

Neurosteroids - Neuropathic pain (NP)

Development status

Preclinical trials

IP protection status

Kudova et al.: Amphipilic 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
PainReduction Induced by Neuropathic Pain (PAIN) Model
PAIN Effect on Mechanical Pain Threshold after Chronic Dosing
Neurosteroid-Induced Peripheral Neuropathy (PINP) Inhibitor

Safety
Standard Plus Tests
Activity Test - sedation 100 mg/kg
Available ADME data
• No CYP 450 inhibition not activation
• Moderate membrane stability in rat, low in human
• No effect on plasma proteins
• No effect on hERG
• DDPDPPD Safety Study on 40 selected receptors and proteins revealed no target hit
• No toxicity to hERG
• Potency: MS-225, 100 mg/kg

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

Preclinical Plan
• Behavioral Pain models: Dorsal skin, Formalin, Dorsal heat
• Clinical relevance: Pain Development, Pain Threshold, Response Development
• Pain Reducers: In vivo testing of Neurosteroids
• Clinical relevance: In vivo testing of Neurosteroids
• Pain Reducers: In vivo testing of Neurosteroids
• Pain Reducers: In vivo testing of Neurosteroids
• Pain Reducers: In vivo testing of Neurosteroids

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

IOCB Tech
Project Manager Contact: Jan Šesták, PhD, IOCB Tech, Prague, Czech Republic, +420 224 121 212, jsestak@iocbtech.cz

This is a project of the Center for Development of Original Drugs (CODO) with the financial support of the Ministry of Education, Youth and Sports of the Czech Republic.

Institution

IOCB Tech

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