Preclinical and translational studies of fenobam, an mGlu5 NAM, for the treatment of pain

Robert W Gereau IV*, Laura F Cavallone

From Seventh Scientific Meeting of The TMJ Association, Genetic, Epigenetic, and Mechanistic Studies of Temporomandibular Disorders and Overlapping Pain Conditions
Bethesda, MD, USA. 7-9 September 2014

Background
Metabotropic glutamate receptor 5 has been suggested by many rodent studies to be a promising target for the development of novel analgesic drugs. The lack of approved compounds has prevented proof-of-concept studies in human subjects. Here we describe preclinical and translational studies of the mGlu5 negative allosteric modulator (NAM), fenobam.

Materials and methods
Fenobam was tested for analgesic efficacy and toxicity in mouse models. We also tested the plasma levels after oral dosing of fenobam in healthy volunteers, and collected any adverse events following oral dosing compared to placebo.

Results
The mGlu5 NAM Fenobam is effective in a wide variety of preclinical pain models in mice with no evidence of the development of analgesic tolerance on daily dosing. No obvious toxicities were observed in mice, or in several studies in healthy human volunteers.

Conclusions
Fenobam has robust analgesic activity and shows a good safety profile. Fenobam therefore represents a useful tool for proof-of-concept studies in human subjects.