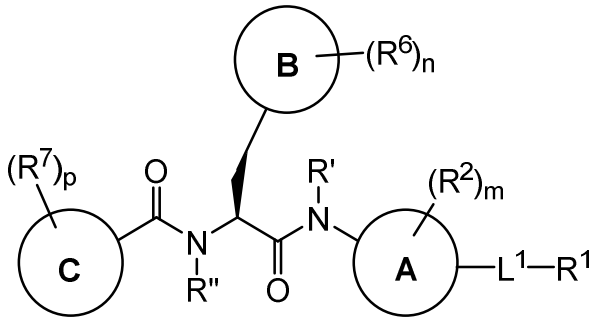
models of PD in multiple species (Bingol et al., The mitochondrial deubiquitinase USP30 opposes parkin-mediated mitophagy. Nature 2014, 510:370-375; Bian et al., Overexpression of parkin ameliorates dopaminergic neurodegeneration induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine in mice. PLoS One 2012, 7:e39953. PMC3390003; Hou et al., Parkin represses 6-hydroxydopamine-induced apoptosis via stabilizing scaffold protein p62 in PC12 cells. Acta Pharmacol Sin 2015, 36:1300-1307. PMC4635325; Lo Bianco et al., Lentiviral vector delivery of parkin prevents dopaminergic degeneration in an alpha-synuclein rat model of Parkinson's disease. Proc Natl Acad Sci USA 2004, 101:17510-17515. PMC536019; Paterna et al., DJ-1 and Parkin modulate dopamine-dependent behavior and inhibit MPTP-induced nigral dopamine neuron loss in mice. Mol Ther 2007, 15:698-704; Vercammen et al., Parkin protects against neurotoxicity in the 6-hydroxydopamine rat model for Parkinson's disease. Mol Ther 2006, 14:716-723; Yasuda et al., Parkin-mediated protection of dopaminergic neurons in a chronic MPTP-minipump mouse model of Parkinson disease. J Neuropathol Exp Neurol 2011, 70:686-697; Yasuda et al., Neuronal specificity of alpha-synuclein toxicity and effect of Parkin co-expression in primates. Neuroscience 2007, 144:743-753; Liang et al., USP30 deubiquitylates mitochondrial Parkin substrates and restricts apoptotic cell death. EMBO Rep 2015, 16:618-627. PMC4428036.). PINK1/Parkin-dependent linear ubiquitination of proteins on the outer mitochondrial membrane (OMM) leads to removal of damaged protein and mitochondria through fission of mitochondrial derived vesicles (MDVs) or recruitment of phagophores to begin the mitophagy process. The deubiquitinating (DUB) enzyme, USP30, is present specifically on the OMM (unlike other DUBs such as USP8,15 and 35 implicated in mitochondrial quality control), and acts as a counterbalance to this process by specifically removing ubiquitin chains on parkin substrates. Involvement of USP30 in regulating mitophagy has been well established through functional genomic studies in mammalian, including human, cells and flies, further validating it as a promising target (Bingol et al., 2014). Without wishing to be bound by any particular theory, it is believed that USP30 inhibitors will promote the clearance of damaged mitochondria to restore mitochondrial homeostasis, attenuating the pathogenic cascade associated with PD pathogenesis.

SUMMARY

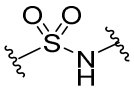
[0006a] In an aspect of the present disclosure, there is provided a compound of formula **II**:



II

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

L^1 is ;

R^1 is hydrogen or 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, $–NHS(O)_2R$, $–N(R)_2$, 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;

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;

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

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

Ring B is a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^6 is independently halogen, phenyl, a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, –CN, $–NO_2$, –NHR, $–N(R)_2$, –OR, –C(O)R, –C(O)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;

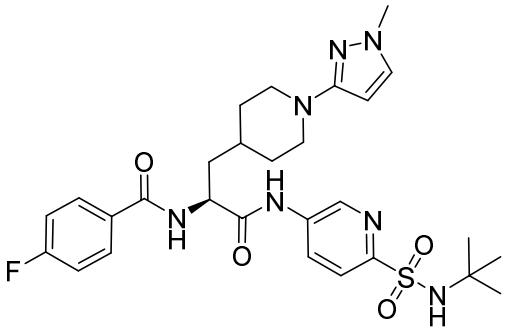
an R^6 group and R" group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur;

Ring C is phenyl, a 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 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; and

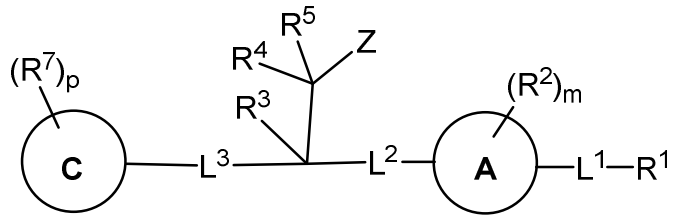
each of m, n, and p is independently 0, 1, 2, 3 or 4.

[0006b] In another aspect of the present disclosure, there is provided a compound having the following structure, or a pharmaceutically acceptable salt thereof

Compound No.	**Structure**
I-293	

.

[0006c] In another aspect of the present disclosure, there is provided a compound of formula **I***:



I*

or a pharmaceutically acceptable salt thereof; wherein

Ring A is a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

L^1 is a covalent bond;
R^1 is hydrogen;
each R^2 is independently $–CF_3$ or –CN;
L^2 is $–C(O)N(R')$;
R' is hydrogen or a C_{1-3} aliphatic group;
L^3 is $–C(O)N(R'')–$;

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

R^3 is hydrogen;

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

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

Z is a C_{1-6} aliphatic group;

Ring C is phenyl or a 5-6 membered heteroaryl ring having 1-4 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; and

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

[0006d] In a further 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.

[0006e] In another aspect of the present disclosure, there is provided a method of inhibiting USP30 in a biological sample comprising contacting the sample with the compound disclosed herein, or a pharmaceutically acceptable salt thereof.

[0006f] In a further aspect of the present disclosure, there is provided a use of a pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating an USP30-mediated disorder, disease, or condition in a patient, wherein the disorder, disease, or condition 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 dehydrogenase deficiency (LCHAD); Leigh disease or syndrome; lethal infantile cardiomyopathy (LIC); Luft disease; glutaric aciduria type II; medium-chain acyl-CoA dehydrogenase deficiency (MCAD); myoclonic epilepsy and ragged-red fiber (MERRF) syndrome; mitochondrial recessive ataxia syndrome; mitochondrial cytopathy; mitochondrial DNA depletion syndrome; myoneurogastrointestinal 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 dehydrogenase (VLCAD) deficiency.

[0006g] In another aspect of the present disclosure, there is provided a use of a pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating an USP30-mediated disorder, disease, or condition in a patient, wherein the disorder, disease, or condition is a neoplastic disease selected from the group consisting of metastatic carcinoma, multiple myeloma, osteosarcoma, chondrosarcoma, Ewing's sarcoma, nasopharyngeal carcinoma, and leukemia.

[0006h] In another aspect of the present disclosure, there is provided a use of a pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating an USP30-mediated disorder, disease, or condition in a patient, wherein the disorder, disease, or condition is cardiovascular disease, kidney disease, pulmonary fibrosis, ophthalmic conditions, cancer, cognitive disease, peroxisome related disease, natural aging, or an age-related disease.

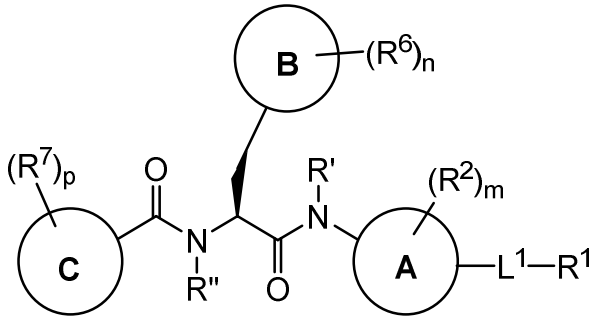
[0006i] In another aspect of the present disclosure, there is provided a pharmaceutical composition disclosed herein, for use in therapy.

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

CLAIMS

We claim:

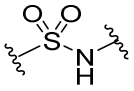
1. A compound of formula **II**:



II

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

L^1 is ;

R^1 is hydrogen or 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, $–NHS(O)_2R$, $–N(R)_2$, 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;

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;

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

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

Ring B is a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^6 is independently halogen, phenyl, a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, –CN, $–NO_2$, –NHR, $–N(R)_2$, –OR, –C(O)R, –C(O)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;

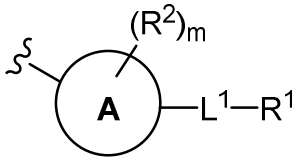
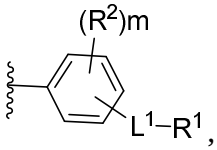
an R^6 group and R' group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur;

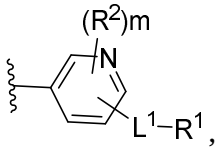
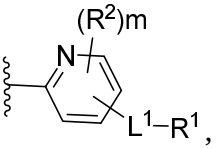
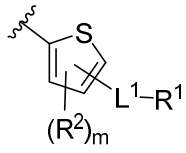
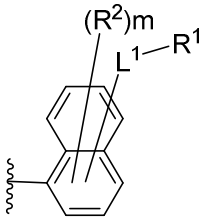
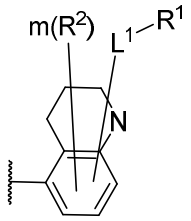
an R^6 group and R" group are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused ring having 0-2 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen or sulfur;

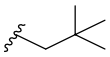
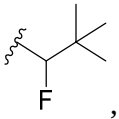
Ring C is phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic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

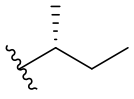
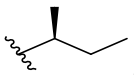
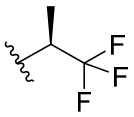
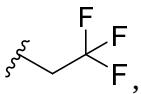
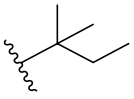
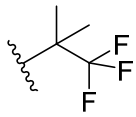
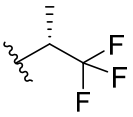
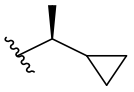
each R^7 is independently halogen, –CN, $–NO_2$, –NHR, $–N(R)_2$, –OR, or an optionally substituted C_{1-6} aliphatic group; and

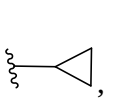
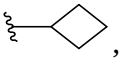
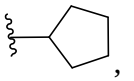
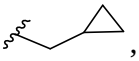
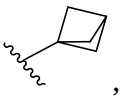
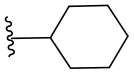
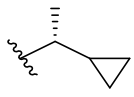
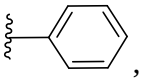
each of m, n, and p is independently 0, 1, 2, 3 or 4.

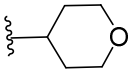
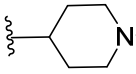
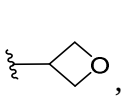
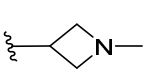
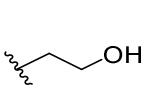
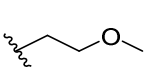
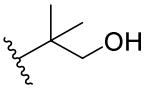
2. The compound of claim 1, wherein  is ,

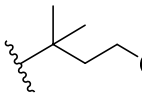
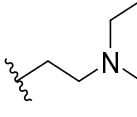
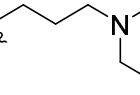
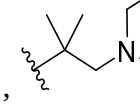
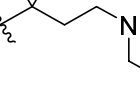
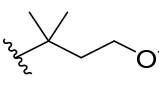
, , , , or .

3. The compound of claim 1 or 2, wherein R^1 is , , , ,

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, , , , , ,

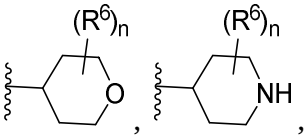
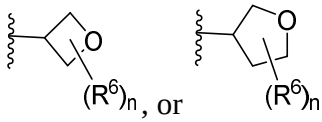
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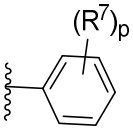
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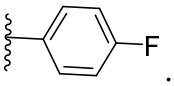
, , , , , ,

, , or .

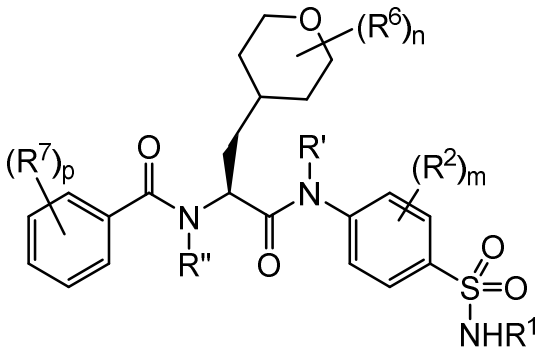
4. The compound of any one of claims 1-3, wherein R^2 is methyl, methoxy, fluoro, chloro, cyano, hydroxyl or trifluoromethyl.

5. The compound of any one of claims 1-4, wherein Ring B$(R^6)_n$ is , , or .

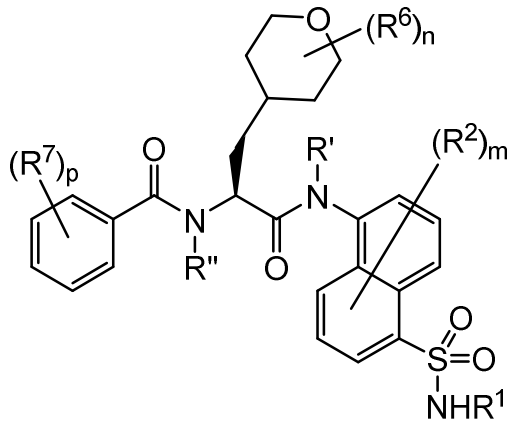
6. The compound of any one of claims 1-5, wherein Ring C-$(R^7)_p$ is .

7. The compound of any one of claims 1-5, wherein Ring C-$(R^7)_p$ is .

8. The compound of claim 1, of formulae **IV-a** or **IV-c**:



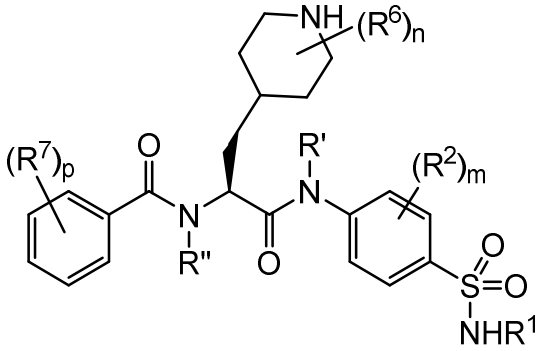
IV-a



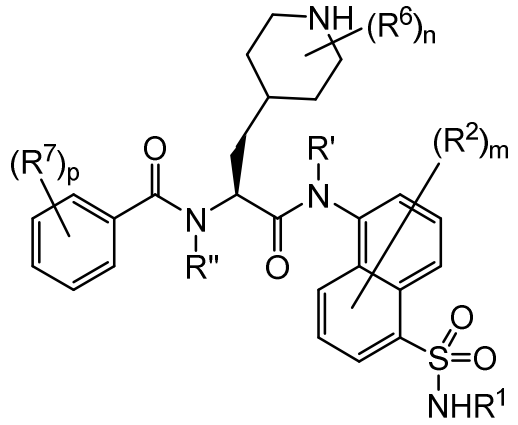
IV-c

or a pharmaceutically acceptable salt thereof.

9. The compound of claim 1, of formulae **VI-a** or **VI-c**:



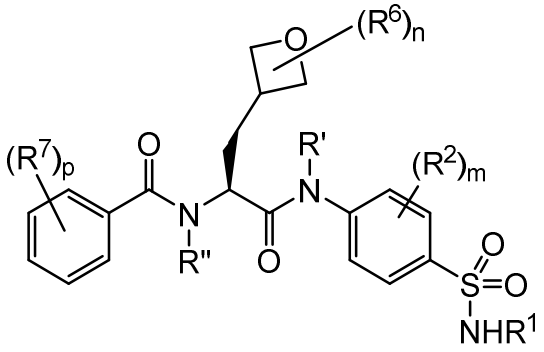
VI-a



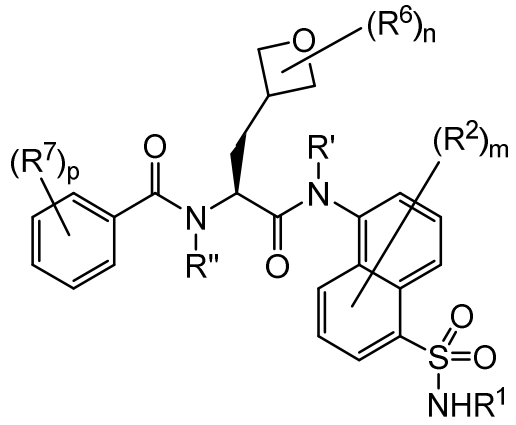
VI-c

or a pharmaceutically acceptable salt thereof.

10. The compound of claim 1, of formulae **X-a** or **X-c**:

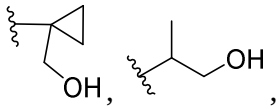
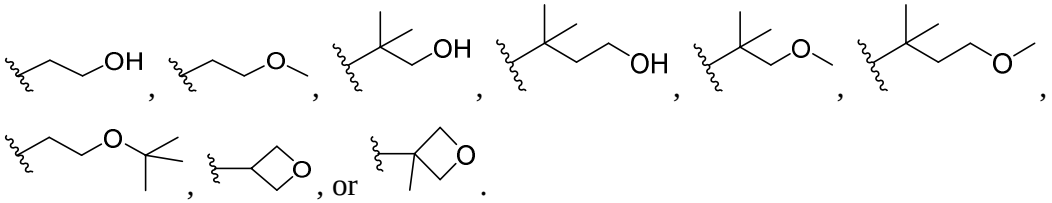


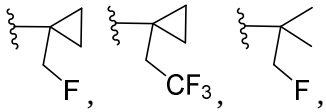
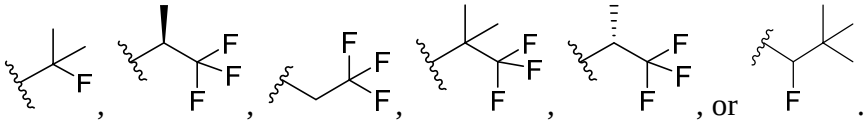
X-a

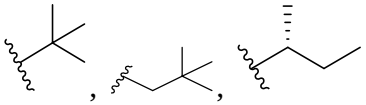
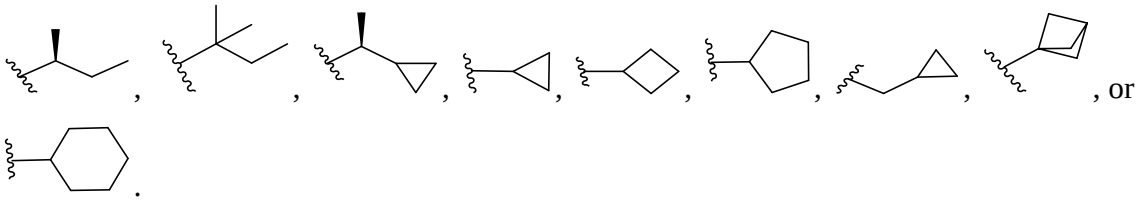


X-c

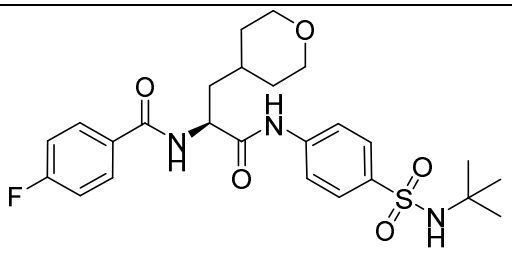
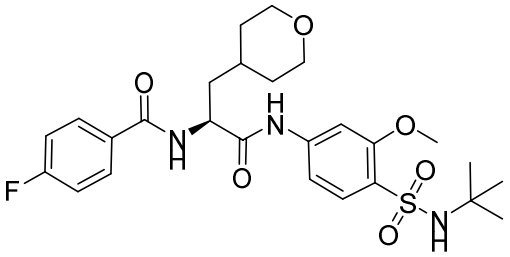
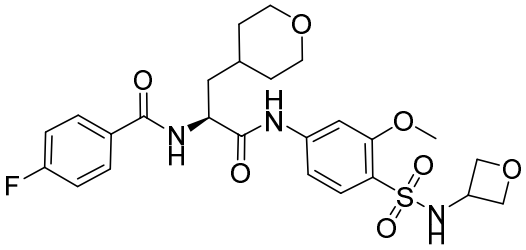
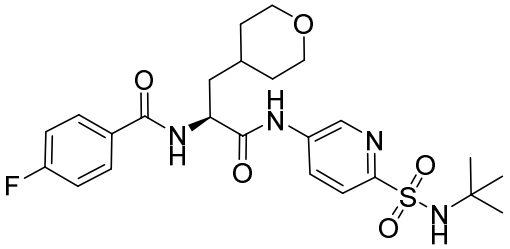
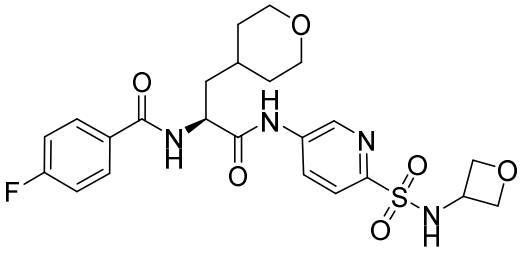
or a pharmaceutically acceptable salt thereof.

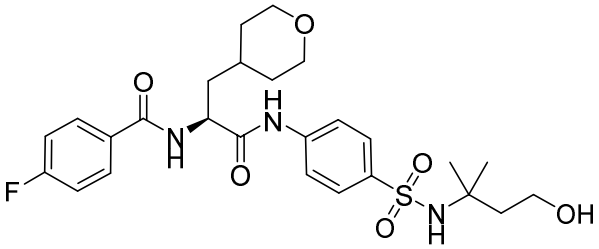
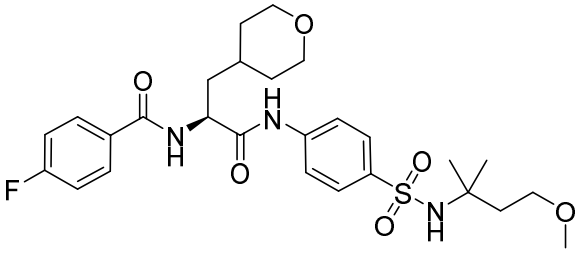
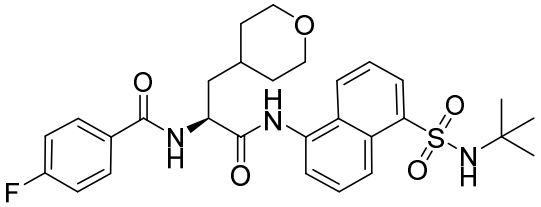
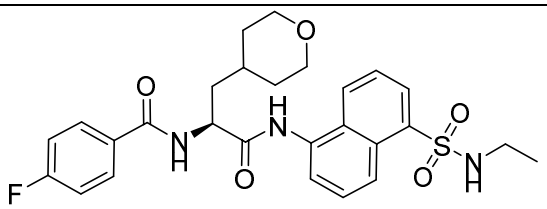
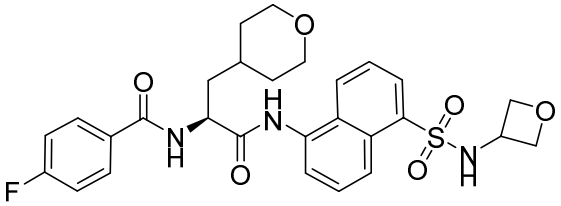
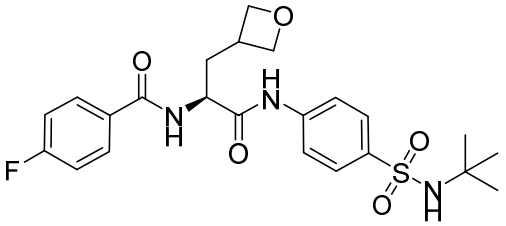
11. The compound of any one of claims 1-3 or 8-11, wherein R^1 is , , or .

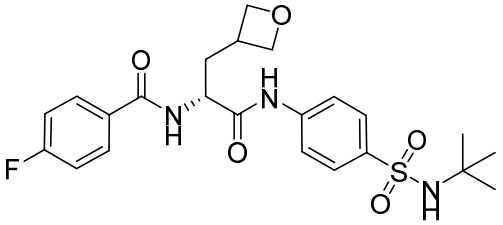
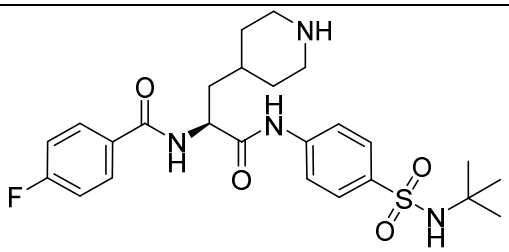
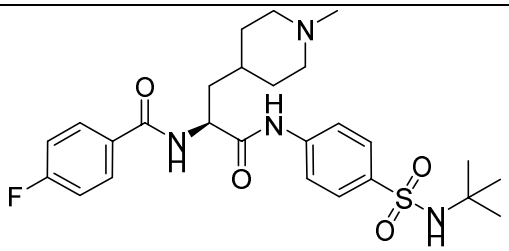
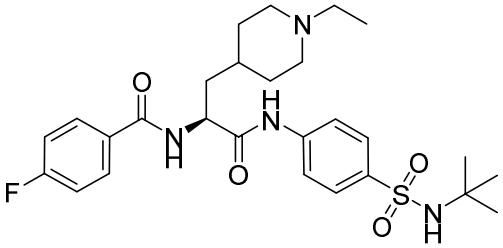
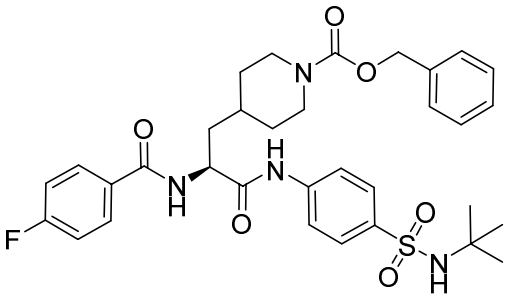
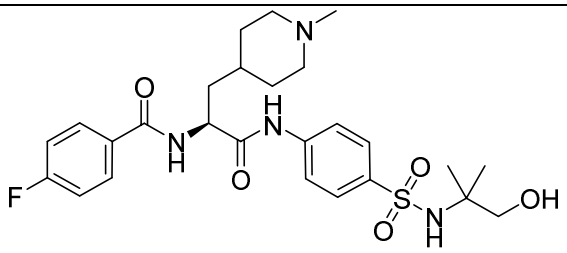
12. The compound of any one of claims 1-3 or 8-11, wherein R^1 is , , or .

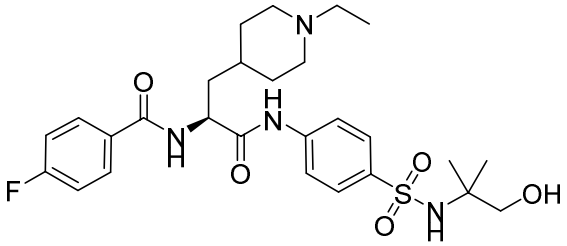
13. The compound of any one of claims 1-11, wherein R^1 is , , or .

14. The compound of claim 1, wherein said compound is selected from those in the following list, or a pharmaceutically acceptable salt thereof.

Compound No.	Structure
I-1	
I-2	
I-3	
I-4	
I-5	

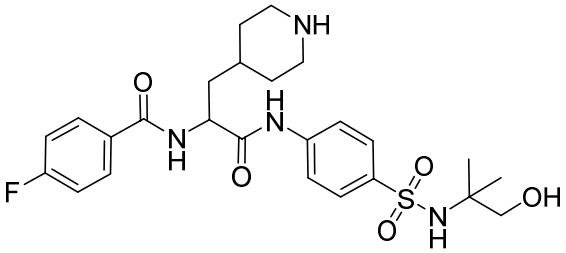
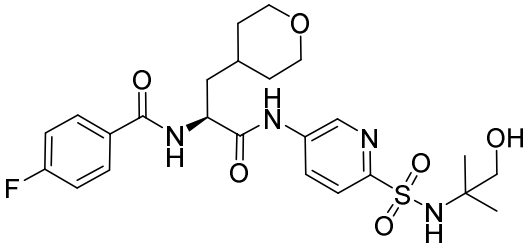
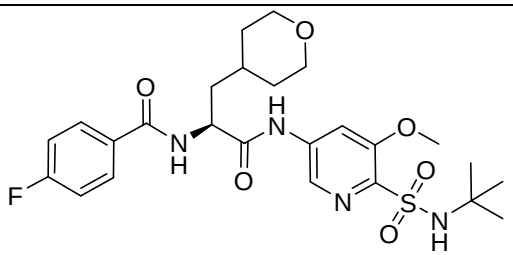
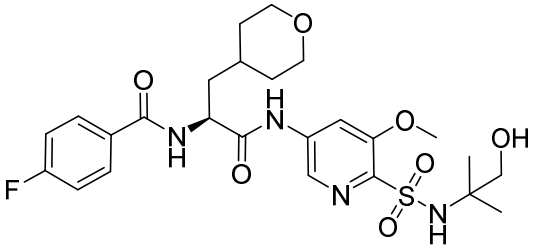
Compound No.	Structure
I-6	
I-7	
I-8	
I-9	
I-10	
I-38	

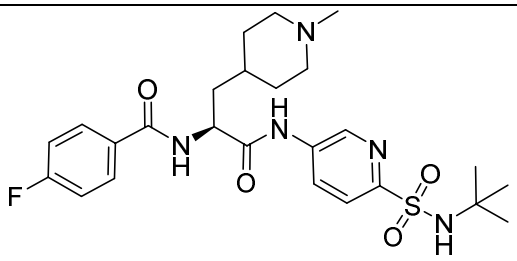
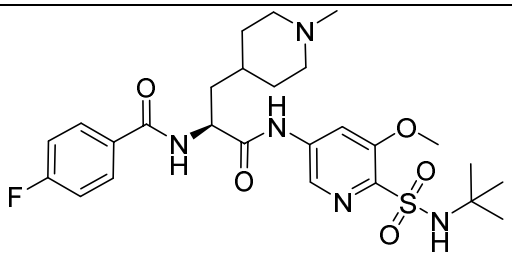
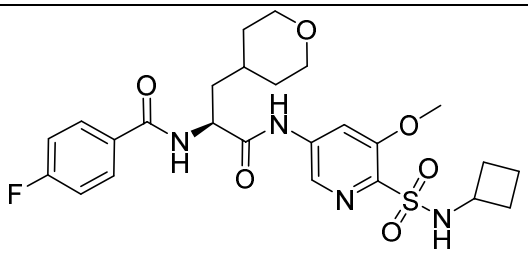
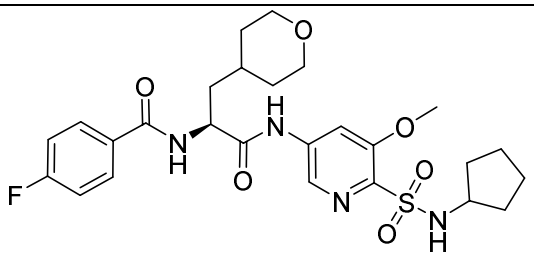
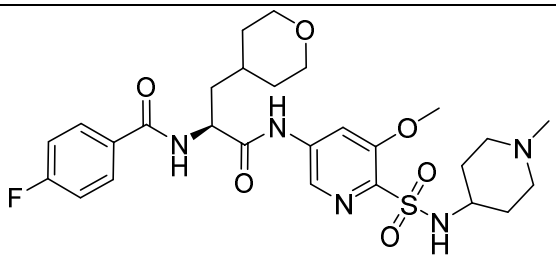
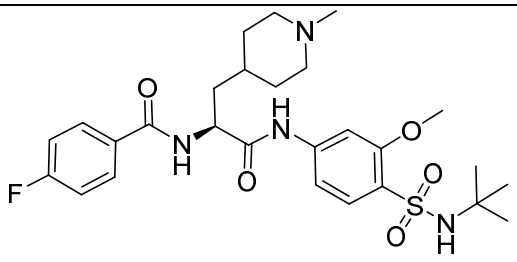
Compound No.	Structure
I-39	
I-40	
I-41	
I-42	
I-43	
I-44	

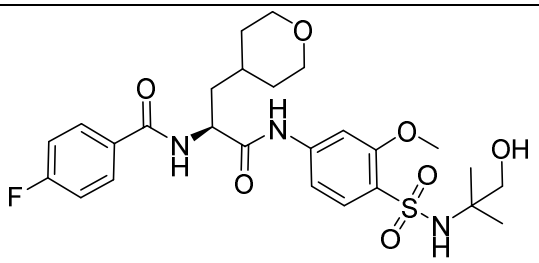
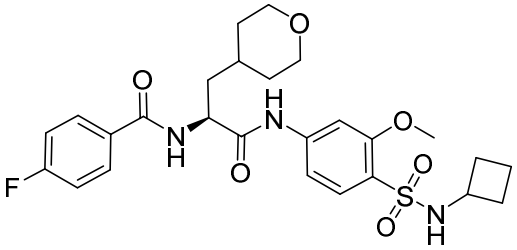
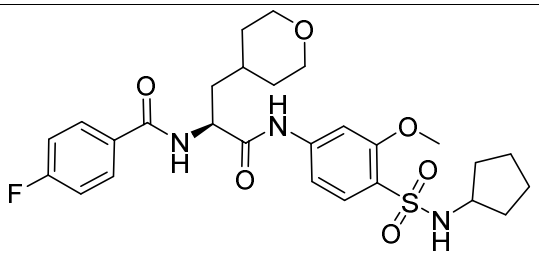
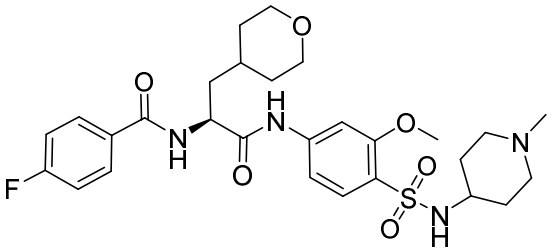
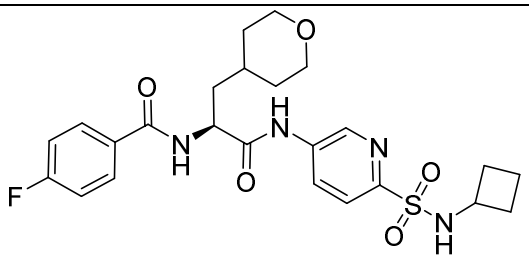
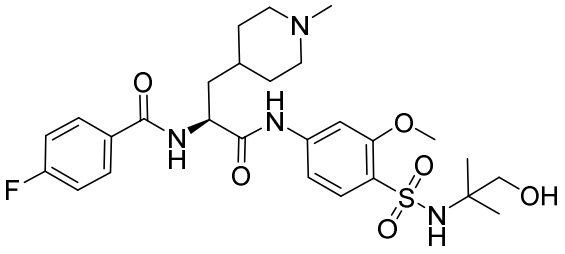
Compound No.	Structure
I-45	

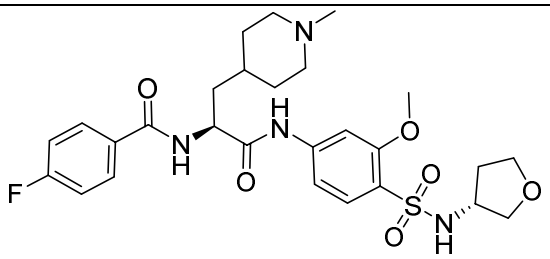
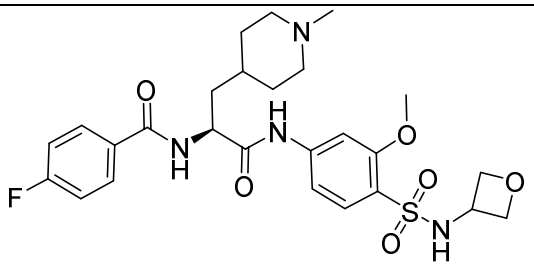
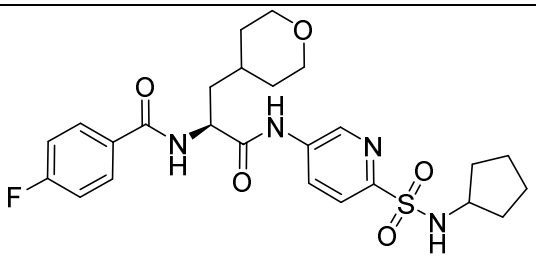
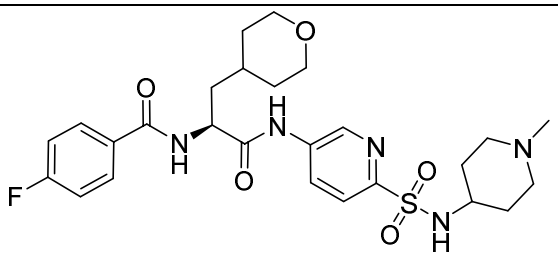
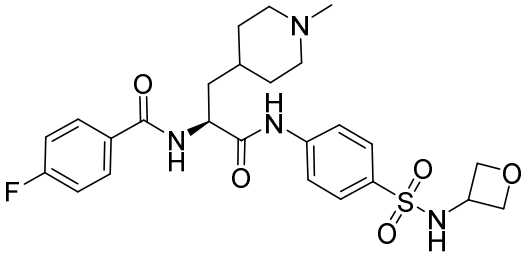
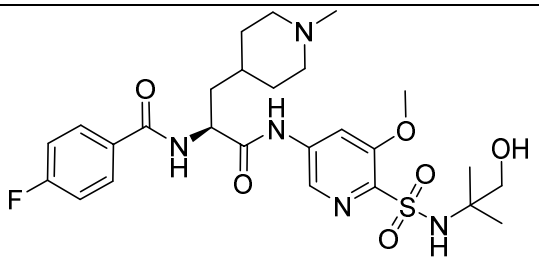
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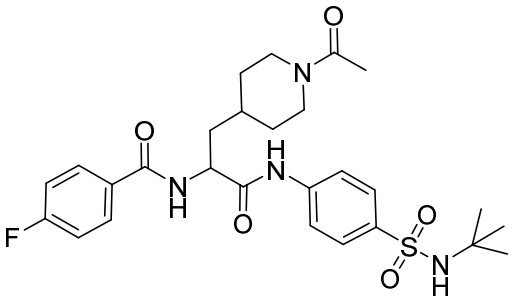
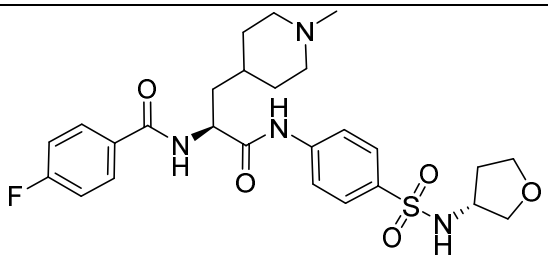
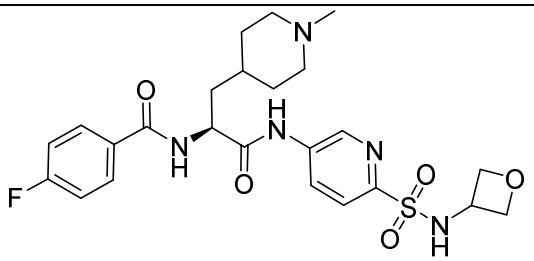
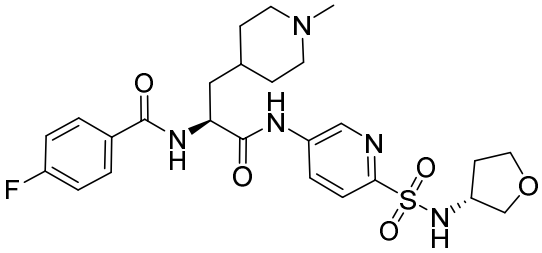
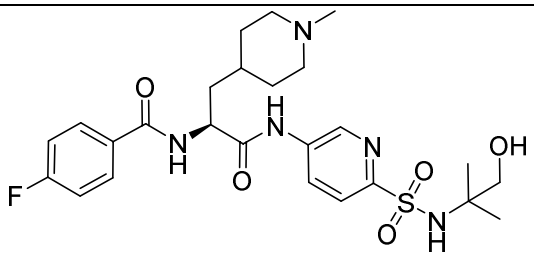
15. The compound of claim 1, wherein said compound is selected from those in the following list, or a pharmaceutically acceptable salt thereof:

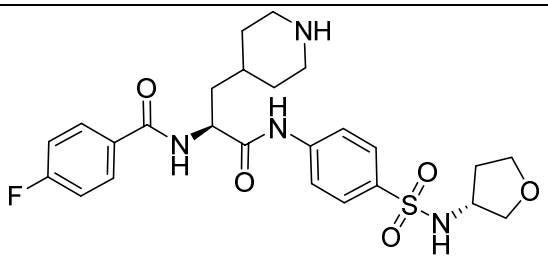
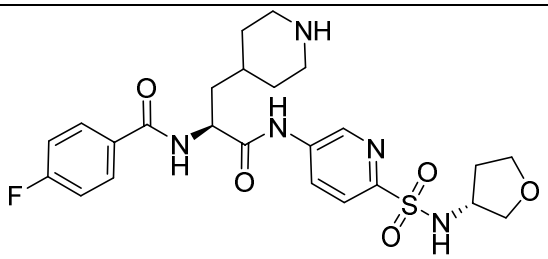
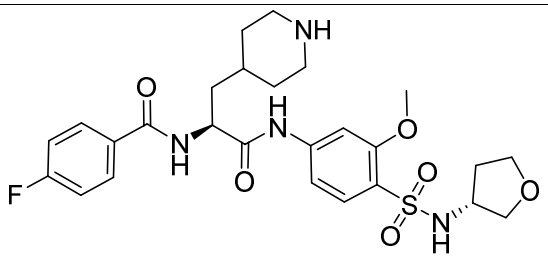
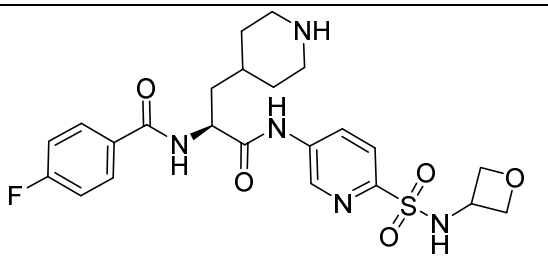
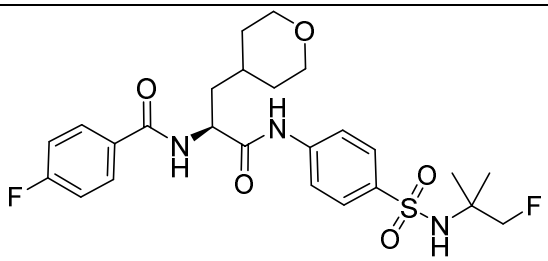
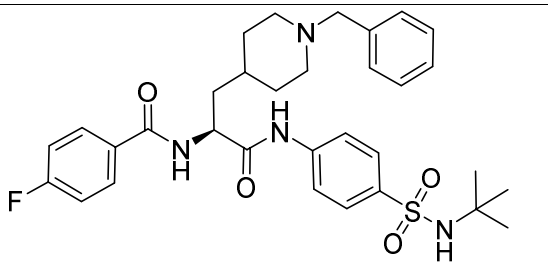
Compound No.	Structure
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I-74	
I-75	
I-76	

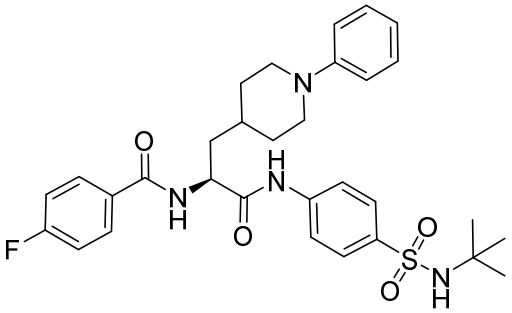
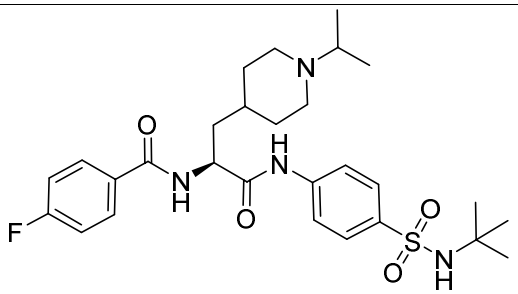
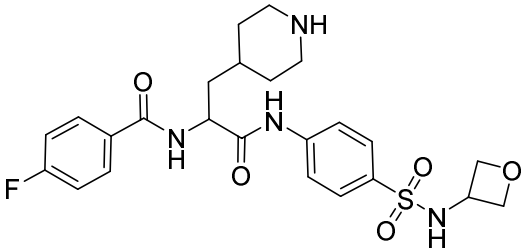
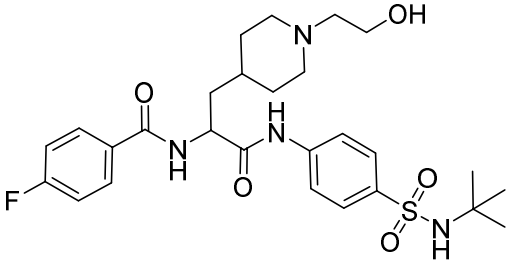
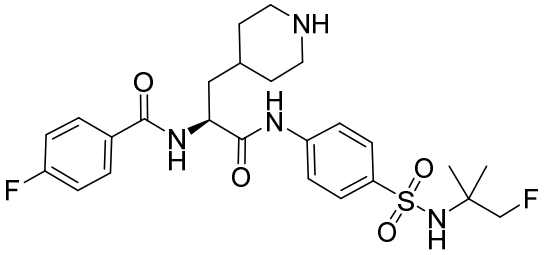
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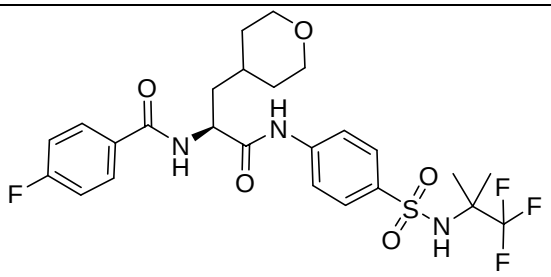
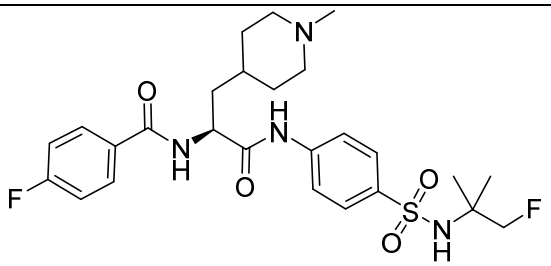
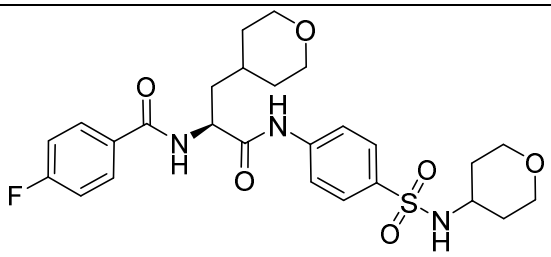
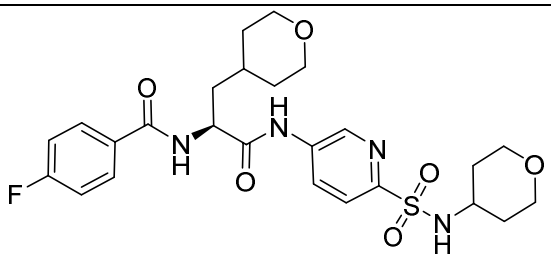
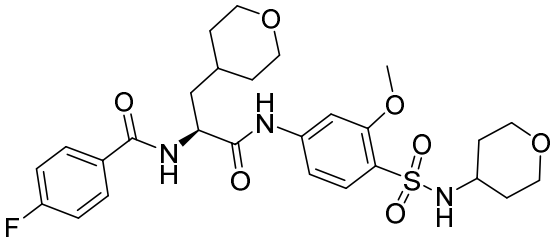
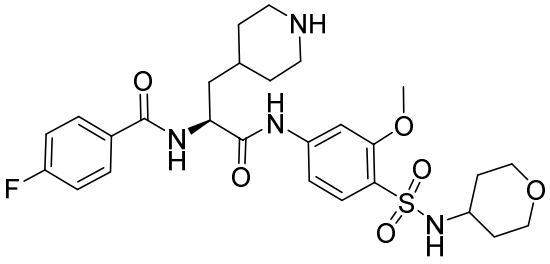
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I-93	

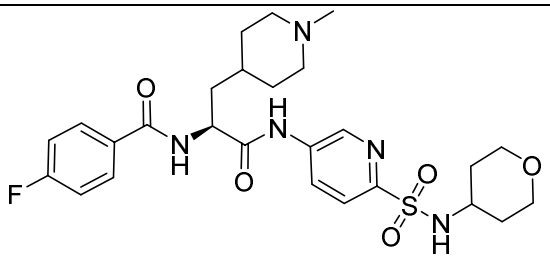
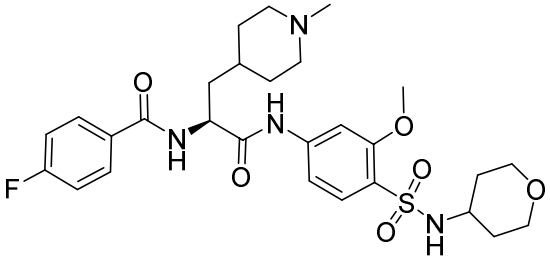
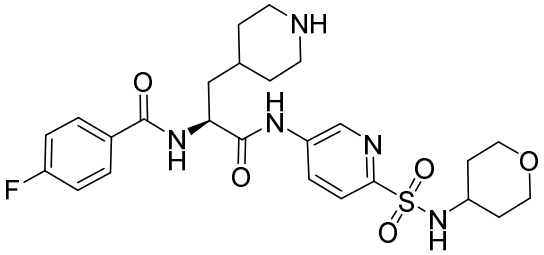
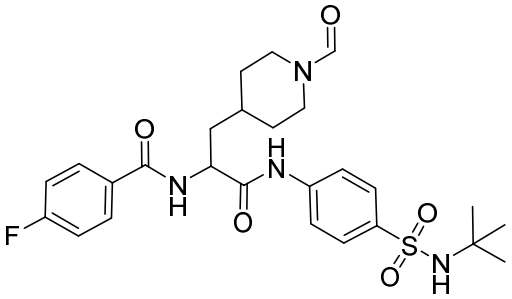
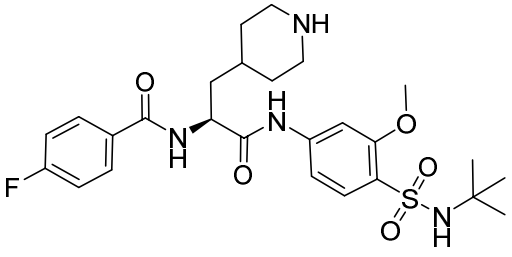
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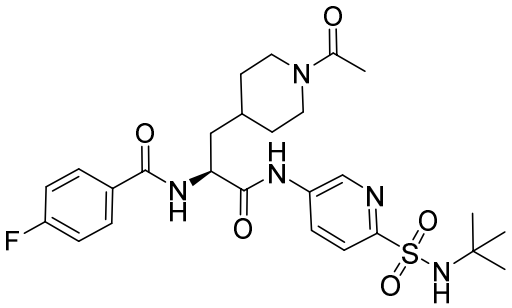
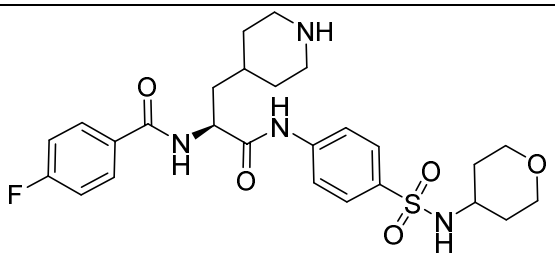
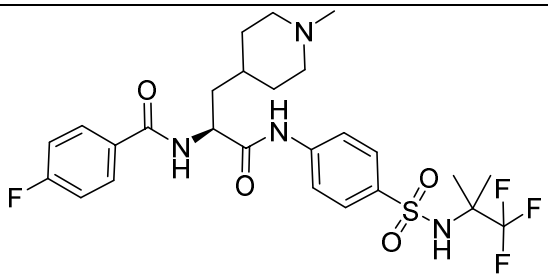
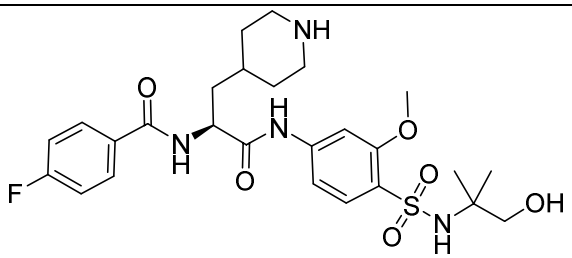
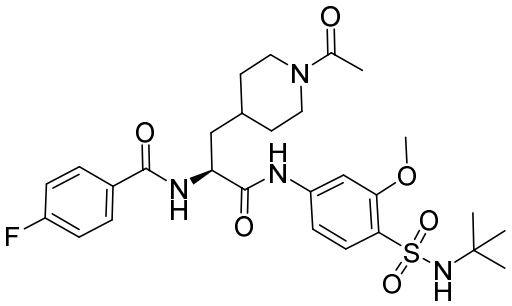
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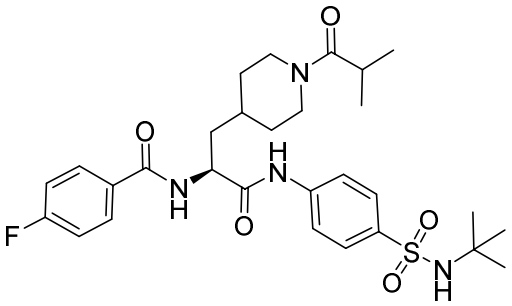
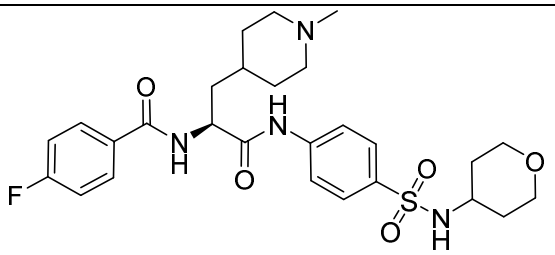
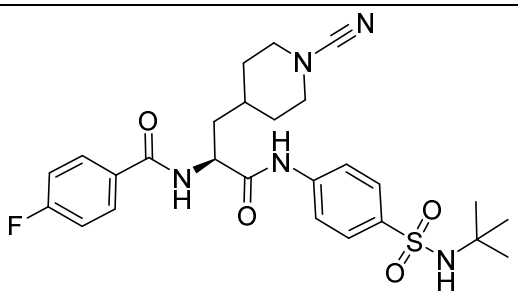
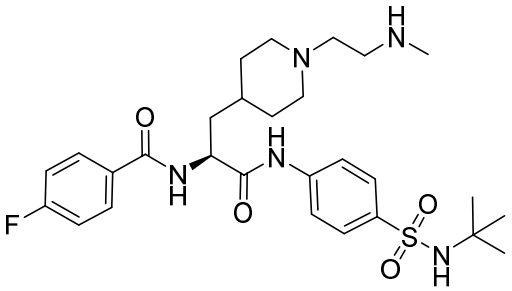
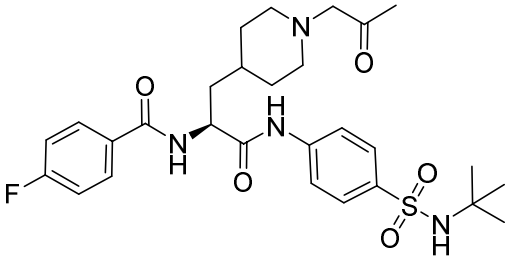
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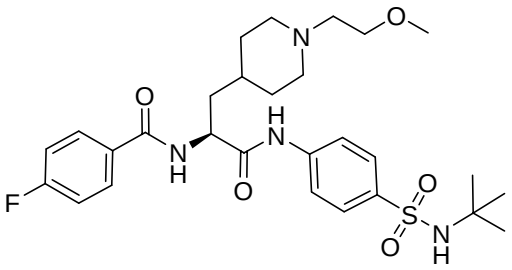
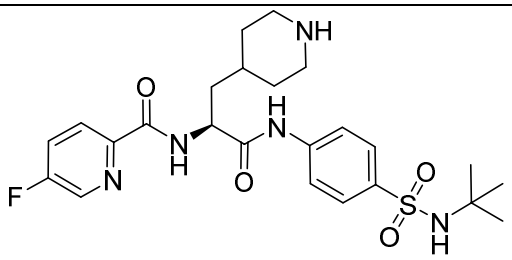
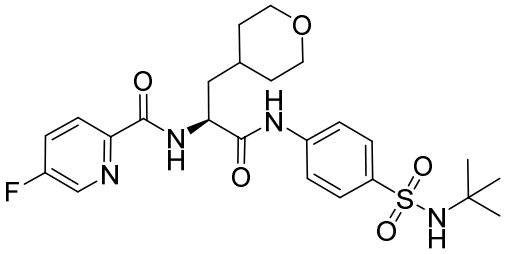
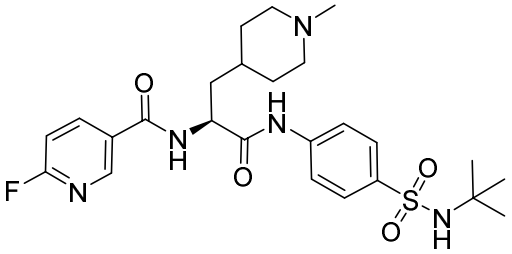
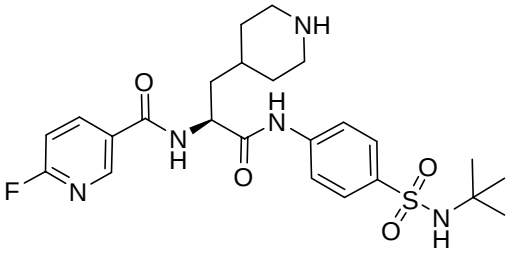
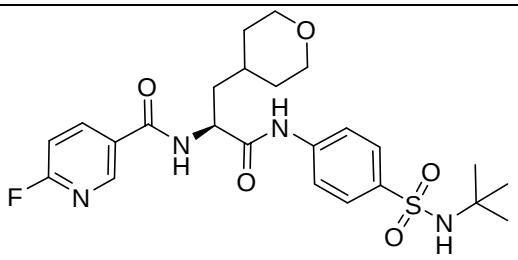
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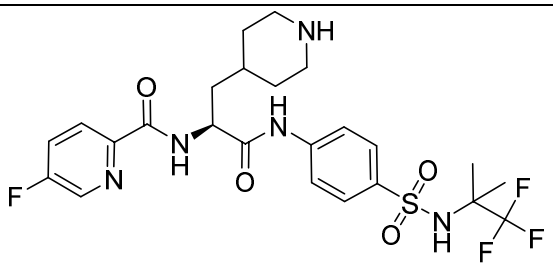
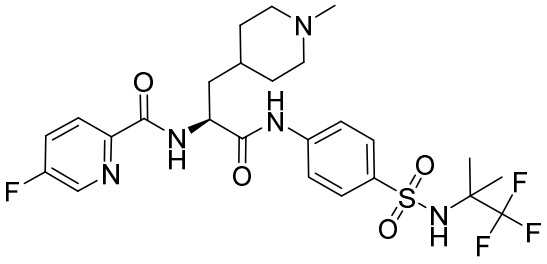
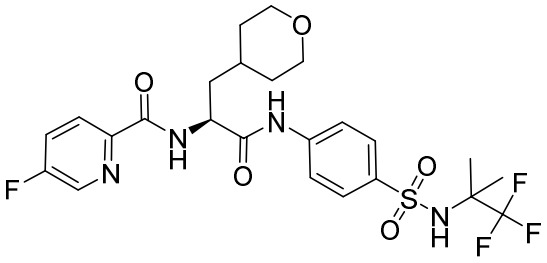
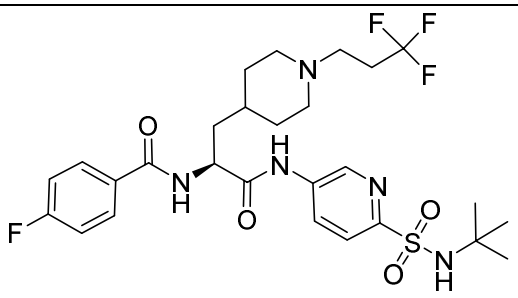
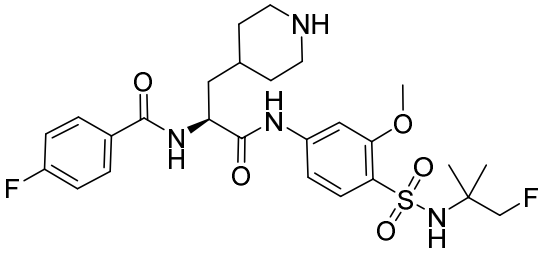
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I-134	
I-135	

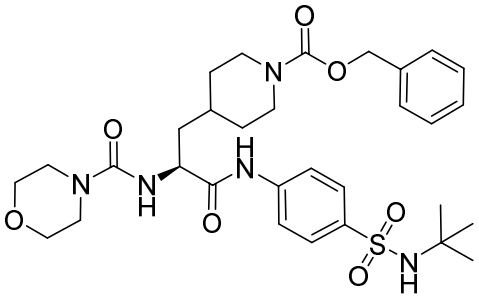
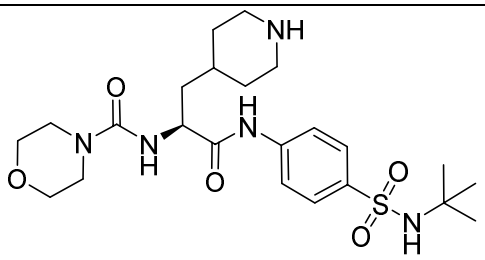
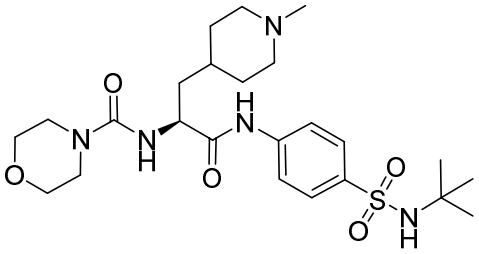
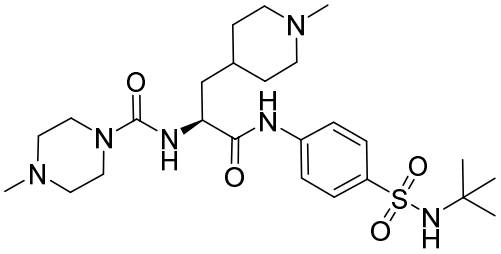
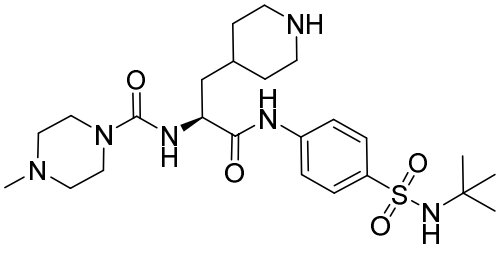
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I-145	
I-155	

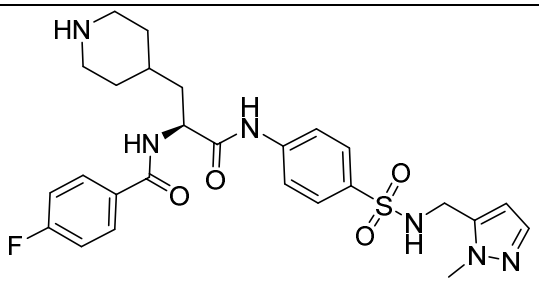
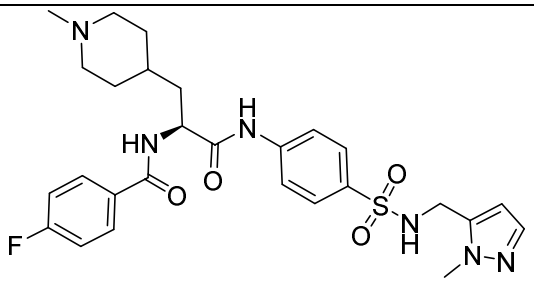
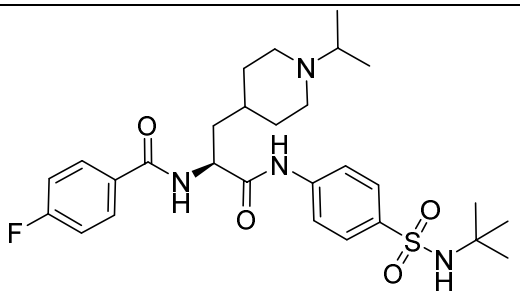
I-156	
I-157	
I-158	
I-159	
I-160	

I-161	
I-164	
I-165	
I-171	
I-172	

I-173	
I-175	
I-177	
I-183	
I-186	
I-196	

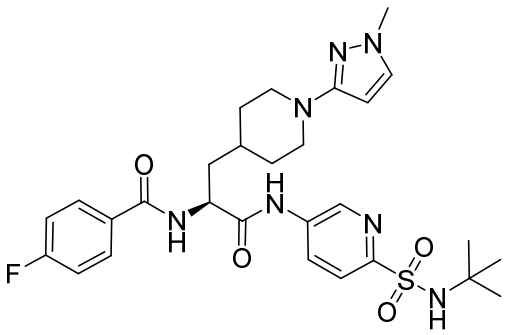
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I-207	
I-208	
I-209	

I-214	
I-215	
I-217	
I-218	
I-219	

I-224	
I-231	
I-287	

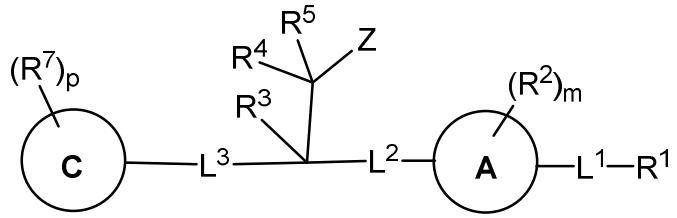
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16. A compound having the following structure, or a pharmaceutically acceptable salt thereof

Compound No.	**Structure**
I-293	

.

17. A compound of formula **I***:



I*

or a pharmaceutically acceptable salt thereof; wherein

Ring A is a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

L^1 is a covalent bond;

R^1 is hydrogen;

each R^2 is independently $–CF_3$ or –CN;

L^2 is –C(O)N(R’);

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

L^3 is –C(O)N(R”)–;

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

R^3 is hydrogen;

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

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

Z is a C_{1-6} aliphatic group;

Ring C is phenyl or a 5-6 membered heteroaryl ring having 1-4 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; and

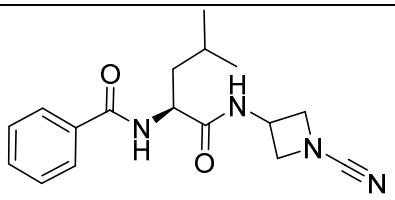
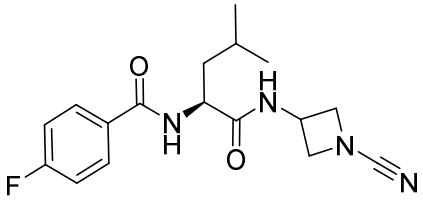
each of m and p is independently 0, 1, 2, 3 or 4.

18. The compound of claim 17, wherein R^2 is –CN.

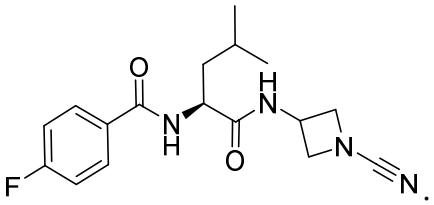
19. The compound of claim 17 or 18, wherein m and p are 1.

20. The compound of any one of claims 17-19, wherein Ring C is phenyl, and R^7 is halogen.

21. The compound of claim 17, wherein the compound is one of the following or a pharmaceutically acceptable salt thereof:

Compound No.	Structure
I-249	
I-251	

22. The compound of claim 17, wherein the compound is the following or a pharmaceutically acceptable salt thereof:



23. A pharmaceutical composition comprising a compound according to any one of claims 1-16, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

24. A pharmaceutical composition comprising a compound according to any one of claims 17-21, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

25. A pharmaceutical composition comprising a compound according to claim 22, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

26. A method of inhibiting USP30 in a biological sample comprising contacting the sample with the compound of any one of claims 1-22, or a pharmaceutically acceptable salt thereof.

27. Use of a pharmaceutical composition of any one of claims 23-25, in the manufacture of a medicament for treating an USP30-mediated disorder, disease, or condition in a patient, wherein the disorder, disease, or condition 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 dehydrogenase deficiency (LCHAD); Leigh disease or syndrome; lethal infantile cardiomyopathy (LIC); Luft disease; glutaric aciduria type II; medium-chain acyl-CoA dehydrogenase deficiency (MCAD); myoclonic epilepsy and ragged-red fiber (MERRF) syndrome; mitochondrial recessive ataxia syndrome; mitochondrial cytopathy; mitochondrial DNA depletion syndrome; myoneurogastrointestinal 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 dehydrogenase (VLCAD) deficiency.

28. The use of claim 27, wherein the disorder, disease, or condition is a neurodegenerative disease 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.

29. The use of claim 28, wherein the neurodegenerative disease is Alzheimer's disease or Parkinson's disease.

30. Use of a pharmaceutical composition of any one of claims 23-25, in the manufacture of a medicament for treating an USP30-mediated disorder, disease, or condition in a patient, wherein the disorder, disease, or condition is a neoplastic disease selected from the group consisting of metastatic carcinoma, multiple myeloma, osteosarcoma, chondrosarcoma, Ewing's sarcoma, nasopharyngeal carcinoma, and leukemia.

31. Use of a pharmaceutical composition of any one of claims 23-25, in the manufacture of a medicament for treating an USP30-mediated disorder, disease, or condition in a patient, wherein the disorder, disease, or condition is cardiovascular disease, kidney disease, pulmonary fibrosis, ophthalmic conditions, cancer, cognitive disease, peroxisome related disease, natural aging, or an age-related disease.

32. The use of claim 31, wherein the disorder, disease, or condition is a peroxisome related disease 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.

33. A pharmaceutical composition of any one of claims 23-25, for use in therapy.