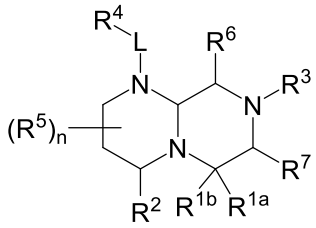
(Matsumoto et al., 2014), stimulation of the HGF/MET signaling system is an ideal target for therapeutics for a range of disease states. Therapeutics involving HGF activity modulation have been proposed for disease and injury in many diverse tissue types including liver, kidney, gastrointestinal tract, cardiovascular components, lung, skin, nervous system, and musculature (Matsumoto et al., 2014). However, highly efficacious compounds useful for the modulation of HGF/MET signaling activity are yet to be explored and discovered.

[0005] Although progress has been made in this field, there remains a need for improved compounds and methods for treatment of HGF-modulated diseases. Accordingly, in one aspect, provided herein are compounds which modulate HGF for use in treating neurodegenerative diseases.

SUMMARY

[0006] Described herein~~, in certain embodiments,~~ are compounds and compositions thereof for modulating hepatocyte growth factor (HGF) for treatment of diseases. Nonlimiting ~~exemplary embodiments~~examples include:

[0007] ~~Embodiment~~Example 1. A compound of Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein:

L is a direct bond, -C(=O)-, -$(CR^aR^b)_m$-C(=O)-, -C(=O)-$(CR^aR^b)_m$-, or -$(CR^aR^b)_m$-;

each R^a and R^b is independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl;

R^{1a} and R^{1b} are independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, halo, or C_6-C_{10} arylalkyl;

R^2 is H, oxo, or thioxo;

R^3 is C_2-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, C_3-C_{12} cycloalkyl, C_3-C_6 cycloalkylalkyl, C_6-C_{10} arylalkyl, 5- to 10-membered heteroarylalkyl, or 5- to 10-membered heterocyclylalkyl,

wherein the 5- to 10-membered heteroarylalkyl or 5- to 10-membered heterocyclylalkyl contains 1-3 heteroatoms selected from nitrogen and oxygen;

R^4 is C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 5- to 10-membered heterocyclyl,

wherein the 5- to 10-membered heteroaryl or 5- to 10-membered heterocyclyl contains 1-3 heteroatoms selected from nitrogen and oxygen;

each R^5 is independently C_1-C_6 alkyl, oxo, or halo;

R^6 is H, C_1-C_6 alkyl, or oxo;

R^7 is H or oxo;

m is 1 or 2; and

n is an integer from 0 to 3;

wherein each C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_{12} cycloalkyl, C_3-C_{12} cycloalkylalkyl, C_6-C_{10} aryl, C_6-C_{10} arylalkyl, 5- to 10-membered heteroaryl, 5- to 10-membered heteroarylalkyl, 5- to 10-membered heterocyclyl, and 5- to 10-membered heterocyclylalkyl is optionally substituted with one to five substituents selected from hydroxyl, halo, amino, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, cyano, -(C=O)NH_2, nitro, -SO_2(C_1-C_6 alkyl), and -CO_2H.

[0008] ~~Embodiment~~Example 2. The compound of ~~embodiment~~example 1, or a pharmaceutically acceptable salt thereof, wherein L is -C(=O)- or -$(CR^aR^b)_m$-.

[0009] ~~Embodiment~~Example 3. The compound of ~~embodiment~~example 1 or 2, or a pharmaceutically acceptable salt thereof, wherein L is a -C(=O)-.

[0010] ~~Embodiment~~Example 4. The compound of ~~embodiment~~example 1 or 2, or a pharmaceutically acceptable salt thereof, wherein L is -$(CR^aR^b)_m$-.

[0011] ~~Embodiment~~Example 5. The compound of ~~embodiment~~example 4, or a pharmaceutically acceptable salt thereof, wherein R^a and R^b are each H, and m is 1.

[0012] ~~Embodiment~~Example 6. The compound of any one of ~~embodiments~~examples 1-5, or a pharmaceutically acceptable salt thereof, wherein R^{1a} and R^{1b} are each independently H; C_1-C_6 alkyl optionally substituted with 1-3 substituents selected from halo, -CO_2H, and -C(=O)NH_2; C_1-C_6 alkoxy; halo; or C_6-C_{10} arylalkyl optionally substituted by 1-3 substituents selected from halo and amino.

[0013] ~~Embodiment~~Example 7. The compound of ~~embodiment~~example 6, or a pharmaceutically acceptable salt thereof, wherein R^{1a} and R^{1b} are each independently H, methyl, fluoro, 2-methylbutyl, $-CH_2F$, methoxy, $-CH_2CO_2H$, $-CH_2C(=O)NH_2$, benzyl, or 4-aminobenzyl.

[0014] ~~Embodiment~~Example 8. The compound of ~~embodiment~~example 6, or a pharmaceutically acceptable salt thereof, wherein R^{1a} and R^{1b} are each independently H or C_1-C_3 alkyl.

[0015] ~~Embodiment~~Example 9. The compound of ~~embodiment~~example 8, or a pharmaceutically acceptable salt thereof, wherein R^{1a} is methyl and R^{1b} is H.

[0016] ~~Embodiment~~Example 10. The compound of ~~embodiment~~example 8, or a pharmaceutically acceptable salt thereof, wherein R^{1a} and R^{1b} are each H.

[0017] ~~Embodiment~~Example 11. The compound of any one of ~~embodiments~~examples 1-10, or a pharmaceutically acceptable salt thereof, wherein R^2 is H.

[0018] ~~Embodiment~~Example 12. The compound of any one of ~~embodiments~~examples 1-10, or a pharmaceutically acceptable salt thereof, wherein R^2 is thioxo.

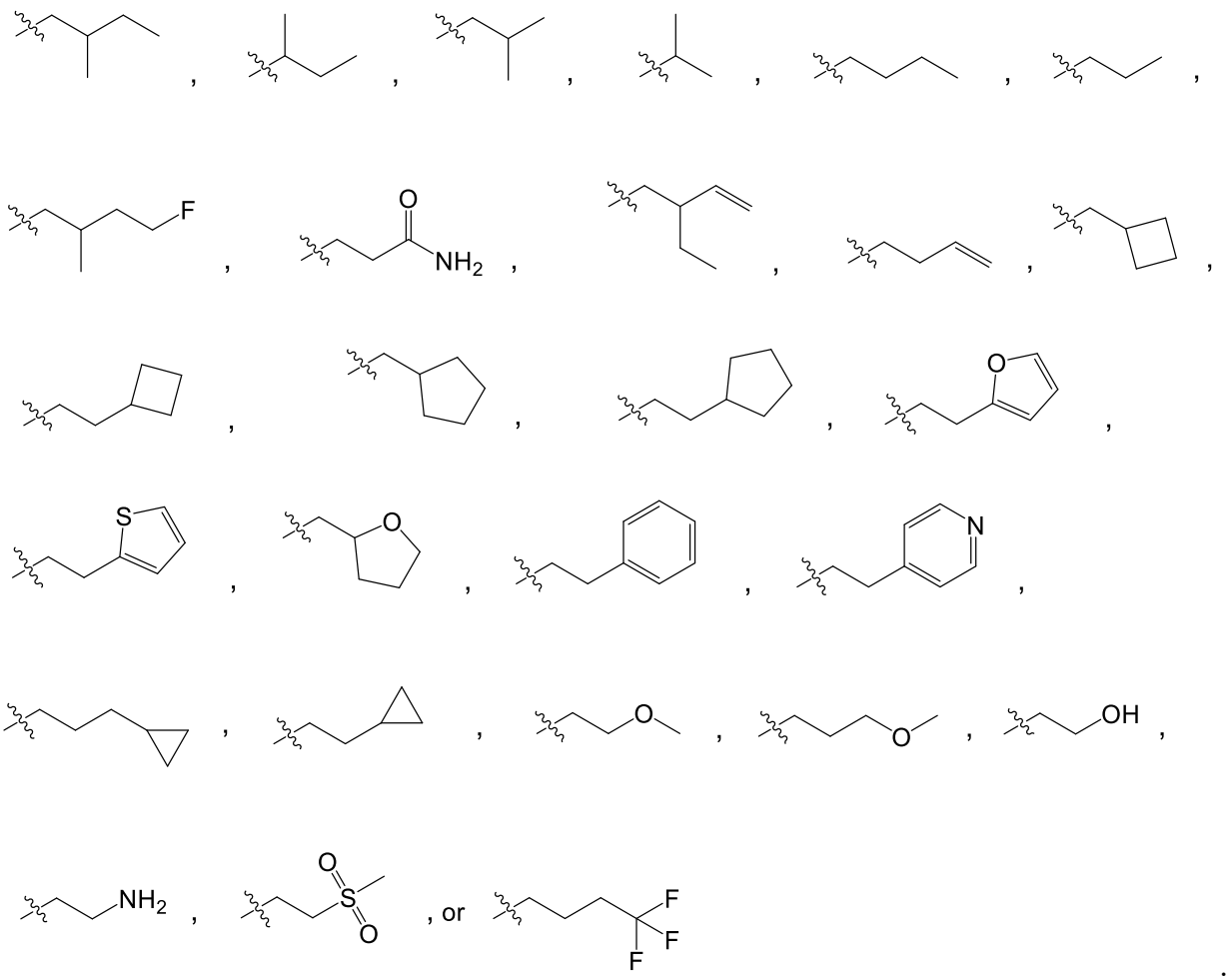
[0019] ~~Embodiment~~Example 13. The compound of any one of ~~embodiments~~examples 1-10, or a pharmaceutically acceptable salt thereof, wherein R^2 is oxo.

[0020] ~~Embodiment~~Example 14. The compound of any one of ~~embodiments~~examples 1-13, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_3-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, C_3-C_{12} cycloalkyl, C_3-C_6 cycloalkylalkyl, C_6-C_{10} arylalkyl, 5- to 10-membered heteroarylalkyl, or 5- to 10-membered heterocyclylalkyl, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, arylalkyl, heteroarylalkyl, or heterocyclylalkyl is optionally substituted with one to five substituents selected from hydroxyl, halo, amino, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, cyano, $-(C=O)NH_2$, nitro, $-SO_2(C_1$-C_6 alkyl), and $-CO_2H$.

[0021] ~~Embodiment~~Example 15. The compound of any one of ~~embodiments~~examples 1-13, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_2-C_6 alkyl optionally substituted by 1-3 substituents selected from halo, C_1-C_3 alkoxy, hydroxy, $-NH_2$, $-SO_2(C_1$-C_3 alkyl), and $-C(=O)NH_2$; C_2-C_6 alkenyl; C_3-C_6 cycloalkylalkyl; 5- to 6-membered heteroarylalkyl; 5- to 6-membered heterocyclylalkyl; or C_6 arylalkyl.

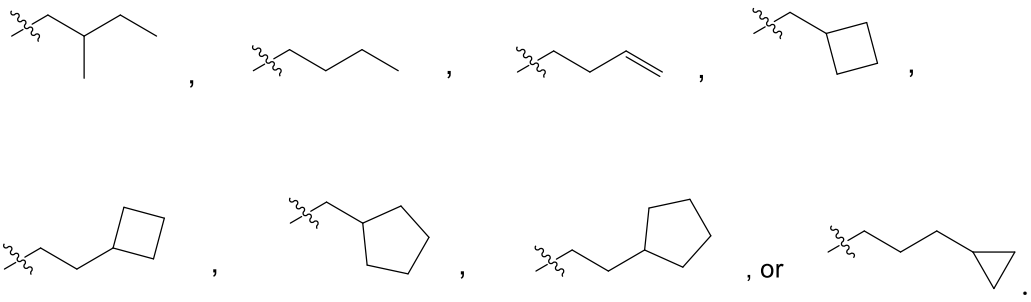
[0022] ~~Embodiment~~Example 16. The compound of ~~embodiment~~example 15, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_2 alkyl substituted by 1-3 substituents selected from C_1-C_3 alkoxy, hydroxy, $-NH_2$, and $-SO_2(C_1$-C_3 alkyl).

[0023] ~~Embodiment~~Example 17. The compound of any one of ~~embodiments~~examples 14-16, or a pharmaceutically acceptable salt thereof, wherein R^3 is:



, or .

[0024] ~~Embodiment~~Example 18. The compound of ~~embodiment~~example 17, or a pharmaceutically acceptable salt thereof, wherein R^3 is:

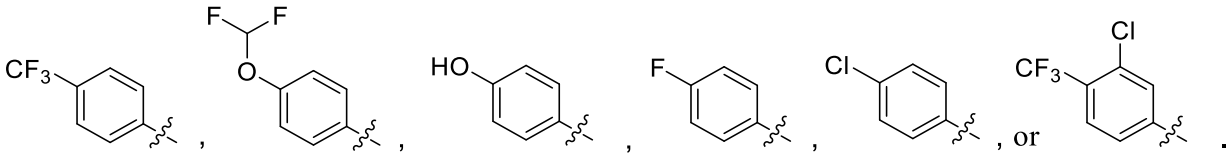


, or .

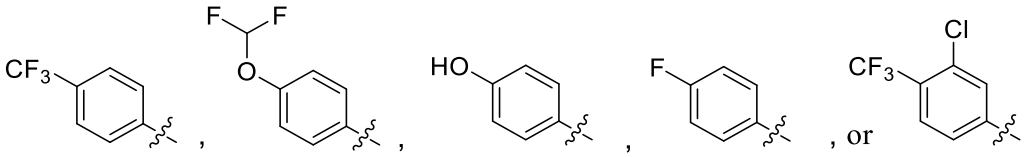
[0025] ~~Embodiment~~Example 19. The compound of any one of ~~embodiments~~examples 1-18, or a pharmaceutically acceptable salt thereof, wherein R^4 is C_6-C_{10} aryl optionally substituted with 1-3 substituents selected from halo, hydroxyl, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy.

[0026] ~~Embodiment~~Example 20. The compound of ~~embodiment~~example 19, or a pharmaceutically acceptable salt thereof, wherein R^4 is phenyl substituted with 1-3 substituents selected from -CF_3, -$OCHF_2$, -OH, fluoro, and chloro.

[0027] ~~Embodiment~~Example 21. The compound of ~~embodiment~~example 20, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



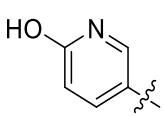
[0028] ~~Embodiment~~Example 22. The compound of ~~embodiment~~example 21, or a pharmaceutically acceptable salt thereof, wherein R^4 is:

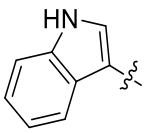


[0029] ~~Embodiment~~Example 23. The compound of any one of ~~embodiments~~examples 1-18, or a pharmaceutically acceptable salt thereof, wherein R^4 is 5- to 10-membered heteroaryl optionally substituted with 1-3 substituents selected from halo, hydroxyl, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy.

[0030] ~~Embodiment~~Example 24. The compound of ~~embodiment~~example 23, or a pharmaceutically acceptable salt thereof, wherein R^4 is pyridyl or indolyl optionally substituted with 1-3 substituents selected from halo, hydroxyl, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy.

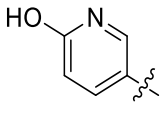
[0031] ~~Embodiment~~Example 25. The compound of ~~embodiment~~example 24, or a pharmaceutically acceptable salt thereof, wherein

R^4 is 

or 

.

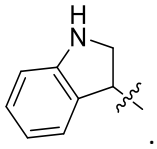
[0032] ~~Embodiment~~Example 26. The compound of ~~embodiment~~example 25, or a pharmaceutically acceptable salt thereof, wherein

R^4 is 

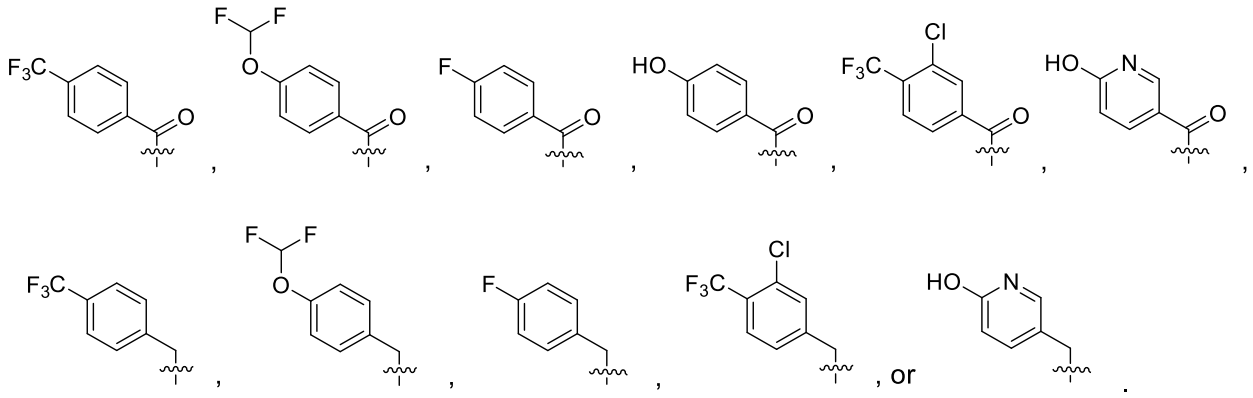
.

[0033] ~~Embodiment~~Example 27. The compound of any one of ~~embodiments~~examples 1-18, or a pharmaceutically acceptable salt thereof, wherein R^4 is 5- to 10-membered heterocyclyl optionally substituted with 1-3 substituents selected from halo, hydroxyl, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy.

[0034] ~~Embodiment~~Example 28. The compound of ~~embodiment~~example 27, or a pharmaceutically acceptable salt thereof, wherein R^4 is indolinyl.

[0035] ~~Embodiment~~Example 29. The compound of ~~embodiment~~example 28, or a pharmaceutically acceptable salt thereof, wherein R^4 is .

[0036] ~~Embodiment~~Example 30. The compound of any one of ~~embodiments~~examples 1-26, or a pharmaceutically acceptable salt thereof, wherein -L-R^4 is:



[0037] ~~Embodiment~~Example 31. The compound of any one of ~~embodiments~~examples 1-30, or a pharmaceutically acceptable salt thereof, wherein n is 0.

[0038] ~~Embodiment~~Example 32. The compound of any one of ~~embodiments~~examples 1-30, or a pharmaceutically acceptable salt thereof, wherein n is 1.

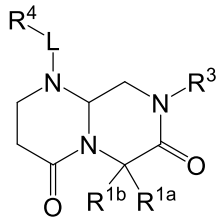
[0039] ~~Embodiment~~Example 33. The compound of ~~embodiment~~example 32, or a pharmaceutically acceptable salt thereof, wherein R^5 is oxo or halo.

[0040] ~~Embodiment~~Example 34. The compound of ~~embodiment~~example 33, or a pharmaceutically acceptable salt thereof, wherein R^5 is oxo or fluoro.

[0041] ~~Embodiment~~Example 35. The compound of any one of ~~embodiments~~examples 1-34, or a pharmaceutically acceptable salt thereof, wherein R^6 is H.

[0042] ~~Embodiment~~Example 36. The compound of any one of ~~embodiments~~examples 1-35, or a pharmaceutically acceptable salt thereof, wherein R^7 is oxo.

[0043] ~~Embodiment~~Example 37. The compound of any one of ~~embodiments~~examples 1-10, 13-31, 35, and 36, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula (V):



(V) .

[0044] ~~Embodiment~~Example 38. The compound of ~~embodiment~~example 37, or a pharmaceutically acceptable salt thereof, wherein:

L is -C(=O)- or -CH_2-;

R^{1a} and R^{1b} are independently H or C_1-C_3 alkyl optionally substituted with -CO_2H;

R^3 is C_4-C_5 alkyl, C_4-C_5 alkenyl, or C_1-C_3 alkyl substituted with C_3-C_5 cycloalkyl; and

R^4 is phenyl or pyridyl substituted with 1-3 substituents selected from -CF_3, -$OCHF_2$, -OH, fluoro, and chloro.

[0045] ~~Embodiment~~Example 39. A compound selected from the compounds of Table 1A and pharmaceutically acceptable salts thereof.

[0046] ~~Embodiment~~Example 40. A pharmaceutical composition comprising the compound of any one of ~~embodiments~~examples 1-39, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

[0047] ~~Embodiment~~Example 41. A method for modulating hepatocyte growth factor in a subject in need thereof, the method comprising administering to the subject an effective amount of the compound of any one of ~~embodiments~~examples 1-39, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of ~~embodiment~~example 40.

[0048] ~~Embodiment~~Example 42. The method of ~~embodiment~~example 41, wherein the modulating comprises treating a disease, condition, or injury.

[0049] ~~Embodiment~~Example 43. The method of ~~embodiment~~example 42, wherein the disease, condition, or injury is a neurodegenerative disease, a spinal cord injury, a traumatic brain injury, or a sensorineural hearing loss.

[0050] ~~Embodiment~~Example 44. The method of ~~embodiment~~example 42 or 43, wherein the disease, condition, or injury is a neurodegenerative disease.

[0051] ~~Embodiment~~Example 45. The method of ~~embodiment~~example 44, wherein the neurodegenerative disease is Alzheimer's disease, Parkinson's disease, Huntington's disease, or amyotrophic lateral sclerosis (ALS).

[0052] ~~Embodiment~~Example 46. The method of ~~embodiment~~example 45, wherein the neurodegenerative disease is Alzheimer's disease or Parkinson's disease.

[0053] ~~Embodiment~~Example 47. A method for treating or slowing progression of dementia in a subject in need thereof, the method comprising administering to the subject an effective amount of the compound of any one of ~~embodiments~~examples 1-39, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of ~~embodiment~~example 40.

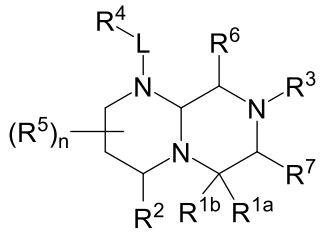
[0054] ~~Embodiment~~Example 48. The method of ~~embodiment~~example 47, wherein the dementia is associated with Alzheimer’s disease or Parkinson’s disease.

[0055] ~~Embodiment~~Example 49. A method for preventing cognitive dysfunction in a subject in need thereof, the method comprising administering to the subject an effective amount of the compound of any one of ~~embodiments~~examples 1-39, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of ~~embodiment~~example 40.

[0056] ~~Embodiment~~Example 50. A method for treating, repairing or preventing a disease, condition or injury related to nerve tissue in a subject in need thereof, the method comprising administering to the subject an effective amount of the compound of any one of ~~embodiments~~examples 1-39, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of ~~embodiment~~example 40.

[0057] ~~Embodiment~~Example 51. A method of treating or preventing a disease or disorder of the central nervous system, a disease or disorder of the peripheral nervous system, neuropathic pain, anxiety, or depression in a subject in need thereof, the method comprising administering to the subject an effective amount of the compound of any one of ~~embodiments~~examples 1-39, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of ~~embodiment~~example 40.

[0057a] In one aspect, the present disclosure provides a compound of Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein:

L is a direct bond, -C(=O)-, -$(CR^aR^b)_m$-C(=O)-, -C(=O)-$(CR^aR^b)_m$-, or -$(CR^aR^b)_m$-;

each R^a and R^b is independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl;

R^{1a} and R^{1b} are independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, halo, or C_6-C_{10} arylalkyl;

R^2 is H, oxo, or thioxo;

R^3 is C_2-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, C_3-C_{12} cycloalkyl, C_3-C_6 cycloalkylalkyl, C_6-C_{10} arylalkyl, 5- to 10-membered heteroarylalkyl, or 5- to 10-membered heterocyclylalkyl,

wherein the 5- to 10-membered heteroarylalkyl or 5- to 10-membered heterocyclylalkyl contains 1-3 heteroatoms selected from nitrogen and oxygen;

R^4 is C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 5- to 10-membered heterocyclyl,

wherein the 5- to 10-membered heteroaryl or 5- to 10-membered heterocyclyl contains 1-3 heteroatoms selected from nitrogen and oxygen;

each R^5 is independently C_1-C_6 alkyl, oxo, or halo;

R^6 is H, C_1-C_6 alkyl, or oxo;

R^7 is H or oxo;

m is 1; and

n is an integer from 0 to 3;

wherein each C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_{12} cycloalkyl, C_3-C_{12} cycloalkylalkyl, C_6-C_{10} aryl, C_6-C_{10} arylalkyl, 5- to 10-membered heteroaryl, 5- to 10-membered heteroarylalkyl, 5- to 10-membered heterocyclyl, and 5- to 10-membered heterocyclylalkyl is optionally substituted with one to five substituents selected from hydroxyl, halo, amino, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, cyano, -(C=O)NH_2, nitro, -SO_2(C_1-C_6 alkyl), and -CO_2H.

[0057b] In another aspect, the present disclosure provides a compound selected from the compounds of Table 1A and pharmaceutically acceptable salts thereof.

[0057c] In another aspect, the present disclosure provides a pharmaceutical composition comprising the compound as described herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

[0057d] In another aspect, the present disclosure provides use of the compound as described herein, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition as described herein, in the manufacture of a medicament for treating or slowing progression of dementia in a subject in need thereof, optionally wherein the dementia is associated with Alzheimer's disease or Parkinson's disease.

[0057e] In another aspect, the present disclosure provides use of the compound as described herein, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition as described herein in the manufacture of a medicament for preventing cognitive dysfunction in a subject in need thereof.

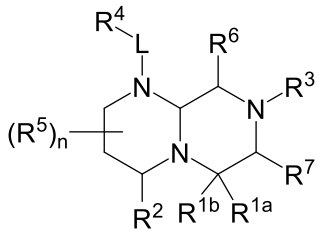
[0057f] In another aspect, the present disclosure provides use of the compound as described herein, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition as described herein in the manufacture of a medicament for treating, repairing or preventing a disease, condition or injury related to nerve tissue in a subject in need thereof.

[0057g] In another aspect, the present disclosure provides use of the compound as described herein, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition as described herein in the manufacture of a medicament for treating or preventing a disease or disorder of the central nervous system, a disease or disorder of the peripheral nervous system, neuropathic pain, anxiety, or depression in a subject in need thereof.

[0057h] In another aspect, the present disclosure provides the compound as described herein, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition as described herein for use in therapy.

CLAIMS

1. A compound of Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein:

L is a direct bond, -C(=O)-, -$(CR^aR^b)_m$-C(=O)-, -C(=O)-$(CR^aR^b)_m$-, or -$(CR^aR^b)_m$-;

each R^a and R^b is independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl;

R^{1a} and R^{1b} are independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, halo, or C_6-C_{10} arylalkyl;

R^2 is H, oxo, or thioxo;

R^3 is C_2-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, C_3-C_{12} cycloalkyl, C_3-C_6 cycloalkylalkyl, C_6-C_{10} arylalkyl, 5- to 10-membered heteroarylalkyl, or 5- to 10-membered heterocyclylalkyl,

wherein the 5- to 10-membered heteroarylalkyl or 5- to 10-membered heterocyclylalkyl contains 1-3 heteroatoms selected from nitrogen and oxygen;

R^4 is C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 5- to 10-membered heterocyclyl,

wherein the 5- to 10-membered heteroaryl or 5- to 10-membered heterocyclyl contains 1-3 heteroatoms selected from nitrogen and oxygen;

each R^5 is independently C_1-C_6 alkyl, oxo, or halo;

R^6 is H, C_1-C_6 alkyl, or oxo;

R^7 is H or oxo;

m is 1~~ or 2~~; and

n is an integer from 0 to 3;

wherein each C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_{12} cycloalkyl, C_3-C_{12} cycloalkylalkyl, C_6-C_{10} aryl, C_6-C_{10} arylalkyl, 5- to 10-membered heteroaryl, 5- to 10-

membered heteroarylalkyl, 5- to 10-membered heterocyclyl, and 5- to 10-membered heterocyclylalkyl is optionally substituted with one to five substituents selected from hydroxyl, halo, amino, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, cyano, -(C=O)NH_2, nitro, -SO_2(C_1-C_6 alkyl), and -CO_2H.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein L is -C(=O)- or -(CR^aR^b)$_m$-, wherein R^a and R^b are each H.

~~3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein L is a -C(=O)-.~~

~~4. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein L is -(CR^aR^b)$_m$-.~~

~~5. The compound of claim 4, or a pharmaceutically acceptable salt thereof, wherein R^a and R^b are each H, and m is 1.~~

~~6. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein R^{1a} and R^{1b} are each independently H; C_1-C_6 alkyl optionally substituted with 1-3 substituents selected from halo, -CO_2H, and -C(=O)NH_2; C_1-C_6 alkoxy; halo; or C_6-C_{10} arylalkyl optionally substituted by 1-3 substituents selected from halo and amino.~~

~~7. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein R^{1a} and R^{1b} are each independently H, methyl, fluoro, 2-methylbutyl, -CH_2F, methoxy, -CH_2CO_2H, -$CH_2C(=O)NH_2$, benzyl, or 4-aminobenzyl.~~

~~8.~~3. The compound of claim ~~6~~1 or 2, or a pharmaceutically acceptable salt thereof, wherein R^{1a} and R^{1b} are each independently H or C_1-C_3 alkyl.

~~9.~~4. The compound of claim ~~8~~3, or a pharmaceutically acceptable salt thereof, wherein R^{1a} is methyl and R^{1b} is H.

~~10. The compound of claim 8, or a pharmaceutically acceptable salt thereof, wherein R^{1a} and R^{1b} are each H.~~

~~11. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt thereof, wherein R^2 is H.~~

~~12. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt thereof, wherein R^2 is thioxo.~~

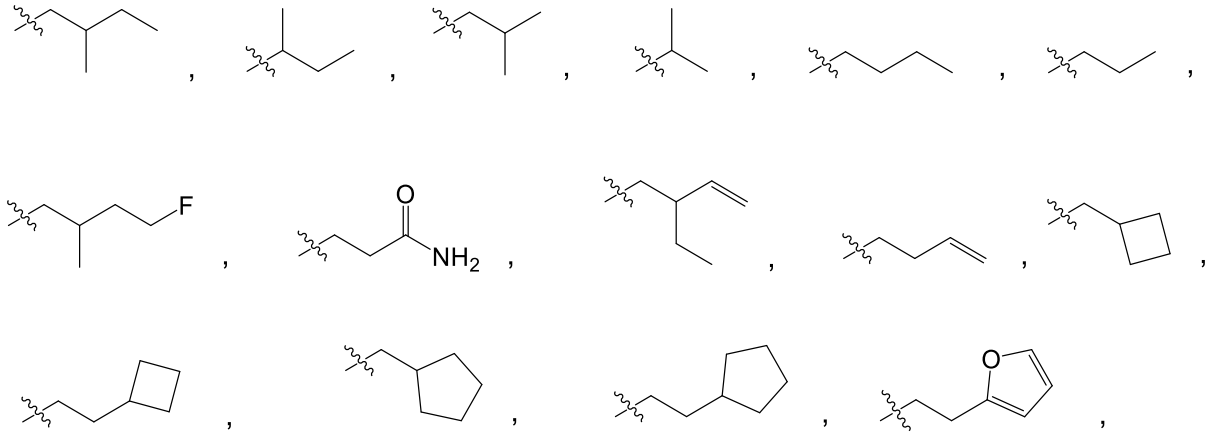
~~13.~~5. The compound of any one of claims 1-~~10~~4, or a pharmaceutically acceptable salt thereof, wherein R^2 is oxo.

~~14. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_3-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, C_3-C_{12} cycloalkyl, C_3-C_6 cycloalkylalkyl, C_6-C_{10} arylalkyl, 5- to 10-membered heteroarylalkyl, or 5- to 10-membered heterocyclylalkyl, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, arylalkyl, heteroarylalkyl, or heterocyclylalkyl is optionally substituted with one to five substituents selected from hydroxyl, halo, amino, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, cyano, -(C=O)NH_2, nitro, -SO_2(C_1-C_6 alkyl), and -CO_2H.~~

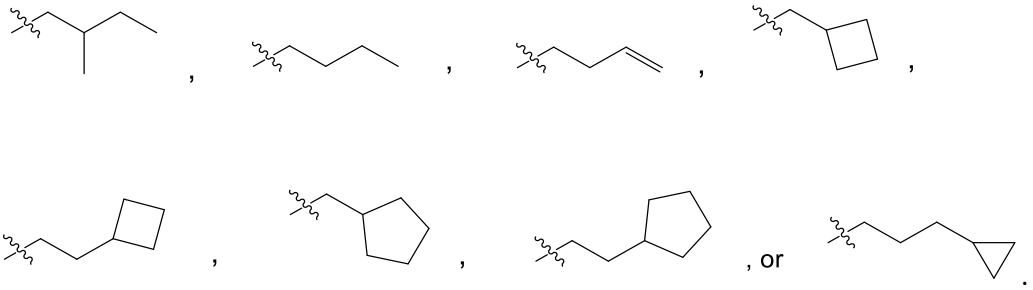
~~15. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_2-C_6 alkyl optionally substituted by 1-3 substituents selected from halo, C_1-C_3 alkoxy, hydroxy, -NH_2, -SO_2(C_1-C_3 alkyl), and -C(=O)NH_2; C_2-C_6 alkenyl; C_3-C_6 cycloalkylalkyl; 5- to 6-membered heteroarylalkyl; 5- to 6-membered heterocyclylalkyl; or C_6 arylalkyl.~~

~~16. The compound of claim 15, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_2 alkyl substituted by 1-3 substituents selected from C_1-C_3 alkoxy, hydroxy, -NH_2, and -SO_2(C_1-C_3 alkyl).~~

~~17. The compound of any one of claims 14-16, or a pharmaceutically acceptable salt thereof, wherein R^3 is:~~



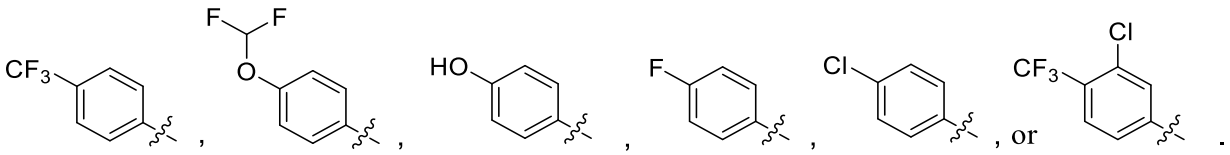
~~18.~~6. The compound of ~~claim 17~~any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein R^3 is:



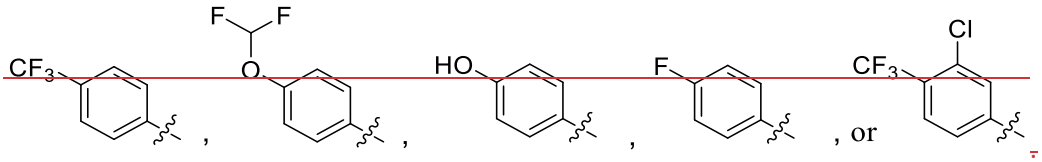
~~19. The compound of any one of claims 1-18, or a pharmaceutically acceptable salt thereof, wherein R^4 is C_6-C_{10} aryl optionally substituted with 1-3 substituents selected from halo, hydroxyl, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy.~~

~~20.~~7. The compound of ~~claim 19~~any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein R^4 is phenyl substituted with 1-3 substituents selected from -CF_3, -$OCHF_2$, -OH, fluoro, and chloro.

~~21.~~8. The compound of claim ~~20~~7, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



~~22. The compound of claim 21, or a pharmaceutically acceptable salt thereof, wherein R^4 is:~~

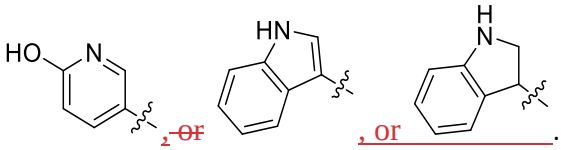


~~23. The compound of any one of claims 1-18, or a pharmaceutically acceptable salt thereof, wherein R^4 is 5- to 10-membered heteroaryl optionally substituted with 1-3 substituents selected from halo, hydroxyl, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy.~~

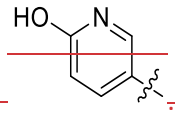
~~24.~~9. The compound of ~~claim 23~~any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein

R^4 is pyridyl or indolyl optionally substituted with 1-3 substituents selected from halo, hydroxyl, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy, or indolinyl.

~~25.~~10. The compound of claim ~~24~~9, or a pharmaceutically acceptable salt thereof, wherein

R^4 is 

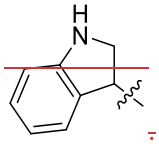
~~26. The compound of claim 25, or a pharmaceutically acceptable salt thereof, wherein~~

~~R^4 is~~ 

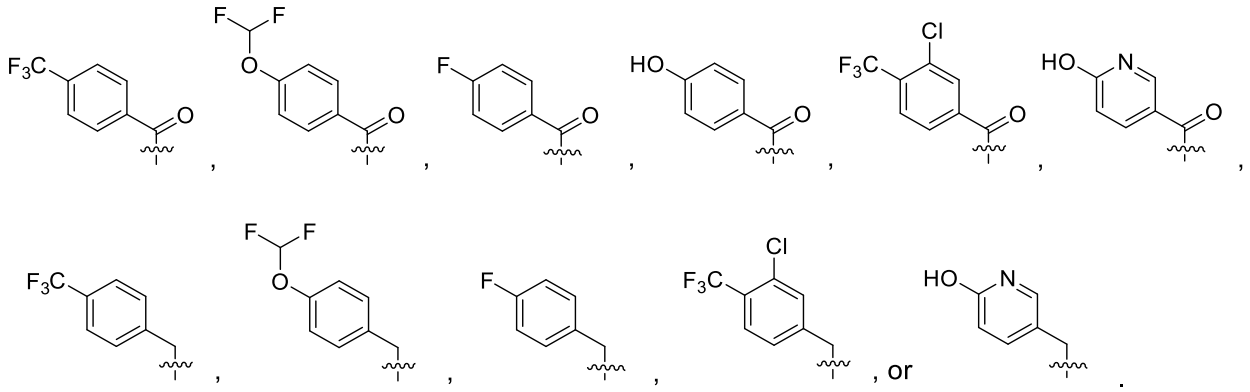
~~27. The compound of any one of claims 1-18, or a pharmaceutically acceptable salt thereof, wherein R^4 is 5- to 10-membered heterocyclyl optionally substituted with 1-3 substituents selected from halo, hydroxyl, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy.~~

~~28. The compound of claim 27, or a pharmaceutically acceptable salt thereof, wherein R^4 is indolinyl.~~

~~29. The compound of claim 28, or a pharmaceutically acceptable salt thereof, wherein R^4 is~~



~~30.~~11. The compound of any one of claims 1-~~26~~10, or a pharmaceutically acceptable salt thereof, wherein -L-R^4 is:



~~31.~~12. The compound of any one of claims 1-~~30~~11, or a pharmaceutically acceptable salt thereof, wherein n is 0.

~~32.~~13. The compound of any one of claims 1-~~30~~11, or a pharmaceutically acceptable salt thereof, wherein n is 1, optionally wherein R^5 is oxo or halo.

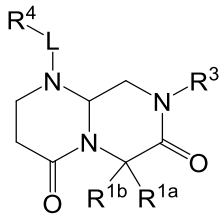
~~33. The compound of claim 32, or a pharmaceutically acceptable salt thereof, wherein R^5 is oxo or halo.~~

~~34. The compound of claim 33, or a pharmaceutically acceptable salt thereof, wherein R^5 is oxo or fluoro.~~

~~35.~~14. The compound of any one of claims 1-~~34~~13, or a pharmaceutically acceptable salt thereof, wherein R^6 is H.

~~36.~~15. The compound of any one of claims 1-~~35~~14, or a pharmaceutically acceptable salt thereof, wherein R^7 is oxo.

~~37.~~16. The compound of any one of claims 1-~~10, 13-31, 35, and 36~~12, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula (V):



(V) .

~~38.~~17. The compound of claim ~~37~~16, or a pharmaceutically acceptable salt thereof, wherein:

L is -C(=O)- or -CH_2-;

R^{1a} and R^{1b} are independently H or C_1-C_3 alkyl optionally substituted with -CO_2H;

R^3 is C_4-C_5 alkyl, C_4-C_5 alkenyl, or C_1-C_3 alkyl substituted with C_3-C_5 cycloalkyl; and

R^4 is phenyl or pyridyl substituted with 1-3 substituents selected from -CF_3, -$OCHF_2$, -OH, fluoro, and chloro.

~~39.~~18. A compound selected from the compounds of Table 1A and pharmaceutically acceptable salts thereof.

~~40.~~19. A pharmaceutical composition comprising the compound of any one of claims 1-~~39~~18, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

~~41. A method for modulating hepatocyte growth factor in a subject in need thereof, the method comprising administering to the subject an effective amount of the compound of any one of claims 1-39, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 40.~~

~~42. The method of claim 41, wherein the modulating comprises treating a disease, condition, or injury.~~

~~43. The method of claim 42, wherein the disease, condition, or injury is a neurodegenerative disease, a spinal cord injury, a traumatic brain injury, or a sensorineural hearing loss.~~

~~44. The method of claim 42 or 43, wherein the disease, condition, or injury is a neurodegenerative disease.~~

~~45. The method of claim 44, wherein the neurodegenerative disease is Alzheimer's disease, Parkinson's disease, Huntington's disease, or amyotrophic lateral sclerosis (ALS).~~

~~46. The method of claim 45, wherein the neurodegenerative disease is Alzheimer's disease or Parkinson's disease.~~

~~47.~~20. ~~A method for treating or slowing progression of dementia in a subject in need thereof, the method comprising administering to the subject an effective amount of the~~ Use of the compound of any one of claims 1-~~39~~18, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim ~~40~~19, in the manufacture of a medicament for treating or slowing progression of dementia in a subject in need thereof, optionally wherein the dementia is associated with Alzheimer’s disease or Parkinson’s disease.

~~48. The method of claim 47, wherein the dementia is associated with Alzheimer’s disease or Parkinson’s disease.~~

~~49.~~21. ~~A method for preventing cognitive dysfunction in a subject in need thereof, the method comprising administering to the subject an effective amount of the~~ Use of the compound of any one of claims 1-~~39~~18, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim ~~40~~19 in the manufacture of a medicament for preventing cognitive dysfunction in a subject in need thereof.

~~50.~~22. ~~A method for treating, repairing or preventing a disease, condition or injury related to nerve tissue in a subject in need thereof, the method comprising administering to the subject an effective amount of the~~ Use of the compound of any one of claims 1-~~39~~18, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim ~~40~~19 in the manufacture of a medicament for treating, repairing or preventing a disease, condition or injury related to nerve tissue in a subject in need thereof.

~~51.~~23. ~~A method of treating or preventing a disease or disorder of the central nervous system, a disease or disorder of the peripheral nervous system, neuropathic pain, anxiety, or depression in a subject in need thereof, the method comprising administering to the subject an effective amount of the~~ Use of the compound of any one of claims 1-~~39~~18, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim ~~40~~19 in the manufacture of a

medicament for treating or preventing a disease or disorder of the central nervous system, a disease or disorder of the peripheral nervous system, neuropathic pain, anxiety, or depression in a subject in need thereof.

24. The compound of any one of claims 1-18, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 19 for use in therapy.