

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
GABAergic and 5-HT 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
Pain threshold after Chronic Dosing (PPH) Model
PPH Effect on Mechanical Pain Threshold after Chronic Dosing
Behavioral effects on neuropathic pain models

Safety
Standard Plus Tests
Activity Test - sedation 100 mg/kg
Acute ADME data
• No CYP 450 inhibition not activation
• Moderate pharmacological stability in rat, low in human
• No CNS depression
• No CNS depression
• No CNS depression
• No CNS depression
• No CNS depression

Pharmacokinetics
PK Study after single i.p. dosing of 1, 3 and 10 mg/kg MS-225 in mice
Comparative PK PK study (i.p. dosing of MS-225 in rat and PK)

Preclinical Plan
• Behavioral Pain models (Original and Formalin, Dexamethasone)
• Behavioral Pain models (Original and Formalin, Dexamethasone)
• Behavioral Pain models (Original and Formalin, Dexamethasone)
• Behavioral Pain models (Original and Formalin, Dexamethasone)
• Behavioral Pain models (Original and Formalin, Dexamethasone)

IP status
• EP3260462 A
• EP3260462 A
• CA 2957906 A
• JP 2017-511948
• US 15/506318
• AU 2015309371

Project Manager Contact
Jan Šesták, PhD
IOCB Tech
IOCB Tech
IOCB Tech

Institution

IOCB Tech

**The Institute of Organic
Chemistry and Biochemistry of
CAS**