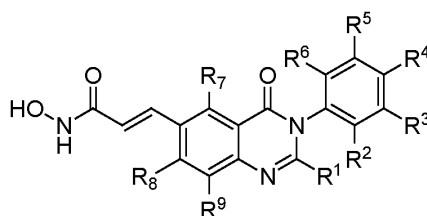


CLAIMS

What is claimed:

1. A compound of Formula (I):



5

Formula (I)

or a pharmaceutically acceptable salt thereof, wherein

R¹ is hydrogen, (C₁₋₂)alkyl, or fluoro(C₁₋₂)alkyl;

R² is hydrogen, halogen, or (C₁₋₃)alkyl;

R³ is hydrogen, or (C₁₋₃)alkyl;

10 R⁴ is hydrogen, halogen, (C₁₋₃)alkyl, or methoxy, N(C₁₋₃)(C₁₋₃);

R⁵ is hydrogen, (C₁₋₃)alkyl, halogen, or trifluoromethyl;

R⁶ is hydrogen, (C₁₋₃)alkyl, halogen;

R⁷ is hydrogen or halogen;

R⁸ is hydrogen, methyl, methoxy, or fluoro; and

15 R⁹ is hydrogen or fluoro.

2. The compound of claim 1, wherein R¹ is methyl.

3. The compound of claim 1, wherein R¹ is ethyl.

4. The compound of claim 1, wherein R² is hydrogen.

5. The compound of claim 1, wherein R² is halogen.

20 6. The compound of claim 1, wherein R² is methyl.

7. The compound of claim 1, wherein R³ is hydrogen.

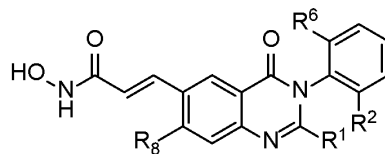
8. The compound of claim 1, wherein R⁶ is methyl.

9. The compound of claim 1, wherein R² is isopropyl.

10. The compound of claim 1, wherein R⁴ is dimethylamino.

11. The compound of claim 1, wherein R⁶ is isopropyl.

12. The compound of claim 1, wherein the compound is of Formula (IA)



13. The compound of claim 12, wherein R² and R⁶ are each methyl.

14. The compound of claim 12, wherein R² and R⁶ are each hydrogen.

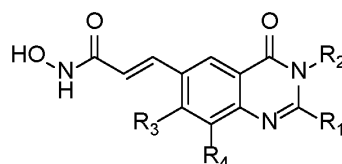
15. The compound of claim 13 or 14, wherein R¹ is ethyl.

16. The compound of claim 13 or 14, wherein R⁸ is fluoro.

17. The compound of claim 1, wherein the compound is of Formula (IB)



18. A compound of Formula (II):



Formula (II)

or a pharmaceutically acceptable salt thereof, wherein

R¹ is methyl, ethyl, or fluoro(C1-2)alkyl;

15 R² is phenyl or phenyl substituted with 1 to 3 substituents independently selected from the group consisting of methyl, ethyl, methoxy, trifluoromethyl, and halogen;

R³ is hydrogen, methyl, methoxy, or fluoro; and

R⁴ is hydrogen or fluoro.

19. The compound of claim 1 or 18, wherein the compound is selected from Table 1.

20. The compound of claim 1 or 18, wherein the compound is selected from the group consisting of

- (E)-3-(3-(2,6-dimethylphenyl)-2-ethyl-8-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 5 (E)-3-(3-(2,6-dimethylphenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(2,6-dimethylphenyl)-5-fluoro-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 10 (E)-3-(2-ethyl-7-fluoro-3-(2-methyl-3-(trifluoromethyl)phenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(2,6-dichlorophenyl)-7-fluoro-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(4-bromo-2-methylphenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 15 (E)-3-(3-(3,5-dimethylphenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(2,6-diisopropylphenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 20 (E)-3-(3-(2,6-diisopropylphenyl)-7-fluoro-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(2,6-dimethylphenyl)-8-fluoro-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(2,6-dimethylphenyl)-2-ethyl-8-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 25 (E)-3-(3-(2,6-difluorophenyl)-7-fluoro-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(2,6-difluorophenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 30 (E)-3-(3-(2,6-dimethylphenyl)-7-fluoro-2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 3-(3-(2,6-dimethylphenyl)-7-fluoro-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxypropanamide,
- (E)-3-(3-(2,6-dimethylphenyl)-2,7-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 35 (E)-3-(3-(2,6-dimethylphenyl)-2-ethyl-7-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,

- (E)-3-(3-(3,5-dimethylphenyl)-7-fluoro-2-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(3,5-dimethylphenyl)-7-fluoro-2-(1-fluoroethyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 5 (E)-3-(3-(4-bromo-2,5-dimethylphenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(4-bromo-3-methylphenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 10 (E)-3-(3-(2,3-dimethylphenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(2,5-dimethylphenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(2-ethyl-7-fluoro-3-(4-fluoro-2,6-dimethylphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 15 (E)-3-(3-(4-chloro-2-methylphenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(2-ethyl-7-fluoro-3-(4-fluoro-2-methylphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 20 (E)-3-(3-(2,4-dimethylphenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(4-bromo-2-fluorophenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(2-bromo-4-chlorophenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 25 (E)-3-(2-ethyl-7-fluoro-3-mesityl-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(4-bromo-2,6-dimethylphenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(3-(2,6-dimethylphenyl)-2-ethyl-7-methoxy-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 30 (E)-3-(2-ethyl-7-fluoro-4-oxo-3-phenyl-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(2-ethyl-7-fluoro-3-(4-methoxy-2-methylphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- (E)-3-(2-ethyl-8-fluoro-3-(4-fluoro-2-methylphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,
- 35 (E)-3-(2-ethyl-3-(2-ethylphenyl)-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,

(E)-3-(2-ethyl-7-fluoro-3-(2-fluoro-6-methylphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,

(E)-3-(2-ethyl-7-fluoro-3-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,

5 (E)-3-(2-ethyl-7-fluoro-4-oxo-3-(p-tolyl)-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,

(E)-3-(2-ethyl-7-fluoro-3-(4-fluorophenyl)-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,

(E)-3-(3-(4-chlorophenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide,

10 (E)-3-(2-ethyl-3-(4-ethylphenyl)-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide and

(E)-3-(3-(4-(dimethylamino)phenyl)-2-ethyl-7-fluoro-4-oxo-3,4-dihydroquinazolin-6-yl)-N-hydroxyacrylamide.

21. A pharmaceutical composition comprising a therapeutically effective amount of the
15 selective HDAC6 inhibitor (HDAC6i) of claim 1 to 20, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or vehicle.

22. A method for promoting neurite outgrowth in a subject in need of, wherein said subject is administered with effective amount of the selective HDAC6 inhibitor of claim 1 to 20, or a pharmaceutically acceptable salt, and a pharmaceutically acceptable carrier or vehicle.

20 23. A method for the prevention or treatment of peripheral neuropathy in a subject in need of, wherein said subject is administered with effective amount of the selective HDAC6 inhibitor of claim 1 to 20, or a pharmaceutically acceptable salt, and a pharmaceutically acceptable carrier or vehicle.

24. The method according to claim 23, wherein said peripheral neuropathy is chemotherapy-induced peripheral neuropathy, diabetic neuropathy, post-herpes zoster pain, or postherpetic neuralgia from shingles.

25. The method according to claim 24, wherein said peripheral neuropathy is chemotherapy-induced peripheral neuropathy.

26. The method according to claim 25, wherein the said chemotherapy is platinum-based
30 chemotherapy, alkaloid-based, or taxane-based chemotherapy.

27. A method for enhancing tubulin hyperacetylation of cells in a subject, wherein said subject is treated is effective amount of the selective HDAC6 inhibitor of claim 1 to 20, or a

pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or vehicle.

28. A method for the prevention or treatment of fibrosis of a subject, wherein said subject is administered with effective amount of the selective HDAC6 inhibitor of claim 1 to 20, or a pharmaceutically acceptable salt, and a pharmaceutically acceptable carrier or vehicle.

29. The method according to claim 28, wherein in said fibrosis is pulmonary fibrosis, hepatic fibrosis, or renal fibrosis.

30. The method according to claim 29, wherein said pulmonary fibrosis is associated with increased expression of IL-1, TNF- α , IL-6 or Collagens in said subject.

31. The method according to claim 29, wherein said pulmonary fibrosis is idiopathic pulmonary fibrosis or virus-induced fibrosis.

32. A method of decreasing expression of IL-1, TNF- α , IL-6 or Collagens in a subject in need, wherein said subject is administered with effective amount of the selective HDAC6 inhibitor of claim 1 to 20, or a pharmaceutically acceptable salt, and a pharmaceutically acceptable carrier or vehicle.

33. A method of treating or ameliorating cytokine-induced inflammatory conditions in a subject in need, wherein said cytokine comprises IL-1, TNF- α , IL-6, M-CSF, VCAM-1, or MCP-1, and said subject is administered with effective amount of the selective HDAC6 inhibitor of Claim 1 to 20, or a pharmaceutically acceptable salt, and a pharmaceutically acceptable carrier or vehicle.

34. The method of claim 33, wherein said conditions are selected from a group consisting of coronavirus-induced pulmonary inflammation, acute respiratory distress syndrome, acute pulmonary inflammation, pulmonary fibrosis, liver fibrosis, and renal fibrosis.

35. Use of the selective HDAC6 inhibitor according to claim 1 to 20 in the manufacture of a medicament for the prevention or treatment of peripheral neuropathy in a subject in need thereof.

36. The use according to claim 35, wherein said peripheral neuropathy is chemotherapy-induced peripheral neuropathy, diabetic neuropathy, post-herpes zoster pain, or postherpetic neuralgia from shingles.

37. The use according to claim 36, wherein said peripheral neuropathy is chemotherapy—
induced peripheral neuropathy.
38. Use of the selective HDAC6 inhibitor according to claim 1 to 20 in the manufacture of a
medicament for the prevention or treatment of fibrosis in a subject in need thereof.
- 5 39. Use of the selective HDAC6 inhibitor according to claim 1 to 20 in the manufacture of a
medicament for the treatment of acute respiratory distress syndrome, acute pulmonary
inflammation, pulmonary fibrosis, pulmonary fibrosis, coronavirus-induced pulmonary
inflammation, liver fibrosis, and renal fibrosis.
- 10 40. A method for the prevention or treatment of diabetes induced neuropathy in a subject,
wherein said subject is administered with effective amount of the selective HDAC6 inhibitor
of claim 1 to 20, or a pharmaceutically acceptable salt, and a pharmaceutically acceptable
carrier or vehicle.