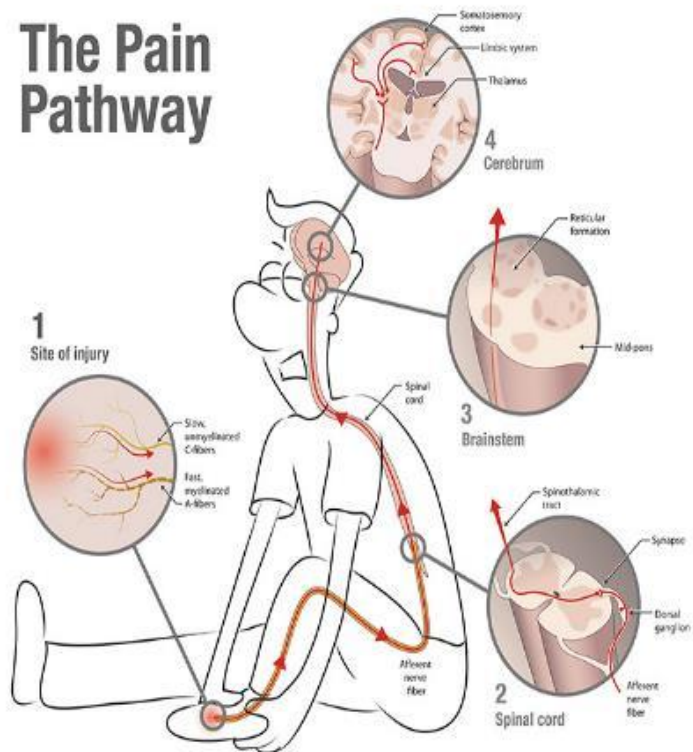


# Neurosteroids for Neuropathic Pain Treatment

Jan Šotola, IOCB TECH

# Neuropathic Pain - Defect Signaling System

## The Pain Pathway



Up to 7% of the population affected!

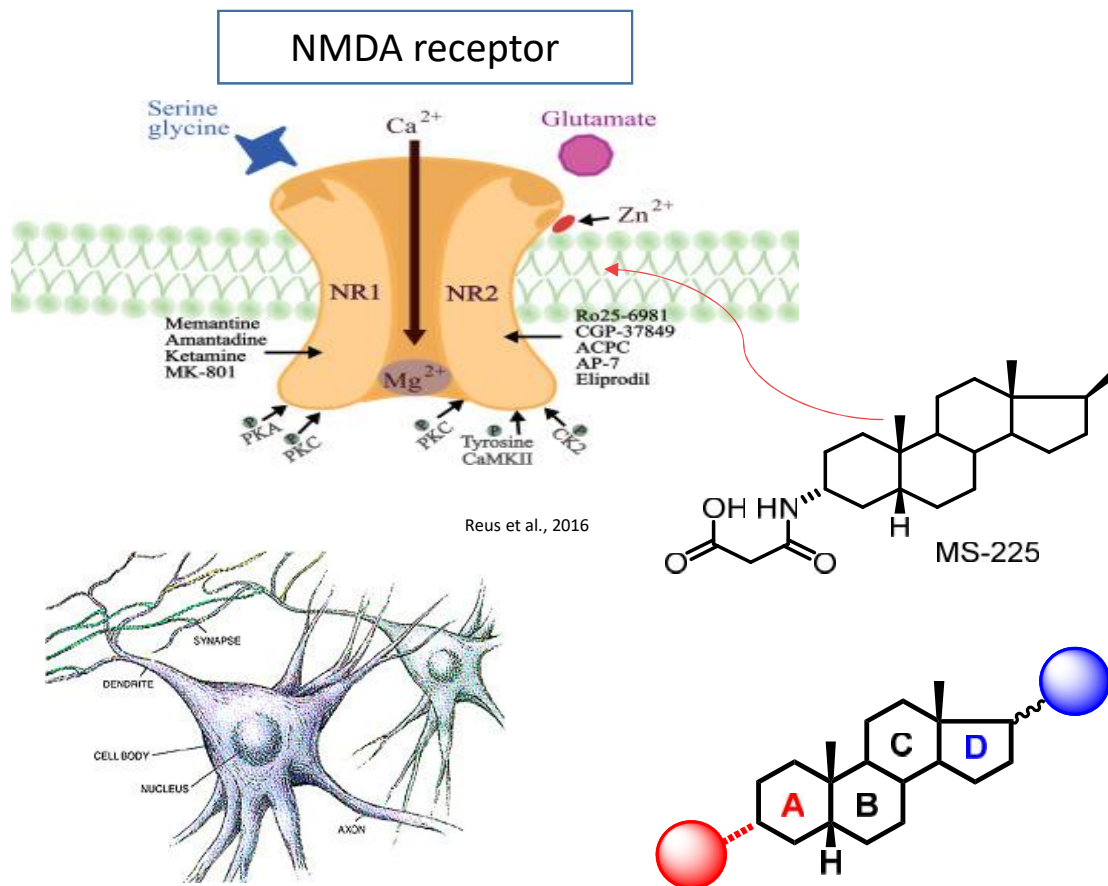
Diabetes, Chemotherapy, Herpes, Ischemia, Spinal cord injury ...

„Analgesics, Lyrica, Duloxetine, Opioids, Qutenza — you name it....

**40% of patients get 30% pain relief.....“**



# Current Treatments are Inadequate



Ketamine, methadon, amantadine, memantin and/or dextromethorphan, are quite efficacious,

**BUT!**

Blocking the ion channel leads to **adverse side effects!**

**SOLUTION?**

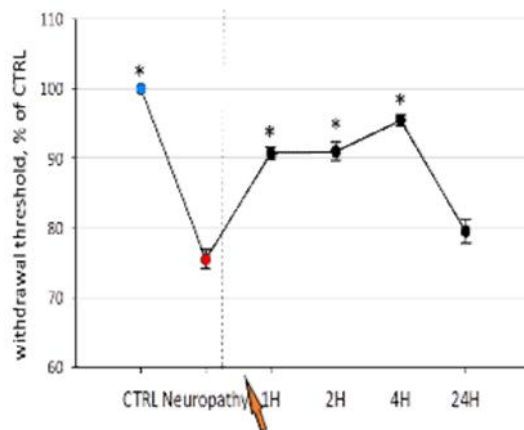
**ALLOSTERIC MODULATION**

- fine modulation on „non-active site“ - not blocking the physiological functions.

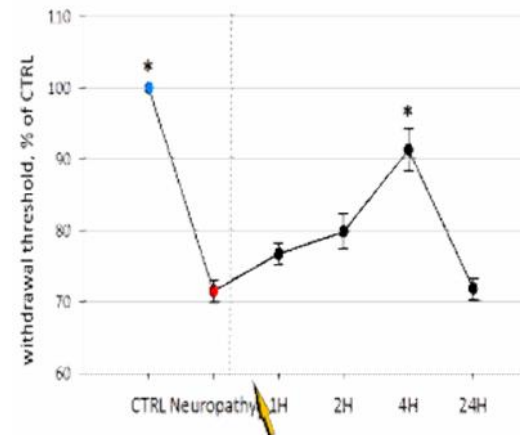
# Our Solution - Proof of Concept

## Paclitaxel-Induced Peripheral Neuropathy (PIPNe) Model

MS-225,  
1 mg/kg



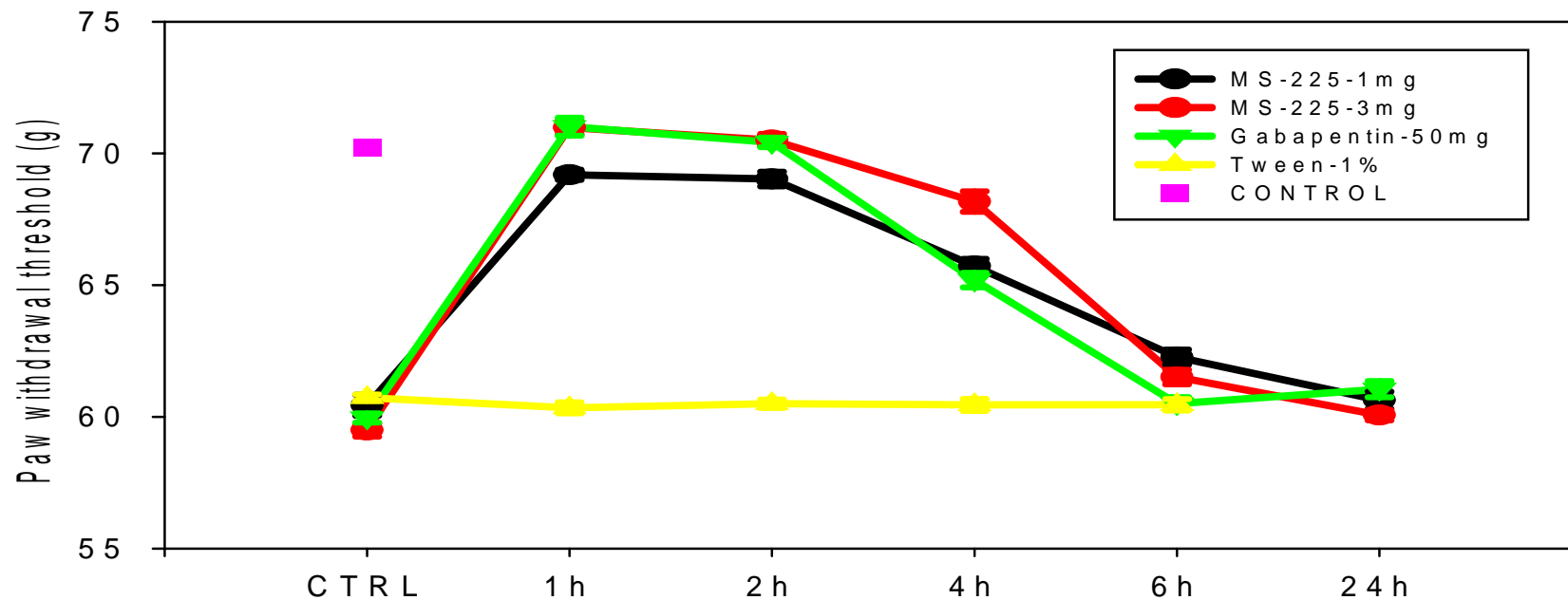
Gabapentin,  
100 mg/kg



MS-225 significantly reduced pathological pain response, is faster and more effective!

# Our Solution - Proof of Concept

## Bortezomib - Induced Peripheral Neuropathy (BIPN) (multiple myeloma treatment)



Reduction of increased sensitivity to mechanical stimuli (mechanical allodynia) after application of MS-225 and Gabapentin [one experimental group n=4]

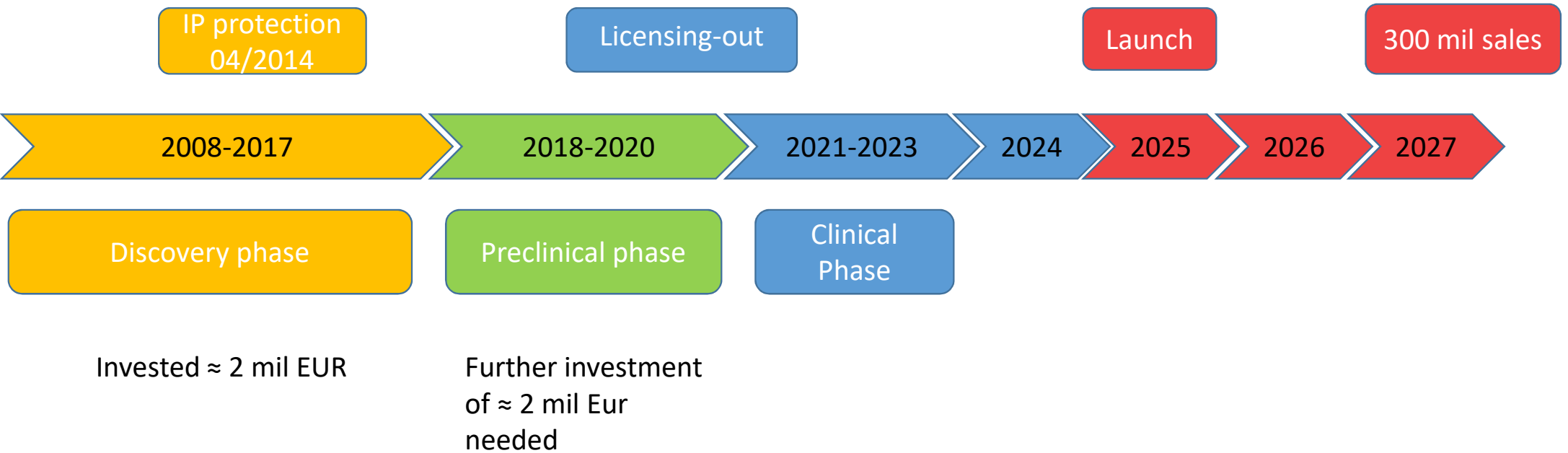
# Market analysis

NP market is estimated to \$3B 2016 and will grow to \$8B by 2026

Marketed drugs	MoA	Sales in mil. USD	
		2016	2023
gabapentin	Ca channel blocker	270	230
pregabalin	Ca channel blocker	5 230	1 300
duloxetine	serotonin uptake blocker	1 100	364
memantine	NMDA antagonist	1 100	264
dextromethorphan	NMDA antagonist	210	400
amantadine	NMDA antagonist	1	290

Pipeline drugs	MoA	Sales		Phase
		2016	2023	
cebranopadol	opioid Mu/ORL1 agonist	0	?	Phase II
cenobamate	sodium channel blocker	0	?	Phase II
mirogabalin bes.	Ca channel blocker	0	278	Phase III

# Timeline



# Preclinical Plan 2018-2020

## ➤ Stronger efficacy evidence

EUR 0.5 mil

- Additional Pain models (Surgical pain, Formalin, Streptozocin)
- Extend Behavioral test to supplement Pain Threshold Response Measurement
- Test the anti-neuro-inflammatory effect of Neurosteroids
- Extend the testing to non human primates (Macaques)
- Localize the place of action: Peripheral / Spinal / Central

## ➤ API Synthesis and Oral-Formulation

EUR 1 mil

## ➤ Start the standard toxicological studies

EUR 0.5 mil



# Team



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Synthesis



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Patch-clamp experiments  
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**IOCB Tech**



**RNDr. Karel Valeš, PhD**  
Behavioral models

# Conclusion

- Efficacy proven in 2 models against positive control.
- Orally bioavailable.
- Behavioral data show no sedation, fuzziness or other mental disorders at therapeutic dosing level (unlike the marketed drugs).
- We are looking for a **partner** for further **pre-clinical** and **clinical development**.
- We prefer **licensing-out** or **co-development** partnership.

Thank you for your attention!