NMDAR antagonists that target various sites of this receptor have been tested to counteract excitotoxicity. Uncompetitive NMDAR antagonists target the ion channel pore thus reducing the calcium entry into postsynaptic neurons. Some of them reached the approval status. As an example, Memantine is currently approved in moderate to severe Alzheimer's disease. It is clinically tested in other indications that include a component of excitotoxicity such as alcohol dependence (phase II), amyotrophic lateral sclerosis (phase III), dementia associated with Parkinson (Phase II), epilepsy, Huntington's disease (phase IV), multiple sclerosis (phase IV), Parkinson's disease (phase IV) and traumatic brain injury (phase IV). This molecule is however of limited benefit to most Alzheimer's disease patients, because it has only modest symptomatic effects. Another approach in limiting excitotoxicity consists in inhibiting the presynaptic release of glutamate. Riluzole, currently approved in amyotrophic lateral sclerosis, showed encouraging results in ischemia and traumatic brain injury models (20-23). It is at present tested in phase II trials in early multiple sclerosis, Parkinson's disease (does not show any better results than placebo) as well as spinal cord injury. In 1995, the drug reached orphan drug status for the treatment of amyotrophic lateral sclerosis and in 1996 for the treatment of Huntington's disease.

WO2009/133128, WO2009/133141, WO2009/133142, and WO2011/054759, disclose molecules which can be used in compositions for treating neurological disorders.

Despite active research in this area, there is still a need for alternative or improved efficient therapies for neurological disorders, and, in particular, neurological disorders which are related to glutamate and/or amyloid beta toxicity. The present invention provides new treatments for such neurological diseases of the central nervous system (CNS) and the peripheral nervous system (PNS).

SUMMARY ~~OF INVENTION~~

An object of the present ~~invention~~disclosure is to provide new therapeutic approaches for treating neurological disorders.

The ~~invention~~disclosure stems, inter alia, from the unexpected discovery by the inventors that Torasemide, Trimetazidine, Mexiletine, Bromocriptine, Ifenprodil and Moxifloxacin, alone or in combinations, represent new and effective therapies for the treatment of neurological disorders.

In an aspect, there is provided the use of a composition comprising Torasemide or a salt, or sustained release formulation thereof, for the manufacture of a medicament for treating Alzheimer's disease (AD), senile dementia of AD type (SDAT), Lewy body dementia, vascular dementia, mild cognitive impairment (MCI), age-associated memory impairment (AAMI), amyotrophic lateral sclerosis (ALS) or spinal cord injury (SCI).

The ~~invention~~disclosure therefore provides novel compositions and methods for treating neurological disorders, particularly AD and related disorders, Multiple Sclerosis (MS), Amyotrophic Lateral Sclerosis (ALS), Parkinson's disease (PD), neuropathies (for instance neuropathic pain or alcoholic neuropathy), alcoholism or alcohol withdrawal, Huntington's disease (HD) and spinal cord injury.

More particularly, the ~~invention~~disclosure relates to a composition, for use in the treatment of a neurological disorder, comprising at least Torasemide, Trimetazidine, Mexiletine, Ifenprodil, Moxifloxacin or Bromocriptine, or a salt, prodrug, derivative, or sustained release formulation thereof.

A further object of the present ~~invention~~disclosure relates to a composition comprising at least one first compound selected from the group consisting of Torasemide, Trimetazidine, Mexiletine, Ifenprodil, Moxifloxacin, and Bromocriptine, or a salt, prodrug, derivative of any chemical purity, or sustained release formulation thereof, in combination with at least one second compound distinct from said first compound, selected from Sulfisoxazole, Methimazole, Prilocaine, Dyphylline, Quinacrine, Carbenoxolone, Acamprosate, Aminocaproic acid, Baclofen, Cabergoline, Diethylcarbamazine, Cinacalcet, Cinnarizine, Eplerenone, Fenoldopam, Leflunomide, Levosimendan, Sulodexide, Terbinafine, Zonisamide, Etomidate, Phenformin, Trimetazidine, Mexiletine, Bromocriptine, Ifenprodil, Torasemide, and Moxifloxacin salts, prodrugs, derivatives of any chemical purity, or sustained release formulation thereof, for simultaneous, separate or sequential administration.

A further object of the present ~~invention~~disclosure relates to a composition, for use in the treatment of a neurological disorder, comprising at least one first compound selected from the group consisting of Torasemide, Trimetazidine, Mexiletine, Ifenprodil, Moxifloxacin, and Bromocriptine, salts, prodrugs, derivatives of any chemical purity, or sustained release formulation thereof, in combination with at least one second compound distinct from said first compound, selected from Sulfisoxazole, Methimazole, Prilocaine, Dyphylline, Quinacrine, Carbenoxolone, Acamprosate, Aminocaproic acid, Baclofen, Cabergoline, Diethylcarbamazine, Cinacalcet, Cinnarizine, Eplerenone, Fenoldopam, Leflunomide, Levosimendan, Sulodexide, Terbinafine, Zonisamide, Etomidate, Phenformin, Trimetazidine, Mexiletine, Bromocriptine, Ifenprodil, Torasemide, and Moxifloxacin, salts, prodrugs, derivatives of any chemical purity, or sustained release formulation thereof, for simultaneous, separate or sequential administration.

The present ~~invention~~disclosure also relates to a composition comprising at least one first compound selected from the group consisting of Torasemide, Trimetazidine, Mexiletine, Ifenprodil, Moxifloxacin and Bromocriptine, salt(s), prodrug(s), derivative(s) of any chemical purity, or sustained release formulation(s) thereof, in combination with at least one second compound distinct from said first compound, selected from Sulfisoxazole, Methimazole, Prilocaine, Dyphylline, Quinacrine, Carbenoxolone, Acamprosate, Aminocaproic acid, Baclofen, Cabergoline, Diethylcarbamazine, Cinacalcet, Cinnarizine, Eplerenone, Fenoldopam, Leflunomide, Levosimendan, Sulodexide, Terbinafine, Zonisamide, Etomidate, Phenformin, Trimetazidine, Mexiletine, Bromocriptine, Ifenprodil, Torasemide, and Moxifloxacin salt(s), prodrug(s), derivative(s) of any chemical purity, or sustained release formulation(s) thereof, and a pharmaceutically acceptable excipient, for simultanous, separate or sequential administration.

Most preferred drug compositions comprise 1, 2, 3, 4 or 5 distinct drugs, even more preferably 2, 3 or 4. Furthermore, the above drug compositions may also be used in further combination with one or several additional drugs or treatments beneficial to subjects with a neurological disorder.

The ~~invention~~disclosure also relates to a method of treating a neurological disorder, the method comprising administering to a subject in need thereof a drug or composition as disclosed above.

A further object of this ~~invention~~disclosure relates to a method of treating a neurological disorder, the method comprising simultaneously, separately or sequentially administering to a subject in need thereof a drug combination as disclosed above.

A further object of this ~~invention~~disclosure relates to the use of at least one compound selected from the group consisting of Torasemide, Trimetazidine, Mexiletine, Ifenprodil, Bromocriptine and Moxifloxacin, or salt(s), prodrug(s), derivative(s) of any chemical purity, or sustained release formulation(s) thereof, for the manufacture of a medicament for the treatment of a neurological disorder.

A further object of this ~~invention~~disclosure relates to the use of drug combinations disclosed above, for the manufacture of a medicament for the treatment of a neurological disorder.

The ~~invention~~disclosure may be used in any mammalian subject, particularly human subject, at any stage of the disease.