pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient, wherein the unit dosage form is a solid gastro-resistant formulation, and wherein when administered to a subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof at a time from 2 to 6 hours after administration, and an in-vivo half-life of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof of 14 to 21 hours.

[0004b] In one aspect, provided herein is a pharmaceutical composition for use in the treatment of a condition in a subject, the pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient, wherein the unit dosage form is a solid gastro-resistant formulation, and wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof at a time from 2 to 6 hours after administration, and an in-vivo half-life of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof of 14 to 21 hours.

[0004c] In one aspect, provided herein is a use of a pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient in the manufacture of a medicament for treating a cardiac condition associated with a leaky ryanodine receptor, wherein the unit dosage form is a solid gastro-resistant formulation, wherein the pharmaceutical composition is to be administered to a subject, and wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof at a time from 2 to 6 hours after administration, and an in-vivo half-life of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof of 14 to 21 hours.

[0004d] In one aspect, provided herein is a use of a pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient in the manufacture of a medicament for treating a musculoskeletal condition associated with a leaky

ryanodine receptor, wherein the unit dosage form is a solid gastro-resistant formulation, wherein the pharmaceutical composition is to be administered to a subject, and wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof at a time from 2 to 6 hours after administration, and an in-vivo half-life of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof of 14 to 21 hours.

[0004e] In one aspect, provided herein is a use of a pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient in the manufacture of a medicament for treating malignant hyperthermia, wherein the unit dosage form is a solid gastro-resistant formulation, wherein the pharmaceutical composition is to be administered to a subject, and wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof at a time from 2 to 6 hours after administration, and an in-vivo half-life of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof of 14 to 21 hours.

[0004f] In one aspect, provided herein is a tablet comprising a core, a sub-coating layer substantially covering the core, and a coating layer substantially covering the sub-coating layer, wherein the core comprises 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid hemifumarate, mannitol, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, maltodextrin, colloidal anhydrous silica, and sodium stearyl fumarate; the sub-coating layer comprises hypromellose, microcrystalline cellulose, and stearic acid; and the coating layer comprises hypromellose acetate succinate, triethyl citrate, sodium lauryl sulfate, and talc.

[0005] In some embodiments, the present disclosure provides a pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-

CLAIMS

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient, wherein the unit dosage form is a solid gastro-resistant formulation, and wherein when administered to a subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof at a time from 2 to 6 hours after administration, and an in-vivo half-life of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof of 14 to 21 hours.
2. The pharmaceutical composition of claim 1, comprising the pharmaceutically-acceptable salt, wherein the pharmaceutically-acceptable salt is a hemifumarate salt.
3. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition provides delayed release of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof.
4. The pharmaceutical composition of any one of claims 1-3, wherein the unit dosage form is suitable for oral administration.
5. The pharmaceutical composition of any one of claims 1-4, wherein the unit dosage form is a solid dosage form.
6. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject a therapeutically-effective amount of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof over a period of time, wherein the period of time occurs after administration, wherein the period of time is at least 12 hours.
7. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject a therapeutically-effective amount of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof over a period of time, wherein the period of time occurs after administration, wherein the period of time is at least 24 hours.

8. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof at a time from 2 to 4 hours after administration.

9. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject an accumulation ratio for C_{max} of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof between 1.4 and 1.8, wherein said accumulation ratio is calculated as a ratio of C_{max} on Day 28/C_{max} on Day 1, wherein C_{max} is maximum observed plasma concentration.

10. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject an accumulation ratio for AUC of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof between 1.4 and 1.8, wherein said accumulation ratio for AUC is calculated as a ratio of AUC_{tau} on Day 28/AUC_{0-24} Day 1,

    wherein

    - AUC is area under the concentration-time curve;
    - AUC_{tau} is area under the concentration-time curve during a dosing interval (tau) at steady-state; and
    - AUC_{0-24} is area under the concentration-time curve, from time 0 to 24 hours post-dose.

11. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject a steady-state plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof in a range of 3 to 7 days after initial administration.

12. The pharmaceutical composition of claim 1, comprising 20 mg of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid hemifumarate, based on mass of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid.

13. The pharmaceutical composition of claim 1, comprising 100 mg of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid hemifumarate, based on mass of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid.

14. The pharmaceutical composition of any one of claims 1-13, wherein the unit dosage form is a gastro-resistant tablet.

15. The pharmaceutical composition of claim 14, wherein the gastro-resistant tablet does not substantially disintegrate at a pH at or below 5.5, wherein disintegration is determined by measuring dissolution of the gastro-resistant tablet in a medium having a pH at or below 5.5.

16. The pharmaceutical composition of claim 14, wherein the gastro-resistant tablet substantially disintegrates at a pH of at least 6.8, wherein disintegration is determined by measuring dissolution of the gastro-resistant tablet in a medium having a pH of 6.8.

17. The pharmaceutical composition of any one of claims 1-16, wherein the unit dosage form is a gastro-resistant tablet, wherein the gastro-resistant tablet comprises a core and a coating layer substantially covering the core.

18. The pharmaceutical composition of claim 17, wherein the coating layer comprises an enteric polymer.

19. The pharmaceutical composition of claim 18, wherein the enteric polymer is hypromellose acetate succinate.

20. The pharmaceutical composition of claim 17, further comprising a sub-coating layer between the core and the coating layer.

21. The pharmaceutical composition of claim 20, wherein the sub-coating layer comprises a polymer.

22. The pharmaceutical composition of claim 21, wherein the polymer is hypromellose.

23. A pharmaceutical composition for use in the treatment of a condition in a subject, the pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient, wherein the unit

dosage form is a solid gastro-resistant formulation, and wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof at a time from 2 to 6 hours after administration, and an in-vivo half-life of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof of 14 to 21 hours.

24. Use of a pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient in the manufacture of a medicament for treating a cardiac condition associated with a leaky ryanodine receptor, wherein the unit dosage form is a solid gastro-resistant formulation, wherein the pharmaceutical composition is to be administered to a subject, and wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof at a time from 2 to 6 hours after administration, and an in-vivo half-life of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof of 14 to 21 hours.

25. The use according to claim 24, wherein the cardiac condition is catecholaminergic polymorphic ventricular tachycardia.

26. The use according to claim 24, wherein the cardiac condition is catecholaminergic polymorphic ventricular tachycardia type 1.

27. The use according to claim 24, wherein the cardiac condition is heart failure.

28. Use of a pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient in the manufacture of a medicament for treating a musculoskeletal condition associated with a leaky ryanodine receptor, wherein the unit dosage form is a solid gastro-resistant formulation, wherein the pharmaceutical composition is to be administered to a subject, and wherein

when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof at a time from 2 to 6 hours after administration, and an in-vivo half-life of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof of 14 to 21 hours.

29. The use according to claim 28, wherein the musculoskeletal condition is a congenital myopathy.

30. The use according to claim 28, wherein the musculoskeletal condition is RYR1-related myopathy.

31. The use according to claim 28, wherein the musculoskeletal condition is a muscular dystrophy.

32. The use according to claim 31, wherein the muscular dystrophy is Duchenne Muscular Dystrophy.

33. The use according to claim 28, wherein the musculoskeletal condition is sarcopenia.

34. Use of a pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient in the manufacture of a medicament for treating malignant hyperthermia, wherein the unit dosage form is a solid gastro-resistant formulation, wherein the pharmaceutical composition is to be administered to a subject, and wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof at a time from 2 to 6 hours after administration, and an in-vivo half-life of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or the pharmaceutically-acceptable ion thereof of 14 to 21 hours.

35. The pharmaceutical composition for use according to claim 23 or the use according to any one of claims 24-34, wherein the pharmaceutical composition is formulated for administration of a therapeutically-effective amount of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable

salt thereof, wherein the therapeutically-effective amount provides to the subject 100 to 400 mg per day of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof.

36. The pharmaceutical composition for use according to claim 23 or the use according to any one of claims 24-35, wherein the pharmaceutical composition is to be orally administered.

37. The pharmaceutical composition for use according to claim 23 or the use according to any one of claims 24-36, wherein the pharmaceutical composition comprises the pharmaceutically-acceptable salt, wherein the pharmaceutically-acceptable salt is a hemifumarate salt.

38. A tablet comprising a core, a sub-coating layer substantially covering the core, and a coating layer substantially covering the sub-coating layer, wherein

- the core comprises 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid hemifumarate, mannitol, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, maltodextrin, colloidal anhydrous silica, and sodium stearyl fumarate;

- the sub-coating layer comprises hypromellose, microcrystalline cellulose, and stearic acid; and

- the coating layer comprises hypromellose acetate succinate, triethyl citrate, sodium lauryl sulfate, and talc.