

## 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**  
Pain-induced Peripheral Neuropathy (PINP) Model  
PINP Effect on Mechanical Pain Threshold after Chronic Dosing  
Brimonidine-Induced Peripheral Neuropathy (BIPNP) Model

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

**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 PK)

**Preclinical Plan**  
• Stereoid Pain models (Optimal dose, Formulation, Dose-toxicity)  
• Effect of Stereoid on Neuropathic Pain Threshold Response (Development)  
• Effect of Stereoid on Neuropathic Pain Threshold Response (Development)  
• Effect of Stereoid on Neuropathic Pain Threshold Response (Development)  
• Effect of Stereoid on Neuropathic Pain Threshold Response (Development)

**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

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

### Institution

**IOCB Tech**

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