PRESS RELEASE
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Asarina Pharma publishes positive results from its Phase IIa study of Sepranolone in Tourette Syndrome

(Stockholm, April 1, 2023) Asarina Pharma today releases results from its Phase IIa study of the endogenous neurosteroid Sepranolone for the treatment of Tourette Syndrome. The primary objective of the study was to investigate the efficacy of Sepranolone, compared to Standard of Care, to reduce tic severity in patients with Tourette Syndrome at twelve weeks, using the change from baseline in Yale Global Tic Severity Scale (YGTSS) total score. The study found that Sepranolone reduced the YGTSS score by 8.6 points or 28.0%. This was compared to a 3.9 point or 12.6% reduction in the control group (p= 0.051) that received only Standard of Care. Improvements in all secondary efficacy endpoints, including improvement in Quality of Life, were observed in the Sepranolone group compared to the control group. Sepranolone maintained its impressive safety profile: no systemic side effects were observed and only 2% of injections resulted in some kind of mild to moderate but reversible skin reaction.

THE STUDY: This was an open label, dual center, add-on study, randomizing 28 Tourette Syndrome patients, 20 males/8 females, 3 adolescents/25 adults between 12 and 47 years of age with an average baseline YGTSS score of 32 points. YGTSS is the validated standard clinical rating instrument used in Tourette Syndrome and tic disorder studies. It measures and evaluates the number, frequency, intensity, complexity, and interference of motor and phonic symptoms.

Seventeen subjects in the active group received Sepranolone 10 mg twice weekly injections in addition to Standard of Care and 9 patients in the control group received Standard of Care alone for 12 weeks. Patient characteristics were evenly distributed between the two groups. Two patients (7%), one from each group, dropped out of the study.

PRIMARY CLINICAL ENDPOINT: Sepranolone is an endogenous neurosteroid that suppresses the effect of positive GABA-A receptor modulators. The study found that the YGTSS total tic score in the Sepranolone group was reduced by 8.6 points or 28.0%, versus 3.9 points or 12.6% in the control group (p= 0.051) in the Intention-To-Treat population, consisting of patients having taken at least 6 injections every 4 weeks. A reduction of 6 to 7 points, or 25%, is considered clinically relevant (1). The treatment effect was further pronounced for the 15 patients in the Per Protocol population, consisting of patients having taken all scheduled injections, with the Sepranolone group reducing the YGTSS score from the baseline by 9.9 points or 30.1%, versus 4.0 points or 12.7% in the control group.

SECONDARY CLINICAL ENDPOINTS: The study showed that the Sepranolone group consistently performed better than the control group for all the TS secondary clinical objectives including Quality of Life. The TS secondary objectives included:

1) **Impairment:** As measured by the YGTSS Impairment scale and assessed by the patient, the number of patients with moderate to marked symptoms was reduced from 50% to 19% for the Sepranolone group versus the unchanged 50% for the control group.

2) **Quality of Life:** The Gilles de la Tourette Syndrome – Quality of Life total score (GTS-QOL) showed a 69% greater increase in life quality for the Sepranolone group versus the control group.

3) **Reducing the Premonitory Urge to Tic:** The Premonitory Urge to Tic scale (PUTS) demonstrated a 44% greater reduction for the Sepranolone group than for the control group.

4) **TS-Clinical Global Impairment** assessed by the investigator showed that 50% of patients in the Sepranolone group improved versus 37% of the controls. 13% of patients in the Sepranolone group had a deteriorated score versus 50% of the controls.

The correlation between the YGTSS total score and the secondary endpoints was strong with Spearman correlation coefficients of 0.57 (p=0.021) for impairment; GTS-QOL total score of 0.54 (p=0.032) and in particular for GTS-QOL-daily living of 0.66 (p=0.006).

Furthermore, a post-hoc analysis was conducted where the Sepranolone patients were divided into two groups; one with a >25% reduction constituting 50% of the ITT population, the other with a <25% reduction of tics. The first group showed a 4.8 times greater decrease of impairment, as measured by the YGTSS-impairment scale, and a 3.7 times greater increase of life quality as measured by the GTS-QOL total score. These metrics are considered the clinically most relevant after YGTSS. In the Per Protocol population 70% showed a reduction > 25% by YGTSS.

SAFETY: Sepranolone was well tolerated in this study, with a safety profile consistent with that observed in more than 300 patients in previous clinical studies in other indications. No systemic side effects were observed and only 2% of injections resulted in some kind of mild to moderate but reversible skin reaction.

CEO Peter Nordkild: “In this small study, the consistent performance of Sepranolone being superior to Standard of Care, as measured by a wide variety of Tourette Syndrome assessment instruments, is very encouraging. The low rate of only mild to moderate and reversible side effects is also very promising in a Tourette Syndrome treatment context, as Tourette Syndrome medications are commonly associated with frequent and severe side effects. The very low drop-out rate of only one patient in the active group (5.9%) is an indication of the acceptance of this new treatment for Tourette Syndrome - an acceptance likely to be further improved when administered with a tailored autoinjector. These consistent clinical results offer encouraging evidence of a safer, more tolerable treatment for patients suffering from Tourette Syndrome. With the good safety profile and the consistent evidence of reduced tics observed in the study, we believe that patients in a phase IIb study could further benefit from slightly higher dose or more frequent dosing. We would like to thank our clinical team at our test centers. Asarina Pharma will now assess our various options for progressing this program to a clinical Phase IIb study starting in 2024.”

Reference:
(1) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3999642/

The information above was provided by Asarina Pharma AB according to EU Market Abuse Regulations. The information was provided, through the below contact person, for publication on April 1, 2023 at 1420 CET.

About Sepranolone

Sepranolone (*isoallopregnanolone)* is an endogenous neurosteroid produced specifically to target and modulate the effects of Allopregnanolone - the powerful neurosteroid implicated in the exacerbation of tics, and other stress- and compulsion-related indications ranging from Tourette to OCD, ADHD, compulsive gambling, PMDD and essential tremor. Sepranolone has been found to reduce tics without inducing off-target Central Nervous System side effects in several preclinical studies and has demonstrated a strong safety profile in multiple clinical studies. Over 300 women have taken Sepranolone in previous trials with no other side effects than mild and reversible local skin irritation. Asarina Pharma is the first company to develop and synthesize isoallopregnanolone / Sepranolone as a medication, patenting it as a pharmaceutical formulation in 2010, after 40 years' research and development. In March 2021, a US patent was granted for the use of Sepranolone for the treatment of Tourette Syndrome.

About Tourette Syndrome

Tourette Syndrome (TS) is a neurological disorder that can cause sudden, unwanted and often uncontrollable rapid, repeated movements or vocal sounds called tics. The first symptoms typically occur at the ages of 4 - 12 years, often causing stigma and/or social exclusion (63% of children with TS reported feeling discriminated against, including being bullied, excluded or suspended from school in the Tourette Association of America's 2018 Impact Survey). Tics typically lessen and become more controllable by the late teens to early 20s. However, for many, tics do persist into adulthood, with the first-line treatment being the behavioral therapy CBIT (Comprehensive Behavioral Intervention for Tics.) There is a pronounced need for an effective but safe pharmaceutical treatment for Tourette Syndrome. (In the 2018 study cited above 44% of parents felt that current Tourette Syndrome treatments failed to adequately control their child's symptoms, and 29% of children had tried five or more different medications.) Currently available pharmaceutical treatments like the anti-psychotic haloperidol (Haldol) can involve extremely severe side effects.

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About Asarina Pharma

Asarina Pharma is 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.