



PRESS RELEASE

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New preclinical study confirms that Sepranolone suppresses tics in Tourette Syndrome

(Stockholm, 11 February 2021.) Two sets of new preclinical data presented by Prof Marco Bortolato (Univ. of Utah) confirm that Sepranolone suppresses tics in Tourette Syndrome (TS) and restores Prepulse Inhibition (PPI), a key phenomenon related to TS with no observable side-effects. The new data also point towards the overproduction of Allopregnanolone in acute stress situations as potentially crucial in triggering negative symptoms in neuropsychiatric conditions from Tourette to OCD, mania and schizophrenia.

Professor Marco Bortolato presented the new preclinical findings at the “Allopregnanolone and its synthetic analogues: from bench to clinical strategies for neuropathology” Conference in Torino, Italy, on February 11 in a presentation entitled *‘The other side of the coin: the neuropsychiatric side effects of allopregnanolone’*. Prof Bortolato: “Our data consistently confirm that acute stress increases Allopregnanolone production in the prefrontal cortex, the major area for decision making that also controls impulse and impulsivity. We have now used multiple complementary experimental models to get an idea of how generalizable this phenomenon might be, and it actually appears to be highly generalizable.”

THE FIRST SET OF FINDINGS is from a newly developed mouse model of TS, developed to confirm 2019 data from a previous D1CT-7 transgenic mouse model. The new model was generated through early-life depletion of cholinergic interneurons in the striatum, an abnormality observed in post-mortem brain samples of individuals affected by TS. The mice subjected to this manipulation in early adolescence develop increased stress-induced stereotypes (akin to tics) and gating impairments, which were mediated by Allopregnanolone and significantly suppressed by Sepranolone.

CEO Peter Nordkild: “This different but complementary preclinical model corroborated previous findings, confirming the role of neurosteroids and in particular Allopregnanolone in the pathophysiology of TS and underlined the therapeutic potential of Sepranolone as an effective treatment for TS.”

THE SECOND SET OF FINDINGS were from mouse and rat models that measured the effect of the overproduction of Allopregnanolone on PPI. PPI is a highly reliable index that measures our ability to filter out redundant information. It is commonly used in preclinical tests in a range of psychiatric disorders. “PPI is a modulated startle reflex that is universal and identical in all normally functioning animals and humans,” Bortolato says. “When we hear a sudden loud noise, we have a startle reflex, but if we hear a quiet pre-pulse directly before it, that startle reflex is reduced. This PPI response is significantly reduced in many psychiatric disorders, from schizophrenia and mania to TS and OCD. In these conditions patients still startle with the same intensity, even when they have heard the pre-pulse, indicating they are not able to filter out irrelevant stimuli. We believe this is probably the

mechanism by which acute stress impairs the ability of TS patients to suppress their tics. It also seems to be a generalized problem in a lot of other conditions that share this type of information processing problems, such as OCD, mania, and schizophrenia.”

The study found that increased production of allopregnanolone interrupted the PPI response during acute stress situations, and that Sepranolone prevented this interruption when injected into the prefrontal cortex. “Increased production of Allopregnanolone in mice and rats, whether manually administered or increased by stress, impaired PPI, and this reduction was blocked by Sepranolone” says Bortolato.

CEO Peter Nordkild: “PPI is a highly reliable measurement in animals so we believe there is a good possibility that the same mechanism might apply in humans. These findings suggest that at least a part of the information processing we see *across all these diverse disorders* could be exacerbated by Allopregnanolone - and attenuated by Sepranolone. Our focus is to develop an efficacious therapy with little or no side effects for TS patients, but it does seem as well that Sepranolone could offer psychiatrists a new adjunctive treatment to reduce stress and improve compliance to psychotherapy in these other highly stress-induced conditions.”

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About Asarina Pharma

We are a Swedish biotech company developing Sepranolone for allopregnanolone-related stress, menstrual and neurological disorders. Our product pipeline is built on over 40 years of research into allopregnanolone-related neurological disorders. With our new family of GAMSAs (GABA_A Modulating Steroid Antagonists) we aim to deliver a new generation of efficacious and safe drugs for still widely untreated neuroendocrinological conditions.

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