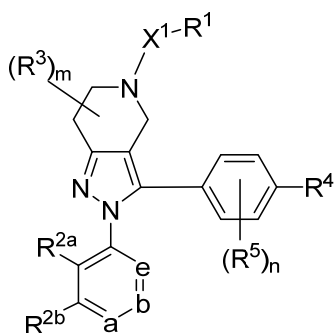


Table 1: Structure, Characterization Data of Specific Embodiments

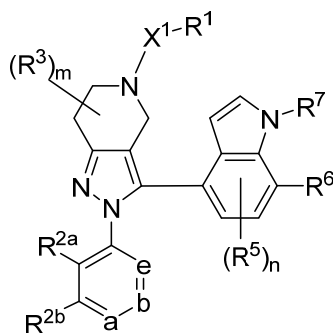
Example No.	Structure	MS: (ES) m/z [M + H] ⁺	R _t (min)
1		783.2	2.37 (Method A)
2		748.2	2.67 (method A)
3		645.4	3.45 (Method A)
4		719.2	2.50 (Method A)
5		737.2	3.07 (Method A)

CLAIMS

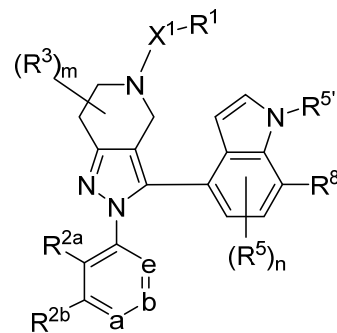
1 1. A compound of any one of Formulae (IA), (IB), (IC), (IIA), (IIB) or
2 (IIC):



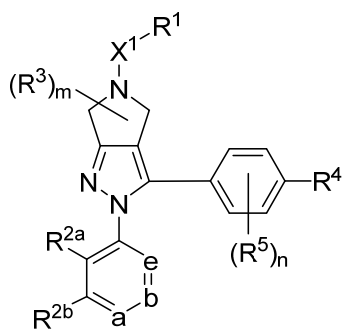
IA



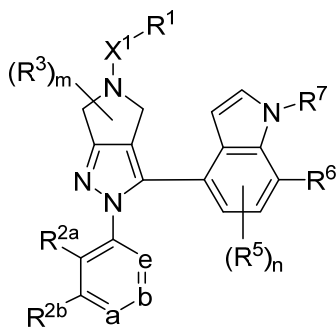
IB



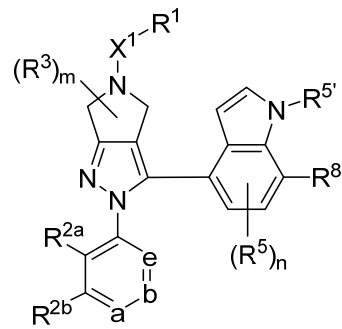
IC



IIA



IIB



IIC

or a pharmaceutically acceptable salt thereof, wherein,

ring vertex a is N or C(R^{2c}), ring vertex b is N or C(R^{2d}), and ring vertex e is N or C(R^{2e}),

wherein no more than one of a, b and e is N;

X¹ is selected from the group consisting of a bond, C₁₋₈ alkylene, C(O), C(O)-C₁₋₄ alkylene,
and S(O)₂;

R¹ is selected from the group consisting of

a) 5- to 10-membered heteroaryl having from 1 to 4 heteroatoms as ring vertices selected
from N, O and S;

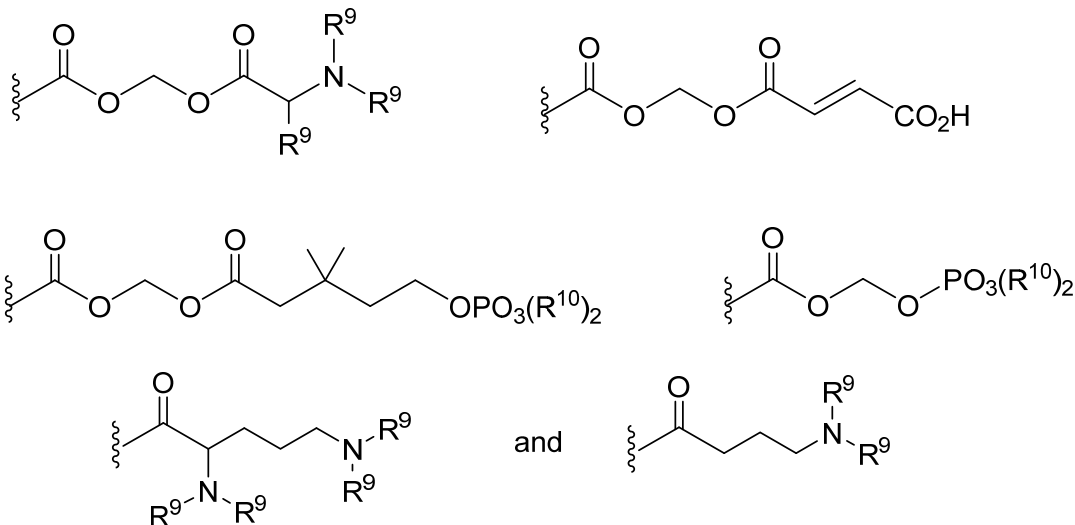
b) C₆₋₁₀ aryl;

c) C₃₋₈ cycloalkyl;

d) 4- to 8-membered heterocycloalkyl having from 1 to 2 heteroatoms as ring vertices
 selected from N, O and S; and
 e) C₁₋₈ alkyl, C₁₋₈ alkoxy, C₁₋₈ haloalkyl, -C(O)NR^{1a}R^{1b}, and -CO₂R^{1a}; wherein R^{1a} and
 R^{1b} are each independently selected from the group consisting of hydrogen, C₁₋₈
 alkyl, C₆₋₁₀ aryl, and -C₁₋₆ alkylene-C₆₋₁₀ aryl;
 wherein the group -X¹-R¹ is unsubstituted or substituted with 1 to 5 R^x substituents;
 R^{2a} and R^{2c} are each independently selected from the group consisting of hydrogen, C₁₋₆
 alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, -O-C₁₋₆ haloalkyl, -S-C₁₋₆ alkyl, -C₁₋₆ alkyl-O-C₁₋₆
 alkyl, -C₁₋₆ alkyl-S-C₁₋₆ alkyl, CN, and halogen, and at least one of R^{2a} and R^{2c} is
 other than hydrogen;
 R^{2b}, R^{2c}, and R^{2d} are each independently selected from the group consisting of hydrogen, C₁₋₆
 alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, -O-C₁₋₆ haloalkyl, -S-C₁₋₆ alkyl, -C₁₋₆ alkyl-O-C₁₋₆
 alkyl, -C₁₋₆ alkyl-S-C₁₋₆ alkyl, cyano, and halogen;
 each R³ is independently selected from the group consisting of hydroxyl, C₁₋₄ alkyl, C₁₋₄
 haloalkyl and C₁₋₄ hydroxyalkyl, and optionally two R³ groups on the same carbon
 atom are combined to form oxo (=O), and optionally two R³ groups and the carbon
 atoms they are attached to form a 3-6 membered ring with 0-2 heteroatoms as ring
 members selected from O, N, and S;
 R⁴ is a member selected from the group consisting of: -NHP¹, -NHC(O)NHP¹, -CH₂NHP¹
 and -CH₂NHC(O)NHP¹;
 each R⁵ is independently selected from the group consisting of C₁₋₈ alkyl, C₁₋₈ alkoxy, C₁₋₈
 haloalkyl, C₁₋₈ haloalkoxy, C₁₋₈ hydroxyalkyl, halogen, OH, CN, C(O)R^{5a} and
 CO₂R^{5a};
 R^{5'} is a member selected from the group consisting of hydrogen, C₁₋₈ alkyl, C₁₋₈ haloalkyl, C₁₋₈
 hydroxyalkyl, C(O)R^{5a} and CO₂R^{5a}; wherein each R^{5a} is independently selected
 from the group consisting of hydrogen, C₁₋₄ alkyl, and C₁₋₄ haloalkyl;
 R⁶ is a member selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆
 haloalkyl, -O-C₁₋₆ haloalkyl, -S-C₁₋₆ alkyl, -C₁₋₆ alkyl-O-C₁₋₆ alkyl, -C₁₋₆ alkyl-S-C₁₋₆
 alkyl, cyano, and halogen;
 R⁷ is P¹; and
 R⁸ is -CH₂OP¹;

each P¹ is a prodrug component

(i) selected from the group consisting of:



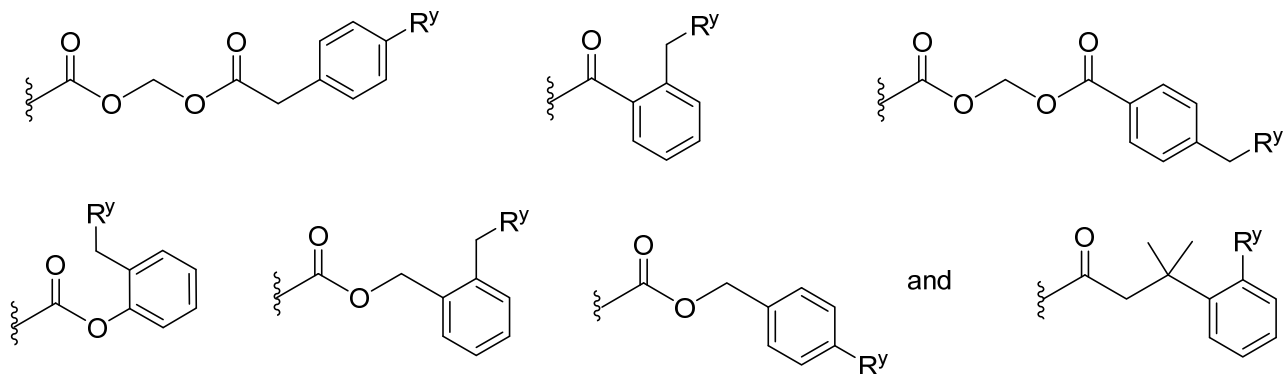
wherein each R⁹ is independently selected from the group consisting of H and C₁₋₃ alkyl;

and

each R¹⁰ is independently selected from the group consisting of H, C₁₋₃ alkyl, phenyl, and

benzyl; or

(ii) selected from the group consisting of:



wherein

each R^y is independently selected from the group consisting of

-OP(O)(OR^{y1})₂, -OC(O)CH₂N(R^{y2})₂, -N(R^{y2})₂, and piperazine;

each R^{y1} is independently selected from the group consisting of H, C₁₋₃ alkyl, and benzyl;

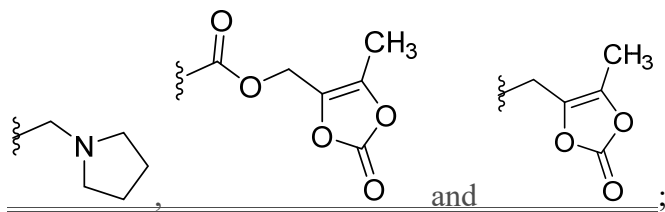
each R^{y2} is independently H or C₁₋₃ alkyl; and

each phenyl ring bearing an R^y or $-CH_2R^y$ substituent is further substituted with from 0 to 3 members independently selected from the group consisting of nitro, halogen, CN, CF_3 , C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, and C_{1-4} hydroxyalkyl; or

(iii) selected from the group consisting of $-CH_2OH$, $-P(O)(OR^{10})_2$, and $-CH_2-O-P(O)(OR^{10})_2$, wherein each R^{10} is independently selected from the group consisting of H, C_{1-3} alkyl, phenyl, and benzyl; or

(iv) selected from the group consisting of an amino acid, a dipeptide, and a tripeptide; or

(v) selected from the group consisting of:



each R^x is independently selected from the group consisting of halogen, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} hydroxyalkyl, C_{2-4} alkenyl, C_{3-6} cycloalkyl, CO_2-C_{1-4} alkyl, and $CONH_2$;
the subscript m is 0, 1, 2, 3 or 4; and
the subscript n is 0, 1, 2 or 3.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof,

(i) having Formula **IA**; or

(ii) having Formula **IB**; or

(iii) having Formula **IC**; or

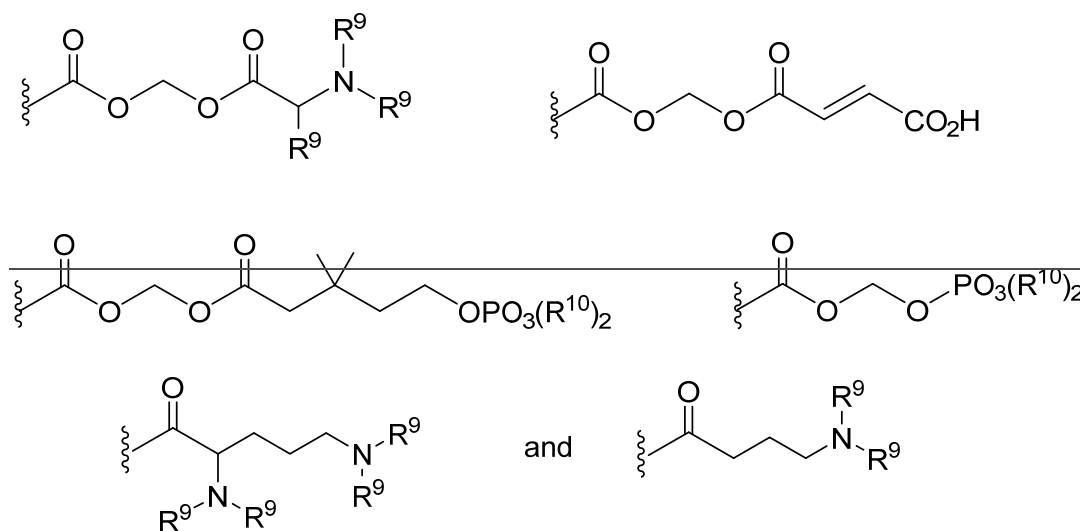
2 ~~3. The compound of claim 1, or a pharmaceutically acceptable salt thereof,~~

3 ~~(i^v) having Formula IIA; or~~

1 ~~(vⁱⁱ) having Formula IIB; or~~

1 ~~(vⁱⁱⁱ) having Formula IIC.~~

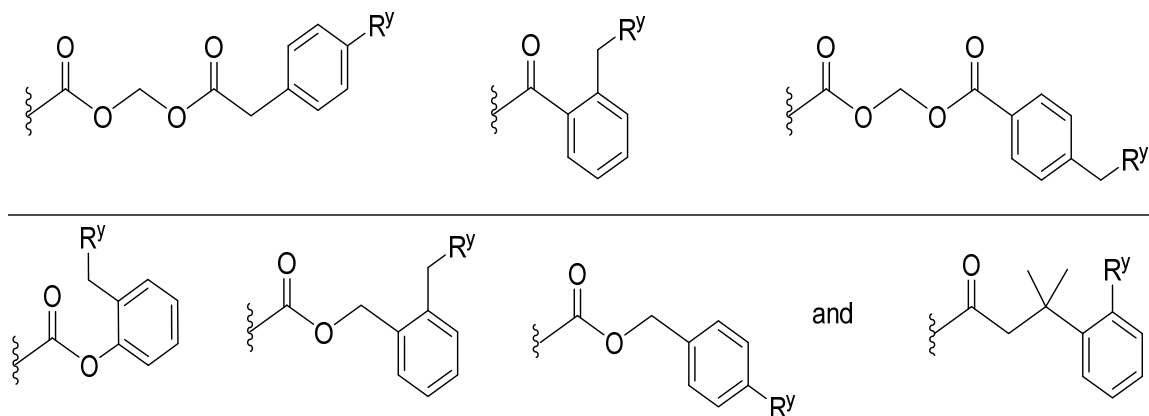
1 ~~3. The compound of any one of claims 1 to 2, or a pharmaceutically~~
2 ~~acceptable salt thereof, (i) wherein P⁺ is selected from the group consisting of:~~



3 ~~wherein each R⁹ is independently selected from the group consisting of H and C₁₋₂~~
4 ~~alkyl; and~~

5 ~~each R¹⁰ is independently selected from the group consisting of H, C₁₋₂ alkyl,~~
6 ~~phenyl, and benzyl; or~~

1 ~~(ii) wherein P⁺ is selected from the group consisting of:~~



wherein

each R^* is independently selected from the group consisting of

~~$OP(O)(OR^{*1})_2$, $OC(O)CH_2N(R^{*2})_2$, $N(R^{*2})_2$, and piperazine;~~

each R^{*1} is independently selected from the group consisting of H, C_{1-2} alkyl, and

benzyl;

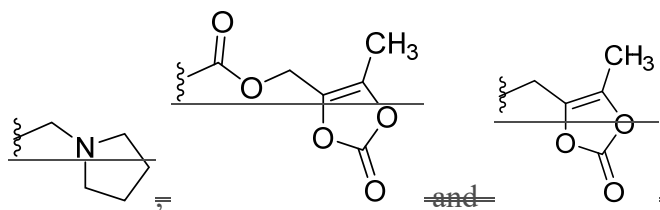
each R^{*2} is independently H or C_{1-2} alkyl; and

each phenyl ring bearing an R^* or CH_2R^* substituent is further substituted with from 0 to 3 members independently selected from the group consisting of nitro, halogen, CN, CF_3 , C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, and C_{1-4} hydroxyalkyl; or

(iii) wherein P^+ is selected from the group consisting of CH_2OH , $P(O)(OR^{+0})_2$, and $CH_2O-P(O)(OR^{+0})_2$, wherein each R^{+0} is independently selected from the group consisting of H, C_{1-2} alkyl, phenyl, and benzyl; or

(iv) wherein P^+ is selected from the group consisting of an amino acid, a dipeptide, and a tripeptide; or

(v) wherein P^+ is selected from the group consisting of:



4. The compound of any one of claims 31 to 3, where said amino acid, dipeptide, or tripeptide moieties are independently selected from the group consisting of glycine, alanine, valine, leucine, isoleucine, lysine, cysteine, aspartate, glutamate, histidine, and phenylalanine, wherein the N atom of each amino acid unit may be methylated or acylated.

5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein X^1 is $C(O)-C_{1-4}$ alkylene or $S(O)_2$.

6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, (i) wherein R^1 is a 5- to 10-membered heteroaryl having from 1 to 4 heteroatoms as ring vertices selected from N, O and S; and wherein the group $-X^1-R^1$ is optionally substituted with 1 to 4 R^x substituents; or

(ii) wherein R^1 is C_{6-10} aryl; and wherein the group $-X^1-R^1$ is optionally substituted with 1 to 4 R^x substituents; or

(iii) wherein R^1 is C_{3-8} cycloalkyl; and wherein the group $-X^1-R^1$ is optionally substituted with 1 to 4 R^x substituents; or

(iv) wherein R^1 is a 4- to 8-membered heterocycloalkyl having from 1 to 2 heteroatoms as ring vertices selected from N, O and S; and wherein the group $-X^1-R^1$ is optionally substituted with 1 to 4 R^x substituents; or

(v) wherein R^1 is selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} haloalkyl, $-C(O)NR^{1a}R^{1b}$, and $-CO_2R^{1a}$; wherein R^{1a} and R^{1b} are each independently selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-10} aryl, and $-C_{1-6}$ alkylene- C_{6-10} aryl; and wherein the group $-X^1-R^1$ is optionally substituted with 1 to 4 R^x substituents; or

(vi) wherein R¹ is selected from the group consisting of phenyl, pyridyl, pyrimidinyl, and pyrazinyl; and wherein the group -X¹-R¹ is optionally substituted with 1 to 4 R^x substituents.

7. The compound of claim 6, (i) wherein R¹ is selected from the group consisting of pyrazolyl, pyridyl, pyrimidinyl, imidazolyl, thiazolyl, thiadiazolyl and pyrazinyl; and wherein the group -X¹-R¹ is optionally substituted with 1 to 4 R^x substituents.

8. The compound of claim 6, (ii) wherein R¹ is phenyl; and wherein the group -X¹-R¹ is optionally substituted with 1 to 4 R^x substituents.

9. The compound of claim 6, (iii) wherein R¹ is selected from the group consisting of cyclobutyl, cyclopentyl and cyclohexyl; and wherein the group -X¹-R¹ is optionally substituted with 1 to 4 R^x substituents

10. The compound of claim 6, (iv) wherein R¹ is selected from the group consisting of oxetanyl, tetrahydrofuranyl, tetrahydropyranyl and morpholinyl; and wherein the group -X¹-R¹ is optionally substituted with 1 to 4 R^x substituents

11. The compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, (i) wherein ring vertices a and b are CH; R^{2b} is H; ring vertex e is C(R^{2e}), and R^{2a} and R^{2e} are independently selected from the group consisting of C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, -O-C₁₋₆ haloalkyl, -S-C₁₋₆ alkyl, -C₁₋₆ alkyl-O-C₁₋₆ alkyl, -C₁₋₆ alkyl-S-C₁₋₆ alkyl, CN, and halogen; or

(ii) wherein ring vertices a and b are CH; R^{2b} is H; ring vertex e is C(R^{2e}), and R^{2a} and R^{2e} are independently selected from the group consisting of C₁₋₆ alkyl, C₁₋₆ alkoxy and halogen.

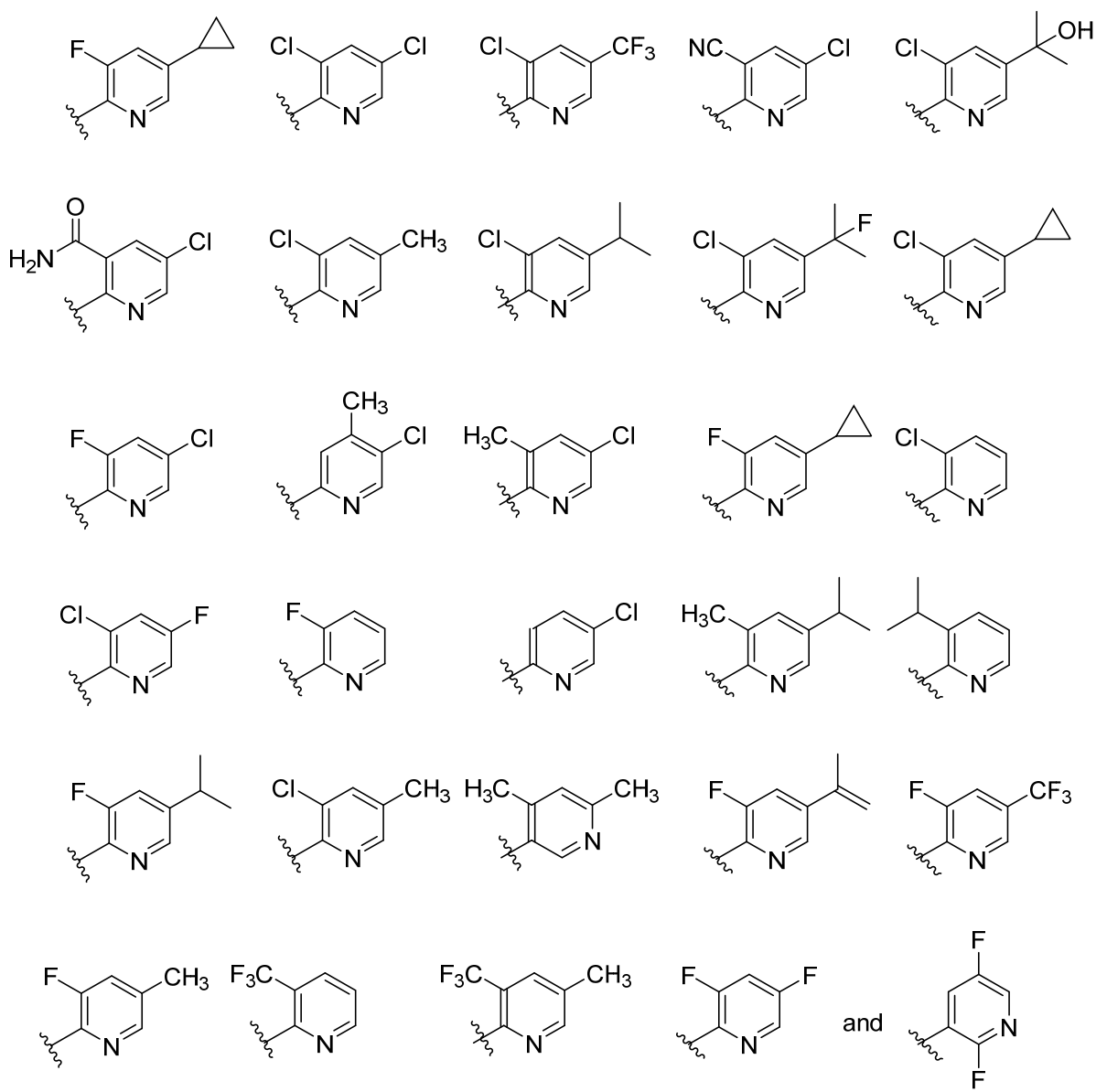
1 **12.** The compound of any one of claims **1** to **11**, or a pharmaceutically
2 acceptable salt thereof, (i) wherein n is 0, 1 or 2 and each R⁵, when present, is selected from the
3 group consisting of F, Cl, CN, C₁₋₄ alkyl and C₁₋₄ alkoxy; or

1 (ii) wherein n is 0, 1 or 2 and each R⁵, when present, is selected from the group
2 consisting of F, Cl, CN, CH₃ and OCH₃; or

1 (iii) wherein m is 0, 1 or 2 and each R³, when present, is C₁₋₄ alkyl.

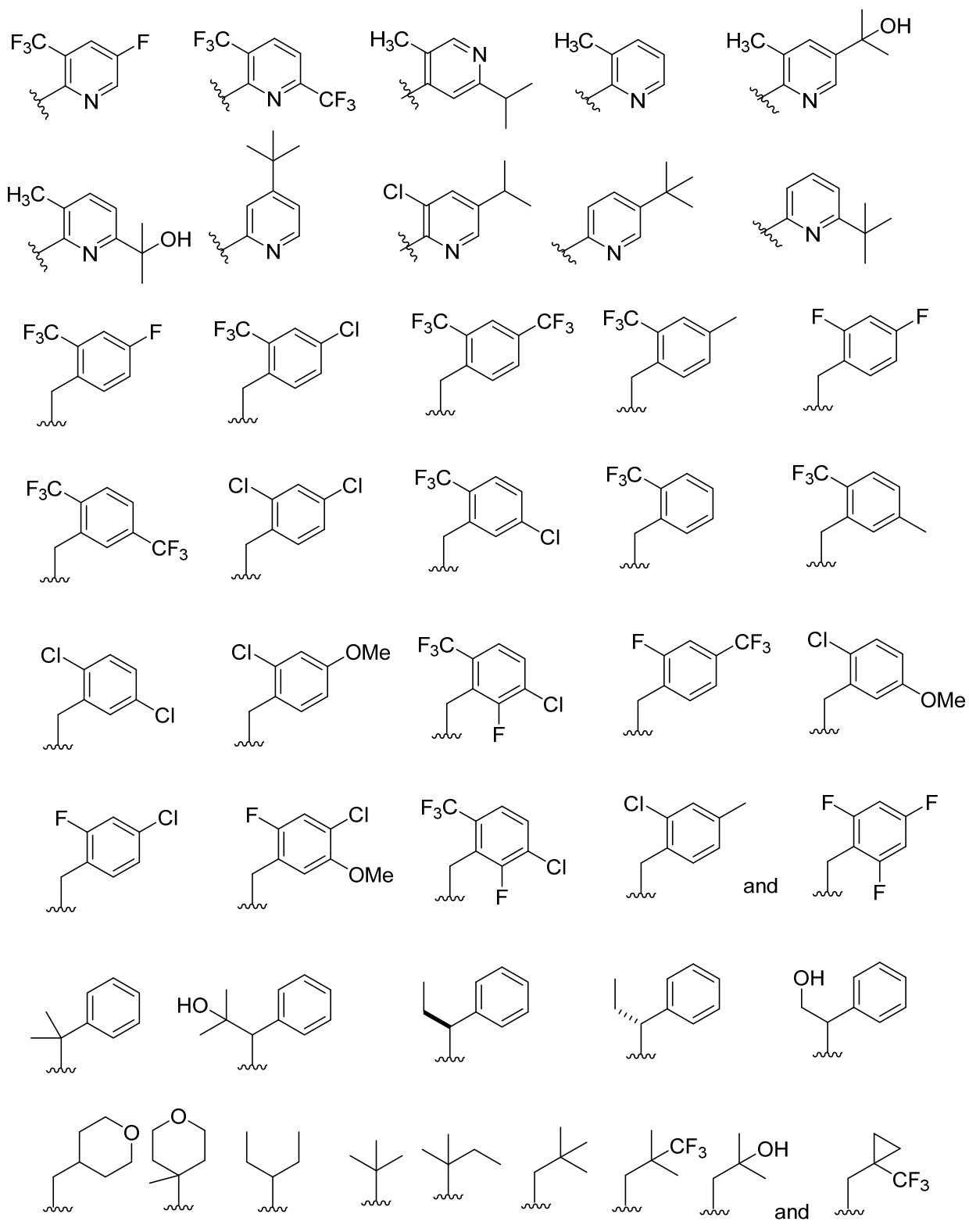
1 **13.** The compound of any one of claims 1 or claim to 32, or a
2 pharmaceutically acceptable salt thereof, wherein R¹ is selected from the group consisting of
3 phenyl or pyridyl, wherein the group -X¹-R¹ is optionally substituted with 1 to 4 R^x substituents;
4 ring vertices a and b are CH; R^{2b} is H; ring vertex e is C(R^{2e}), and R^{2a} and R^{2e} are independently
5 selected from the group consisting of C₁₋₆ alkyl, C₁₋₆ alkoxy and halogen; m is 0, 1 or 2 and each
6 R³, when present, is CH₃; ~~R⁴, when present, is selected from the group consisting of:~~ n is 0, 1 or
7 2, and each R⁵, when present, is selected from the group consisting of F, Cl, CN, CH₃ and OCH₃.

1 **14.** The compound of any one of claims 1 or claim to 32, or a
2 pharmaceutically acceptable salt thereof, (i) wherein R¹ is selected from the group consisting of



; or

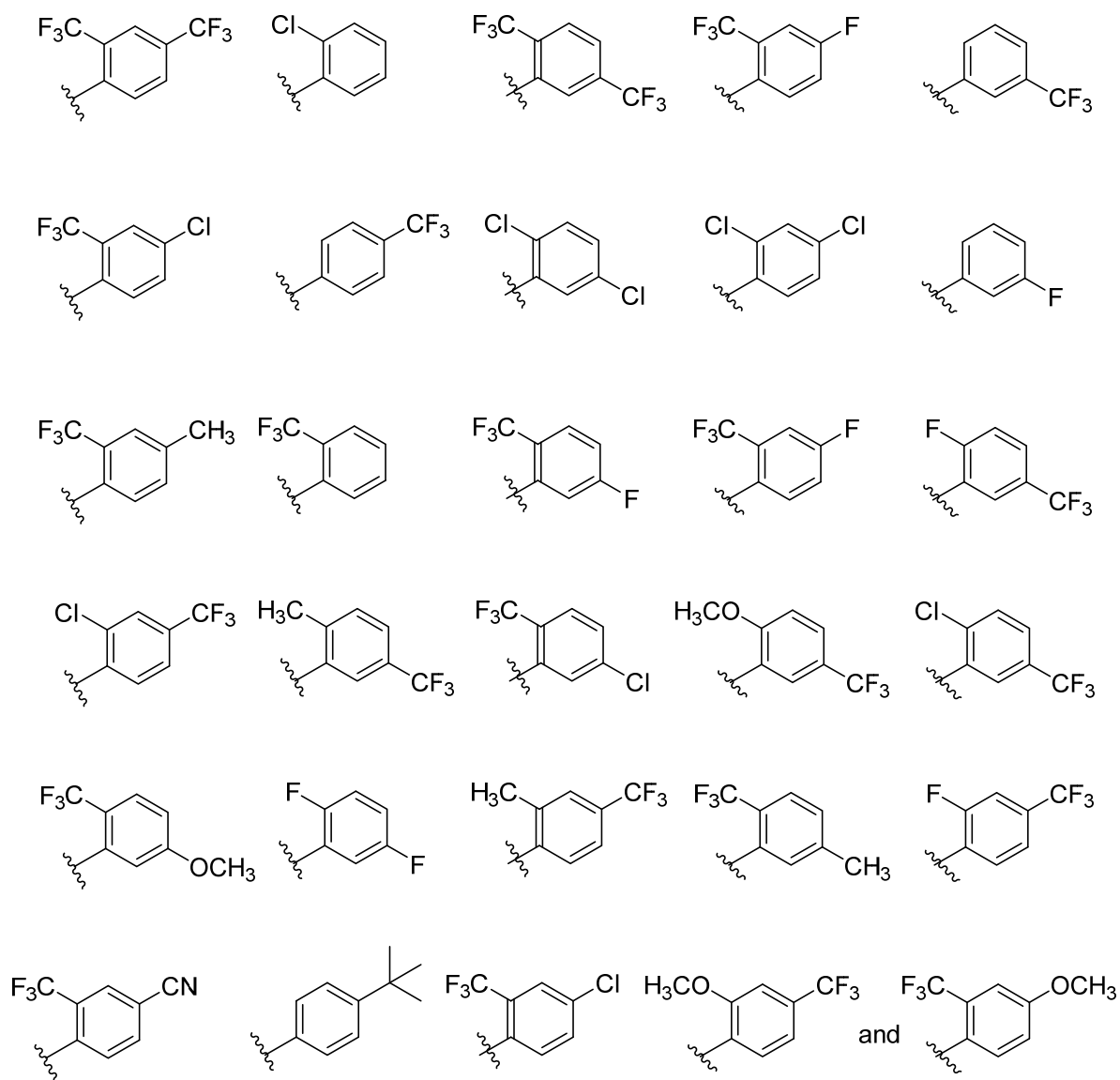
(ii) wherein $-X^1-R^1$ is selected from the group consisting of:



2
3

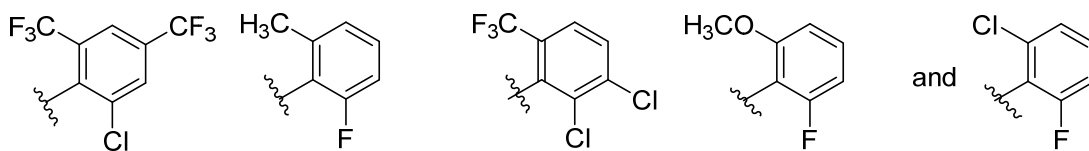
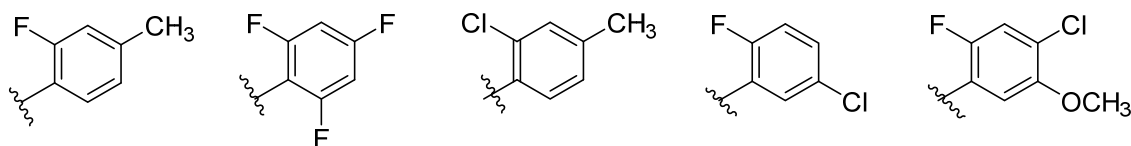
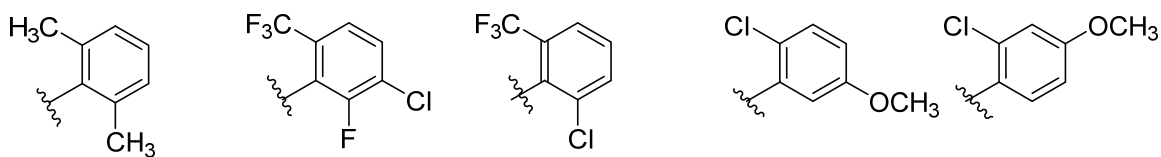
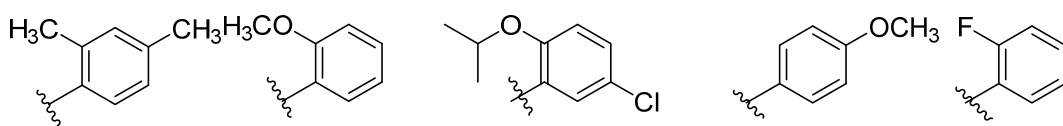
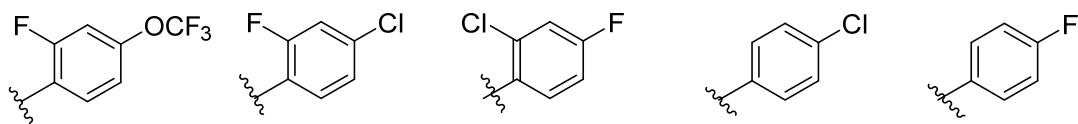
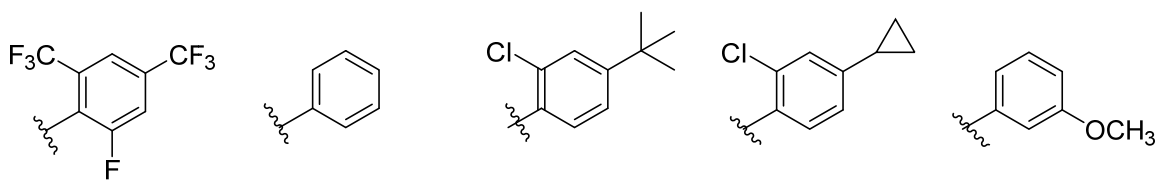
1

(iii) wherein R¹ is selected from the group consisting of:



; or

(iv) wherein R^1 is selected from the group consisting of:

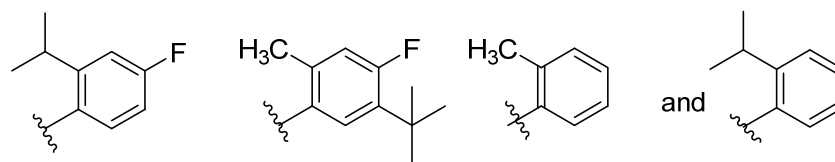
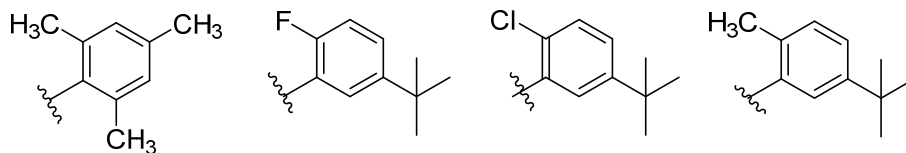


3

; or

1

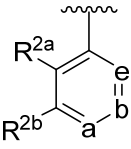
(v) wherein R^1 is selected from the group consisting of:

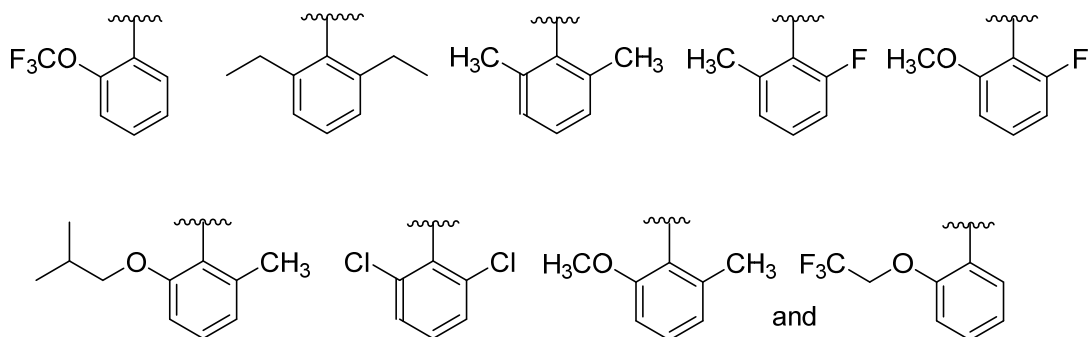


2

.

1 **15.** The compound of any one of claims **1** to **14**, or a pharmaceutically

2 acceptable salt thereof, wherein  is selected from the group consisting of



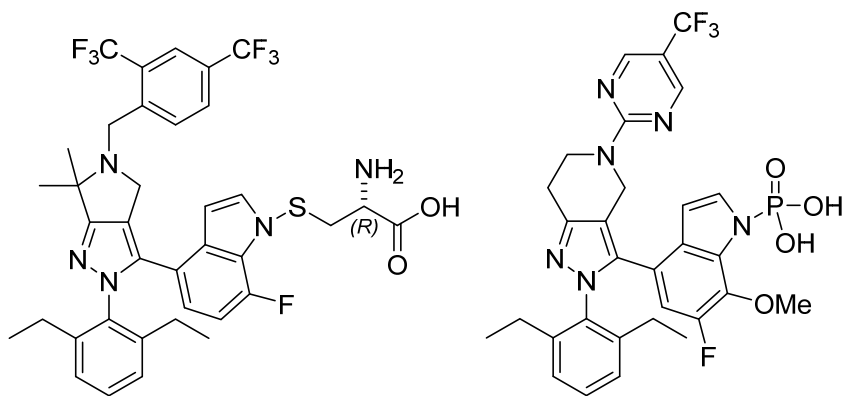
1 **16.** The compound of any one of claims **1** to **15**, or a pharmaceutically

2 acceptable salt thereof, (i) wherein n is 0; or

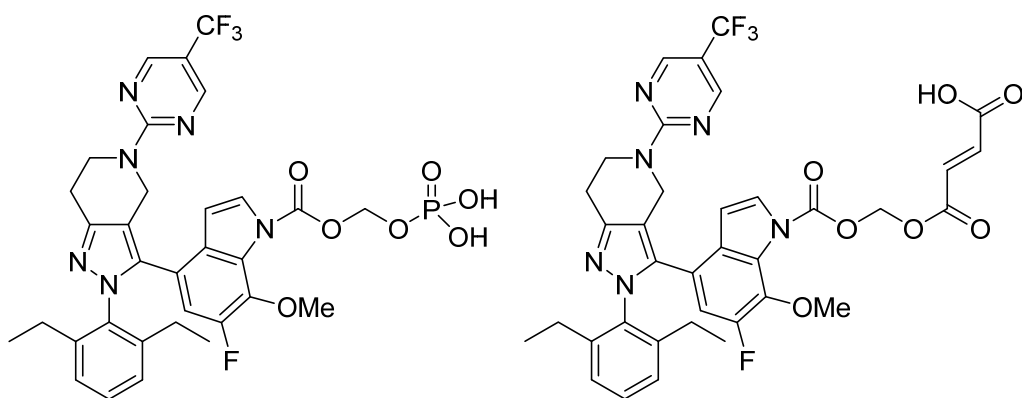
1 (ii) wherein n is 2 and the two R³ groups are on the same carbon atom and are
2 combined to form oxo (=O).

1
2 **17.** The compound of claim **1**, or a pharmaceutically acceptable salt
3 thereof, having the structure selected from

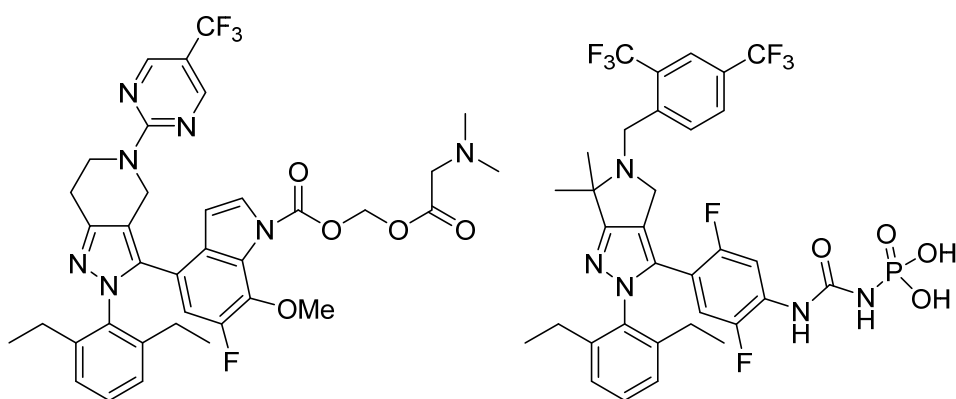
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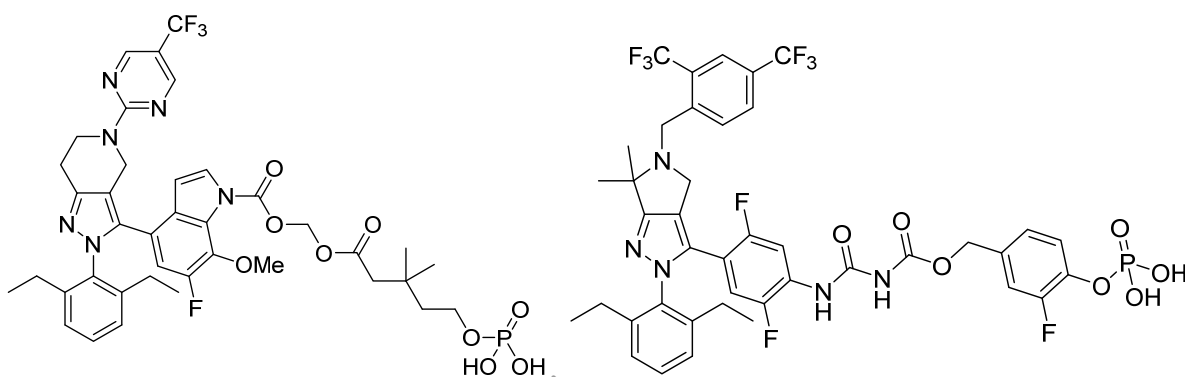
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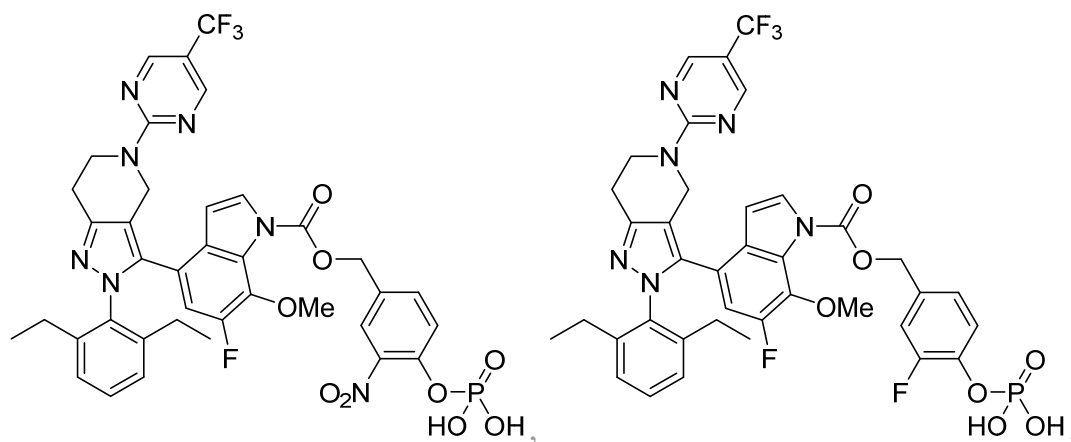


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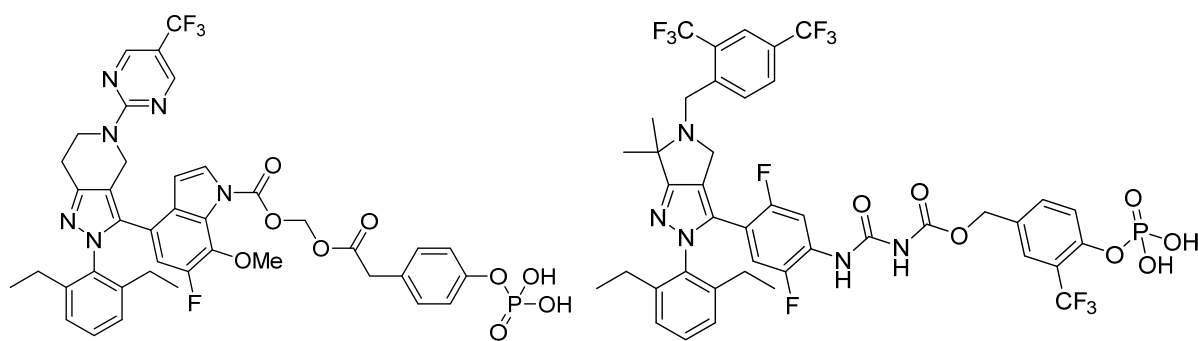


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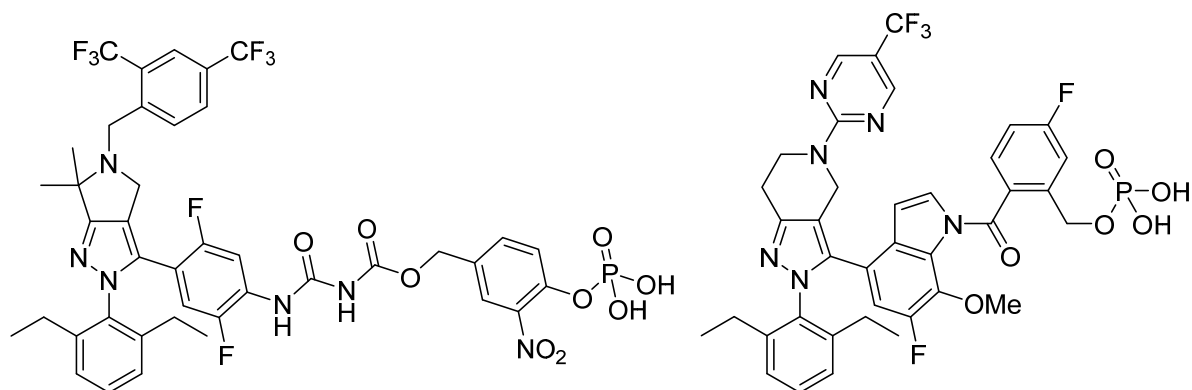




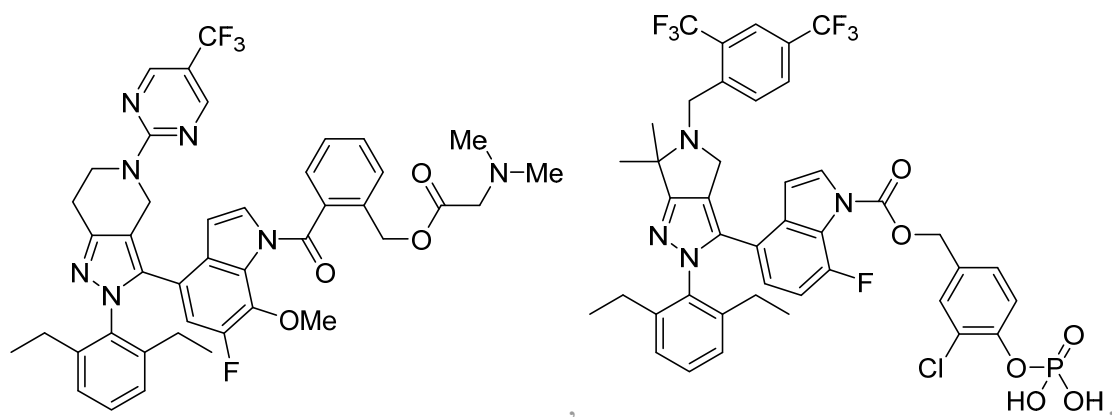
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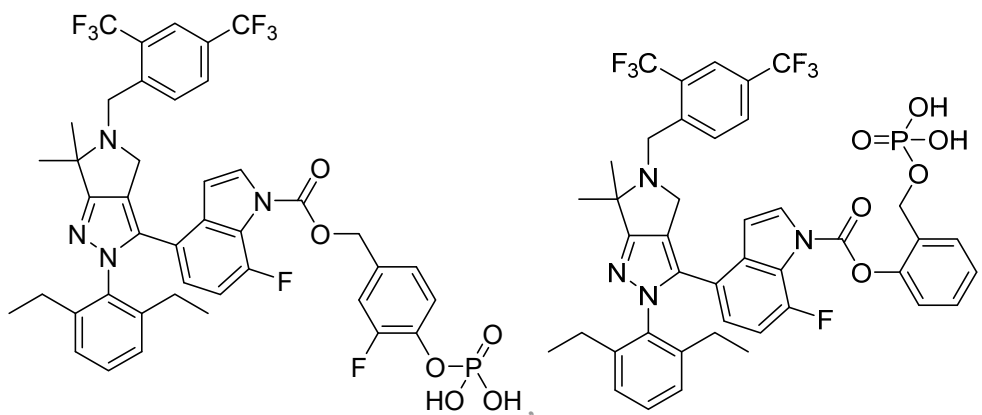


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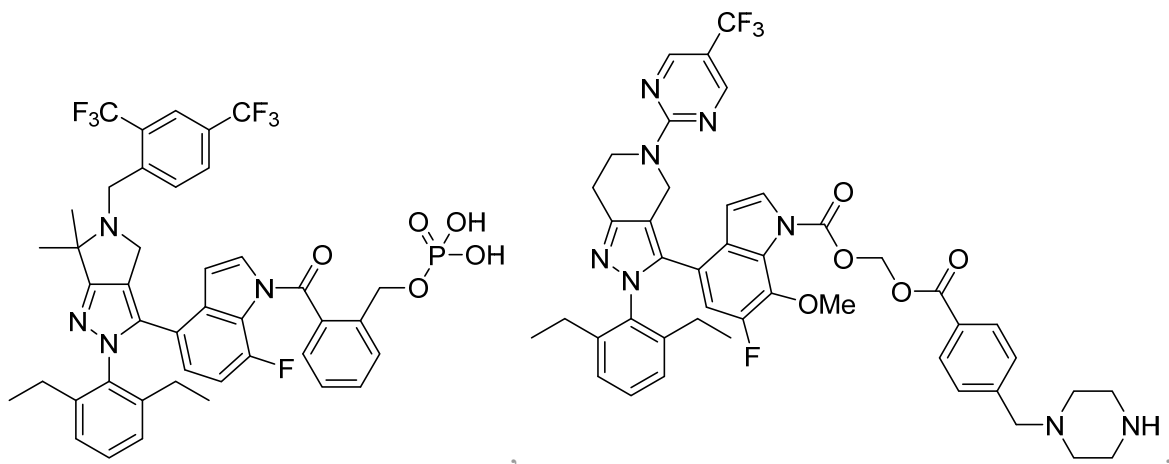


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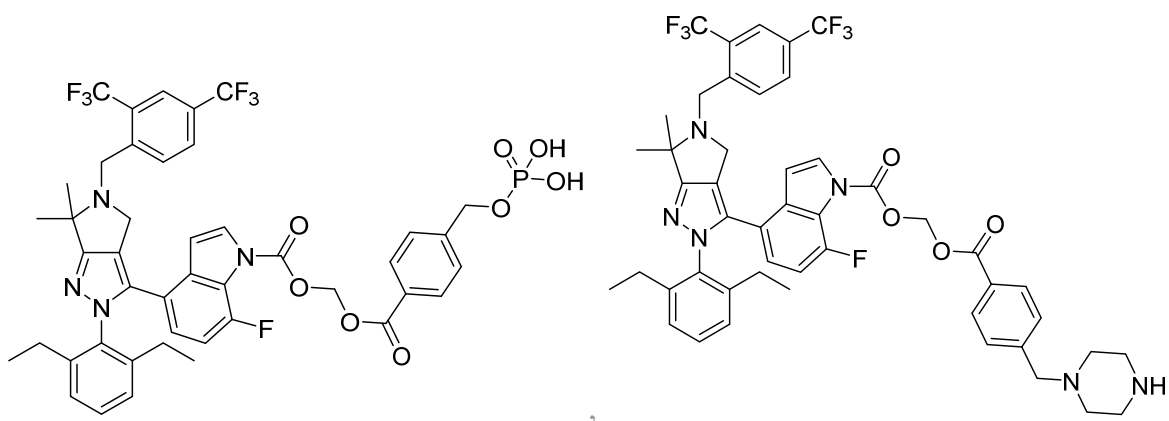
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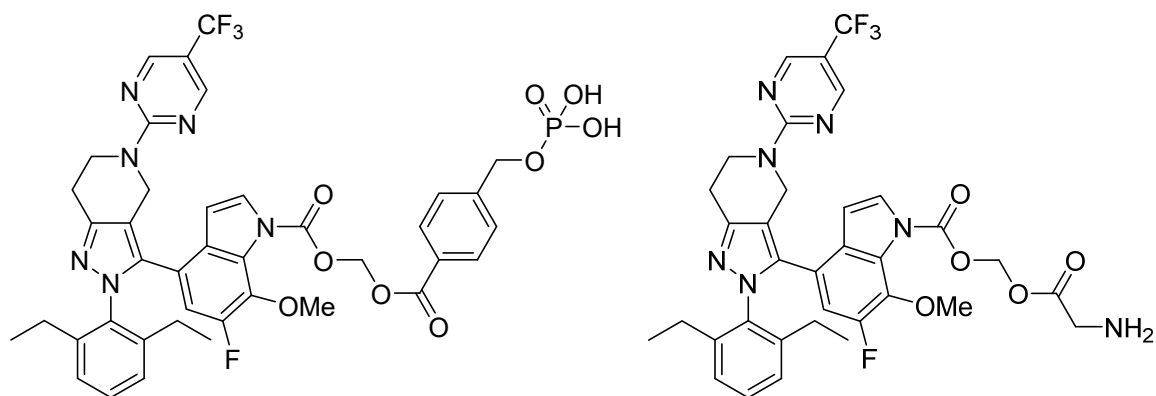
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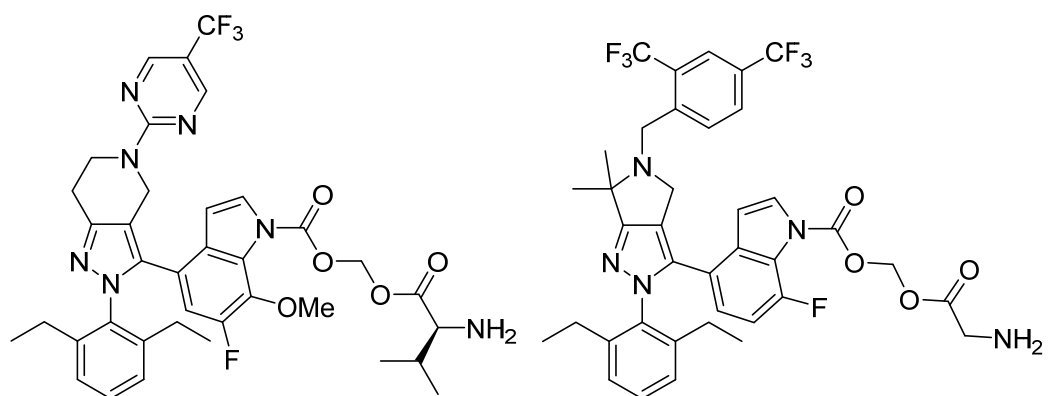
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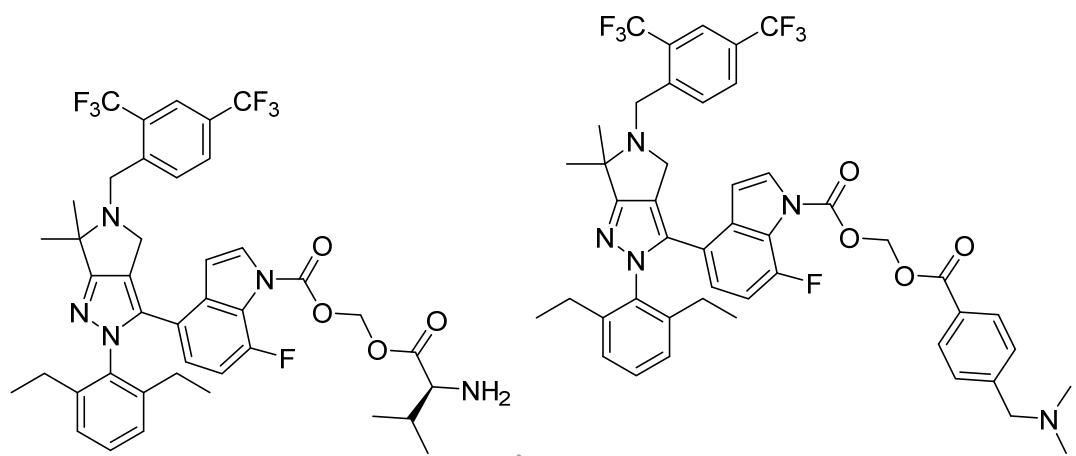
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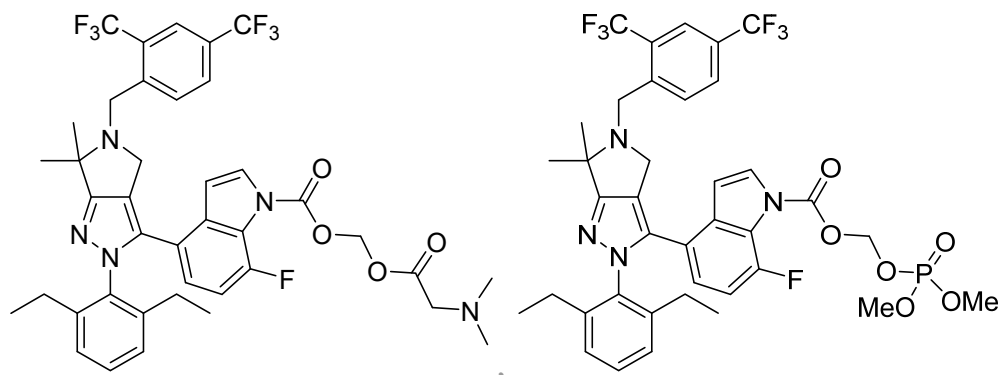
16

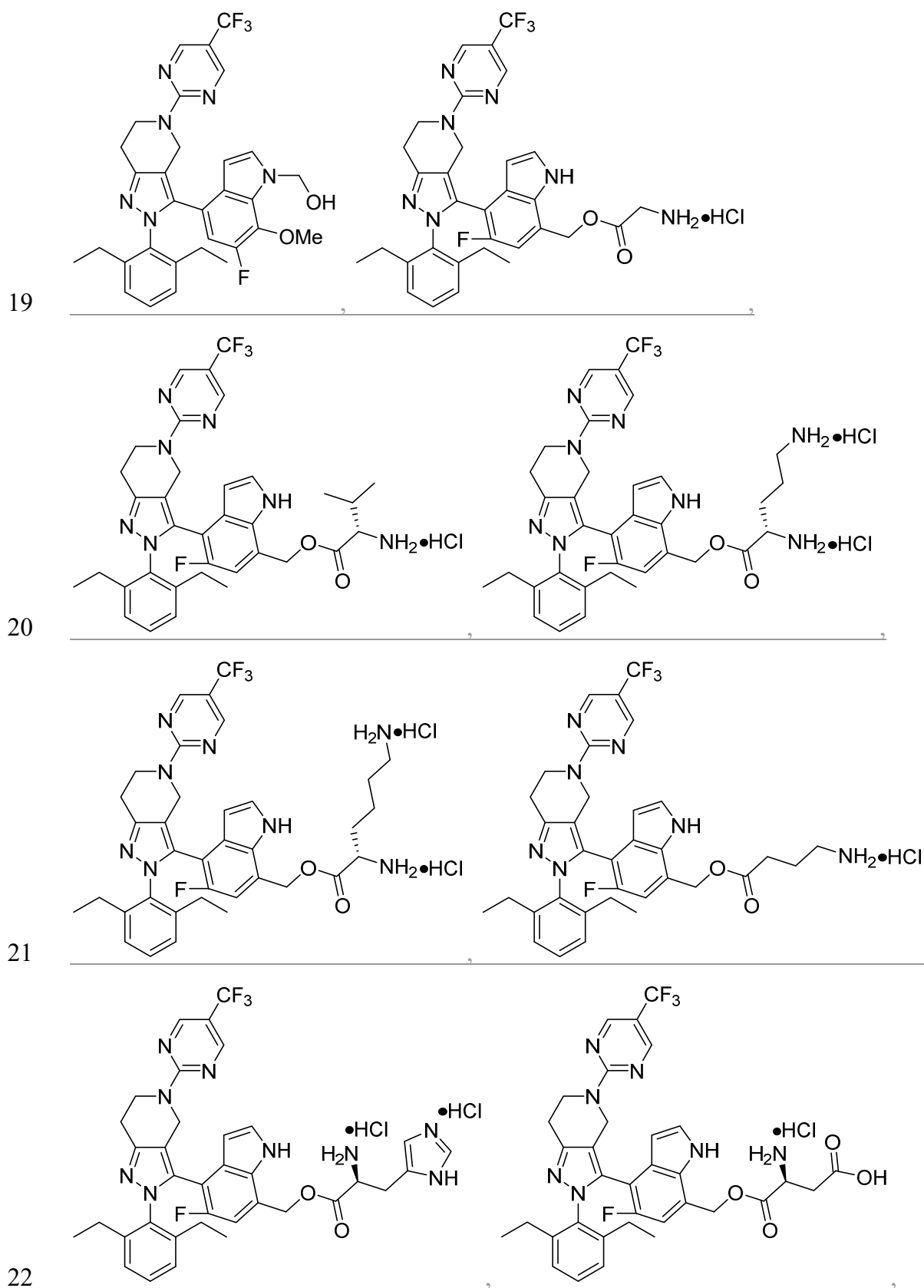


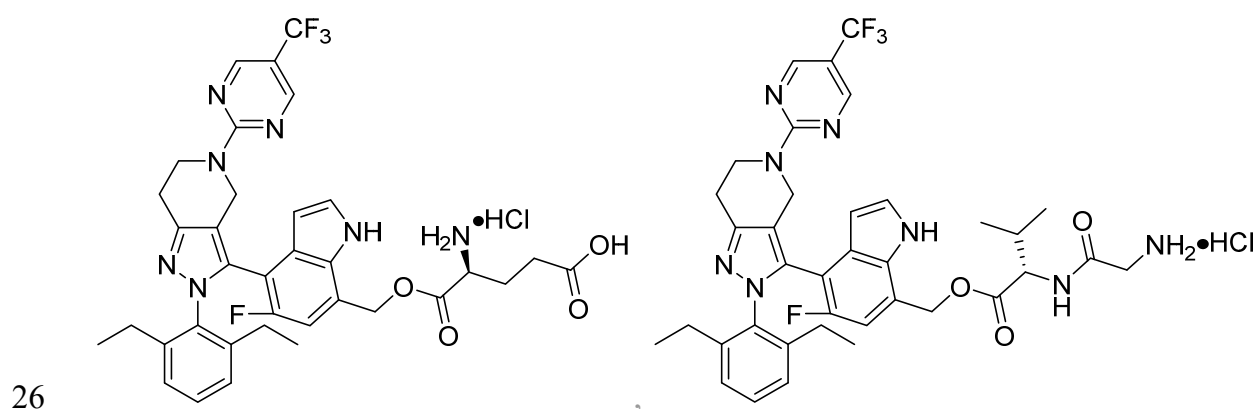
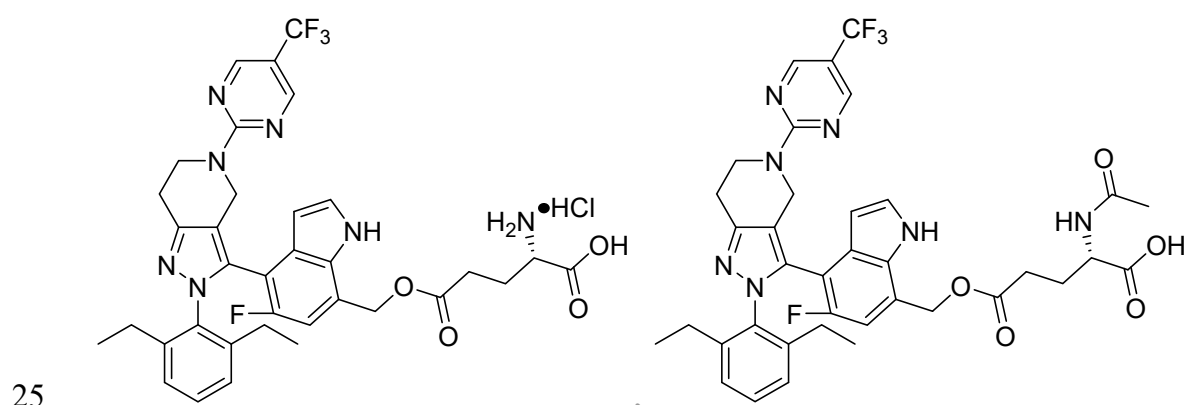
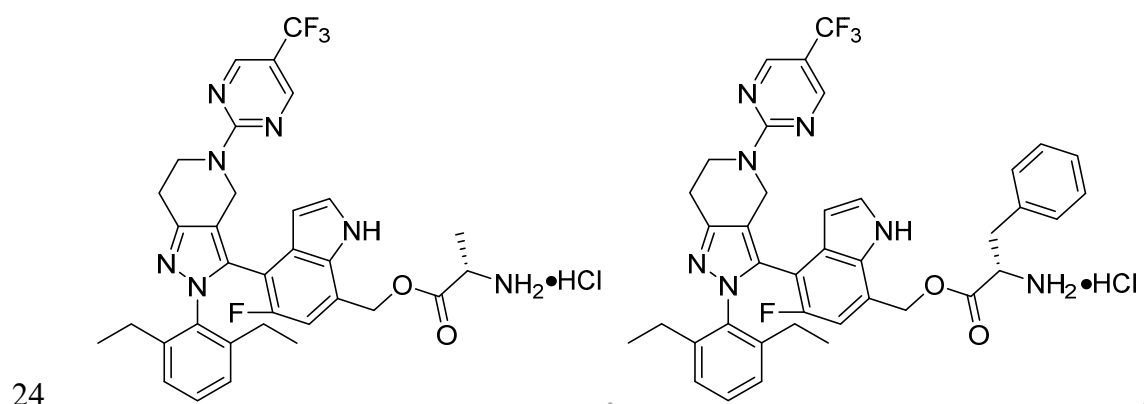
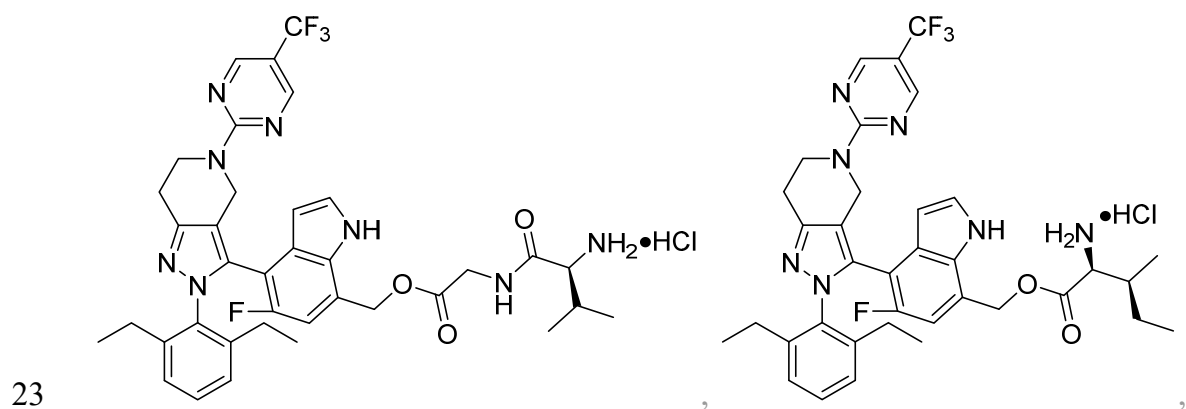
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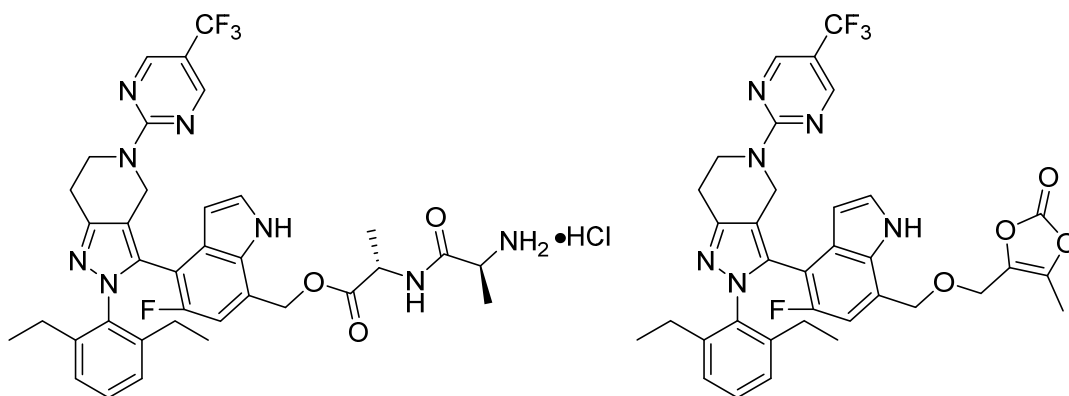
18



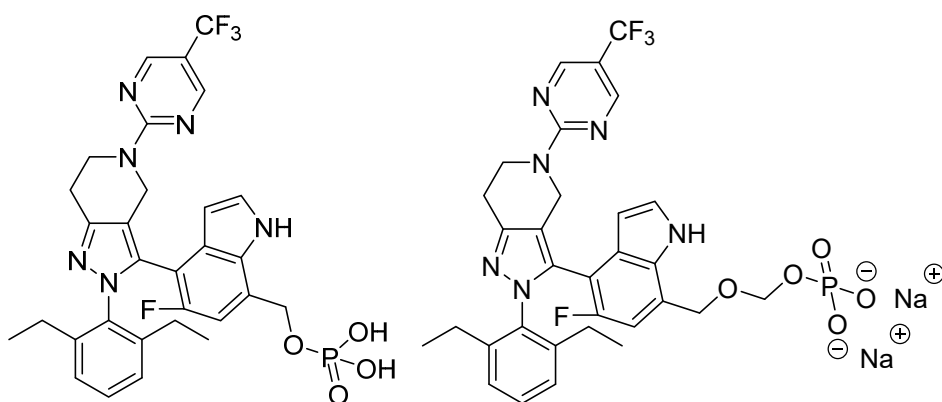




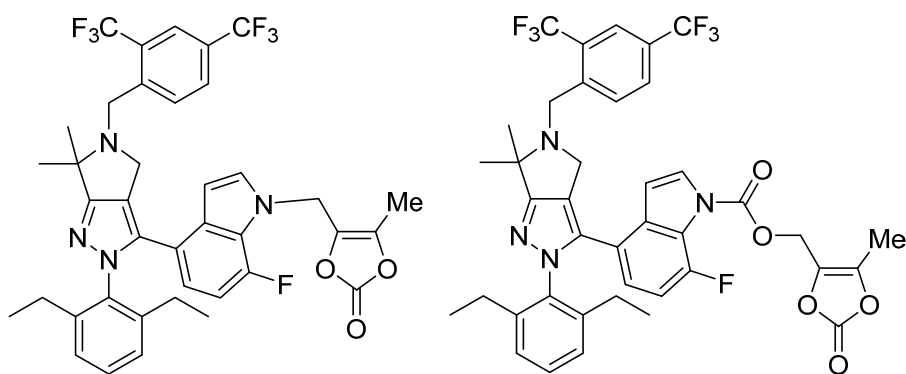
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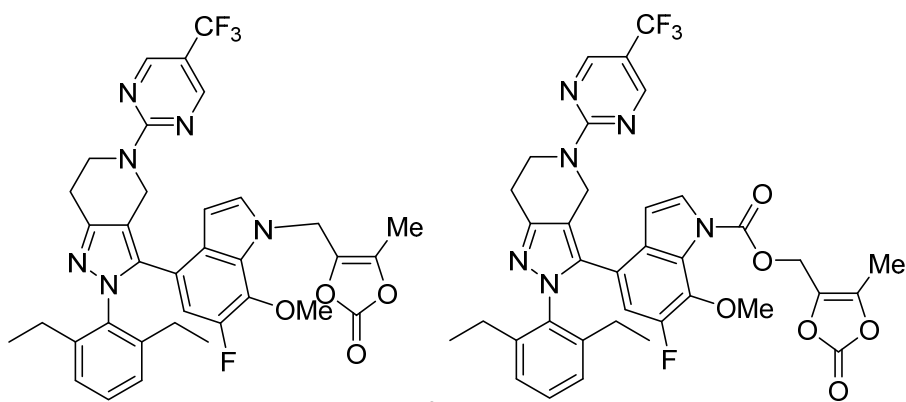
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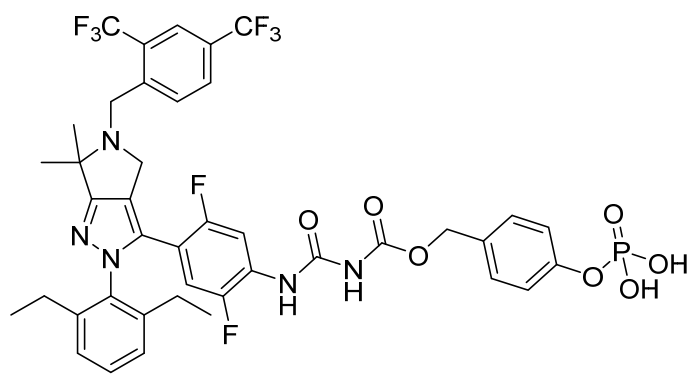
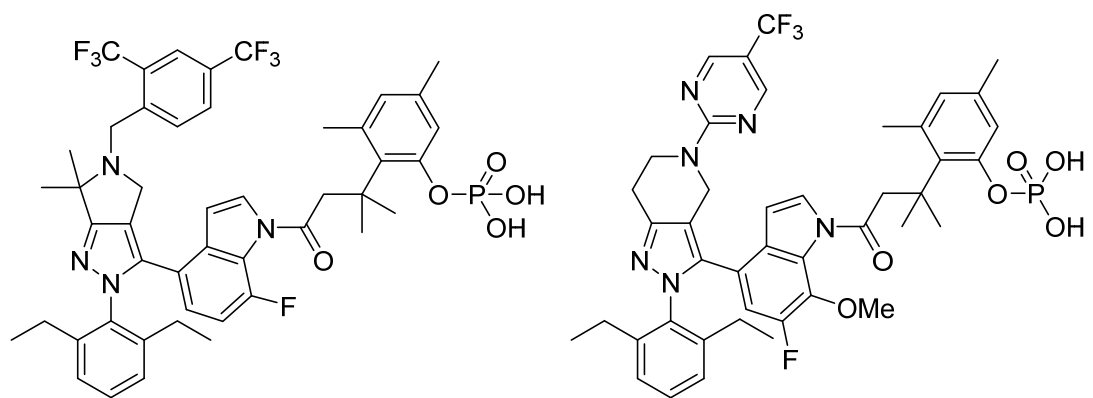
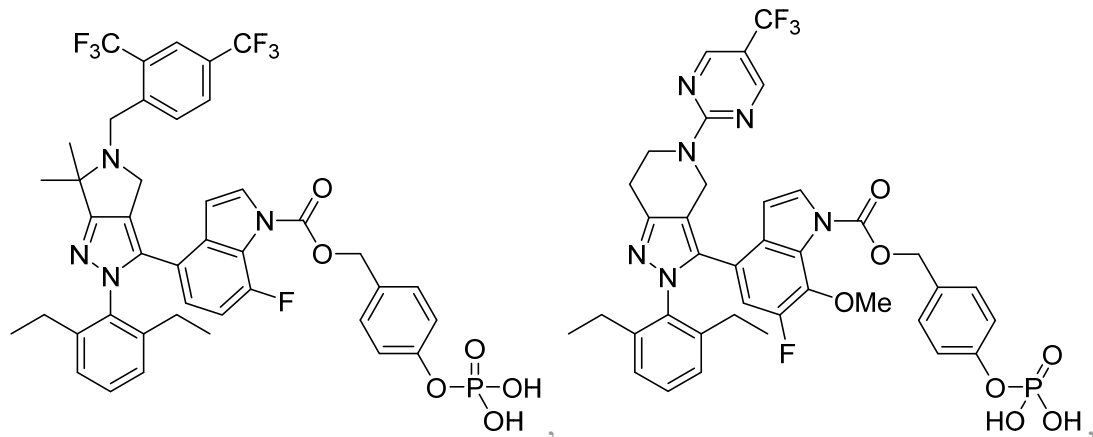


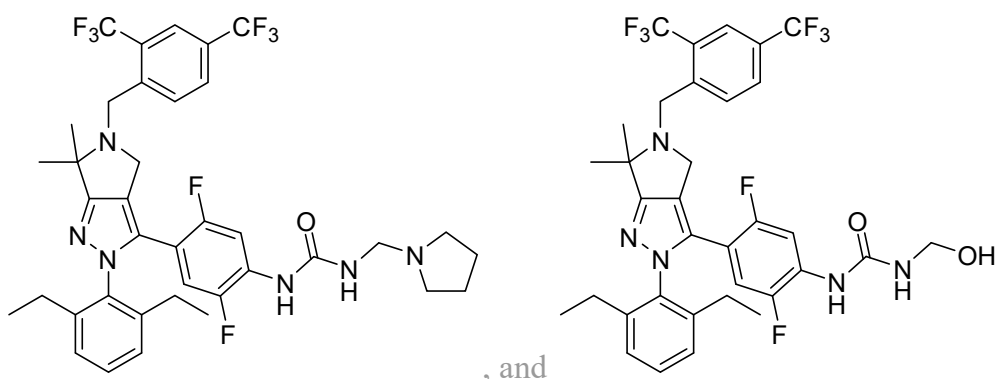
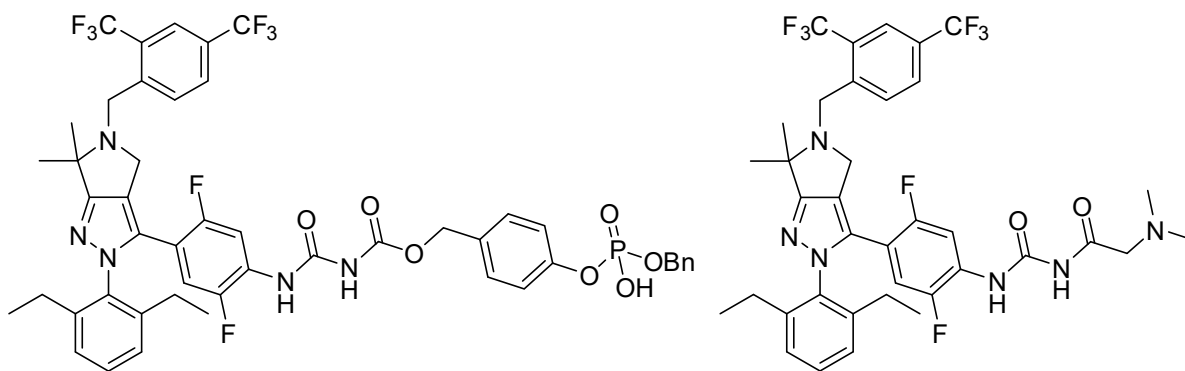
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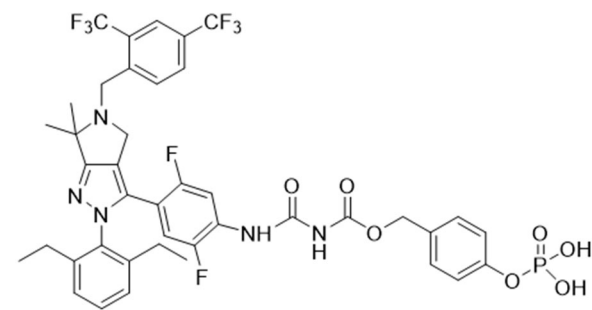




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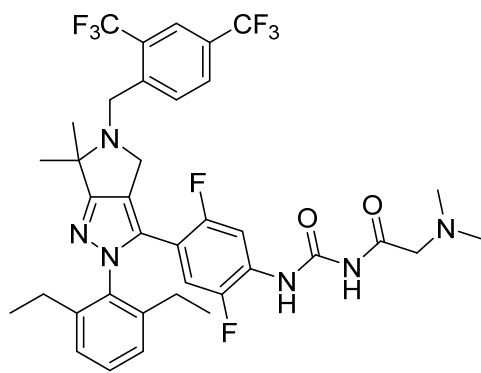
37 18. The compound of claim 17, or a pharmaceutically acceptable salt

38 thereof, having the structure

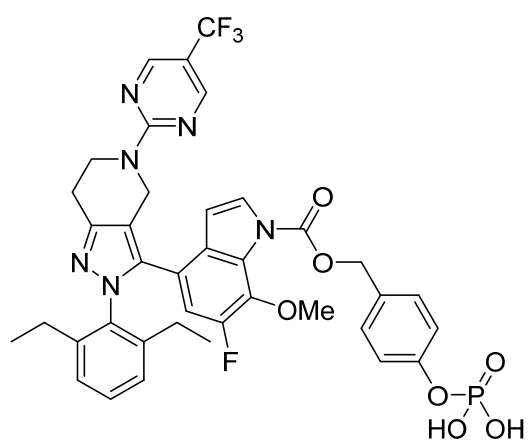


40 19. The compound of claim 17, or a pharmaceutically acceptable salt

41 thereof, having the structure



20. The compound of claim 17, or a pharmaceutically acceptable salt thereof, having the structure



1721. A pharmaceutical composition comprising a compound of any one of claims 1 to ~~16~~**20** or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

1822. The pharmaceutical composition of claim ~~17~~**21**, formulated for oral, intravenous, transdermal or subcutaneous administration.

1923. The pharmaceutical composition of claim ~~17-21~~ or ~~18~~**22**, further comprising one or more additional therapeutic agents.

~~2024~~. The pharmaceutical composition of claim ~~1923~~, wherein the one or more additional therapeutic agent is selected from the group consisting of corticosteroids, steroids, immunosuppressants, Immunoglobulin G agonists, Dipeptidyl peptidase IV inhibitors, Lymphocyte function antigen-3 receptor antagonists, Interleukin-2 ligands, Interleukin-1 beta ligand inhibitors, IL-2 receptor alpha subunit inhibitors, HGF gene stimulators, IL-6 antagonists, IL-5 antagonists, Alpha 1 antitrypsin stimulators, Cannabinoid receptor antagonists, Histone deacetylase inhibitors, AKT protein kinase inhibitors, CD20 inhibitors, Abl tyrosine kinase inhibitors, JAK tyrosine kinase inhibitors, TNF alpha ligand inhibitors, Hemoglobin modulators, TNF antagonists, proteasome inhibitors, CD3 modulators, Hsp 70 family inhibitors, Immunoglobulin agonists, CD30 antagonists, tubulin antagonists, Sphingosine-1-phosphate receptor-1 agonists, connective tissue growth factor ligand inhibitors, caspase inhibitors, adrenocorticotrophic hormone ligands, Btk tyrosine kinase inhibitors, Complement C1s subcomponent inhibitors, Erythropoietin receptor agonists, B-lymphocyte stimulator ligand inhibitors, Cyclin-dependent kinase-2 inhibitors, P-selectin glycoprotein ligand-1 stimulators, mTOR inhibitors, Elongation factor 2 inhibitors, Cell adhesion molecule inhibitors, Factor XIII agonists, Calcineurin inhibitors, Immunoglobulin G1 agonists, Inosine monophosphate dehydrogenase inhibitors, Complement C1s subcomponent inhibitors, Thymidine kinase modulators, Cytotoxic T-lymphocyte protein-4 modulators, Angiotensin II receptor antagonists, Angiotensin II receptor modulators, TNF superfamily receptor 12A antagonists, CD52 antagonists, Adenosine deaminase inhibitors, T-cell differentiation antigen CD6 inhibitors, FGF-7 ligands, dihydroorotate dehydrogenase inhibitors, Syk tyrosine kinase inhibitors, Interferon type I receptor antagonists, Interferon alpha ligand inhibitors, Macrophage migration inhibitory factor inhibitors, Integrin alpha-V/beta-6 antagonists, Cysteine protease stimulators, p38 MAP kinase inhibitors, TP53 gene inhibitors, Shiga like toxin I inhibitors, Fucosyltransferase 6 stimulators, Interleukin 22 ligands, IRS1 gene inhibitors, Protein kinase C stimulators, Protein kinase C alpha inhibitors, CD74 antagonists, Immunoglobulin gamma Fc receptor IIB antagonists, T-cell antigen CD7 inhibitors, CD95 antagonists, N acetylmannosamine kinase stimulators, Cardiotrophin-1 ligands, Leukocyte elastase inhibitors, CD40 ligand

receptor antagonists, CD40 ligand modulators, IL-17 antagonists, TLR-2 antagonists, Mannan-binding lectin serine protease-2 (MASP-2) inhibitors, Factor B inhibitors, Factor D inhibitors, C3aR modulators, C5aR2 modulators, T cell receptor antagonists, PD-1 inhibitors, PD-L1 inhibitors, TIGIT inhibitors, TIM-3 inhibitors, LAG-3 inhibitors, VISTA inhibitors, STING agonists, IDO inhibitors, adenosine receptor modulators, CD39 inhibitors, CD73 inhibitors, antagonists of the chemokine receptors, especially CXCR1, CXCR2, CXCR3, CXCR4, CXCR7, CCR1, CCR2, CCR3, CCR4, CCR5, CCR7, CCR7, CCR9, CX3CR1 and CXCR6, and combinations thereof.

2125. The pharmaceutical composition of any one of claims ~~19-23~~ or ~~2024~~, wherein the one or more additional therapeutic agent is selected from the group consisting of obinutuzumab, rituximab, ocrelizumab, cyclophosphamide, prednisone, hydrocortisone, hydrocortisone acetate, cortisone acetate, tixocortol pivalate, prednisolone, methylprednisolone, triamcinolone acetonide, triamcinolone alcohol, mometasone, amcinonide, budesonide, desonide, fluocinonide, fluocinolone acetonide, halcinonide, betamethasone, betamethasone sodium phosphate, dexamethasone, dexamethasone sodium phosphate, fluocortolone, hydrocortisone-17-valerate, halometasone, alclometasone dipropionate, beclomethasone, betamethasone valerate, betamethasone dipropionate, prednicarbate, clobetasone-17-butyrate, clobetasol-17-propionate, fluocortolone caproate, fluocortolone pivalate, fluprednidene acetate, hydrocortisone-17-butyrate, hydrocortisone-17-aceponate, hydrocortisone-17-buteprate, ciclesonide and prednicarbate, GB-0998, immuglo, begelomab, alefacept, aldesleukin, gevokizumab, daclizumab, basiliximab, inolimomab, beperminogene perplasmid, sirukumab, tocilizumab, clazakizumab, mepolizumab, fingolimod, panobinostat, tricitiribine, nilotinib, imatinib, tofacitinib, momelotinib, peficitinib, itacitinib, infliximab, PEG-bHb-CO, etanercept, ixazomib, bortezomib, muromonab, orelizumab, gusperimus, brentuximab vedotin, Ponesimod, KRP-203, FG-3019, emricasan, corticotropin, ibrutinib, cinryze, conestat, methoxy polyethylene glycol-epoetin beta, belimumab, blisibimod, atacicept, seliciclib, neihulizumab, everolimus, sirolimus, denileukin diftitox, LMB-2, natalizumab, catridecacog, ciclosporin, tacrolimus, voclosporin, voclosporin, canakinumab, mycophenolate, mizoribine, CE-1145, TK-DLI, abatacept, belatacept,

olmesartan medoxomil, sparsentan, TXA-127, BIIB-023, alemtuzumab, pentostatin, itolizumab, palifermin, leflunomide, PRO-140, cenicriviroc, fostamatinib, anifrolumab, sifalimumab, BAX-069, BG-00011, losmapimod, QPI-1002, ShigamAbs, TZ-101, F-652, reparixin, ladarixin, PTX-9908, aganirsen, APH-703, sotrastaurin, sotrastaurin, milatuzumab, SM-101, T-Guard, APG-101, DEX-M74, cardiotrophin-1, tiprelestat, ASKP-1240, BMS-986004, HPH-116, KD-025, OPN-305, TOL-101, defibrotide, pomalidomide, Thymoglobulin, laquinimod, remestemcel-L, Equine antithymocyte immunoglobulin, Stempeucel, LIV-Gamma, Octagam 10%, t2c-001, 99mTc-sestamibi, Clairyg, Prosorba, pomalidomide, laquinimod, teplizumab, FCRx, solnatide, foralumab, ATIR-101, BPX-501, ACP-01, ALLO-ASC-DFU, irbesartan + propagermanium, ApoCell, cannabidiol, RGI-2001, saratin, anti-CD3 bivalent antibody-diphtheria toxin conjugate, NOX-100, LT-1951, OMS721, ALN-CC5, ACH-4471, AMY-101, Acthar gel, and CD4+CD25+ regulatory T-cells, MEDI7814, P32, P59, pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, CCX354, CCX721, CCX9588, CCX140, CCX872, CCX598, CCX6239, CCX587, CCX624, CCX282, CCX025, CCX507, CCX430, CCX765, CCX758, CCX771, CCX662, CCX650, and combinations thereof..

~~2226.~~ Use of a compound of any one of claims **1** to ~~16-20~~ or a pharmaceutical composition of any one of claims ~~17-21~~ to ~~21-25~~ in the preparation of a medicament for treating a human suffering from or susceptible to a disease or disorder involving pathologic activation of C5a receptors.

~~23.~~ — ~~The use of claim 22,~~ wherein the disease or disorder is (i) an inflammatory disease or disorder, an autoimmune disease, or an oncologic disease or disorder; or

(ii) a cardiovascular or cerebrovascular disorder; or

(iii) is selected from the group consisting of neutropenia, neutrophilia, Wegener's granulomatosis, microscopic polyangiitis, C3-glomerulopathy, C3-glomerulonephritis, dense deposit disease, membranoproliferative glomerulonephritis, Kawasaki disease, sepsis, septic shock, Hemolytic uremic syndrome, atypical hemolytic

uremic syndrome (aHUS), Alzheimer's disease, multiple sclerosis, stroke, inflammatory bowel disease, chronic obstructive pulmonary disorder, inflammation associated with burns, lung injury, osteoarthritis, atopic dermatitis, chronic urticaria, ischemia-reperfusion injury, acute respiratory distress syndrome, systemic inflammatory response syndrome, multiple organ dysfunction syndrome, Uveitis, tissue graft rejection, hyperacute rejection of transplanted organs, myocardial infarction, coronary thrombosis, vascular occlusion, post-surgical vascular reocclusion, arteriosclerosis, polypoidal choroidal vasculopathy, traumatic central nervous system injury, ischemic heart disease, rheumatoid arthritis, systemic lupus erythematosus, Guillain- Barre syndrome, pancreatitis, lupus nephritis, lupus glomerulonephritis, psoriasis, Crohn's disease, vasculitis, ANCA vasculitis, irritable bowel syndrome, dermatomyositis, multiple sclerosis, bronchial asthma, pemphigus, pemphigoid, scleroderma, myasthenia gravis, autoimmune hemolytic and thrombocytopenic states, Goodpasture's syndrome, immuno vasculitis, Graft versus host disease, Paroxysmal nocturnal hemoglobinuria, Sjogrens syndrome, insulin-dependent diabetes, mellitus, lupus nephropathy, Heyman nephritis, membranous nephritis, glomerulonephritis, IGA nephropathy, Membranoproliferative glomerulonephritis, Antiphospholipid syndrome, Age related macular degeneration; Dry age related macular degeneration, Wet age related macular degeneration, Motor neurone disease, contact sensitivity responses, hidradenitis suppurativa, and inflammation resulting from contact of blood with artificial surfaces; or

(iv) is selected from the group consisting of neutropenia, neutrophilia, Wegener's granulomatosis, microscopic polyangiitis, C3-glomerulopathy, C3-glomerulonephritis, dense deposit disease, membranoproliferative glomerulonephritis, Kawasaki disease, Hemolytic uremic syndrome, atypical hemolytic uremic syndrome (aHUS), tissue graft rejection, hyperacute rejection of transplanted organs, rheumatoid arthritis, systemic lupus erythematosus, lupus nephritis, lupus glomerulonephritis, vasculitis, ANCA vasculitis, autoimmune hemolytic and thrombocytopenic states, immuno vasculitis, Graft versus host disease, lupus nephropathy, Heyman nephritis, membranous nephritis, glomerulonephritis, IGA nephropathy, hidradenitis suppurativa, and Membranoproliferative glomerulonephritis; or

(v) is selected from the group consisting of melanoma, lung cancer, lymphoma, sarcoma, carcinoma, fibrosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, angiosarcoma, lymphangiosarcoma, synovioma, mesothelioma, meningioma, leukemia, lymphoma, leiomyosarcoma, rhabdomyosarcoma, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, papillary carcinoma, cystadenocarcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatocellular carcinoma, transitional cell carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, wilm's tumor, pleomorphic adenoma, liver cell papilloma, renal tubular adenoma, cystadenoma, papilloma, adenoma, leiomyoma, rhabdomyoma, hemangioma, lymphangioma, osteoma, chondroma, lipoma and fibroma.

2427. The use of ~~any one of claims 22-26 to 23~~, further comprising a therapeutically effective amount of one or more additional therapeutic agents to be administered to the human.

2528. The use of claim 2427, wherein the one or more additional therapeutic agents is (i) selected from the group consisting of corticosteroids, steroids, immunosuppressants, Immunoglobulin G agonists, Dipeptidyl peptidase IV inhibitors, Lymphocyte function antigen-3 receptor antagonists, Interleukin-2 ligands, Interleukin-1 beta ligand inhibitors, IL-2 receptor alpha subunit inhibitors, HGF gene stimulators, IL-6 antagonists, IL-5 antagonists, Alpha 1 antitrypsin stimulators, Cannabinoid receptor antagonists, Histone deacetylase inhibitors, AKT protein kinase inhibitors, CD20 inhibitors, Abl tyrosine kinase inhibitors, JAK tyrosine kinase inhibitors, TNF alpha ligand inhibitors, Hemoglobin modulators, TNF antagonists, proteasome inhibitors, CD3 modulators, Hsp 70 family inhibitors, Immunoglobulin agonists, CD30 antagonists, tubulin antagonists, Sphingosine-1-phosphate receptor-1 agonists, connective tissue growth factor ligand inhibitors, caspase inhibitors, adrenocorticotrophic hormone ligands, Btk tyrosine kinase inhibitors, Complement C1s subcomponent inhibitors, Erythropoietin receptor agonists, B-lymphocyte stimulator ligand inhibitors, Cyclin-dependent kinase-2 inhibitors, P-selectin glycoprotein ligand-1 stimulators, mTOR inhibitors, Elongation factor 2 inhibitors, Cell adhesion molecule inhibitors, Factor XIII agonists, Calcineurin

inhibitors, Immunoglobulin G1 agonists, Inosine monophosphate dehydrogenase inhibitors, Complement C1s subcomponent inhibitors, Thymidine kinase modulators, Cytotoxic T-lymphocyte protein-4 modulators, Angiotensin II receptor antagonists, Angiotensin II receptor modulators, TNF superfamily receptor 12A antagonists, CD52 antagonists, Adenosine deaminase inhibitors, T-cell differentiation antigen CD6 inhibitors, FGF-7 ligands, dihydroorotate dehydrogenase inhibitors, Syk tyrosine kinase inhibitors, Interferon type I receptor antagonists, Interferon alpha ligand inhibitors, Macrophage migration inhibitory factor inhibitors, Integrin alpha-V/beta-6 antagonists, Cysteine protease stimulators, p38 MAP kinase inhibitors, TP53 gene inhibitors, Shiga like toxin I inhibitors, Fucosyltransferase 6 stimulators, Interleukin 22 ligands, IRS1 gene inhibitors, Protein kinase C stimulators, Protein kinase C alpha inhibitors, CD74 antagonists, Immunoglobulin gamma Fc receptor IIB antagonists, T-cell antigen CD7 inhibitors, CD95 antagonists, N acetylmannosamine kinase stimulators, Cardiotrophin-1 ligands, Leukocyte elastase inhibitors, CD40 ligand receptor antagonists, CD40 ligand modulators, IL-17 antagonists, TLR-2 antagonists, Mannan-binding lectin serine protease-2 (MASP-2) inhibitors, Factor B inhibitors, Factor D inhibitors, C3aR modulators, C5aR2 modulators, T cell receptor antagonists, PD-1 inhibitors, PD-L1 inhibitors, TIGIT inhibitors, TIM-3 inhibitors, LAG-3 inhibitors, VISTA inhibitors, STING agonists, IDO inhibitors, adenosine receptor modulators, CD39 inhibitors, CD73 inhibitors, antagonists of the chemokine receptors, especially CXCR1, CXCR2, CXCR3, CXCR4, CXCR7, CCR1, CCR2, CCR3, CCR4, CCR5, CCR7, CCR7, CCR9, CX3CR1 and CXCR6, and combinations thereof; or

(ii) selected from the group consisting of obinutuzumab, rituximab, ocrelizumab, cyclophosphamide, prednisone, hydrocortisone, hydrocortisone acetate, cortisone acetate, tixocortol pivalate, prednisolone, methylprednisolone, triamcinolone acetonide, triamcinolone alcohol, mometasone, amcinonide, budesonide, desonide, fluocinonide, fluocinolone acetonide, halcinonide, betamethasone, betamethasone sodium phosphate, dexamethasone, dexamethasone sodium phosphate, fluocortolone, hydrocortisone-17-valerate, halometasone, alclometasone dipropionate, beclomethasone, betamethasone valerate, betamethasone dipropionate, prednicarbate, clobetasone-17-

butyrate, clobetasol-17-propionate, fluocortolone caproate, fluocortolone pivalate, fluprednidene acetate, hydrocortisone-17-butyrate, hydrocortisone-17-aceponate, hydrocortisone-17-buteprate, ciclesonide and prednicarbate, GB-0998, immuglo, begelomab, alefacept, aldesleukin, gevokizumab, daclizumab, basiliximab, inolimomab, beperminogene perplasmid, sirukumab, tocilizumab, clazakizumab, mepolizumab, fingolimod, panobinostat, tricitiribine, nilotinib, imatinib, tofacitinib, momelotinib, peficitinib, itacitinib, infliximab, PEG-bHb-CO, etanercept, ixazomib, bortezomib, muromonab, orelizumab, gusperimus, brentuximab vedotin, Ponesimod, KRP-203, FG-3019, emricasan, corticotropin, ibrutinib, cinryze, conestat, methoxy polyethylene glycol-epoetin beta, belimumab, blisibimod, atacicept, seliciclib, neihulizumab, everolimus, sirolimus, denileukin diftitox, LMB-2, natalizumab, catridecacog, ciclosporin, tacrolimus, voclosporin, voclosporin, canakinumab, mycophenolate, mizoribine, CE-1145, TK-DLI, abatacept, belatacept, olmesartan medoxomil, sparsentan, TXA-127, BIIB-023, alemtuzumab, pentostatin, itolizumab, palifermin, leflunomide, PRO-140, cenicriviroc, fostamatinib, anifrolumab, sifalimumab, BAX-069, BG-00011, losmapimod, QPI-1002, ShigamAbs, TZ-101, F-652, reparixin, ladarixin, PTX-9908, aganirsen, APH-703, sotrastaurin, sotrastaurin, milatuzumab, SM-101, T-Guard, APG-101, DEX-M74, cardiotrophin-1, tiprelestat, ASKP-1240, BMS-986004, HPH-116, KD-025, OPN-305, TOL-101, defibrotide, pomalidomide, Thymoglobulin, laquinimod, remestemcel-L, Equine antithymocyte immunoglobulin, Stempeucel, LIV-Gamma, Octagam 10%, t2c-001, 99mTc-sestamibi, Clairyg, Prosorba, pomalidomide, laquinimod, teplizumab, FCRx, solnatide, foralumab, ATIR-101, BPX-501, ACP-01, ALLO-ASC-DFU, irbesartan + propagermanium, ApoCell, cannabidiol, RGI-2001, saratin, anti-CD3 bivalent antibody-diphtheria toxin conjugate, NOX-100, LT-1951, OMS721, ALN-CC5, ACH-4471, AMY-101, Acthar gel, and CD4+CD25+ regulatory T-cells, MEDI7814, P32, P59, pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, CCX354, CCX721, CCX9588, CCX140, CCX872, CCX598, CCX6239, CCX587, CCX624, CCX282, CCX025, CCX507, CCX430, CCX765, CCX758, CCX771, CCX662, CCX650, and combinations thereof.