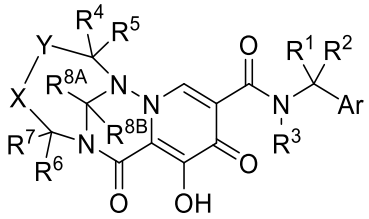
CLAIMS

1. A compound of Formula I:



Formula I,

or a pharmaceutically acceptable salt thereof, wherein

Ar is C_6-C_{10} aryl or six to ten membered heteroaryl containing one, two or three heteroatoms selected from N, O, and S; wherein the C_6-C_{10} aryl or six to ten membered heteroaryl is optionally substituted with 1-4 substituents independently selected from the group consisting of halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 alkyloxy;

R^1 is H, C_1-C_3 alkyl or phenyl;

R^2 is H or C_1-C_3 alkyl;

R^3 is H or C_1-C_3 alkyl;

R^4 and R^5 are each independently H, halogen, cyano, C_1-C_6 alkyl, C_1-C_6 alkyloxy, C_6-C_{10} aryl, or six to ten membered heteroaryl containing one, two or three heteroatoms selected from N, O, and S; wherein the C_1-C_6 alkyl, C_1-C_6 alkyloxy, C_6-C_{10} aryl, or six to ten membered heteroaryl is optionally substituted with one, two or three groups independently selected from halogen, C_1-C_3 alkyloxy, or C_1-C_3 haloalkyloxy; or

R^4 and R^5 are joined together to form a 3-6 membered carbocyclic ring or 4-6 membered heterocyclic ring comprising one heteroatom selected from N, O, and S;

R^6 is H, halogen, C_1-C_6 alkyl, C_1-C_6 alkyloxy or C_1-C_6 haloalkyl;

R^7 is H, halogen, C_1-C_6 alkyl, C_1-C_6 alkyloxy, or C_1-C_6 haloalkyl;

R^{8A} and R^{8B} are independently H, C_1-C_3 alkyl or benzyl; and

-X-Y- is $–(CR^{13A}R^{13B})_p$-CR^9=CR^{10}-; wherein

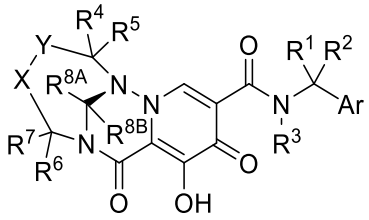
R^9 is H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl or C_1-C_6 alkyloxy;

R^{10} is H, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl or C_1-C_6 alkyloxy; and

R^{13A} and R^{13B} are each independently H, halogen, C_1-C_6 alkyl, C_1-C_6 alkyloxy; or C_1-C_6 haloalkyl; and

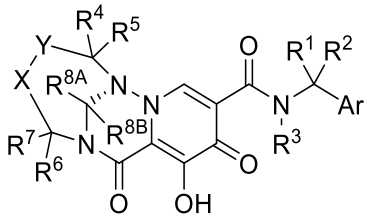
p is 0 or 1.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is of a Formula Ia:



Formula Ia; or

wherein the compound is of a Formula Ib:



Formula Ib.

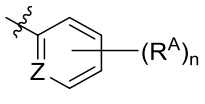
3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein Ar is C_6-C_{10} aryl or six to ten membered heteroaryl containing one heteroatom selected from N, O, and S; wherein the C_6-C_{10} aryl or six to ten membered heteroaryl is optionally substituted with

(a) 1-4 substituents independently selected from the group consisting of halogen, C_1-C_6 alkyl, and C_1-C_6 alkyloxy; or

(b)1-4 halogens; or

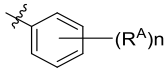
(c) 1-3 substituents independently selected from Cl and F.

4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein Ar is a group of Formula:



;

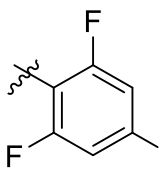
wherein Z is N or CR^A; n is 0, 1, 2, 3, or 4; and each R^A is independently halogen, C_1-C_6 alkyl, and C_1-C_6 alkyloxy, optionally wherein Z is CH or N.

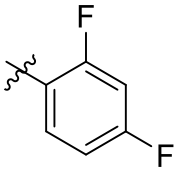
5. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein Ar is 

; n is 1, 2, 3, or 4; and each R^A is

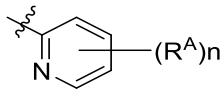
(a) independently selected from halogen and C_1-C_6 alkyloxy; or

(b) independently halo or -O-C_{1-4}alkyl.

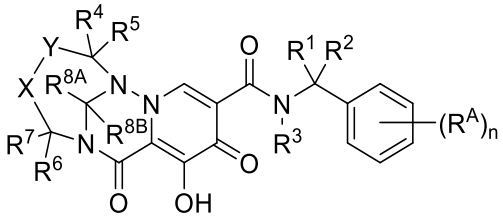
6. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein Ar is 

or 

.

7. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein Ar is  , n is 1, 2, or 3 , and each R^A is independently fluoro or chloro.

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



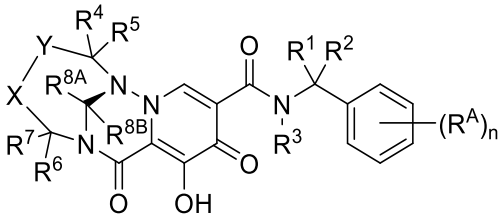
Formula II,

wherein

n is 0, 1, 2, 3, or 4; and

each R^A is independently halogen, C_1-C_6 alkyl, and C_1-C_6 alkyloxy.

9. The compound of any one of claims 1-5 and 8, or a pharmaceutically acceptable salt thereof, wherein the compound has a Formula IIa:



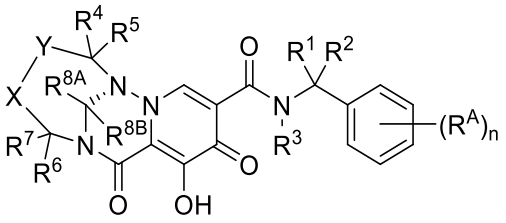
Formula IIa,

wherein

n is 0, 1, 2, 3, or 4; and

each R^A is independently halogen, C_1-C_6 alkyl, and C_1-C_6 alkyloxy; or

wherein the compound has a Formula IIb:



Formula IIb,

wherein

n is 0, 1, 2, 3, or 4; and

each R^A is independently halogen, C_1-C_6 alkyl, and C_1-C_6 alkyloxy.

10. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein

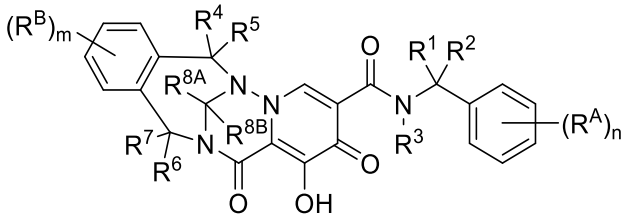
(a) -X-Y- is $–CR^{13A}R^{13B}$-CR^9=CR^{10}-; or

(b) -X-Y- is $–CH_2$-CR^9=CR^{10}-; or

(c) -X-Y- is -CR^9=CR^{10}-.

11. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt thereof, wherein R^9 is H or halogen; and R^{10} is H or halogen.

12. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt thereof, wherein the compound has a Formula III:



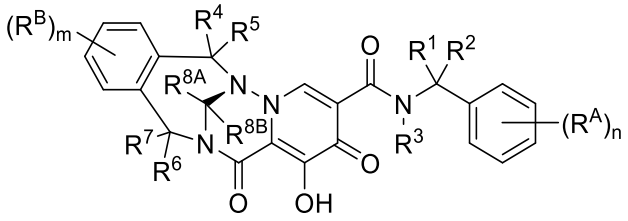
Formula III;

wherein

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

each R^B is independently halogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, or C_1-C_3 alkyloxy.

13. The compound of any one of claims 1-12, or a pharmaceutically acceptable salt thereof, wherein the compound has a Formula IIIa:



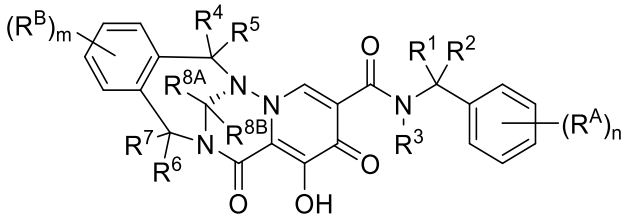
Formula IIIa;

wherein

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

each R^B is independently halogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, or C_1-C_3 alkyloxy; or

wherein the compound has a Formula IIIb:



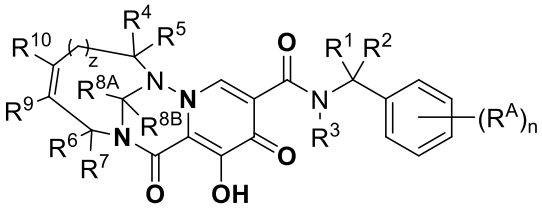
Formula IIIb;

wherein

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

each R^B is independently halogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, or C_1-C_3 alkyloxy.

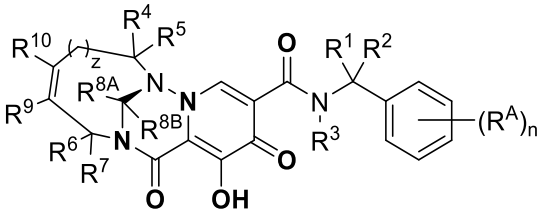
14. The compound of any one of claims 1-11, or a pharmaceutically acceptable salt thereof, wherein the compound has a Formula IV:



Formula IV;

wherein z is 0 or 1.

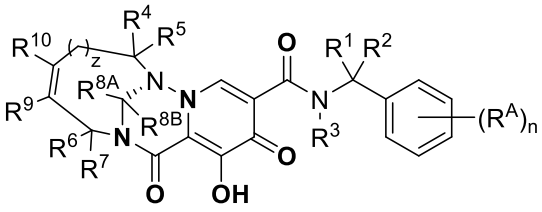
15. The compound of any one of claims 1-11 and 14, or a pharmaceutically acceptable salt thereof, wherein the compound has a Formula IVa:



Formula IVa;

wherein z is 0 or 1; or

wherein the compound has a Formula IVb:



Formula IVb;

wherein z is 0 or 1.

16. The compound of any one of claims 1-15, or a pharmaceutically acceptable salt thereof, wherein each R^9 and R^{10} is independently H, halogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl.

17. The compound of claim 14, or a pharmaceutically acceptable salt thereof, wherein:

z is 0;

R^1, R^2, and R^3 are each H;

R^4 and R^5 are independently H, halogen, cyano, C_1-C_6 alkyl, C_1-C_6 alkyloxy, C_6-C_{10} aryl, or six to ten membered heteroaryl containing one, two or three heteroatoms selected from N, O, and S;

R^6 and R^7 are independently H, halogen, C_1-C_6 alkyl, C_1-C_6 alkyloxy or C_1-C_6 haloalkyl;

R^{8A} and R^{8B} are both H;

R^9 and R^{10} is each independently H, halogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl; each R^A is independently fluoro or chloro; and

n is 1, 2, or 3.

18. The compound of claim 14, or a pharmaceutically acceptable salt thereof, wherein:

z is 0;

R^1, R^2, and R^3 are each H;

R^4 and R^5 are independently H, halogen, cyano, C_1-C_6 alkyl, or C_1-C_6 alkyloxy;

R^6 and R^7 are independently H, halogen, C_1-C_6 alkyl, C_1-C_6 alkyloxy or C_1-C_6 haloalkyl;

R^{8A} and R^{8B} are both H;

R^9 and R^{10} is each independently H, halogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

each R^A is independently fluoro or chloro; and

n is 1, 2, or 3.

19. The compound of claim 14, or a pharmaceutically acceptable salt thereof, wherein:

z is 0;

R^1, R^2, and R^3 are each H;

R^4 and R^5 are independently H, halogen, or C_1-C_6 alkyl;

R^6 and R^7 are independently H, halogen or C_1-C_6 alkyl;

R^{8A} and R^{8B} are both H;

R^9 and R^{10} is each independently H, halogen or C_1-C_6 alkyl;

each R^A is independently fluoro or chloro; and

n is 1, 2, or 3.

20. The compound of any one of claims 1-19, or a pharmaceutically acceptable salt thereof, wherein R^{8B} is H.

21. The compound of any one of claims 1-20, or a pharmaceutically acceptable salt thereof, wherein R^{8A} is H.

22. The compound of any one of claims 1-21, or a pharmaceutically acceptable salt thereof, wherein R^3 is H.

23. The compound of any one of claims 1-21, or a pharmaceutically acceptable salt thereof, wherein R^1 and R^2 are both H.

24. The compound of any one of claims 1-23, or a pharmaceutically acceptable salt thereof, wherein

(a) each R^4 and R^5 is independently H, or C_1-C_6 alkyl, wherein the C_1-C_6 alkyl is optionally substituted with one two or three groups independently selected from halogen, C_1-C_3 alkyloxy, or C_1-C_3 haloalkyloxy; or

(b) R^4 is H or C_1-C_6 alkyl, wherein the C_1-C_6 alkyl is optionally substituted with one two or three groups independently selected from halogen, C_1-C_3 alkyloxy, or C_1-C_3 haloalkyloxy; and R^5 is H or C_1-C_6 alkyl; or

(c) R^4 is H or C_1-C_6 alkyl, wherein the C_1-C_6 alkyl is optionally substituted with one two or three groups independently selected from halogen, C_1-C_3 alkyloxy, or C_1-C_3 haloalkyloxy; and R^5 is H; or

(d) R^4 and R^5 are independently H, Me, OMe, or -CH_2F; or

(e) R^4 and R^5 are joined together to form a 4-6 membered heterocyclic ring comprising one heteroatom selected from N, O, and S.

25. The compound of any one of claims 1-23, or a pharmaceutically acceptable salt thereof, wherein R^6 is

(a) H, halogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;.

(b) H, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

(c) H, methyl, or CH_2F;

(d) H, halogen or C_1-C_6 alkyl;

(e) halogen or C_1-C_6 alkyl;

(f) C_1-C_6 alkyl.

(g) methyl; or

(h) H.

26. The compound of any one of claims 1-25, or a pharmaceutically acceptable salt thereof, wherein R^7 is

(a) H, halogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

(b) H, halogen, or C_1-C_6 alkyl;

(c) halogen or C_1-C_6 alkyl;

(d) C_1-C_6 alkyl; or

(e) H.

27. The compound of any one of claims 1-26, or a pharmaceutically acceptable salt thereof, wherein R^{13A} and R^{13B} are each independently

(a) H, halogen, C_1-C_6 alkyl, or C_1-C_6 alkyloxy; or

(b) H, halogen, or C_1-C_6 alkyloxy; or

(c) H, halogen, or methoxy; or

(d) H, fluoro, or methoxy.

28. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is (1S,2R,5S)-8-hydroxy-2,5-dimethyl-7,9-dioxo-N-(2,4,6-trifluorobenzyl)-2,5,7,9-tetrahydro-1,6-methanopyrido[1,2-b][1,2,5]triazonine-10-carboxamide.

29. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is (1S,2S,5S)-8-hydroxy-2,5-dimethyl-7,9-dioxo-N-(2,4,6-trifluorobenzyl)-2,5,7,9-tetrahydro-1,6-methanopyrido[1,2-b][1,2,5]triazonine-10-carboxamide.

30. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is (1S,2R,5S)-N-(2,4-difluorobenzyl)-8-hydroxy-2,5-dimethyl-7,9-dioxo-2,5,7,9-tetrahydro-1,6-methanopyrido[1,2-b][1,2,5]triazonine-10-carboxamide.

31. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is (1S,2S,5S)-N-(2,4-difluorobenzyl)-8-hydroxy-2,5-dimethyl-7,9-dioxo-2,5,7,9-tetrahydro-1,6-methanopyrido[1,2-b][1,2,5]triazonine-10-carboxamide.

32. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is (2S,5S)-N-(2,4-difluorobenzyl)-2-(fluoromethyl)-8-hydroxy-5-methyl-

7,9-dioxo-2,5,7,9-tetrahydro-1,6-methanopyrido[1,2-b][1,2,5]triazonine-10-carboxamide.

33. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is (1S,2R,5S)-N-(3-chloro-2,4-difluorobenzyl)-8-hydroxy-2,5-dimethyl-7,9-dioxo-2,5,7,9-tetrahydro-1,6-methanopyrido[1,2-b][1,2,5]triazonine-10-carboxamide.

34. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is (1S,2R,5S)-2-ethyl-8-hydroxy-5-methyl-7,9-dioxo-N-(2,4,6-trifluorobenzyl)-2,5,7,9-tetrahydro-1,6-methanopyrido[1,2-b][1,2,5]triazonine-10-carboxamide.

35. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is (1S,2S,5S)-2-(fluoromethyl)-8-hydroxy-5-methyl-7,9-dioxo-N-(2,4,6-trifluorobenzyl)-2,5,7,9-tetrahydro-1,6-methanopyrido[1,2-b][1,2,5]triazonine-10-carboxamide.

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. A compound of any one of claims 1-35, or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 36, for use in a medical therapy.

38. Use of a compound of any one of claims 35, or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 36, in the manufacture of a medicament for treating an HIV infection in a human having or at risk of having the infection.

39. The use according to claim 38, wherein the compound is for use by oral, intravenous, subcutaneous, or intramuscular administration.