



PRESS RELEASE

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Extensive new preclinical study significantly increases the Translatability of Asarina Pharma's findings on key stress mechanism implicated in Tourette Syndrome and OCD

(Stockholm, 6 October 2022.) A new study in the journal *Neurobiology of Stress* reconfirms the central role the neurosteroid Allopregnanolone (ALLO) plays in stress-related conditions such as Tourette syndrome and OCD, and the efficacy of its endogenous modulator isoallopregnanolone in modulating its negative effects. This is the most extensive of four preclinical studies confirming these findings, significantly increasing the Translatability of data. Asarina Pharma is testing isoallopregnanolone (under the name Sepranolone) for Tourette syndrome in a Phase IIa study, with the last patient soon to be randomized. The dropout rate has so far been unexpectedly low.

A new study, the fourth and most comprehensive in a series of four (1), reconfirms that acute stress increases the overproduction of the powerful neurosteroid Allopregnanolone in the medial prefrontal cortex (mPFC) of the brain, and that the administration of its endogenous modulator isoallopregnanolone (being developed as the novel treatment Sepranolone) counters those effects. The study, *Acute stress impairs sensorimotor gating via the neurosteroid allopregnanolone in the prefrontal cortex*, was carried out by Professor Marco Bortolato and his team at the Dept. of Pharmacology and Toxicology, University of Utah.

Positive PPI findings – a key metric in Tourette, OCD and schizophrenia

The study significantly strengthened evidence that increased production of ALLO reduces Prepulse Inhibition (PPI), the universal ability to reduce the startle reflex in response to repeated stressors. PPI is a key metric used in clinical tests for Tourette, OCD, schizophrenia and others. With reduced PPI, Tourette patients, for example, are unable to manage their startle response and react with the same level of startle to the same, repeated stressor. The current and very solid study demonstrates i) ALLO's harmful effect on PPI from four different kinds of stress triggers tested in three different breeds of rodents, and ii) how both systemic and intra-PFC administration of isoallopregnanolone (Sepranolone) countered that negative effect.

Broader study increases translatability

The study significantly increased the number and range of subjects and stress stimuli in comparison to previous studies. It tested four very different types of stress factors on three different breeds of rodents. This significantly increases the Translatability of these and earlier findings: "The confirmation of these mechanisms across distinct animal models and several different acute stressors strongly supports the translational value of these findings and warrants future research on the role of ALLO in information processing." (2)

Tourette and Sepranolone

Previous preclinical studies carried out by the University of Utah team demonstrated that Sepranolone suppresses tics in Tourette and restores PPI. Currently no safe, effective pharmaceutical therapy without serious side effects exists for Tourette. Anti-psychotic neuroleptics like haloperidol (Haldol), associated with frequent and serious side effects, are still prescribed. In June 2022 a new study by the U.S. CDC (Centers for Disease Control and Prevention) estimated that double the number of Tourette patients than previously thought (1-in-50 children compared to previous estimates of 1-in-100) may be affected by Tourette or persistent tic disorders.

Asarina Pharma CEO Peter Nordkild: “This new study powerfully extends the Translatability of our data demonstrating ALLO’s role as a key component in the mechanism of action in Tourette, OCD and other stress-related conditions. Test subjects were exposed to very different types of stress all reacting with reduced PPI – a recognized clinical metric in Tourette and OCD worldwide. The study is a highly positive and encouraging end to this ambitious, comprehensive cycle of preclinical tests. We now have a highly compelling case for further clinical tests in Tourette and an initial trial in OCD.”

- (1) 2017, <https://www.nature.com/articles/s41598-017-03649-1> 2019 <https://pubmed.ncbi.nlm.nih.gov/31175669/> 2022 <https://pubmed.ncbi.nlm.nih.gov/34423500/>
- (2) <https://www.sciencedirect.com/science/article/pii/S2352289522000649>

For further information, please contact:

Peter Nordkild, CEO, Asarina Pharma AB

Phone: +45 25 47 16 46

E-mail: peter.nordkild@asarinapharma.com

About Asarina Pharma

We are a Swedish biotech company developing Sepranolone for allopregnanolone-induced stress- and compulsivity-driven disorders. Our product pipeline is built on over 40 years of research into allopregnanolone-related neurological disorders. With our new family of GAMSA compounds (GABA-A Modulating Steroid Antagonists) we aim to deliver a new generation of safe, efficacious drugs for neurological conditions from Tourette syndrome to Obsessive Compulsive Disorder that still lack safe, efficacious pharmaceutical treatments.