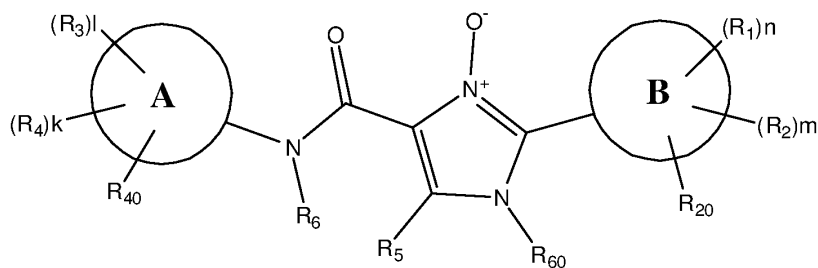


WHAT IS CLAIMED:

1. A compound represented by the structure of formula I:



I

- 5 **A** and **B** rings are each independently a single or fused aromatic or heteroaromatic ring system (e.g., phenyl, indole, benzofuran, 2-, 3- or 4-pyridine, naphthalene, thiazole, thiophene, imidazole, 1-methylimidazole, benzimidazole), a single or fused C₃-C₁₀ cycloalkyl (e.g. cyclohexyl), or a single or fused C₃-C₁₀ heterocyclic ring (e.g., benzofuran-2(3H)-one, benzo[d][1,3]dioxole, tetrahydrothiophene 1,1-dioxide, piperidine, 1-methylpiperidine, isoquinoline, 1,3-dihydroisobenzofuran);
- 10 **R₁**, **R₂** and **R₂₀** are each independently H, F, Cl, Br, I, OH, SH, R₈-OH (e.g., CH₂-OH), R₈-SH, -R₈-O-R₁₀, (e.g., -CH₂-O-CH₃), R₈-(C₃-C₈ cycloalkyl) (e.g., cyclohexyl), R₈-(C₃-C₈ heterocyclic ring) (e.g., CH₂-morpholine, CH₂-imidazole, CH₂-indazole), CF₃, CD₃, OCD₃, CN, NO₂, -CH₂CN, -R₈CN, NH₂, NHR (e.g., NH-CH₃), N(R)₂ (e.g., N(CH₃)₂), R₈-N(R₁₀)(R₁₁) (e.g., CH₂-CH₂-N(CH₃)₂, CH₂-NH₂, CH₂-N(CH₃)₂), R₉-R₈-N(R₁₀)(R₁₁) (e.g., C≡C-CH₂-NH₂), B(OH)₂, -OC(O)CF₃, -OCH₂Ph, NHC(O)-R₁₀
- 15 (e.g., NHC(O)CH₃), NHCO-N(R₁₀)(R₁₁) (e.g., NHC(O)N(CH₃)₂), COOH, -C(O)Ph, C(O)O-R₁₀ (e.g. C(O)O-CH₃, C(O)O-CH(CH₃)₂, C(O)O-CH₂CH₃), R₈-C(O)-R₁₀ (e.g., CH₂C(O)CH₃), C(O)H, C(O)-R₁₀ (e.g., C(O)-CH₃, C(O)-CH₂CH₃, C(O)-CH₂CH₂CH₃), C₁-C₅ linear or branched C(O)-haloalkyl (e.g., C(O)-CF₃), -C(O)NH₂, C(O)NHR, C(O)N(R₁₀)(R₁₁) (e.g., C(O)N(CH₃)₂), SO₂R, SO₂N(R₁₀)(R₁₁) (e.g., SO₂N(CH₃)₂, SO₂NHC(O)CH₃), C₁-C₅ linear or branched, substituted or unsubstituted alkyl (e.g.,
- 20 C(H)(OH)-CH₃, methyl, 2, 3, or 4-CH₂-C₆H₄-Cl, ethyl, propyl, iso-propyl, butyl, t-Bu, iso-butyl, pentyl, benzyl), C₂-C₅ linear or branched, substituted or unsubstituted alkenyl (e.g., CH=C(Ph)₂), C₁-C₅ linear, branched or cyclic haloalkyl (e.g., CF₃, CF₂CH₃, CH₂CF₃, CF₂CH₂CH₃, CH₂CH₂CF₃, CF₂CH(CH₃)₂, CF(CH₃)-CH(CH₃)₂), substituted or unsubstituted C₁-C₅ linear or branched or C₃-C₈ cyclic alkoxy (e.g. methoxy, O-(CH₂)₂-pyrrolidine, ethoxy, propoxy, isopropoxy, O-CH₂-cyclopropyl,
- 25 O-cyclobutyl, O-cyclopentyl, O-cyclohexyl, 1-butoxy, 2-butoxy, O-tBu), optionally wherein at least one methylene group (CH₂) in the alkoxy is replaced with an oxygen atom (e.g., O-1-oxacyclobutyl, O-2-oxacyclobutyl), C₁-C₅ linear or branched thioalkoxy, C₁-C₅ linear or branched haloalkoxy (e.g., OCF₃, OCHF₂), C₁-C₅ linear or branched alkoxyalkyl, substituted or unsubstituted C₃-C₈ cycloalkyl (e.g., cyclopropyl, cyclopentyl, cyclohexyl), substituted or unsubstituted C₃-C₈ heterocyclic ring (e.g., morpholine, piperidine, piperazine, 3-methyl-4H-1,2,4-triazole, 5-methyl-1,2,4-oxadiazole, thiophene, oxazole, oxadiazole, imidazole, furane, triazole, tetrazole, pyridine (2, 3, or 4-pyridine), 3-methyl-2-pyridine, pyrimidine, pyrazine, pyridazine, oxacyclobutane (1 or 2-oxacyclobutane), indole, protonated
- 30

or deprotonated pyridine oxide), substituted or unsubstituted aryl (e.g., phenyl, xylyl, 2,6-difluorophenyl, 4-fluoroxyl), substituted or unsubstituted benzyl (e.g., benzyl, 4-Cl-benzyl, 4-OH-benzyl), or $\text{CH}(\text{CF}_3)(\text{NH-R}_{10})$;

or R_2 and R_1 are joint together to form a 5 or 6 membered substituted or unsubstituted, aliphatic or aromatic, carbocyclic or heterocyclic ring (e.g., pyrrol, [1,3]dioxole, furan-2(3H)-one, benzene, pyridine);

R_3 , R_4 and R_{40} are each independently H, F, Cl, Br, I, OH, SH, $\text{R}_8\text{-OH}$ (e.g., $\text{CH}_2\text{-OH}$), $\text{R}_8\text{-SH}$, $\text{-R}_8\text{-O-R}_{10}$, (e.g., $\text{CH}_2\text{-O-CH}_3$) CF_3 , CD_3 , OCD_3 , CN, NO_2 , $\text{-CH}_2\text{CN}$, $\text{-R}_8\text{CN}$, NH_2 , NHR , N(R)_2 , $\text{R}_8\text{-N(R}_{10})(\text{R}_{11})$ (e.g., $\text{CH}_2\text{-NH}_2$, $\text{CH}_2\text{-N(CH}_3)_2$) $\text{R}_9\text{-R}_8\text{-N(R}_{10})(\text{R}_{11})$, B(OH)_2 , -OC(O)CF_3 , $\text{-OCH}_2\text{Ph}$, -NHCO-R_{10} (e.g., NHC(O)CH_3), $\text{NHCO-N(R}_{10})(\text{R}_{11})$ (e.g., $\text{NHC(O)N(CH}_3)_2$), COOH , -C(O)Ph , C(O)O-R_{10} (e.g., C(O)O-CH_3 , $\text{C(O)O-CH}_2\text{CH}_3$), $\text{R}_8\text{-C(O)-R}_{10}$ (e.g., $\text{CH}_2\text{C(O)CH}_3$), C(O)H , C(O)-R_{10} (e.g., C(O)-CH_3 , $\text{C(O)-CH}_2\text{CH}_3$, $\text{C(O)-CH}_2\text{CH}_2\text{CH}_3$), $\text{C}_1\text{-C}_5$ linear or branched C(O)-haloalkyl (e.g., C(O)-CF_3), -C(O)NH_2 , C(O)NHR (e.g., $\text{C(O)NH(CH}_3)_2$), $\text{C(O)N(R}_{10})(\text{R}_{11})$ (e.g., $\text{C(O)N(CH}_3)_2$, $\text{C(O)N(CH}_3)(\text{CH}_2\text{CH}_3)$, $\text{C(O)N(CH}_3)(\text{CH}_2\text{CH}_2\text{-O-CH}_3)$, $\text{C(S)N(R}_{10})(\text{R}_{11})$ (e.g., $\text{C(S)NH(CH}_3)_2$), C(O)-pyrrolidine , C(O)-azetidine , $\text{C(O)-methylpiperazine}$, C(O)-piperidine , C(O)-morpholine , SO_2R , $\text{SO}_2\text{N(R}_{10})(\text{R}_{11})$ (e.g., $\text{SO}_2\text{NH(CH}_3)_2$, $\text{SO}_2\text{N(CH}_3)_2$), $\text{C}_1\text{-C}_5$ linear or branched, substituted or unsubstituted alkyl (e.g., methyl, $\text{C(OH)(CH}_3)(\text{Ph})$, ethyl, propyl, iso-propyl, t-Bu, iso-butyl, pentyl), substituted or unsubstituted $\text{C}_1\text{-C}_5$ linear or branched or $\text{C}_3\text{-C}_8$ cyclic haloalkyl (e.g., CF_3 , CF_2CH_3 , $\text{CF}_2\text{-cyclobutyl}$, $\text{CF}_2\text{-cyclopropyl}$, $\text{CF}_2\text{-methylcyclopropyl}$, CH_2CF_3 , $\text{CF}_2\text{CH}_2\text{CH}_3$, $\text{CH}_2\text{CH}_2\text{CF}_3$, $\text{CF}_2\text{CH(CH}_3)_2$, $\text{CF(CH}_3)_2\text{-CH(CH}_3)_2$, $\text{C(OH)}_2\text{CF}_3$, cyclopropyl- CF_3), $\text{C}_1\text{-C}_5$ linear, branched or cyclic alkoxy (e.g. methoxy, ethoxy, propoxy, isopropoxy, $\text{O-CH}_2\text{-cyclopropyl}$), $\text{C}_1\text{-C}_5$ linear or branched thioalkoxy, $\text{C}_1\text{-C}_5$ linear or branched haloalkoxy, $\text{C}_1\text{-C}_5$ linear or branched alkoxyalkyl, substituted or unsubstituted $\text{C}_3\text{-C}_8$ cycloalkyl (e.g., $\text{CF}_3\text{-cyclopropyl}$, cyclopropyl, cyclopentyl), substituted or unsubstituted $\text{C}_3\text{-C}_8$ heterocyclic ring (e.g., oxadiazole, pyrrol, *N*-methyloxetane-3-amine, 3-methyl-4H-1,2,4-triazole, 5-methyl-1,2,4-oxadiazole, thiophene, oxazole, isoxazole, imidazole, furane, triazole, methyl-triazole, pyridine (2, 3, or 4-pyridine), pyrimidine, pyrazine, oxacyclobutane (1 or 2-oxacyclobutane), indole), substituted or unsubstituted aryl (e.g., phenyl), $\text{CH}(\text{CF}_3)(\text{NH-R}_{10})$;

or R_3 and R_4 are joint together to form a 5 or 6 membered substituted or unsubstituted, aliphatic or aromatic, carbocyclic or heterocyclic ring (e.g., imidazole, [1,3]dioxole, furan-2(3H)-one, benzene, cyclopentane, imidazole);

R_5 is H, $\text{C}_1\text{-C}_5$ linear or branched, substituted or unsubstituted alkyl (e.g., methyl, CH_2SH , ethyl, iso-propyl), $\text{C}_2\text{-C}_5$ linear or branched, substituted or unsubstituted alkenyl, $\text{C}_2\text{-C}_5$ linear or branched, substituted or unsubstituted alkynyl (e.g., CCH), $\text{C}_1\text{-C}_5$ linear or branched haloalkyl (e.g., CF_3 , CF_2CH_3 , CH_2CF_3 , $\text{CF}_2\text{CH}_2\text{CH}_3$, $\text{CH}_2\text{CH}_2\text{CF}_3$, $\text{CF}_2\text{CH(CH}_3)_2$, $\text{CF(CH}_3)_2\text{-CH(CH}_3)_2$), $\text{R}_8\text{-aryl}$ (e.g., $\text{CH}_2\text{-Ph}$), $\text{C(=CH}_2\text{)-R}_{10}$ (e.g., $\text{C(=CH}_2\text{)-C(O)-OCH}_3$, $\text{C(=CH}_2\text{)-CN}$) substituted or unsubstituted aryl (e.g., phenyl), or substituted or unsubstituted heteroaryl (e.g., pyridine (2, 3, and 4-pyridine);

R_6 is H, $\text{C}_1\text{-C}_5$ linear or branched alkyl (e.g., methyl), C(O)R , or $\text{S(O)}_2\text{R}$;

R₆₀ is H, substituted or unsubstituted C₁-C₅ linear or branched alkyl (e.g., methyl, CH₂-OC(O)CH₃, CH₂-PO₄H₂, CH₂-PO₄H-tBu, CH₂-OP(O)(OCH₃)₂), C(O)R, or S(O)₂R;

R₈ is [CH₂]_p

wherein **p** is between 1 and 10;

5 **R₉** is [CH]_q, [C]_q

wherein **q** is between 2 and 10;

R₁₀ and **R₁₁** are each independently H, CN, C₁-C₅ linear or branched alkyl (e.g., methyl, ethyl), R₈-O-R₁₀ (e.g., CH₂CH₂-O-CH₃), C(O)R (e.g., C(O)(OCH₃)), or S(O)₂R;

10 or **R₁₀** and **R₁₁** are joined to form a substituted or unsubstituted C₃-C₈ heterocyclic ring (e.g., pyrrolidine, piperazine, methylpiperazine, azetidine, piperidine, morpholine),

15 wherein substitutions include: F, Cl, Br, I, OH, C₁-C₅ linear or branched alkyl (e.g. methyl, ethyl, propyl), C₁-C₅ linear or branched alkyl-OH (e.g., C(CH₃)₂CH₂-OH, CH₂CH₂-OH), C₂-C₅ linear or branched alkenyl (e.g., *E*- or *Z*-propylene), C₂-C₅ linear or branched, substituted or unsubstituted alkynyl (e.g., CH≡C-CH₃), alkoxy, ester (e.g., OC(O)-CH₃), N(R)₂, CF₃, aryl, phenyl, R₈-aryl (e.g., CH₂CH₂-Ph), heteroaryl (e.g., imidazole) C₃-C₈ cycloalkyl (e.g., cyclohexyl), C₃-C₈ heterocyclic ring (e.g., pyrrolidine), halophenyl, (benzyloxy)phenyl, alkyl-hydrogen-phosphate (e.g., tBu-PO₄H), dihydrogen-phosphate (i.e., OP(O)(OH)₂), dialkylphosphate (e.g., OP(O)(OCH₃)₂), CN and NO₂;

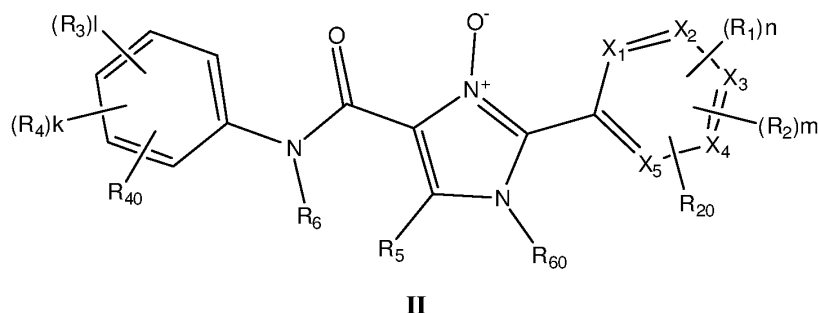
R is H, C₁-C₅ linear or branched alkyl (e.g., methyl, ethyl), C₁-C₅ linear or branched alkoxy (e.g., methoxy), phenyl, aryl or heteroaryl,

20 or two gem R substituents are joint together to form a 5 or 6 membered heterocyclic ring;

m, **n**, **l** and **k** are each independently an integer between 0 and 4 (e.g., 0, 1 or 2);

or its pharmaceutically acceptable salt, stereoisomer, tautomer, hydrate, *N*-oxide, reverse amide analog, prodrug, isotopic variant (e.g., deuterated analog), PROTAC, pharmaceutical product or any combination thereof.

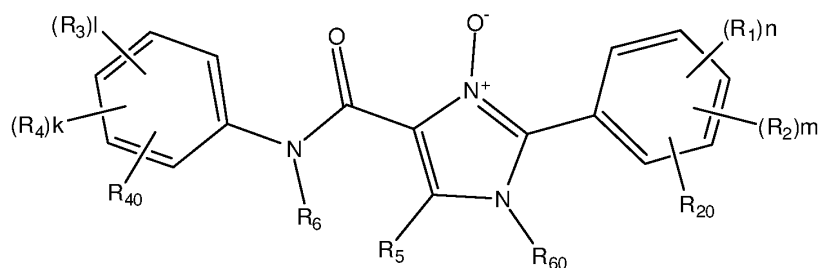
25 2. The compound of claim 1, represented by the structure of formula **II**:



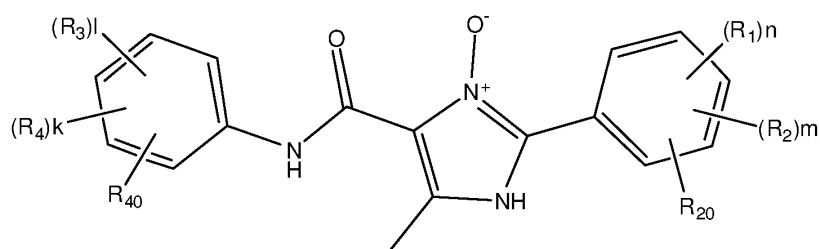
wherein

X₁, **X₂**, **X₃**, **X₄** and **X₅** are each independently C or N.

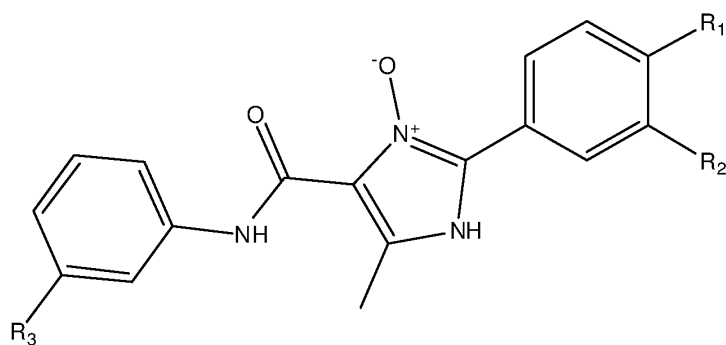
3. The compound of claim 1 or 2, represented by the structure of formula **III**:

**III.**

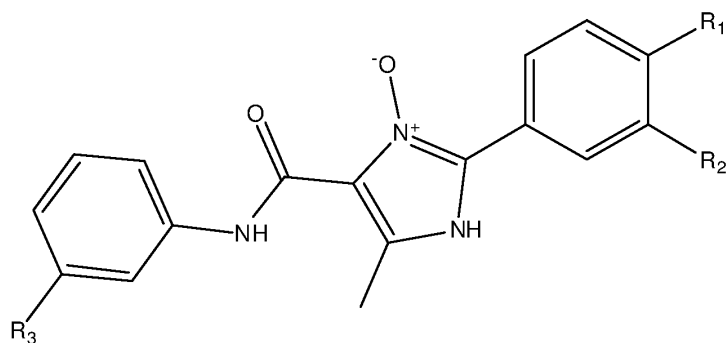
4. The compound of any one of the preceding claims, represented by the structure of formula **IV**:

**IV.**

5. The compound of any one of the preceding claims, represented by the structure of formula **VI**:

**VI.**

- 10 6. The compound of any one of the preceding claims, represented by the structure of formula **VII**:

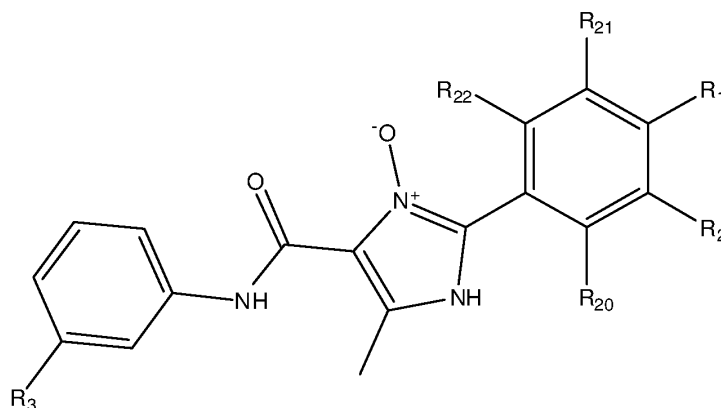
**VII**

wherein

R₃ is C(O)NH₂, C(O)NHR (e.g., C(O)NH(CH₃)), C(O)N(R₁₀)(R₁₁) (e.g., C(O)N(CH₃)₂, C(O)N(CH₃)(CH₂CH₃), C(O)N(CH₃)(CH₂CH₂-O-CH₃), C(S)N(R₁₀)(R₁₁) (e.g., C(S)NH(CH₃)), C(O)-pyrrolidine, C(O)-azetidine, C(O)-methylpiperazine, C(O)-piperidine, C(O)-morpholine, SO₂N(R₁₀)(R₁₁) (e.g., SO₂NH(CH₃), SO₂N(CH₃)₂), or substituted or unsubstituted C₁-C₅ linear or

5 branched or C₃-C₈ cyclic haloalkyl (e.g., CF₃, CF₂CH₃, CF₂-cyclobutyl, CF₂-cyclopropyl, CF₂-methylcyclopropyl, CH₂CF₃, CF₂CH₂CH₃, CH₂CH₂CF₃, CF₂CH(CH₃)₂, CF(CH₃)-CH(CH₃)₂, C(OH)₂CF₃, cyclopropyl-CF₃).

7. The compound of any one of claims 1 to 4, represented by the structure of formula **VIII**:



VIII

10

wherein

R₂₁ and **R₂₂** are each independently H, F, Cl, Br, I, OH, SH, R₈-OH (e.g., CH₂-OH), R₈-SH, -R₈-O-R₁₀, (e.g., -CH₂-O-CH₃), R₈-(C₃-C₈ cycloalkyl) (e.g., cyclohexyl), R₈-(C₃-C₈ heterocyclic ring) (e.g., CH₂-morpholine, CH₂-imidazole, CH₂-indazole), CF₃, CD₃, OCD₃, CN, NO₂, -CH₂CN, -R₈CN, NH₂, NHR (e.g., NH-CH₃), N(R)₂ (e.g., N(CH₃)₂), R₈-N(R₁₀)(R₁₁) (e.g., CH₂-CH₂-N(CH₃)₂, CH₂-NH₂, CH₂-N(CH₃)₂), R₉-R₈-N(R₁₀)(R₁₁) (e.g., C≡C-CH₂-NH₂), B(OH)₂, -OC(O)CF₃, -OCH₂Ph, NHC(O)-R₁₀ (e.g., NHC(O)CH₃), NHCO-N(R₁₀)(R₁₁) (e.g., NHC(O)N(CH₃)₂), COOH, -C(O)Ph, C(O)O-R₁₀ (e.g., C(O)O-CH₃, C(O)O-CH(CH₃)₂, C(O)O-CH₂CH₃), R₈-C(O)-R₁₀ (e.g., CH₂C(O)CH₃), C(O)H, C(O)-R₁₀ (e.g., C(O)-CH₃, C(O)-CH₂CH₃, C(O)-CH₂CH₂CH₃), C₁-C₅ linear or branched C(O)-haloalkyl (e.g., C(O)-CF₃), -C(O)NH₂, C(O)NHR, C(O)N(R₁₀)(R₁₁) (e.g., C(O)N(CH₃)₂), SO₂R, SO₂N(R₁₀)(R₁₁) (e.g., SO₂N(CH₃)₂, SO₂NHC(O)CH₃), C₁-C₅ linear or branched, substituted or unsubstituted alkyl (e.g., C(H)(OH)-CH₃, methyl, 2, 3, or 4-CH₂-C₆H₄-Cl, ethyl, propyl, iso-propyl, butyl, t-Bu, iso-butyl, pentyl, benzyl), C₂-C₅ linear or branched, substituted or unsubstituted alkenyl (e.g., CH=C(Ph)₂), C₁-C₅ linear, branched or cyclic haloalkyl (e.g., CF₃, CF₂CH₃, CH₂CF₃, CF₂CH₂CH₃, CH₂CH₂CF₃, CF₂CH(CH₃)₂, CF(CH₃)-CH(CH₃)₂), substituted or unsubstituted C₁-C₅ linear or branched or C₃-C₈ cyclic alkoxy (e.g. methoxy, O-(CH₂)₂-pyrrolidine, ethoxy, propoxy, isopropoxy, O-CH₂-cyclopropyl, O-cyclobutyl, O-cyclopentyl, O-cyclohexyl, 1-butoxy, 2-butoxy, O-tBu), optionally wherein at least one methylene group (CH₂) in the alkoxy is replaced with an oxygen atom (e.g., O-1-oxacyclobutyl, O-2-oxacyclobutyl), C₁-C₅ linear or branched thioalkoxy, C₁-C₅ linear or branched haloalkoxy (e.g., OCF₃,

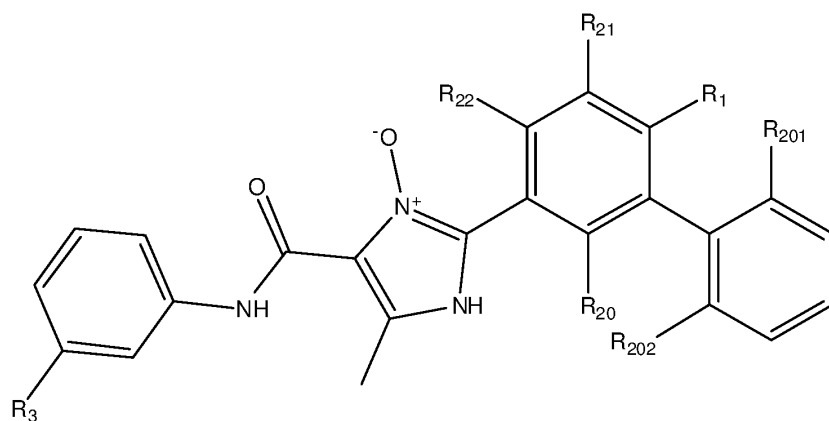
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OCHF₂), C₁-C₅ linear or branched alkoxyalkyl, substituted or unsubstituted C₃-C₈ cycloalkyl (e.g., cyclopropyl, cyclopentyl, cyclohexyl), substituted or unsubstituted C₃-C₈ heterocyclic ring (e.g., morpholine, piperidine, piperazine, 3-methyl-4H-1,2,4-triazole, 5-methyl-1,2,4-oxadiazole, thiophene, oxazole, oxadiazole, imidazole, furane, triazole, tetrazole, pyridine (2, 3, or 4-pyridine), 3-methyl-2-pyridine, pyrimidine, pyrazine, pyridazine, oxacyclobutane (1 or 2-oxacyclobutane), indole, protonated or deprotonated pyridine oxide), substituted or unsubstituted aryl (e.g., phenyl, xylyl, 2,6-difluorophenyl, 4-fluorophenyl), substituted or unsubstituted benzyl (e.g., benzyl, 4-Cl-benzyl, 4-OH-benzyl), or CH(CF₃)(NH-R₁₀).

8. The compound of any one of claims 1-4 and 7, represented by the structure of formula **IX**:



IX

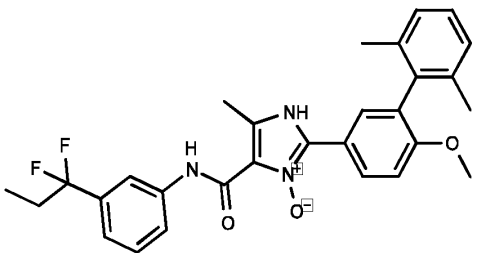
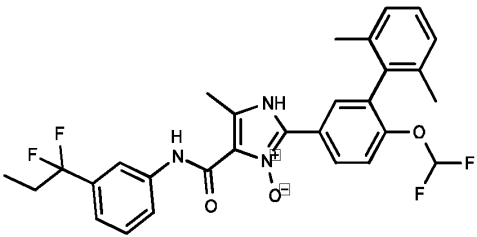
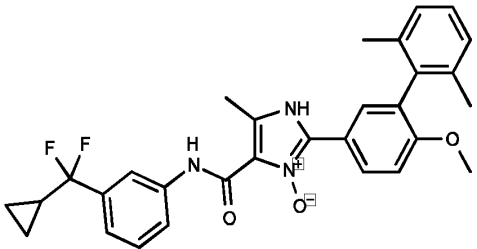
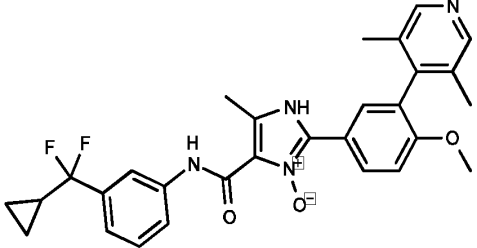
wherein

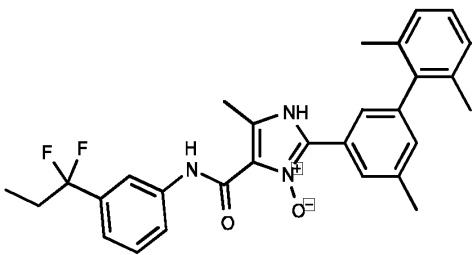
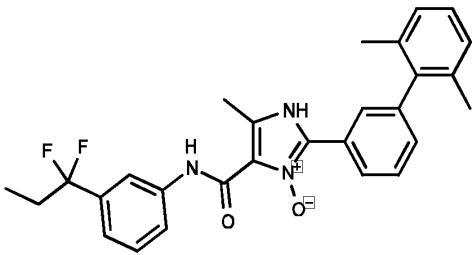
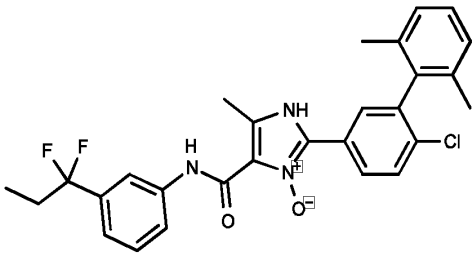
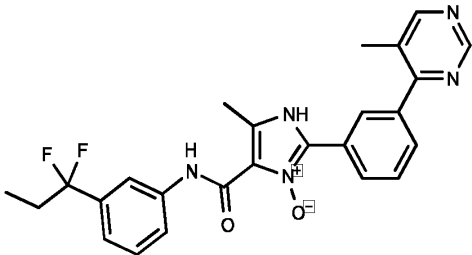
R₁, R₂₀, R₂₁ and R₂₂ are each independently H, F, Cl, Br, I, OH, SH, R₈-OH (e.g., CH₂-OH), R₈-SH, -R₈-O-R₁₀, (e.g., -CH₂-O-CH₃), R₈-(C₃-C₈ cycloalkyl) (e.g., cyclohexyl), R₈-(C₃-C₈ heterocyclic ring) (e.g., CH₂-morpholine, CH₂-imidazole, CH₂-indazole), CF₃, CD₃, OCD₃, CN, NO₂, -CH₂CN, -R₈CN, NH₂, NHR (e.g., NH-CH₃), N(R)₂ (e.g., N(CH₃)₂), R₈-N(R₁₀)(R₁₁) (e.g., CH₂-CH₂-N(CH₃)₂, CH₂-NH₂, CH₂-N(CH₃)₂), R₉-R₈-N(R₁₀)(R₁₁) (e.g., C≡C-CH₂-NH₂), B(OH)₂, -OC(O)CF₃, -OCH₂Ph, NHC(O)-R₁₀ (e.g., NHC(O)CH₃), NHCO-N(R₁₀)(R₁₁) (e.g., NHC(O)N(CH₃)₂), COOH, -C(O)Ph, C(O)O-R₁₀ (e.g., C(O)O-CH₃, C(O)O-CH(CH₃)₂, C(O)O-CH₂CH₃), R₈-C(O)-R₁₀ (e.g., CH₂C(O)CH₃), C(O)H, C(O)-R₁₀ (e.g., C(O)-CH₃, C(O)-CH₂CH₃, C(O)-CH₂CH₂CH₃), C₁-C₅ linear or branched C(O)-haloalkyl (e.g., C(O)-CF₃), -C(O)NH₂, C(O)NHR, C(O)N(R₁₀)(R₁₁) (e.g., C(O)N(CH₃)₂), SO₂R, SO₂N(R₁₀)(R₁₁) (e.g., SO₂N(CH₃)₂, SO₂NHC(O)CH₃), C₁-C₅ linear or branched, substituted or unsubstituted alkyl (e.g., C(H)(OH)-CH₃, methyl, 2, 3, or 4-CH₂-C₆H₄-Cl, ethyl, propyl, iso-propyl, butyl, t-Bu, iso-butyl, pentyl, benzyl), C₂-C₅ linear or branched, substituted or unsubstituted alkenyl (e.g., CH=C(Ph)₂), C₁-C₅ linear, branched or cyclic haloalkyl (e.g., CF₃, CF₂CH₃, CH₂CF₃, CF₂CH₂CH₃, CH₂CH₂CF₃, CF₂CH(CH₃)₂, CF(CH₃)-CH(CH₃)₂), substituted or unsubstituted C₁-C₅ linear or branched or C₃-C₈ cyclic alkoxy (e.g. methoxy, O-(CH₂)₂-pyrrolidine, ethoxy, propoxy, isopropoxy, O-CH₂-cyclopropyl, O-cyclobutyl, O-cyclopentyl, O-cyclohexyl, 1-butoxy, 2-butoxy, O-tBu), optionally wherein at least one methylene group (CH₂) in the alkoxy is replaced with an oxygen atom (e.g., O-1-

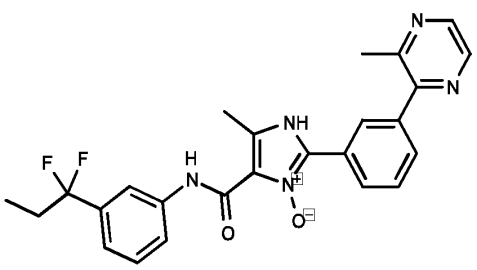
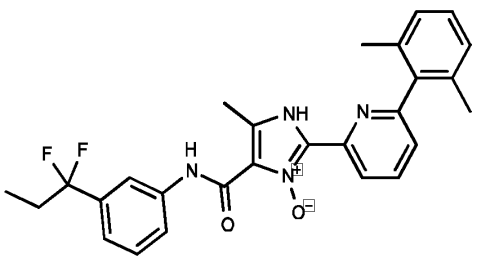
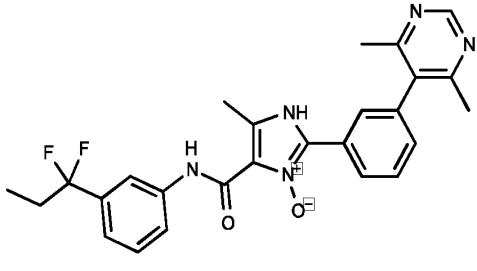
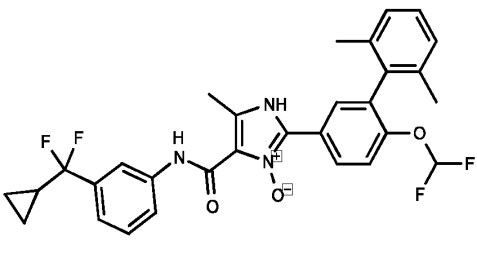
- oxacyclobutyl, O-2-oxacyclobutyl), C₁-C₅ linear or branched thioalkoxy, C₁-C₅ linear or branched haloalkoxy (e.g., OCF₃, OCHF₂), C₁-C₅ linear or branched alkoxyalkyl, substituted or unsubstituted C₃-C₈ cycloalkyl (e.g., cyclopropyl, cyclopentyl, cyclohexyl), substituted or unsubstituted C₃-C₈ heterocyclic ring (e.g., morpholine, piperidine, piperazine, 3-methyl-4H-1,2,4-triazole, 5-methyl-1,2,4-oxadiazole, thiophene, oxazole, oxadiazole, imidazole, furane, triazole, tetrazole, pyridine (2, 3, or 4-pyridine), 3-methyl-2-pyridine, pyrimidine, pyrazine, pyridazine, oxacyclobutane (1 or 2-oxacyclobutane), indole, protonated or deprotonated pyridine oxide), substituted or unsubstituted aryl (e.g., phenyl, xylyl, 2,6-difluorophenyl, 4-fluoroxyl), substituted or unsubstituted benzyl (e.g., benzyl, 4-Cl-benzyl, 4-OH-benzyl), CH(CF₃)(NH-R₁₀);
- 10 or **R**₂₁ and **R**₁ are joint together to form a 5 or 6 membered substituted or unsubstituted, aliphatic or aromatic, carbocyclic or heterocyclic ring (e.g., pyrrol, [1,3]dioxole, furan-2(3H)-one, benzene, pyridine);
- or **R**₂₁ and **R**₂₂ are joint together to form a 5 or 6 membered substituted or unsubstituted, aliphatic or aromatic, carbocyclic or heterocyclic ring (e.g., pyrrol, [1,3]dioxole, furan-2(3H)-one, benzene, pyridine); and
- 15 **R**₂₀₁ and **R**₂₀₂ are each independently H, F, Cl, Br, I, CF₃, or C₁-C₅ linear or branched, substituted or unsubstituted alkyl (e.g., methyl).

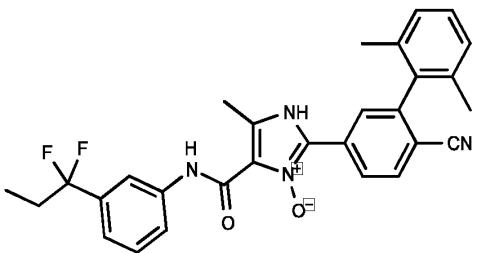
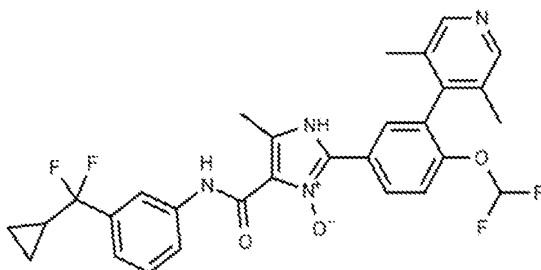
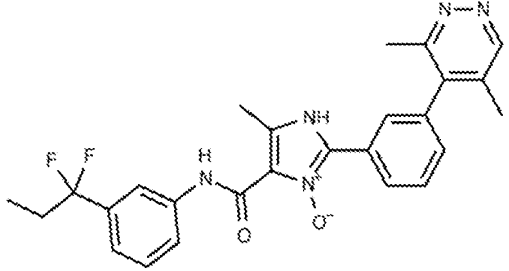
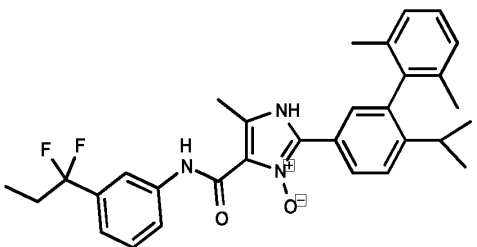
9. The compound of any one of the preceding claims, selected from the following:

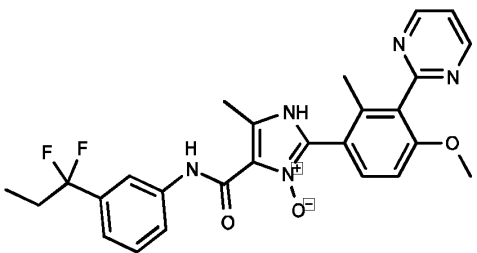
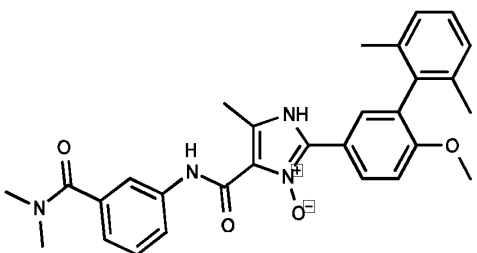
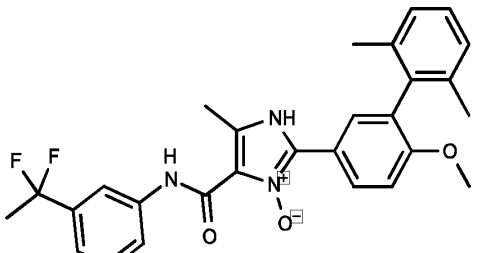
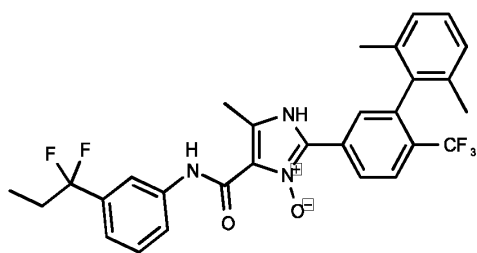
Compound Number	Compound Structure
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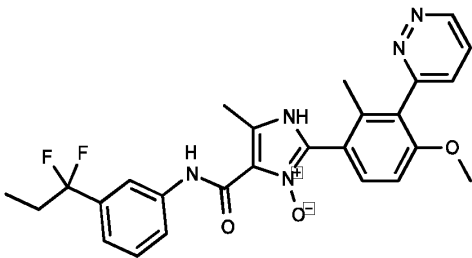
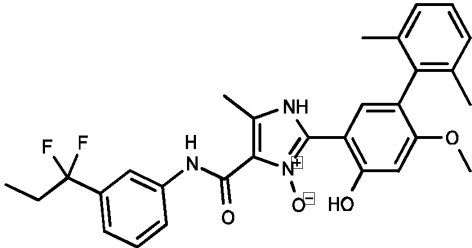
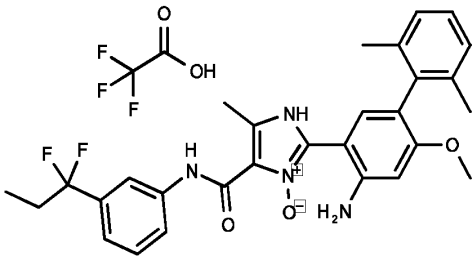
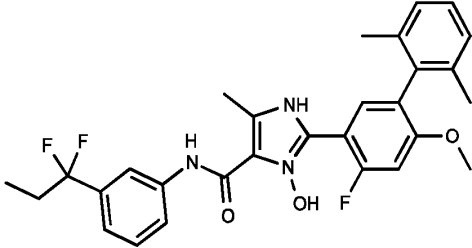
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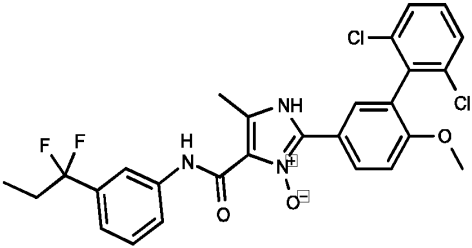
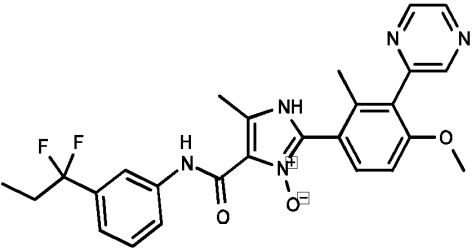
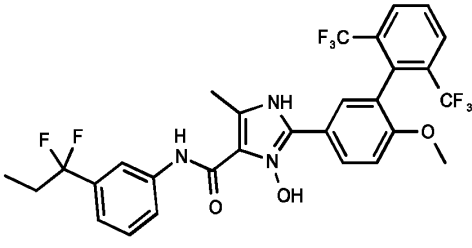
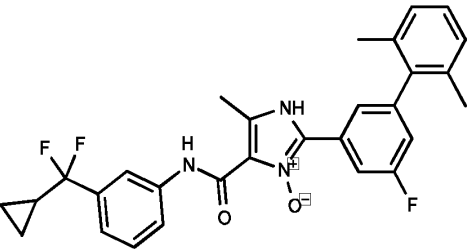
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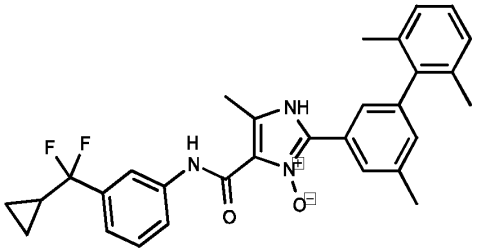
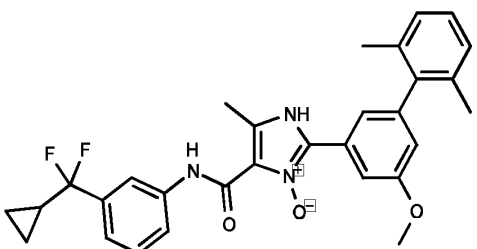
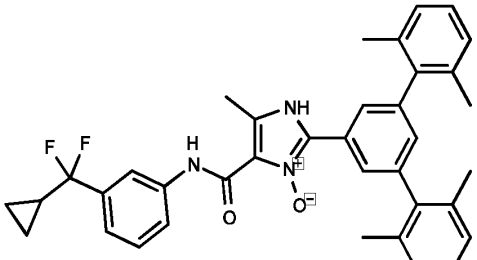
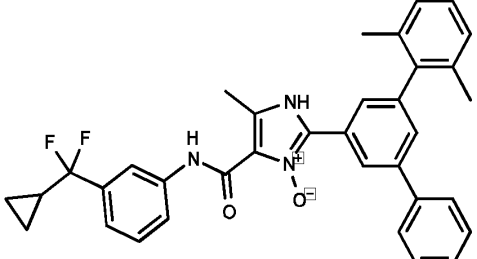
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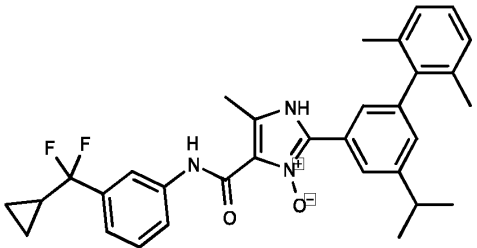
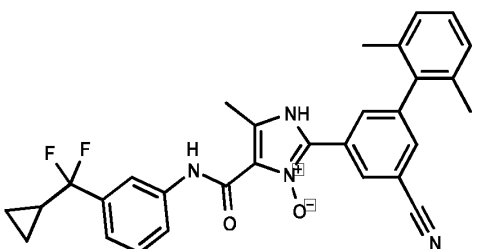
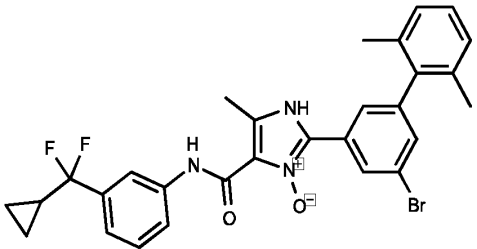
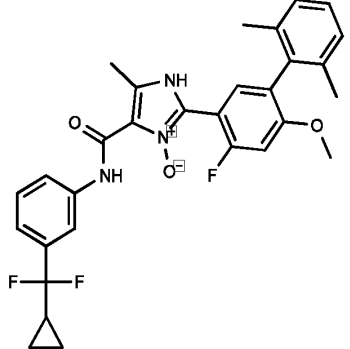
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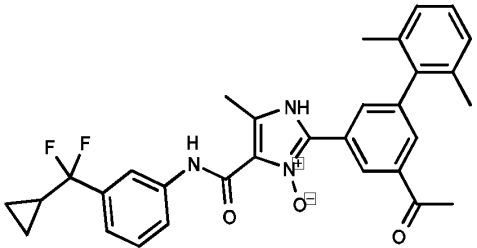
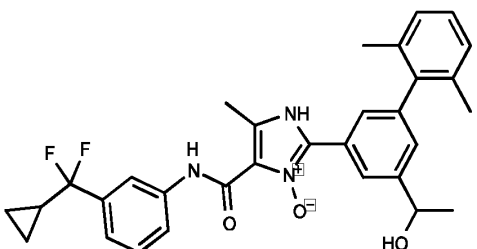
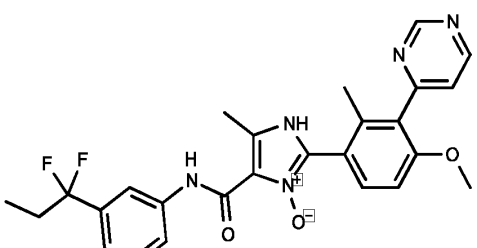
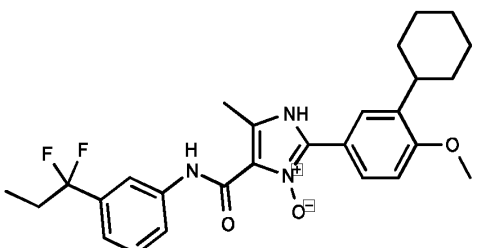
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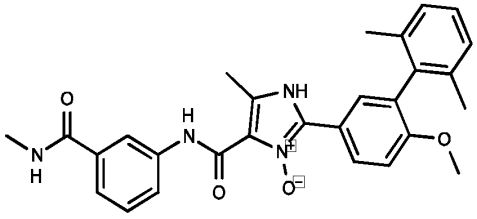
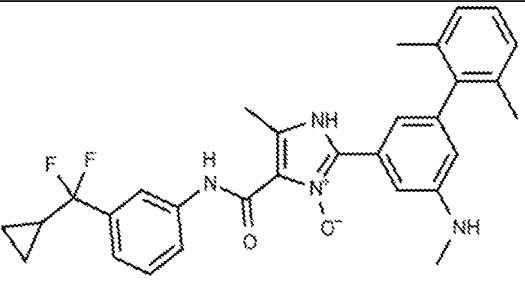
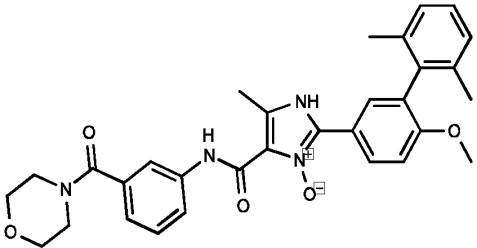
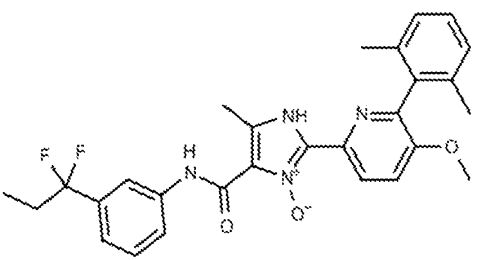
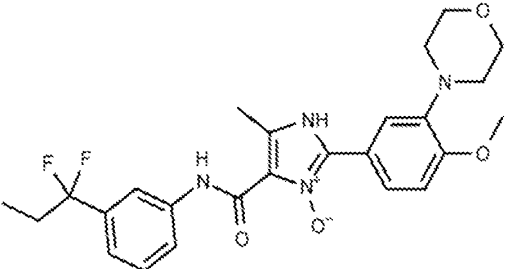
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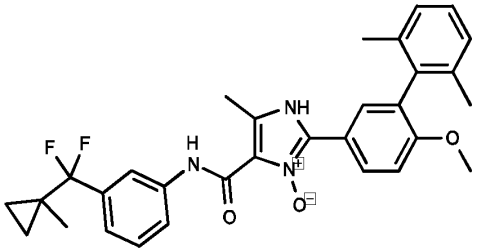
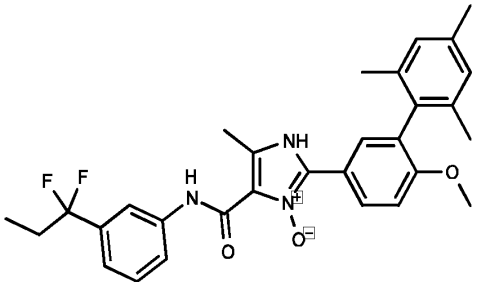
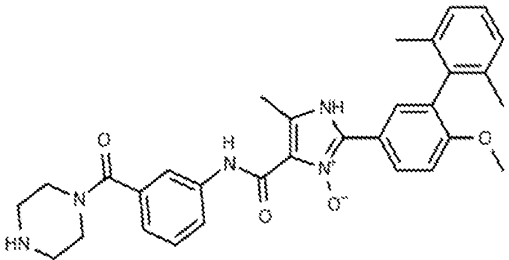
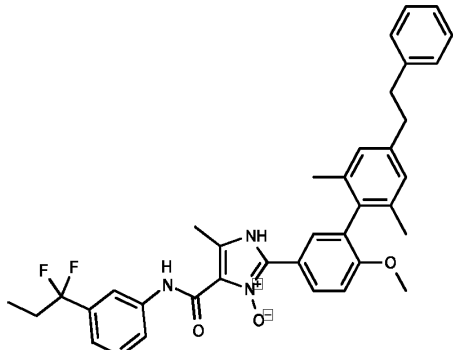
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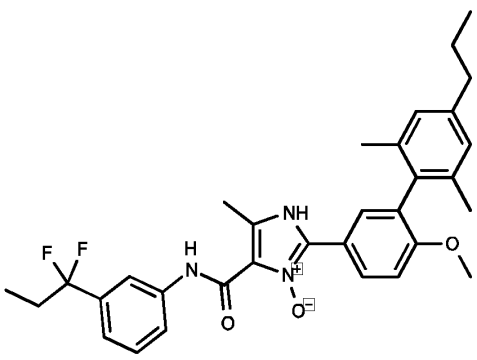
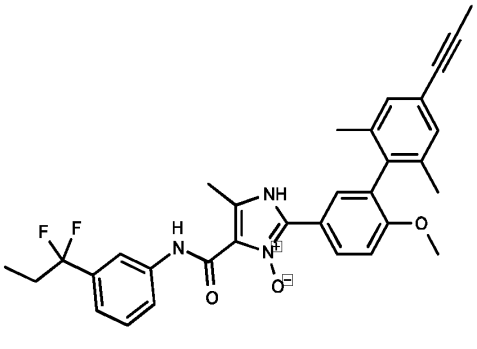
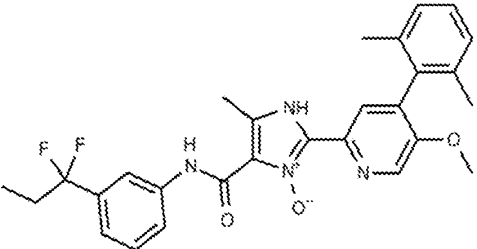
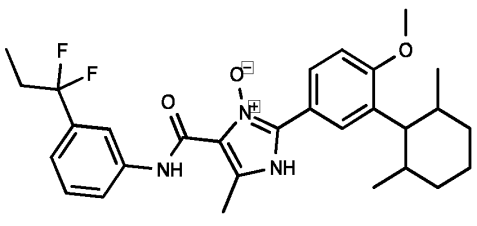
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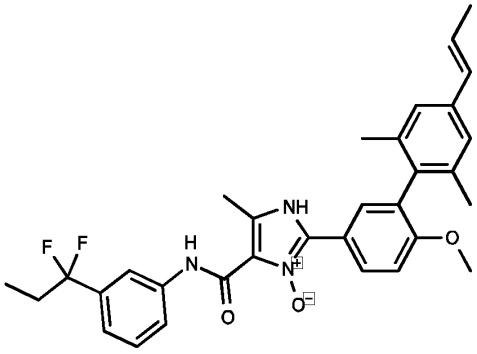
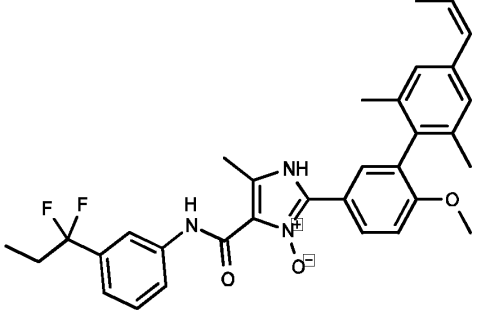
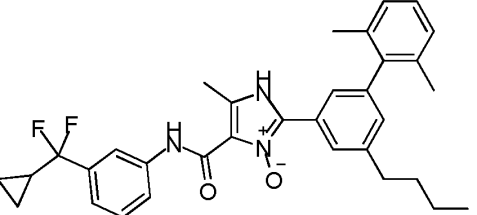
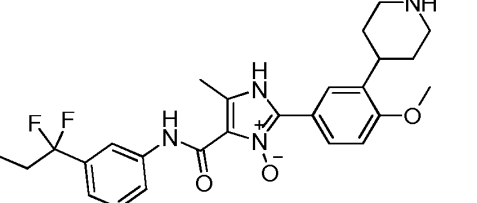
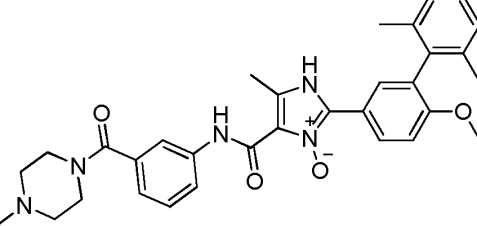
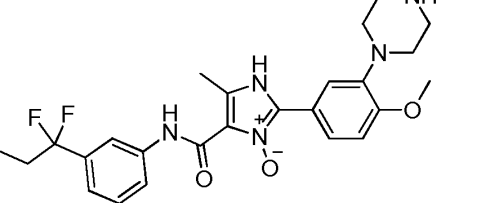
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139	 <chem>CC1=CN(C(=O)Nc2ccc(cc2)C(=O)N3CCCCC3)c4cc(OC)c(C)c4</chem>
140	 <chem>CCN(C)C(=O)c1ccc(cc1)C(=O)Nc2cc(C)c([N-]([O-])=Nc3cc(OC)c(C)c3)c2</chem> <chem>OC(=O)O</chem>
141	 <chem>COCN(C)C(=O)c1ccc(cc1)C(=O)Nc2cc(C)c([N-]([O-])=Nc3cc(OC)c(C)c3)c2</chem> <chem>OC(=O)O</chem>

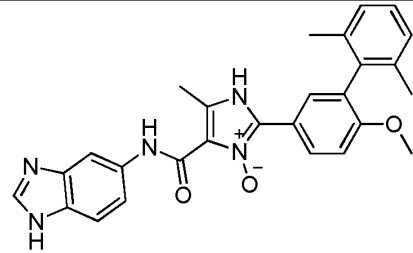
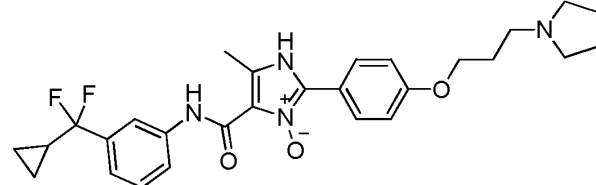
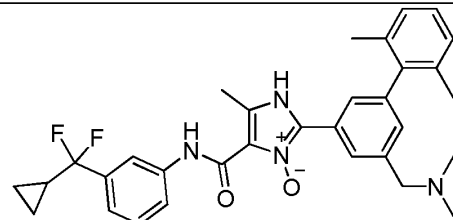
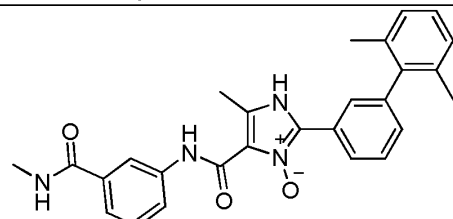
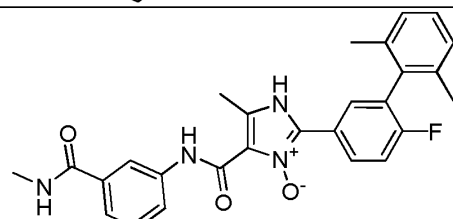
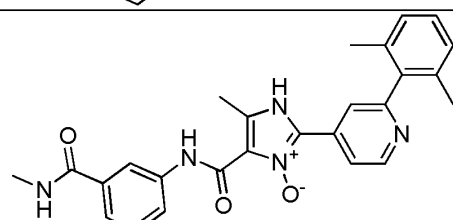
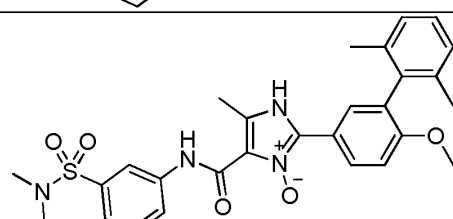
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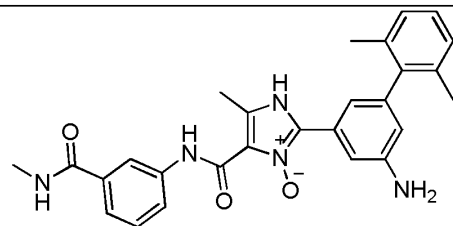
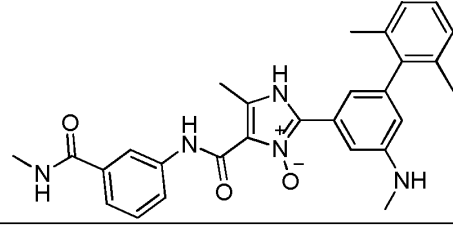
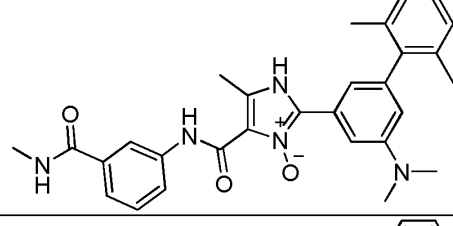
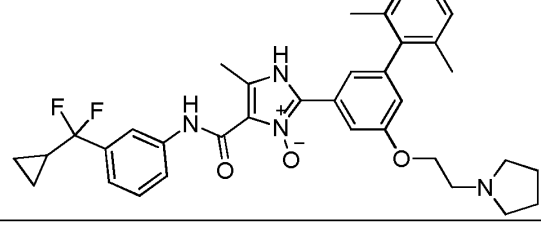
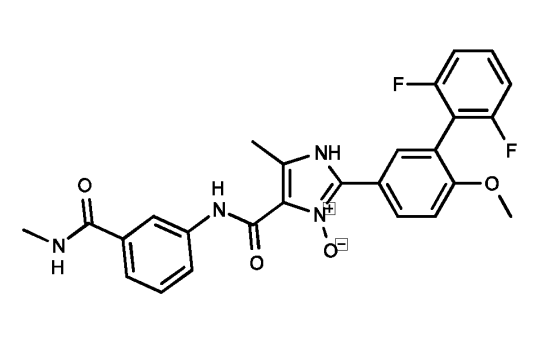
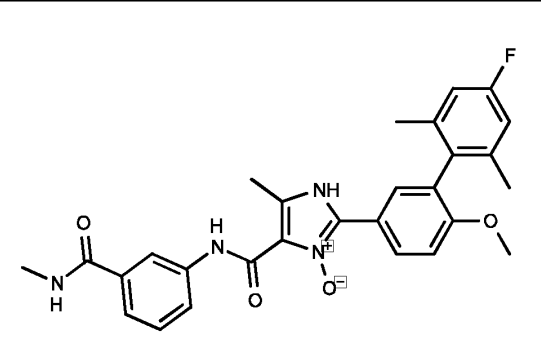
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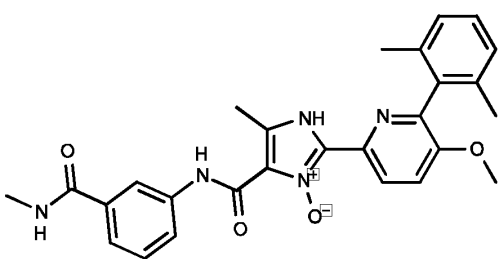
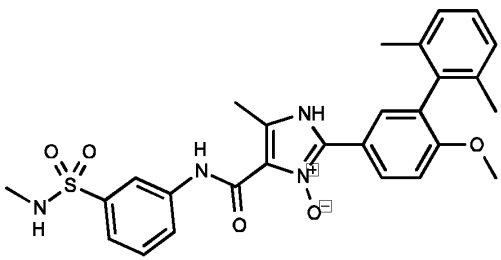
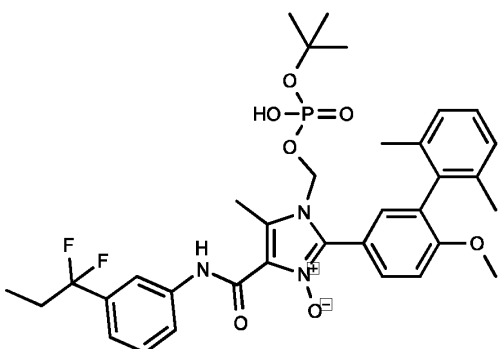
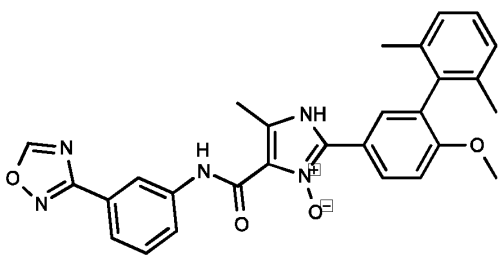
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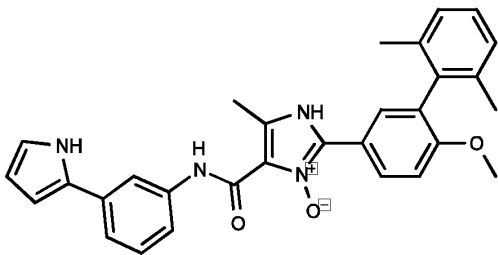
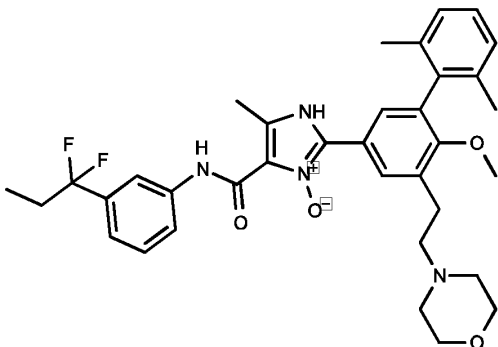
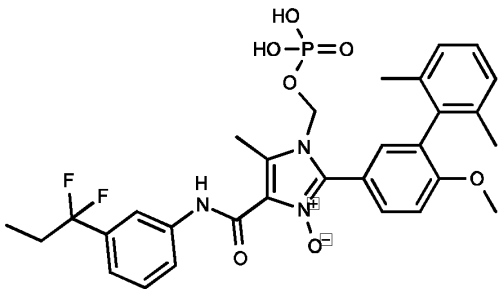
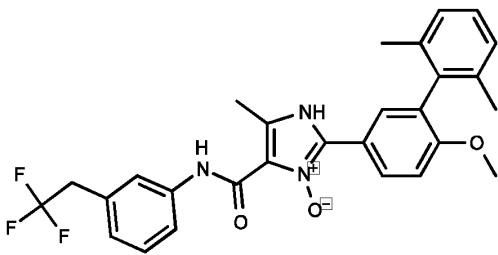
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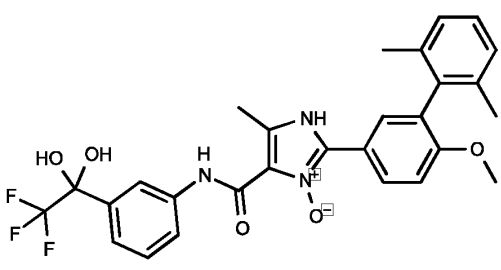
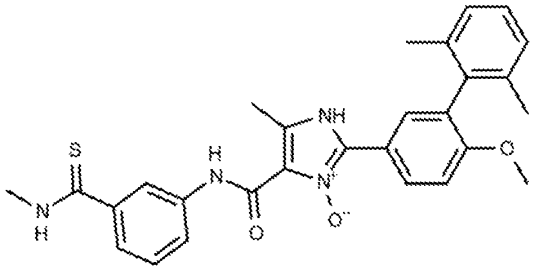
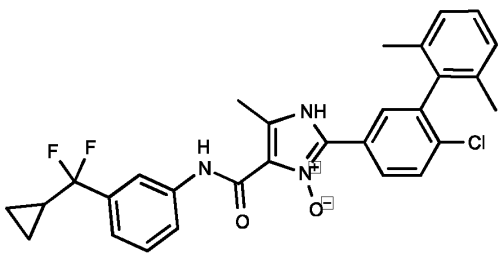
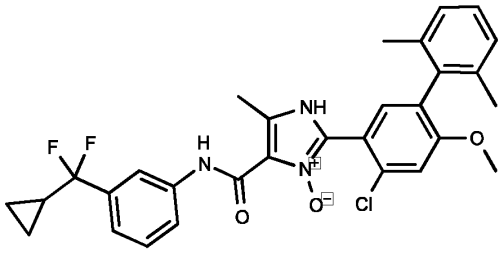
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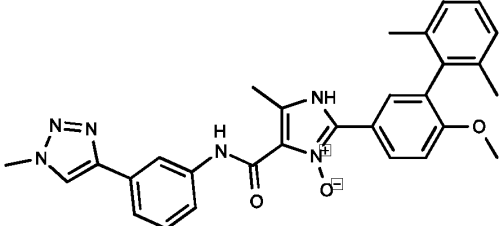
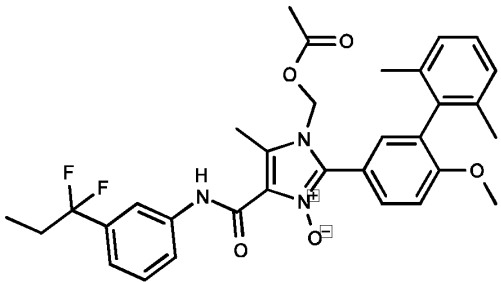
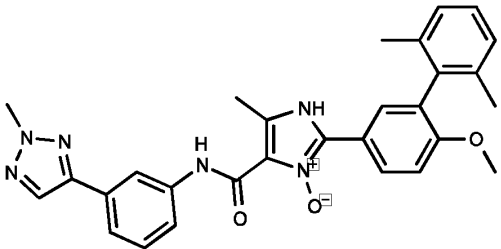
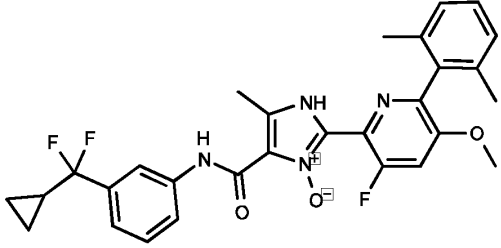
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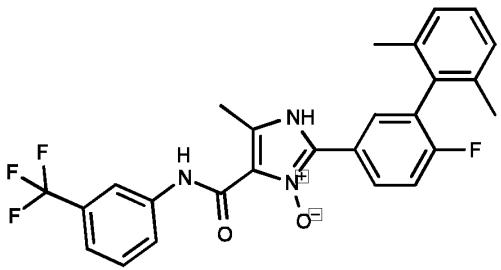
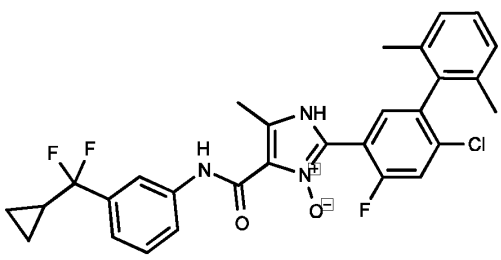
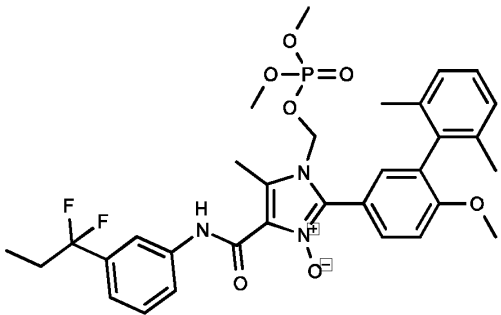
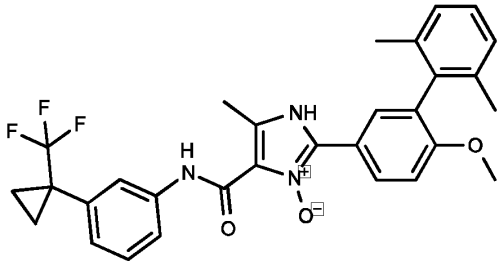
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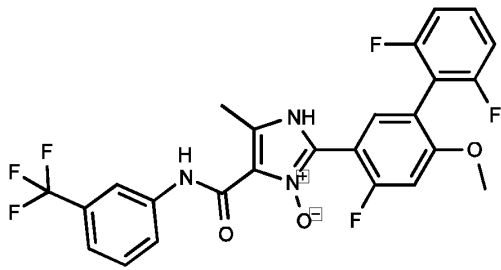
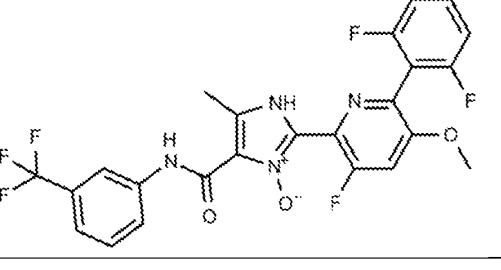
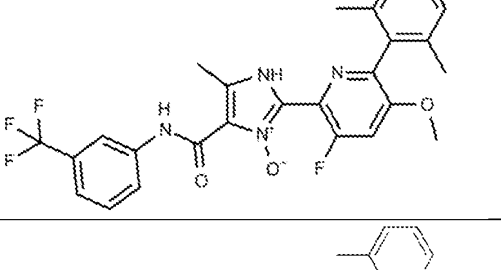
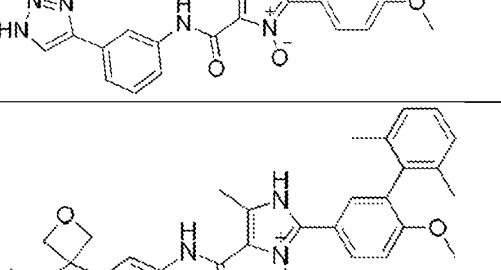
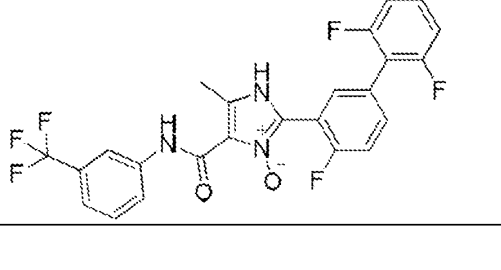
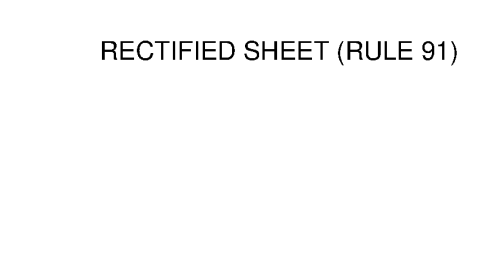
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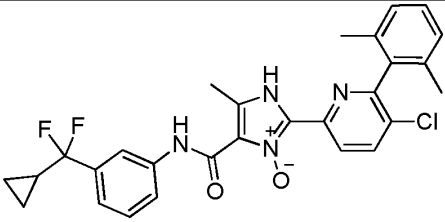
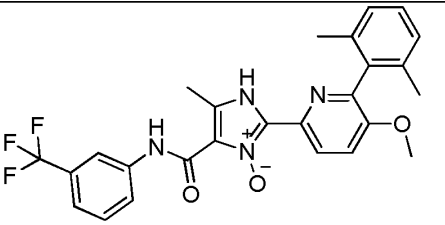
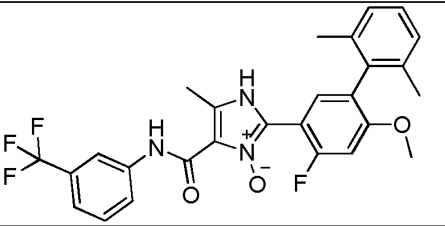
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or its pharmaceutically acceptable salt, stereoisomer, tautomer, hydrate, *N*-oxide, reverse amide analog, prodrug, isotopic variant (e.g., deuterated analog), PROTAC, pharmaceutical product or any combination thereof.

10. A pharmaceutical composition comprising a compound according to any one of claims 1 to 9 and a pharmaceutically acceptable carrier.
11. A compound according to any one of claims 1 to 9, for use in treating, suppressing, reducing the severity, reducing the risk of developing or inhibiting cancer in a subject.
12. The compound of claim 11, wherein the cancer is selected from the list of: hepatocellular carcinoma, melanoma (e.g., BRAF mutant melanoma), glioblastoma, breast cancer (e.g., invasive ductal carcinomas of the breast, triple-negative breast cancer), prostate cancer, liver cancer, brain cancer,

ovarian cancer, lung cancer, Lewis lung carcinoma (LLC), colon carcinoma, pancreatic cancer, renal cell carcinoma and mammary carcinoma.

13. The compound of claim 11 or 12, wherein the cancer is early cancer, advanced cancer, invasive cancer, metastatic cancer, drug resistant cancer or any combination thereof.
- 5 14. The compound of any one of claims 11 to 13, wherein the subject has been previously treated with chemotherapy, immunotherapy, radiotherapy, biological therapy, surgical intervention, or any combination thereof.
15. The compound of any one of claims 11 to 14, wherein the compound is administered in combination with an anti-cancer therapy.
- 10 16. The compound of claim 15, wherein the anti-cancer therapy is chemotherapy, immunotherapy, radiotherapy, biological therapy, surgical intervention, or any combination thereof.
17. A compound according to any one of claims 1 to 9, for use in suppressing, reducing or inhibiting tumour growth in a subject suffering from cancer.
18. The compound of claim 17, wherein the tumor growth is enhanced by increased acetate uptake by
15 cancer cells of said cancer.
19. The compound of claim 18, wherein the increased acetate uptake is mediated by ACSS2.
20. The compound of claim 18 or 19, wherein the cancer cells are under hypoxic stress.
21. The compound of claim 17, wherein the tumor growth is suppressed due to suppression of lipid (e.g., fatty acid) synthesis and/or regulating histones acetylation and function induced by ACSS2 mediated
20 acetate metabolism to acetyl-CoA.
22. A method of suppressing, reducing or inhibiting lipid synthesis and/or regulating histones acetylation and function in a cell, comprising contacting a compound according to any one of claims 1 to 9, with a cell under conditions effective to suppress, reduce or inhibit lipid synthesis and/or regulating histones acetylation and function in said cell.
- 25 23. The method of claim 22, wherein the cell is a cancer cell.
24. A method of binding an ACSS2 inhibitor compound to an ACSS2 enzyme, comprising the step of contacting an ACSS2 enzyme with an ACSS2 inhibitor compound according to any one of claims 1 to 9, in an amount effective to bind the ACSS2 inhibitor compound to the ACSS2 enzyme.
25. A method of suppressing, reducing or inhibiting acetyl-CoA synthesis from acetate in a cell, comprising
30 contacting a compound according to any one of claims 1 to 9 with a cell, under conditions effective to suppress, reduce or inhibit acetyl-CoA synthesis from acetate in said cell.
26. The method of claim 25, wherein the cell is a cancer cell.
27. The method of claim 25 or 26, wherein the synthesis is mediated by ACSS2.
28. A method of suppressing, reducing or inhibiting acetate metabolism in a cancer cell, comprising
35 contacting a compound according to any one of claims 1 to 9 with a cancer cell, under conditions effective to suppress, reduce or inhibit acetate metabolism in said cells.
29. The method of claim 28, wherein the acetate metabolism is mediated by ACSS2.
30. The method of claim 28 or 29, wherein the cancer cell is under hypoxic stress.

31. A compound according to any one of claims 1 to 9, for use in treating, suppressing, reducing the severity, reducing the risk of developing or inhibiting human alcoholism in a subject.
32. A compound according to any one of claims 1 to 9, for use in treating, suppressing, reducing the severity, reducing the risk of developing or inhibiting a viral infection in a subject.
- 5 33. The compound of claim 32, wherein the viral infection is human cytomegalovirus (HCMV) infection.
34. A compound according to any one of claims 1 to 9, for use in treating, suppressing, reducing the severity, reducing the risk of developing or inhibiting alcoholic steatohepatitis (ASH) in a subject.
35. A compound according to any one of claims 1 to 9, for use in treating, suppressing, reducing the severity, reducing the risk of developing or inhibiting non alcoholic fatty liver disease (NAFLD) in a
10 subject.
36. A compound according to any one of claims 1 to 9, for use in treating, suppressing, reducing the severity, reducing the risk of developing or inhibiting non-alcoholic steatohepatitis (NASH) in a subject.
37. A compound according to any one of claims 1 to 9, for use in treating, suppressing, reducing the
15 severity, reducing the risk of developing or inhibiting a metabolic disorder in a subject.
38. The compound of claim 37, wherein the metabolic disorder is selected from: obesity, weight gain, hepatic steatosis and fatty liver disease.
39. A compound according to any one of claims 1 to 9, for use in treating, suppressing, reducing the severity, reducing the risk of developing or inhibiting a neuropsychiatric disease or disorder in a subject.
- 20 40. The compound of claim 39, wherein the neuropsychiatric disease or disorder is selected from: anxiety, depression, schizophrenia, autism and post-traumatic stress disorder.
41. A compound according to any one of claims 1 to 9, for use in treating, suppressing, reducing the severity, reducing the risk of developing or inhibiting inflammatory condition in a subject.
42. A compound according to any one of claims 1 to 9, for use in treating, suppressing, reducing the
25 severity, reducing the risk of developing or inhibiting an autoimmune disease or disorder in a subject.