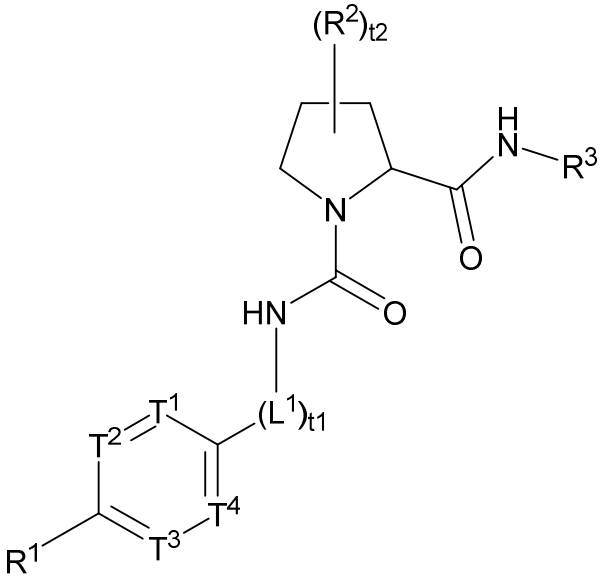
CLAIMS

1. A compound of Formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

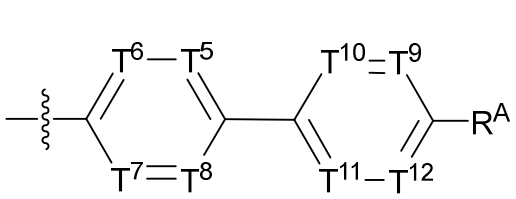
R^1 is H, halogen, -CN, C_{1-8} alkyl, C_{2-8} alkenyl, (C_{3-6} cycloalkyl)-C_{1-4} alkyl-, or C_{3-6} cycloalkyl, wherein each of the C_{1-8} alkyl, C_{2-8} alkenyl, (C_{3-6} cycloalkyl)-C_{1-4} alkyl-, or C_{3-6} cycloalkyl is optionally substituted with 1, 2, 3, 4, 5, or 6 substituents each independently selected from halogen, -OH, -CN, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy;

each R^2 is independently halogen, -OH, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, or (C_{3-4} cycloalkyl)-C_{1-4} alkyl-, wherein each of the C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, or (C_{3-4} cycloalkyl)-C_{1-4} alkyl- is optionally substituted with 1, 2, or 3 substituents each independently selected from halogen, -OH, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy;

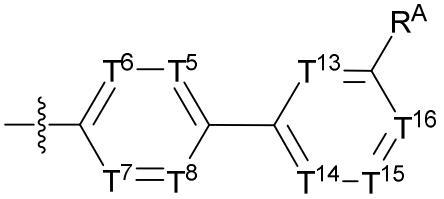
or two R^2 , when attached to a same ring carbon atom of the proline ring in Formula I, together with the ring carbon atom to which they are attached, optionally form C_{3-6} cycloalkyl or a 4- to 7- membered heterocycloalkyl, each of which is optionally substituted with 1, 2, 3, or 4 substituents each independently selected from halogen, -OH, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy;

or two R^2 , when attached to two adjacent ring carbon atoms of the proline ring in Formula I, together with the two ring carbon atoms to which they are attached, optionally form C_{3-6} cycloalkyl or a 4- to 7-membered heterocycloalkyl, each of which is optionally substituted with 1, 2, 3, or 4 substituents each independently selected from halogen, -OH, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy;

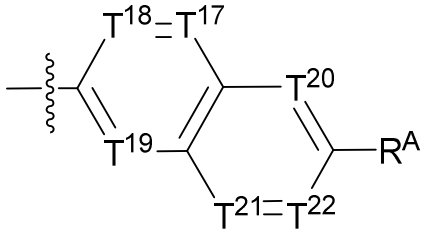
R^3 is R^{3a}, R^{3b}, R^{3c}, or R^{3d}:



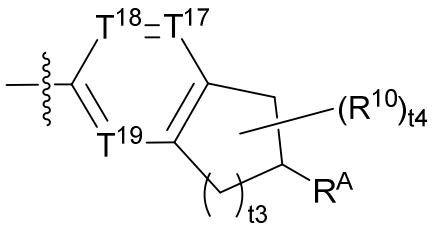
R^{3a},



R^{3b},



R^{3c}, or



R^{3d};

each of T^1, T^2, T^3, and T^4 is independently CR^4 or N, provided that only 0, 1, or 2 of T^1, T^2, T^3, and T^4 can be N;

each R^4 is independently H, halogen, -CN, C_{3-6} cycloalkyl, (C_{3-6} cycloalkyl)-C_{1-2} alkyl-, C_{1-4} alkyl, C_{1-4} cyanoalkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy;

each of T^5, T^6, T^7, and T^8 is independently CR^5 or N, provided that only 0, 1, or 2 of T^5, T^6, T^7, and T^8 can be N;

each R^5 is independently H, halogen, -CN, C_{3-6} cycloalkyl, (C_{3-6} cycloalkyl)-C_{1-2} alkyl-, C_{1-4} alkyl, C_{1-4} cyanoalkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy;

each of T^9, T^{10}, T^{11}, and T^{12} is independently CR^6 or N, provided that only 0, 1, or 2 of T^9, T^{10}, T^{11}, and T^{12} can be N;

each R^6 is independently H, halogen, -CN, C_{3-6} cycloalkyl, (C_{3-6} cycloalkyl)-C_{1-2} alkyl-, C_{1-4} alkyl, C_{1-4} cyanoalkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy;

each of T^{13}, T^{14}, T^{15}, and T^{16} is independently CR^7 or N, provided that only 0, 1, or 2 of T^{13}, T^{14}, T^{15}, and T^{16} can be N;

each R^7 is independently H, halogen, -CN, C_{3-6} cycloalkyl, (C_{3-6} cycloalkyl)-C_{1-2} alkyl-, C_{1-4} alkyl, C_{1-4} cyanoalkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy;

each of T^{17}, T^{18}, and T^{19} is independently CR^8 or N, provided that only 0, 1, or 2 of T^{17}, T^{18}, and T^{19} can be N;

each R^8 is independently H, halogen, -CN, C_{3-6} cycloalkyl, (C_{3-6} cycloalkyl)-C_{1-2} alkyl-, C_{1-4} alkyl, C_{1-4} cyanoalkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy;

each of T^{20}, T^{21}, and T^{22} is independently CR^9 or N, provided that only 0, 1, or 2 of T^{20}, T^{21}, and T^{22} can be N;

each R^9 is independently H, halogen, -CN, C_{3-6} cycloalkyl, (C_{3-6} cycloalkyl)-C_{1-2} alkyl-, C_{1-4} alkyl, C_{1-4} cyanoalkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy;

each R^{10} is independently halogen, -OH, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, or (C_{3-4} cycloalkyl)-C_{1-4} alkyl-, wherein each of the C_{1-4} alkyl, C_{1-4}

haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, or (C_{3-4} cycloalkyl)-C_{1-4} alkyl- is optionally substituted with 1, 2, or 3 substituents each independently selected from halogen, -OH, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy;

R^A is -C(=O)-OH, 1*H*-tetrazol-5-yl, OH, -C(=O)-N(R^{11})(R^{12}), -C(=O)-OR^{13}, 3-hydroxyisoxazol-5-yl, or -S(=O)$_2$NHCF_3;

each of R^{11} and R^{12} is independently H, C_{1-6} alkyl, C_{3-6} cycloalkyl, (C_{3-6} cycloalkyl)-C_{1-4} alkyl-, phenyl, or phenyl-C_{1-4} alkyl-, wherein each of the C_{1-6} alkyl, C_{3-6} cycloalkyl, (C_{3-6} cycloalkyl)-C_{1-4} alkyl-, phenyl, or phenyl-C_{1-4} alkyl- is optionally substituted with 1, 2, 3, 4, or 5 substituents each independently selected from halogen, -OH, -CN, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, or (C_{3-4} cycloalkyl)-C_{1-4} alkyl-;

or R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 8-membered heterocycloalkyl optionally substituted with 1, 2, 3, 4, or 5 substituents each independently selected from halogen, -OH, -CN, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, or (C_{3-4} cycloalkyl)-C_{1-4} alkyl-, wherein each of the C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, or (C_{3-4} cycloalkyl)-C_{1-4} alkyl- is optionally substituted with 1, 2, or 3 substituents each independently selected from halogen, -OH, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy;

R^{13} is C_{1-6} alkyl, C_{3-6} cycloalkyl, (C_{3-6} cycloalkyl)-C_{1-4} alkyl-, phenyl, or phenyl-C_{1-4} alkyl-, each of which is optionally substituted with 1, 2, 3, 4, or 5 substituents each independently selected from halogen, -OH, -CN, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, or (C_{3-4} cycloalkyl)-C_{1-4} alkyl-;

L^1 is C(R^L)$_2$;

each R^L is independently H, C_{1-2} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy, or C_{1-2} haloalkoxy;

or two R^L together with the carbon atom to which they are attached, optionally form C_{3-6} cycloalkyl or a 3- to 6-membered heterocycloalkyl, each of which is optionally substituted with 1, 2, 3, or 4 substituents each independently selected from halogen, -OH, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy;

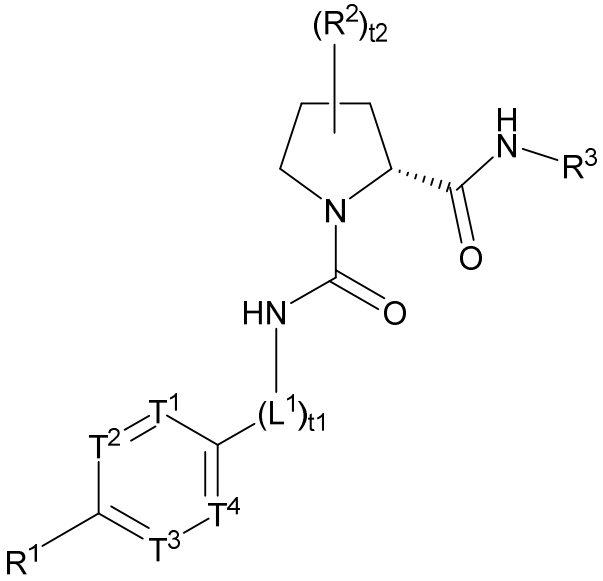
t1 is 0 or 1;

t2 is 0, 1, 2, 3, or 4;

t3 is 1 or 2; and

t4 is 0, 1, 2, 3, or 4.

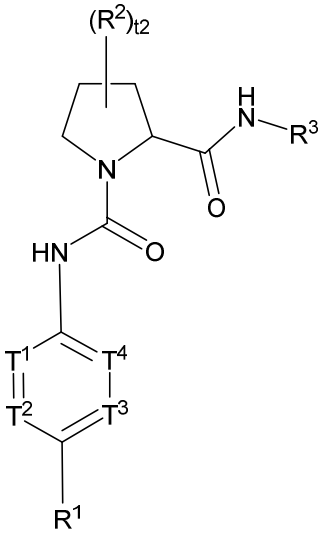
2. The compound of claim 1, wherein the compound is a compound of Formula Ia:



Ia

or a pharmaceutically acceptable salt thereof.

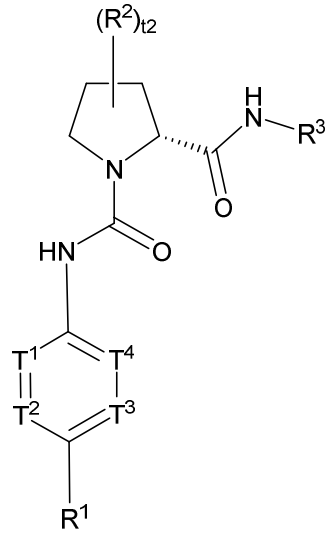
3. The compound of claim 1, wherein the compound is a compound of Formula II:



II

or a pharmaceutically acceptable salt thereof.

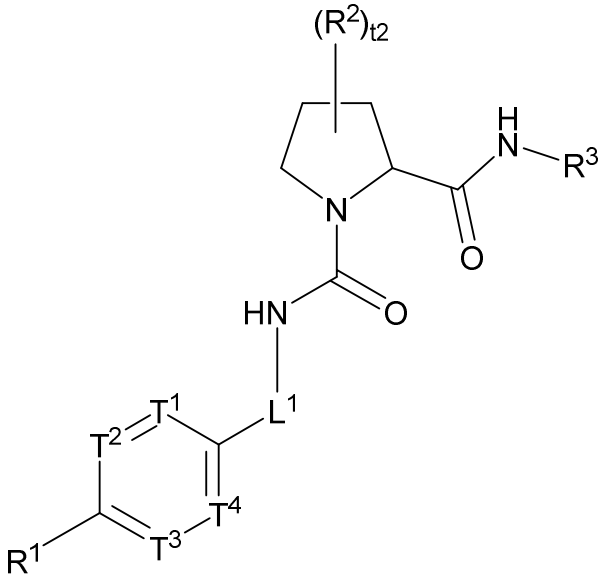
4. The compound of claim 1, wherein the compound is a compound of Formula IIa:



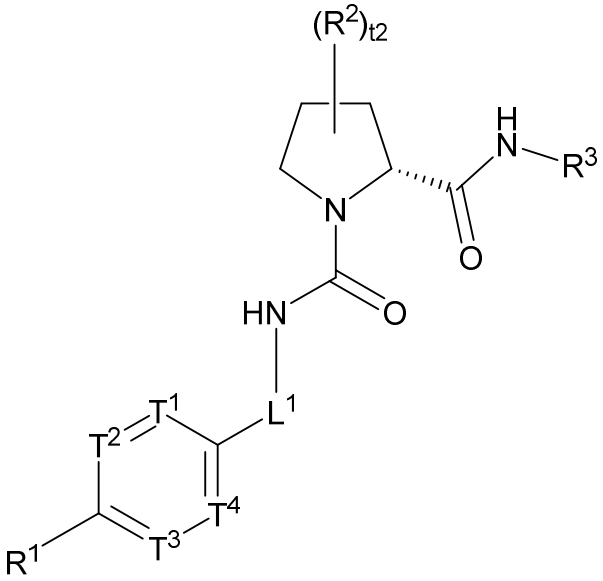
IIa

or a pharmaceutically acceptable salt thereof.

5. The compound of claim 1, wherein the compound is a compound of Formula III or IIIa:



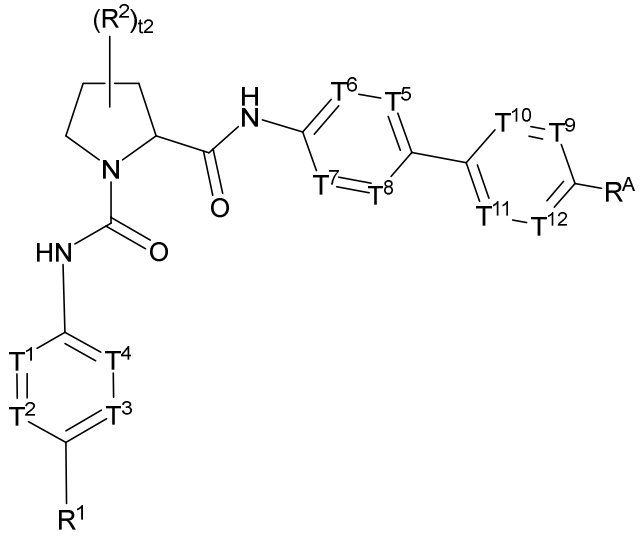
III



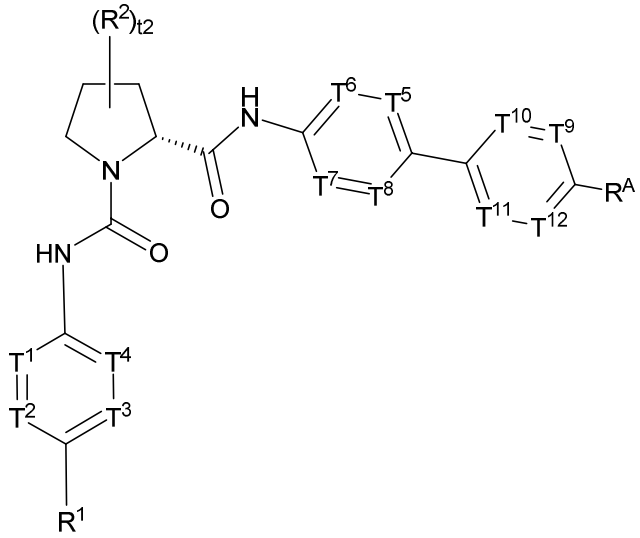
IIIa

or a pharmaceutically acceptable salt thereof.

6. The compound of claim 1, wherein the compound is a compound of Formula IV or IVa:



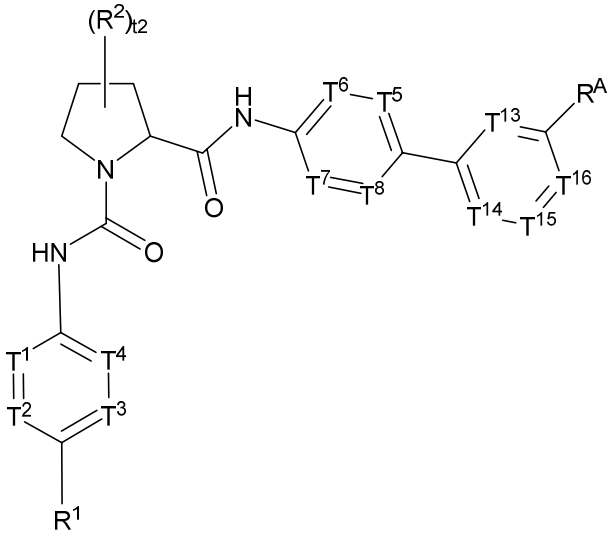
IV



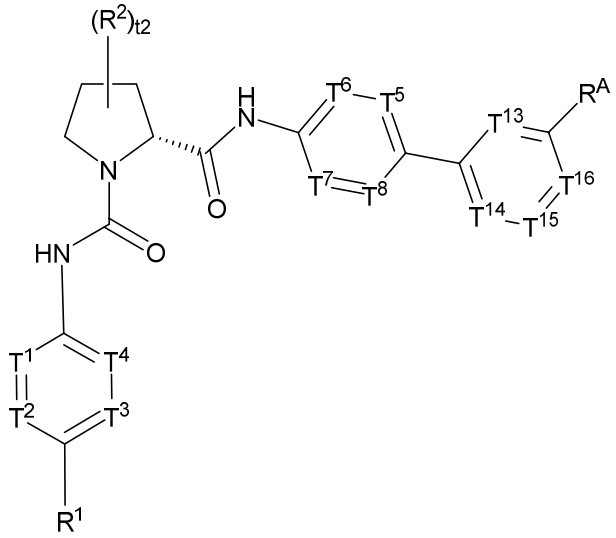
IVa

or a pharmaceutically acceptable salt thereof.

7. The compound of claim 1, wherein the compound is a compound of Formula V or Va:



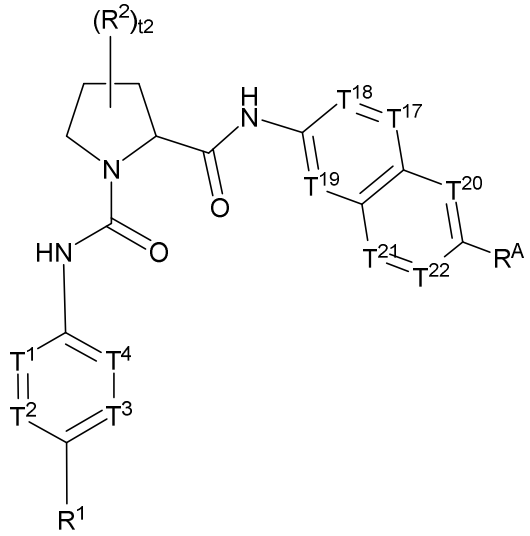
V



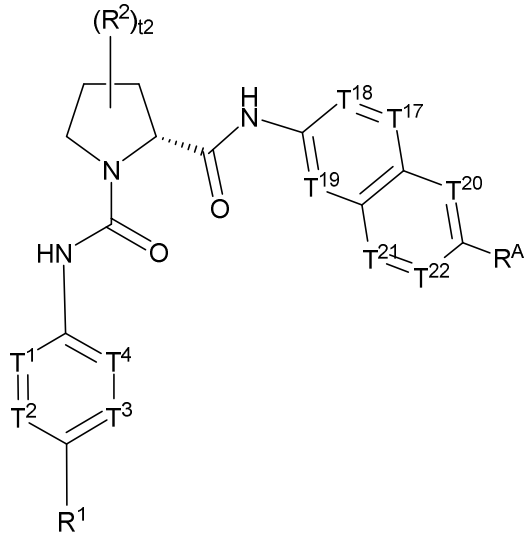
Va

or a pharmaceutically acceptable salt thereof.

8. The compound of claim 1, wherein the compound is a compound of Formula VI or VIa:



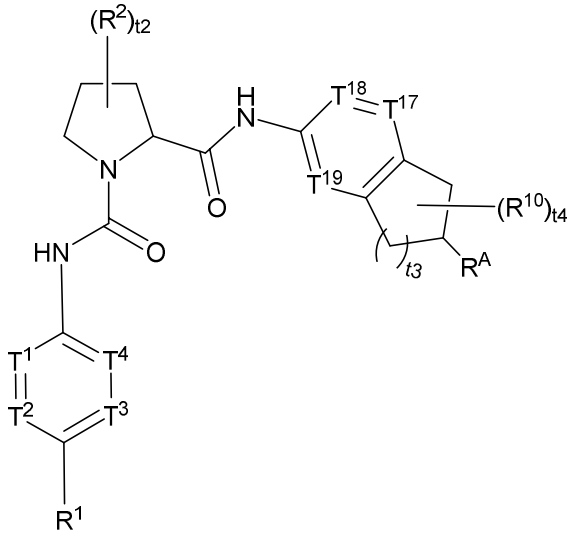
VI



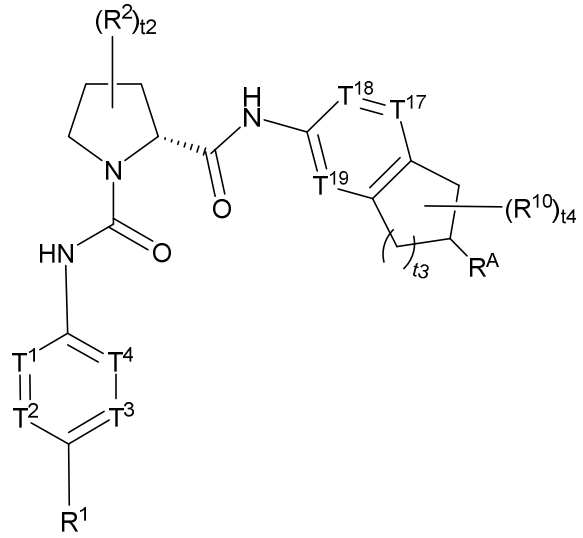
VIa

or a pharmaceutically acceptable salt thereof.

9. The compound of claim 1, wherein the compound is a compound of Formula VII or VIIa:



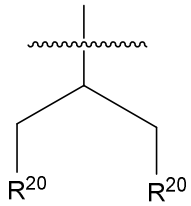
VII



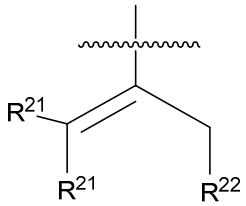
VIIa

or a pharmaceutically acceptable salt thereof.

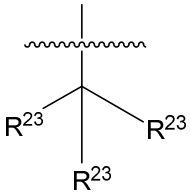
10. The compound of any one of claims 1 to 9, wherein R^1 is cyclopropyl, cyclobutyl, R^{1a}, R^{1b}, or R^{1c},



R^{1a}



R^{1b}



R^{1c}

wherein each of the cyclopropyl or cyclobutyl is optionally substituted with 1, 2, 3, or 4 R^S;

each R^{20} is independently H, halogen, -OH, C_{1-2} alkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy, or C_{1-2} haloalkoxy;

each R^{21} is independently H, C_{1-2} alkyl, or C_{1-2} haloalkyl;

R^{22} is H, halogen, C_{1-2} alkyl, C_{1-2} hydroxylalkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy, or C_{1-2} haloalkoxy;

each R^{23} is independently halogen, C_{1-2} alkyl, C_{1-2} hydroxylalkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy, or C_{1-2} haloalkoxy; and

each R^S is independently halogen, -OH, C_{1-2} alkyl, C_{1-2} hydroxylalkyl, C_{1-2} haloalkyl, C_{1-2} alkoxy, or C_{1-2} haloalkoxy.

11. The compound of any one of claims 1 to 10, wherein R^1 is propan-2-yl, prop-1-en-2-yl, or cyclopropyl.

12. The compound of any one of claims 1 to 11, wherein R^1 is propan-2-yl.

13. The compound of any one of claims 1 to 12, wherein each of T^1, T^2, T^3, and T^4 is independently CR^4.

14. The compound of any one of claims 1 to 12, wherein one of T^1, T^2, T^3, and T^4 is N, and the other three are each independently CR^4.

15. The compound of any one of claims 1 to 14, wherein each R^2 is independently halogen, -OH, C_{1-4} alkyl, C_{1-4} hydroxylalkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, or (C_{3-4} cycloalkyl)-C_{1-4} alkyl-; and t2 is 0, 1, or 2.

16. The compound of any one of claims 1 to 7 and 10 to 15, wherein each of T^5, T^6, T^7, and T^8 is independently CR^5.

17. The compound of any one of claims 1 to 7 and 10 to 15, wherein one of T^5, T^6, T^7, and T^8 is N and the other three are each independently CR^5.

18. The compound of any one of claims 1 to 6 and 10 to 17, wherein each of T^9, T^{10}, T^{11}, and T^{12} is independently CR^6.

19. The compound of any one of claims 1 to 6 and 10 to 17, wherein one of T^9, T^{10}, T^{11}, and T^{12} is N and the other three are each independently CR^6.

20. The compound of any one of claims 1 to 5, 7, and 10 to 15, wherein each of T^{13}, T^{14}, T^{15}, and T^{16} is independently CR^7.

21. The compound of any one of claims 1 to 5, 7, and 10 to 15, wherein one of T^{13}, T^{14}, T^{15}, and T^{16} is N and the other three are each independently CR^7.

22. The compound of any one of claims 1 to 5, 8, 9, and 10 to 15, wherein each of T^{17}, T^{18}, and T^{19} is independently CR^8.

23. The compound of any one of claims 1 to 5, 8, 9, and 10 to 15, wherein one of T^{17}, T^{18}, and T^{19} is N, and the other two are each independently CR^8.

24. The compound of any one of claims 1 to 5, 8, 10 to 15, 22, and 23, wherein each of T^{20}, T^{21}, and T^{22} is independently CR^9.

25. The compound of any one of claims 1 to 5, 8, 10 to 15, 22, and 23, wherein one of T^{20}, T^{21}, and T^{22} is N, and the other two are each independently CR^9.

26. The compound of any one of claims 1 to 5, 9, 10 to 15, 22, and 23, wherein t3 is 2.

27. The compound of any one of claims 1 to 5, 9, 10 to 15, 22, 23, and 26, wherein t4 is 0,1, or 2; and each R^{10} is independently halogen, -OH, C_{1-4} alkyl, C_{1-4} hydroxylalkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, or (C_{3-4} cycloalkyl)-C_{1-4} alkyl-.

28. The compound of any one of claims 1 to 27 wherein R^A is -C(=O)-OH.

29. A compound selected from:

5-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

6-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}pyridine-3-carboxylic acid;

4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-3-carboxylic acid;

4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

4-{6-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]pyridin-3-yl}benzoic acid;

3'-fluoro-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

4'-({1-[(4-cyclopropylphenyl)carbamoyl]-DL-prolyl}amino)[1,1'-biphenyl]-4-carboxylic acid;

2-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}pyrimidine-5-carboxylic acid;

6-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

6-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]naphthalene-2-carboxylic acid;

8-methyl-6-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]quinoline-2-carboxylic acid;

4'-[(1-{[4-(prop-1-en-2-yl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

4'-({1-[(4-chlorophenyl)carbamoyl]-DL-prolyl}amino)[1,1'-biphenyl]-4-carboxylic acid;

4-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}pyridine-2-carboxylic acid; and

3',5'-difluoro-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid,
or a pharmaceutically acceptable salt thereof.

30. A compound selected from:

5-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

6-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}pyridine-3-carboxylic acid;

4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-3-carboxylic acid;

4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

4-{6-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]pyridin-3-yl}benzoic acid;

3'-fluoro-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

4'-({1-[(4-cyclopropylphenyl)carbamoyl]-D-prolyl}amino)[1,1'-biphenyl]-4-carboxylic acid;

2-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}pyrimidine-5-carboxylic acid;

6-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

6-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]naphthalene-2-carboxylic acid;

8-methyl-6-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]quinoline-2-carboxylic acid;

4'-[(1-{[4-(prop-1-en-2-yl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

4'-({1-[(4-chlorophenyl)carbamoyl]-D-prolyl}amino)[1,1'-biphenyl]-4-carboxylic acid;

4-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}pyridine-2-carboxylic acid; and

3',5'-difluoro-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid,
or a pharmaceutically acceptable salt thereof.

31. A compound selected from:

4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

5-{4-[(1-{[3-methyl-4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

6-methyl-5-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

3-methoxy-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

5-{4-[(1-{[3-fluoro-4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}-6-methylpyridine-2-carboxylic acid;

3-fluoro-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

4-{6-[(1-{[4-(trifluoromethyl)phenyl]carbamoyl}-DL-prolyl)amino]pyridin-3-yl}benzoic acid;

4'-[(1-{[3-fluoro-4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]-3-methoxy[1,1'-biphenyl]-4-carboxylic acid;

4-{3-fluoro-5-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]pyridin-2-yl}benzoic acid; and

6-methyl-5-{4-[(1-{[3-methyl-4-(trifluoromethyl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}pyridine-2-carboxylic acid,

or a pharmaceutically acceptable salt thereof.

32. A compound selected from:

4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

5-{4-[(1-{[3-methyl-4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

6-methyl-5-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

3-methoxy-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

5-{4-[(1-{[3-fluoro-4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}-6-methylpyridine-2-carboxylic acid;

3-fluoro-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

4-{6-[(1-{[4-(trifluoromethyl)phenyl]carbamoyl}-D-prolyl)amino]pyridin-3-yl}benzoic acid;

4'-[(1-{[3-fluoro-4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]-3-methoxy[1,1'-biphenyl]-4-carboxylic acid;

4-{3-fluoro-5-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]pyridin-2-yl}benzoic acid; and

6-methyl-5-{4-[(1-{[3-methyl-4-(trifluoromethyl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}pyridine-2-carboxylic acid,

or a pharmaceutically acceptable salt thereof.

33. A compound selected from

4'-[(1-{[4-(trifluoromethyl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

5-{4-[(1-{[3-methyl-4-(trifluoromethyl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

4-{5-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]pyridin-2-yl}benzoic acid;

5-{4-[(1-{[3-methyl-4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

6-methyl-5-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

3-methoxy-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

4-{5-[(1-{[4-(trifluoromethyl)phenyl]carbamoyl}-DL-prolyl)amino]pyridin-2-yl}benzoic acid;

4'-({1-[(4-cyclobutylphenyl)carbamoyl]-DL-prolyl}amino)[1,1'-biphenyl]-4-carboxylic acid;

4-{5-fluoro-6-[(1-{[4-(trifluoromethyl)phenyl]carbamoyl}-DL-prolyl)amino]pyridin-3-yl}benzoic acid;

4-{5-fluoro-6-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]pyridin-3-yl}benzoic acid;

4'-[(1-{[4-cyclopropyl-3-(trifluoromethyl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

5-{4-[(1-{[3-fluoro-4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]phenyl}-6-methylpyridine-2-carboxylic acid;

3-fluoro-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

2-methoxy-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

3-methoxy-4'-[(1-{[3-methyl-4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

4-{6-[(1-{[4-(trifluoromethyl)phenyl]carbamoyl}-DL-prolyl)amino]pyridin-3-yl}benzoic acid;

4'-[(1-{[3-fluoro-4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]-3-methoxy[1,1'-biphenyl]-4-carboxylic acid;

4-{3-fluoro-5-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl)amino]pyridin-2-yl}benzoic acid;

4'-{[3-methyl-1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid;

4'-{[(*trans*)-3-methyl-1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid;

4'-{[3-methyl-1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid;

4'-{[(3-*trans*)-3-methyl-1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid;

4'-{[4-methoxy-1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid;

4'-{[(4-*cis*)-4-methoxy-1-{[4-(propan-2-yl)phenyl]carbamoyl}-DL-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid;

4'-{[1-({1-[4-(propan-2-yl)phenyl]ethyl}carbamoyl)-DL-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid; and

3-[6-({1-[(4-cyclobutylphenyl)carbamoyl]-DL-prolyl}amino)pyridin-3-yl]benzoic acid,

or a pharmaceutically acceptable salt thereof.

34. A compound selected from

4'-[(1-{[4-(trifluoromethyl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

5-{4-[(1-{[3-methyl-4-(trifluoromethyl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

4-{5-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]pyridin-2-yl}benzoic acid;

5-{4-[(1-{[3-methyl-4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

6-methyl-5-{4-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}pyridine-2-carboxylic acid;

3-methoxy-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

4-{5-[(1-{[4-(trifluoromethyl)phenyl]carbamoyl}-D-prolyl)amino]pyridin-2-yl}benzoic acid;

4'-({1-[(4-cyclobutylphenyl)carbamoyl]-D-prolyl}amino)[1,1'-biphenyl]-4-carboxylic acid;

4-{5-fluoro-6-[(1-{[4-(trifluoromethyl)phenyl]carbamoyl}-D-prolyl)amino]pyridin-3-yl}benzoic acid;

4-{5-fluoro-6-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]pyridin-3-yl}benzoic acid;

4'-[(1-{[4-cyclopropyl-3-(trifluoromethyl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

5-{4-[(1-{[3-fluoro-4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]phenyl}-6-methylpyridine-2-carboxylic acid;

3-fluoro-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

2-methoxy-4'-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

3-methoxy-4'-[(1-{[3-methyl-4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino][1,1'-biphenyl]-4-carboxylic acid;

4-{6-[(1-{[4-(trifluoromethyl)phenyl]carbamoyl}-D-prolyl)amino]pyridin-3-yl}benzoic acid;

4'-[(1-{[3-fluoro-4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]-3-methoxy[1,1'-biphenyl]-4-carboxylic acid;

4-{3-fluoro-5-[(1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl)amino]pyridin-2-yl}benzoic acid;

4'-{[(3S)-3-methyl-1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid;

4'-{[(3R)-3-methyl-1-{[4-(propan-2-yl)phenyl]carbamoyl}-L-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid;

4'-{[(3R)-3-methyl-1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid;

4'-{[(3S)-3-methyl-1-{[4-(propan-2-yl)phenyl]carbamoyl}-L-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid;

4'-{[(4R)-4-methoxy-1-{[4-(propan-2-yl)phenyl]carbamoyl}-D-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid;

4'-{[1-({(1S)-1-[4-(propan-2-yl)phenyl]ethyl}carbamoyl)-D-prolyl]amino}[1,1'-biphenyl]-4-carboxylic acid; and

3-[6-({1-[(4-cyclobutylphenyl)carbamoyl]-D-prolyl}amino)pyridin-3-yl]benzoic acid,

or a pharmaceutically acceptable salt thereof.

35. A pharmaceutical composition comprising a compound of any one of claims 1 to 34 and a pharmaceutically acceptable excipient.

36. Use of a compound of any one of claims 1 to 34, in the manufacture of a medicament for treating or preventing a condition, disease, or disorder, wherein the condition, disease, or disorder is selected from the group consisting of diabetes [e.g. Type 1 diabetes mellitus (T1D), Type 2 diabetes mellitus (T2DM), including pre-diabetes], idiopathic T1D (Type 1b), latent autoimmune diabetes in adults (LADA), early-onset T2DM (EOD), youth-onset atypical diabetes (YOAD), maturity onset diabetes of the young (MODY), malnutrition-related diabetes, gestational diabetes, hyperglycemia, insulin resistance, hepatic insulin resistance, impaired glucose tolerance, diabetic neuropathy, diabetic nephropathy, kidney disease [e.g., acute kidney disorder, tubular dysfunction, proinflammatory changes to the proximal tubules, or chronic kidney disease (CKD)], diabetic retinopathy, adipocyte dysfunction, visceral adipose deposition, sleep apnea [e.g. obstructive sleep apnea (OSA)], obesity (including hypothalamic

obesity and monogenic obesity) and related comorbidities (e.g., osteoarthritis and urine incontinence), eating disorders (including binge eating syndrome, bulimia nervosa, and syndromic obesity such as Prader-Willi and Bardet-Biedl syndromes), weight gain such as weight gain caused by use of other agents (e.g., caused by use of steroids and/or antipsychotics, or caused by treatment of depression, or caused by use of agents on cognitive function), overweight, excessive sugar craving, dyslipidemia [including hyperlipidemia, hypertriglyceridemia, increased total cholesterol, high LDL (low-density lipoprotein) cholesterol, and low HDL (high-density lipoprotein) cholesterol], hyperinsulinemia, nonalcoholic fatty liver disease [NAFLD, including related diseases such as steatosis, nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma], cardiovascular disease, atherosclerosis (including coronary artery disease), peripheral vascular disease, hypertension, endothelial dysfunction, impaired vascular compliance, heart failure [e.g. congestive heart failure, heart failure with preserved ejection fraction (HFpEF), heart failure with reduced ejection fraction (HFrEF)], myocardial infarction (e.g. necrosis and apoptosis), stroke, hemorrhagic stroke, ischemic stroke, traumatic brain injury, pulmonary hypertension, restenosis after angioplasty, intermittent claudication, post-prandial lipemia, metabolic acidosis, ketosis, arthritis, osteoporosis, osteoarthritis, Parkinson's disease, left ventricular hypertrophy, peripheral arterial disease (PAD), macular degeneration, cataract, glomerulosclerosis, chronic renal failure, metabolic syndrome, syndrome X, premenstrual syndrome, angina pectoris, thrombosis, atherosclerosis, transient ischemic attacks, vascular restenosis, impaired glucose metabolism, conditions of impaired fasting plasma glucose, hyperuricemia, gout, erectile dysfunction, skin and connective tissue disorders, psoriasis, foot ulcerations, ulcerative colitis, hyper apo B lipoproteinemia, Alzheimer's Disease, schizophrenia, impaired cognition, inflammatory bowel disease, short bowel syndrome, Crohn's disease, colitis, irritable bowel syndrome, polycystic ovary syndrome (PCOS), and addiction (e.g., addition to alcohol, nicotine, and/or drug); or use of a compound of any one of claims 1 to 32, in the manufacture of a medicament for weight management (e.g. chronic weight management).

37. A compound of any one of claims 1 to 34, for use in therapy.

38. A method for modulating a glucose-dependent insulinotropic polypeptide receptor (GIPR) comprising contacting the GIPR with a compound of any one of clams 1 to 34.