceptable salt thereof, wherein:

Ring A is phenyl, a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic aryl or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

L^1 is a C_{1-3} bivalent hydrocarbon chain wherein one methylene unit of the chain is replaced by –$C(CF_3)H$–, –N(R)–, –O–, –C(O)–, –C(O)N(R)–, –N(R)C(O)–, –S(O)–, –$S(O)_2$–, –S(O)N(R)–, –$S(O)_2$N(R)–, or –S(O)(R)=N–;

each R is independently hydrogen or an optionally substituted C_{1-3} aliphatic group; or:

two R groups on the same nitrogen are optionally 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, or sulfur; or

an R group and R^1 on the same nitrogen are optionally 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, or sulfur;

R^1 is an optionally substituted group selected from a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, C_{1-6} aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, a 5-8 membered saturated or partially unsaturated bridged bicyclic carbocyclic ring, phenyl, or a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^2 is independently halogen, $–CF_3$, –CN, –C(O)NHR, $–NO_2$, –NHR, –NHC(O)R, $–NHS(O)_2R$, $–N(R)_2$, or –OR, or an optionally substituted C_{1-6} aliphatic group; or

two R^2 on the same carbon are optionally taken together to form =O; or

two R^2 groups are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms independently selected from nitrogen, oxygen or sulfur;

L^2 is selected from the group consisting of $–C(O)N(R')–$, $–CH_2O–$, $–CH_2N(R')–$, and $–C(OH)(H)CH_2N(R')–$;

R' is hydrogen or a C_{1-3} aliphatic group;

L^3 is selected from the group consisting of –C(O)N(R")–, –OC(O)N(R")–, and $–CH_2O–$;

R" is hydrogen or a C_{1-3} aliphatic group;

R^3 is hydrogen or C_{1-3} aliphatic; or:

R^3 and R^4 are optionally taken together with their intervening atoms to form a 3-5 membered saturated carbocyclic ring; or

R^3 and R^5 are optionally taken together with their intervening atoms to form a 3-5 membered saturated carbocyclic ring;

R^4 is hydrogen or C_{1-3} aliphatic;

R^5 is hydrogen or C_{1-3} aliphatic;

Ring B is phenyl, a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic aryl or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^6 is independently halogen, –CN, $–NO_2$, –NHR, $–N(R)_2$, –OR, or an optionally substituted C_{1-6} aliphatic group; or:

two R^6 on the same carbon are optionally taken together to form =O;

an R^6 group and R' group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur;

an R^6 group and R^3 group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated spiro-fused ring having 0-2 heteroatoms independently selected from nitrogen, oxygen or sulfur; or

an R^6 group and R'' group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur;

Ring C is phenyl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic aryl or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^7 is independently halogen, –CN, $–NO_2$, –NHR, $–N(R)_2$, –OR, or an C_{1-6} aliphatic group; or two R^7 on the same carbon are optionally taken together to form =O; or

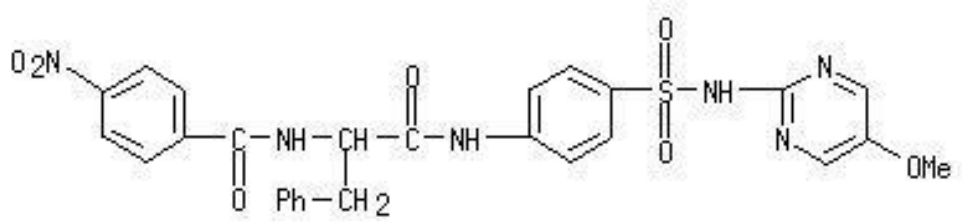
an R^7 group and R'' group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur; and

each of m, n, and p is independently 0, 1, 2, 3 or 4;

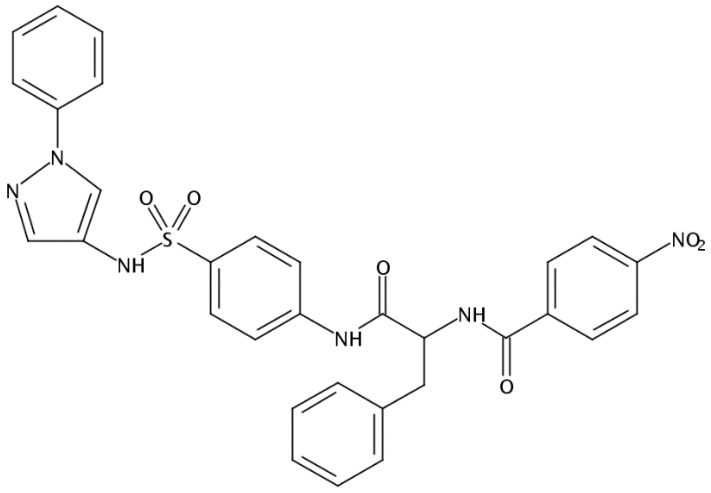
provided that R^1 is other than isopropyl, t-butyl, 1-methylcyclopropyl, 1-fluoromethylcyclopropyl, 1-difluoromethylcyclopropyl, 1-trifluoromethylcyclopropyl, or 3-methyl-3-oxetanyl when L^1 is $–S(O)_2N(R)$-;

R^1 is other than ethyl when L^1 is $–S(O)_2N(R)$- and Ring A is naphthyl; and

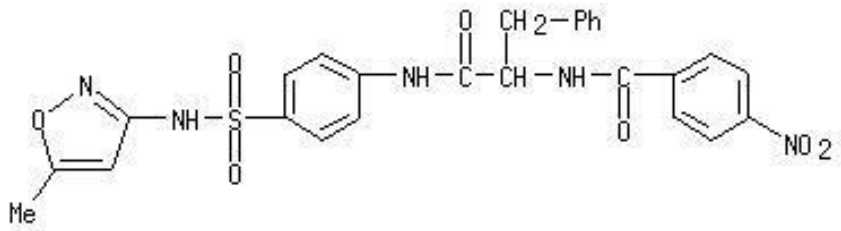
the compound is other than



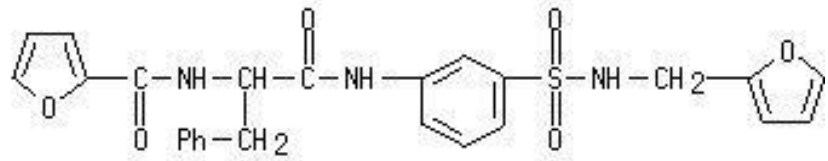
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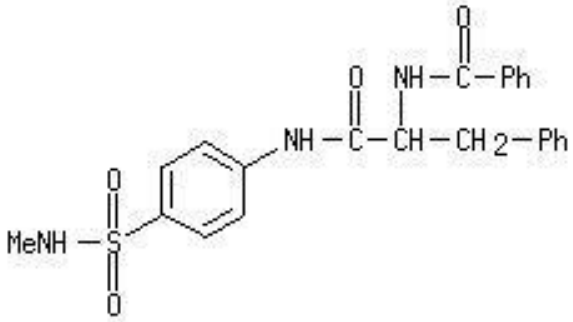
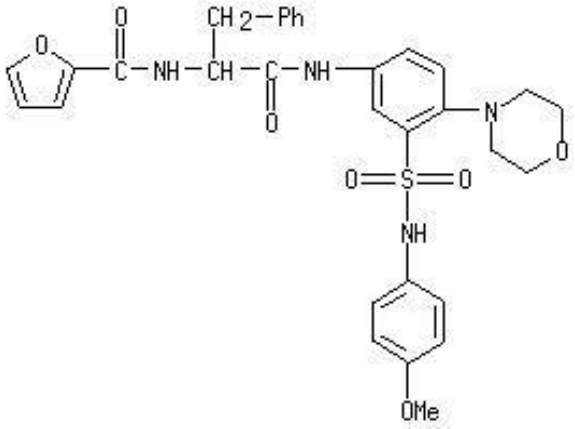


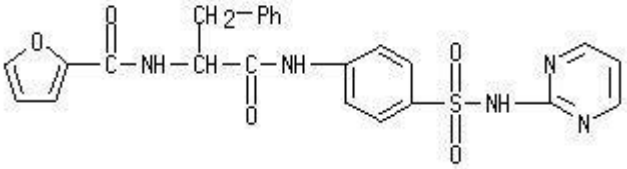
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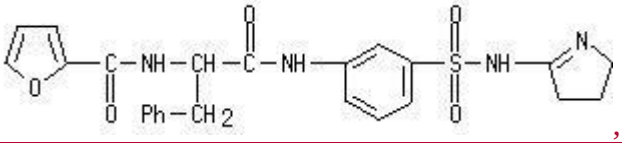
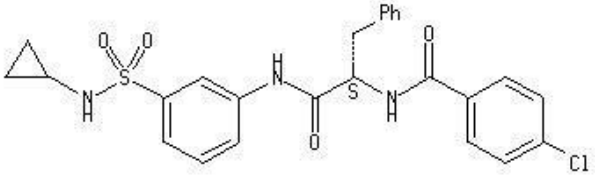


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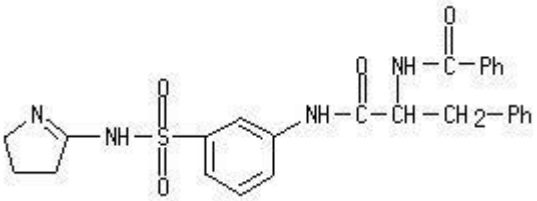
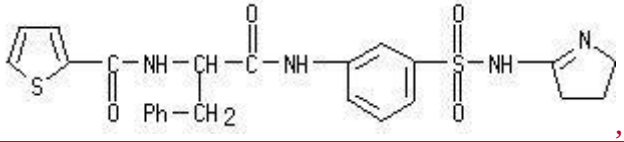
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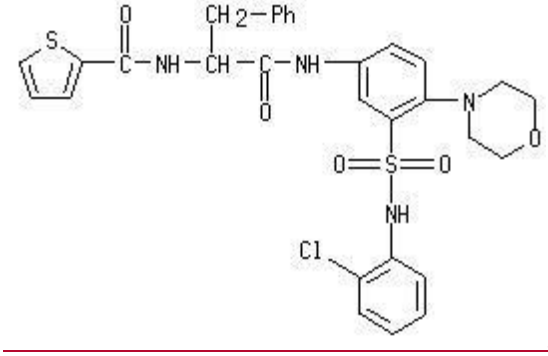
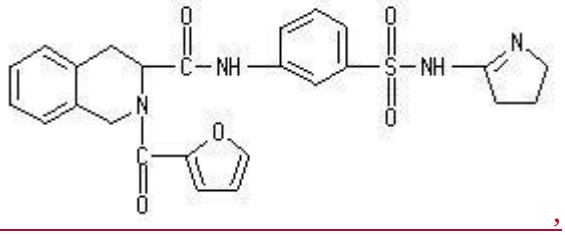

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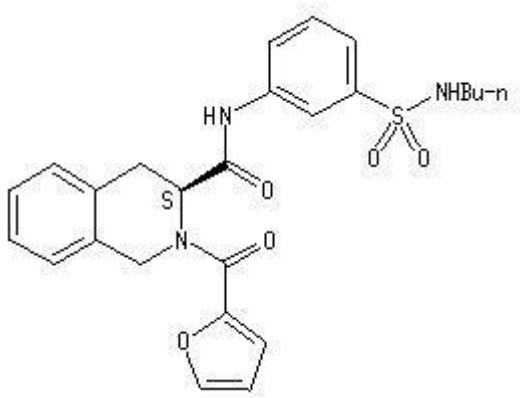

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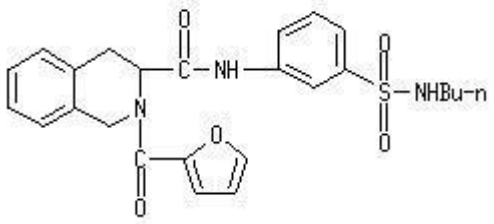

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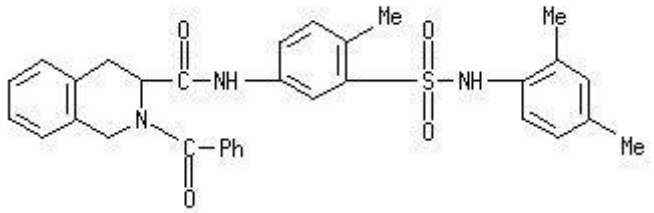

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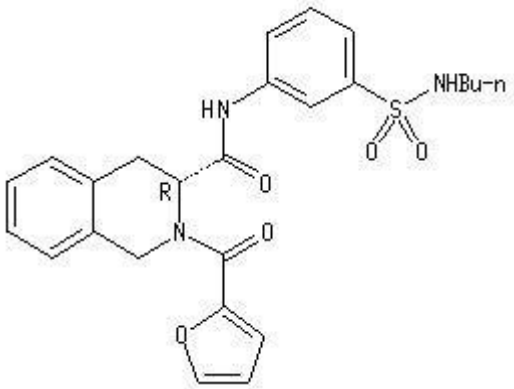

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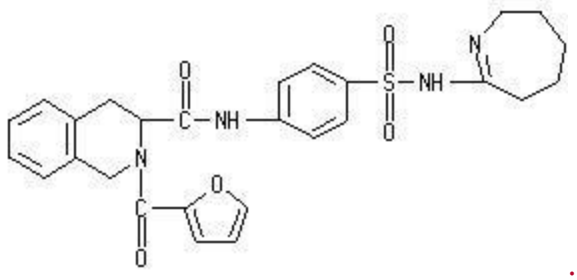
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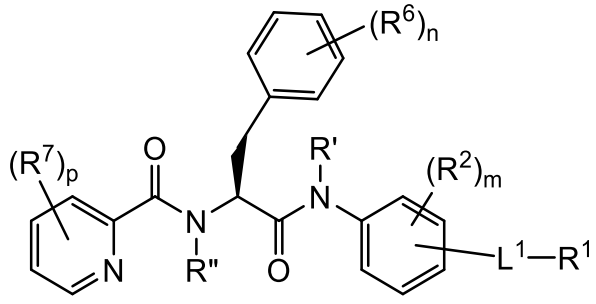
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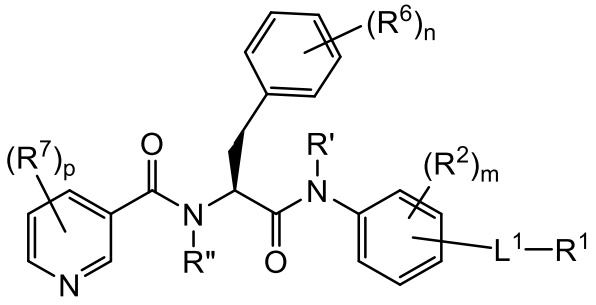
, or



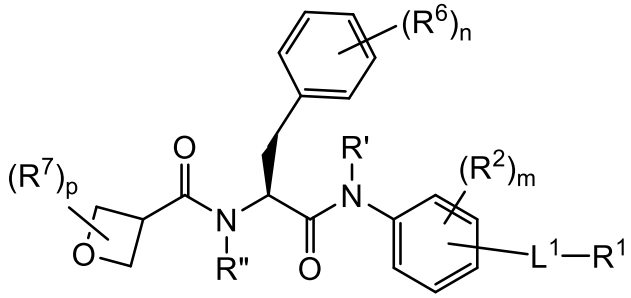
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[0007b] In another aspect of the present disclosure, there is provided a compound of any one of formulas **XV-a**, **XV-b**, **XV-c**, **XV-d**, **XVII-a**, **XVII-b**, **XVII-c**, **XVII-d**, **XIX-a**, **XIX-b**, **XIX-c**, **XIX-d**, **XXI**, **XXIII-a**, **XXIII-b**, **XXV-a**, **XXV-b**, **XXV-c**, or **XXV-d**:

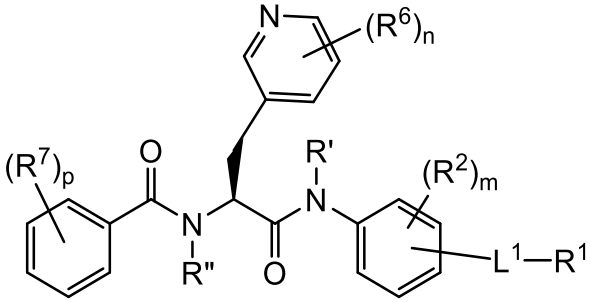




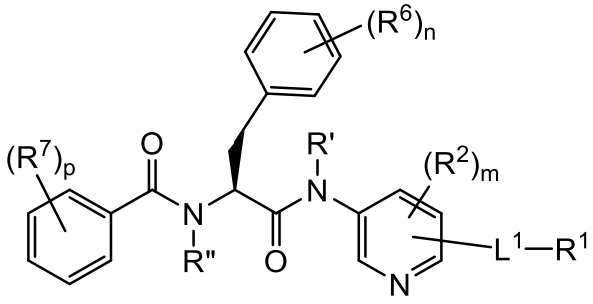
XV-a



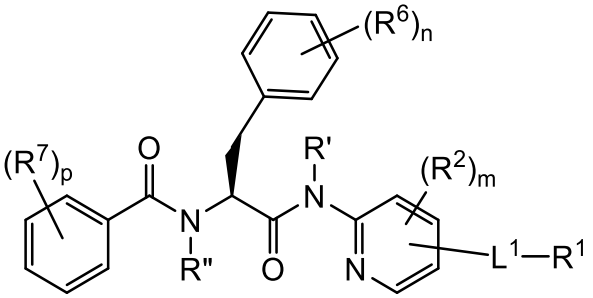
XV-b



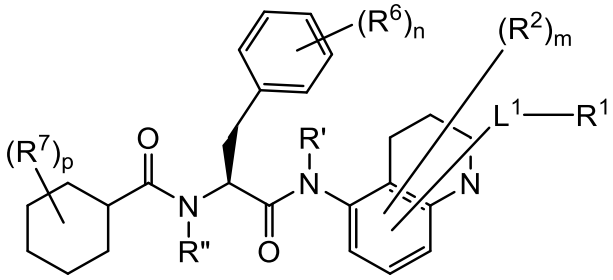
XV-c



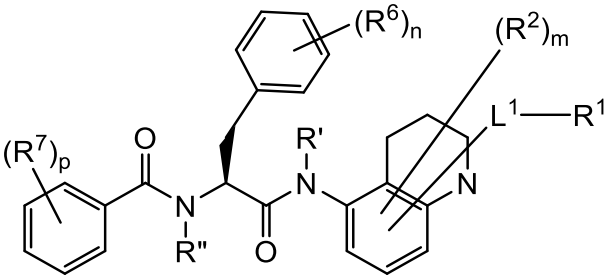
XV-d



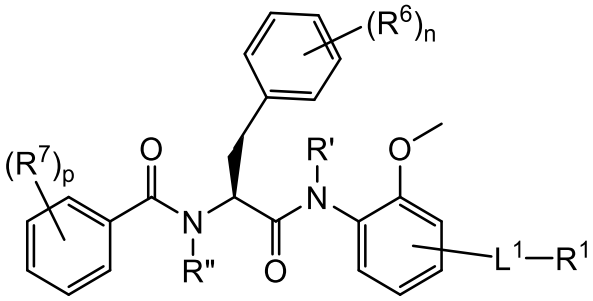
XVII-a



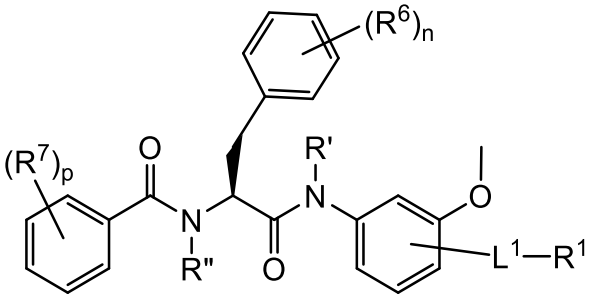
XVII-b



XVII-c

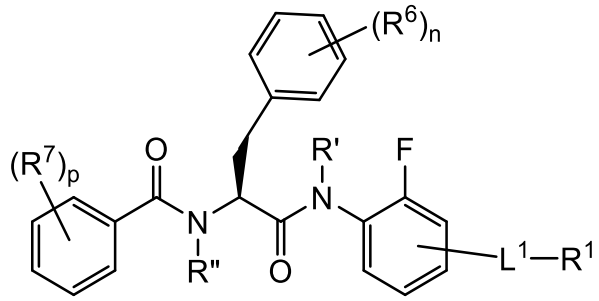


XVII-d

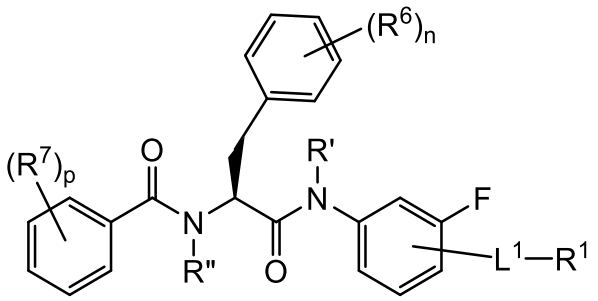


XIX-a

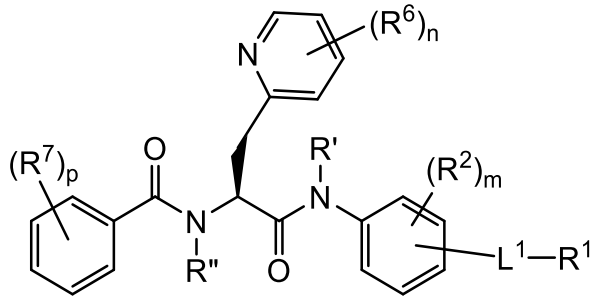
XIX-b



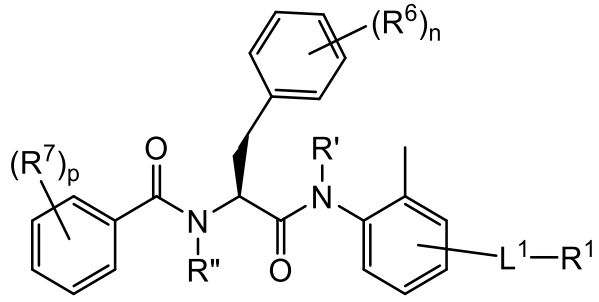
XIX-c



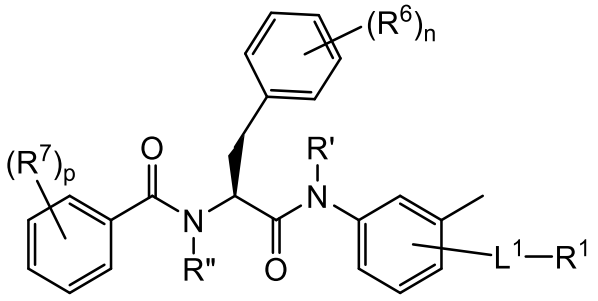
XIX-d



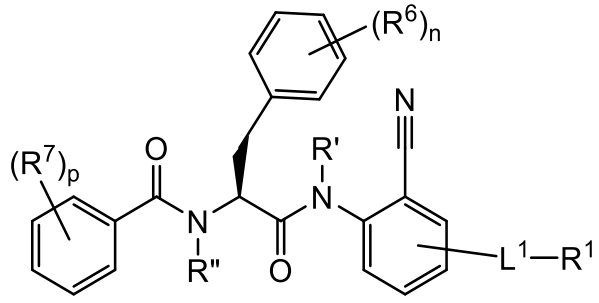
XXI



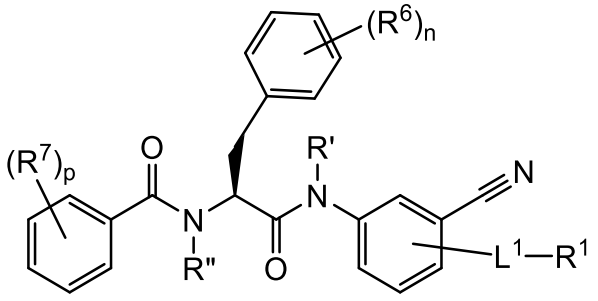
XXIII-a



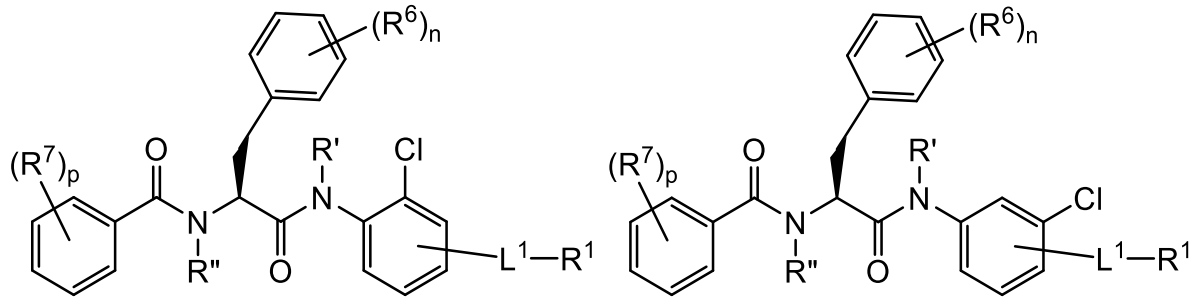
XXIII-b



XXV-a



XXV-b



XXV-c **XXV-d**

or a pharmaceutically acceptable salt thereof, wherein:

L^1 is a C_{1-3} bivalent hydrocarbon chain wherein one methylene unit of the chain is replaced by –C(CF_3)H–, –N(R)–, –O–, –C(O)–, –C(O)N(R)–, –N(R)C(O)–, –S(O)–, –$S(O)_2$–, –S(O)N(R)–, –$S(O)_2$N(R)–, or –S(O)(R)=N–;

each R is independently hydrogen or an optionally substituted C_{1-3} aliphatic group; or:

two R groups on the same nitrogen are optionally 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, or sulfur; or

an R group and R^1 on the same nitrogen are optionally 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, or sulfur;

R^1 is an optionally substituted group selected from C_{1-6} aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, a 5-8 membered saturated or partially unsaturated bridged bicyclic carbocyclic ring, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^2 is independently halogen, –CF_3, –CN, –C(O)NHR, –NO_2, –NHR, –NHC(O)R, –$NHS(O)_2$R, –$N(R)_2$, or –OR, or an optionally substituted C_{1-6} aliphatic group; or

two R^2 on the same carbon are optionally taken together to form =O; or

two R^2 groups are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms independently selected from nitrogen, oxygen or sulfur;

R' is hydrogen or a C_{1-3} aliphatic group;

R'' is hydrogen or a C_{1-3} aliphatic group;

each R^6 is independently halogen, –CN, $–NO_2$, –NHR, $–N(R)_2$, –OR, or an optionally substituted C_{1-6} aliphatic group; or:

two R^6 on the same carbon are optionally taken together to form =O;

an R^6 group and R' group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur; or

an R^6 group and R'' group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur;

each R^7 is independently halogen, –CN, $–NO_2$, –NHR, $–N(R)_2$, –OR, or an C_{1-6} aliphatic group; or

two R^7 on the same carbon are optionally taken together to form =O; or

an R^7 group and R'' group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur; and

each of m, n, and p is independently 0, 1, 2, 3 or 4;

provided that R^1 is other than isopropyl, t-butyl, 1-methylcyclopropyl, 1-fluoromethylcyclopropyl, 1-difluoromethylcyclopropyl, 1-trifluoromethylcyclopropyl, or 3-methyl-3-oxetanyl when L^1 is $–S(O)_2N(R)-$.

[0007c] In a further aspect of the present disclosure, there is provided a compound selected from those depicted in **Table 1** of the specification, or a pharmaceutically acceptable salt thereof.

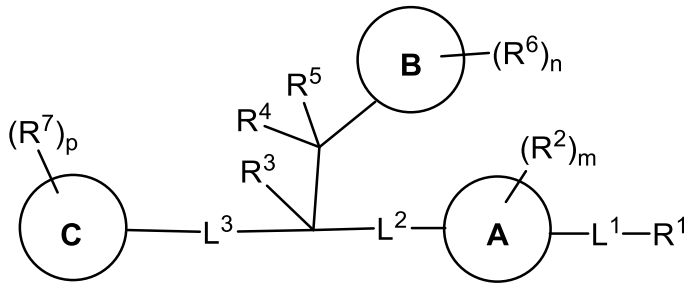
[0007d] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound disclosed herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

[0007e] In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein in the preparation of a medicament for inhibiting USP30.

[0007f] In another aspect of the present disclosure, there is provided a use of a compound disclosed herein in the preparation of a medicament for treating an USP30-mediated disorder, disease, or condition.

[0007g] In a further aspect of the present disclosure, there is provided a compound disclosed herein, for use in therapy.

[0008] In some ~~embodiment~~examples, such compounds have the general formula **I'**:



I'

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

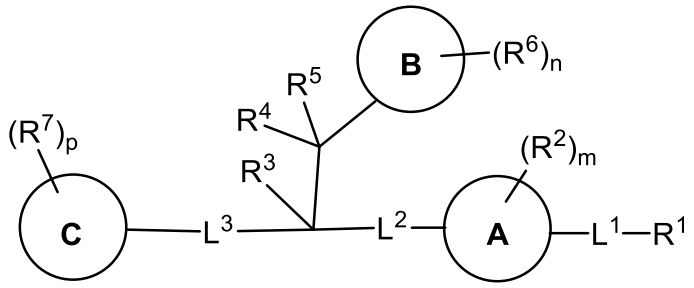
[0009] Compounds of the present ~~invention~~disclosure, and pharmaceutically acceptable compositions thereof, are useful for treating a variety of diseases, disorders or conditions, associated with mitochondrial homeostasis implicating USP30. Such diseases, disorders, or conditions include those described herein.

[0010] Compounds provided by this ~~invention~~ present disclosure are also useful for the study of USP30 in biological and pathological phenomena; the study of mitochondrial homeostasis occurring in bodily tissues; and the comparative evaluation of new USP30 inhibitors or other regulators of mitochondrial homeostasis *in vitro* or *in vivo*.

CLAIMS

We claim:

1. A compound of formula **I'**:



I'

or a pharmaceutically acceptable salt thereof, wherein:

Ring A is phenyl, a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic aryl or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

L^1 is a ~~covalent bond or a~~ C_{1-3} bivalent hydrocarbon chain wherein one ~~or two~~ methylene unit~~s~~ of the chain is~~are optionally and independently~~ replaced by –C(CF_3)H–, –N(R)–, –O–, –C(O)–, ~~–OC(O) –, –C(O)O –,~~ –C(O)N(R)–, –N(R)C(O)–, –S(O)–, –$S(O)_2$–, –S(O)N(R)–, –$S(O)_2$N(R)–, or –S(O)(R)=N–;

each R is independently hydrogen or an optionally substituted C_{1-3} aliphatic group; or:

two R groups on the same nitrogen are optionally 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, or sulfur; or

an R group and R^1 on the same nitrogen are optionally 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, or sulfur;

R^1 is ~~hydrogen or~~ an optionally substituted group selected from a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, C_{1-6} aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, a 5-8 membered saturated or partially unsaturated bridged

bicyclic carbocyclic ring, phenyl, ~~a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur,~~ or a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^2 is independently halogen, $–CF_3$, –CN, –C(O)NHR, $–NO_2$, –NHR, –NHC(O)R, $–NHS(O)_2R$, $–N(R)_2$, or –OR, or an optionally substituted C_{1-6} aliphatic group; or

two R^2 on the same carbon are optionally taken together to form =O; or

two R^2 groups are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms independently selected from nitrogen, oxygen or sulfur;

L^2 is selected from the group consisting of $–C(O)N(R')–$, $–CH_2O–$, $–CH_2N(R')–$, and $–C(OH)(H)CH_2N(R')–$;

R' is hydrogen or a C_{1-3} aliphatic group;

L^3 is selected from the group consisting of –C(O)N(R")–, –OC(O)N(R")–, and $–CH_2O–$;

R" is hydrogen or a C_{1-3} aliphatic group;

R^3 is hydrogen or C_{1-3} aliphatic; or:

R^3 and R^4 are optionally taken together with their intervening atoms to form a 3-5 membered saturated carbocyclic ring; or

R^3 and R^5 are optionally taken together with their intervening atoms to form a 3-5 membered saturated carbocyclic ring;

R^4 is hydrogen or C_{1-3} aliphatic;

R^5 is hydrogen or C_{1-3} aliphatic;

Ring B is phenyl, a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic aryl or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^6 is independently halogen, –CN, $–NO_2$, –NHR, $–N(R)_2$, –OR, or an optionally substituted C_{1-6} aliphatic group; or:

two R^6 on the same carbon are optionally taken together to form =O;

an R^6 group and $R^{'}$ group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur;

an R^6 group and R^3 group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated spiro-fused ring having 0-2 heteroatoms independently selected from nitrogen, oxygen or sulfur; or

an R^6 group and $R^{"}$ group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur;

Ring C is phenyl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic aryl or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^7 is independently halogen, –CN, $–NO_2$, –NHR, $–N(R)_2$, –OR, or an ~~optionally substituted~~ C_{1-6} aliphatic group; or

two R^7 on the same carbon are optionally taken together to form =O; or

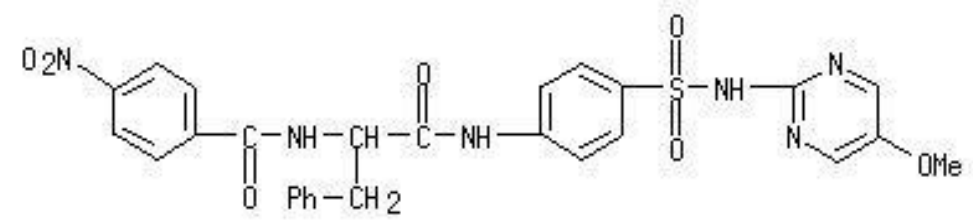
an R^7 group and $R^{"}$ group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur; and

each of m, n, and p is independently 0, 1, 2, 3 or 4;

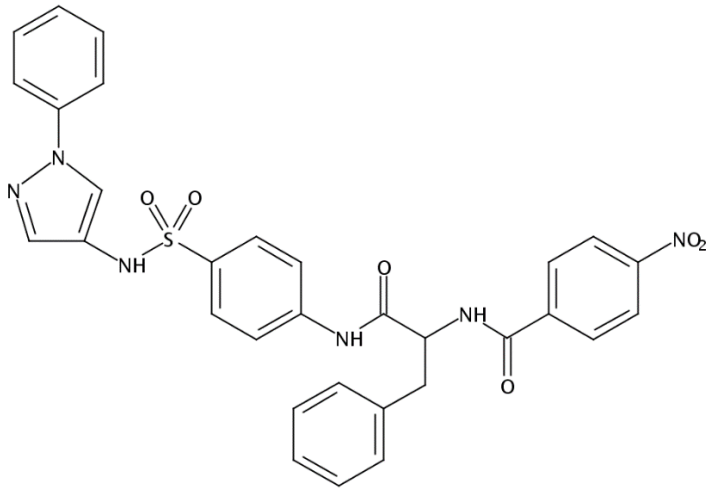
provided that R^1 is other than ~~hydrogen,~~ isopropyl, t-butyl, 1-methylcyclopropyl, 1-fluoromethylcyclopropyl, 1-difluoromethylcyclopropyl, 1-trifluoromethylcyclopropyl, or 3-methyl-3-oxetanyl when L^1 is $–S(O)_2N(R)$-;

R^1 is other than ethyl when L^1 is $–S(O)_2N(R)$- and Ring A is naphthyl; and

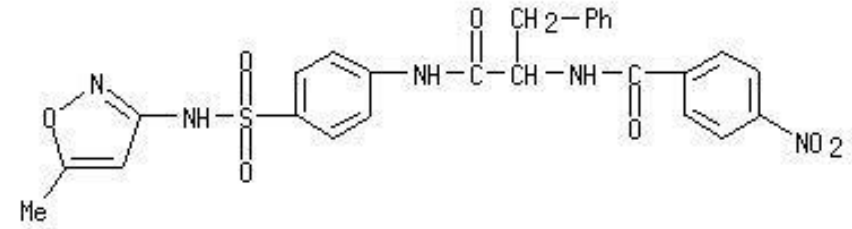
the compound is other than ~~one depicted in **Table 1-1.**~~



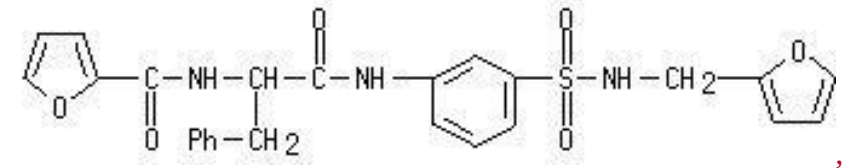
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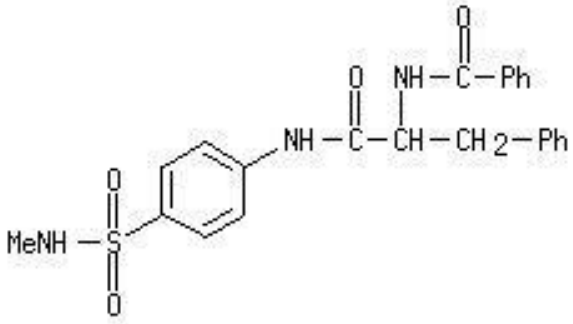
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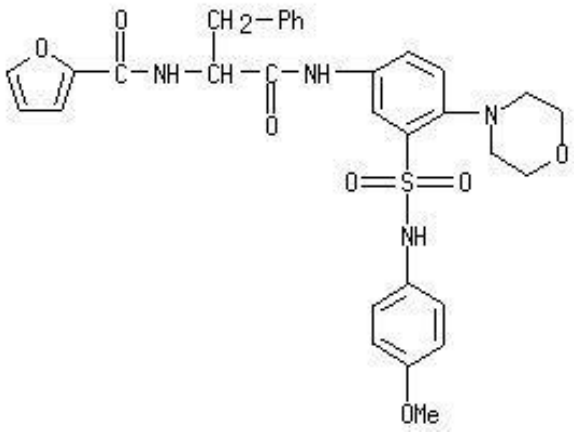
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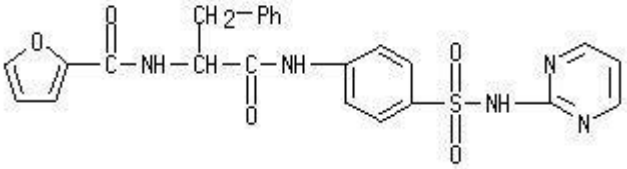
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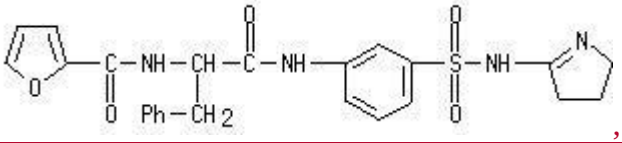
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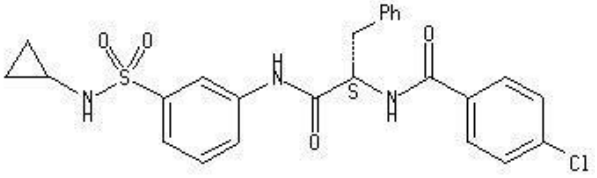
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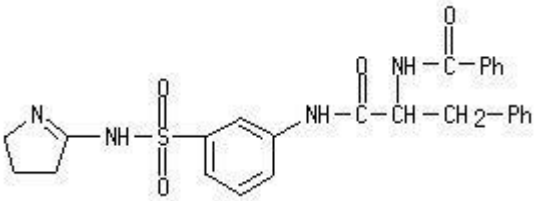
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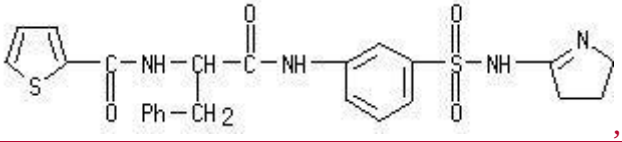
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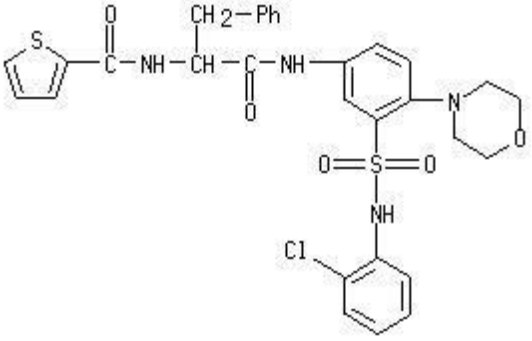
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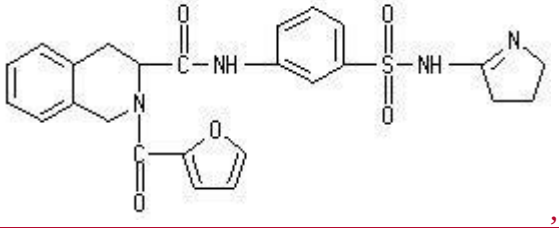
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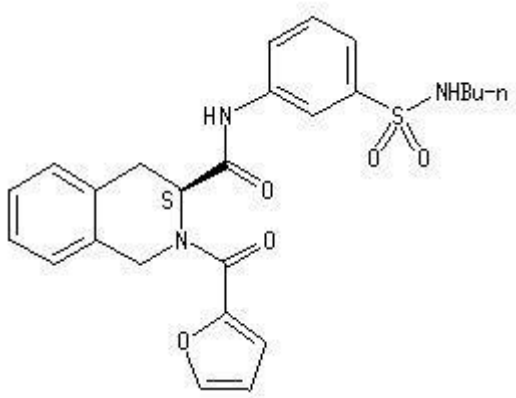
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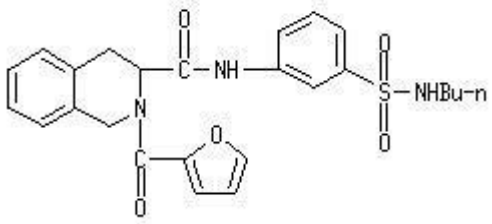


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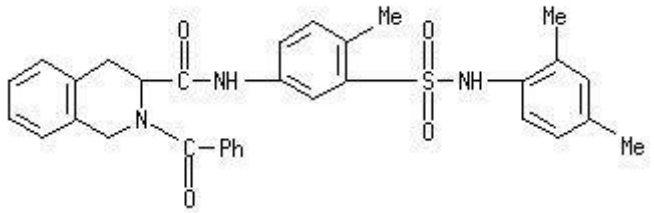


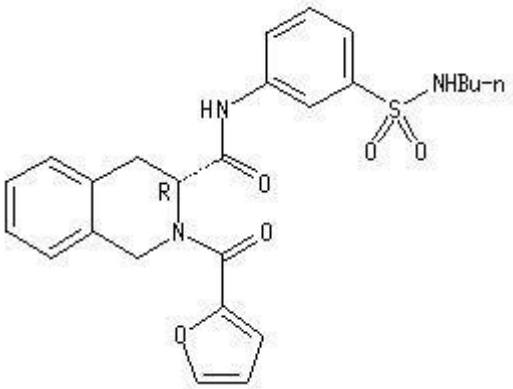
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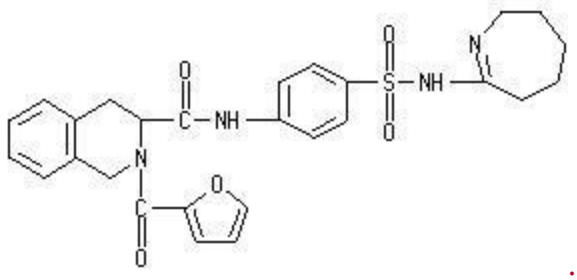
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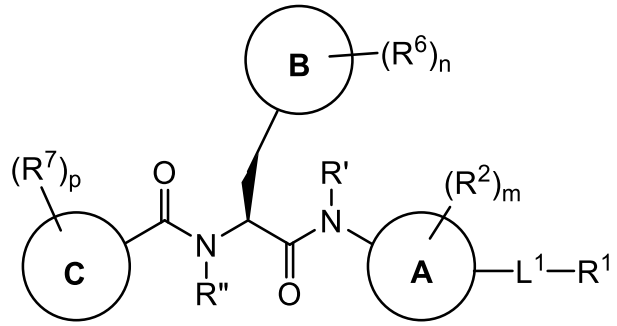
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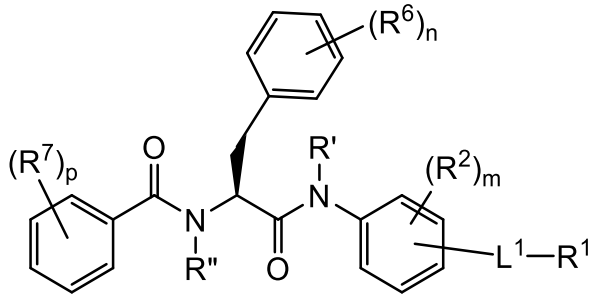
2. The compound of claim 1 of formula **II**:



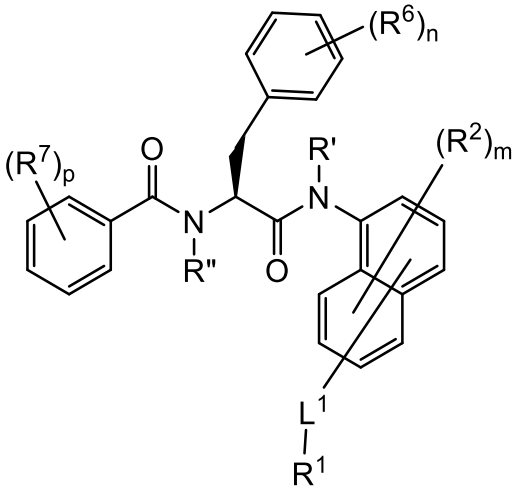
II

or a pharmaceutically acceptable salt thereof

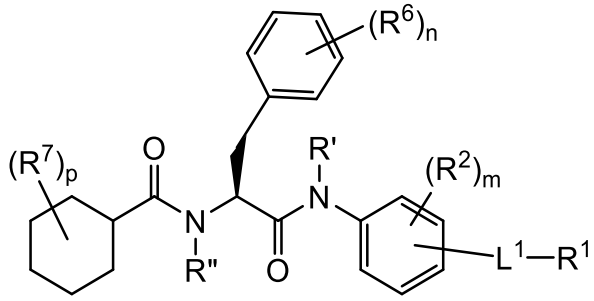
3. The compound of claim 1 of one of formulas **III-a**, **III-b**, **III-c**, or **III-d**:



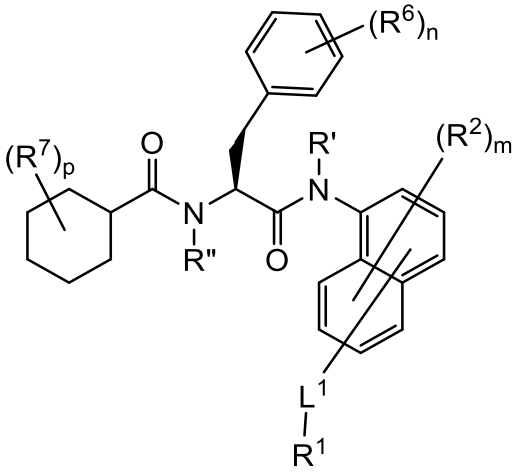
III-a



III-b



III-c

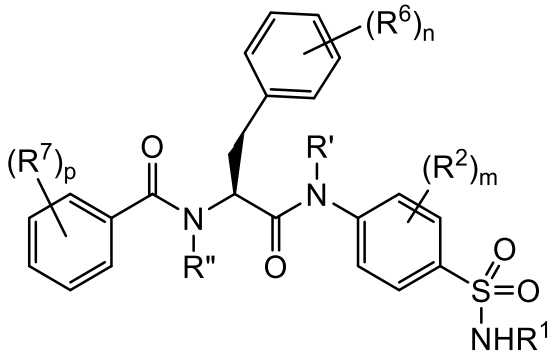


III-d

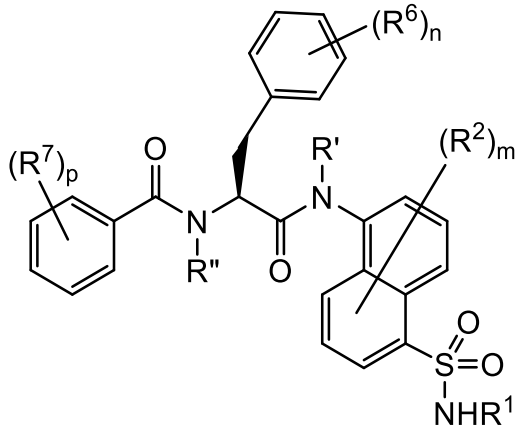
or a pharmaceutically acceptable salt thereof.

4. The compound of any one of the preceding claims where L^1 is $–S(O)_2NH-$, -S(O)NH-, -C(O)NH-, $-S(O)_2-$, -S(O)(NH)-, -S(O)-, S(O)NH-, -S(O)(N-*t*-Bu)-, or $-C(CF_3)(H)NH-$.

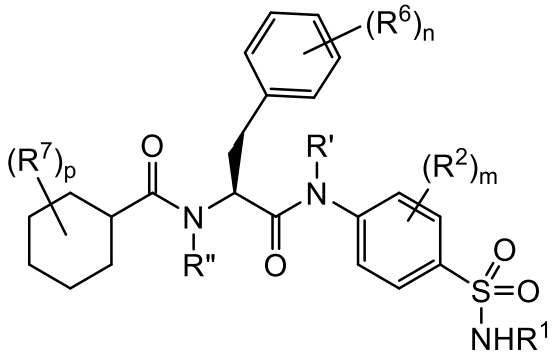
5. The compound of claim 1 of one of formulas **IV-a**, **IV-b**, **IV-c**, or **IV-d**:



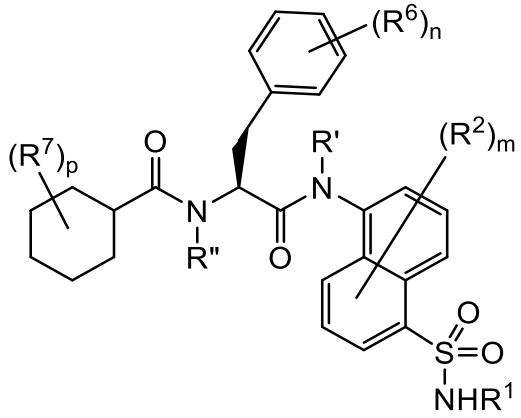
IV-a



IV-b



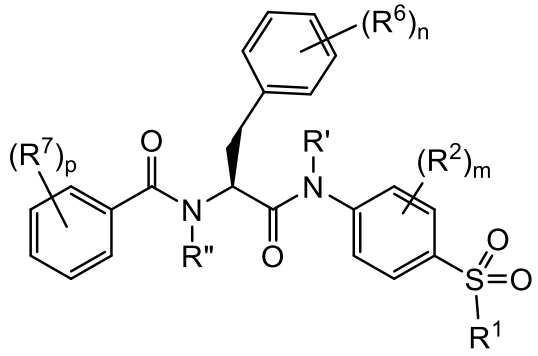
IV-c



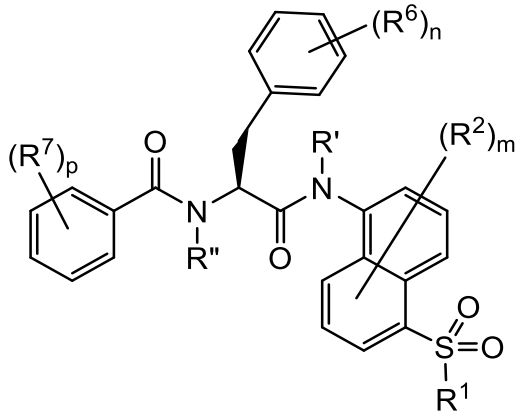
IV-d

or a pharmaceutically acceptable salt thereof.

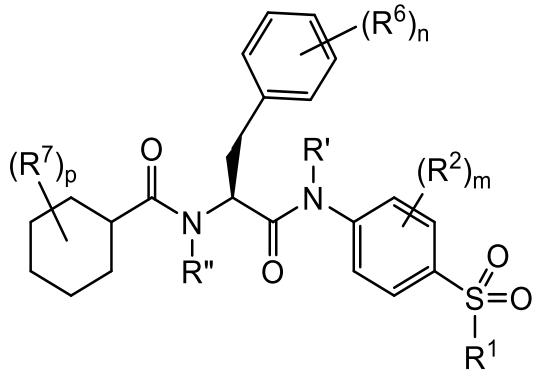
6. The compound of claim 1 of one of formulas **V-a**, **V-b**, **V-c**, or **V-d**:



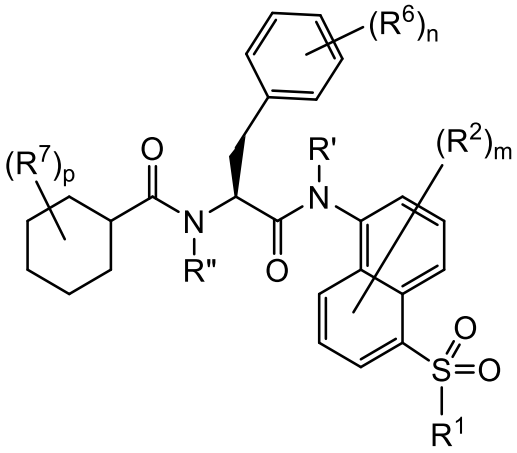
V-a



V-b



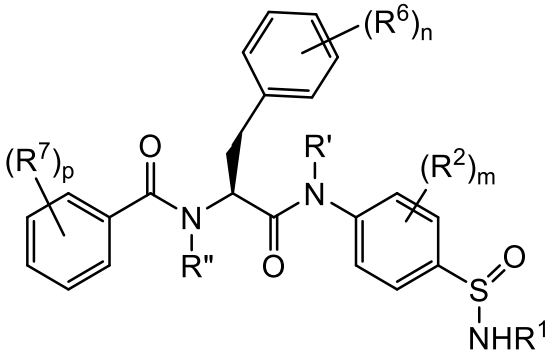
V-c



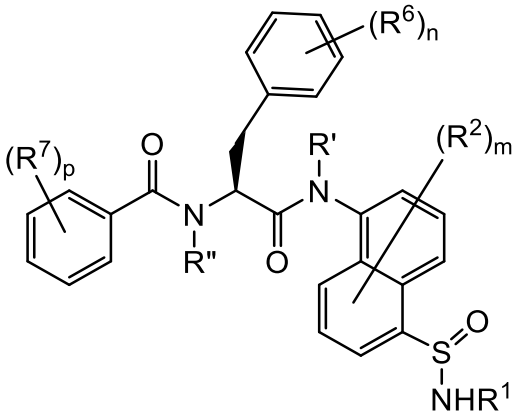
V-d

or a pharmaceutically acceptable salt thereof.

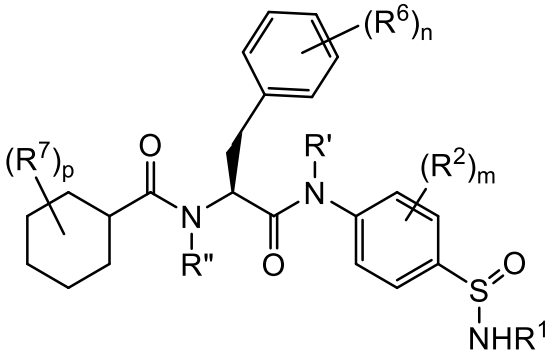
7. The compound of claim 1 of one of formulas **VI-a**, **VI-b**, **VI-c**, or **VI-d**:



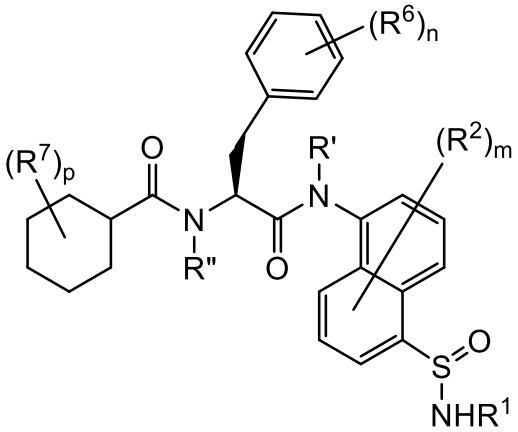
VI-a



VI-b



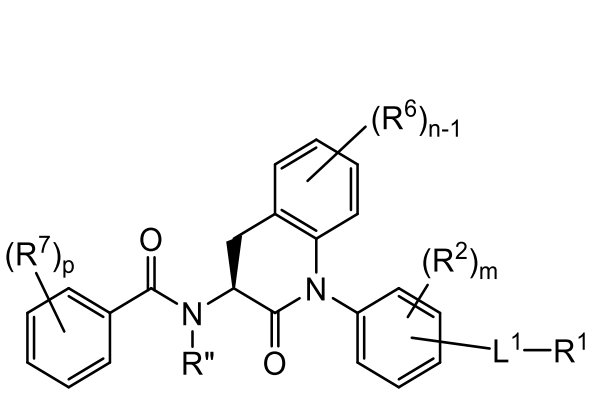
VI-c



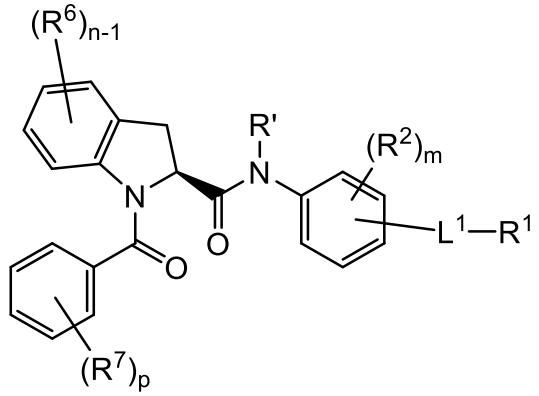
VI-d

or a pharmaceutically acceptable salt thereof.

8. The compound of claim 1 of one of formulas **VII-a** or **VII-b**:



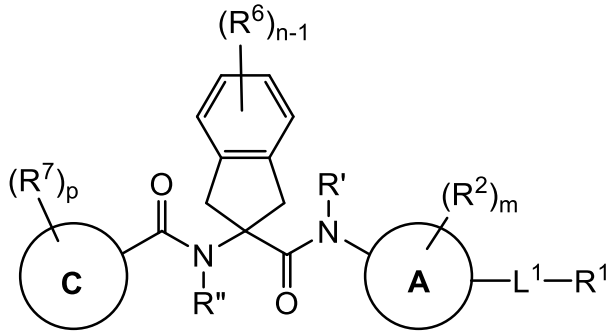
VII-a



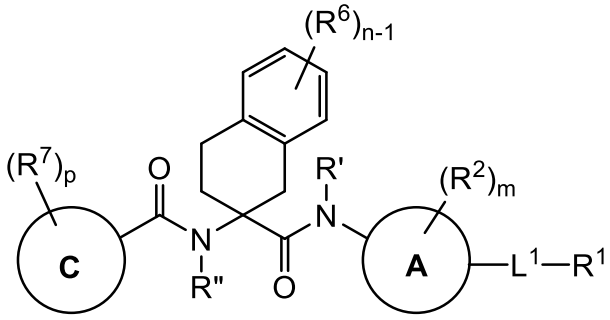
VII-b

or a pharmaceutically acceptable salt thereof.

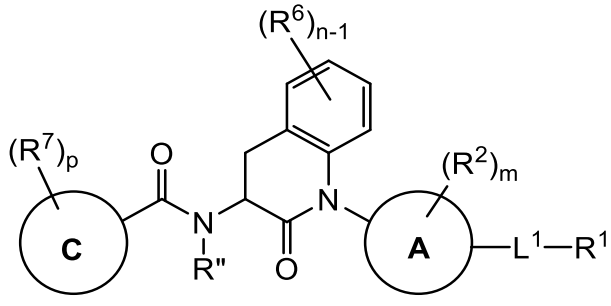
9. The compound of claim 1 of one of formulas **VIII**, **IX**, **X**, **XI**, **XII**, **XIII**, **XIV-a**, or **XIV-b**:



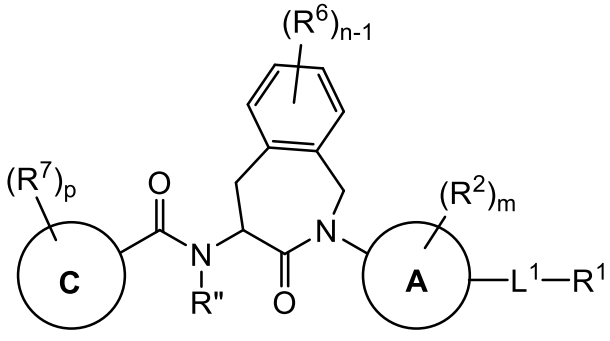
VIII



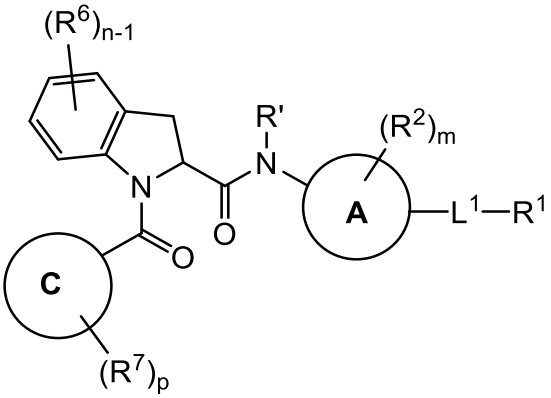
IX



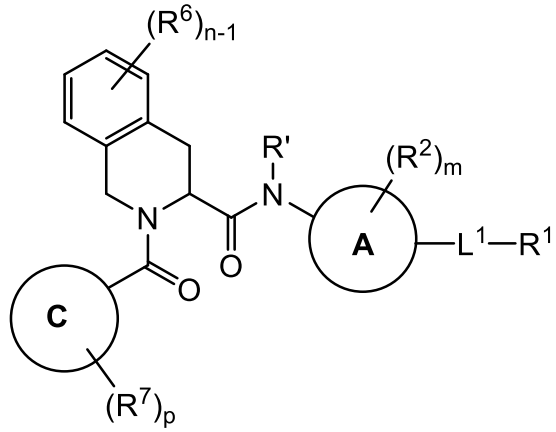
X



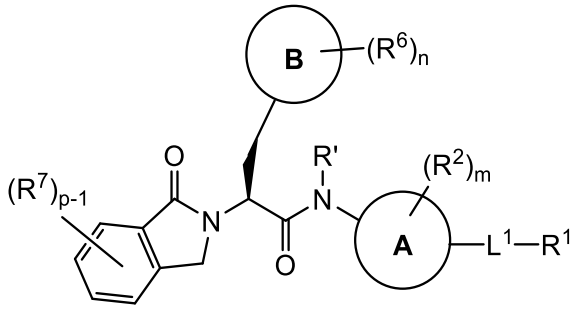
XI



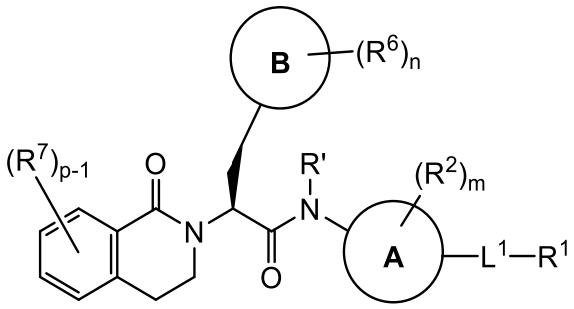
XII



XIII



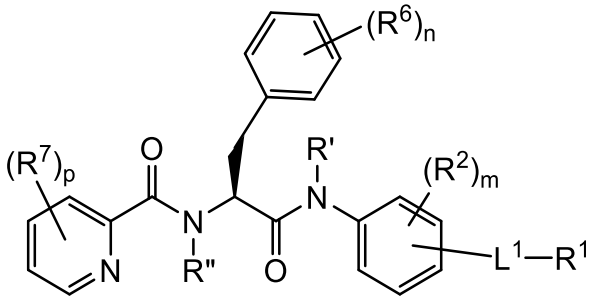
XIV-a



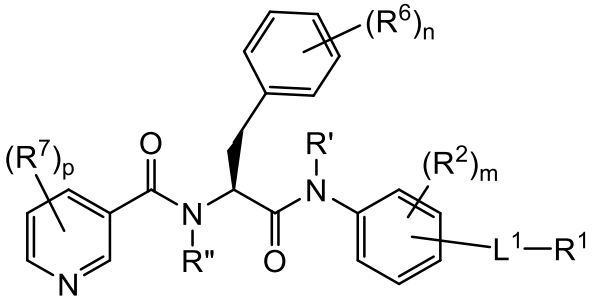
XIV-b

or a pharmaceutically acceptable salt thereof.

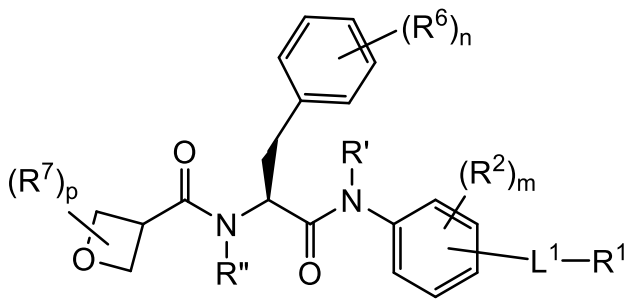
10. A~~The~~ compound of ~~claim 1 of~~ any one of formulas **XV-a**, **XV-b**, **XV-c**, **XV-d**, **XVII-a**, **XVII-b**, **XVII-c**, **XVII-d**, **XIX-a**, **XIX-b**, **XIX-c**, **XIX-d**, **XXI**, **XXIII-a**, **XXIII-b**, **XXV-a**, **XXV-b**, **XXV-c**, or **XXV-d**:



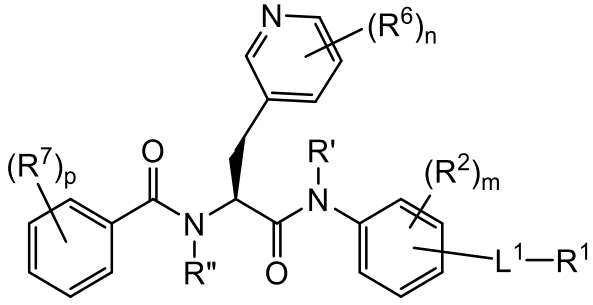
XV-a



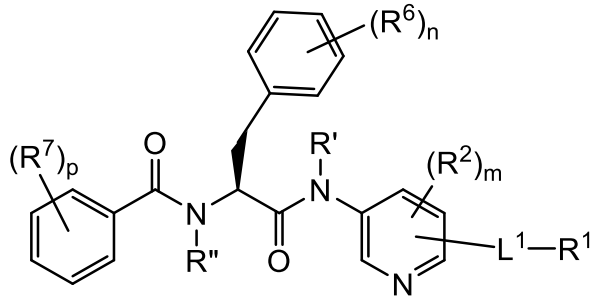
XV-b



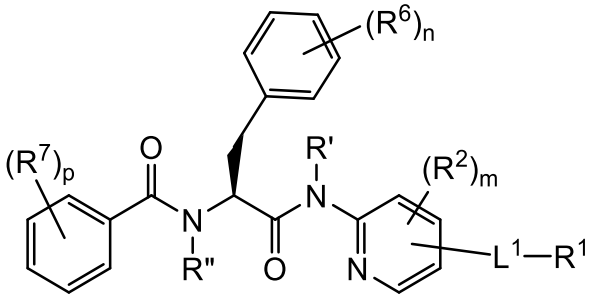
XV-c



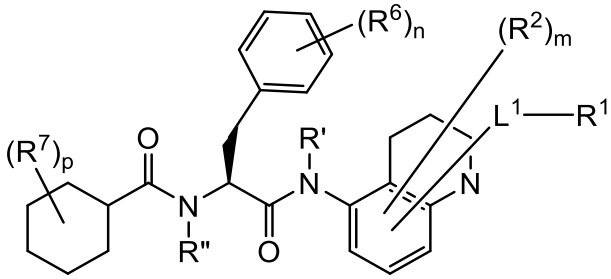
XV-d



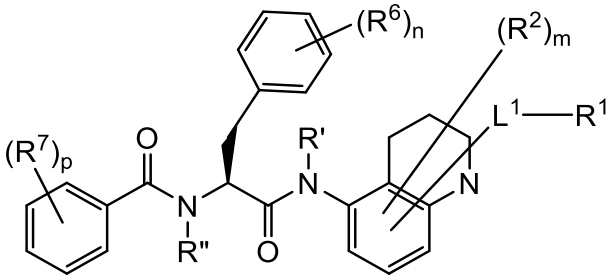
XVII-a



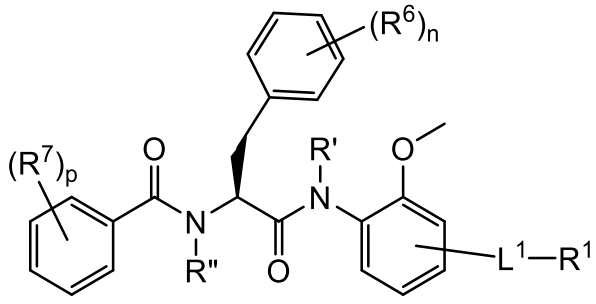
XVII-b



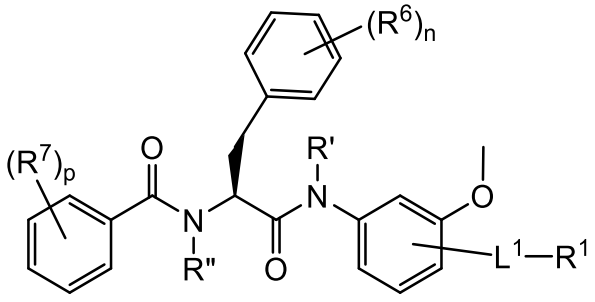
XVII-c



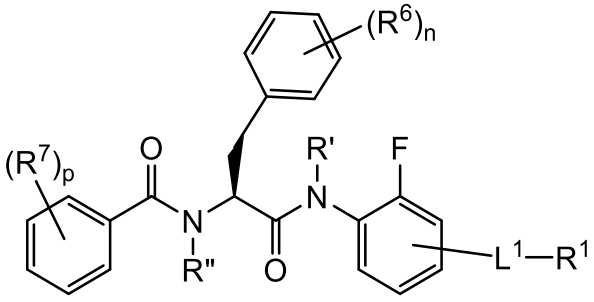
XVII-d



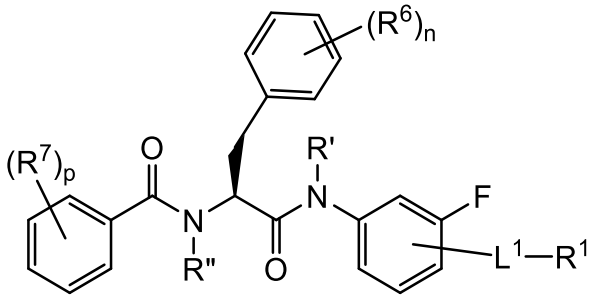
XIX-a



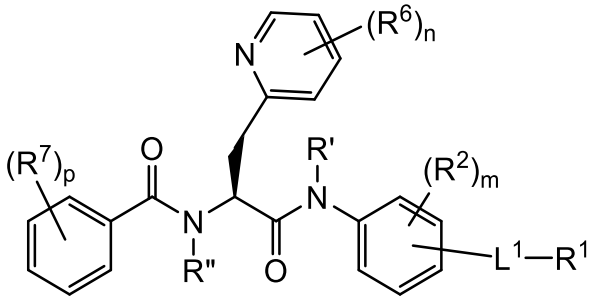
XIX-b



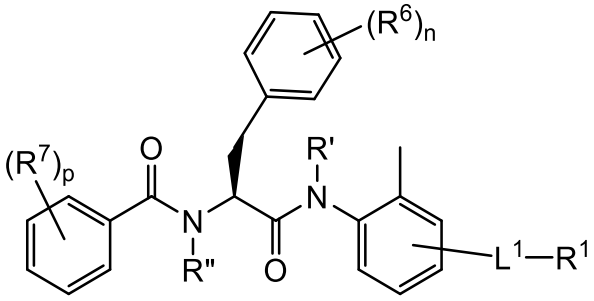
XIX-c



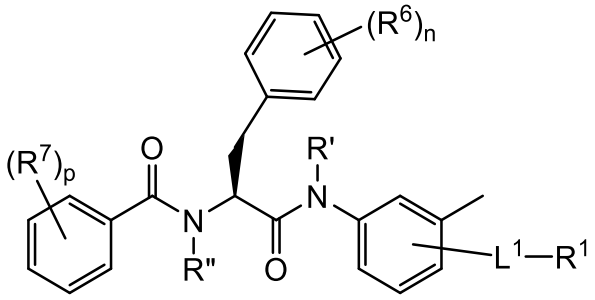
XIX-d



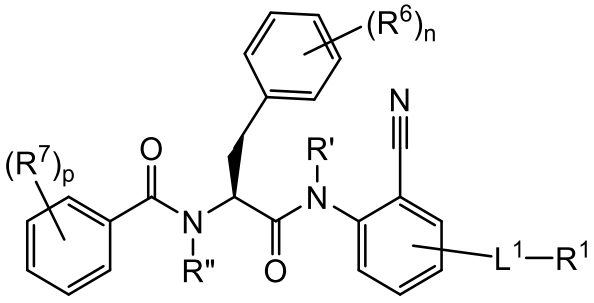
XXI



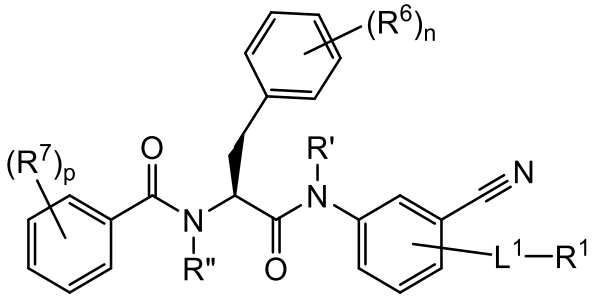
XXIII-a



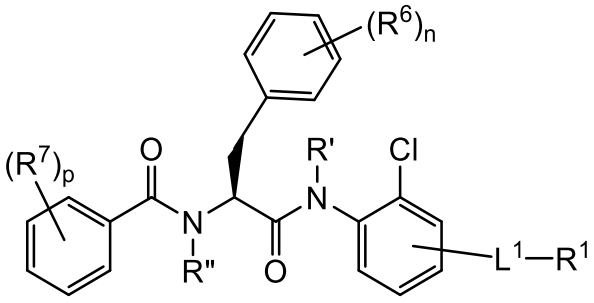
XXIII-b



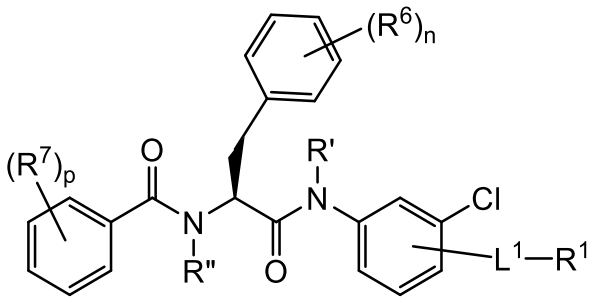
XXV-a



XXV-b



XXV-c



XXV-d

or a pharmaceutically acceptable salt thereof, wherein:

L^1 is a C_{1-3} bivalent hydrocarbon chain wherein one methylene unit of the chain is replaced by –$C(CF_3)H$–, –N(R)–, –O–, –C(O)–, –C(O)N(R)–, –N(R)C(O)–, –S(O)–, –$S(O)_2$–, –S(O)N(R)–, –$S(O)_2$N(R)–, or –S(O)(R)=N–;

each R is independently hydrogen or an optionally substituted C_{1-3} aliphatic group; or:

two R groups on the same nitrogen are optionally 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, or sulfur; or

an R group and R^1 on the same nitrogen are optionally 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, or sulfur;

R^1 is an optionally substituted group selected from C_{1-6} aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, a 5-8 membered saturated or partially unsaturated bridged bicyclic carbocyclic ring, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^2 is independently halogen, –CF_3, –CN, –C(O)NHR, –NO_2, –NHR, –NHC(O)R, –$NHS(O)_2$R, –$N(R)_2$, or –OR, or an optionally substituted C_{1-6} aliphatic group; or

two R^2 on the same carbon are optionally taken together to form =O; or

two R^2 groups are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms independently selected from nitrogen, oxygen or sulfur;

R' is hydrogen or a C_{1-3} aliphatic group;

R'' is hydrogen or a C_{1-3} aliphatic group;

each R^6 is independently halogen, –CN, $–NO_2$, –NHR, $–N(R)_2$, –OR, or an optionally substituted C_{1-6} aliphatic group; or:

two R^6 on the same carbon are optionally taken together to form =O;

an R^6 group and R' group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur; or

an R^6 group and R'' group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur;

each R^7 is independently halogen, –CN, $–NO_2$, –NHR, $–N(R)_2$, –OR, or an C_{1-6} aliphatic group; or

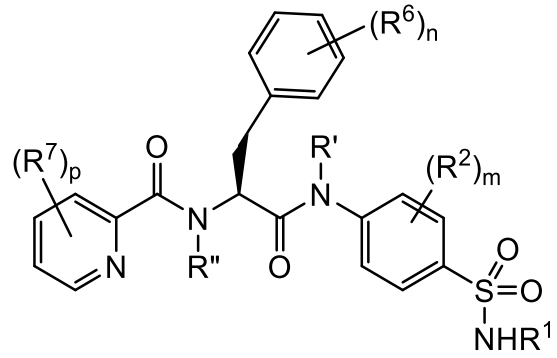
two R^7 on the same carbon are optionally taken together to form =O; or

an R^7 group and R'' group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur; and

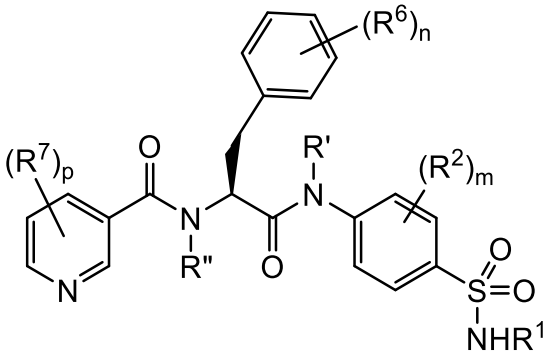
each of m, n, and p is independently 0, 1, 2, 3 or 4;

provided that R^1 is other than isopropyl, t-butyl, 1-methylcyclopropyl, 1-fluoromethylcyclopropyl, 1-difluoromethylcyclopropyl, 1-trifluoromethylcyclopropyl, or 3-methyl-3-oxetanyl when L^1 is $–S(O)_2N(R)-$.

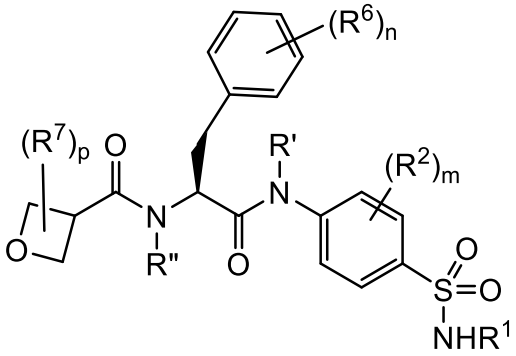
11. The compound of claim 10 of any one of formulas **XVI-a**, **XVI-b**, **XVI-c**, **XVI-d**, **XVIII-a**, **XVIII-b**, **XVIII-c**, **XVIII-d**, **XX-a**, **XX-b**, **XX-c**, **XX-d**, **XXII**, **XXIV-a**, **XXIV-b**, **XXVI-a**, **XXVI-b**, **XXVI-c**, or **XXVI-d**:



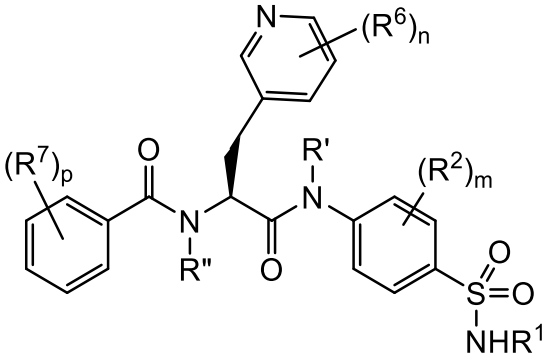
XVI-a



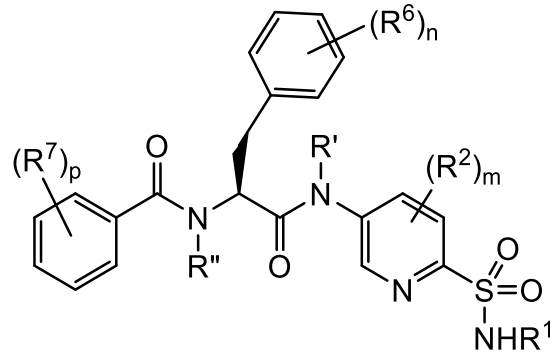
XVI-b



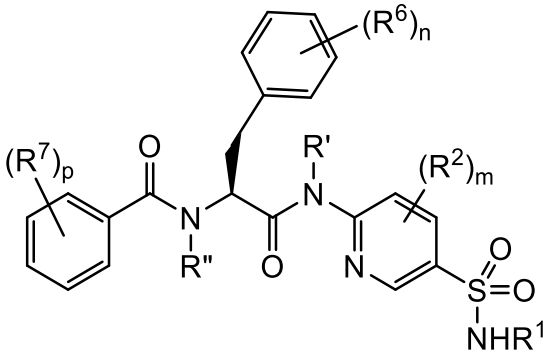
XVI-c



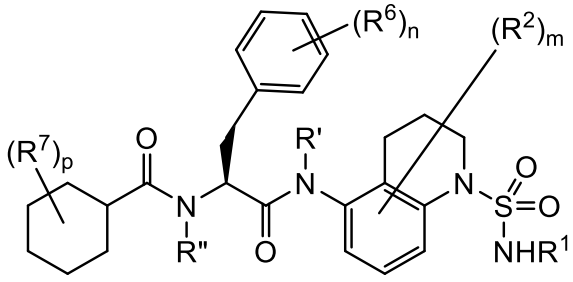
XVI-d



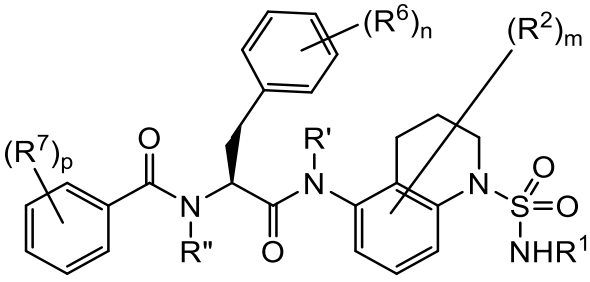
XVIII-a



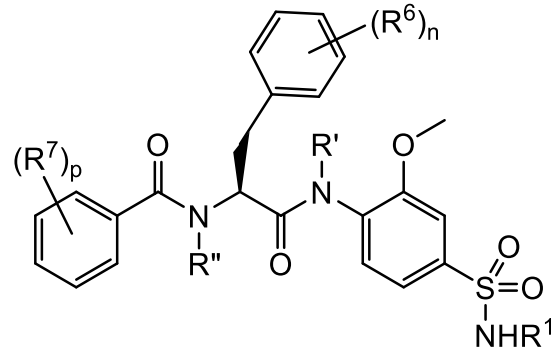
XVIII-b



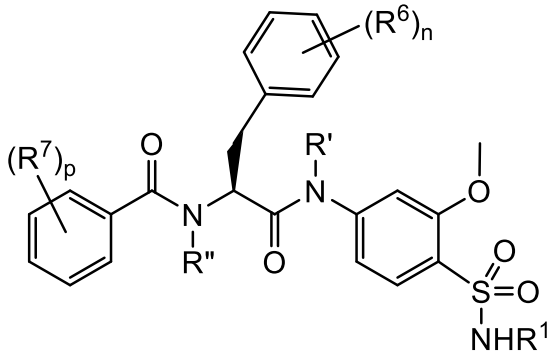
XVIII-c



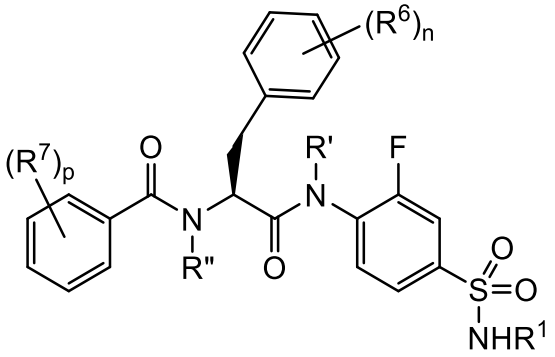
XVIII-d



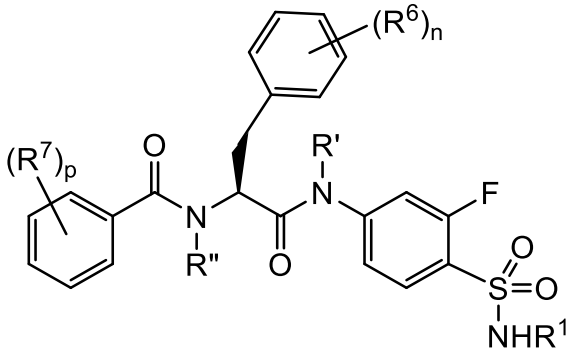
XX-a



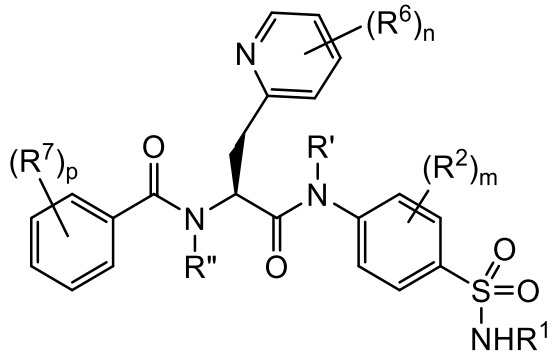
XX-b



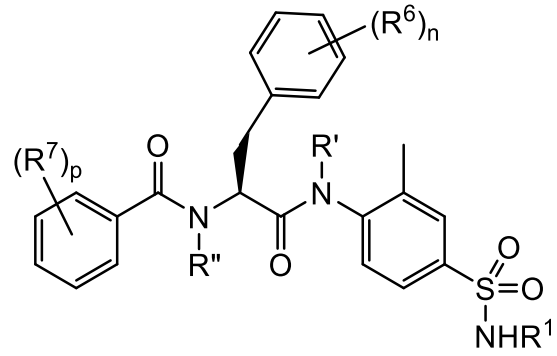
XX-c

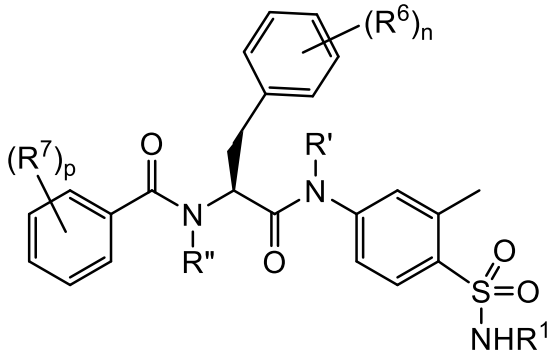


XX-d

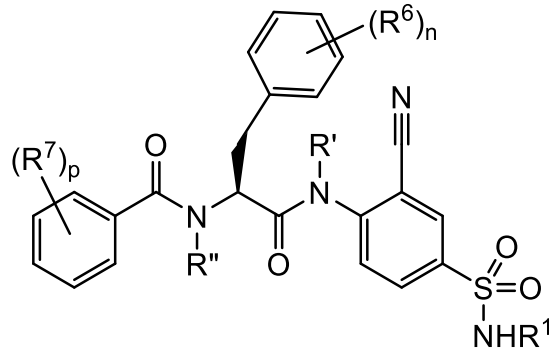


XXII

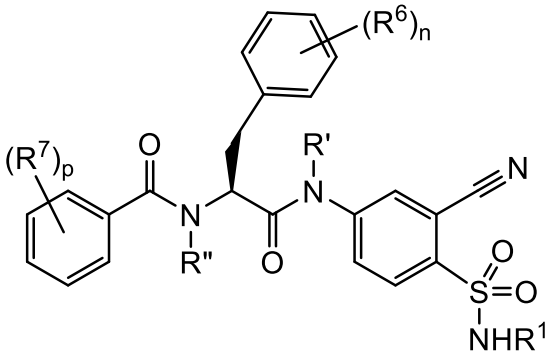




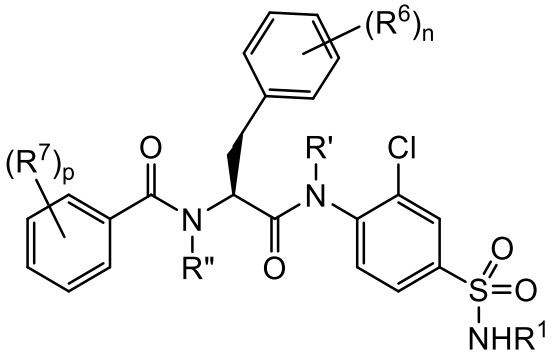
XXIV-a



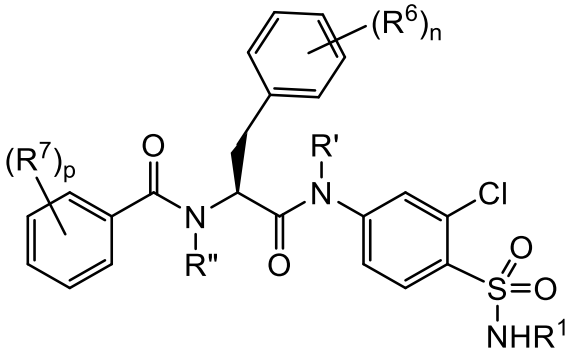
XXIV-b



XXVI-a



XXVI-b



XXVI-c

XXVI-d

or a pharmaceutically acceptable salt thereof.

12. The compound of any one of claims 1-9, wherein at least one R^2 is fluoro, methyl, or methoxy.

13. The compound of any one of the preceding claims, wherein m is 0, 1, 2, or 3.

14. The compound of any one of the preceding claims, wherein p is 0, 1, 2, or 3.

15. The compound of any one of the preceding claims, wherein at least one R^7 is fluoro.

16. A~~The~~ compound ~~of claim 1 wherein said compound is~~ selected from those depicted in **Table 1** of the specification, or a pharmaceutically acceptable salt thereof.

17. 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.

18. ~~A method of~~ Use of a compound of any one of claims 1-16 in the preparation of a medicament for inhibiting USP30 ~~in a biological sample comprising contacting the sample with the compound of any one of claims 1-16, or a pharmaceutically acceptable salt thereof~~.

19. Use of a compound of any one of claims 1-16 in the preparation of a medicament for~~A method of~~ treating an USP30-mediated disorder, disease, or condition ~~in a patient comprising administering to said patient the pharmaceutical composition of claim 17~~.

20. The use~~method~~ of claim 19, wherein the disorder is selected from the group consisting of a neurodegenerative disease; mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome; Leber's hereditary optic neuropathy (LHON); neuropathy, ataxia, retinitis pigmentosa- maternally inherited Leigh syndrome (NARP-MILS); Danon disease; ischemic heart disease leading to myocardial infarction; multiple sulfatase deficiency (MSD); mucolipidosis II (ML II); mucolipidosis III (ML III); mucolipidosis IV (ML IV); GM1 -gangliosidosis (GM1); neuronal ceroid- lipofuscinoses (NCL1); Alpers disease; Barth syndrome; Beta-oxidation defects; carnitine- acyl-carnitine deficiency; carnitine deficiency; creatine deficiency syndromes; coenzyme Q10 deficiency; complex I deficiency; complex II deficiency; complex III deficiency; complex IV deficiency; complex V deficiency; COX deficiency; chronic progressive external ophthalmoplegia syndrome (CPEO); CPT I deficiency; CPT II deficiency; glutaric aciduria type II; Kearns-Sayre syndrome; lactic acidosis; long-chain acyl-CoA dehydrongenase deficiency (LCHAD); Leigh disease or syndrome; lethal infantile cardiomyopathy (LIC); Luft disease; glutaric aciduria type II; medium-chain acyl-CoA dehydrongenase deficiency (MCAD); myoclonic epilepsy and ragged-red fiber (MERRF) syndrome; mitochondrial recessive ataxia syndrome; mitochondrial cytopathy; mitochondrial DNA depletion syndrome; myoneurogastointestinal disorder and encephalopathy; Pearson syndrome; pyruvate carboxylase deficiency; pyruvate dehydrogenase deficiency; POLG

mutations; medium/short-chain 3-hydroxyacyl-CoA dehydrogenase (M/SCHAD) deficiency; and very long-chain acyl-CoA dehydrongenase (VLCAD) deficiency.

21. The use~~method~~ of claim 20, wherein the neurodegenerative disease is selected from the group consisting of Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS), Huntington's disease, ischemia, stroke, dementia with Lewy bodies, and frontotemporal dementia.

22. The use~~method~~ of claim 21, wherein the neurodegenerative disease is Alzheimer's disease or Parkinson's disease.

23. The use~~method~~ of claim 19, wherein the disorder is a neoplastic disease selected from the group consisting of metastatic carcinoma, multiple myeloma, osteosarcoma, chondosarcoma, Ewing's sarcoma, nasopharyngeal carcinoma, and leukemia.

24. The use~~method~~ of claim 19, wherein the disease is cardiovascular disease, kidney disease, pulmonary fibrosis, ophthalmic conditions, cancer, cognitive disease, peroxisome related disease, natural aging, or an age-related disease.

25. The use~~method~~ of claim 24, wherein the peroxisome related disease is selected from the group consisting of Ataxia-telangiectasia mutated, Heimler syndrome, Infantile refsum disease, Neonatal adrenoleukodystrophy, Rhizomelic chondrodysplasia punctate, White matter dementia, Zellweger syndrome, and Zellweger spectrum disorder.

26. A compound of any one of claims 1-16, for use in therapy.