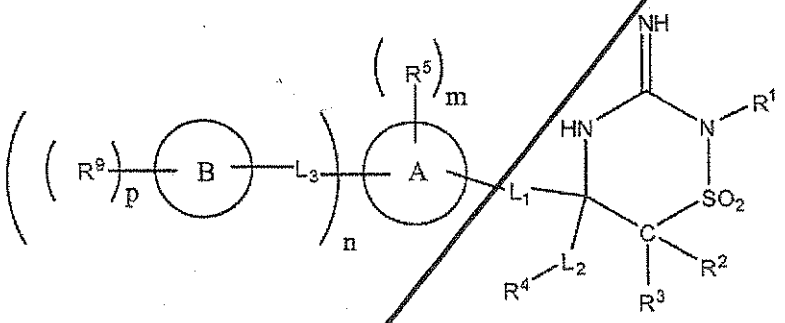
WE CLAIM:

1. A compound, or a tautomer thereof, or a stereoisomer of said compound or said tautomer, or a pharmaceutically acceptable salt thereof, said compound having the structural Formula (I):



(I)

wherein:

$-L_1-$ represents a bond or a divalent moiety selected from the group consisting of -alkyl-, -haloalkyl-, -heteroalkyl-, -alkenyl-, and -alkynyl-;

$-L_2-$ represents a bond or a divalent moiety selected from the group consisting of -alkyl-, -haloalkyl-, -heteroalkyl-, -alkenyl-, and -alkynyl-;

each $-L_3-$ independently represents a bond or a divalent moiety independently selected from the group consisting of -alkyl-, -haloalkyl-, -heteroalkyl-, -alkenyl-, -alkynyl-, $-N(R^7)-$, –NHC(O)-, -C(O)NH-, $-NHS(O)_2-$, $-S(O)_2NH-$, -O-alkyl-, -alkyl-O-, $-N(R^7)$-alkyl-, -alkyl-$N(R^7)$-, -haloalkyl-NH-, and –NH-haloalkyl-;

m, n, and p are each independently selected integers, wherein:

m is 0 or more;

n is 0 or more; and

p is 0 or more,

wherein the maximum value of the sum of m and n is the maximum number of available substitutable hydrogen atoms on ring A, and wherein the maximum value of p is the maximum number of available substitutable hydrogen atoms on ring B;

R^1 is selected from the group consisting of: H, alkyl, heteroalkyl, heterohaloalkyl, cycloalkyl, cycloalkylalkyl-, heterocycloalkyl, heterocycloalkylalkyl-, aryl, arylalkyl-, heteroaryl, and heteroarylalkyl-,

wherein each of said alkyl, heteroalkyl, heterohaloalkyl, cycloalkyl, cycloalkylalkyl-, heterocycloalkyl, heterocycloalkylalkyl-, aryl, arylalkyl-, heteroaryl, and heteroarylalkyl- of R^1 is unsubstituted or substituted with one or more independently selected R^{10} groups;

R^2 is selected from the group consisting of H, halo, alkyl, haloalkyl, and heteroalkyl,

wherein each of said alkyl and said haloalkyl of R^2 is unsubstituted or substituted with one or more independently selected R^{10} groups;

R^3 is selected from the group consisting of H, halo, alkyl, haloalkyl, and heteroalkyl,

wherein each of said alkyl and said haloalkyl of R^2 is unsubstituted or substituted with one or more independently selected R^{10} groups;

R^4 is selected from the group consisting of alkyl, aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocycloalkyl, and heterocycloalkenyl,

wherein each of said alkyl, aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocycloalkyl, and heterocycloalkenyl of R^4 is unsubstituted or substituted with one or more independently selected R^{10} groups;

ring A is selected from the group consisting of monocyclic aryl, monocyclic heteroaryl, monocyclic cycloalkyl, monocyclic cycloalkenyl, monocyclic heterocycloalkyl, monocyclic heterocycloalkenyl, and a multicyclic group;

each ring B (when present) is independently selected from the group consisting of monocyclic aryl, monocyclic heteroaryl, monocyclic cycloalkyl, monocyclic cycloalkenyl, monocyclic heterocycloalkyl, monocyclic heterocycloalkenyl, and a multicyclic group;

each R^5 (when present) is independently selected from the group consisting of halo, -CN, $-SF_5$, $-OSF_5$, $-NO_2$, $-Si(R^6)_3$, $-P(O)(OR^7)_2$, $-P(O)(OR^7)(R^7)$, $-N(R^8)_2$, $-NR^8C(O)R^7$, $-NR^8S(O)_2R^7$, $-NR^8C(O)N(R^8)_2$, $-NR^8C(O)OR^7$, $-C(O)R^7$, $-C(O)_2R^7$, $-C(O)N(R^8)_2$, $-S(O)R^7$, $-S(O)_2R^7$, $-S(O)_2N(R^8)_2$, $-OR^7$, $-SR^7$, alkyl, haloalkyl, haloalkoxy, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl,

wherein each said alkyl, haloalkyl, haloalkoxy, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl of R^5 (when present) is optionally

independently unsubstituted or further substituted with one or more independently selected groups selected from the group consisting of lower alkyl, lower alkenyl, lower alkynyl, lower heteroalkyl, halo, -CN, $-SF_5$, $-OSF_5$, $-NO_2$, $-N(R^8)_2$, $-OR^7$, $-C(O)N(R^8)_2$, and cycloalkyl;

each R^6 (when present) is independently selected from the group consisting of alkyl, aryl, arylalkyl-, haloalkyl, cycloalkyl, cycloalkylalkyl-, heteroaryl, and heteroarylalkyl-;

each R^7 (when present) is independently selected from the group consisting of H, alkyl, alkenyl, heteroalkyl, haloalkyl, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, cycloalkyl, cycloalkylalkyl-, heterocycloalkyl, and heterocycloalkylalkyl-;

each R^8 (when present) is independently selected from the group consisting of H, alkyl, alkenyl, heteroalkyl, haloalkyl, haloalkenyl, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, cycloalkyl, cycloalkylalkyl-, heterocycloalkyl, and heterocycloalkylalkyl-;

each R^9 (when present) is independently selected from the group consisting of: halogen, -CN, $-SF_5$, $-OSF_5$, $-NO_2$, $-Si(R^6)_3$, $-P(O)(OR^7)_2$, $-P(O)(OR^7)(R^7)$, $-N(R^8)_2$, $-NR^8C(O)R^7$, $-NR^8S(O)_2R^7$, $-NR^8C(O)N(R^8)_2$, $-NR^8C(O)OR^7$, $-C(O)R^7$, $-C(O)_2R^7$, $-C(O)N(R^8)_2$, $-S(O)R^7$, $-S(O)_2R^7$, $-S(O)_2N(R^8)_2$, $-OR^7$, $-SR^7$, alkyl, haloalkyl, heteroalkyl, alkenyl, alkynyl, aryl, arylalkyl-, cycloalkyl, heteroaryl, heteroarylalkyl-, and heterocycloalkyl;

each R^{10} (when present) is independently selected from the group consisting of halo, -CN, $-NO_2$, $-Si(R^6)_3$, $-P(O)(OR^7)_2$, $-P(O)(OR^7)(R^7)$, $-N(R^8)_2$, $-NR^8C(O)R^7$, $-NR^8S(O)_2R^7$, $-NR^8C(O)N(R^8)_2$, $-NR^8C(O)OR^7$, $-C(O)R^7$, $-C(O)_2R^7$, $-C(O)N(R^8)_2$, $-S(O)R^7$, $-S(O)_2R^7$, $-S(O)_2N(R^8)_2$, $-OR^7$, $-SR^7$, alkyl, haloalkyl, haloalkoxy, heteroalkyl, alkenyl, alkynyl, and cycloalkyl,

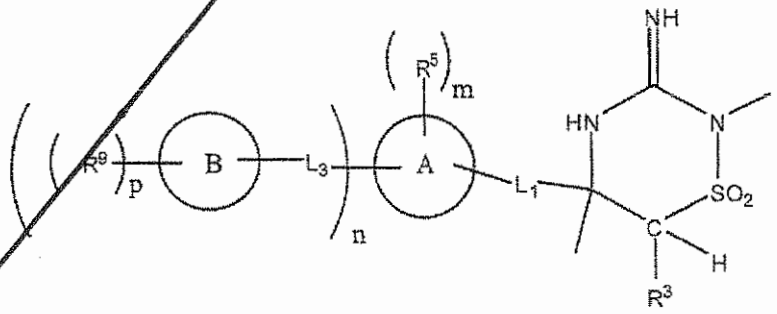
wherein each said alkyl, haloalkyl, haloalkoxy, heteroalkyl, alkenyl, alkynyl, and cycloalkyl of R^{10} (when present) is optionally independently unsubstituted or further substituted with one or more independently selected groups selected from the group consisting of lower alkyl, lower alkenyl, lower alkynyl, lower heteroalkyl, halo, -CN, $-NO_2$, $-N(R^8)_2$, $-OR^7$, and $-C(O)N(R^8)_2$.

2. A compound of claim 1, or a tautomer thereof, or a stereoisomer of said compound or said tautomer, or a pharmaceutically acceptable salt thereof, wherein:
R^1 is selected from the group consisting of H, lower alkyl, and cyclopropyl.

3. A compound of claim 1, or a tautomer thereof, or a stereoisomer of said compound or said tautomer, or a pharmaceutically acceptable salt thereof, wherein:
R^2 is H.

4. A compound of claim 1, or a tautomer thereof, or a stereoisomer of said compound or said tautomer, or a pharmaceutically acceptable salt thereof, wherein:
R^3 is selected from the group consisting H, alkyl, haloalkyl, and heteroalkyl.

5. A compound of claim 1, or a tautomer thereof, or a stereoisomer of said compound or said tautomer, or a pharmaceutically acceptable salt thereof, said compound having a structural Formula (II):



(II).

6. A compound of claim 5, or a tautomer thereof, or a stereoisomer of said compound or said tautomer, or a pharmaceutically acceptable salt thereof, wherein:

ring A is selected from the group consisting of phenyl, pyridyl, pyrazinyl, furanyl, thienyl, pyrimidinyl, pyridazinyl, thiazolyl, oxazolyl, benzothienyl, benzimidazolyl, indazolyl, indolyl, and thienopyrazolyl;

m is 0 or more;

each R^5 group (when present) is independently selected from the group consisting of halogen, -CN, $-SF_5$, $-N(R^8)_2$, $-OR^7$, $-SR^7$, lower alkyl, lower haloalkyl, lower heteroalkyl, lower alkynyl, and cycloalkyl;

n is 1;

$-L_3-$ represents a bond or a divalent moiety selected from the group consisting of –NHC(O)- and –C(O)NH-;

ring B is selected from the group consisting of phenyl, pyridyl, pyrazinyl, furanyl, thienyl, pyrimidinyl, pyridazinyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, pyrrolopyridyl, and pyrrolopyrimidinyl;

p is 0 or more; and

each R^9 group (when present) is independently selected from the group consisting of halogen, -CN, $-SF_5$, $-N(R^8)_2$, $-OR^7$, $-SR^7$, lower alkyl, lower haloalkyl, lower heteroalkyl, lower alkynyl, phenyl, benzyl, and cycloalkyl.

7. A compound of claim 5, or a tautomer thereof, or a stereoisomer of said compound or said tautomer, or a pharmaceutically acceptable salt thereof, wherein:

n is 0;

m is 1 or more;

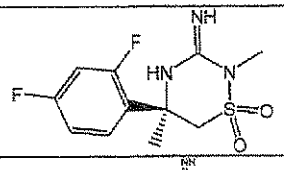
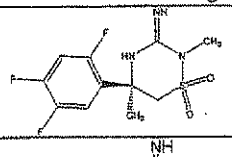
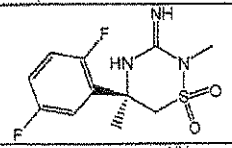
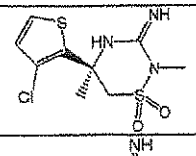
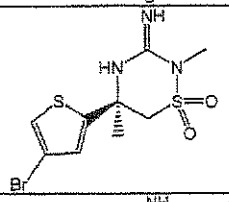
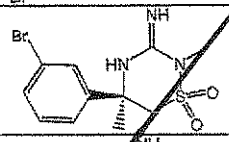
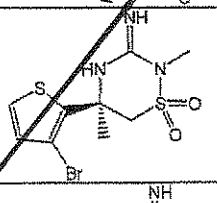
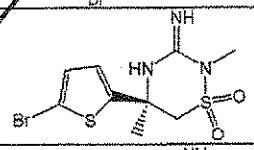
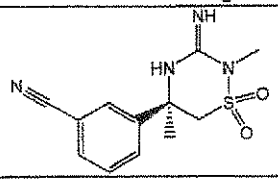
$-L_1-$ represents a bond, $-CH_2-$, or $-CH_2CH_2-$;

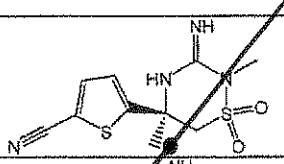
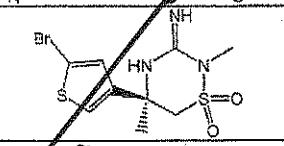
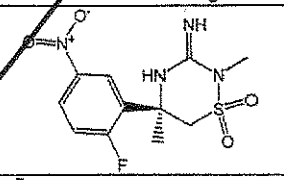
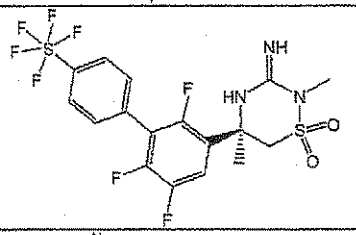
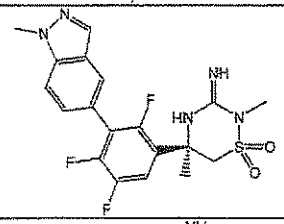
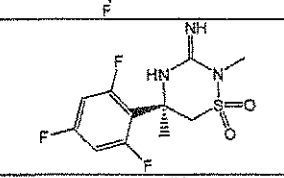
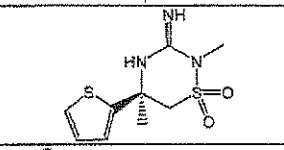
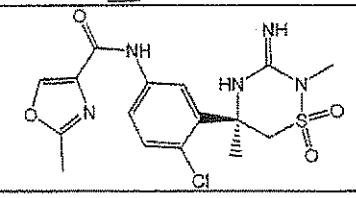
ring A is selected from the group consisting of phenyl, pyridyl, pyrazinyl, furanyl, thienyl, pyrimidinyl, pyridazinyl, thiazolyl, oxazolyl, imidazolyl, pyrazolyl, quinazolinyl, benzofuranyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, benzothienyl, naphthyl, quinolyl, isoquinolyl, indazolyl, indolyl, and thienopyrazolyl; and

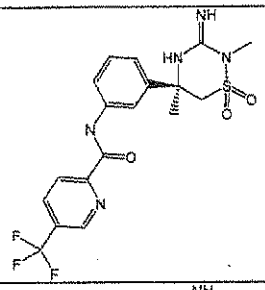
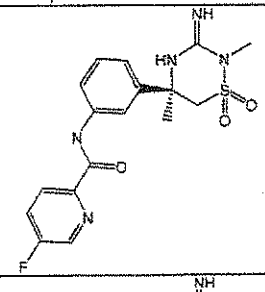
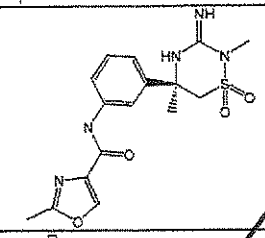
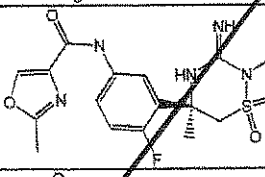
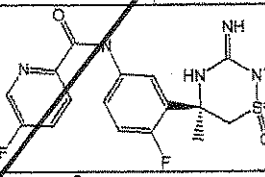
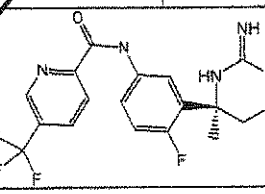
each R^5 group (when present) is independently selected from the group consisting of halogen, -CN, $-SF_5$, $-N(R^8)_2$, $-OR^7$, $-SR^7$, lower alkyl, lower haloalkyl, lower heteroalkyl, lower alkynyl, and cycloalkyl.

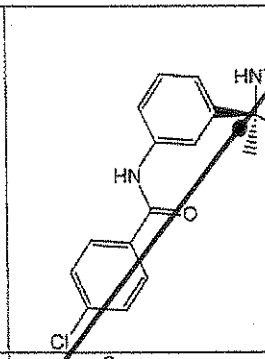
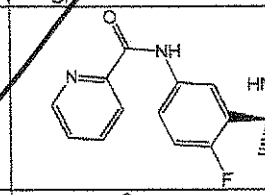
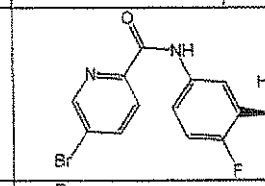
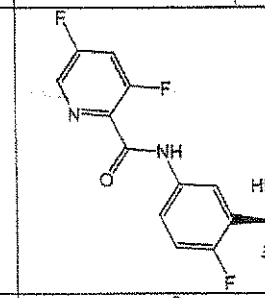
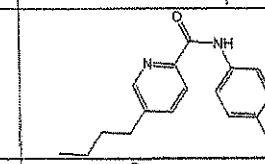
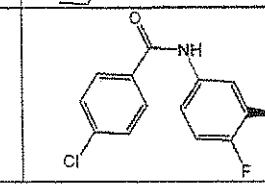
8. A compound, or a tautomer thereof, or a stereoisomer of said compound or said tautomer, or a pharmaceutically acceptable salt thereof, said compound being selected from the group consisting of:

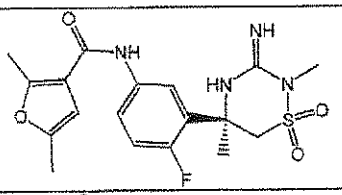
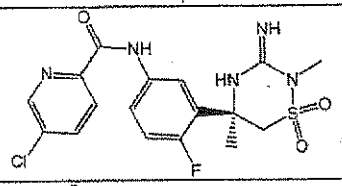
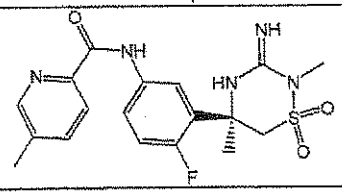
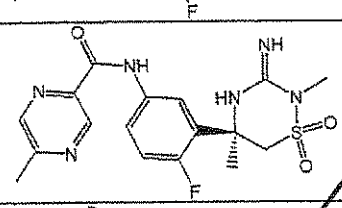
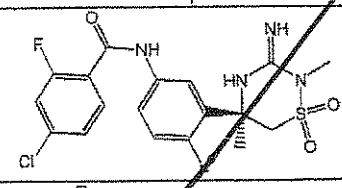
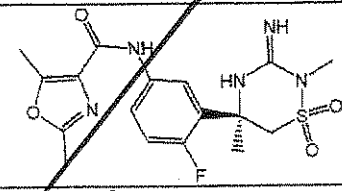
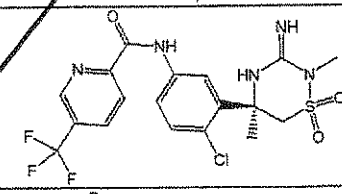
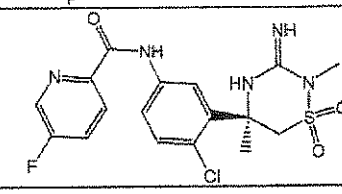
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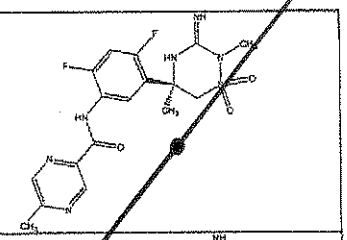
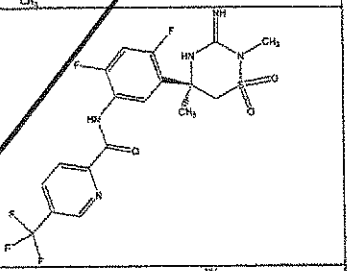
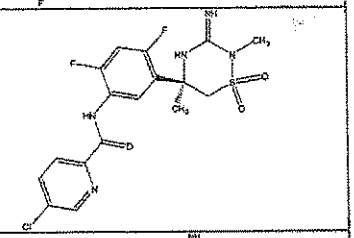
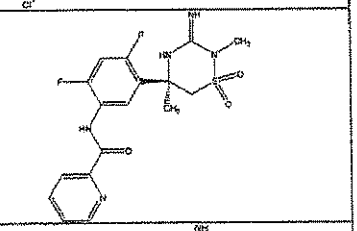
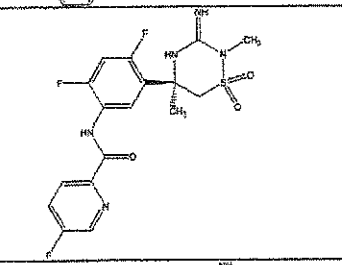
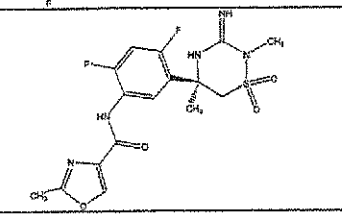
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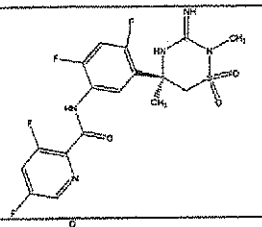
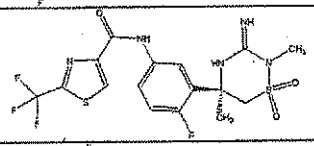
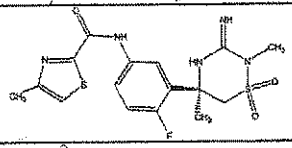
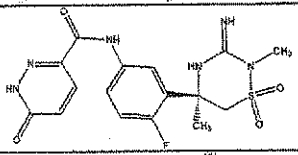
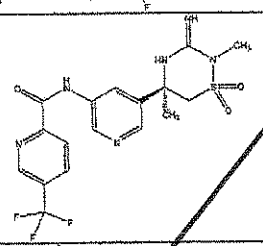
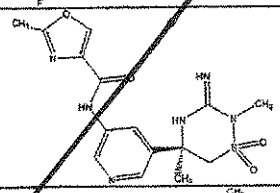
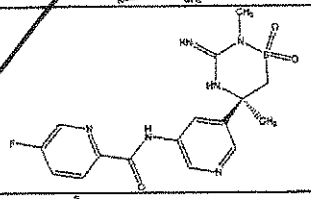
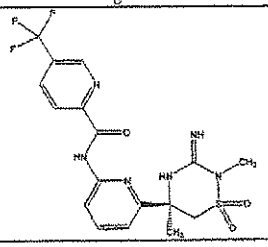
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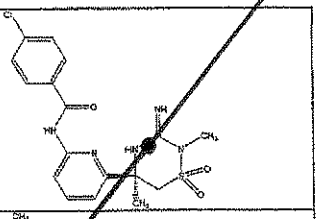
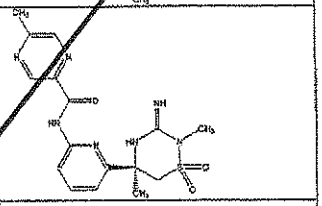
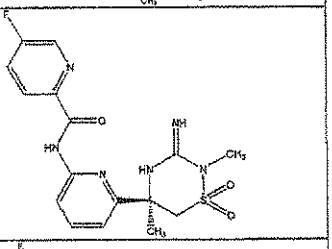
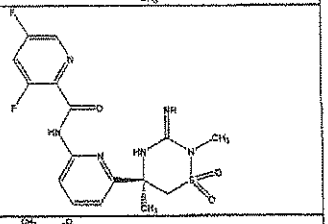
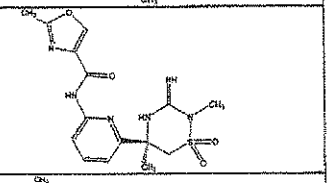
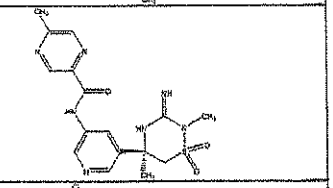
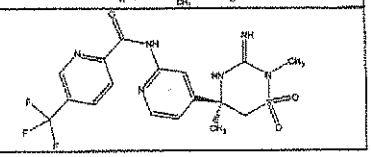
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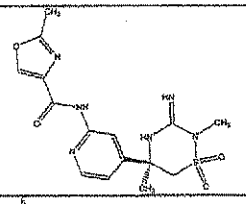
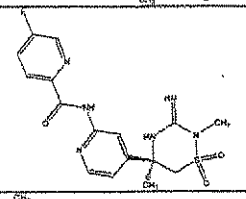
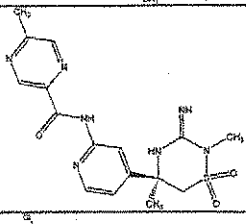
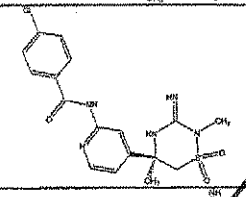
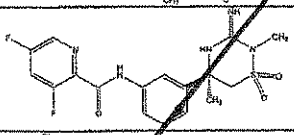
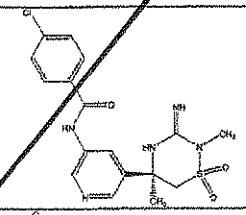
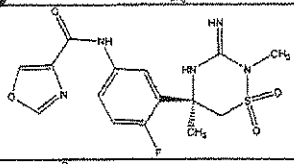
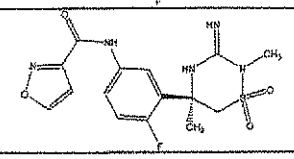
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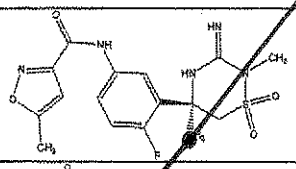
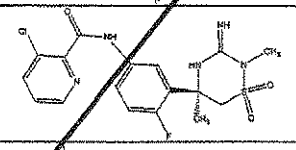
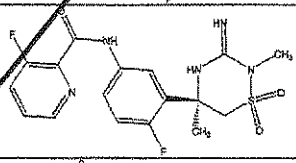
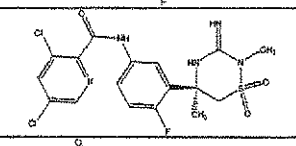
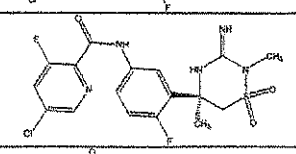
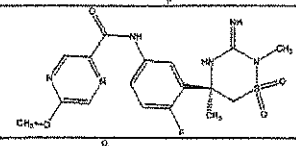
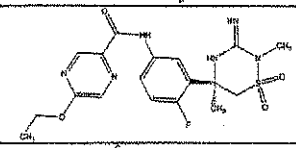
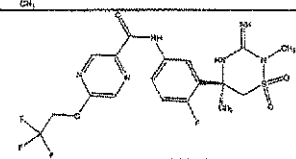
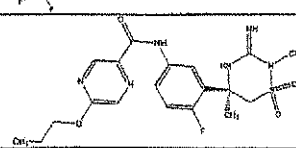
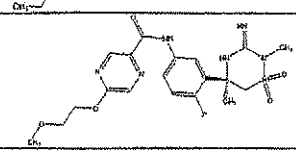
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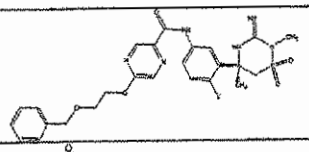
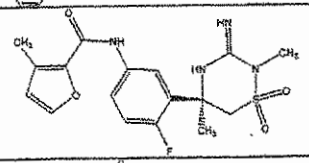
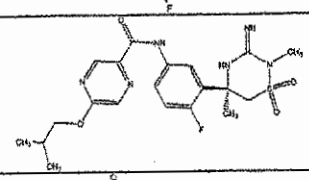
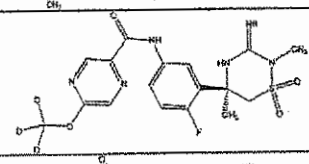
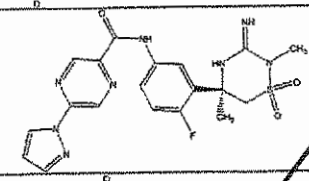
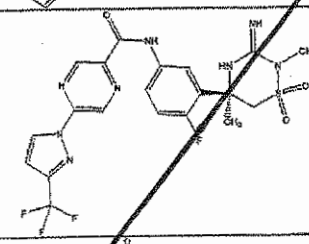
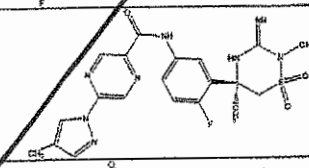
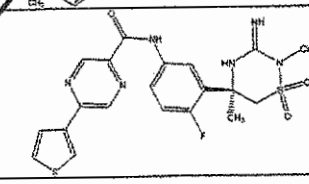
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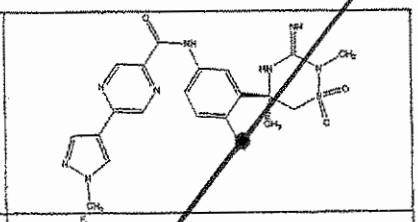
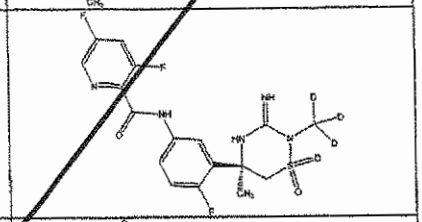
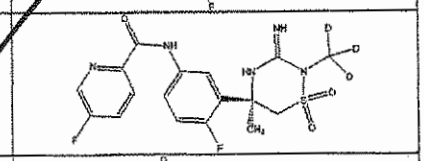
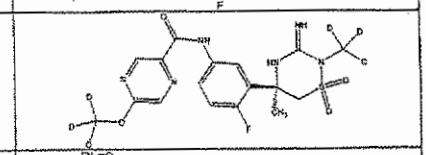
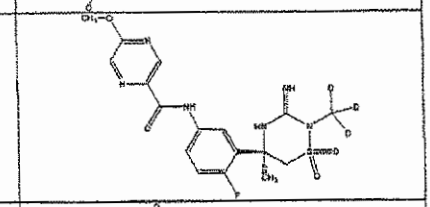
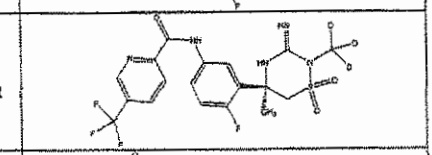
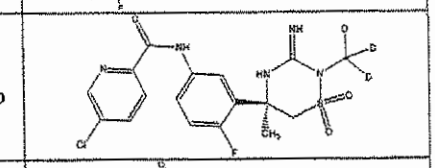
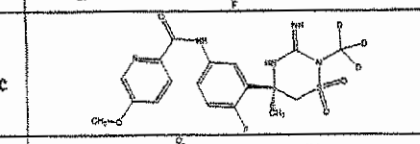
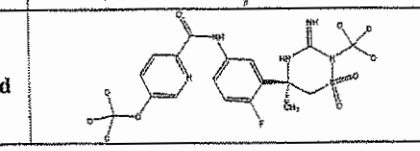
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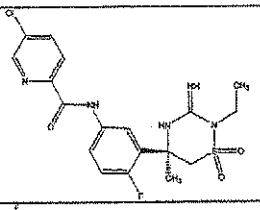
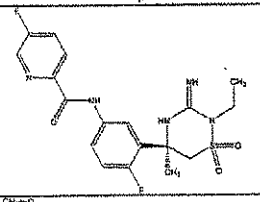
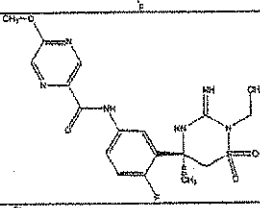
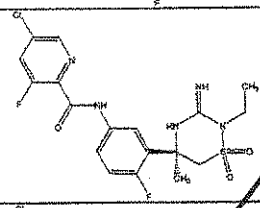
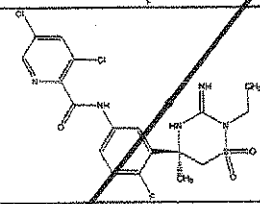
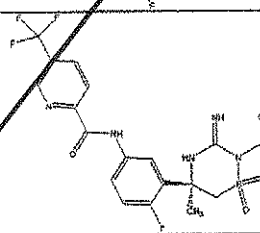
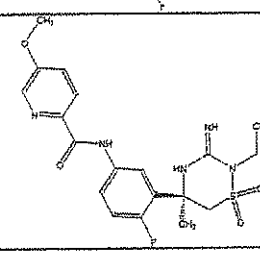
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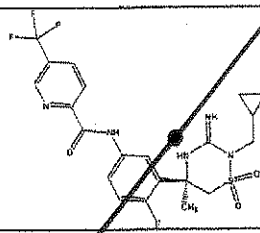
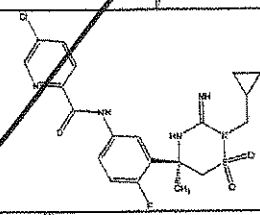
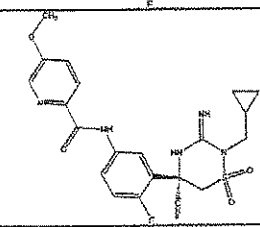
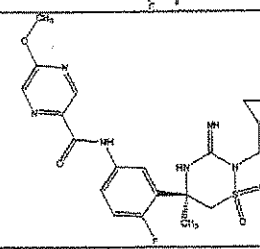
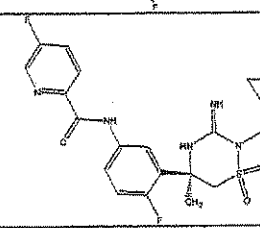
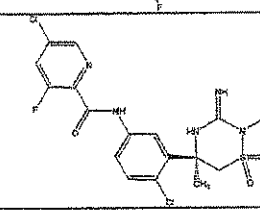
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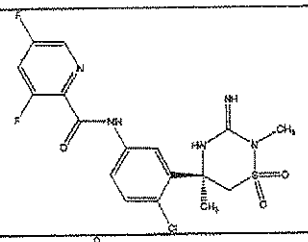
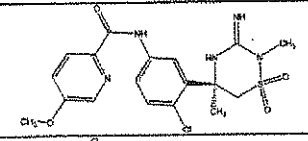
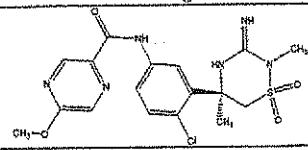
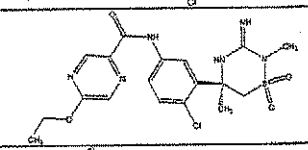
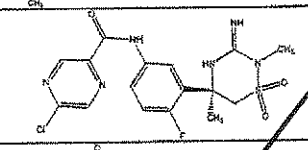
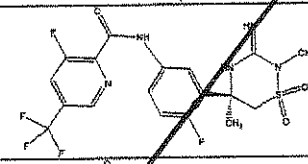
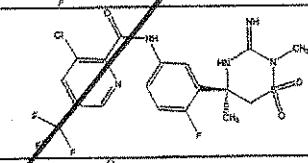
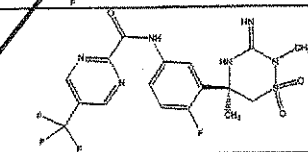
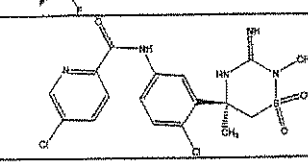
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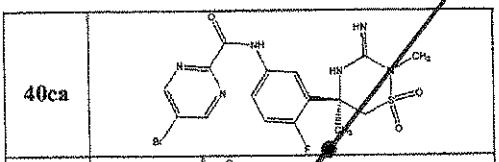
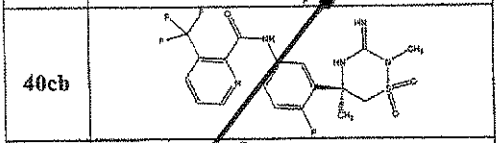
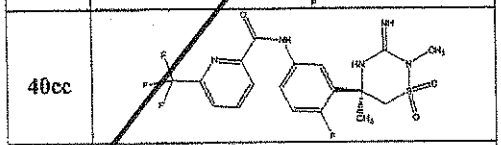
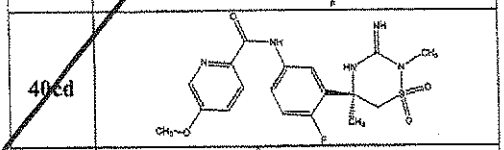
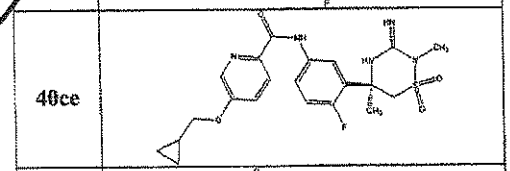
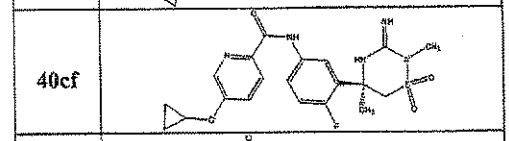
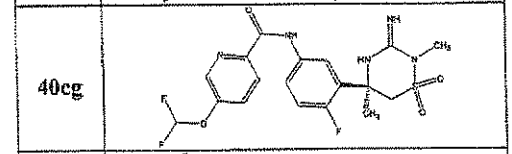
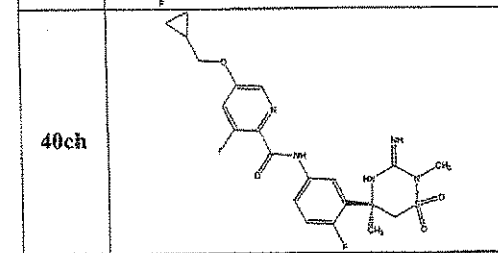
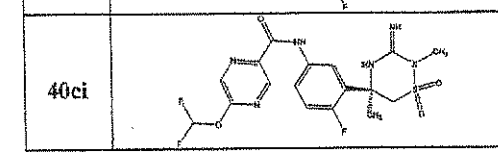
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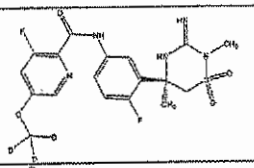
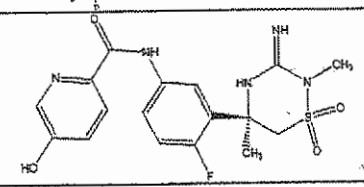
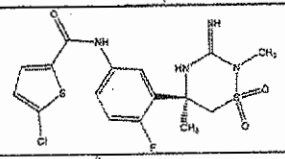
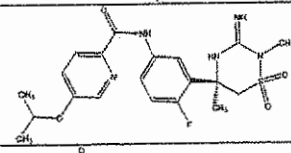
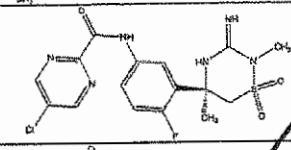
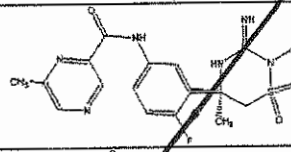
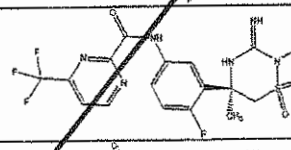
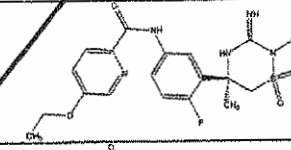
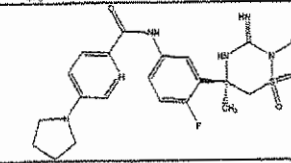
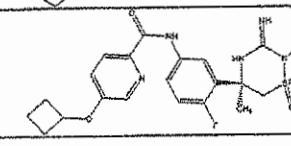
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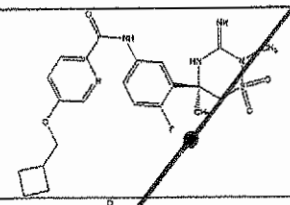
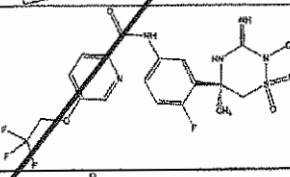
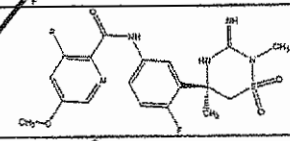
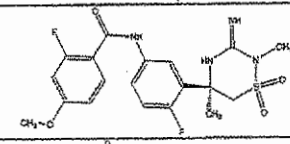
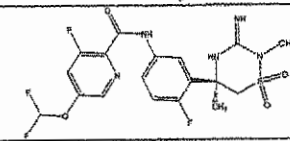
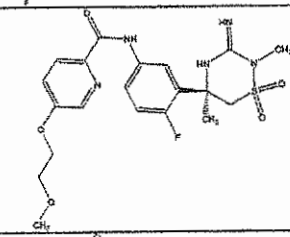
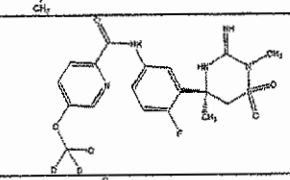
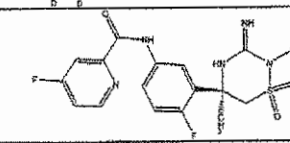
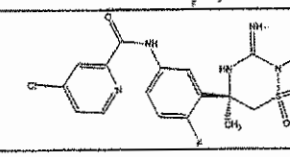
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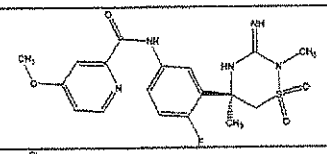
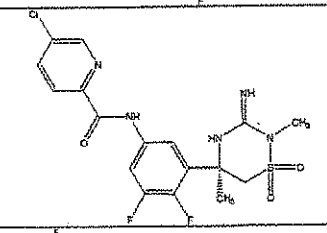
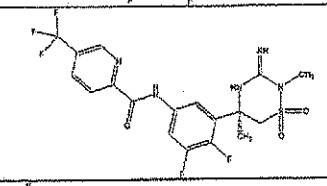
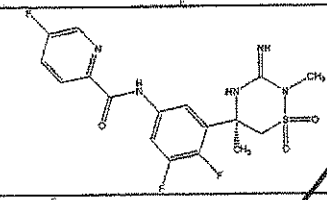
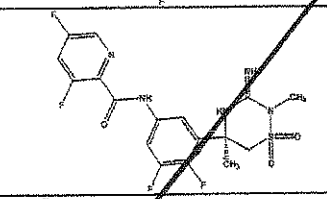
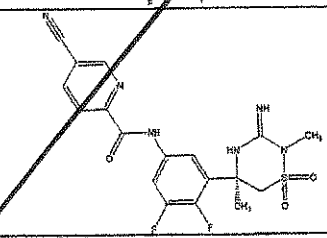
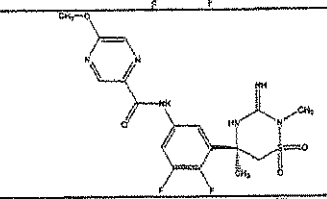
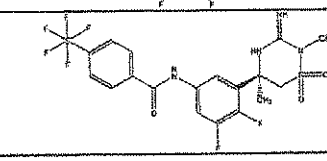
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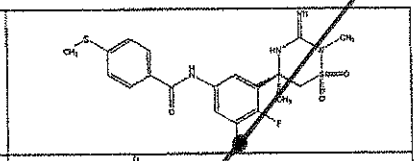
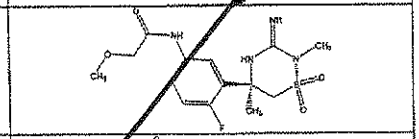
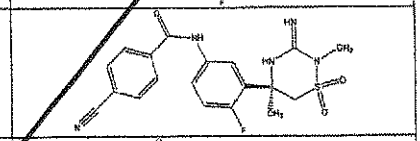
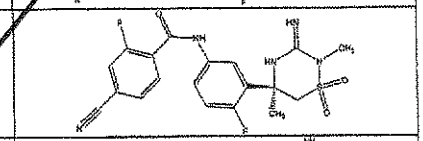
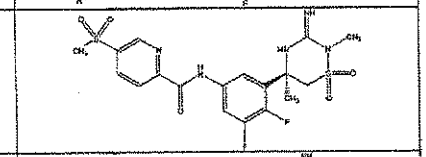
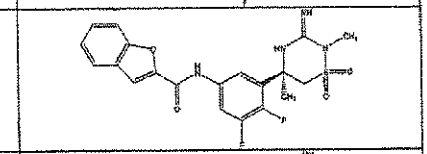
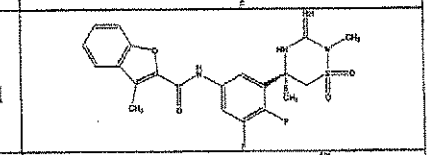
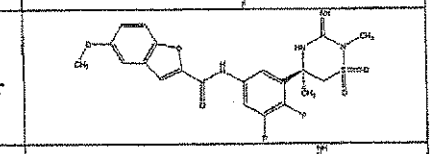
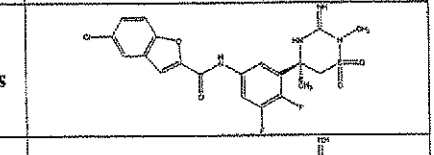
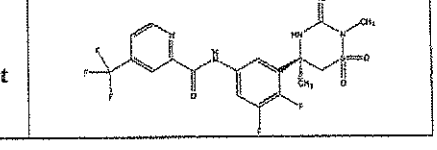
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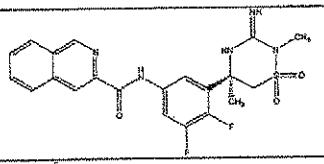
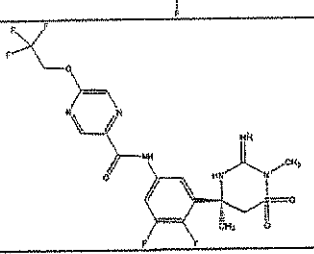
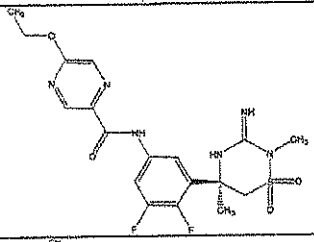
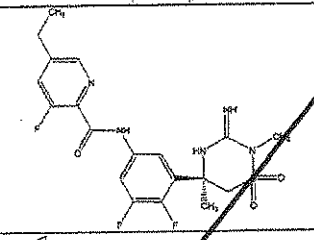
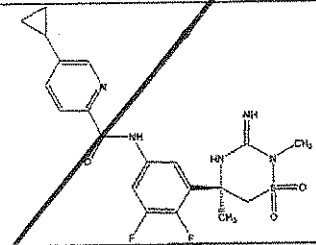
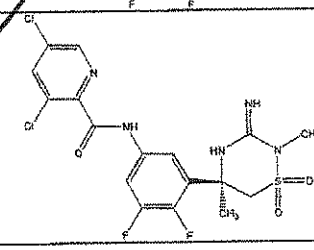
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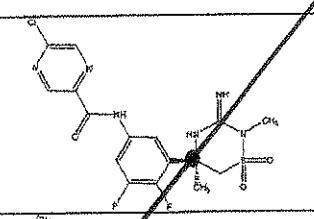
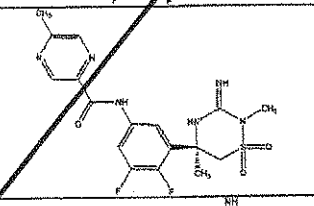
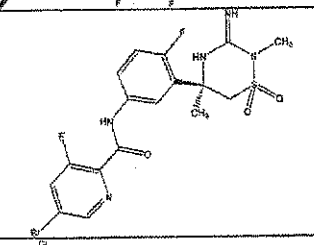
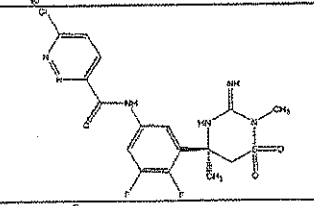
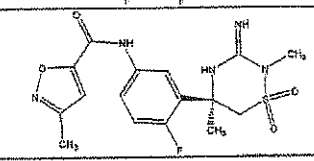
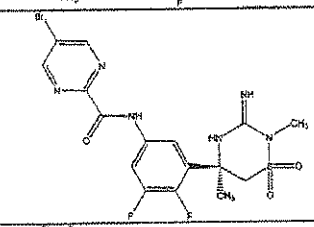
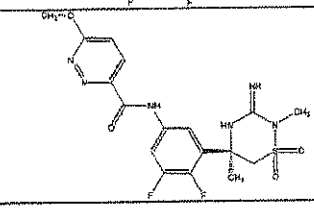
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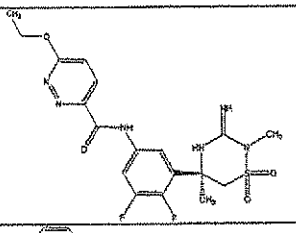
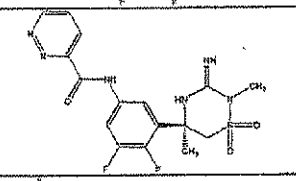
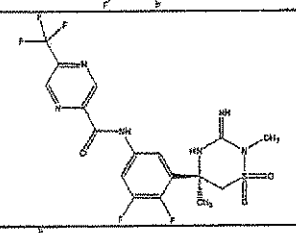
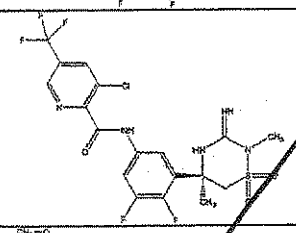
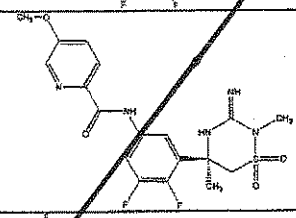
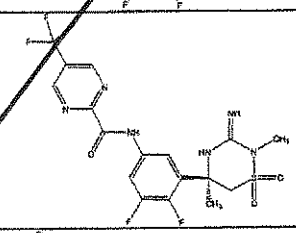
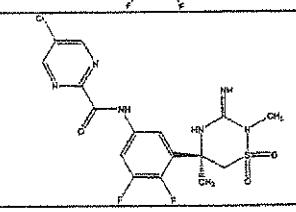
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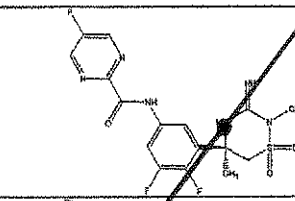
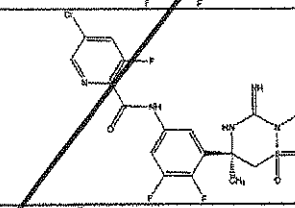
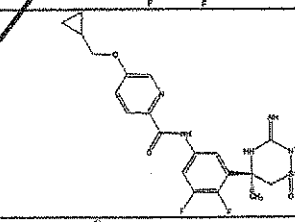
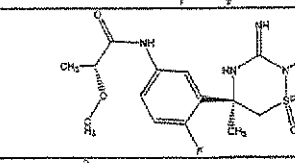
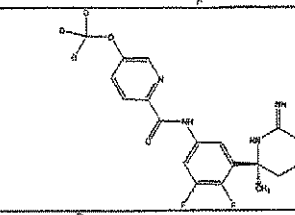
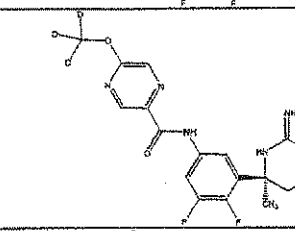
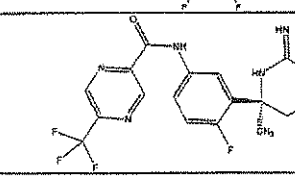
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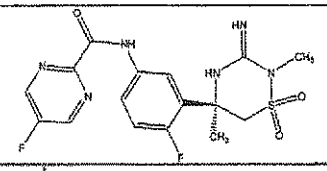
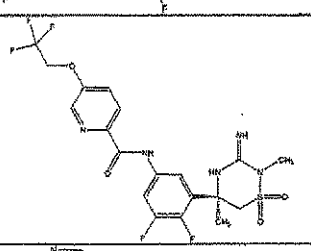
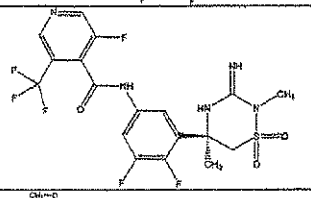
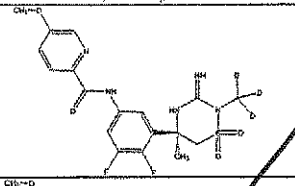
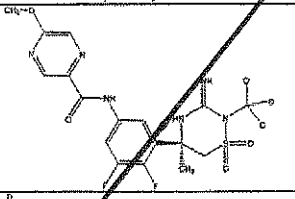
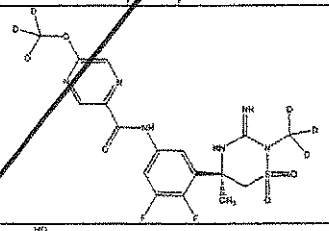
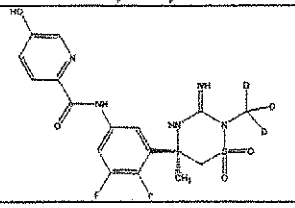
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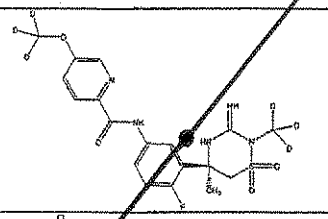
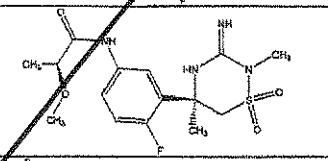
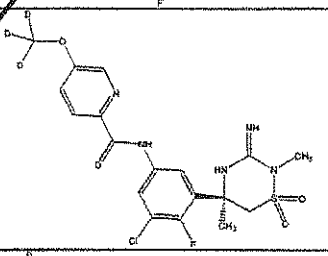
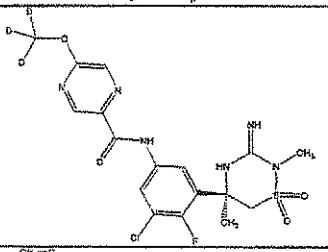
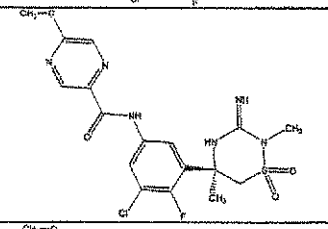
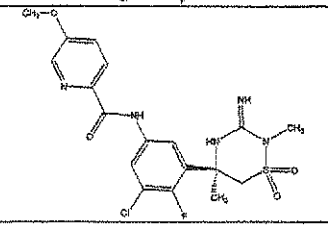
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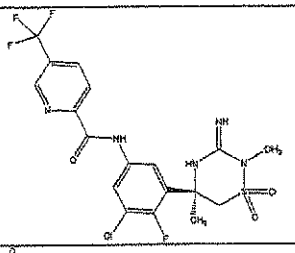
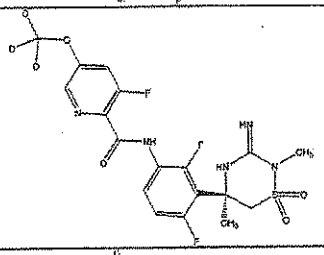
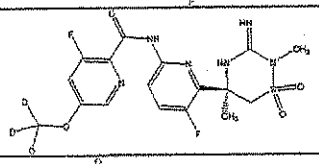
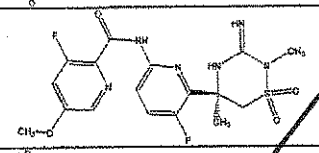
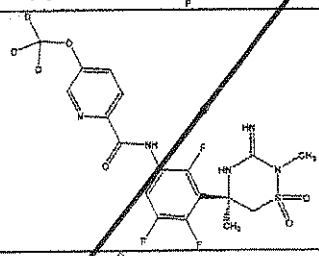
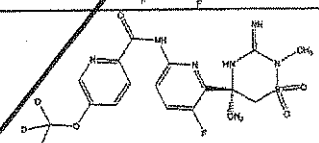
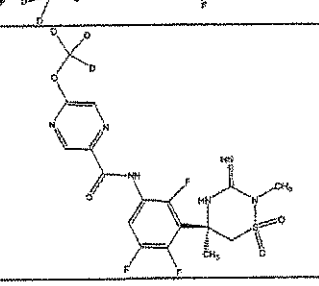
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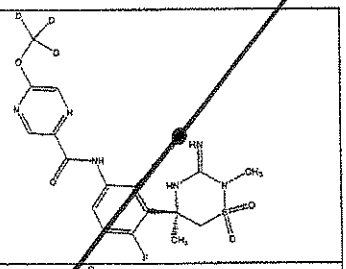
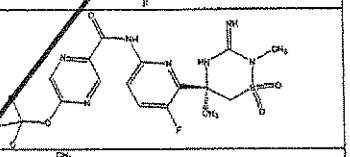
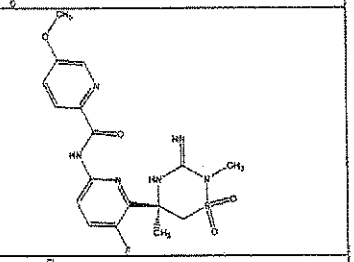
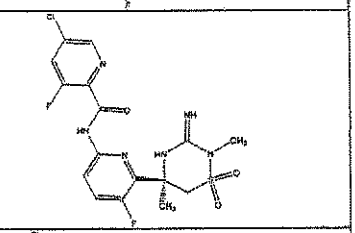
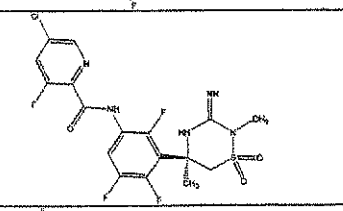
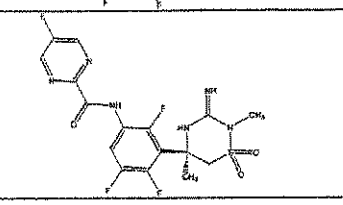
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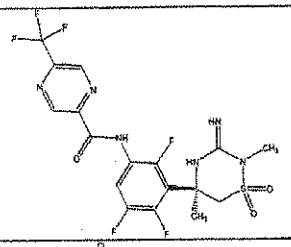
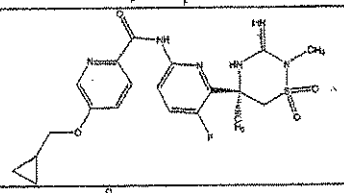
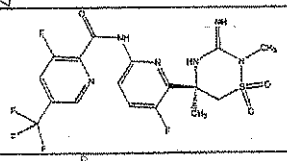
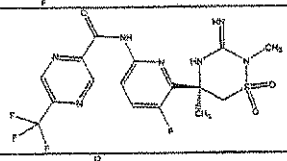
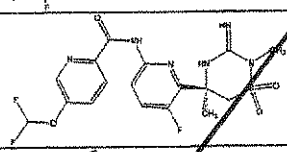
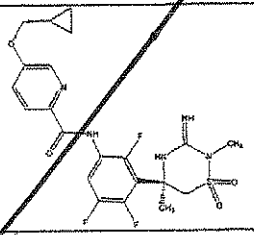
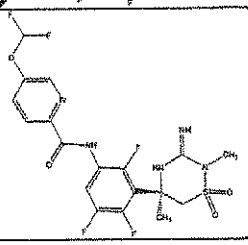
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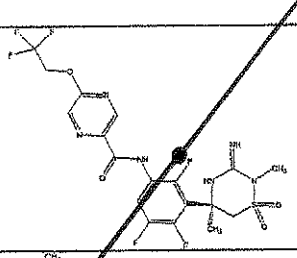
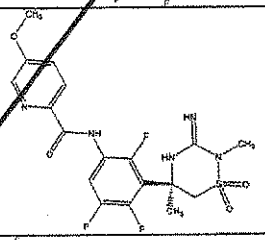
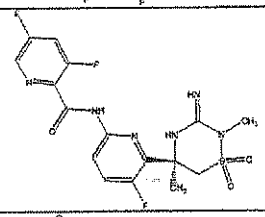
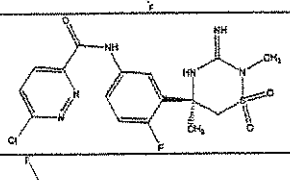
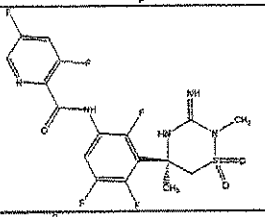
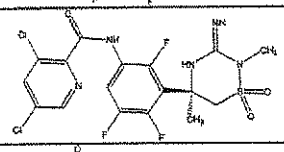
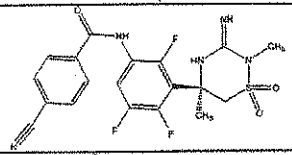
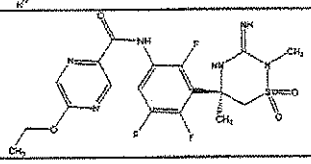
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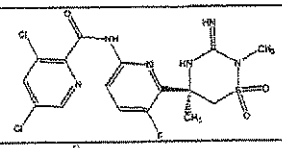
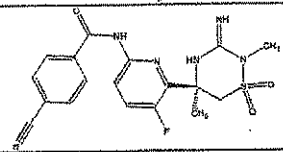
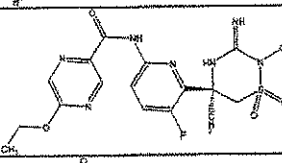
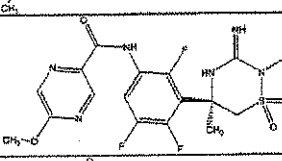
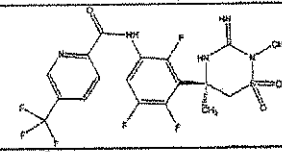
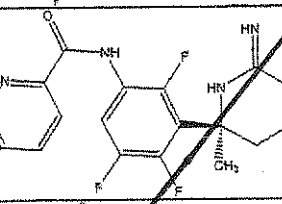
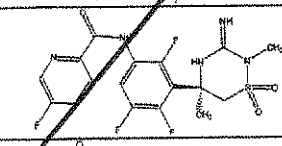
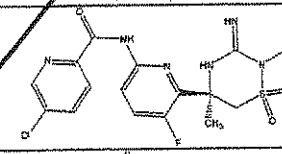
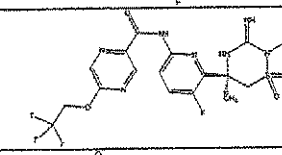
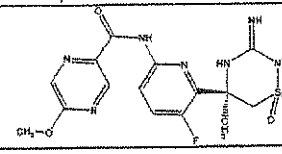
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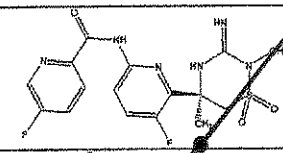
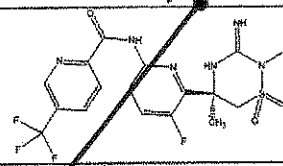
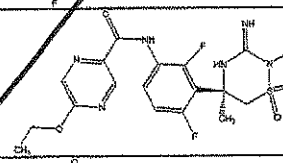
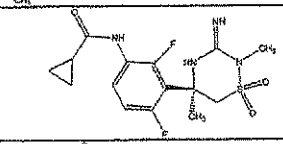
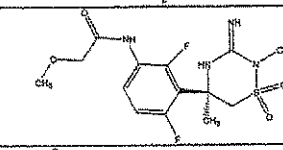
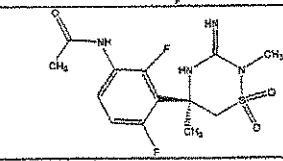
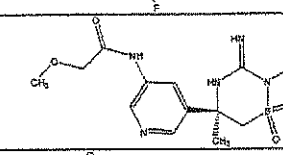
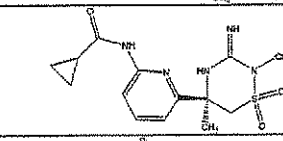
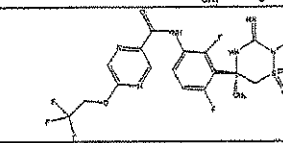
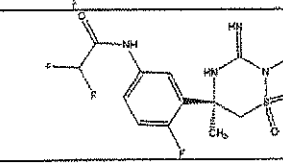
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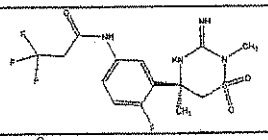
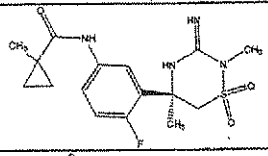
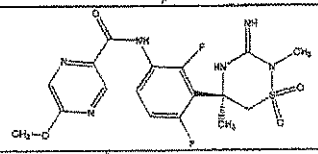
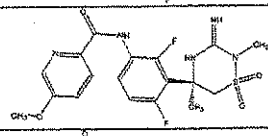
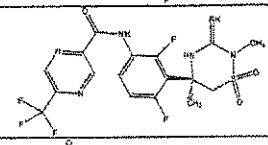
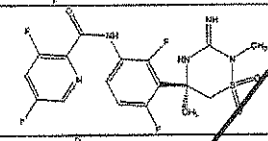
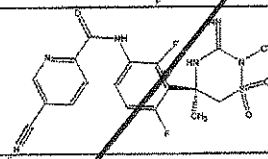
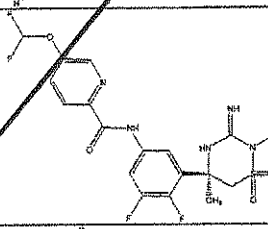
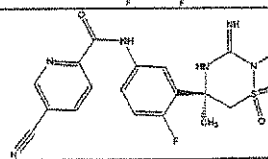
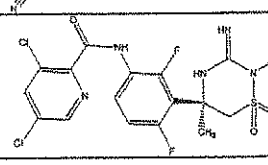
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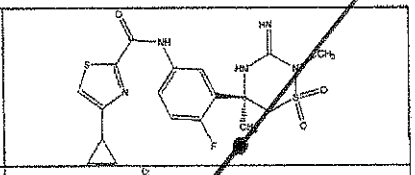
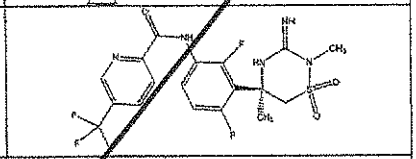
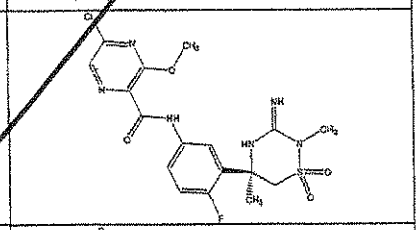
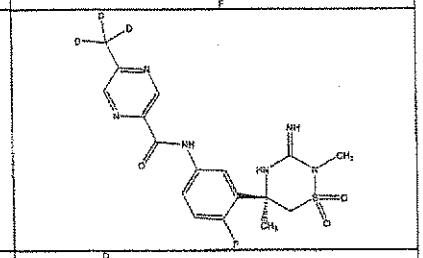
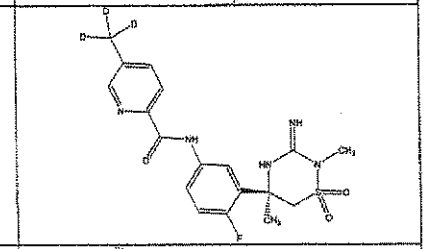
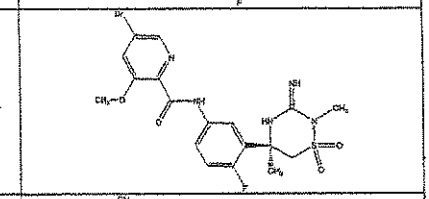
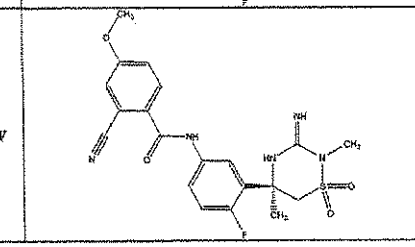
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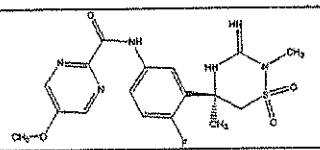
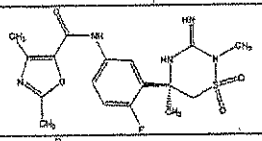
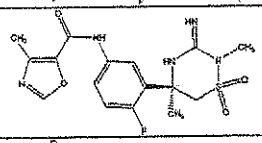
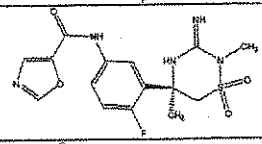
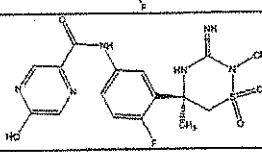
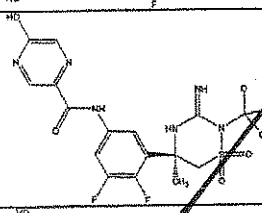
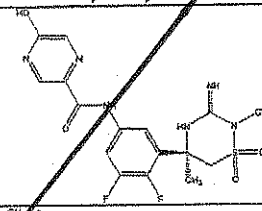
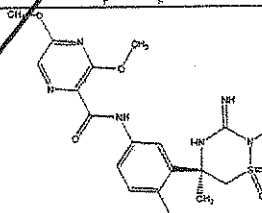
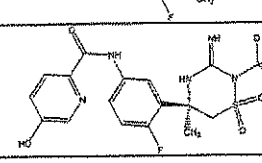
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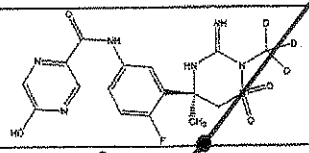
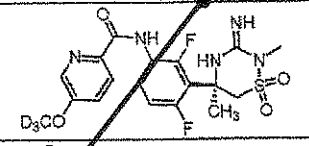
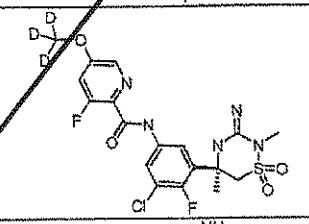
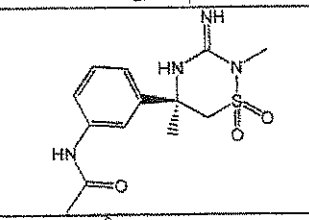
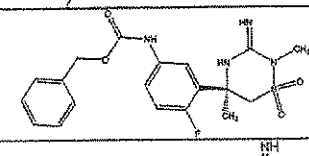
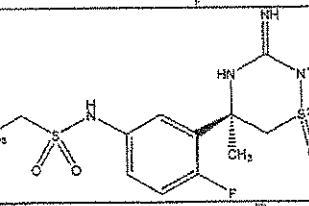
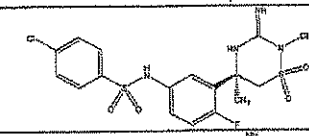
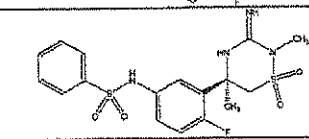
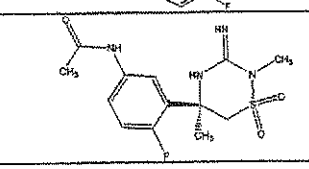
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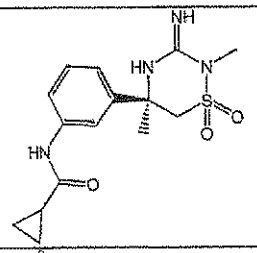
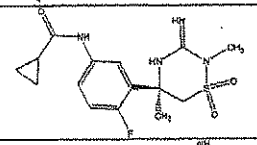
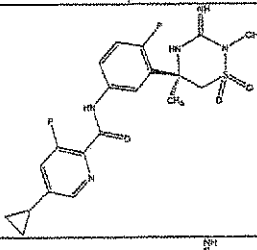
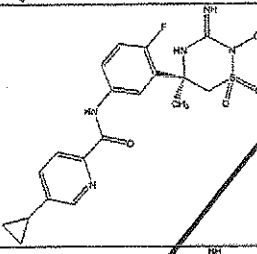
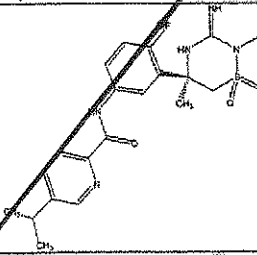
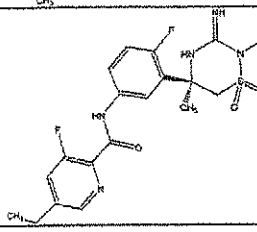
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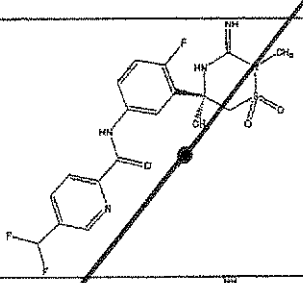
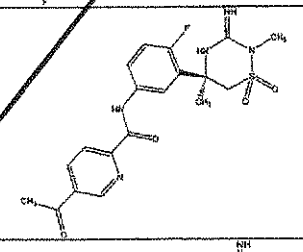
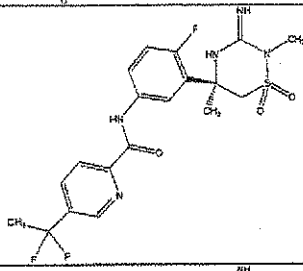
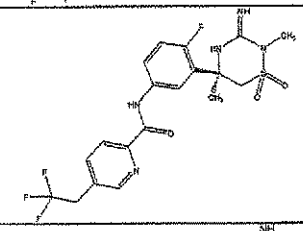
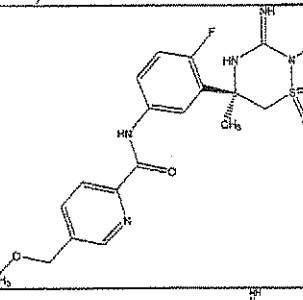
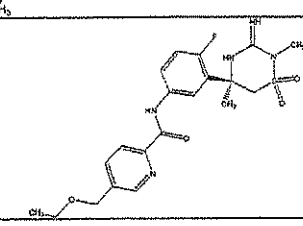
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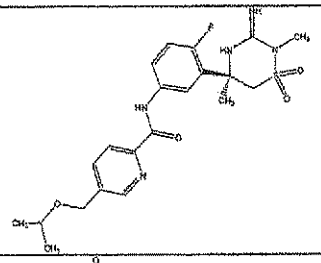
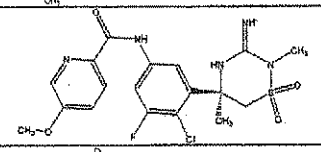
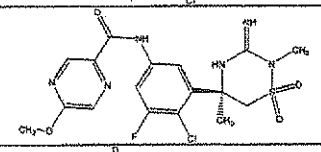
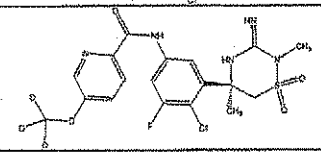
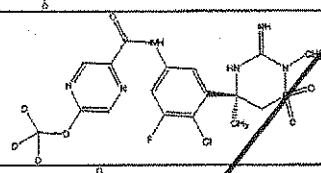
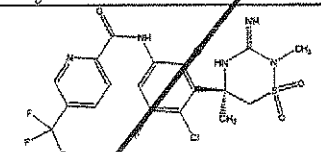
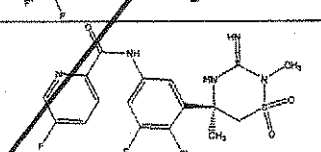
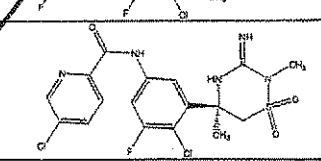
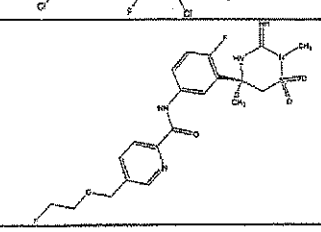
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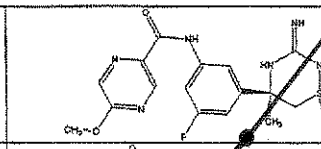
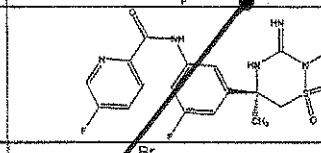
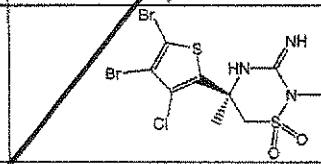
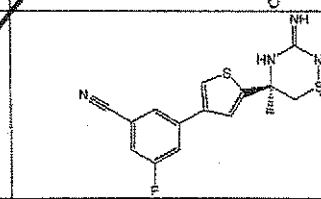
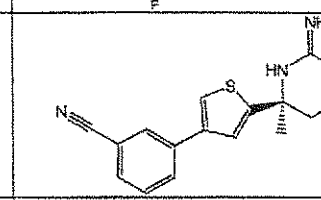
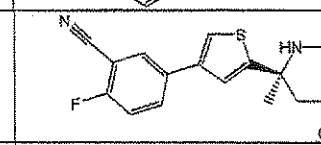
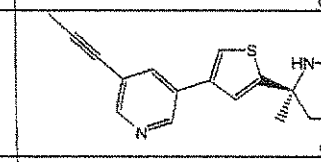
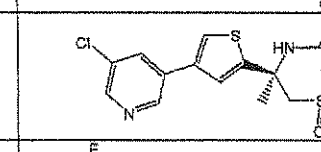
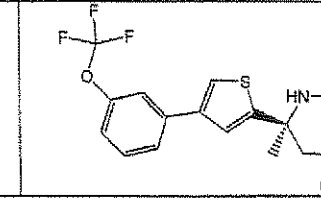
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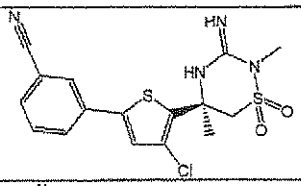
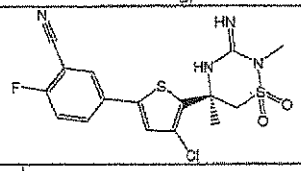
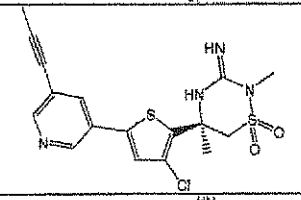
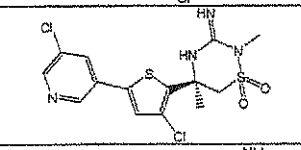
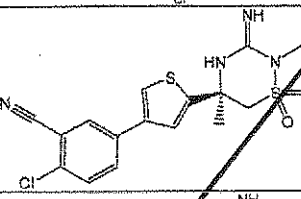
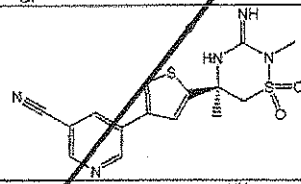
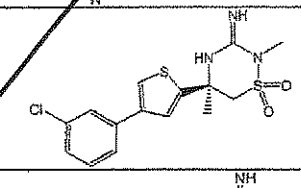
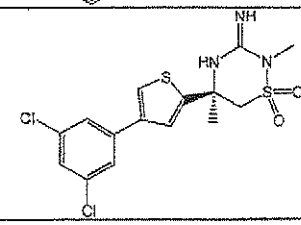
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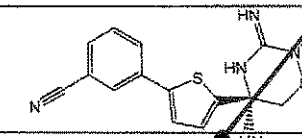
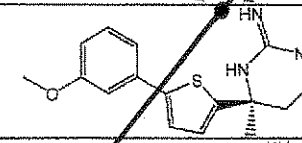
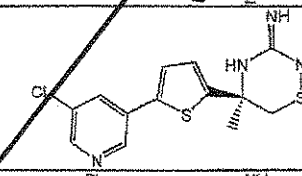
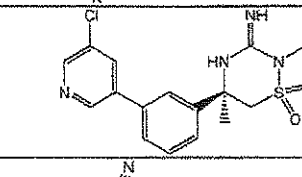
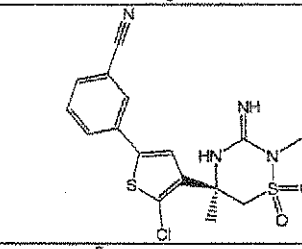
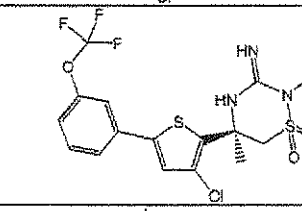
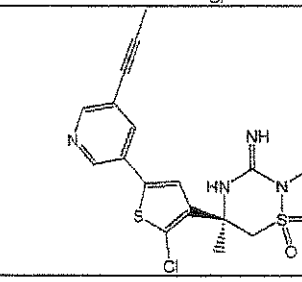
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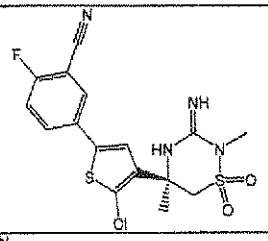
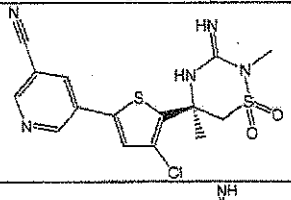
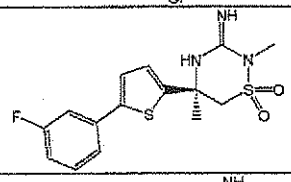
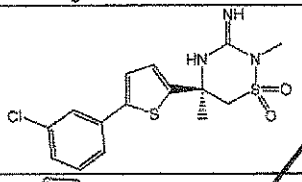
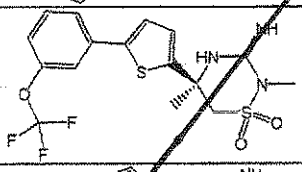
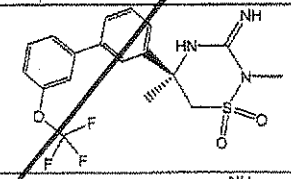
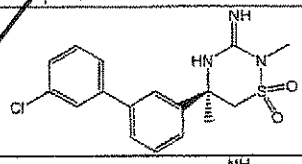
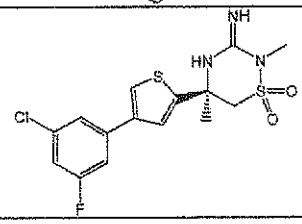
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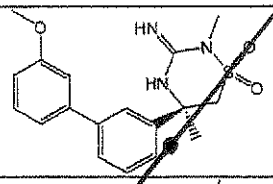
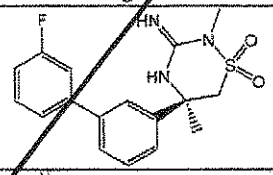
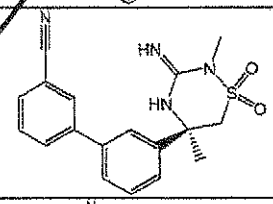
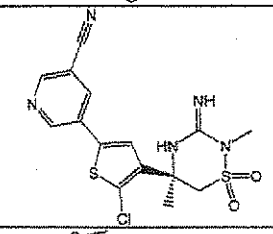
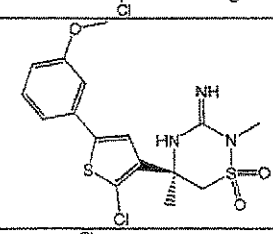
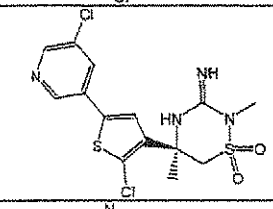
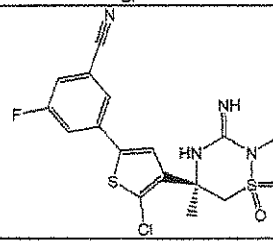
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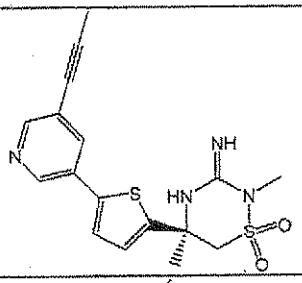
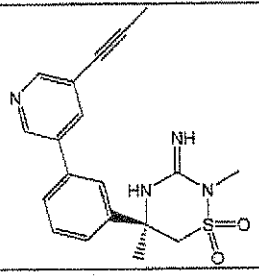
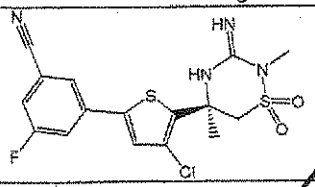
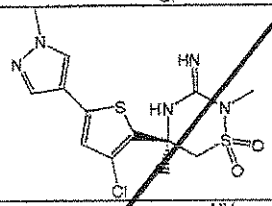
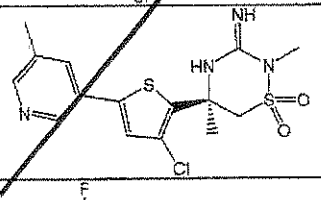
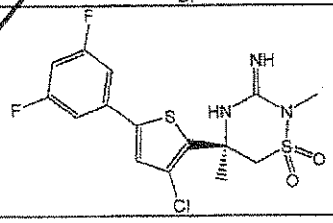
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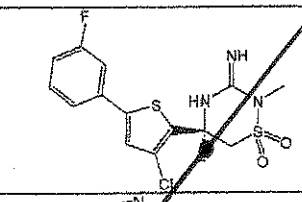
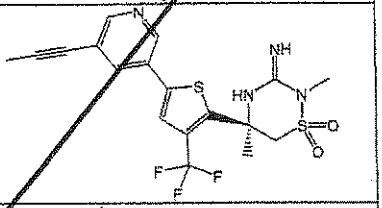
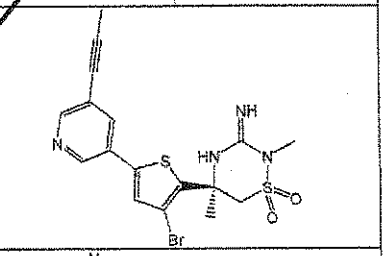
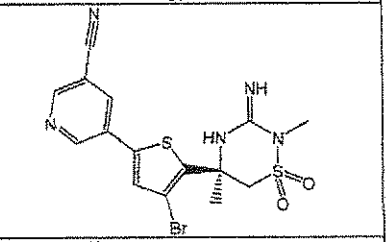
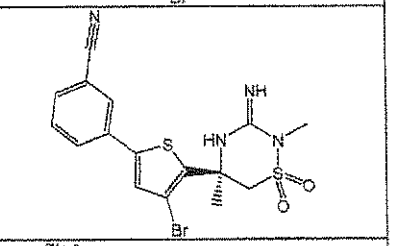
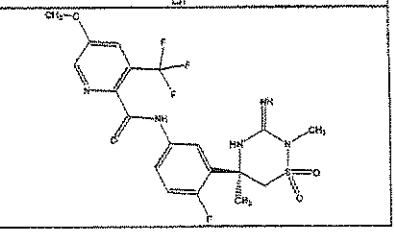
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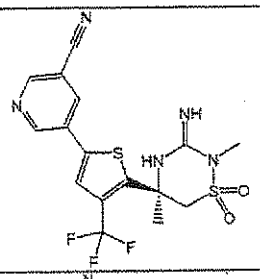
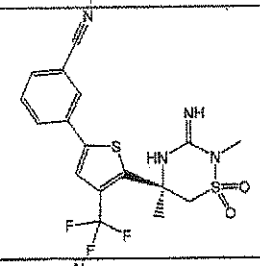
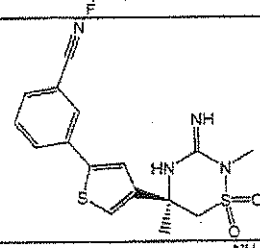
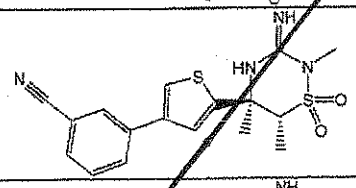
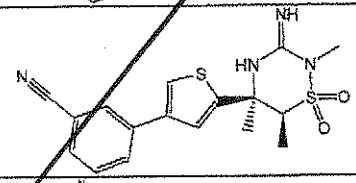
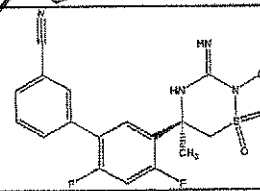
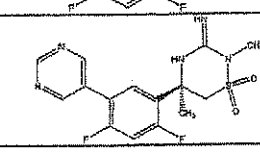
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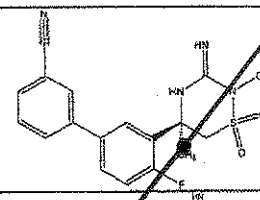
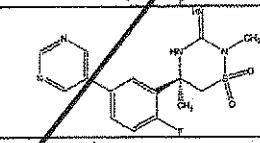
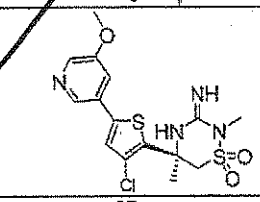
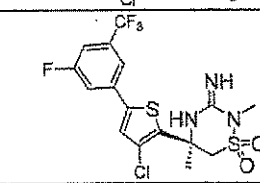
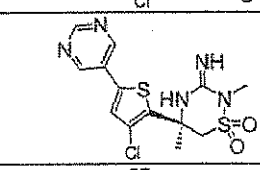
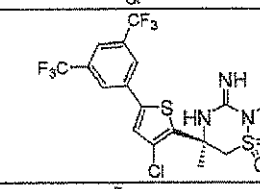
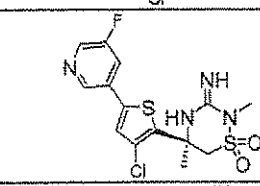
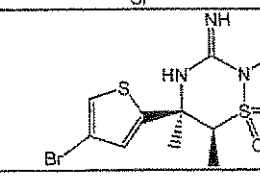
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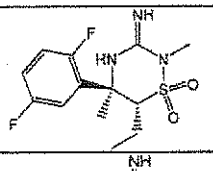
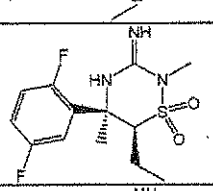
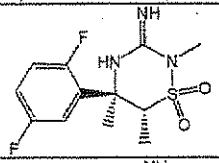
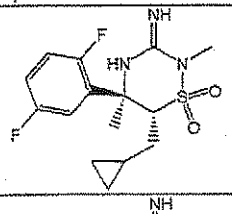
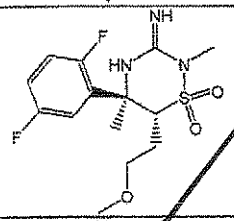
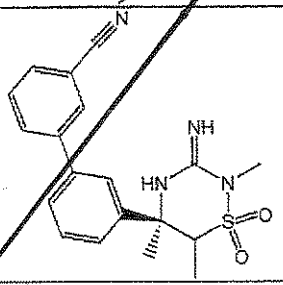
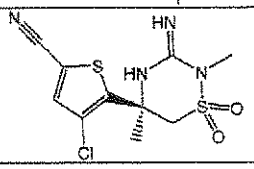
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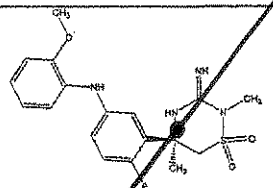
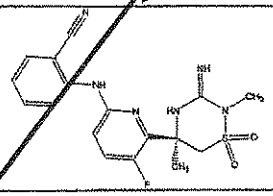
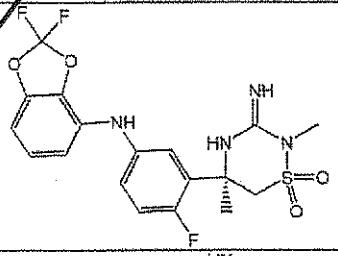
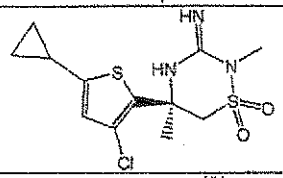
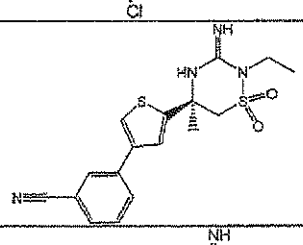
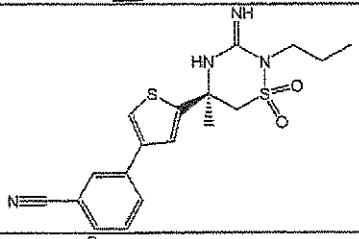
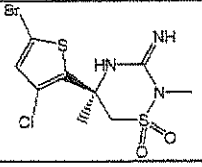
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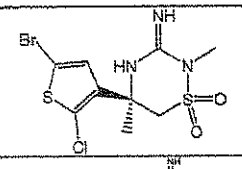
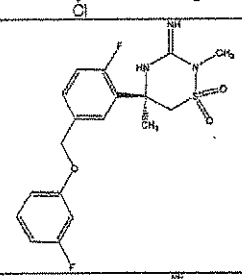
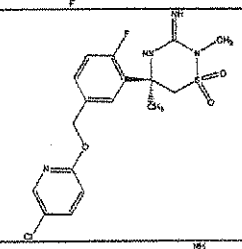
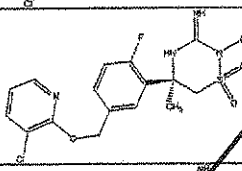
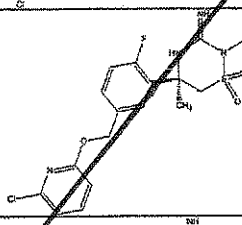
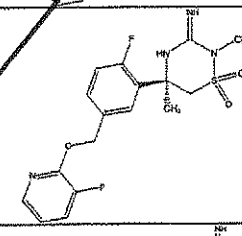
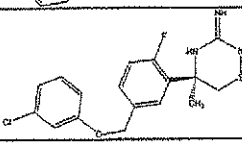
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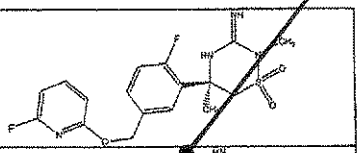
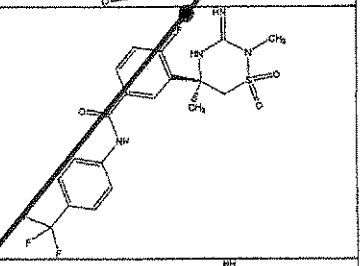
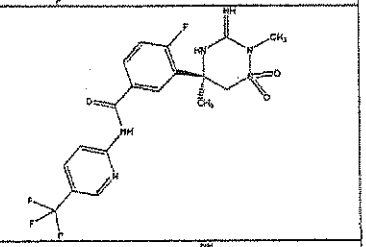
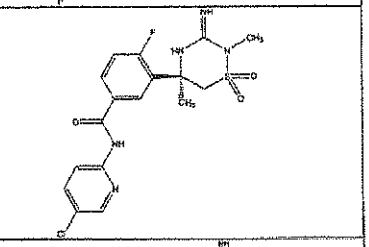
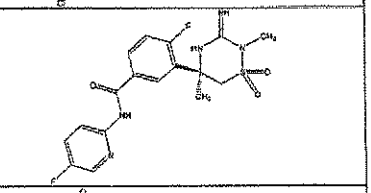
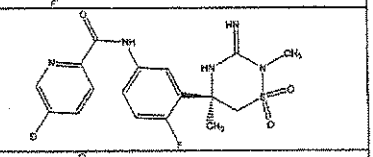
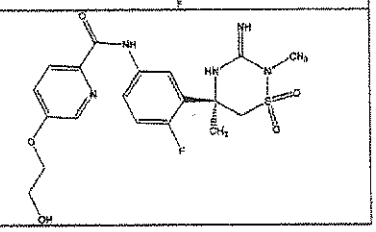
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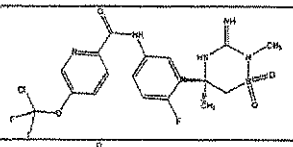
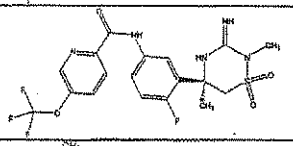
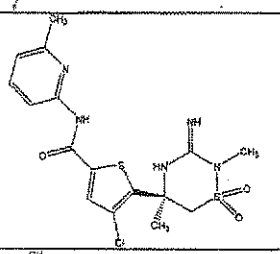
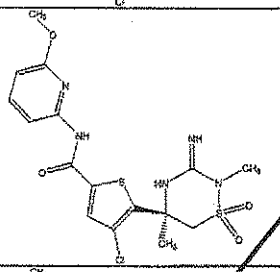
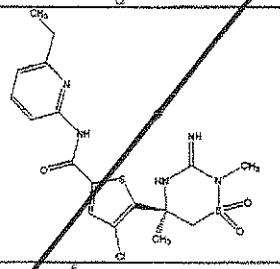
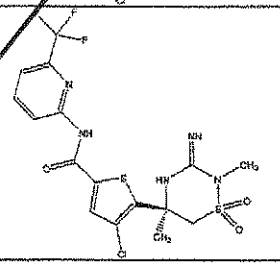
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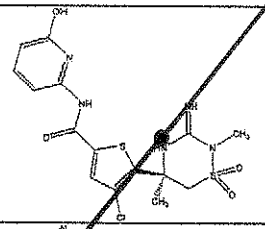
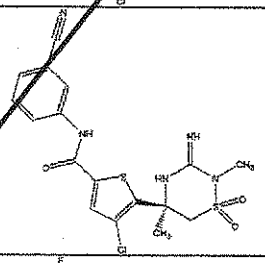
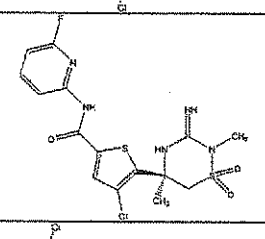
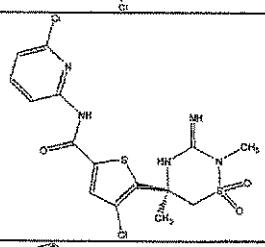
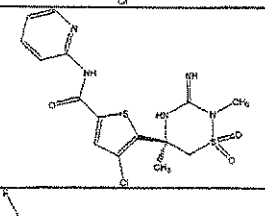
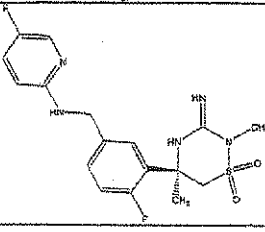
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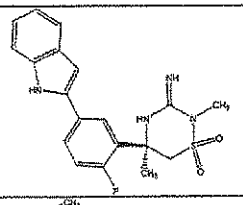
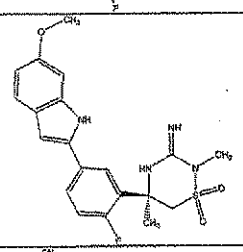
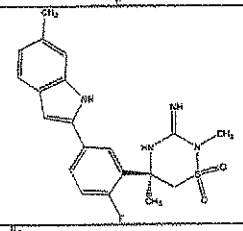
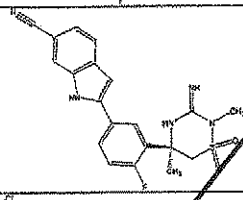
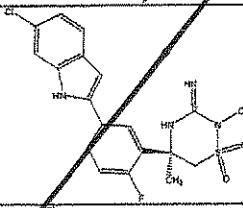
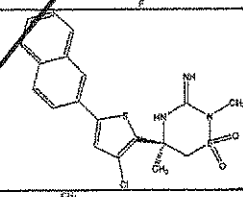
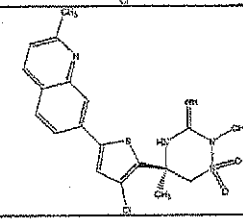
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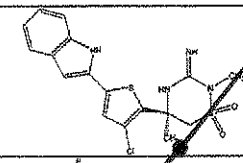
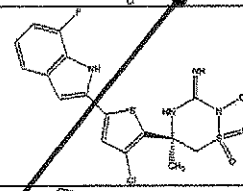
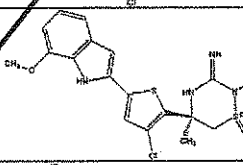
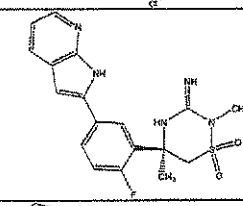
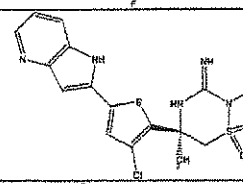
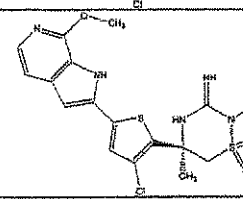
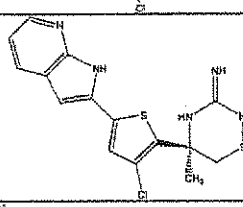
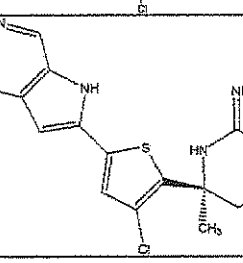
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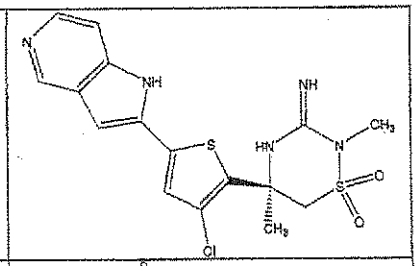
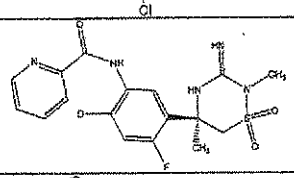
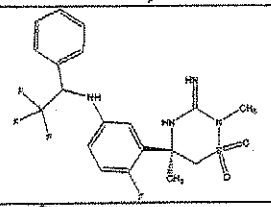
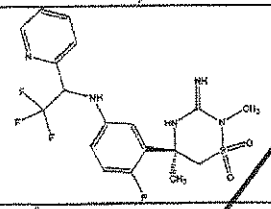
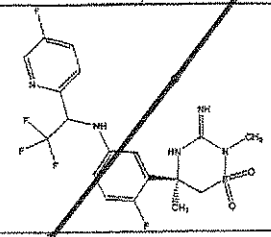
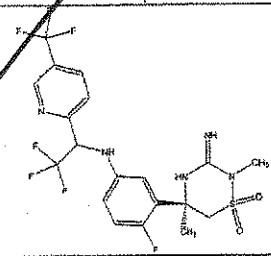
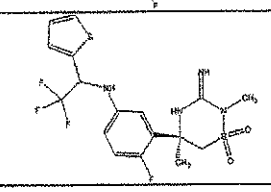
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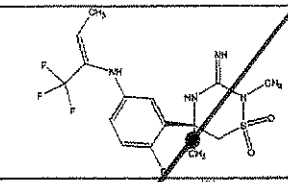
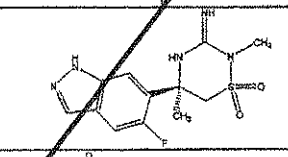
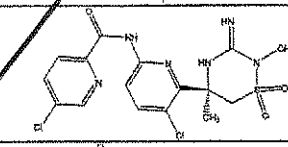
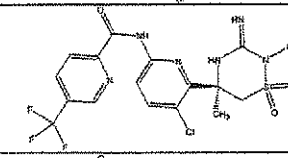
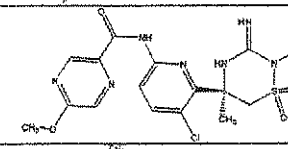
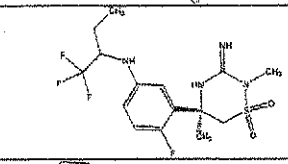
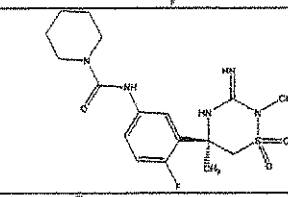
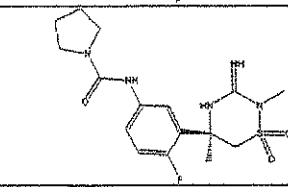
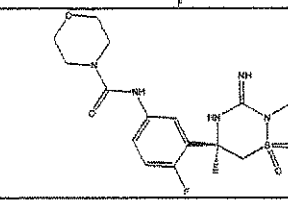
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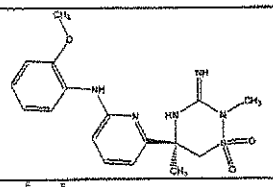
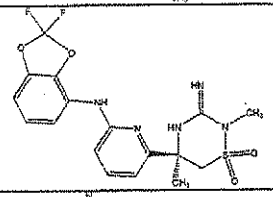
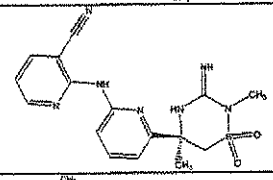
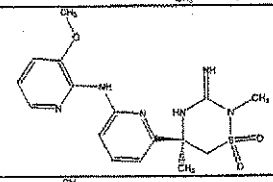
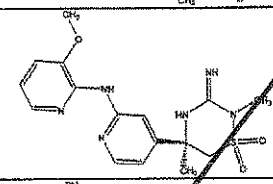
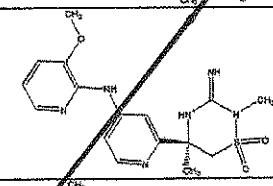
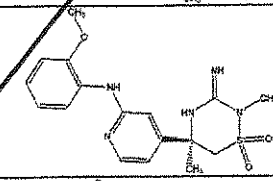
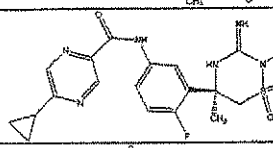
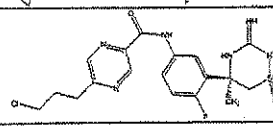
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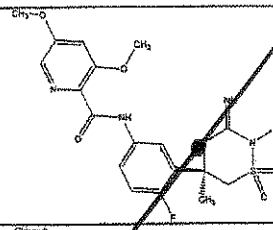
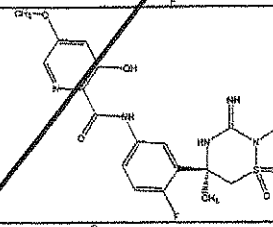
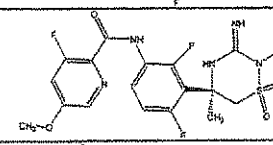
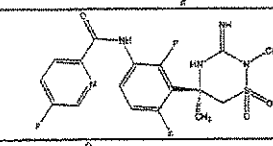
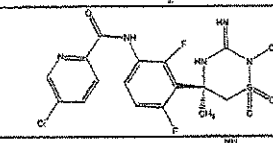
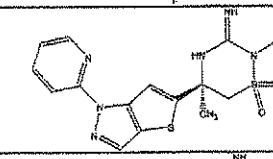
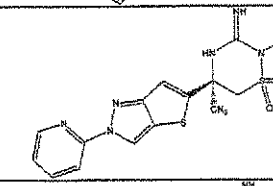
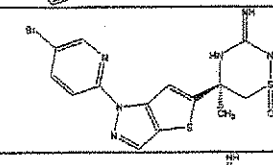
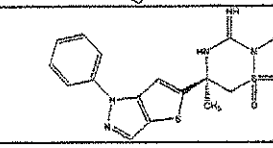
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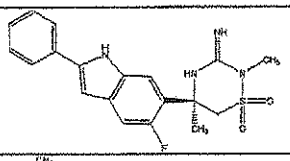
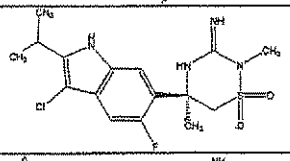
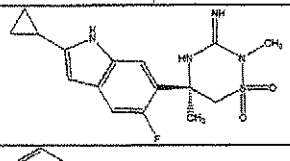
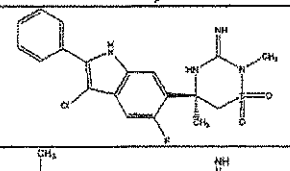
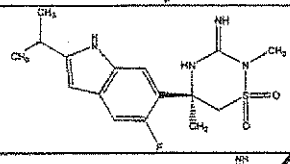
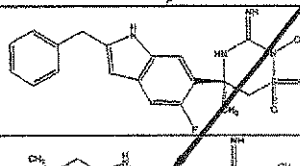
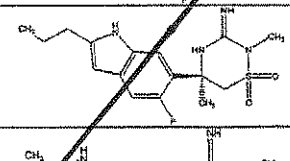
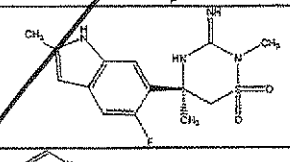
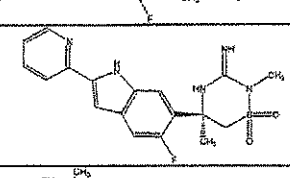
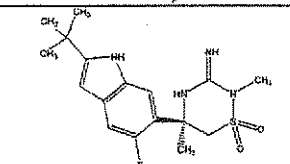
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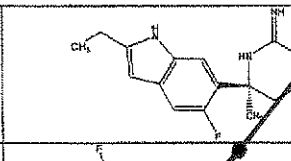
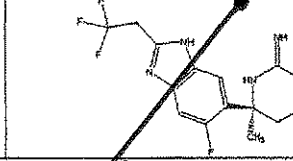
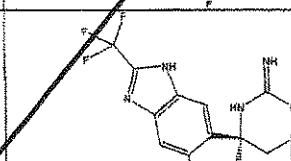
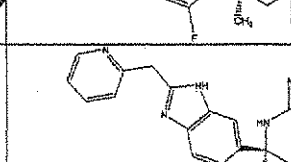
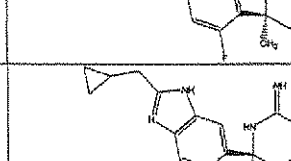
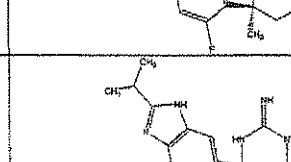
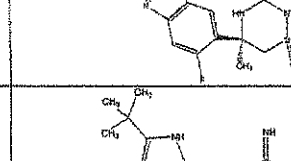
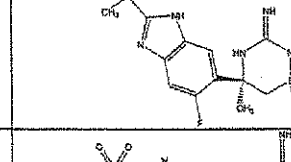
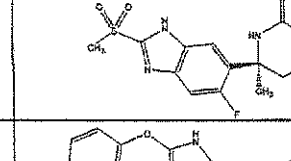
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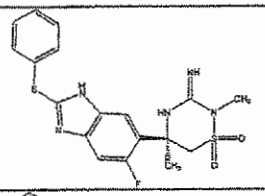
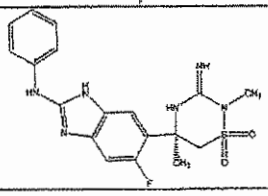
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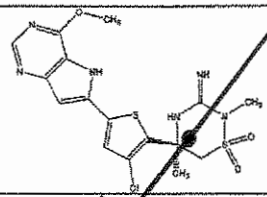
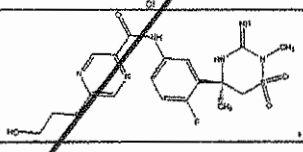
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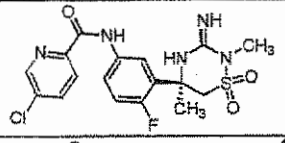
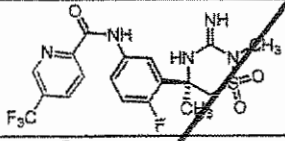
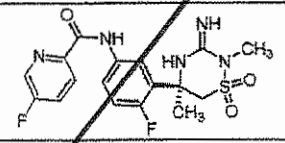
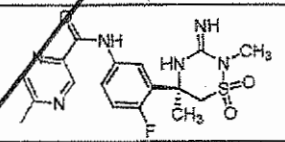
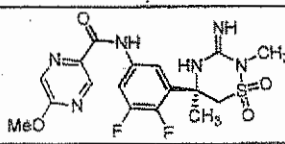
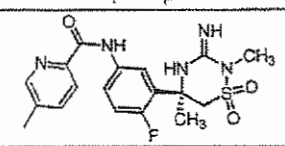
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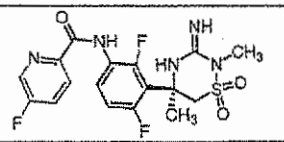
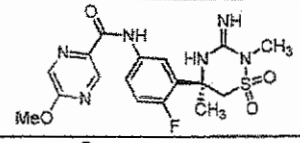
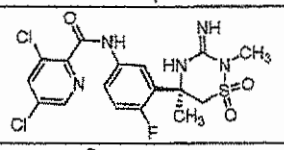
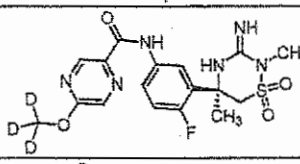
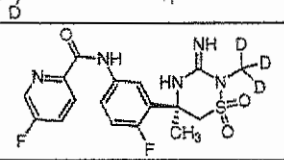
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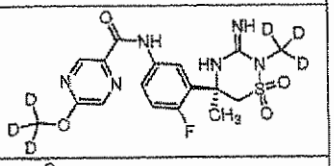
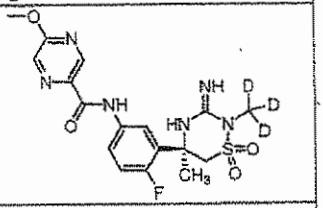
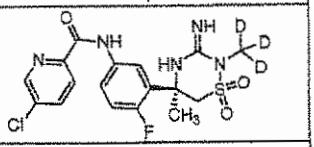
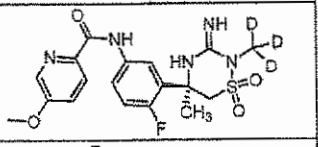
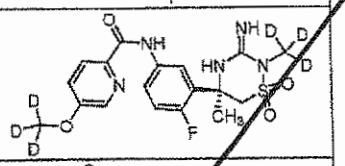
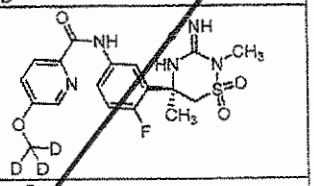
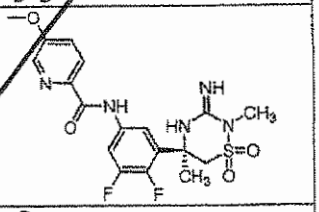
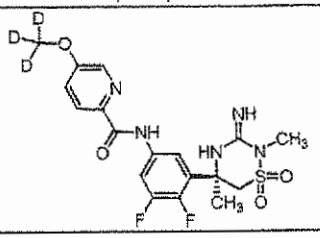
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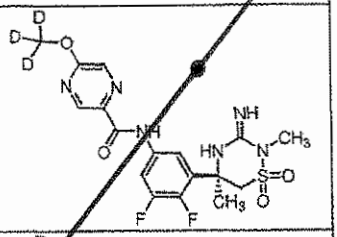
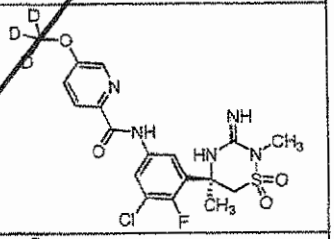
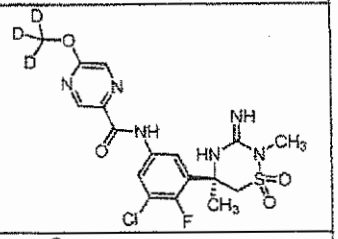
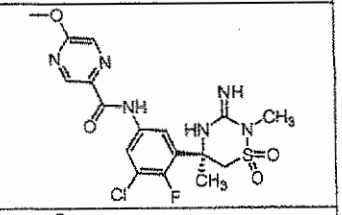
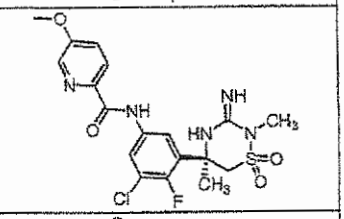
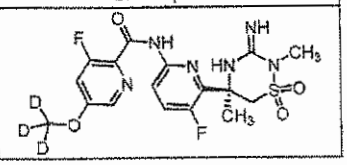
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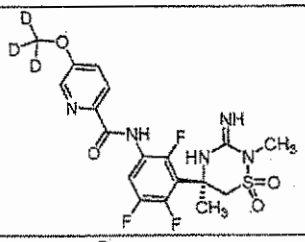
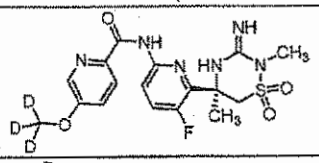
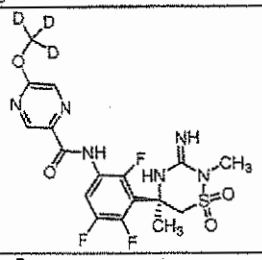
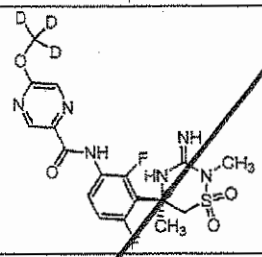
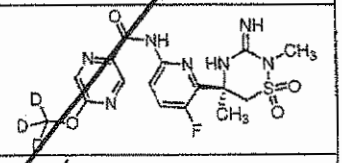
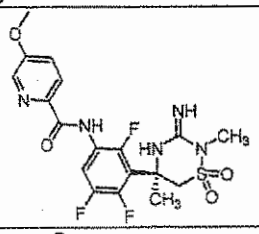
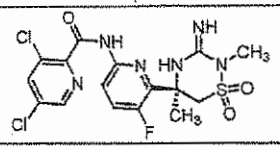
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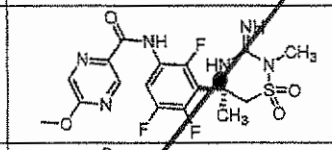
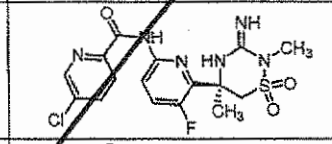
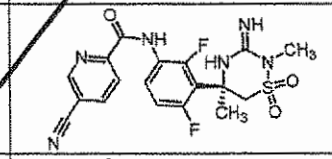
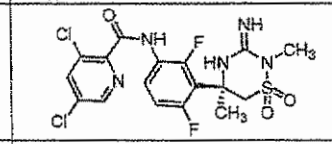
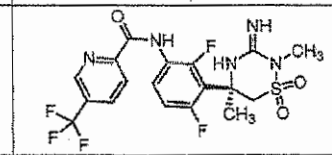
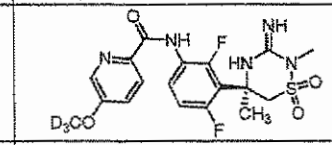
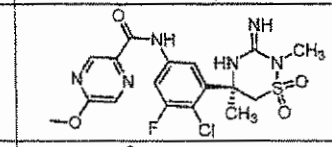
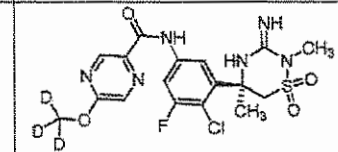
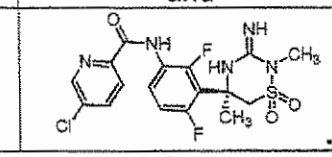
Ex. #	Structure
34	
26	
25	
36	
40di	
35	

Ex. #	Structure
173	
40ai	
40ag	
40aq	
40ax	

Ex. #	Structure
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40az	
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40bc	
40bd	
40cz	
40el	
40es	

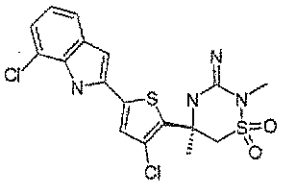
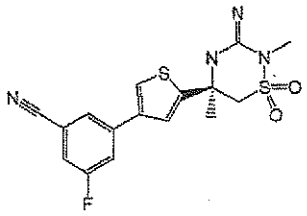
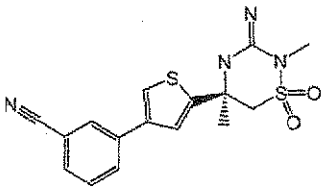
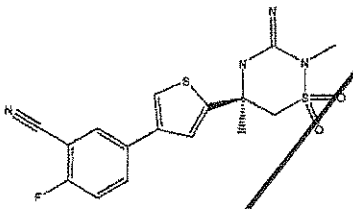
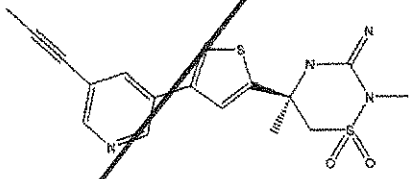
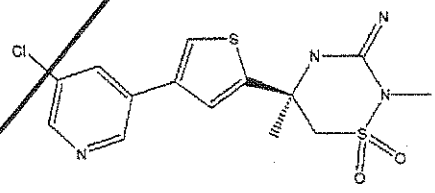
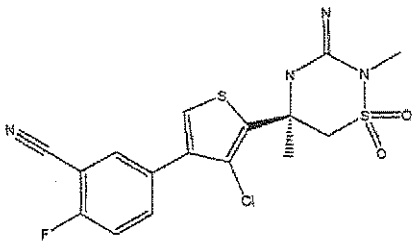
Ex. #	Structure
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40ff	
40fg	
40fh	
40fi	
40fl	

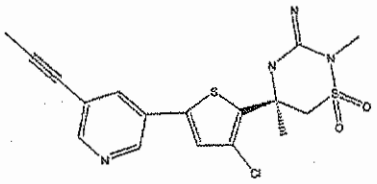
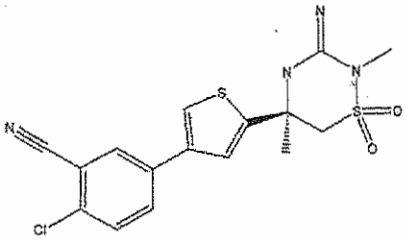
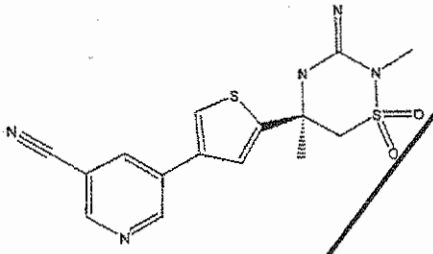
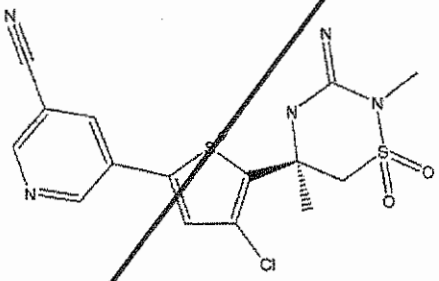
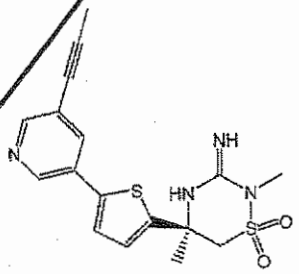
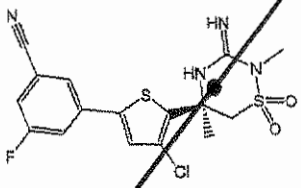
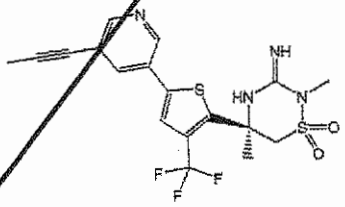
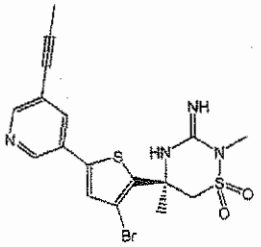
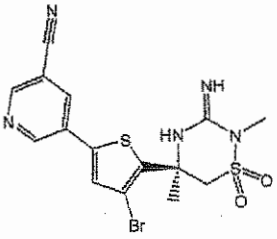
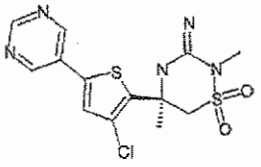
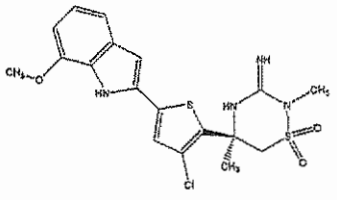
Ex. #	Structure
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40fo	
40fp	
40fq	
40fr	
40ge	
40gl	

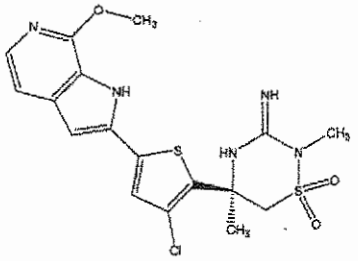
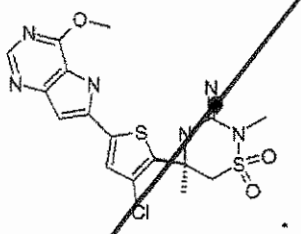
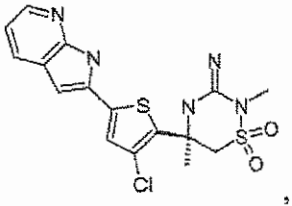
Ex. #	Structure
40go	
40gs	
40hm	
40hp	
40hr	
40ii	
42n	
42p	
	and
174	

10. A compound, or a tautomer thereof,

10. A compound, or a tautomer thereof, or a stereoisomer of said compound or said tautomer, or a pharmaceutically acceptable salt thereof, said compound being selected from the group consisting of

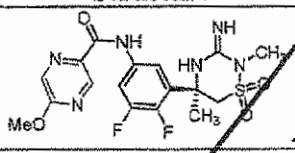
Ex.	Structure
141a	
44	
45	
46	
47	
48	
51	

Ex.	Structure
52	
54	
55	
66	
80	
82	
87	
88	
89	
95g	
141	

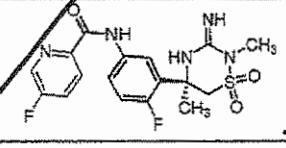
Ex.	Structure	Ex.	Structure
144		200	
145			

, and

11. A compound, or a tautomer thereof, or a pharmaceutically acceptable salt of said compound or said tautomer, said compound having a structure:

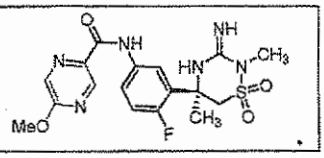
Ex #	Structure
40di	

12. A compound, or a tautomer thereof, or a pharmaceutically acceptable salt of said compound or said tautomer, said compound having a structure:

Ex #	Structure
25	

13. A compound, or a tautomer thereof, or a pharmaceutically acceptable salt of said compound or said tautomer, said compound having a structure:

Ex #	Structure

40ai	

14. A pharmaceutical composition comprising at least one compound of any one of claims 1-13, or a tautomer thereof, or a stereoisomer of said compound or said tautomer, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

15. A pharmaceutical composition comprising a compound of any one of claims 1-13, or a tautomer thereof, or a stereoisomer of said compound or said tautomer, or a pharmaceutically acceptable salt thereof, together with at least one additional therapeutic agent, and a pharmaceutically acceptable carrier or diluent.

16. A pharmaceutical composition of claim 15, wherein said at least one additional therapeutic agent is at least one agent selected from:

m_1 agonists; m_2 antagonists; cholinesterase inhibitors; galantamine; rivastigimine; N-methyl-D-aspartate receptor antagonists; combinations of cholinesterase inhibitors and N-methyl-D-aspartate receptor antagonists; gamma secretase modulators; gamma secretase inhibitors; non-steroidal anti-inflammatory agents; anti-inflammatory agents that can reduce neuroinflammation; anti-amyloid antibodies; vitamin E; nicotinic acetylcholine receptor agonists; CB1 receptor inverse agonists; CB1 receptor antagonists; antibiotics; growth hormone secretagogues; histamine H3 antagonists; AMPA agonists; PDE4 inhibitors; $GABA_A$ inverse agonists; inhibitors of amyloid aggregation; glycogen synthase kinase beta inhibitors; promoters of alpha secretase activity; PDE-10 inhibitors; Tau kinase inhibitors; Tau aggregation inhibitors; RAGE inhibitors; anti-Abeta vaccine; APP ligands; agents that upregulate insulin, cholesterol lowering agents; cholesterol absorption inhibitors; combinations of HMG-CoA reductase inhibitors and cholesterol absorption inhibitors; fibrates; combinations of fibrates and cholesterol lowering agents and/or cholesterol absorption inhibitors; nicotinic receptor agonists; niacin; combinations of niacin and cholesterol absorption inhibitors and/or cholesterol lowering agents; LXR agonists; LRP mimics; H3 receptor antagonists; histone deacetylase inhibitors; hsp90 inhibitors; 5-HT4

agonists; 5-HT6 receptor antagonists; mGluR1 receptor modulators or antagonists; mGluR5 receptor modulators or antagonists; mGluR2/3 antagonists; Prostaglandin EP2 receptor antagonists; PAI-1 inhibitors; agents that can induce Abeta efflux; Metal-protein attenuating compound; GPR3 modulators; and antihistamines.

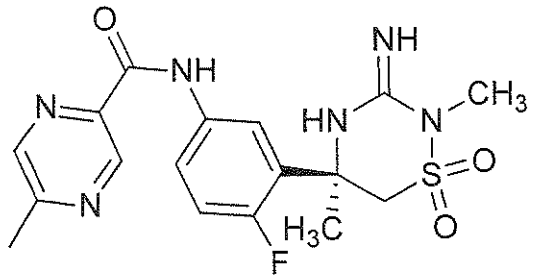
17. A method of treating, preventing, and/or delaying the onset of an amyloid β pathology ("Aβ pathology") and/or one or more symptoms of said pathology comprising administering at least one compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof, to a patient in need thereof in an amount effective to treat said pathology.

18. A method of claim 17, wherein said Aβ pathology is selected from Alzheimer's disease, Down's syndrome, Parkinson's disease, memory loss, memory loss associated with Alzheimer's disease, memory loss associated with Parkinson's disease, attention deficit symptoms, attention deficit symptoms associated with Alzheimer's disease, Parkinson's disease, and/or Down's syndrome, dementia, stroke, microgliosis and brain inflammation, pre-senile dementia, senile dementia, dementia associated with Alzheimer's disease, Parkinson's disease, and/or Down's syndrome, progressive supranuclear palsy, cortical basal degeneration, neurodegeneration, olfactory impairment, olfactory impairment associated with Alzheimer's disease, Parkinson's disease, and/or Down's syndrome, β-amyloid angiopathy, cerebral amyloid angiopathy, hereditary cerebral hemorrhage, mild cognitive impairment ("MCI"), glaucoma, amyloidosis, type II diabetes, diabetes-associated amyloidogenesis, hemodialysis complications (from β_2 microglobulins and complications arising therefrom in hemodialysis patients), scrapie, bovine spongiform encephalitis, traumatic brain injury ("TBI"), Creutzfeld-Jakob disease, and traumatic brain injury.

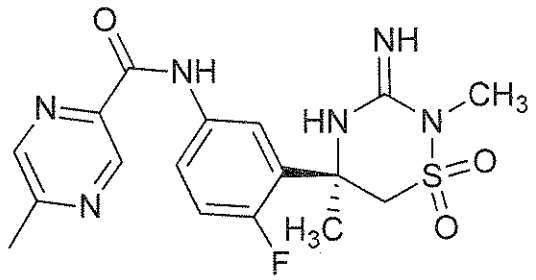
19. A method of claim 18, wherein said Aβ pathology is Alzheimer's disease.

WE CLAIM:

1. A compound, or a tautomer thereof, said compound having a structure:



2. A pharmaceutically acceptable salt of a compound or a tautomer thereof, said compound having a structure:

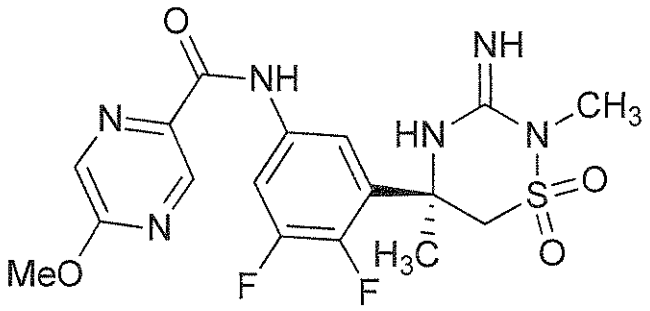


3. The pharmaceutically acceptable salt of claim 2, wherein said salt is selected from the group consisting of acetate, ascorbate, benzoate, benzenesulfonate, bisulfate, borate, butyrate, citrate, camphorate, camphorsulfonate, fumarate, hydrochloride, hydrobromide, hydroiodide, lactate, maleate, methanesulfonate, naphthalenesulfonate, nitrate, oxalate, phosphate, propionate, salicylate, succinate, sulfate, tartarate, thiocyanate, and toluenesulfonate.

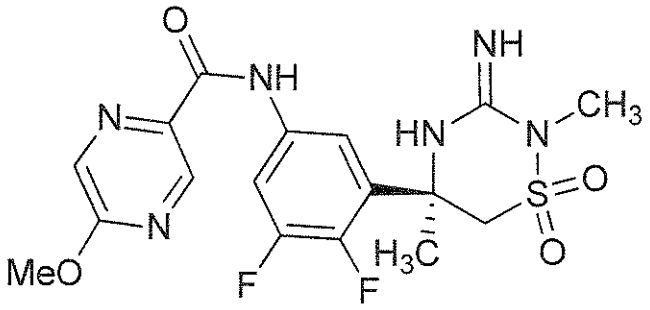
4. The pharmaceutically acceptable salt of claim 2, wherein said salt is a hydrochloride salt.

5. The pharmaceutically acceptable salt of claim 2, wherein said salt is a toluenesulfonate salt.

6. A compound, or a tautomer thereof, said compound having a structure:



7. A pharmaceutically acceptable salt of a compound or a tautomer thereof, said compound having a structure:

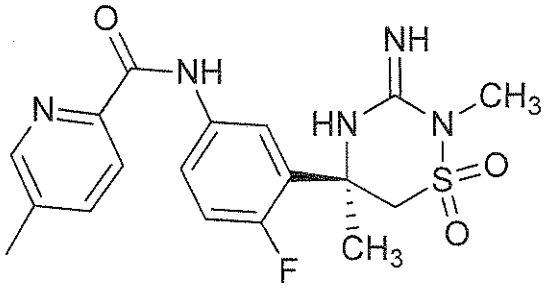


8. The pharmaceutically acceptable salt of claim 7, wherein said salt is selected from the group consisting of acetate, ascorbate, benzoate, benzenesulfonate, bisulfate, borate, butyrate, citrate, camphorate, camphorsulfonate, fumarate, hydrochloride, hydrobromide, hydroiodide, lactate, maleate, methanesulfonate, naphthalenesulfonate, nitrate, oxalate, phosphate, propionate, salicylate, succinate, sulfate, tartarate, thiocyanate, and toluenesulfonate.

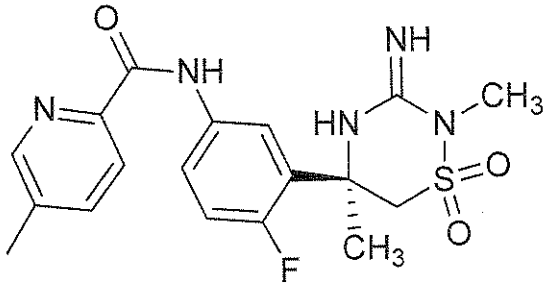
9. The pharmaceutically acceptable salt of claim 7, wherein said salt is a hydrochloride salt.

10. The pharmaceutically acceptable salt of claim 7, wherein said salt is a toluenesulfonate salt.

11. A compound, or a tautomer thereof, said compound having a structure:



12. A pharmaceutically acceptable salt of a compound or a tautomer thereof, said compound having a structure:

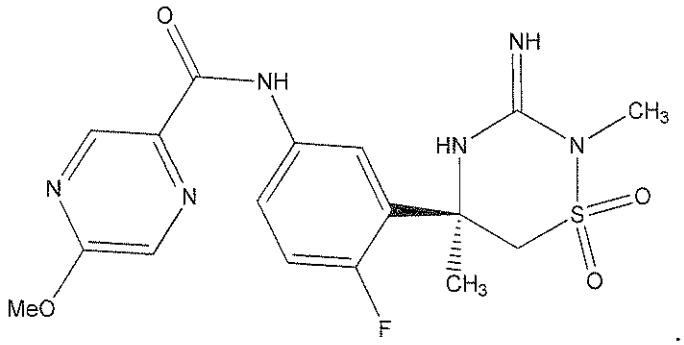


13. The pharmaceutically acceptable salt of claim 12, wherein said salt is selected from the group consisting of acetate, ascorbate, benzoate, benzenesulfonate, bisulfate, borate, butyrate, citrate, camphorate, camphorsulfonate, fumarate, hydrochloride, hydrobromide, hydroiodide, lactate, maleate, methanesulfonate, naphthalenesulfonate, nitrate, oxalate, phosphate, propionate, salicylate, succinate, sulfate, tartarate, thiocyanate, and toluenesulfonate.

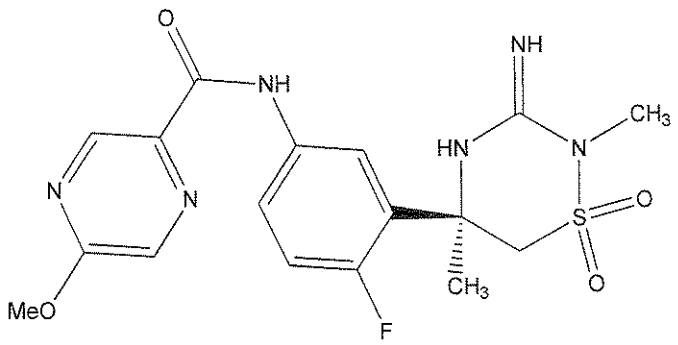
14. The pharmaceutically acceptable salt of claim 12, wherein said salt is a hydrochloride salt.

15. The pharmaceutically acceptable salt of claim 12, wherein said salt is a toluenesulfonate salt.

16. A compound, or a tautomer thereof, said compound having a structure:



17. A pharmaceutically acceptable salt of a compound or a tautomer thereof, said compound having a structure:

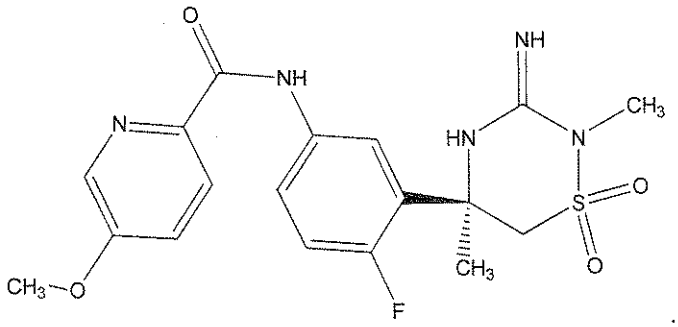


18. The pharmaceutically acceptable salt of claim 17, wherein said salt is selected from the group consisting of acetate, ascorbate, benzoate, benzenesulfonate, bisulfate, borate, butyrate, citrate, camphorate, camphorsulfonate, fumarate, hydrochloride, hydrobromide, hydroiodide, lactate, maleate, methanesulfonate, naphthalenesulfonate, nitrate, oxalate, phosphate, propionate, salicylate, succinate, sulfate, tartarate, thiocyanate, and toluenesulfonate.

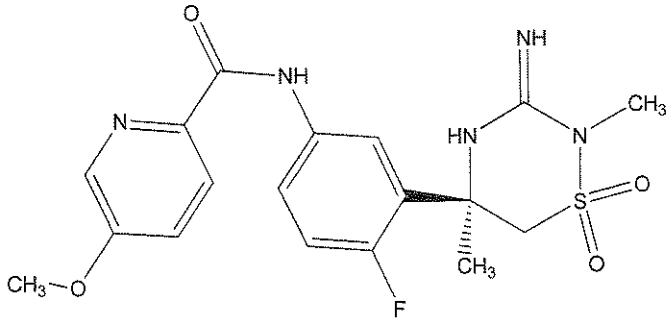
19. The pharmaceutically acceptable salt of claim 17, wherein said salt is a hydrochloride salt.

20. The pharmaceutically acceptable salt of claim 17, wherein said salt is a toluenesulfonate salt.

21. A compound, or a tautomer thereof, said compound having a structure:



22. A pharmaceutically acceptable salt of a compound or a tautomer thereof, said compound having a structure:



23. The pharmaceutically acceptable salt of claim 21, wherein said salt is selected from the group consisting of acetate, ascorbate, benzoate, benzenesulfonate, bisulfate, borate, butyrate, citrate, camphorate, camphorsulfonate, fumarate, hydrochloride, hydrobromide, hydroiodide, lactate, maleate, methanesulfonate, naphthalenesulfonate, nitrate, oxalate, phosphate, propionate, salicylate, succinate, sulfate, tartarate, thiocyanate, and toluenesulfonate.

24. The pharmaceutically acceptable salt of claim 21, wherein said salt is a hydrochloride salt.

25. The pharmaceutically acceptable salt of claim 21, wherein said salt is a toluenesulfonate salt.

26. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent and the compound of any one of claims 1, 6, 11, 16 and 21.

27. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent and the pharmaceutically acceptable salt of any one of claims 2 to 5, 7 to 10, 12 to 15, 17 to 20 or 22 to 25.

28. Use of a compound, or a tautomer thereof, according to any one of claims 1, 6, 11, 16, and 21, or a pharmaceutically acceptable salt of said compound or said tautomer in the manufacture of a medicament for the treatment of an indication selected from the group consisting of Alzheimer's disease, Down's syndrome, Parkinson's disease, stroke, microgliosis, brain inflammation, pre-senile dementia, senile dementia, progressive supranuclear palsy, cortical basal degeneration, olfactory impairment associated with Alzheimer's disease, olfactory impairment associated with Parkinson's disease, olfactory impairment associated with Down's syndrome, β-amyloid angiopathy, cerebral amyloid angiopathy, hereditary cerebral hemorrhage, mild cognitive impairment, glaucoma, amyloidosis, type II diabetes, diabetes-associated amyloidogenesis, scrapie, bovine spongiform encephalitis, traumatic brain injury, and Creutzfeld-Jakob disease.

29. The use of claim 28, wherein said indication is Alzheimer's disease.

30. The use of claim 28, wherein said indication is olfactory impairment associated with Alzheimer's disease.

31. The use of claim 28, wherein said indication is Down's syndrome.

32. The use of claim 28, wherein said indication is olfactory impairment associated with Down's syndrome.

33. The use of claim 28, wherein said indication is pre-senile dementia.

34. The use of claim 28, wherein said indication is is β-amyloid angiopathy.

35. The use of claim 28, wherein said indication is cerebral amyloid angiopathy.

36. The use of claim 28, wherein said indication is mild cognitive impairment.

37. The use of claim 28, wherein said indication is type II diabetes.

38. The use of claim 28, wherein said indication is traumatic brain injury.