

## 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.

**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
<ul style="list-style-type: none"> <li>Pain Relief in Neuropathic Pain (PNP) Model</li> <li>Effect on Mechanical Pain Threshold after Chronic Dosing</li> <li>Behavioral/Neurological Parameters (B/NP) Inhibition</li> </ul>	<ul style="list-style-type: none"> <li>Standard Plus Tests</li> <li>Activity Test - sedation 100 mg/kg</li> <li>Acute ADME data</li> <li>No CYP 450 inhibition not activation</li> <li>Stable in vitro stability in rat, low in human</li> <li>Not bound to plasma proteins</li> <li>LogP 2.8</li> <li>ELISA/MS Safety Study on 40 selected receptors and proteins revealed no target hit</li> <li>No binding to NMDA</li> <li>Preferential MS-225 100 mg/kg</li> </ul>	<ul style="list-style-type: none"> <li>PK Study after single i.p. dosing of 1, 3 and 10 mg/kg MS-225 in mice</li> <li>Comparative PK PK study (i.p. dosing of MS-225 in rat and 010)</li> </ul>

**Preclinical Plan:** Strategic Pain models (Optimal dose, Formulation, Dosing schedule), Targeted Neuroprotective and Neuroregenerative Treatment, Study the effect on the sensory effect of Neurosteroids, Clinical trials in animal models, Safety studies, and other studies, MS-225 and other Steroidal Compounds, and other studies, and other studies.

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**Project Manager Contact:** Jiri Saska, PhD, IOCB Tech, saska@iocbtech.cz, +420 732 222 222, IOCB Tech, saska@iocbtech.cz

This is a project of the Center for Development of Original Drugs (CDO) with the financial support of the Ministry of Health of the Czech Republic.

### 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.

### Institution

## IOCB Tech

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