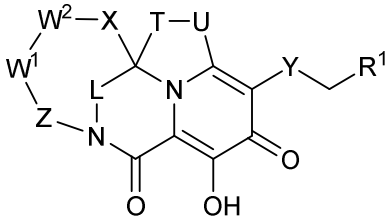
CLAIMS

We claim:

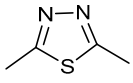
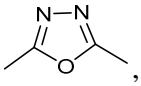
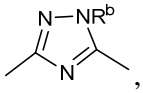
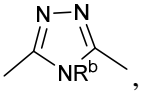
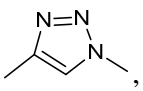
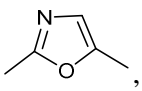
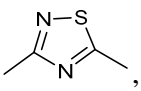
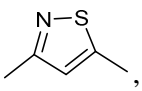
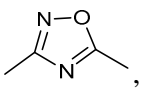
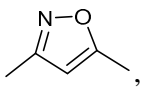
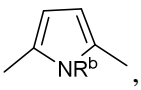
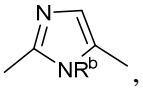
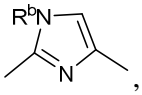
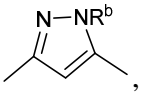
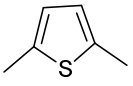
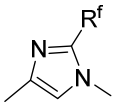
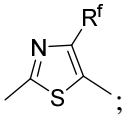
1. A compound of Formula I:



Formula I

or a pharmaceutically acceptable salt thereof, wherein

R^1 is H, C_{6-10}aryl or C_{6-10}heteroaryl, wherein the C_{6-10}aryl or C_{6-10}heteroaryl are optionally substituted with one to four R^{A1}, wherein each R^{A1} is independently halo, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, cyano, –O–C_{1-4}alkyl, –O–C_{3-6}cycloalkyl, or C_{1-4}alkyl–O–C_{1-4}alkyl;

Y is selected from the group consisting of –C(O)NH–, , , , , , , , , , , , , , , , , and ;

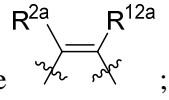
L is $–CR^{3a}R^{3b}–$, –C(O)–, $–SO_2–$, $–CR^{3a}R^{3b}–CR^{3c}R^{3d}–$, or $–N(R^a)–$;

W^1 is a bond or $–CR^{4a}R^{4b}–$;

W^2 is $–CR^{5a}R^{5b}–$, $–CR^{5a}R^{5b}CR^{5c}R^{5d}–$, $–CR^{6a}=CR^{6b}–$, $–N(R^7)–$, $–O–$, $–S(O)_n–$, $–C(O)NR^e–$, $–CR^{5a}R^{5b}–N(R^7)–$, $–CR^{5a}R^{5b}–O–$, $–CR^{5a}R^{5b}–S(O)_n–$, $-CR^{5a}R^{5b}–C(O)NR^e–$, $–CR^{5a}R^{5b}–NR^e–C(O)–$, $–S(O)_nN(R^e)–CR^{5a}R^{5b}–$, or $–N(R^e)–S(O)_n–CR^{5a}R^{5b}–$;

X is a bond or $–CR^{8a}R^{8b}–$;

Z is $–CR^{9a}R^{9b}–$, $–CR^{9a}R^{9b}CR^{9c}R^{9d}–$, or $–CR^{10a}=CR^{10b}–$;

T is $–CR^{2a}R^{2b}–$ or $—CR^{2a}R^{2b}–CR^{2c}R^{2d}$; U is $–NR^{11}–$, $–CR^{12a}R^{12b}–$, $–S(O)_n–$, $–C(O)–$, or $–O–$; or T and U together are ;

R^{2a}, R^{2b}, R^{2c}, R^{2d}, R^{12a}, and R^{12b} are independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, cyano, $–CH_2R^a–$, $–CH_2OR^a$, $–CH_2–S(O)_nR^a–$, $–OR^a$, $–O–C(O)–NHR^a$, $–NHR^a–$, $–C(O)–NH(R^a)–$, $–NR^e–C(O)R^a–$, $–NR^e–S(O)_nR^a–$, $–S(O)_n–NH(R^a)–$, or $–S(O)_n–R^a–$;

R^{3a}, R^{3b}, R^{3c}, and R^{3d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or $–O–C_{1-4}$alkyl;

R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{5c}, R^{5d}, R^{8a}, R^{8b}, R^{9a}, R^{9b}, R^{9c}, and R^{9d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, halo, hydroxyl, cyano, $–O–C_{1-4}$alkyl, or C_{1-4}alkylene$–O–C_{1-4}$alkyl;

each R^{6a}, R^{6b}, R^{10a}, and R^{10b} is independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl;

R^7 is H, C_{1-6}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, $C(O)R^c$, or SO_2R^c;

R^{11} is H, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, $–C(O)–R^a$, $–S(O)_n–R^a$, $–CH_2–R^a$;

each R^a is independently (i) H, (ii) C_{1-6}alkyl, (iii) C_{3-6}cycloalkyl, (iv) a 5 to 10 membered carbocyclic ring, (v) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (vi) a 6 to 10 membered aromatic ring, or (iv) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S;

wherein the C_{1-6}alkyl, C_{3-6}cycloalkyl, 5 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring or 5 to 10 membered heteroaromatic ring is optionally substituted with 0 to 4 substituents independently selected from the group consisting of (i) oxo (ii) halo, (iii) cyano, (iv) –O–C_{1-4}alkyl, (v) C_{1-6}alkyl, (vi) –OR^e (vii) 3 to 10 membered carbocyclic ring, (viii) 5 to 10 membered heterocyclic ring containing 1 or 2 heteroatom selected from N, O, and S, (ix) 6 to 10 membered aromatic ring, or (x) a 5 to 10 membered heteroaromatic ring containing 1 to 3 heteroatoms selected from N, O and S;
wherein the 3 to 10 membered carbocyclic ring, 5 to 10 membered heterocyclic ring, 6 to 10 membered aromatic ring, or 5 to 10 membered heteroaromatic ring is optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or –OR^e;

R^b is H, C_{1-4}alkyl, C_{1-4}haloalkyl or C_{3-6}cycloalkyl;

R^f is H, halo, C_{1-4}alkyl, or C_{1-4}haloalkyl;

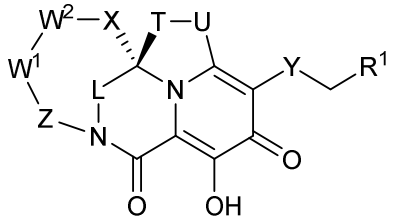
each R^c is independently, H, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl; C(O)R^d, or –SO_2R^d;

each R^d is independently C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl, C_{3-6}halocycloalkyl, –NR^e_2, or –OR^e;

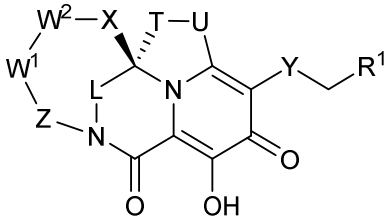
each R^e is independently H, C_{1-4}alkyl or C_{3-6}cycloalkyl wherein each C_{1-4}alkyl or C_{3-6}cycloalkyl is optionally substituted by a halo or a cyano; and

each n is 0, 1, or 2.

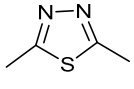
2. The compound of claims 1, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula Ia or Formula Ib:



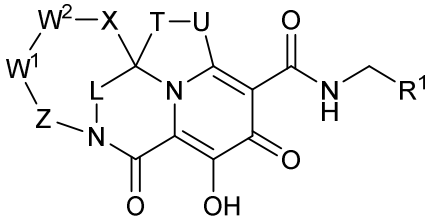
Formula Ia



Formula Ib.

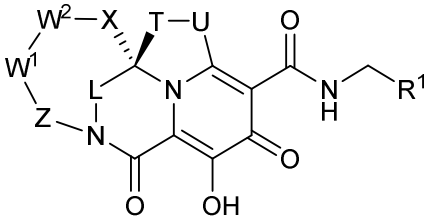
3. The compound of claim 1 or 2, or the pharmaceutically acceptable salt thereof, wherein Y is selected from the group consisting of –C(O)NH– or .

4. The compound of any one of claims 1-3, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula II:

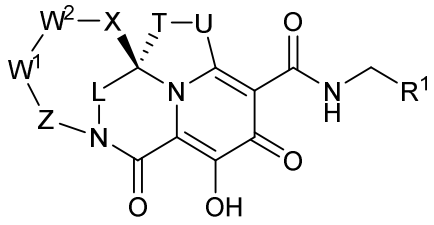


Formula II.

5. The compound of claim4, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula IIa or Formula IIb:



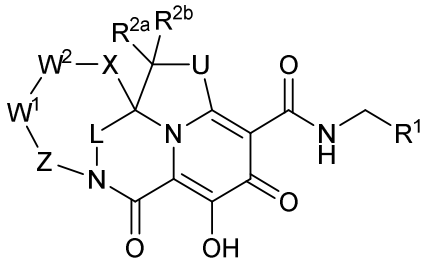
Formula IIa



Formula IIb.

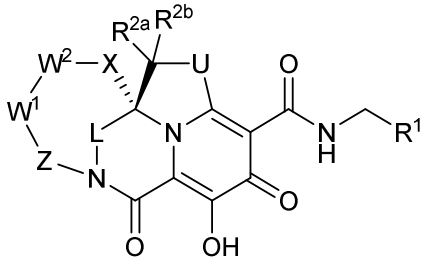
6. The compound of any one of claims 1-5, or the pharmaceutically acceptable salt thereof, wherein R^{2a}, R^{2b}, R^{2c}, and R^{2d} are independently H, halo, $C_{1\text{-}6}$alkyl, -CH_2OR^a or –OR^a; and wherein each R^a is independently H or $C_{1\text{-}6}$alkyl.

7. The compound of any one of claims 1-6, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula III:

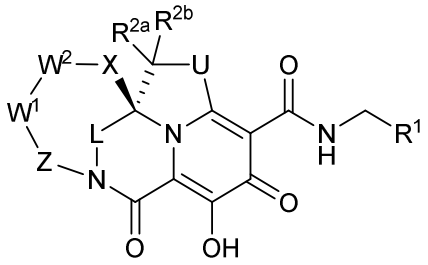


Formula III.

8. The compound of claim 7, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula IIIa or Formula IIIb:

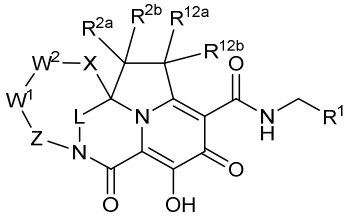


Formula IIIa



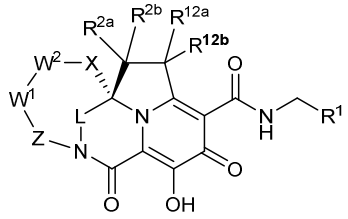
Formula IIIb.

9. The compound of any one of claims 1-8, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula IV:

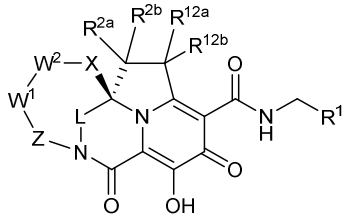


Formula IV.

10. The compound of claim 9, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula IVa or Formula IVb:



Formula IVa



Formula IVb.

11. The compound of claim 9 or 10, or the pharmaceutically acceptable salt thereof, wherein:

X is $–CR^{8a}R^{8b}–$;

W^1 is a bond or $–CR^{4a}R^{4b}–$;

W^2 is $–CR^{5a}R^{5b}–$ or $–CR^{6a}=CR^{6b}–$;

Z is $–CR^{9a}R^{9b}–$;

L is $–CH_2–$;

R^{2a}, R^{2b}, R^{12a}, and R^{12b} are independently H, $C_{1\text{-}6}$alkyl, halo, $–OR^a–$, or $–CH_2OR^a$;

R^a is H or $C_{1\text{-}6}$alkyl;

R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a}, R^{9b} are independently H, hydroxyl, $C_{1\text{-}6}$alkyl, or $–O–C_{1\text{-}4}$alkyl;

both R^{6a} and R^{6b} are H; and

R^1 is $C_{6\text{-}10}$aryl optionally substituted with one to four R^{A1}, wherein each R^{A1} is independently fluoro or chloro.

12. The compound of claim 1, or the pharmaceutically acceptable salt thereof, wherein R^{12a} and R^{12b} are independently H, halo, $C_{1\text{-}6}$alkyl, $-CH_2OR^a$, or $–OR^a$; and wherein each R^a is H or $C_{1\text{-}6}$alkyl.

13. The compound of any one of claims 1-12, or the pharmaceutically acceptable salt thereof, wherein W^1 is a bond.

14. The compound of any one of claims 1-12, or the pharmaceutically acceptable salt thereof, wherein W^1 is $–CR^{4a}R^{4b}–$.

15. The compound of any one of claims 1-14, or the pharmaceutically acceptable salt thereof, wherein W^2 is $–CR^{5a}R^{5b}–$ or $–CR^{6a}=CR^{6b}–$.

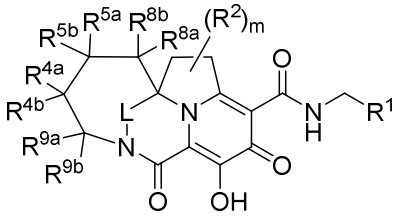
16. The compound of any one of claims 1-15, or the pharmaceutically acceptable salt thereof, wherein W^2 is $–CR^{5a}R^{5b}–$.

17. The compound of any one of claims 1-16, or the pharmaceutically acceptable salt thereof, wherein X is a bond.

18. The compound of any one of claims 1-16, or the pharmaceutically acceptable salt thereof, wherein X is $–CR^{8a}R^{8b}–$.

19. The compound of any one of claims 1-18, or the pharmaceutically acceptable salt thereof, wherein Z is $–CR^{9a}R^{9b}–$.

20. The compound of any one of claims 1-19, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VI:

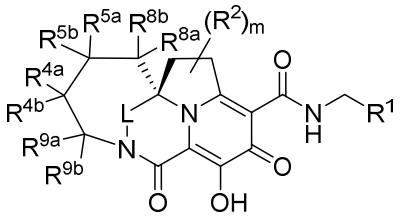


Formula VI;

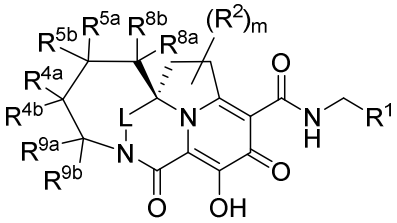
wherein m is 0, 1, 2, 3, or 4; and

each R^2 is independently C_{1-6}alkyl, C_{3-6}cycloalkyl, halo, cyano, $–CH_2R^a–$, $–CH_2OR^a$, $–CH_2–S(O)_nR^a–$, $–OR^a$, $–O–C(O)–NHR^a$, $–NHR^a–$, $–C(O)–NH(R^a)–$, $–NR^e–C(O)R^a–$ $–NR^e–S(O)_nR^a–$, $–S(O)_n–NH(R^a)–$, or $–S(O)_n–R^a–$; or two R^2 on same carbon atom, together with the carbon atom to which they both are attached form a (i) 3 to 7 membered carbocyclic ring or (ii) 4 to 7 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 4 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl or $–OR^e$.

21. The compound of claim 20, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VIa or Formula VIb:



Formula VIa;

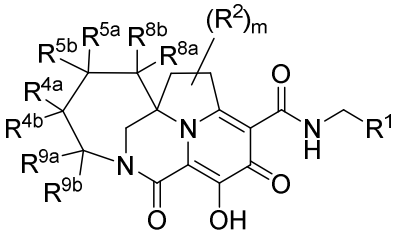


Formula VIb;

wherein m is 0, 1, 2, 3, or 4; and

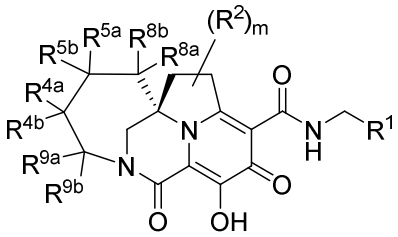
each R^2 is independently $C_{1\text{-}6}$alkyl, $C_{3\text{-}6}$cycloalkyl, halo, cyano, $–CH_2R^a–$, $–CH_2OR^a$, $–CH_2–S(O)_nR^a–$, $–OR^a$, $–O–C(O)–NHR^a$, $–NHR^a–$, $–C(O)–NH(R^a)–$, $–NR^e–C(O)R^a–$ $–NR^e–S(O)_nR^a–$, $–S(O)_n–NH(R^a)–$, or $–S(O)_n–R^a–$; or two R^2 on same carbon atom, together with the carbon atom to which they both are attached form a (i) 3 to 7 membered carbocyclic ring or (ii) 4 to 7 membered heterocyclic ring containing 1 or 2 heteroatoms selected from N, O, and S, wherein the 3 to 7 membered carbocyclic ring or the 4 to 7 membered heterocyclic ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently oxo, halo, cyano, $C_{1\text{-}6}$alkyl, $C_{3\text{-}6}$cycloalkyl or $–OR^e$.

22. The compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VII:

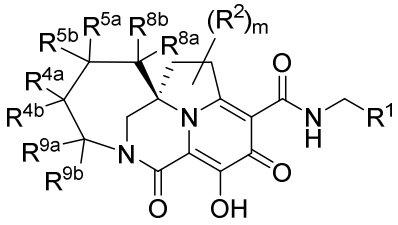


Formula VII.

23. The compound of claim 22, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VIIa or Formula VIIb:



Formula VIIa



Formula VIIb.

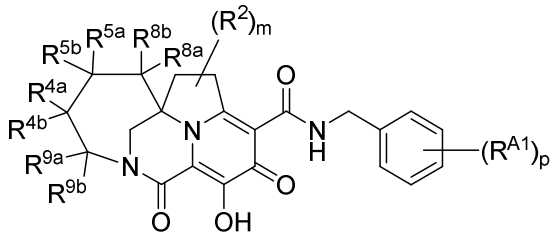
24. The compound of any one of claims 1-23, or the pharmaceutically acceptable salt thereof, wherein R^1 is phenyl or pyridyl, wherein the phenyl or pyridyl is optionally substituted with one, two, three, or four R^{A1}, wherein each R^{A1} is independently halo, C_{1-4}alkyl, C_{1-4}haloalkyl, or –O–C_{1-4}alkyl.

25. The compound of any one of claims 1-24, or the pharmaceutically acceptable salt thereof, wherein R^1 is phenyl or pyridyl, wherein the phenyl or pyridyl is substituted with one, two, three, or four halogens.

26. The compound of any one of claims 1-24, or the pharmaceutically acceptable salt thereof, wherein R^1 is phenyl, optionally substituted with one, two, three, or four R^{A1}, wherein each R^{A1} is independently halo, C_{1-4}alkyl, C_{1-4}haloalkyl, or –O–C_{1-4}alkyl.

27. The compound of any one of claims 1-21, and 26, or the pharmaceutically acceptable salt thereof, wherein R^1 is phenyl substituted with two or three halogens selected from chloro and fluoro.

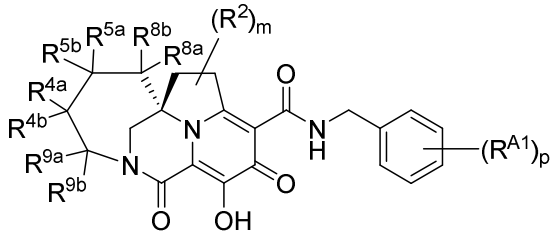
28. The compound of any one of claims 1-26, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VIII:



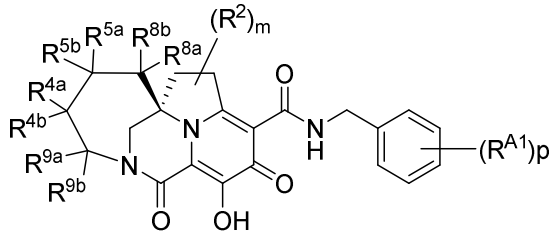
Formula VIII;

wherein p is 2 or 3.

29. The compound of claim 28, or the pharmaceutically acceptable salt thereof, wherein the compound has a Formula VIIIa or Formula VIIIb:



Formula VIIIa;



Formula VIIIb;

wherein p is 2 or 3.

30. The compound of any one of claims 1-29, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, C_1-C_6 alkyl, halo, or –O–C_{1-4}alkyl.

31. The compound of any one of claims 1-29, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, $-CH_3$, or $-OCH_3$.

32. The compound of any one of claims 20-30, wherein m is 0, 1, or 2.

33. The compound of any one of claims 1-32, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently halo, C_1-C_6 alkyl, $-CH_2OR^a$, or $–OR^a$; wherein each R^a is independently H or C_1-C_6 alkyl.

34. The compound of any one of claims 1-33or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently halo, C_1-C_6 alkyl, $-CH_2OR^a$, or $–OR^a$; wherein each R^a is independently H or methyl.

35. The compound of any one of claims 28-34, wherein each R^{A1} is independently a halo.

36. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1-35, or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

37. Use of a compound of any one of claims 1-35 or pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an HIV infection in a human having or at risk of having the infection.

38. The compound of claim 28, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each independently H, C_1-C_6 alkyl, halo, or $–O$-$C_{1\text{-}4}$alkyl.

39. The compound of claim 38, or the pharmaceutically acceptable salt thereof, wherein m is 0, 1, or 2.

40. The compound of claim 39, or the pharmaceutically acceptable salt thereof, wherein each R^2 is independently halo, $C_{1\text{-}6}$alkyl, $-CH_2OR^a$ or $–OR^a$; wherein each R^a is independently H or C_1-C_6 alkyl.

41. The compound of claim 40, or the pharmaceutically acceptable salt thereof, wherein each R^{A1} is independently a halo.

42. The compound of claim 41, or the pharmaceutically acceptable salt thereof, wherein R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{8a}, R^{8b}, R^{9a} and R^{9b} are each H.

43. The compound of claim 42, or the pharmaceutically acceptable salt thereof, wherein m is 0.

44. A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 42, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

45. Use of the compound of claim 42, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an HIV infection in a human having or at risk of having the infection.