

Neurosteroids - Neuropathic pain (NP)

Development status

Preclinical trials

IP protection status

Kudova et al.: Amphiphilic Compounds with Neuroprotective Properties. EP3260462 A, EP3260462 A, CA 2957906 A, JP 2017-511948, US 15/506318, AU 2015309371

Partnering strategy

Collaboration, licensing, spin-off

Challenge

The NP market is rife with unmet needs. The main classes of drugs used in the treatment of NP have traditionally consisted of antidepressants, anticonvulsants, opioid analgesics, and topical analgesics. Although many of the available drugs offer some degree of efficacy in terms of pain relief, there still remains vast room for improvement in efficacy, safety, drug delivery, and dosing convenience. Market size 2017 is about 3 bil. USD, CAGR 3%

Description

Neurosteroids act as multi-target allosteric modulators of various neuro-receptors. Among others, the NMDA receptor modulators influence the ion flow in synapses. Allosteric NMDAr modulators do not reveal typical adverse effects (in animal models) like dizziness, nausea, somnolence or cognitive difficulties as the current therapeutics often acting as Ca or Na channel blockers. MS-225 shows inhibitory effect at micromolar concentrations. However, there are other receptor families involved in the pain perception. MS-225 modulates their function at nanomolar concentrations. This might be the dominant mode of action and as such is a subject of further research and a new application for extended patent protection. Besides the NP, some steroidal analogues has proven its efficacy in epilepsy or neuroprotection models.

Commercial opportunity

If the clinical trials confirm its efficacy and low adverse effects, the molecule can easily acquire 10-30% of the market counting from 300 mil. to 1 bil. USD.

STEROIDS for Neuropathic Pain Treatment

The Pain Pathway: Glutamate and its receptors represent a major neurotransmitter system at the first spinal synapse. NMDA antagonists are conceivable analgesics, clinically proven as quite efficacious, however, due to the presence of NMDA receptors in the whole CNS, systemic administration of NMDA antagonists brings a number of adverse side effects like memory impairment, psychomotoric changes, ataxia, disturbance of motor coordination, sedation etc.

Our proprietary, specifically designed steroidal molecules act as ALLOSTERIC MODULATORS of NMDA receptor with no observed side effects at the therapeutic dosing level.

Efficacy	Safety	Pharmacokinetics
<p>Preclinical-induced Neuropathic Pain (PINP) Model</p> <ul style="list-style-type: none"> MS-225 (100 ng/kg) MS-225 (1000 ng/kg) MS-225 (10000 ng/kg) <p>Effect on Mechanical Pain Threshold after Chronic Dosing</p> <p>MS-225 Inhibits Peripheral Neuroinflammation (PNI) Inhibits</p>	<p>Standard Plus Tests</p> <p>Activity Test – sedation 100 mg/kg</p> <p>Acute ADME data</p> <ul style="list-style-type: none"> No CYP 450 inhibition not activation Stable pharmacokinetic stability in rat, low in human Highly bound to plasma proteins Low logP ELICITING Safety Study on 40 selected receptors and proteins revealed no target hit No toxicity to MSD Proprietary MS-225: 100 mg/kg 	<p>PK Study after single i.p. dosing of 1, 3 and 10 mg/kg MS-225 in mice</p> <p>Comparative PK Study (i.p. dosing of MS-225 in rat and PK)</p>

Preclinical Plan

- Strategic efficacy studies
- Strategic safety studies (toxicology, safety, reproductive toxicology)
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Institution

IOCB Tech

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Chemistry and Biochemistry of
CAS**