Seaport Therapeutics Presents Additional Data from Phase 1 Study of SPT-300 at ACNP Annual Meeting 2024

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Multiple well-tolerated doses with pharmacodynamic activity were identified and will be included in a planned Phase 2b study in major depressive disorder

BOSTON, December 11, 2024 – Seaport Therapeutics ("Seaport" or the "Company"), a clinical-stage biopharmaceutical company that is advancing novel neuropsychiatric medicines with a proven strategy and team, today announced the presentation of additional data from its first-in-human, multi-part Phase 1 study of SPT-300 in healthy volunteers at the American College of Neuropsychopharmacology (ACNP) Annual Meeting, held December 8-11, 2024 in Phoenix, Arizona. SPT-300 is an oral prodrug of allopregnanolone that is designed to retain the pharmacological activity of allopregnanolone, an endogenous neurosteroid. Allopregnanolone has been clinically validated in third-party trials as a rapidly acting antidepressant with anxiolytic effects.

The Phase 1 study enrolled 99 participants (in three parts: double-blind single ascending dose, multiple ascending dose, and open-label food effect) and evaluated oral bioavailability, safety, tolerability, pharmacokinetics and $GABA_A$ target engagement. Pharmacodynamic assessments included quantitative electroencephalography (EEG) analyses of brain function and video-oculography (VOG) assessments of eye movement. SPT-300 was well-tolerated, with all adverse events (AE) being mild or moderate, transient and dose-dependent. The most common AE was somnolence, which was mild and transient in all cases. The study showed that SPT-300 had therapeutically relevant blood levels that were up to approximately nine times greater than published data on orally administered unmodified allopregnanolone, which has minimal bioavailability.

New data in the poster presented at the conference include further safety analyses and pharmacokinetic and pharmacodynamic data. In the Phase 1 study, increases in EEG beta frequency power and reduction in saccadic eye velocity were observed at approximately 4 hours post-dose. Somnolence peaked in this same timeframe and diminished by 6 to 8 hours post-dose, consistent with both pharmacodynamic markers and blood levels of allopregnanolone. Based on the Phase 1 study results, the profile of SPT-300 is suitable for chronic dosing and oral administration at night in the planned Phase 2b placebo-controlled study in major depressive disorder with or without anxious distress.

"Together with previous clinical efficacy data, the further analyses of the Phase 1 study demonstrate that these doses of SPT-300 are well-tolerated and have rapidly acting pharmacodynamic activity. This reinforces our confidence in SPT-300 as an oral modulator of $GABA_A$ receptors and as a potential rapidly acting antidepressant and anxiolytic agent," said Tony Loebel, M.D., Chief Medical Officer and President of Clinical Development of Seaport Therapeutics. "There is a great need for innovative neuropsychiatric medicines, and an oral form of allopregnanolone has the potential to provide important advantages that we believe will allow for once-daily use on a chronic basis. We look forward to the next phase of our clinical development plan for SPT-300."

About SPT-300

SPT-300 (Glyph allopregnanolone), an oral prodrug of allopregnanolone, an endogenous neurosteroid, is in clinical stage development for the treatment of major depressive disorder (MDD) with or without anxious distress. Allopregnanolone has demonstrated therapeutic benefit in a range of neuropsychiatric conditions, but is currently only approved as an intravenous infusion, which has limited the scope of its clinical use. Using the Glyph™ platform, SPT-300 is designed to retain the activity, potency and the breadth of the natural biological response of endogenous allopregnanolone in an oral form, which has the potential to capture clinically important antidepressant and anxiolytic effects. In a Phase 2a clinical study, SPT-300 demonstrated initial proof-of-concept in a validated clinical model of anxiety in healthy volunteers. SPT-300 also demonstrated oral bioavailability, tolerability and γ-aminobutyric-acid type A ($GABA_A$) receptor target engagement in healthy volunteers in a Phase 1 clinical study.

About Seaport Therapeutics

Seaport Therapeutics is a clinical-stage biopharmaceutical company advancing the development of novel neuropsychiatric medicines in areas of high unmet patient needs. The Company has a proven strategy of advancing clinically validated mechanisms previously held back by limitations that are overcome with its proprietary Glyph technology platform. All the therapeutic candidates in its pipeline of potentially first and best-in-class medicines are based on the Glyph platform, which is uniquely designed to enable oral bioavailability, bypass first-pass metabolism and reduce liver enzyme elevations or hepatotoxicity and other side effects. Seaport is led by an experienced team that invented and advanced important neuropsychiatric medicines and is guided by an extensive network of renowned scientists, clinicians and key opinion leaders. For more information, please visit www.seaporttx.com.