Other examples provide a method of treating a disease caused by changes in motor neuron excitability comprising administering to a patient in need thereof an effective amount of a compound of FORMULA I (or a pharmaceutically acceptable salt thereof). In some particularly preferred examples, the disease caused by changes in motor neuron excitability is ALS.

The present examples also provides the compounds of FORMULA I (or pharmaceutically acceptable salts thereof) for use in therapy. In one aspect, the present disclosure refers to a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, for use in therapy. More particularly, the present examples provide a compound of FORMULA I (or a pharmaceutically acceptable salt thereof) for use in the treatment of a disease caused by changes in motor neuron excitability. In one aspect, the present disclosure refers to a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, for use in the treatment of a disease caused by changes in motor neuron excitability, wherein the disease is selected from the group consisting of ALS, primary lateral sclerosis, pseudobulbar palsy, progressive bulbar palsy, epilepsy and progressive muscular atrophy. In some examples, such a disease may be ALS.

Further, the present examples provide the use of a compound of FORMULA I (or pharmaceutically acceptable salts thereof) in the manufacture of a medicament for the treatment of a disease caused by changes in motor neuron excitability. In one aspect, the present disclosure refers to use of a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease caused by changes in motor neuron excitability in a patient in need thereof, wherein the disease is selected from the group consisting of ALS, primary lateral sclerosis, pseudobulbar palsy, progressive bulbar palsy, epilepsy and progressive muscular atrophy. In another aspect, the present disclosure refers to use of the pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating a disease caused by changes in motor neuron excitability in a patient in need thereof, wherein the disease is selected from the group consisting of ALS, primary lateral sclerosis, pseudobulbar palsy, progressive bulbar palsy, epilepsy and progressive muscular atrophy. In some such examples, the disease is ALS.

In one aspect, the present disclosure refers to a process for preparing a pharmaceutical composition, comprising admixing a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, with one or more pharmaceutically acceptable carriers, diluents, or excipients.

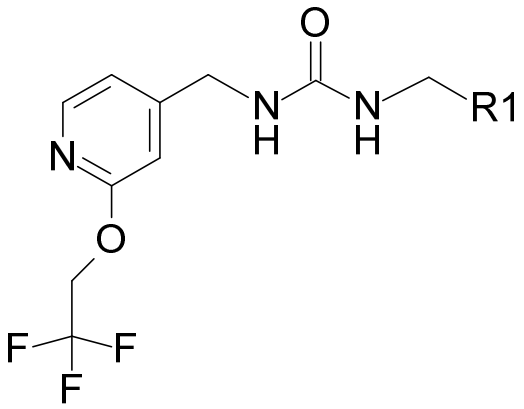
DESCRIPTION

As used herein, the term “disease associated with changes in motor neuron excitability” or a “disease caused by changes in motor neuron excitability” include a disease selected from the group consisiting of ALS, primary lateral sclerosis, pseudobulbar palsy, progressive bulbar palsy, epilepsy and progressive muscular atrophy. These terms also include all of the diseases listed in A. Verma, *et al.*, “Atypical Motor Neuron Disease and Related Motor Syndromes,” *Seminars in Neurology*, Volume 21, Number 2, 2001. Such terms also include PNH (peripheral nerve hyper excitability) disorders. Information about PNH disorders can be found at C. Küçükali *et al.*, “Peripheral nerve hyperexcitability syndromes” *Rev Neurosci.* 2015;26(2):239-51. Accordingly, the compounds and pharmaceutically acceptable salts herein may be used to treat one or more of these diseases.

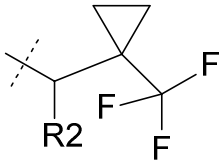
As used interchangeably herein, the term “patient,” “subject,” and “individual,” refers to a human, a more particularly, a patient in need thereof. In certain embodiments, the patient is further characterized with a disease, disorder, or condition (e.g., ALS or another disease) that would benefit from a potentiation

WE CLAIM:

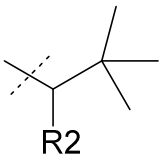
1. A compound of the Formula:



wherein R1 is



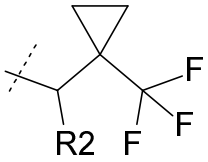
or



and wherein R2 is H or OH,

or a pharmaceutically acceptable salt thereof.

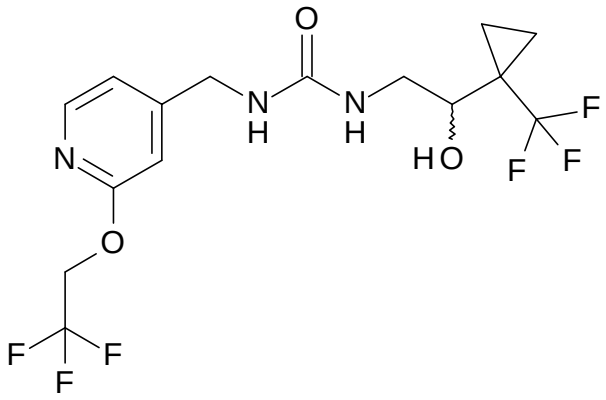
2. The compound according to claim 1 wherein R1 is:



or a pharmaceutically acceptable salt thereof.

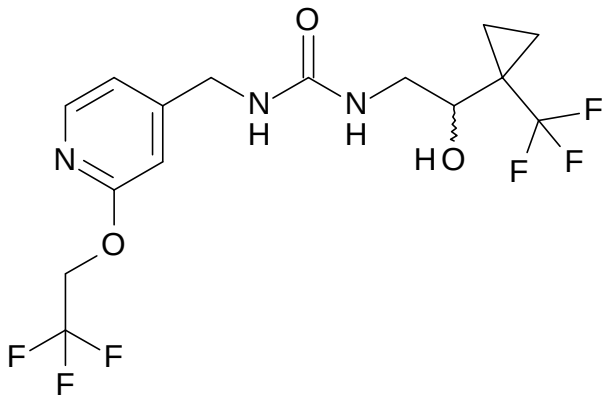
3. The compound according to claim 2, wherein R2 is OH, or a pharmaceutically acceptable salt thereof.

4. The compound according to claim 3 of the Formula:



wherein the compound comprises a single enantiomer that has the (+) optical rotation in methanol, or a pharmaceutically acceptable salt thereof.

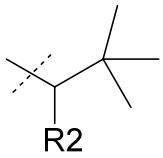
5. The compound according to claim 3 of the Formula:



wherein the compound comprises a single enantiomer that has the (-) optical rotation in methanol, or a pharmaceutically acceptable salt thereof.

6. The compound according to claim 2, wherein R2 is H, or a pharmaceutically acceptable salt thereof.

7. The compound according to claim 1, wherein R1 is

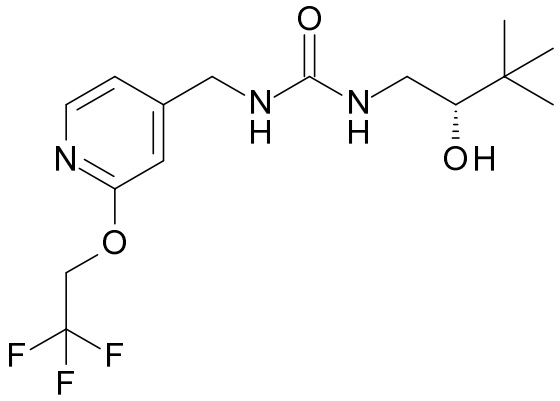


or a pharmaceutically acceptable salt thereof.

8. The compound according to claim 7, wherein R2 is H, or a pharmaceutically acceptable salt thereof.

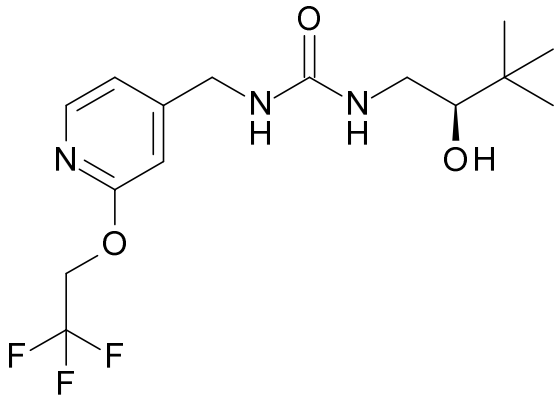
9. The compound according to claim 7, wherein R2 is OH, or a pharmaceutically acceptable salt thereof.

10. The compound according to claim 9 of the Formula:



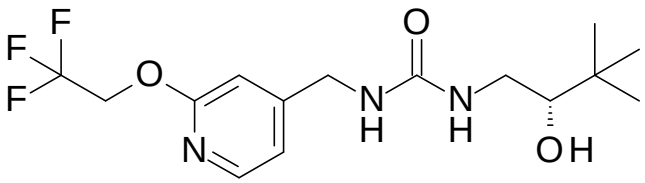
or a pharmaceutically acceptable salt thereof.

11. The compound according to claim 9 of the Formula:



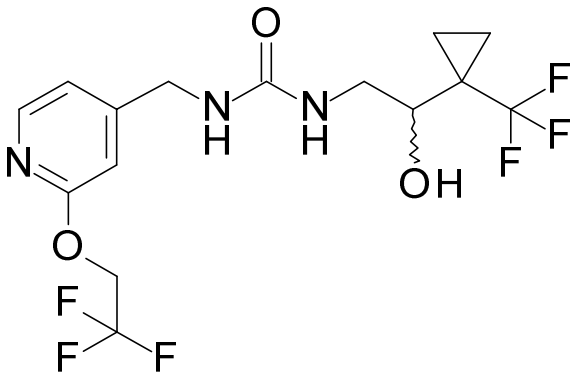
or a pharmaceutically acceptable salt thereof.

12. A compound of the Formula:



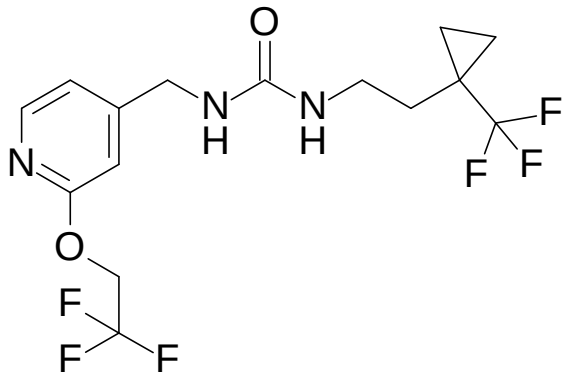
or a pharmaceutically acceptable salt thereof.

13. A compound of the Formula:



wherein the compound comprises a single enantiomer that has the (+) optical rotation in methanol, or a pharmaceutically acceptable salt thereof.

14. A compound of the Formula:



,

or a pharmaceutically acceptable salt thereof.

15. A pharmaceutical composition comprising a compound according to any one of claims 1-14, or a pharmaceutically acceptable salt thereof, with one or more pharmaceutically acceptable carriers, diluents or excipients.

16. Use of a compound according to any one of claims 1-14, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for

treating a disease caused by changes in motor neuron excitability in a patient in need thereof, wherein the disease is selected from the group consisting of ALS, primary lateral sclerosis, pseudobulbar palsy, progressive bulbar palsy, epilepsy and progressive muscular atrophy.

17. The use of claim 16, wherein the disease caused by changes in motor neuron excitability is ALS.

18. Use of the pharmaceutical composition of Claim 15 in the manufacture of a medicament for treating a disease caused by changes in motor neuron excitability in a patient in need thereof, wherein the disease is selected from the group consisting of ALS, primary lateral sclerosis, pseudobulbar palsy, progressive bulbar palsy, epilepsy and progressive muscular atrophy.

19. The use of claim 18, wherein the disease caused by changes in motor neuron excitability is ALS.

20. A compound according to any one of claims 1-14, or a pharmaceutically acceptable salt thereof, for use in therapy.

21. A compound according to any one of claims 1-14, or a pharmaceutically acceptable salt thereof, for use in the treatment of a disease caused by changes in motor neuron excitability, wherein the disease is selected from the group consisting of ALS, primary lateral sclerosis, pseudobulbar palsy, progressive bulbar palsy, epilepsy and progressive muscular atrophy.

22. The compound for use according to claim 21, or a pharmaceutically acceptable salt thereof, wherein the disease caused by changes in motor neuron excitability is ALS.

23. A process for preparing a pharmaceutical composition, comprising admixing a compound according to any one of claims 1-14, or a pharmaceutically

acceptable salt thereof, with one or more pharmaceutically acceptable carriers, diluents, or excipients.