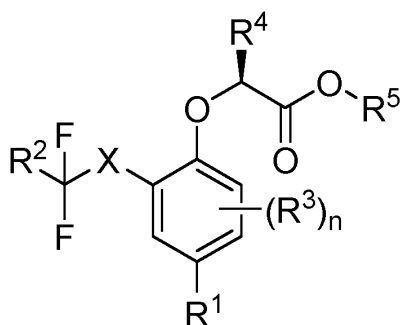


Claims

1. A compound of Formula (I):



Formula (I)

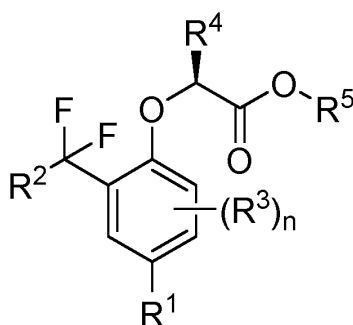
5 wherein:

- R¹ is selected from the group consisting of C₁₋₂ alkyl, C₂ alkenyl, C₂ alkynyl, CN, CF₃, NO₂, F, Cl, Br, and I;
- R² is selected from the group consisting of C₁₋₅ alkyl optionally be substituted with one or more, identical or different, substituents R⁶, C₂₋₅ alkenyl optionally be substituted with one or more, identical or different, substituents R⁶, C₂₋₅ alkynyl optionally be substituted with one or more, identical or different, substituents R⁶, C₃₋₅ cycloalkyl optionally substituted with one or more, identical or different, substituents R⁶, phenyl optionally substituted with one or more, identical or different, substituents R⁹, and 5-6 membered aromatic heterocycle optionally substituted with one or more, identical or different, substituents R⁷;
- R³ is selected from the group consisting of deuterium, Cl and F;
- R⁴ is selected from the group consisting of H, deuterium, C₁₋₅ alkyl, C₂₋₅ alkenyl, C₂₋₅ alkynyl, and C₃₋₅ cycloalkyl, each of which may be optionally substituted with one or more, identical or different, substituents R⁷;
- R⁵ is selected from the group consisting of H, C₁₋₅ alkyl optionally substituted with one or more, identical or different, substituents R⁶, C₂₋₅ alkenyl optionally substituted with one or more, identical or different, substituents R⁶, C₂₋₅ alkynyl optionally substituted with one or more, identical or different, substituents R⁶, C₃₋₆ cycloalkyl optionally substituted with one or more, identical or different, substituents R⁶,

phenyl optionally substituted with one or more, identical or different, substituents R^9 , and benzyl optionally substituted with one or more, identical or different, substituents R^9 ;

- 5 - R^6 is independently selected from the group consisting of deuterium, F, -CN, -O-C₁₋₅ alkyl, -O-C₃₋₅ cycloalkyl, -S-C₁₋₅ alkyl, and -S-C₃₋₅ cycloalkyl, wherein the -O-C₁₋₅ alkyl, -O-C₃₋₅ cycloalkyl, -S-C₁₋₅ alkyl, and -S-C₃₋₅ cycloalkyl may optionally be substituted with one or more, identical or different, substituents R^8 ;
- 10 - R^7 is independently selected from the group consisting deuterium, F, Cl, -CN, C₃₋₅ cycloalkyl, -O-C₁₋₅ alkyl, -O-C₃₋₅ cycloalkyl, -S-C₁₋₅ alkyl, and -S-C₃₋₅ cycloalkyl, wherein the C₃₋₅ cycloalkyl, -O-C₁₋₅ alkyl, -O-C₃₋₅ cycloalkyl, -S-C₁₋₅ alkyl, and -S-C₃₋₅ cycloalkyl may optionally be substituted with one or more, identical or different, substituents R^8 ;
- 15 - R^8 is independently selected from the group consisting of deuterium and F;
- R^9 is independently selected from the group consisting of deuterium, methoxy, nitro, cyano, Cl, Br, I, and F;
- X is a bond or selected from the group consisting of -O-, -S-, -CH₂-, -CHR⁶-, and -C(R⁶)₂-; and
- n is an integer 0, 1, 2, or 3;
- 20 or a pharmaceutically acceptable salt, hydrate, polymorph, tautomer, or solvate thereof.

2. The compound according to claim 1, wherein the compound is of Formula (II)



Formula (II)

- 25 wherein:

- R¹ is selected from the group consisting of C₁₋₂ alkyl, C₂ alkenyl, C₂ alkynyl, CN, CF₃, NO₂, F, Cl, Br, and I;
- R² is selected from the group consisting of C₁₋₅ alkyl optionally be substituted with one or more, identical or different, substituents R⁶, C₂₋₅ alkenyl optionally be substituted with one or more, identical or different, substituents R⁶, C₂₋₅ alkynyl optionally be substituted with one or more, identical or different, substituents R⁶, C₃₋₅ cycloalkyl optionally substituted with one or more, identical or different, substituents R⁶, phenyl optionally substituted with one or more, identical or different, substituents R⁹, and 5-6 membered aromatic heterocycle optionally substituted with one or more, identical or different, substituents R⁷;
- R³ is selected from the group consisting of deuterium, Cl and F;
- R⁴ is selected from the group consisting of H, deuterium, C₁₋₅ alkyl, C₂₋₅ alkenyl, C₂₋₅ alkynyl, and C₃₋₅ cycloalkyl, each of which may be optionally substituted with one or more, identical or different, substituents R⁷;
- R⁵ is selected from the group consisting of H, C₁₋₅ alkyl optionally substituted with one or more, identical or different, substituents R⁸, C₂₋₅ alkenyl optionally substituted with one or more, identical or different, substituents R⁸, C₂₋₅ alkynyl optionally substituted with one or more, identical or different, substituents R⁸, C₃₋₆ cycloalkyl optionally substituted with one or more, identical or different, substituents R⁸, phenyl optionally substituted with one or more, identical or different, substituents R⁹, and benzyl optionally substituted with one or more, identical or different, substituents R⁹;
- R⁶ is independently selected from the group consisting of deuterium, F, -CN, -O-C₁₋₅ alkyl, -O-C₃₋₅ cycloalkyl, -S-C₁₋₅ alkyl, and -S-C₃₋₅ cycloalkyl, wherein the -O-C₁₋₅ alkyl, -O-C₃₋₅ cycloalkyl, -S-C₁₋₅ alkyl, and -S-C₃₋₅ cycloalkyl may optionally be substituted with one or more, identical or different, substituents R⁸;
- R⁷ is independently selected from the group consisting deuterium, F, Cl, -CN, C₃₋₅ cycloalkyl, -O-C₁₋₅ alkyl, -O-C₃₋₅ cycloalkyl, -S-C₁₋₅ alkyl, and -S-C₃₋₅ cycloalkyl, wherein the C₃₋₅ cycloalkyl, -O-C₁₋₅ alkyl, -O-C₃₋₅ cycloalkyl, -S-C₁₋₅ alkyl, and -S-C₃₋₅ cycloalkyl may optionally be substituted with one or more, identical or different, substituents R⁸;
- R⁸ is independently selected from the group consisting of deuterium and F;

- R⁹ is independently selected from the group consisting of deuterium, methoxy, nitro, cyano, Cl, Br, I, and F; and
- n is an integer 0, 1, 2, or 3;
or a pharmaceutically acceptable salt, hydrate, polymorph, tautomer, or solvate thereof.
- 5
3. The compound according to any of claims 1 to 2, wherein R¹ is Cl or Br.
4. The compound according to any of claims 1 to 3, wherein R² is C₁₋₃ alkyl optionally substituted with one or more, identical or different, substituents R⁶.
5. The compound according to any of claims 1 to 4, wherein R³ is F and n is 1.
- 10 6. The compound according to any of claims 1 to 5, wherein R⁴ is C₁₋₅ alkyl optionally substituted with one or more, identical or different, substituents R⁶.
7. The compound according to any of claims 1 to 6, wherein R⁴ is CH₂F.
8. The compound according to any of claims 1 to 5, wherein R⁴ is C₂₋₅ alkynyl optionally substituted with one or more, identical or different, substituents R⁶.
- 15 9. The compound according to any of claims 1 to 8, wherein R⁵ is H.
10. The compound for use according to any one of claims 1 to 11, wherein the compound is selected from the group consisting of:
- (2S)-2-[4-bromo-2-(1,1-difluoroethyl)phenoxy]-3-cyclopropylpropanoic acid;
(2S)-2-[4-bromo-2-(1,1-difluoroethyl)phenoxy]butanoic acid;
20 (2S)-2-[4-bromo-2-(1,1-difluoropropyl)phenoxy]propanoic acid;
(2S)-2-[4-bromo-2-(1,1-difluoroethyl)phenoxy]propanoic acid;
(2S)-2-[4-chloro-2-(1,1-difluoropropyl)phenoxy]propanoic acid;
2-[4-bromo-2-(1,1-difluoropropyl)phenoxy]acetic acid;
(2S)-2-[4-bromo-2-(1,1-difluoro-2-methylpropyl)phenoxy]propanoic acid;
25 (2S)-2-[4-bromo-2-[difluoro(phenyl)methyl]phenoxy]propanoic acid;
(2S)-2-[4-bromo-2-(1,1-difluoroethyl)phenoxy]-2-cyclopropylacetic acid;
(2S)-2-[4-bromo-2-(1,1-difluorobutyl)phenoxy]propanoic acid;
(2R)-2-[4-bromo-2-(1,1-difluoropropyl)phenoxy]-3-fluoropropanoic acid;
(2S)-2-[4-bromo-2-(cyclopropyldifluoromethyl)phenoxy]propanoic acid;
30 (2S)-2-[4-bromo-2-[difluoro(1,3-thiazol-2-yl)methyl]phenoxy]propanoic acid;

- (2S)-2-[4-bromo-2-(1,1-difluoroethyl)phenoxy]pent-4-ynoic acid;
(2S)-2-[4-bromo-2-(cyclobutylidifluoromethyl)phenoxy]propanoic acid;
(2R)-2-[4-bromo-2-(1,1-difluoroethyl)phenoxy]-3-fluoropropanoic acid;
(2R)-2-[4-bromo-2-(1,1-difluoropropyl)phenoxy]-3-chloropropanoic acid;
5 (2S)-2-[4-bromo-2-(1,1-difluoropropyl)phenoxy]pent-4-ynoic acid;
(2S)-2-[4-chloro-2-(1,1-difluoroethyl)phenoxy]pent-4-ynoic acid;
(2S)-2-[2-(1,1-difluoropropyl)-4-iodophenoxy]propanoic acid;
(2S)-2-[4-bromo-2-(1,1-difluoropropyl)phenoxy](2-²H)propanoic acid;
(2R)-2-[4-chloro-2-(1,1-difluoropropyl)phenoxy]-3-fluoropropanoic acid;
10 (2S)-2-[2-(1,1-difluoropropyl)-4-ethynylphenoxy]propanoic acid;
(2S)-2-[4-bromo-2-(1,1-difluoropropyl)-5-fluorophenoxy]propanoic acid;
(2S)-2-[4-bromo-2-(1,1-difluoropropyl)-6-fluorophenoxy]propanoic acid;
(2S)-2-[4-cyano-2-(1,1-difluoropropyl)phenoxy]propanoic acid;
(2R)-2-[4-chloro-2-(1,1-difluoroethyl)phenoxy]-3-fluoropropanoic acid;
15 (2S)-2-[4-bromo-2-(1,1-difluoroethyl)-5-fluorophenoxy]propanoic acid;
(2S)-2-[4-bromo-2-(1,1-difluoropropyl)(3,5,6-²H₃)phenoxy]propanoic acid;
2-[4-bromo-2-(1,1-difluoropropyl)-5-fluorophenoxy]acetic acid;
(2S)-2-[4-chloro-2-(1,1-difluoropropyl)-5-fluorophenoxy]propanoic acid;
(2S)-2-[2-(1,1-difluoropropyl)-4-(trifluoromethyl)phenoxy]propanoic acid;
20 (2R)-2-[4-bromo-2-(1,1-difluoropropyl)-5-fluorophenoxy]-3-fluoropropanoic
acid;
(2S)-2-[2-(1,1-difluoropropyl)-4-ethenylphenoxy]propanoic acid;
2-[4-bromo-2-(1,1-difluoroethyl)-5-fluorophenoxy]acetic acid;
(2S)-2-[2-(1,1-difluoropropyl)-4-methylphenoxy]propanoic acid;
25 2-[4-bromo-2-(1,1-difluoro-2-methylpropyl)phenoxy]acetic acid;
2-[4-chloro-2-(1,1-difluoropropyl)-5-fluorophenoxy]acetic acid;
(2S)-2-[2-(1,1-difluoroethyl)-4-ethynylphenoxy]propanoic acid;
(2R)-2-[4-chloro-2-(1,1-difluoropropyl)-5-fluorophenoxy]-3-fluoropropanoic
acid;
30 (2S)-2-[4,5-dichloro-2-(1,1-difluoropropyl)phenoxy]propanoic acid;
(2R)-2-[4-bromo-2-(1,1-difluoroethyl)-5-fluorophenoxy]-3-fluoropropanoic acid;
(2R)-2-[4,5-dichloro-2-(1,1-difluoroethyl)phenoxy]-3-fluoropropanoic acid;
(2S)-2-[4-bromo-2-(1,1-difluoroethyl)phenoxy]-4-fluorobutanoic acid;
(2S)-2-[4-bromo-2-(1,1-difluoro-2-methylpropyl)phenoxy]butanoic acid;
35 (2S)-2-[2-(1,1-difluoropropyl)-4-ethenyl-5-fluorophenoxy]propanoic acid;

- (2S)-2-[4-bromo-2-(1,1-difluoropropyl)-5-fluorophenoxy]butanoic acid;
(2S)-2-[4-chloro-2-(1,1-difluoropropyl)-5-fluorophenoxy]butanoic acid;
(2R)-2-[5-chloro-2-(1,1-difluoropropyl)-4-fluorophenoxy]-3-fluoropropanoic acid;
5 (2S)-2-[2-(1,1-difluoropropyl)-4-nitrophenoxy]propanoic acid;
(2S)-2-[5-chloro-2-(1,1-difluoropropyl)-4-fluorophenoxy]propanoic acid;
(2S)-2-[4-bromo-2-(1,1-difluoropropyl)phenoxy]-4-methoxybutanoic acid;
(2R)-2-[2-(1,1-difluoropropyl)-4,5-difluorophenoxy]-3-fluoropropanoic acid;
(2S)-2-[2-(1,1-difluoropropyl)-4,5-difluorophenoxy]propanoic acid; and
10 (2S)-2-[4-bromo-2-(1,1-difluoro-3-methoxypropyl)phenoxy]propanoic acid.
11. The compound according to any one of claims 1 to 10, wherein the compound is an inhibitor of the CIC-1 ion channel.
12. A composition comprising the compound according to any one of claims 1 to 11 and a pharmaceutically acceptable carrier.
- 15 13. The compound according to any one of claims 1 to 11 or composition according to claim 12 for use as a medicament.
14. The compound according to any one of claims 1 to 11 or composition according to claim 12 for use in the treatment of symptoms of an indication selected from the group consisting of myasthenia gravis, Lambert-Eaton Syndrome, critical
20 illness myopathy, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), critical illness myopathy (CIM), reversal diabetic polyneuropathy, Guillain-Barré syndrome, poliomyelitis, post-polio syndrome, chronic fatigue syndrome, critical illness polyneuropathy, periodic paralysis, sarcopenia, hypokalemic periodic paralysis, hyperkalemic periodic paralysis, myotubular myopathy and
25 Duchenne muscular dystrophy.
15. The compound according to any one of claims 1 to 11 or composition according to claim 12 for use in reversing and/or ameliorating a neuromuscular blockade.