

Neurosteroidy - Neuropatická bolest (NP)

Fáze vývoje technologie

Preklinické testy

Status IP ochrany

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

Strategie pro hledání partnera

Licencování, Spin-off, Spolupráce

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 (the sensory impairment, psychomotoric changes, ataxia, disturbances of motor coordination, sensation 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
Preclinical Model: PPRN Model, PPRN Effect on Mechanical Pain Threshold after Chronic Dosing, Steroid-induced Peripheral Neuropathy (SIPN) Model.

Safety
Dose-toxicity studies, Activity Test - sedation 100 mg/kg.

Pharmacokinetics
PK study after single IP dosing of 0.2 and 10 mg/kg MS-225 in mice, Comparative PK study (2 to 6 h dosing of MS-225 in rat (p.o)).

Available ADME data

- No CNS ADME dependent activation
- Modestly improved stability in rat, low in human
- 100% bioavailability in rat
- LogP=4.8
- CSF:PK:PB Study on 40 selected receptors and ion channels
- No binding to MDR1
- Pharmacology MTD is 100 mg/kg

Preclinical Plan

- Design of new molecules
- Preclinical studies: Dose-toxicity, Pain, Sensation, Motoric, Behavioral, Neurophysiological, PK, Pharmacokinetic Measurement
- Lead and lead-lead optimization
- Preclinical studies in human: Safety, Pharmacokinetic, PK:PK:PB Study on 40 selected receptors and ion channels
- ADME studies and CSF:PK:PB studies
- Lead selection

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Motivace

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%

Popis

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. 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.

Komerční využití

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.

Institute

IOCB Tech

Ústav organické chemie a
biochemie AV ČR, v.v.i.