closely resembling human ALS [11-12]. Among other genes implicated in development of ALS or related motor neuron diseases, alsin, an exchange factor for Rab5A [13], senataxin, potentially involved in RNA processing, VAPB protein regulating vesicle transport, the major axonal retrograde motor protein dynactin, mitochondrial genes for cytochrome c oxidase and isoleucine tRNA synthetase [14-15], angiogenic modulatorsVEGF and angiogenin [16], can be mentioned.

ALS is a complex disease with multiple causes and the precise mechanisms involved in the pathogenesis of this disease are not yet resolved. This challenges the discovery of effective pharmacologic therapies. Clinical trials had shown that survival, but not function, is modestly prolonged by riluzole in ALS [18]. Nevertheless, riluzole is currently the only drug approved and the only known therapy for ALS. Regarding to the severity of disease, it is consequently administered as a disease-modifying compound to all the patients suffering from ALS.

WO 2009/133128, WO 2009/133141, WO 2009/133142, WO 2011/054759, WO 2009/068668 and WO 2009/153291 disclose potential treatments for several neurodegenerative diseases, among which ALS.

First attempts at establishing guidelines for non-pharmacological therapies were performed. However, standards are still based on expert opinion and differ between countries.

Accordingly, there is still a strong need in the art for novel and effective therapies for treating amyotrophic lateral sclerosis.

SUMMARY ~~OF INVENTION~~

The present ~~invention~~ disclosure provides novel compositions and methods for treating ALS and related disorders. The ~~invention~~ disclosure stems, inter alia, from the identification of drug combinations which provide improved therapeutic effect and clinical benefit to subjects having ALS.

More particularly, an object of the disclosure~~invention~~ relates to a composition for use in the treatment of ALS or a related disorder, comprising at least two drugs selected from

acamprosate, baclofen, cinacalcet, mexiletine, sulfisoxazole and torasemide, or a salt, prodrug, derivative of any chemical purity, or sustained-release formulation thereof.

A further object ~~of the invention~~ is a method for treating ALS or a related disorder in a subject in need thereof, comprising administering to the subject at least two drugs selected from acamprosate, baclofen, cinacalcet, mexiletine, sulfisoxazole and torasemide, or a salt, prodrug, derivative of any chemical purity, or sustained-release formulation thereof.

Preferred examples of drug combinations ~~for use in the invention~~ include, *e.g.*, baclofen and acamprosate; torasemide and baclofen; baclofen and cinacalcet; torasemide and sulfisoxazole; mexiletine and cinacalcet; or baclofen and acamprosate and torasemide.

In a particular embodiment ~~of the invention~~, the composition further comprises riluzole, or a salt, prodrug, derivative of any chemical purity, or sustained-release formulation thereof.

The disclosed compositions ~~in the invention~~ may further comprise one or several pharmaceutically acceptable carrier(s) or excipient(s), and they may be administered repeatedly to the subject. Preferred compositions are administered orally. Moreover, the drugs may be formulated or administered together, separately or sequentially.

The ~~invention~~ disclosure is suitable for treating ALS in any mammalian subject, particularly in a human subject, at any stage of the disease. The ~~invention~~ disclosure may be used to retard the development of the disease, to reduce, delay or prevent paralysis, motor neuron degeneration and/or pain, and/or to increase survival.

In one aspect, there is provided the use of a composition comprising acamprosate and baclofen, or a salt, a prodrug, a derivative of any chemical purity or a sustained-release formulation thereof, in the manufacture of a medicament, for treating ALS or a related disorder in a subject in need thereof.

In another aspect, there is provided the use of acamprosate, or a salt, a prodrug, a derivative of any chemical purity, or a sustained-release formulation thereof, in the manufacture of a medicament for treating ALS or a related disorder, wherein said medicament is to be administered in combination with baclofen, or a salt, prodrug, derivative of any chemical purity, or sustained-release formulation thereof.

In still another aspect, there is provided the use of acamprosate, or a salt, a prodrug, a derivative of any chemical purity, or a sustained-release formulation thereof, in the manufacture of a medicament for treating ALS or a related disorder, wherein said medicament is to be administered in combination with baclofen and riluzole, or a salt, prodrug, derivative of any chemical purity, or sustained-release formulation thereof.

LEGEND TO THE FIGURES

Figure 1: Effect of baclofen and acamprosate combination therapy against glutamate toxicity on neuronal cortical cells. Glutamate intoxication is significantly prevented by

CLAIMS

1. Use of a composition comprising acamprosate and baclofen~~or~~, or a salt, a prodrug, a derivative of any chemical purity or a sustained-release formulation thereof, in the manufacture of a medicament, for treating ALS or a related disorder in a subject in need thereof.

2. The use of claim 1, wherein the composition comprises at least one of the following drug combinations:
   - baclofen and acamprosate,
   - baclofen and acamprosate and torasemide or a salt, prodrug, derivative of any chemical purity, or sustained-release formulation thereof.

3. The use of claim 1 or 2, wherein the composition further comprises riluzole, or a salt, prodrug, derivative of any chemical purity, or sustained-release formulation thereof.

4. The use of any one of the preceding claims, wherein the medicament further comprises a pharmaceutically acceptable carrier or excipient.

5. The use of any one of the preceding claims, wherein the compounds of said composition are formulated or administered together, separately or sequentially.

6. The use of any one of the preceding claims, wherein said medicament is to be administered repeatedly to the subject.

7. The use of any one of claims 3 to 6, wherein riluzole is to be administered in a dosage from 0.1 to 50 mg per day.

8. The use of any one of claims 1 to 7, wherein acamprosate is to be administered in a dosage of less than 50 mg per day, more preferably less than 10 mg per day.

9. The use of any one of claims 1 to 8, wherein baclofen is to be administered in a dosage of less than 30 mg per day.