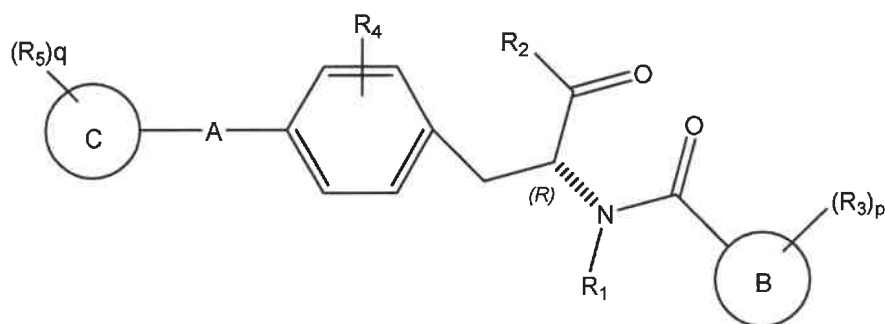
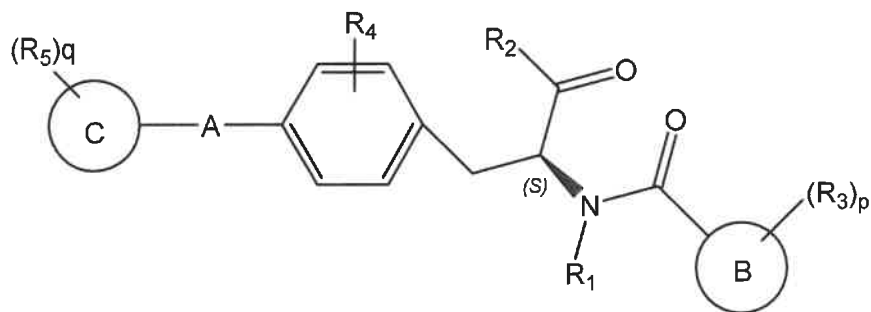


CLAIMS

1. A compound having the structure of Formula **I-R** or **I-S** or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof:



I-R



I-S

wherein

A is pyrimidinyl, pyridinyl, pyridazinyl or pyrazinyl, each of which may be optionally substituted with one or more of R_4 ;

B is phenyl or heterocycle;

C is a nonaromatic carbocyclyl;

each R_1 is independently H or C_{1-4} alkyl;

R_2 is $-OH$, $-O-R_8$, $-N(R_1)-SO_2-R_7$, $-NR_{41}R_{42}$, $-N(R_1)-(CR_aR_b)_m-COOR_8$, $-N(R_1)-(CR_aR_b)_m-CO-N(R_1)(R_{40})$, $-N(R_1)-(CR_aR_b)_m-N(R_1)C(O)O(R_8)$, $-N(R_1)-(CR_aR_b)_m-N(R_1)(R_{40})$, $-N(R_1)-(CR_aR_b)_m-CO-N(R_1)-heterocyclyl$, or $-N(R_1)-(CR_aR_b)_m-$

heterocyclyl, which heterocyclyl may be optionally (singly or multiply) substituted with R₇;

each R₃ and R₄ is independently H, halo, alkyl, alkyl substituted (singly or multiply) with R₃₁, alkoxy, haloalkyl, perhaloalkyl, haloalkoxy, perhaloalkoxy, aryl, heterocyclyl, -OH, -OR₇, -CN, -NO₂, -NR₁R₇, -C(O)R₇, -(O)NR₁R₇, -NR₁C(O)R₇, -SR₇, -S(O)R₇, -S(O)₂R₇, -OS(O)₂R₇, -S(O)₂NR₁R₇, -NR₁S(O)₂R₇, -(CR_aR_b)_mNR₁R₇, -(CR_aR_b)_mO(CR_aR_b)_mR₇, -(CR_aR_b)_mNR₁(CR_aR_b)_mR₇ or -(CR_aR_b)_mNR₁(CR_aR_b)_mCOOR₈; or any two R₃ or R₄ groups on the same carbon atom taken together form oxo;

R₅ is R₇, -(CR_aR_b)_m-(CR_aR_b)_m-R₇, or -(L₃-(CR_aR_b)_r-L₃-R₇, wherein the carbon atoms of any two adjacent -(CR_aR_b)_m or (CR_aR_b)_r groups may be taken together to form a double bond -(C(R_a)=C(R_a)-) or triple bond (-C≡C-);

R₆ is H, alkyl, aryl, heteroaryl, heterocyclyl, heterocycloalkyl, any of which may be optionally substituted (singly or multiply) with R₇ or -(CR_aR_b)_m-L₂-(CR_aR_b)_m-R₇;

each R₇ is independently R₁₀; a ring moiety selected from cycloalkyl, aryl, aralkyl, heterocyclyl or heterocyclalkyl, where such ring moiety is optionally (singly or multiply) substituted with R₁₀; or when a carbon atom bears two R₇ groups such two R₇ groups are taken together to form oxo or thioxo, or are taken together to form a ring moiety selected from cycloalkyl, aryl, heterocyclyl or heterocyclalkyl, wherein such ring moiety is optionally singly or multiply substituted with R₁₀;

each R₈ is independently H, alkyl, haloalkyl, aryl, -(CR_aR_b)_m-L₂-(CR_aR_b)_m-R₁ or -(L₃-(CR_aR_b)_r-L₃-R₁;

each R₁₀ is independently H, halo, alkyl, haloalkyl, haloalkoxy, perhaloalkyl, perhaloalkoxy, -(CR_aR_b)_mOH, -(CR_aR_b)_mOR₈, -(CR_aR_b)_mCN, -(CR_aR_b)_mNH(C=NH)NH₂, -(CR_aR_b)_mNR₁R₈, -(CR_aR_b)_mO(CR_aR_b)_mR₈, -(CR_aR_b)_mNR₁(CR_aR_b)_mR₈, -(CR_aR_b)_mC(O)R₈, -(CR_aR_b)_mC(O)OR₈, -(CR_aR_b)_mC(O)NR₁R₈, -(CR_aR_b)_mNR₁(CR_aR_b)_mC(O)OR₈, -(CR_aR_b)_mNR₁C(O)R₈, -(CR_aR_b)_mC(O)NR₁S(O)₂R₈, -(CR_aR_b)_mSR₈, -(CR_aR_b)_mS(O)R₈, -(CR_aR_b)_mS(O)₂R₈, -(CR_aR_b)_mS(O)₂NR₁R₈ or -(CR_aR_b)_mNR₁S(O)₂R₈;

each R₃₁ is independently H, halo, hydroxyl, -NR₄₁R₄₂, or alkoxy;

each R_{40} is independently H, R_7 , alkyl which may be optionally (singly or multiply) substituted with R_7 , or R_{40} and R_1 taken together with the N atom to which they are attached form a 3- to 7-membered heterocyclyl which may be optionally (singly or multiply) substituted with R_7 ;

each R_{41} and R_{42} is independently R_{40} , $-(CHR_{40})_n-C(O)O-R_{40}$, $-(CHR_{40})_n-C(O)-R_{40}$, $-(CH_2)_n-N(R_1)(R_7)$, aryl or heteroaryl any of which aryl or heteroaryl may be optionally (singly or multiply) substituted with R_7 ; or any two R_{41} and R_{42} taken together with the N atom to which they are attached form a 3- to 7-membered heterocyclyl which may be optionally (singly or multiply) substituted with R_7 ;

each R_a and R_b is independently H, halo, alkyl, alkoxy, aryl, aralkyl, heterocyclyl, heterocyclylalkyl (any of which alkyl, alkoxy, aryl, aralkyl, heterocyclyl or heterocyclylalkyl may be optionally (singly or multiply) substituted with R_7 , $-(CHR_{40})_mC(O)OR_{40}$, $-(CHR_{40})_mOR_{40}$, $-(CHR_{40})_mSR_{40}$, $-(CHR_{40})_mNR_{41}R_{42}$, $-(CHR_{40})_mC(O)NR_{41}R_{42}$, $-(CHR_{40})_mC(O)N(R_1)(CHR_{40})_mNR_{41}R_{42}$, $-(CHR_{40})_mC(O)N(R_1)(CHR_{40})_mC(O)NR_{41}R_{42}$, $-(CHR_{40})_mC(O)N(R_1)-(CHR_{40})_mC(O)OR_{40}$, or $-(CHR_{40})_m-S-S-R_{40}$; or any two R_a and R_b taken together with the carbon atom(s) to which they are attached form a cycloalkyl or heterocyclyl optionally substituted (singly or multiply) with R_7 ; or R_1 and any one of R_a or R_b taken together with the atoms to which they are attached form heterocyclyl optionally substituted (singly or multiply) with R_7 ;

L_2 is independently, from the proximal to distal end of the structure of Formula **I-R** or **I-S**, null, $-O-$, $-OC(O)-$, $-NR_1-$, $-C(O)NR_1-$, $-N(R_1)-C(O)-$, $-S(O_2)-$, $-S(O)-$, $-S-$, $-C(O)-$ or $-S(O_2)-N(R_1)-$;

each L_3 is independently null, $-O-$, or $-N(R_1)-$

each m is independently 0, 1, 2, 3, 4, 5 or 6;

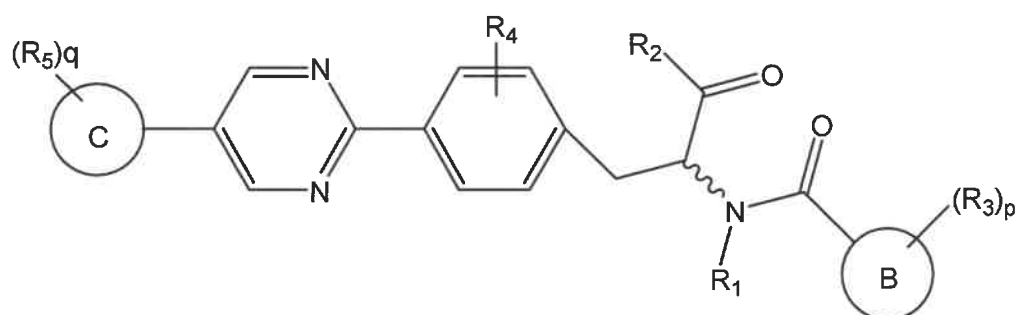
p is 0, 1, 2 or 3;

q is 0, 1, 2 or 3;

each r is independently 2, 3, or 4; and

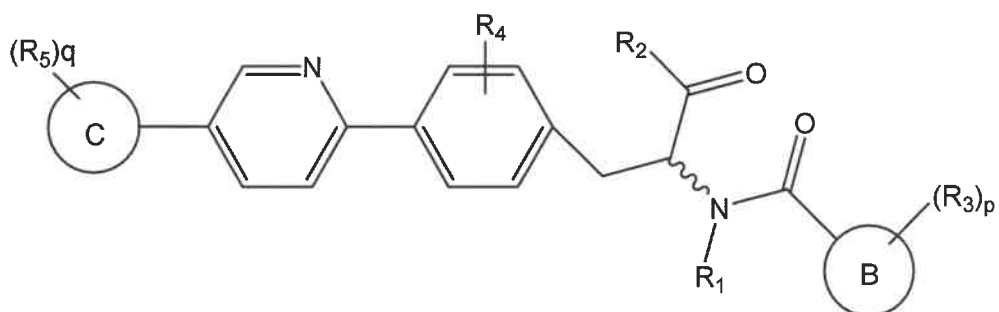
each s is independently 1, 2, 3, or 4.

2. The compound of claim 1 having the following structure:

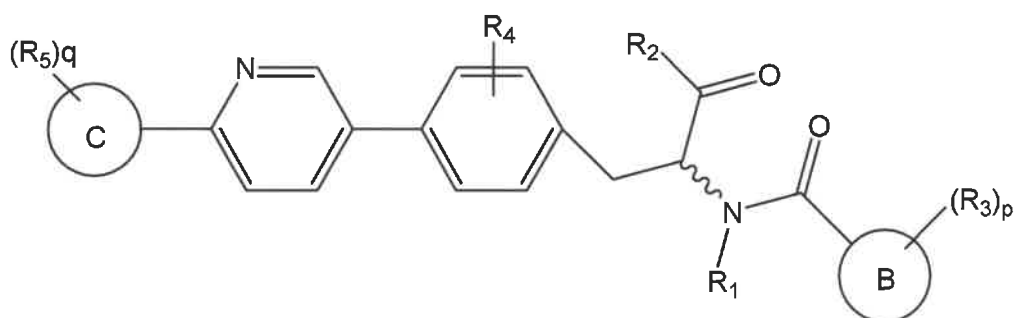


I-R/S (1).

3. The compound of claim 1 having the following structure:

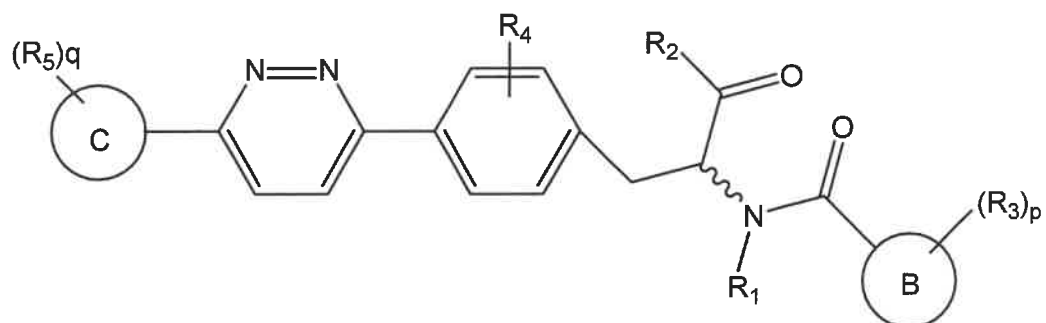


I-R/S (2) or

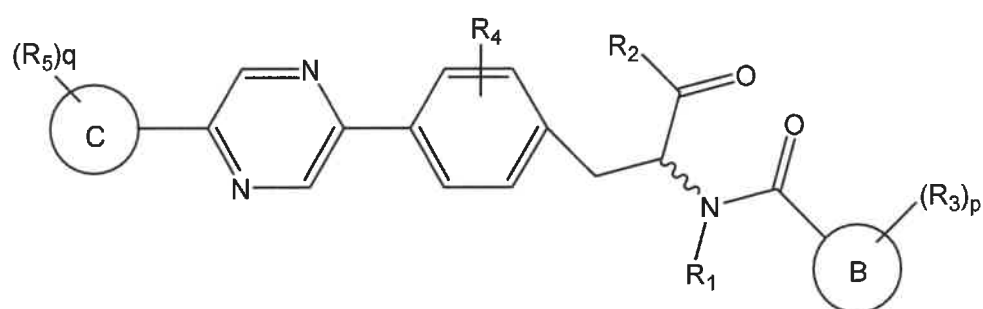


I-R/S (3).

4. The compound of claim 1 having the following structure:

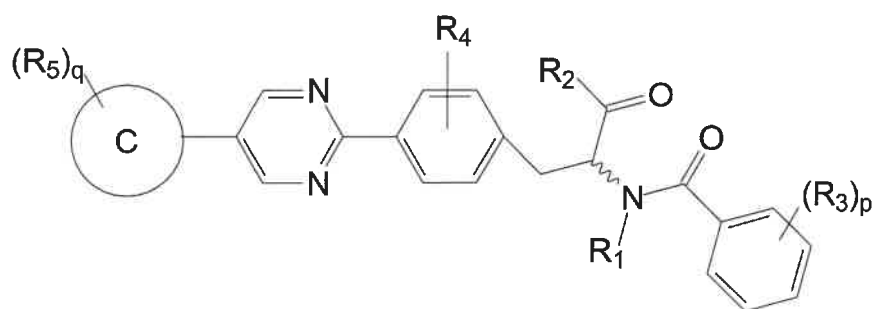


I-R/S (4) or



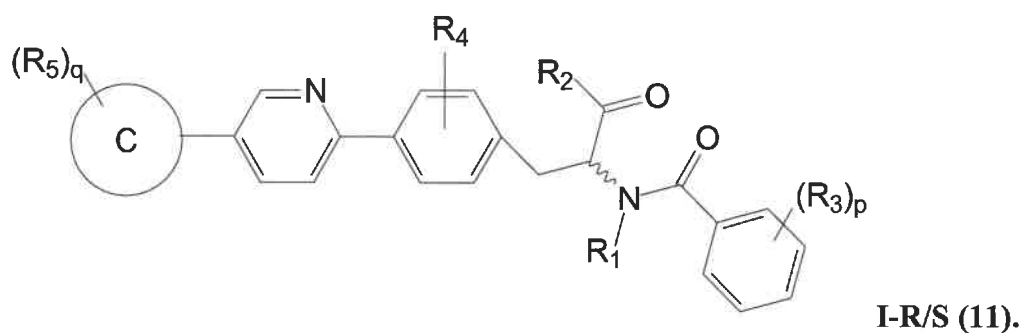
I-R/S (5).

5. The compound of claim 1 having the following structure:

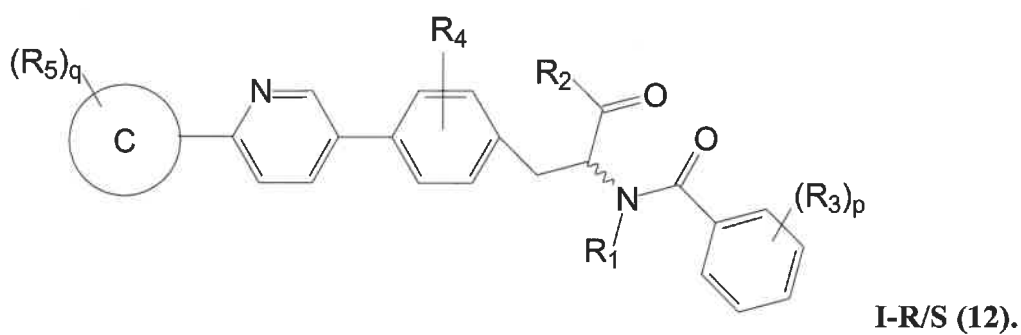


I-R/S (10).

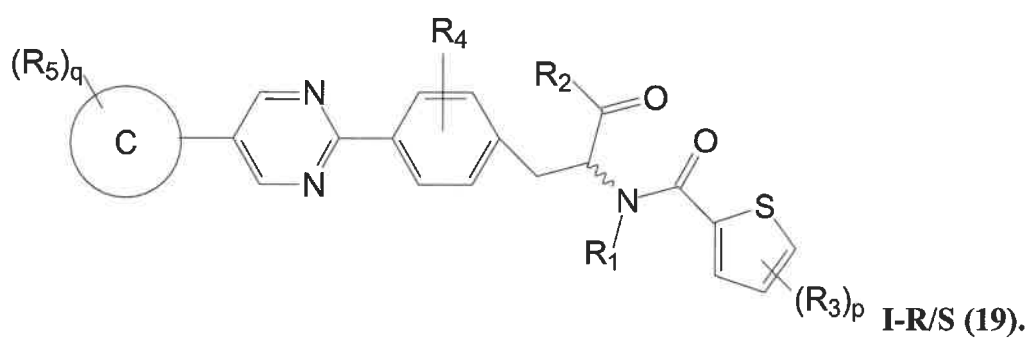
6. The compound of claim 1 having the following structure:



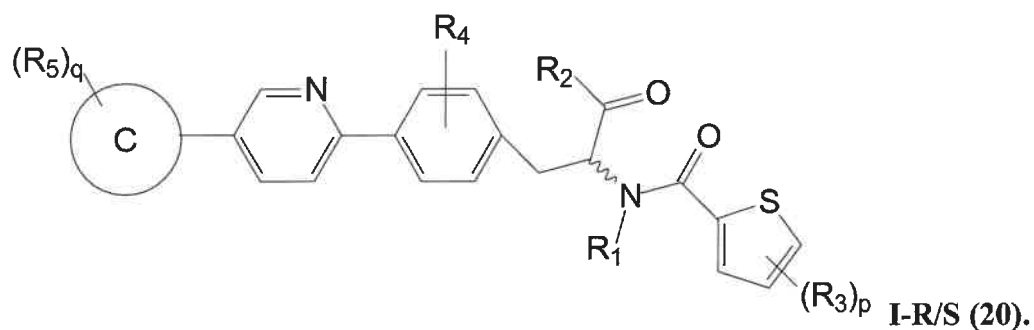
7. The compound of claim 1 having the following structure:



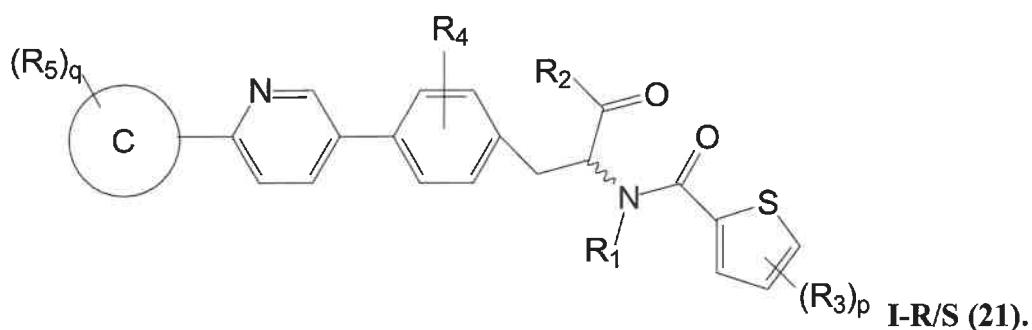
8. The compound of claim 1 having the following structure:



9. The compound of claim 1 having the following structure:

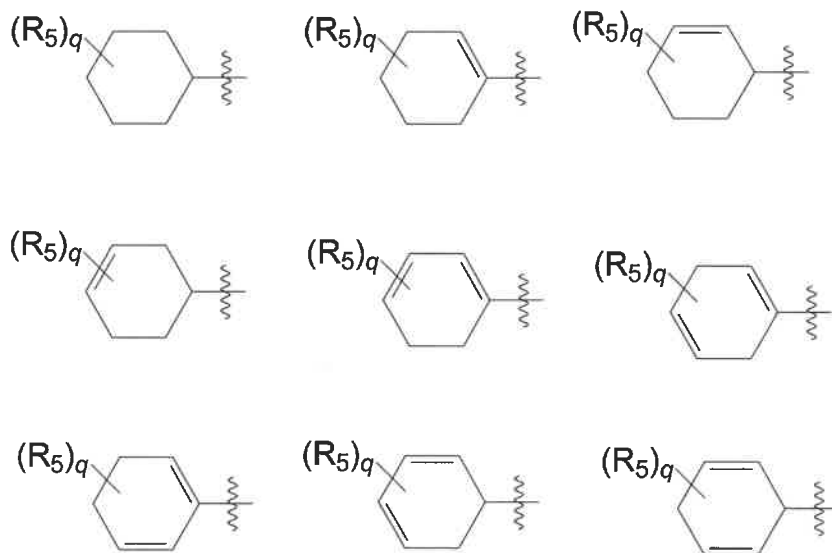


10. The compound of claim 1 having the following structure:

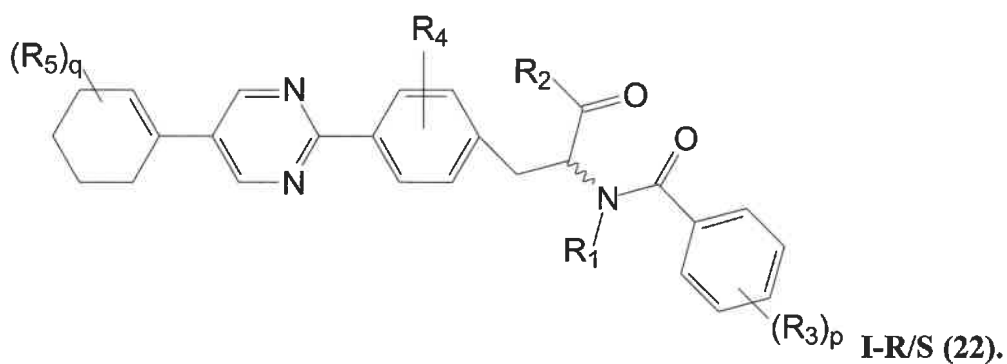


11. The compound of claim 1 wherein B is pyrimidinyl.
12. The compound of claim 1 wherein B is pyrazolyl.
13. The compound of claim 1 wherein B is pyridinyl.
14. The compound of claim 1 wherein B is indolyl.
15. The compound of claim 1 wherein nonaromatic carbocyclyl is cycloalkyl.
16. The compound of claim 1 wherein nonaromatic carbocyclyl is cycloalkenyl.

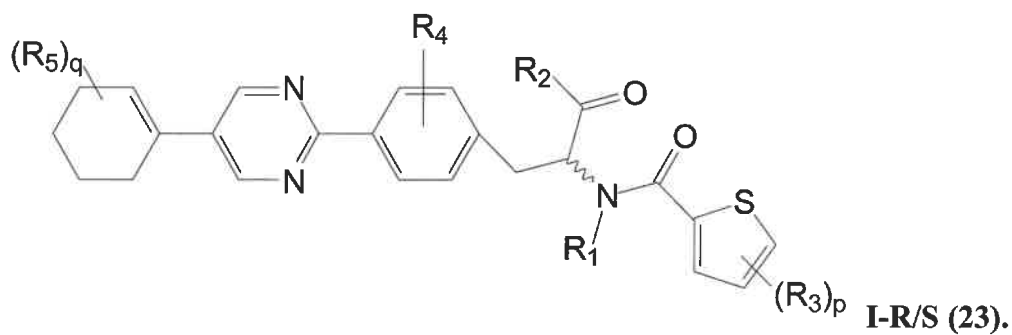
17. The compound of any one of claims 1-14 wherein C is selected from:



18. The compound of claim 1 having the following structure:

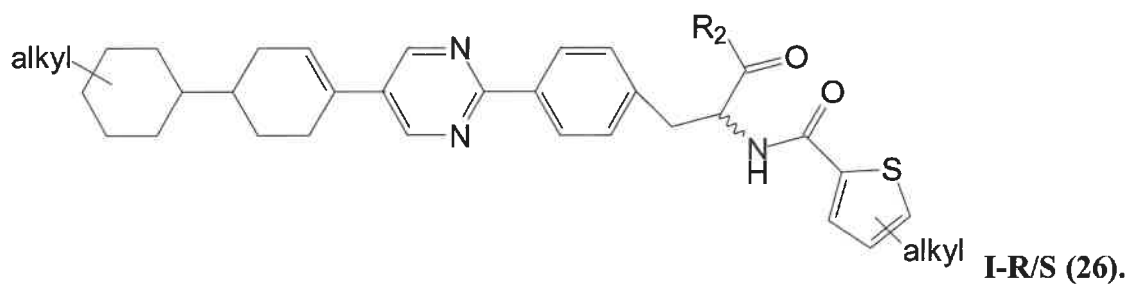


19. The compound of claim 1 having the following structure:

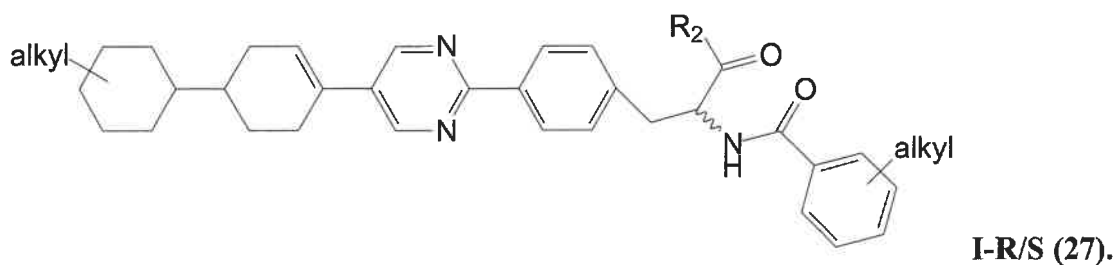


20. The compound of any one of claims 1-19 wherein R_1 is H.
21. The compound of any one of claims 1-19 wherein R_4 is H.
22. The compound of any one of claims 1-19 wherein q is one.
23. The compound of claim 22 wherein R_5 is alkyl.
24. The compound of any one of claims 1-19 wherein p is one.
25. The compound of claim 24 wherein R_3 is alkyl.
26. The compound of claim 25 wherein alkyl is a straight or branched alkyl.
27. The compound of claim 25 wherein alkyl is cycloalkyl.

28. The compound of claim 1 having the following structure:



29. The compound of claim 1 having the following structure:



30. The compound of any one of claims 28-29 wherein each alkyl is independently a C₁-C₈ straight or branched alkyl.

31. The compound of any one of claims 28-29 wherein each alkyl is independently methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl or tert-butyl.

32. The compound of any one of claims 1-31 wherein R₂ is – N(R₁)(CR_aR_b)_mCOOR₈.

33. The compound of claim 32 wherein m is 2, R₁ is hydrogen, each occurrence of R_a and R_b are hydrogen, and R₈ is hydrogen.

34. The compound of claim 32 wherein m is 1, R₁, R_b and R₈ are hydrogen, and R_a is as defined in claim 1.

35. The compound of claim 32 wherein m is 2, a single R_a is hydrogen and the other R_a is as defined in claim 1, each occurrence of R_b is hydrogen, and R₁ and R₈ are hydrogen.

36. The compound of claim 35 wherein the other R_a is alkyl optionally substituted with R₇.

37. The compound of claim 35 wherein the other R_a is a straight or branched alkyl selected from methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl and tert-butyl.

38. The compound of claim 37 wherein the other R_a is methyl.

39. The compound of claim 35 wherein the other R_a is cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl.

40. The compound of claim 35 wherein the other R_a is heterocyclyl optionally substituted with R_7 or heterocyclylalkyl optionally substituted with R_7 .

41. The compound of claim 35 wherein the other R_a is aryl optionally substituted with R_7 or aralkyl optionally substituted with R_7 .

42. The compound of claim 35 wherein the other R_a is $-(CHR_{40})_mC(O)OR_{40}$, $-(CHR_{40})_mOR_{40}$, $-(CHR_{40})_mSR_{40}$, $-(CHR_{40})_mNR_{41}R_{42}$, $-(CHR_{40})_mC(O)NR_{41}R_{42}$, $-(CHR_{40})_mC(O)N(R_1)(CHR_{40})_mNR_{41}R_{42}$, $-(CHR_{40})_mC(O)N(R_1)(CHR_{40})_mC(O)NR_{41}R_{42}$, $-(CHR_{40})_mC(O)N(R_1)(CHR_{40})_mC(O)OR_{40}$, or $-(CHR_{40})_m-S-S-R_{40}$.

43. The compound of claim 32 wherein m is 1, R_b is hydrogen and R_1 and R_a taken together with the atoms to which they are attached form a heterocyclyl optionally substituted with R_7 .

44. The compound of claim 32 wherein m is 2, R_b of the second (CR_aR_b) group is hydrogen and R_1 and R_a of the second (CR_aR_b) group taken together with the atoms to which they are attached form a heterocyclyl optionally substituted with R_7 .

45. The compound of any one of claims 1-31 wherein R_2 is $-OH$

46. The compound of any one of claim 1-31 wherein R_2 is $-N(R_1)-SO_2-R_8$.

47. The compound of any one of claims 1-31 wherein R_2 is $-N(R_{41})(R_{42})$.

48. The compound of claim 47 wherein R_{41} and R_{42} are independently R_{40} , $-(CHR_{40})_n-C(O)OR_{40}$, $-(CHR_{40})_n-C(O)R_{40}$, $-(CH_2)_nN(R_1)(R_7)$, aryl optionally substituted with R_7 , or heteroaryl optionally substituted with R_7 .

49. The compound of claim 47 wherein R_{41} is hydrogen and R_{42} is alkyl optionally substituted with R_7 .

50. The compound of claim 47 wherein R_{41} is hydrogen and R_{42} is $-(CHR_{40})_n-C(O)OR_{40}$, $-(CHR_{40})_n-C(O)R_{40}$, $-(CH_2)_nN(R_1)(R_7)$, aryl optionally substituted with R_7 , or heteroaryl optionally substituted with R_7 .

51. The compound of claim 47 wherein R_{41} and R_{42} taken together with the N atom to which they are attached form a 3- to 7-membered heterocyclyl optionally substituted with R_7 .

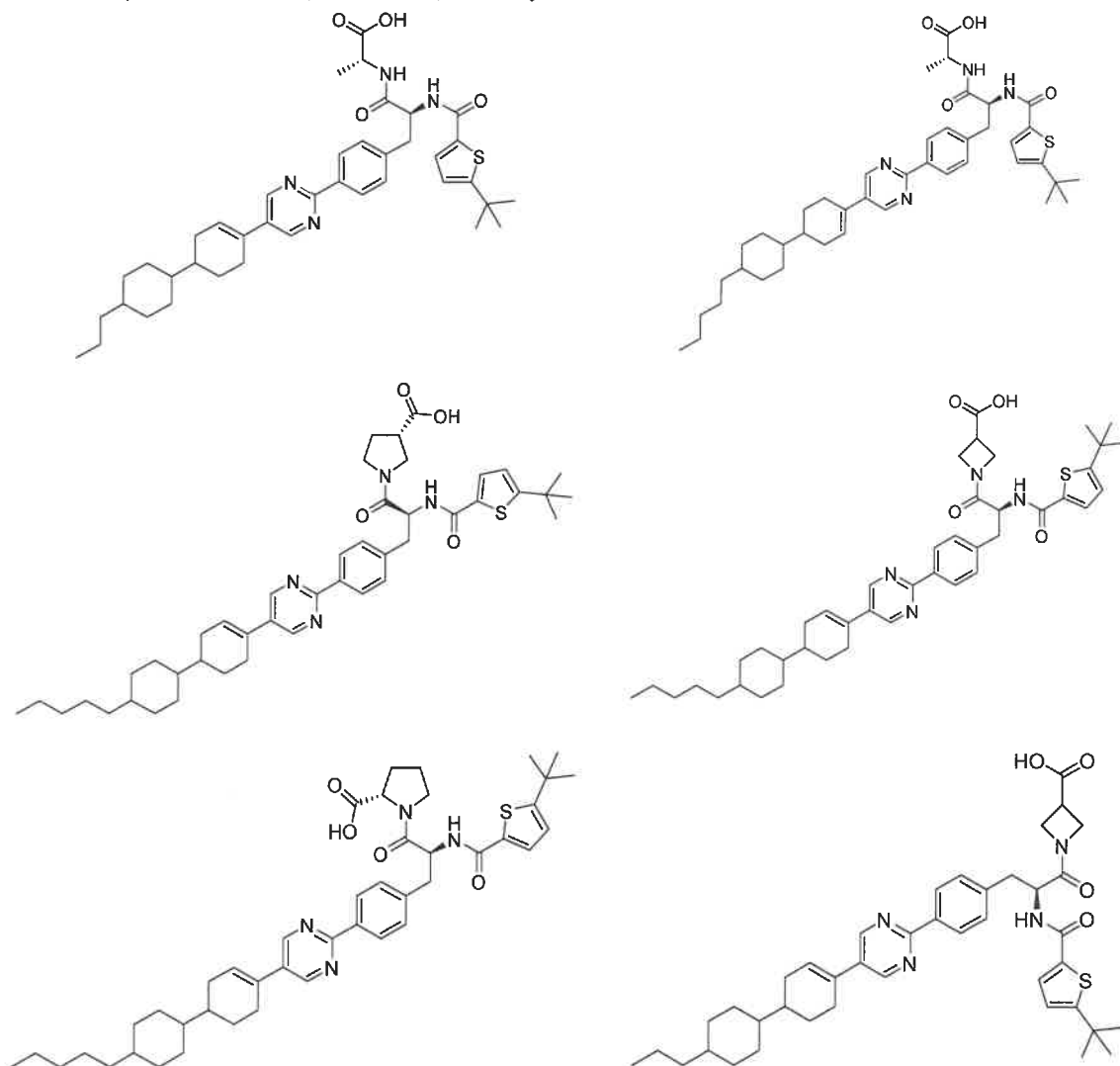
52. The compound of any one of claims 1-31 wherein R_2 is $-N(R_1)(CR_aR_b)_mCON(R_1)(R_{40})$.

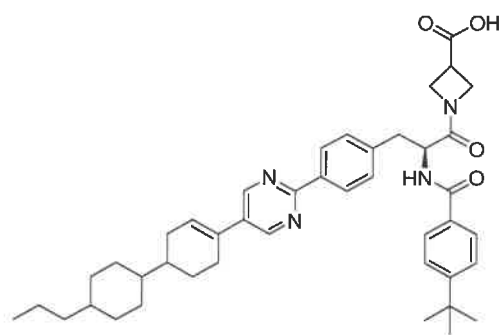
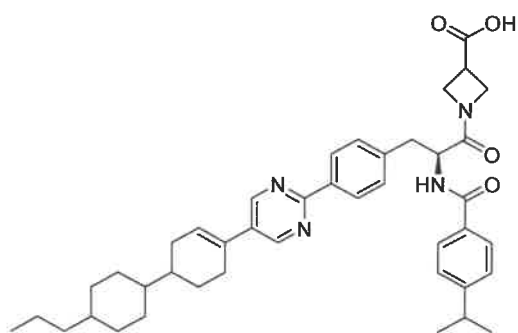
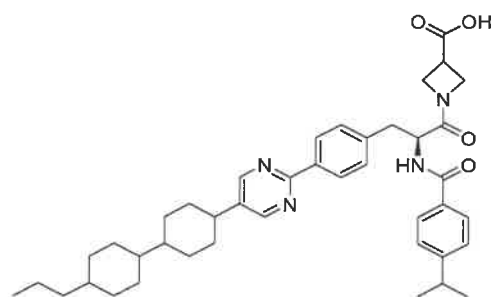
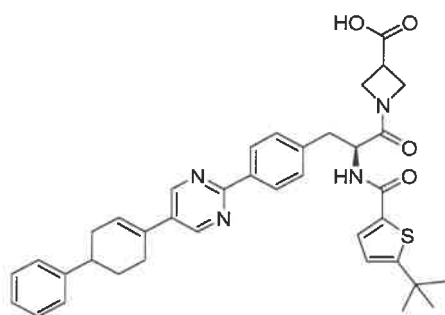
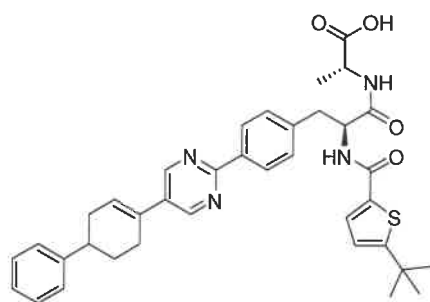
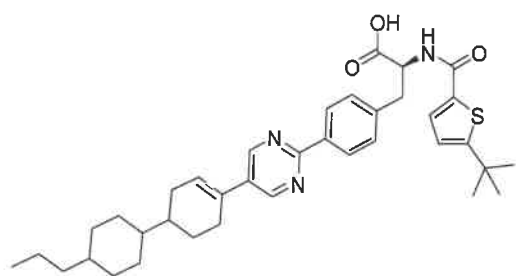
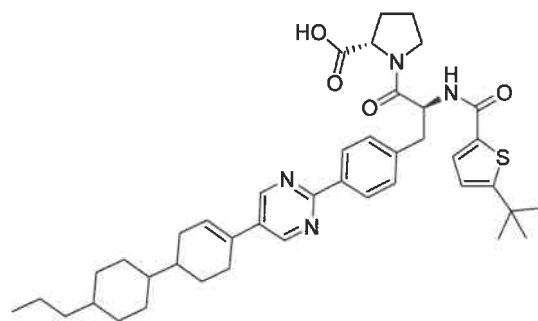
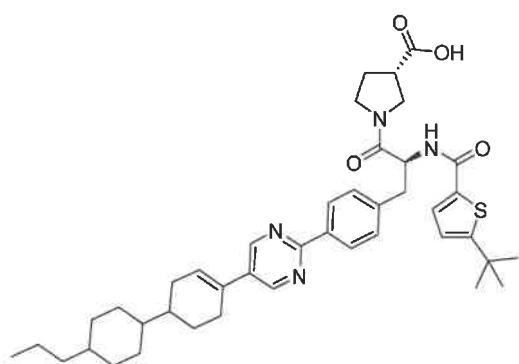
53. The compound of claim 52 wherein m is 1, R_b is hydrogen and R_1 and R_a taken together with the atoms to which they are attached form a heterocyclyl optionally substituted with R_7 .

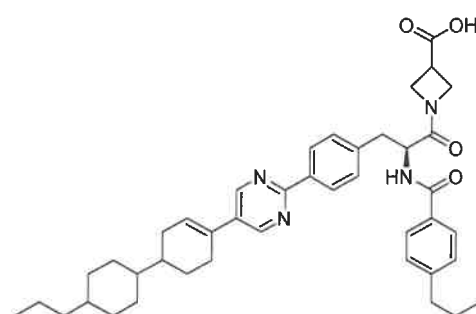
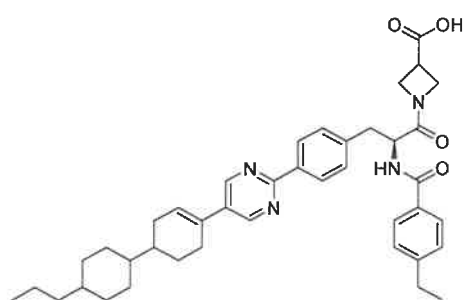
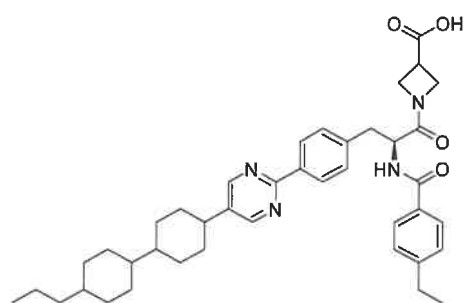
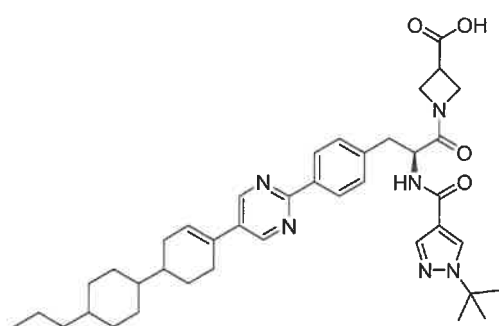
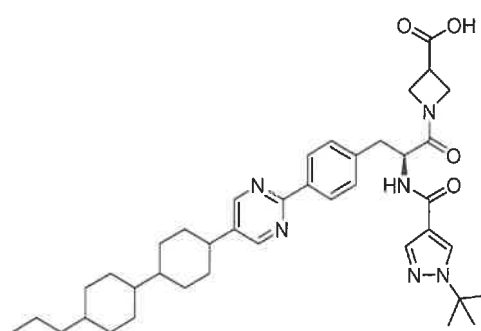
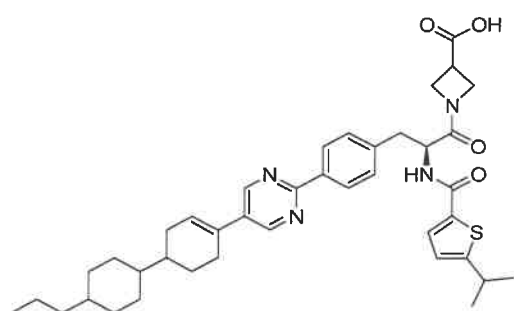
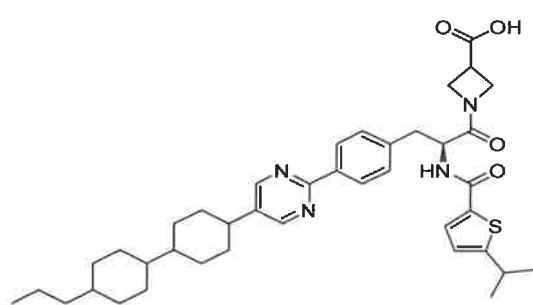
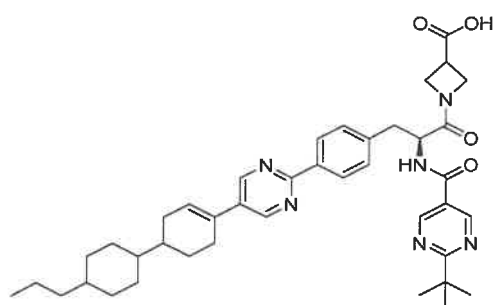
54. The compound of claim 52 wherein m is 2, R_b of the second (CR_aR_b) group is hydrogen and R_1 and R_a of the second (CR_aR_b) group taken together with the atoms to which they are attached form a heterocyclyl optionally substituted with R_7 .

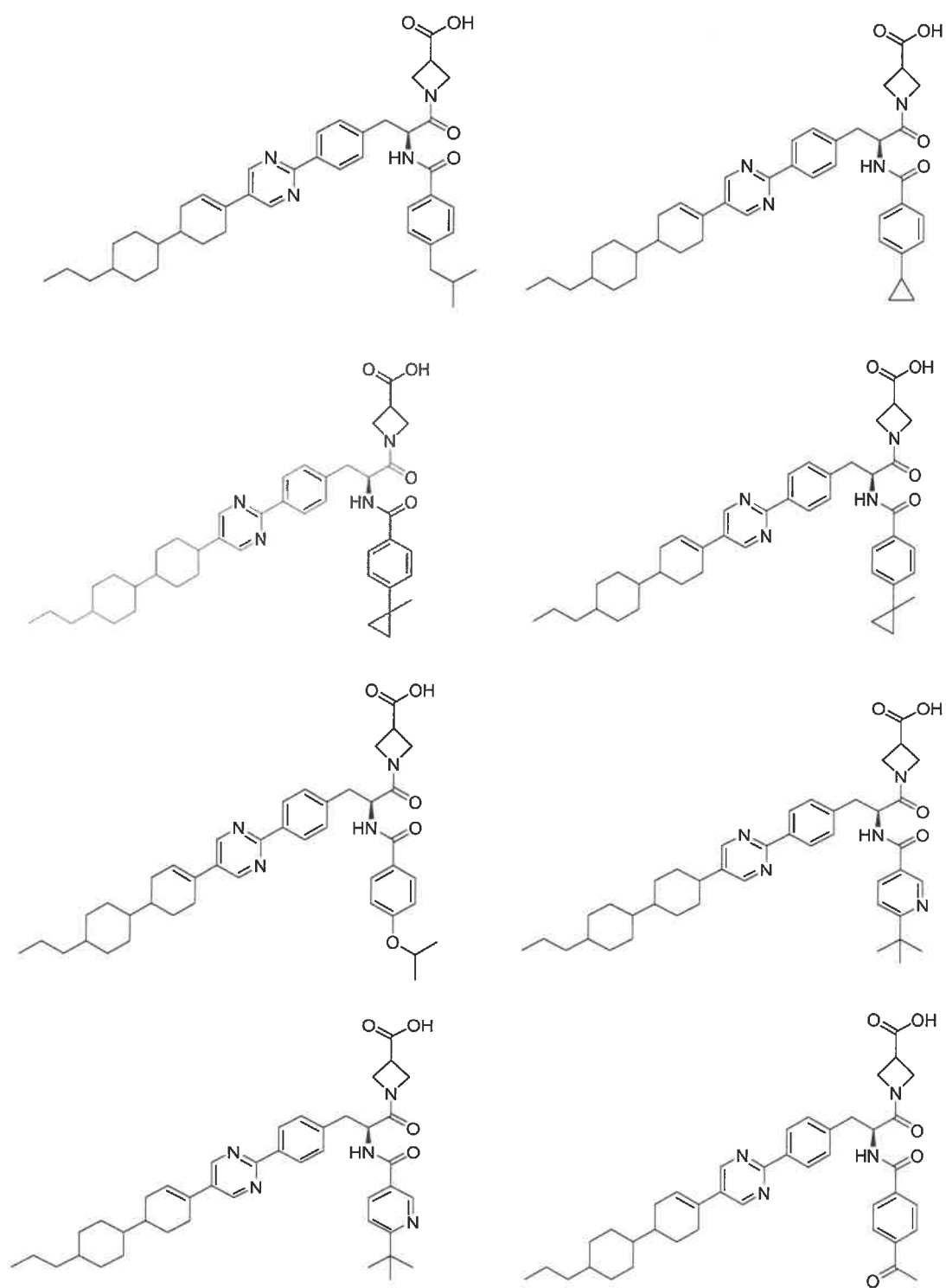
55. The compound of any one of claims 1-31 wherein R_2 is $-N(R_1)(CR_aR_b)_mN(R_1)C(O)OR_8$, $-N(R_1)(CR_aR_b)_mN(R_1)(R_7)$, $-N(R_1)(CR_aR_b)_mCON(R_1)$ -heterocyclyl, or $-(CR_aR_b)_mN(R_1)$ -heterocyclyl.

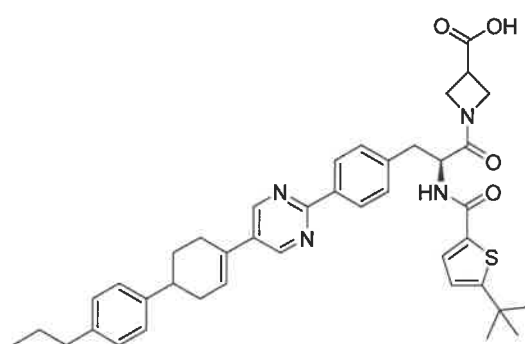
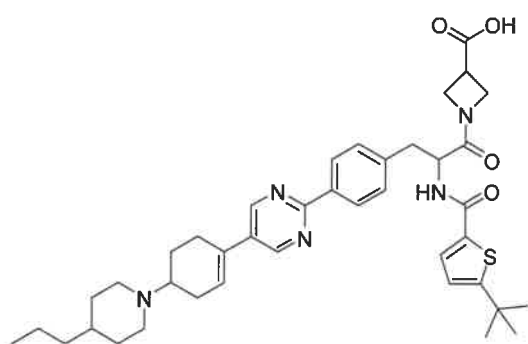
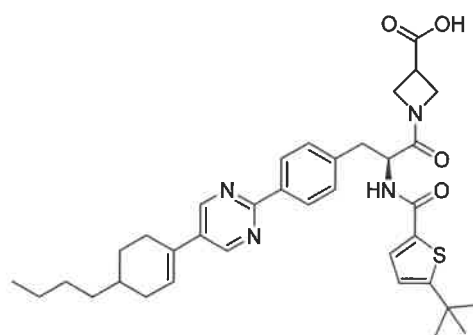
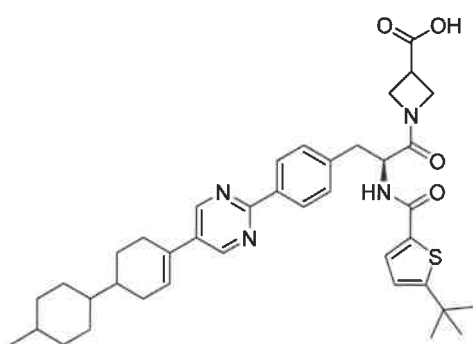
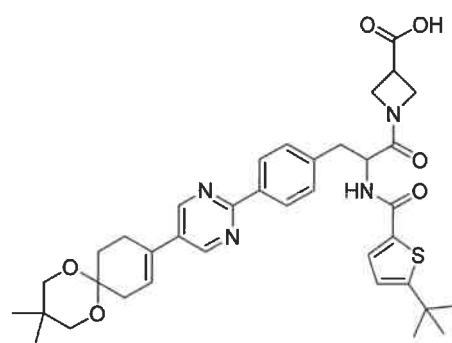
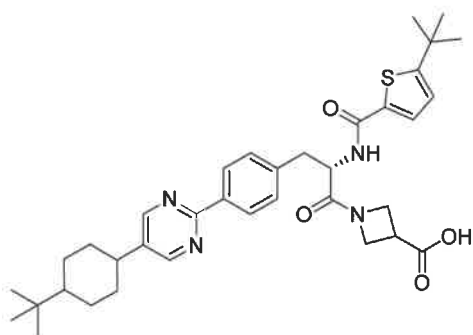
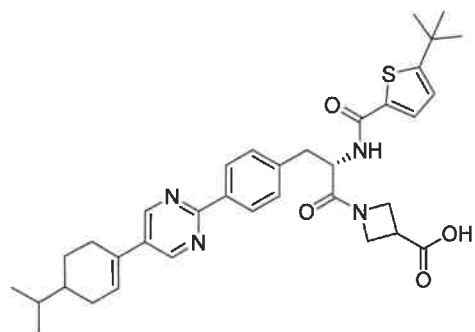
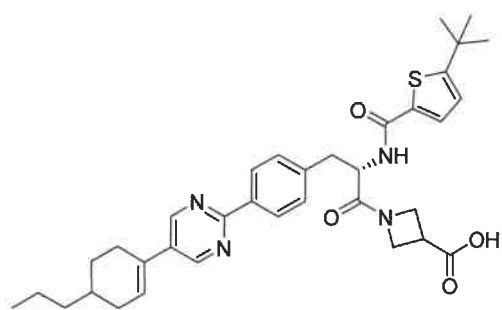
56. The compound of claim 1, wherein the compound has the structure of any one of the following compounds, or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof:

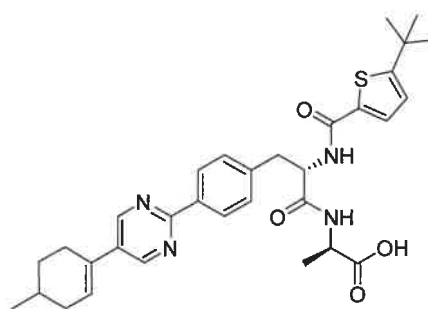
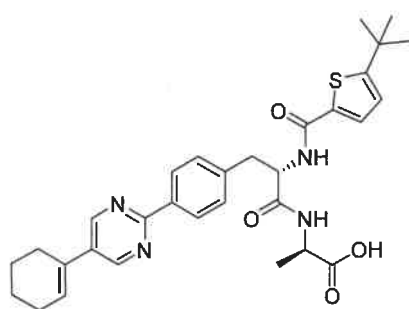
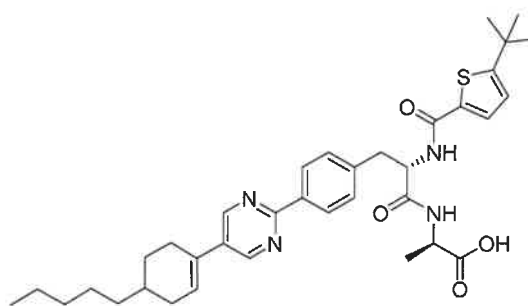
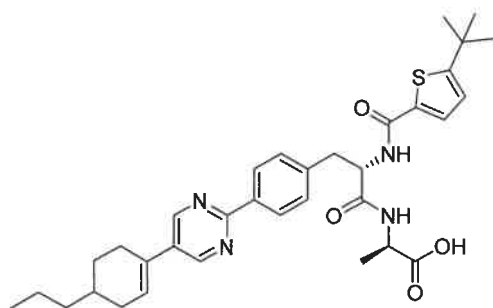
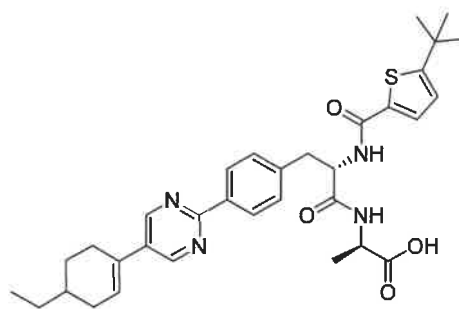
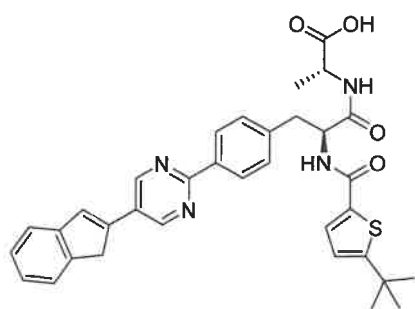
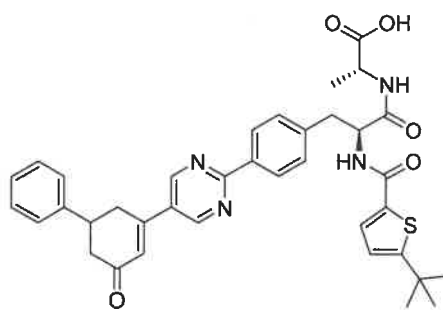
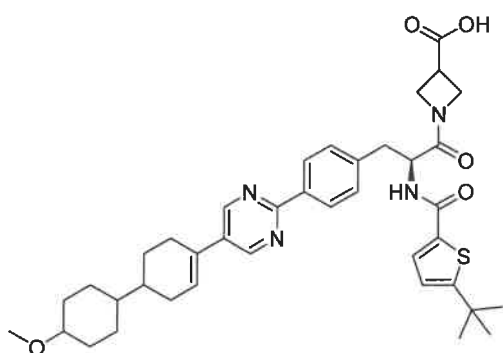


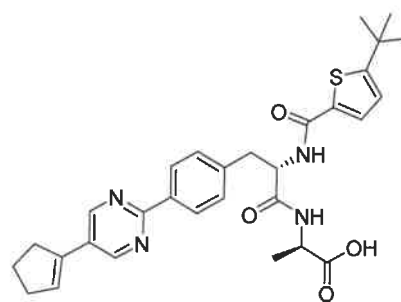
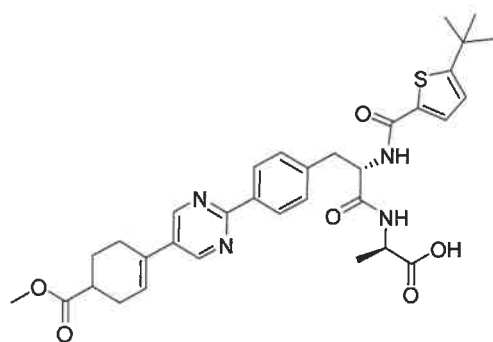
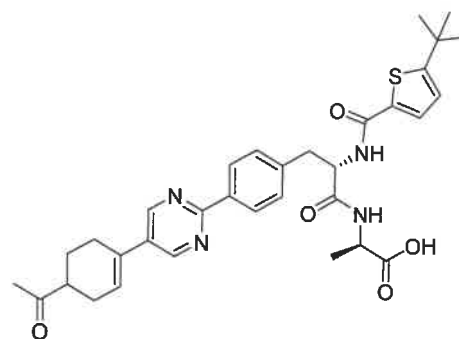
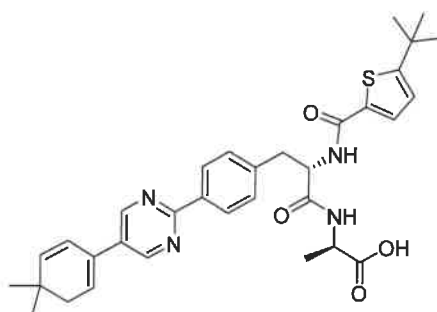
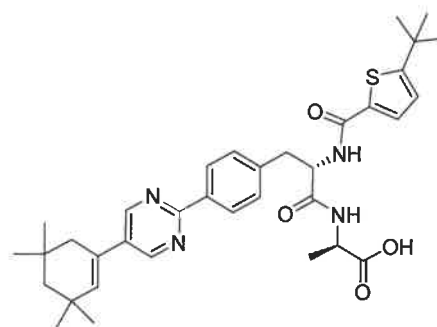
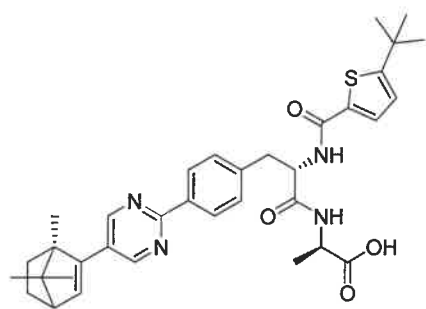
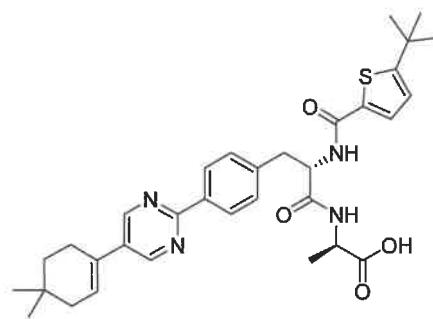
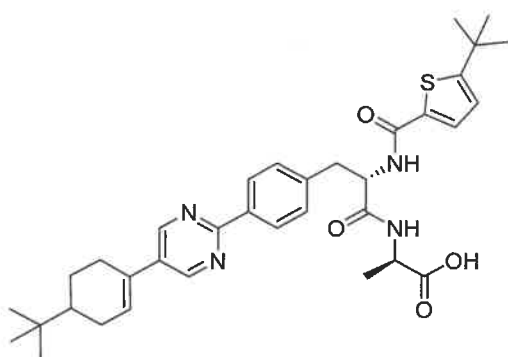


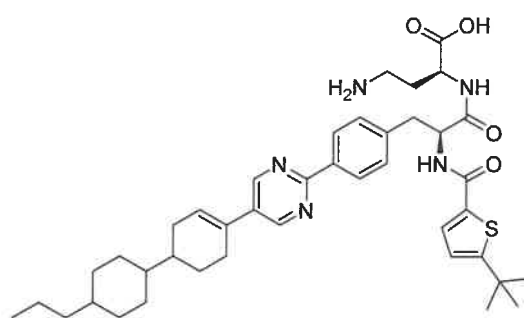
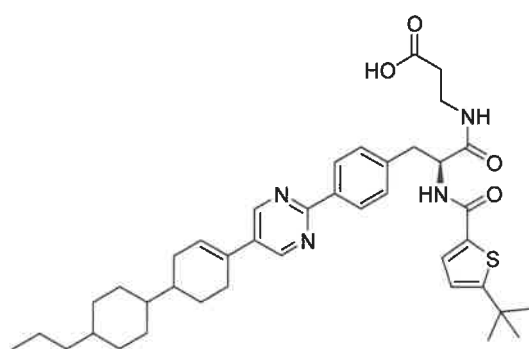
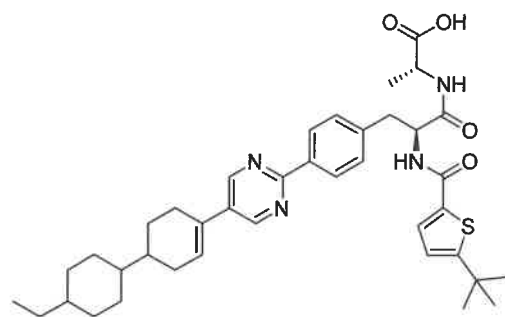
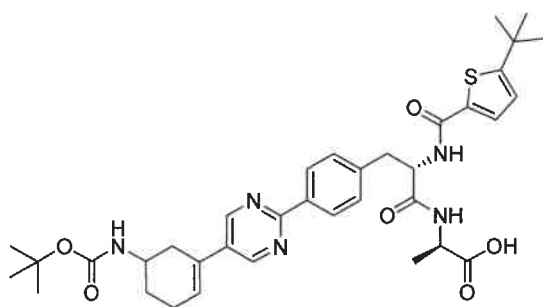
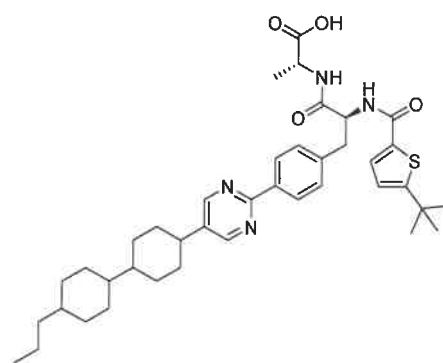
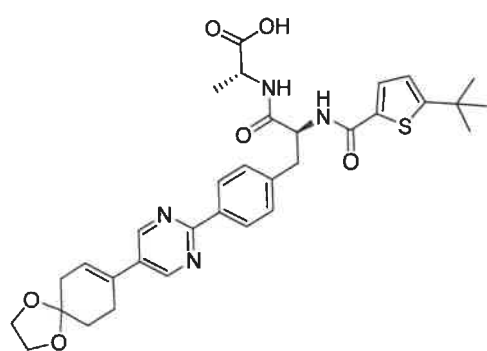
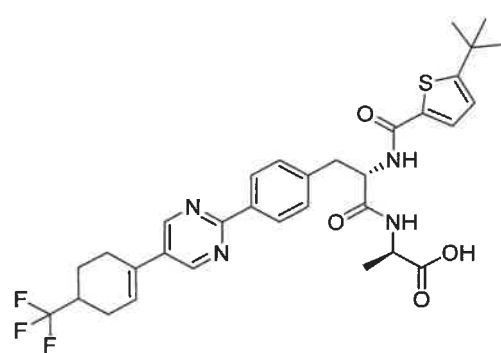
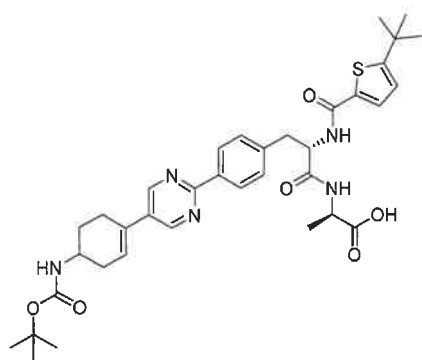


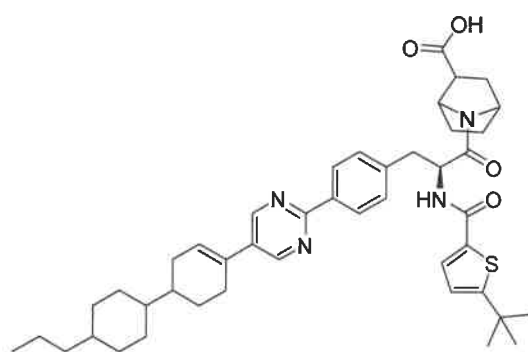
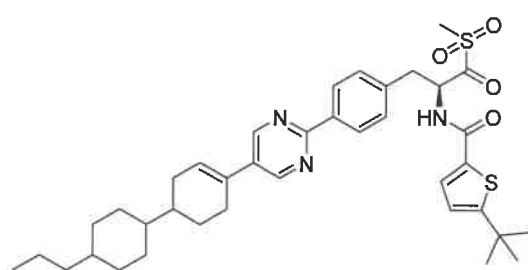
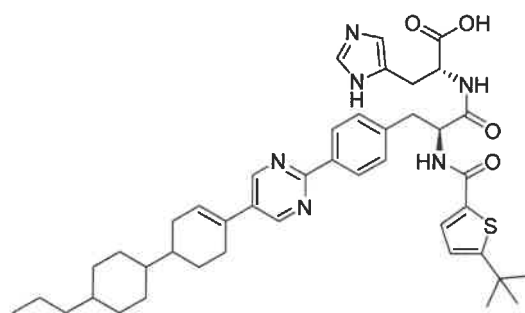
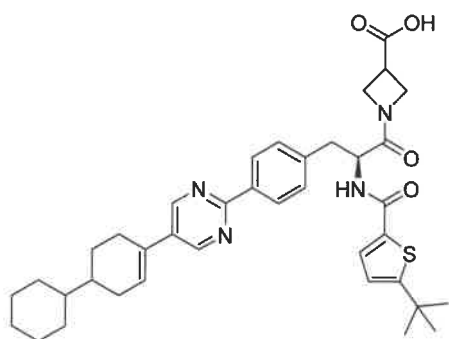
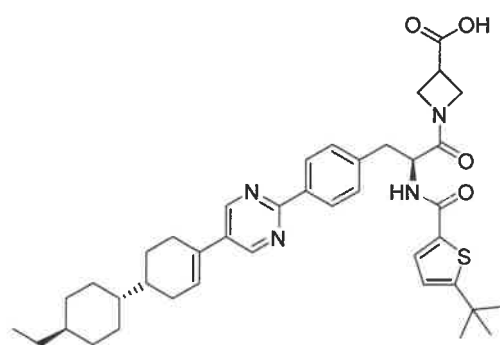
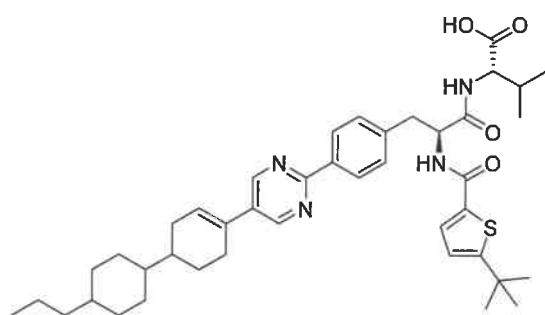
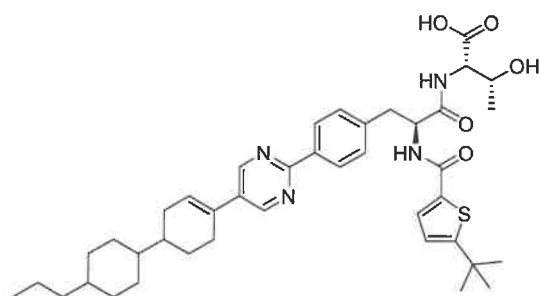
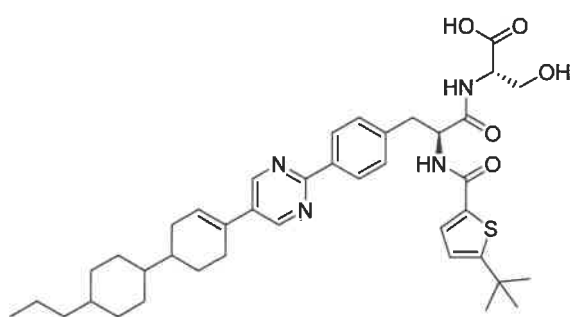


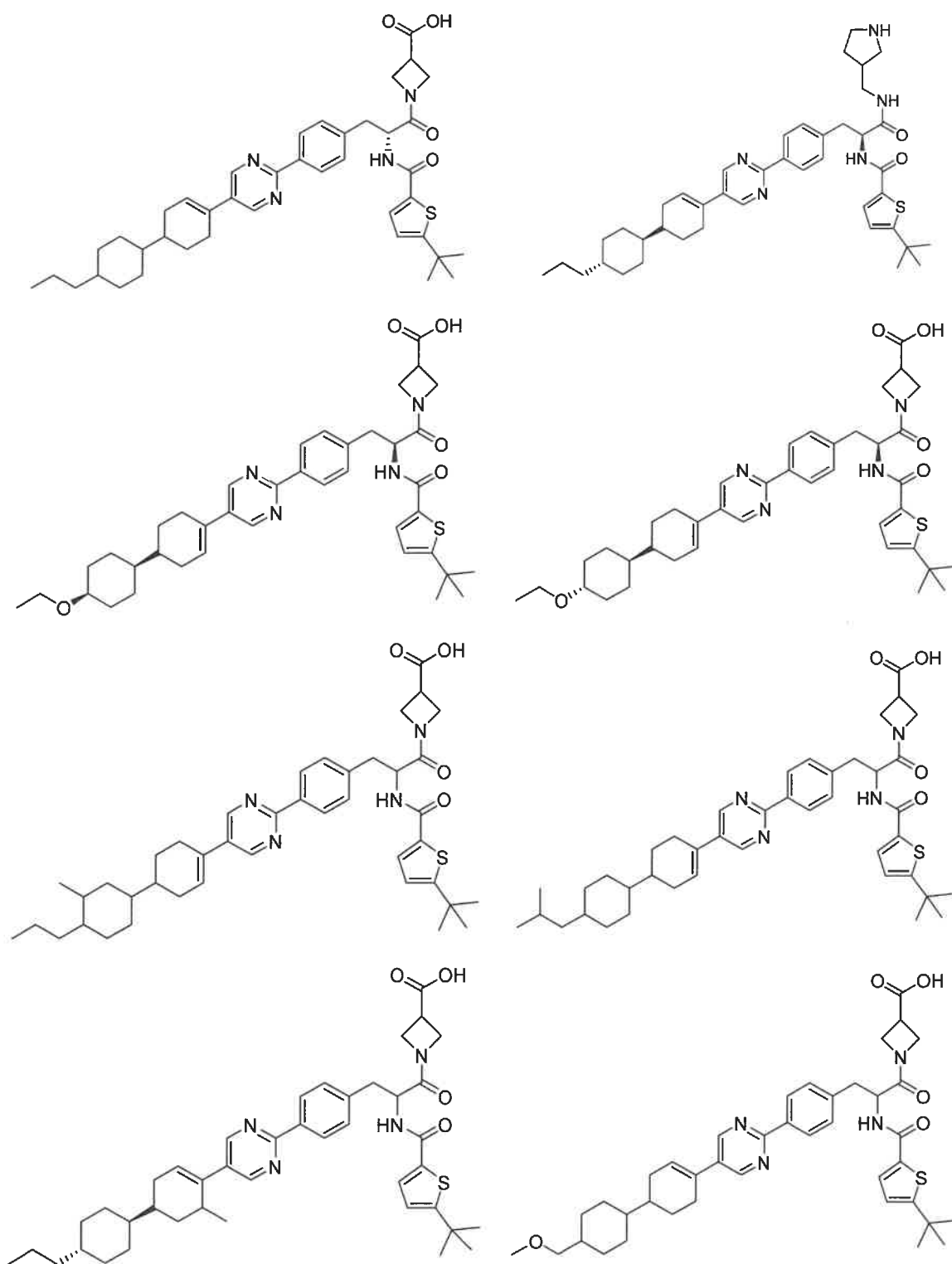


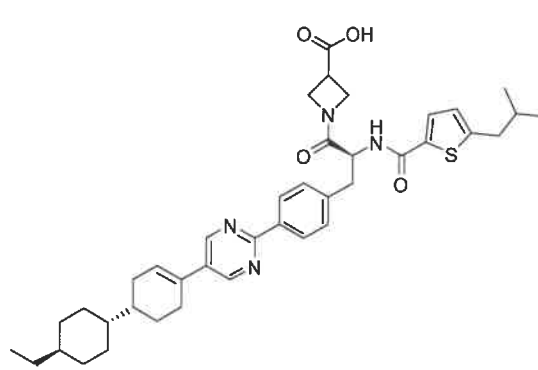
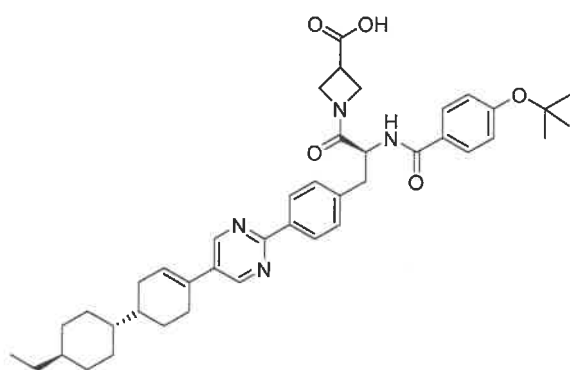
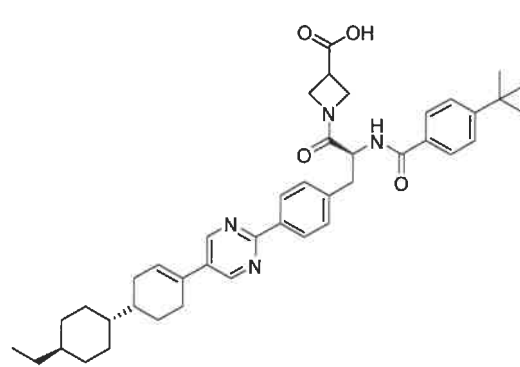
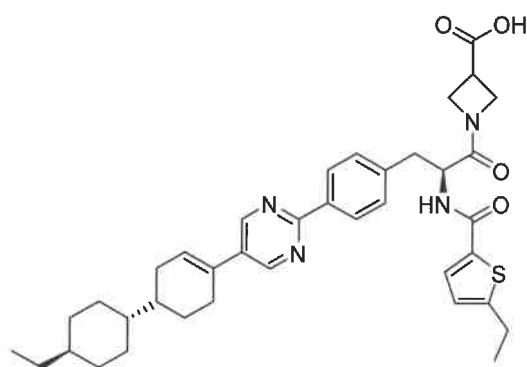
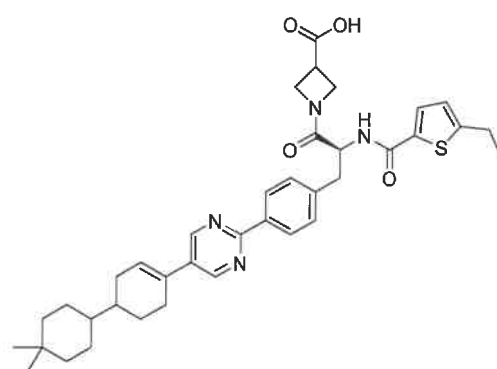
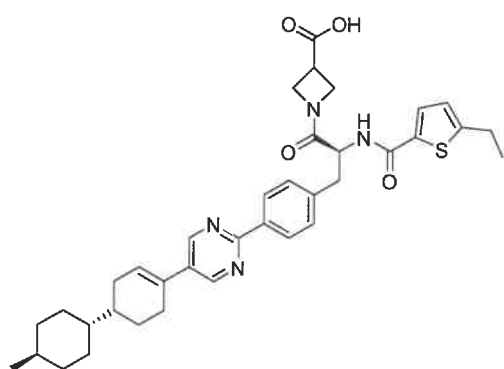
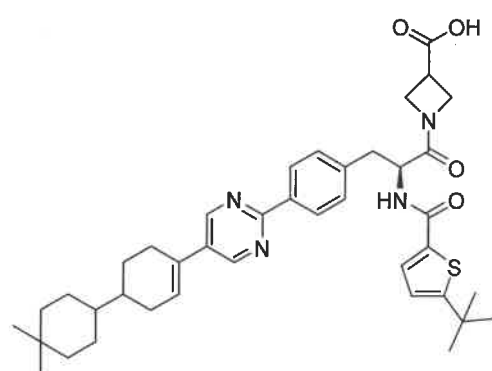
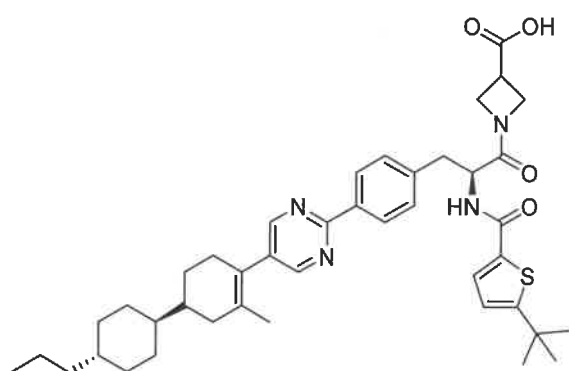


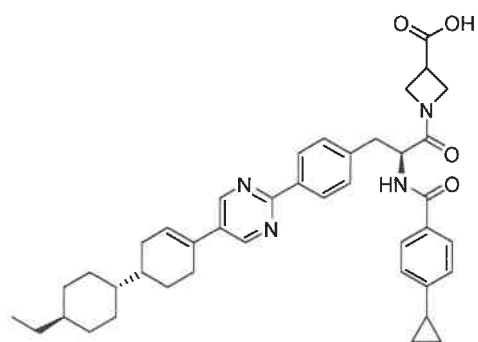
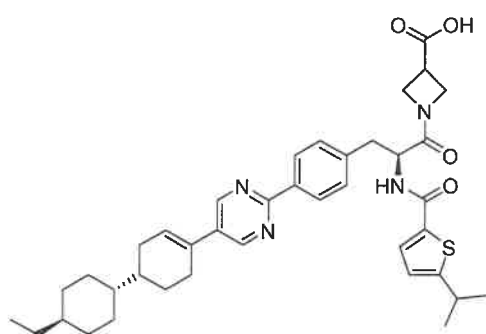
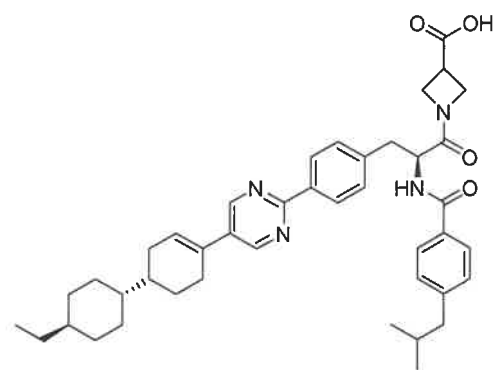
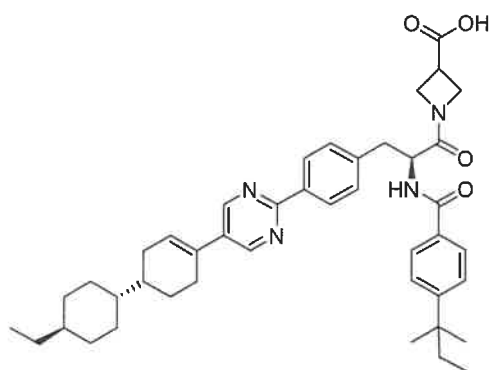
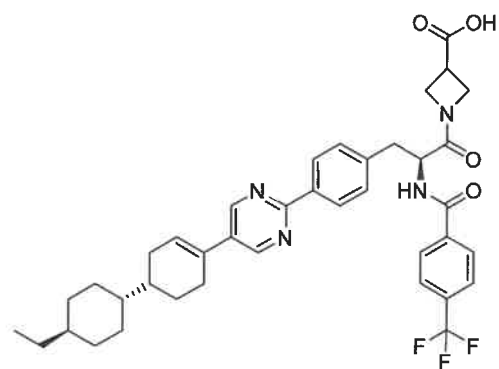
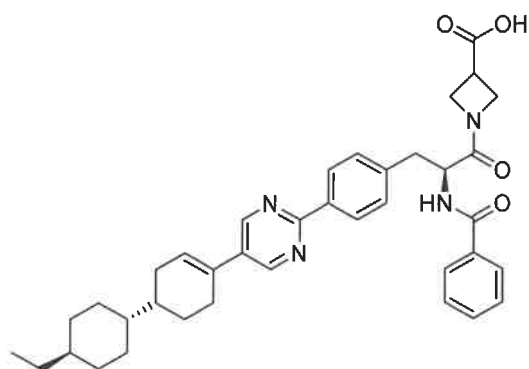
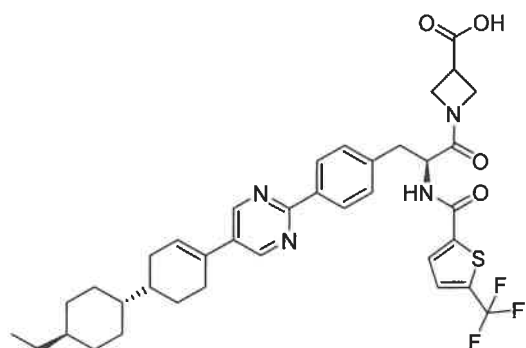
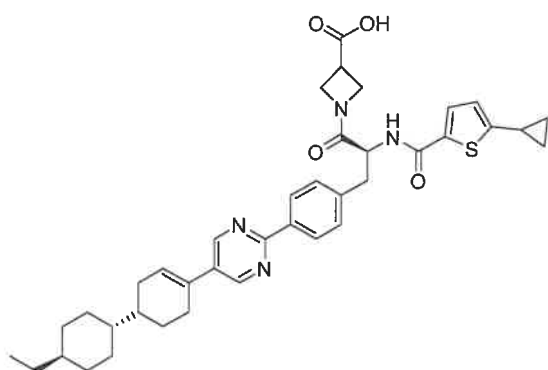


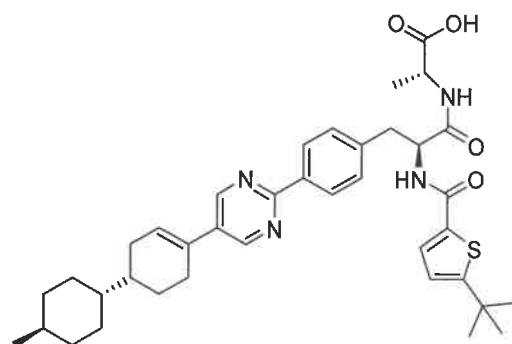
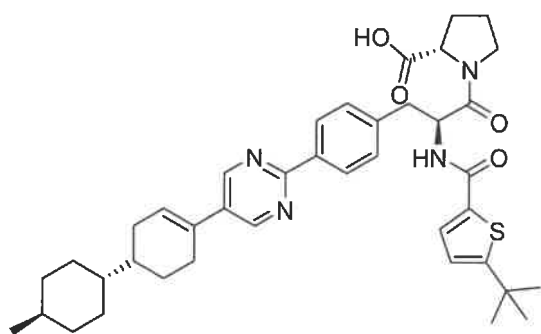
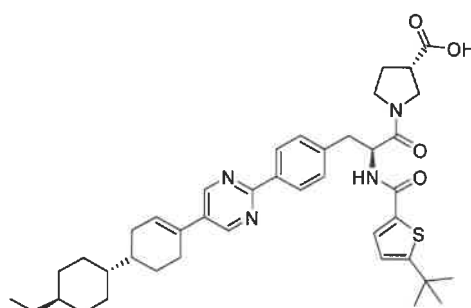
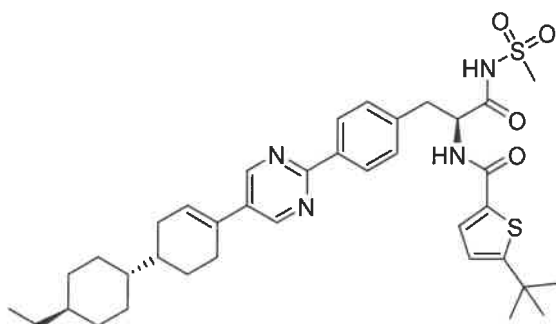
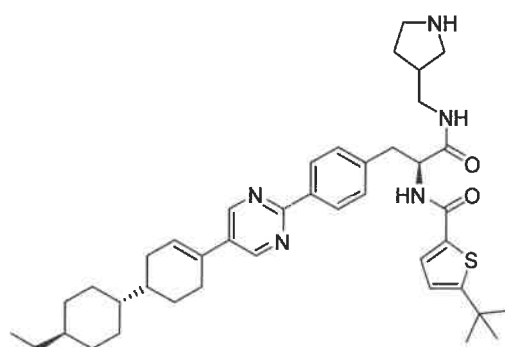
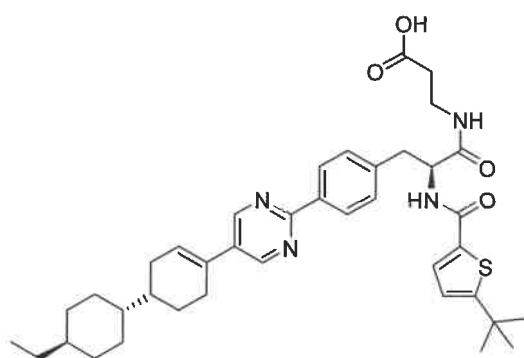
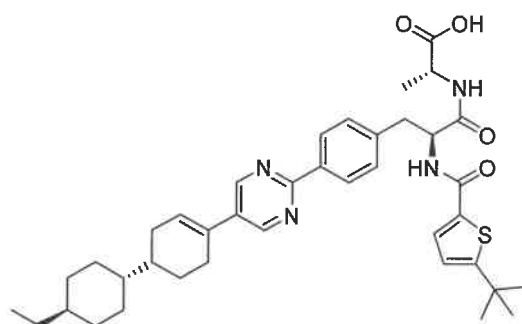
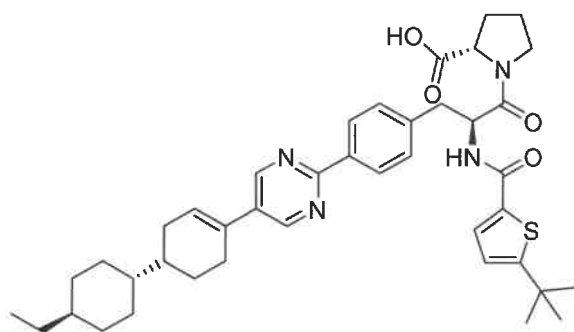


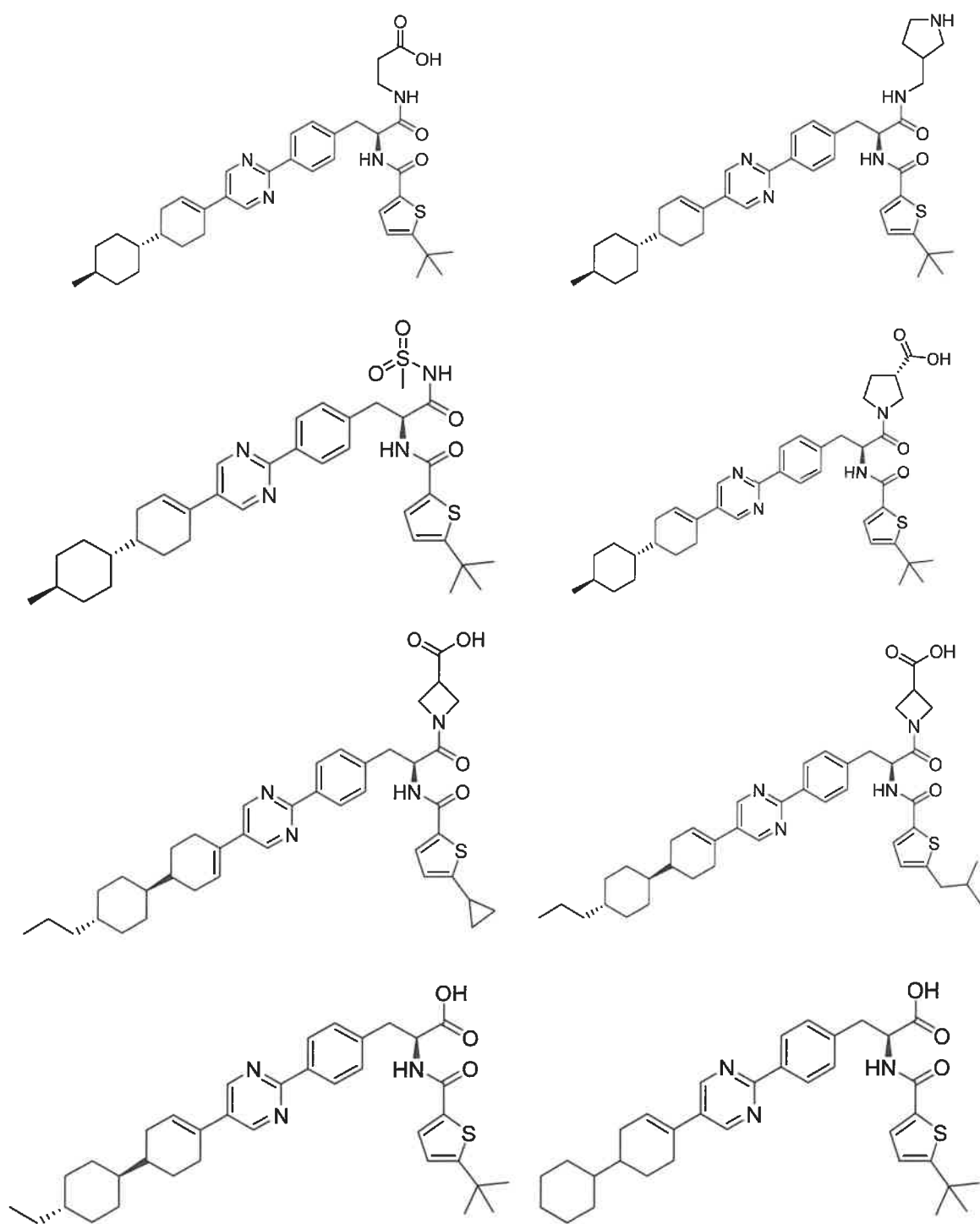


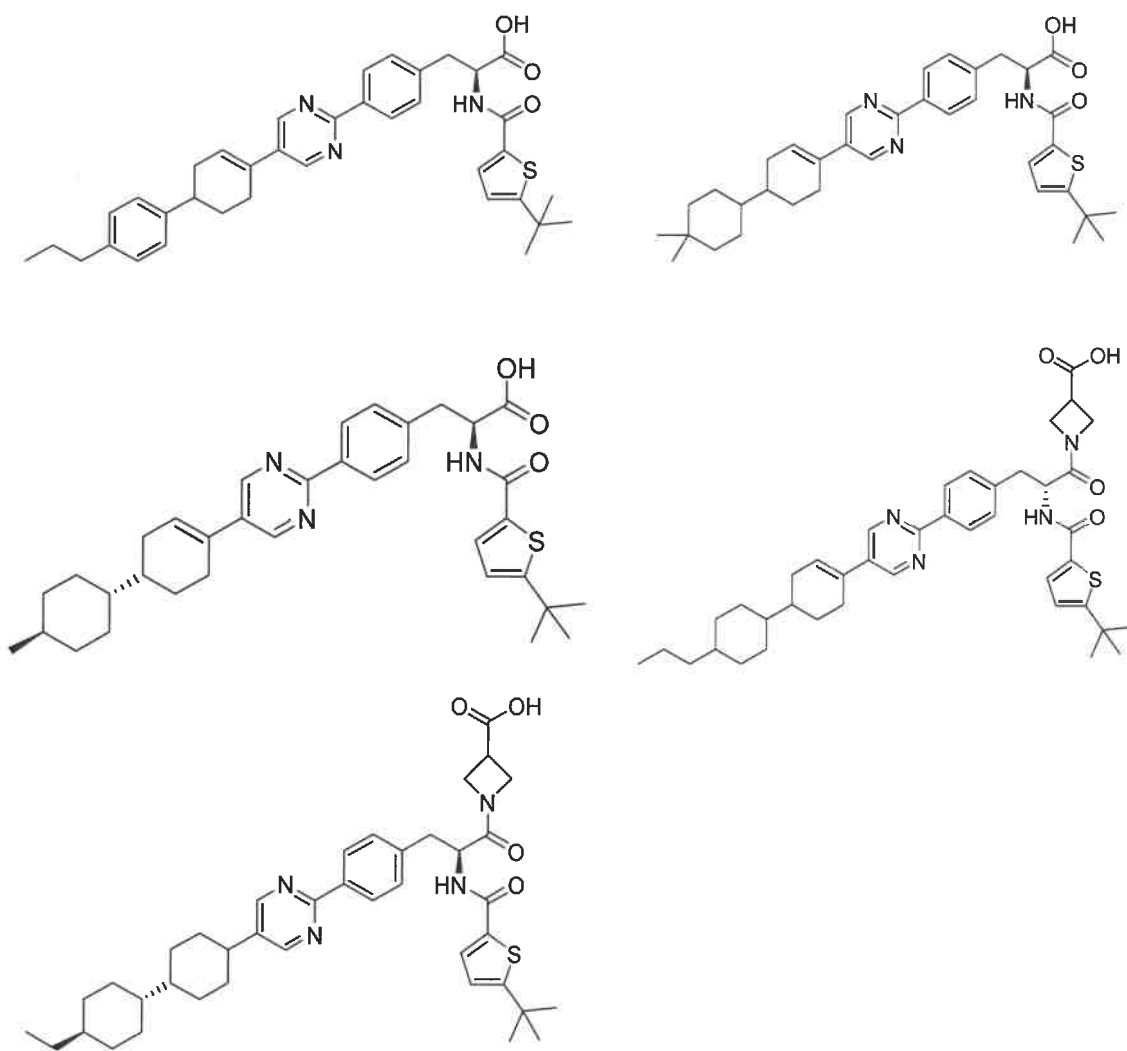












57. A pharmaceutical composition comprising a compound of any one of claims 1-56 together with at least one pharmaceutically acceptable carrier, diluent or excipient.

58. A pharmaceutical combination comprising the compound of any one of claims 1-56 and a second medicament.

59. The pharmaceutical combination of claim 58 wherein the second medicament is an agonist or modulator for glucagon receptor, GIP receptor, GLP-2 receptor, or PTH receptor, or glucagon-like peptide 1 (GLP-1) receptor.

60. The pharmaceutical combination of claim 58 wherein the second medicament is exenatide, liraglutide, taspoglutide, albiglutide, or lixisenatide.

61. The pharmaceutical combination of claim 58 wherein the second medicament is a DPPIV inhibitor.

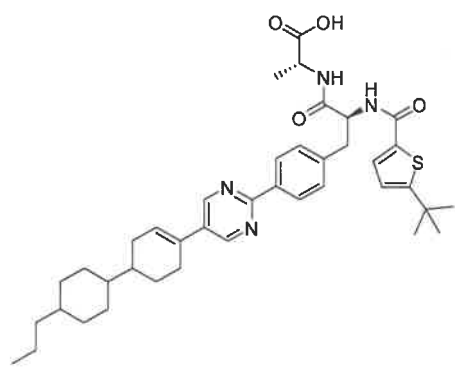
62. The pharmaceutical combination of claim 58 wherein the second medicament is sitagliptin.

63. The pharmaceutical combination of claim 58 wherein the second medicament is a biguanide, a sulfonylurea, a meglitinide, a thiazolidinedione, an α -glucosidase inhibitor, an SGLT2 inhibitor, a bile acid sequestrant, and/or a dopamine-2 agonist.

64. The pharmaceutical combination of claim 58 wherein the second medicament is metformin.

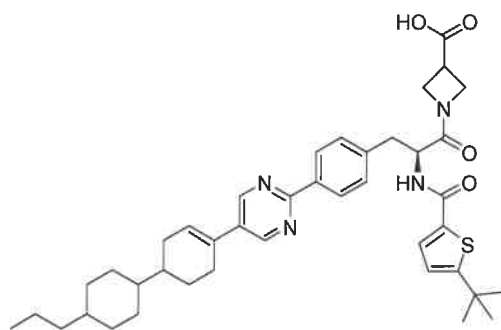
65. The pharmaceutical combination of claim 58 wherein the second medicament is dapagliflozin, empagliflozin or canagliflozin.

66. The compound of claim 1, wherein the compound has the following structure:



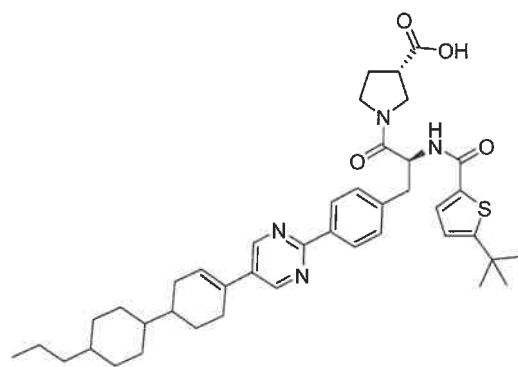
or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof.

67. The compound of claim 1, wherein the compound has the following structure:



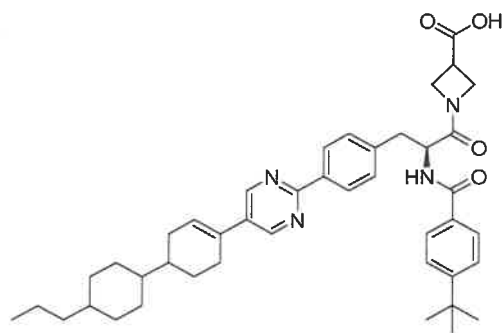
or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof.

68. The compound of claim 1, wherein the compound has the following structure:



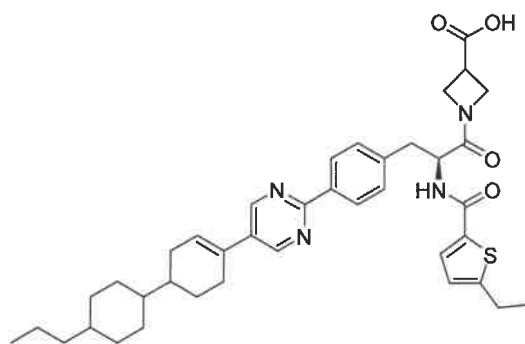
or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof.

69. The compound of claim 1, wherein the compound has the following structure:



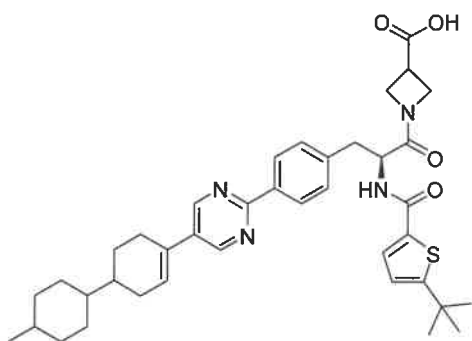
or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof.

70. The compound of claim 1, wherein the compound has the following structure:



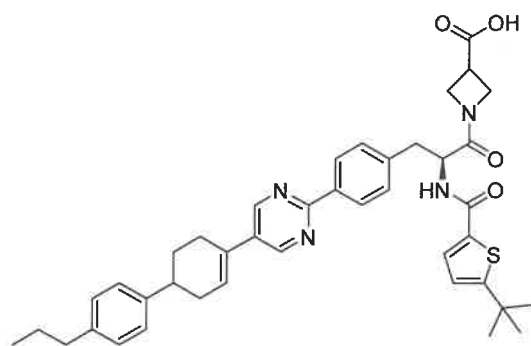
or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof.

71. The compound of claim 1, wherein the compound has the following structure:



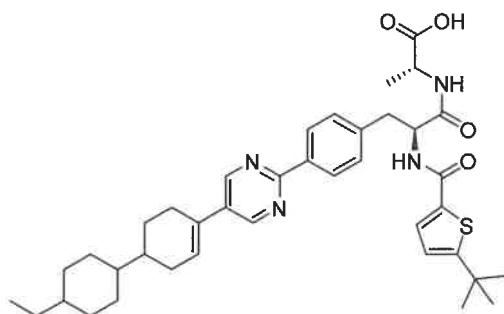
or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof.

72. The compound of claim 1, wherein the compound has the following structure:



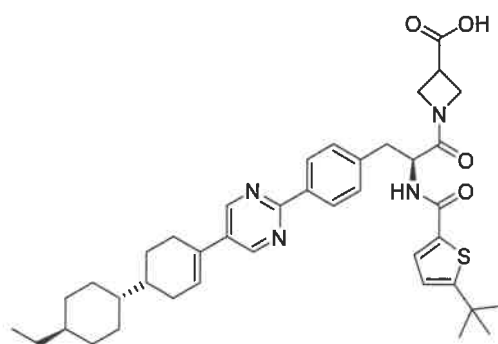
or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof.

73. The compound of claim 1, wherein the compound has the following structure:



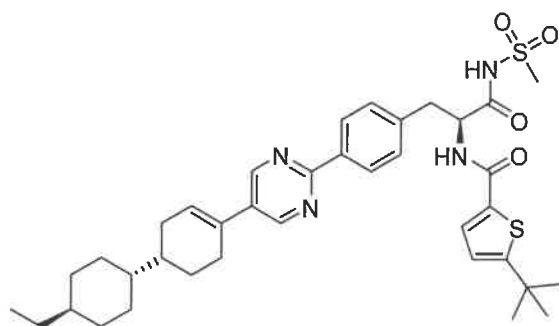
or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof.

74. The compound of claim 1, wherein the compound has the following structure:



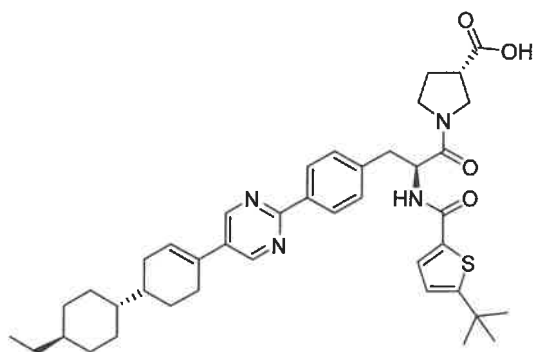
or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof.

75. The compound of claim 1, wherein the compound has the following structure:



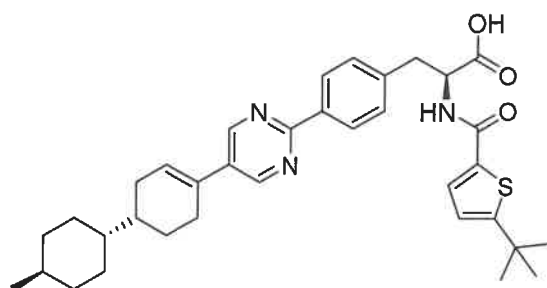
or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof.

76. The compound of claim 1, wherein the compound has the following structure:



or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof.

77. The compound of claim 1, wherein the compound has the following structure:



or a pharmaceutically acceptable enantiomer, diastereomer, racemate, salt, hydrate or solvate thereof.