PureTech Founded Entity 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

PureTech Health plc (Nasdaq: PRTC, LSE: PRTC) ("PureTech" or the "Company"), a clinical-stage biotherapeutics company, noted that its Founded Entity, Seaport Therapeutics, ("Seaport") 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.

New data presented at the conference include further safety analyses and pharmacokinetic and pharmacodynamic data. 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.

The full text of the announcement from Seaport is as follows:

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

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.

About PureTech Health

PureTech is a clinical-stage biotherapeutics company dedicated to giving life to new classes of medicine to change the lives of patients with devastating diseases. The Company has created a broad and deep pipeline through its experienced research and development team and its extensive network of scientists, clinicians and industry leaders that is being advanced both internally and through its Founded Entities. PureTech's R&D engine has resulted in the development of 29 therapeutics and therapeutic candidates, including three that have been approved by the U.S. Food and Drug Administration. A number of these programs are being advanced by PureTech or its Founded Entities in various indications and stages of clinical development, including registration enabling studies. All of the underlying programs and platforms that resulted in this pipeline of therapeutic candidates were initially identified or discovered and then advanced by the PureTech team through key validation points.

For more information, visit www.puretechhealth.com or connect with us on X (formerly Twitter) @puretechh.

Cautionary Note Regarding Forward-Looking Statements

This press release contains statements that are or may be forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation those related to Seaport's development plans for its pipeline of therapeutics for the treatment of depression, anxiety and other neuropsychiatric disorders, potential benefits to patients, and Seaport's and our future prospects, developments and strategies. The forward-looking statements are based on current expectations and are subject to known and unknown risks, uncertainties and other important factors that could cause actual results, performance and achievements to differ materially from current expectations, including, but not limited to, those risks, uncertainties and other important factors described under the caption "Risk Factors" in our Annual Report on Form 20-F for the year ended December 31, 2023, filed with the SEC and in our other regulatory filings. These forward-looking statements are based on assumptions regarding the present and future business strategies of the Company and the environment in which it will operate in the future. Each forward-looking statement speaks only as at the date of this press release. Except as required by law and regulatory requirements, we disclaim any obligation to update or revise these forward-looking statements, whether as a result of new information, future events or otherwise.

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