



PureTech Founded Entity Seaport Therapeutics Announces First Patient Dosed in Phase 2a Clinical Trial Evaluating GlyphAgo™ in Patients with Generalized Anxiety Disorder and Sleep Disturbance

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PureTech Founded Entity Seaport Therapeutics Announces First Patient Dosed in Phase 2a Clinical Trial Evaluating GlyphAgo™ in Patients with Generalized Anxiety Disorder and Sleep Disturbance

[PureTech Health plc](#) (LSE: PRTC) ("PureTech" or the "Company"), a hub-and-spoke biotherapeutics company dedicated to giving life to science and transforming innovation into value, notes that its Founded Entity, Seaport Therapeutics, today announced that the first patient has been dosed in a Phase 2a clinical trial in Australia evaluating GlyphAgo™ (SPT-320 or Glyph Agomelatine) in adults with generalized anxiety disorder ("GAD") and sleep disturbance. The six-week trial is designed to establish proof-of-pharmacology by evaluating the effects of GlyphAgo on sleep. Seaport expects to report topline data from the trial in early 2028.

GlyphAgo is a novel, "Glyphed" oral prodrug of agomelatine, a clinically validated MT1/MT2 melatonin receptor agonist and serotonin 2C (5-HT2C) receptor antagonist. Agomelatine has demonstrated statistically significant separation from placebo in four third-party placebo-controlled studies in GAD.¹ Based on published meta-analyses using indirect comparisons across placebo-controlled trials, agomelatine ranked highest for efficacy and tolerability relative to benzodiazepines and selective serotonin-reuptake inhibitors (SSRIs),² which are standard-of-care drugs for GAD.

Seaport also plans to initiate a global, randomized, double-blind, placebo-controlled Phase 2/3 clinical trial evaluating the efficacy and safety of GlyphAgo in patients with GAD in the first half of 2027. Seaport expects topline data from the Phase 2/3 trial by the end of 2028.

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

Seaport Therapeutics Announces First Patient Dosed in Phase 2a Clinical Trial Evaluating GlyphAgo™ in Patients with Generalized Anxiety Disorder and Sleep Disturbance

Trial is designed to demonstrate proof-of-pharmacology by evaluating the effects of GlyphAgo on sleep and anxiety symptoms in patients with generalized anxiety disorder

In Phase 1, GlyphAgo demonstrated a statistically significant 6.8-fold increase in bioavailability compared to unmodified agomelatine, achieving therapeutically relevant exposures of agomelatine at doses designed to reduce liver exposure

Topline data from the Phase 2a clinical trial are expected in early 2028

BOSTON , Oct. 7, 2026 -- [Seaport Therapeutics, Inc.](#), (Nasdaq: SPTX) ("Seaport" or the "Company"), a clinical-stage therapeutics company that is inventing and developing novel neuropsychiatric medicines, today announced that the first patient has been dosed in a Phase 2a clinical trial in Australia evaluating GlyphAgo™ (SPT-320 or Glyph Agomelatine), in adults with generalized anxiety disorder ("GAD") and sleep disturbance. GlyphAgo is a novel, "Glyphed" oral prodrug of agomelatine, a clinically validated MT1/MT2 melatonin receptor agonist and serotonin 2C (5-HT2C) receptor antagonist. Agomelatine has demonstrated statistically significant separation from placebo in four third-party placebo-controlled studies in GAD¹. Based on published meta-analyses using indirect comparisons across placebo-controlled trials, agomelatine ranked highest for efficacy and tolerability relative to benzodiazepines and selective serotonin-reuptake inhibitors (SSRIs)², which are standard-of-care drugs for GAD.

"Anxiety disorders affect more than 300 million people globally³, and place a substantial burden on patients, families, and healthcare systems," said Daphne Zohar, Co-Founder and Chief Executive Officer at Seaport Therapeutics. "Patients with generalized anxiety disorder experience persistent anxiety symptoms that can make it difficult to carry out normal activities, and sleep disturbances are among the most frequently reported debilitating symptoms. Despite the widespread impact of GAD, there have been no new approved therapies in almost two decades, and many patients continue to experience inadequate symptom relief or tolerability issues that limit treatment. The initiation of this trial is an important step in bringing this potential new medicine to patients and their families."

In the six-week Phase 2a clinical trial, patients with GAD and co-morbid sleep disturbance are randomized in a double-blind manner to one of two dose levels of GlyphAgo, 16 mg/day (containing approximately 5 mg agomelatine) or 32 mg/day (containing approximately 10 mg agomelatine). The trial is designed to establish proof-of-pharmacology by evaluating the effects of GlyphAgo on sleep, assessed by patient-reported sleep outcomes, including the Insomnia Severity Index (ISI), and EEG-based measures of sleep architecture. Additional endpoints include anxiety severity as measured by the Hamilton Anxiety Scale (HAM-A), overall illness severity (Clinical Global Impression-Severity (CGI-S)) and safety, tolerability, and pharmacokinetics. Seaport expects to report topline data from the trial in early 2028.

"Agomelatine has been shown to improve sleep quality and sleep architecture without the daytime sleepiness seen with other therapies, making it a compelling candidate for patients with GAD and sleep disturbance," said Daniel Bonner, Ph.D., Co-Founder and Senior Vice President, Platform, at Seaport Therapeutics. "We designed GlyphAgo with our Glyph™ platform to bypass first-pass liver metabolism and address the bioavailability and hepatic limitations of unmodified agomelatine. We believe that GlyphAgo represents a potentially important treatment advance for people with GAD."

The two GlyphAgo dose levels selected for the Phase 2a trial are supported by Phase 1 data showing that GlyphAgo achieves clinically relevant agomelatine exposures while delivering substantially less drug than the 25 mg dose of agomelatine that is approved for the treatment of GAD in Australia and major depressive disorder in Australia and the European Union. At GlyphAgo doses delivering approximately 5 mg or 10 mg agomelatine, geometric mean agomelatine AUC₀₋₂₄ was at or above that observed with the approved 25 mg dose of unmodified agomelatine.

GlyphAgo also showed markedly lower inter-subject variability, with a geometric CV% for agomelatine AUC₀₋₂₄ approximately 10-fold lower than that of agomelatine 25 mg.

GlyphAgo is designed for absorption via the intestinal lymphatic system, which is intended to bypass first-pass hepatic metabolism and achieve therapeutically relevant agomelatine exposure at substantially lower doses and with reduced liver exposure. Seaport believes this approach has the potential to reduce the risk of liver enzyme elevations which may reduce the need for routine liver function monitoring that has historically limited agomelatine's clinical use.

In a Phase 1 trial in healthy volunteers, GlyphAgo demonstrated a statistically significant 6.8-fold increase in bioavailability compared to unmodified agomelatine, exceeding the program's pre-specified two-fold target. After seven days of once-daily dosing, the 16 mg and 32 mg doses (5 mg and 10 mg agomelatine equivalent) of GlyphAgo achieved therapeutically relevant exposures of agomelatine and were well tolerated, with no serious or severe adverse events (AEs), no liver-related AEs, and no clinically significant changes in liver-related laboratory parameters, including ALT, AST, or bilirubin.

Seaport also plans to initiate a global, randomized, double-blind, placebo-controlled Phase 2/3 clinical trial evaluating the efficacy and safety of GlyphAgo in patients with GAD in the first half of 2027. Topline data from the Phase 2/3 trial are expected by the end of 2028.

About GlyphAgo™ (SPT-320 or Glyph Agomelatine)

GlyphAgo is a novel, "Glyphed" oral prodrug of agomelatine, a clinically validated anti-anxiety and antidepressant that is approved for the treatment of GAD in Australia and Major Depressive Disorder in Australia and the European Union. Using Seaport's proprietary Glyph™ platform, GlyphAgo is designed to enhance lymphatic absorption and avoid first-pass liver metabolism, thereby enhancing oral bioavailability and reducing side effects. By leveraging an alternative absorption pathway via the intestinal lymphatic system used by dietary fats, GlyphAgo is designed to increase systemic exposure of agomelatine, enabling exposure levels within the range observed to be effective in prior third-party placebo-controlled studies in GAD at a lower dose that is designed to reduce liver exposure. Based on the data generated to date, Seaport believes GlyphAgo has the potential to become a leading treatment for GAD.

About Seaport Therapeutics

Seaport Therapeutics (Nasdaq: SPTX) is a clinical-stage therapeutics company focused on inventing and developing new medicines for patients with depression, anxiety, and other debilitating neuropsychiatric disorders. Through its differentiated approach, the Company identifies clinically validated mechanisms with established efficacy and safety which had historically been limited by high first-pass metabolism, low bioavailability, and/or side effects. Seaport applies its proprietary Glyph™ platform to overcome those limitations and invent innovative oral therapies. With an experienced team of industry leaders, Seaport has a proven track record in neuropsychiatry drug discovery and development and delivering successful business outcomes. Seaport aims to develop novel, leading treatment options that will make a significant impact for patients and their families. For more information, please visit www.seaporttx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The words "anticipate," "believe," "contemplate," "continue," "could," "design," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "seek," "should," "target," "would," "will" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, but are not limited to, express or implied statements regarding our product candidates, including: the therapeutic potential of GlyphAgo, including its potential

to achieve therapeutic exposures of agomelatine at lower doses, reduce liver exposure, and reduce or eliminate the need for liver function testing; the design, progress, enrollment and results of the Phase 2a trial of GlyphAgo and the anticipated timing of topline data in early 2028; and the planned initiation of the Phase 2/3 trial of GlyphAgo in the first half of 2027 and the anticipated timing of topline data by the end of 2028.

Forward-looking statements are based on management's current expectations and are subject to risks and uncertainties that could negatively affect Seaport's business, operating results, financial condition and stock value. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to the Company's research and development activities, including with respect to the GlyphAgo Phase 2a trial and planned Phase 2/3 trial; risks that results from earlier trials, including the Phase 1 trial of GlyphAgo, or from third-party trials of agomelatine may not be predictive of future results, including with respect to liver safety; Seaport's ability to execute on its strategy including obtaining the requisite regulatory approvals on the expected timeline, if at all; uncertainties relating to Seaport's preclinical and clinical development activities; the Company's dependence on third parties to conduct clinical trials, manufacture its product candidates and develop and commercialize its product candidates, if approved; Seaport's ability to attract, integrate and retain key personnel; risks related to the Company's financial condition, including Seaport's limited operating history and history of significant losses, its need for substantial additional funding and its ability to raise capital when needed, on acceptable terms, or at all, to complete development activities and commercialize a product candidate, if approved; risks related to regulatory developments and approval processes of the U.S. Food and Drug Administration and comparable foreign regulatory authorities; risks related to establishing and maintaining Seaport's intellectual property protections; and risks related to the competitive landscape for Seaport's product candidates; as well as other risks and uncertainties described in "Risk Factors," in Seaport's Quarterly Report on Form 10-Q for the three months ended June 30, 2026 filed with the Securities and Exchange Commission ("SEC"), as well as in subsequent filings with the SEC. Seaport expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in its expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law, and claims the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

Seaport uses and intends to continue to use its Investor Relations website as a means of disclosing material nonpublic information and for complying with its disclosure obligations under Regulation FD. Accordingly, investors should monitor the Company's Investor Relations website, in addition to following the Company's press releases, SEC filings, public conference calls, presentations, and webcasts.

About PureTech Health

PureTech Health is a hub-and-spoke biotherapeutics company dedicated to giving life to science and transforming innovation into value. We do this through a proven, capital-efficient R&D model focused on opportunities with validated pharmacology and untapped potential to address significant patient needs. This strategy has produced dozens of therapeutic candidates, including three that have received U.S. FDA approval. By identifying, shaping, and de-risking these high-conviction assets, and scaling them through dedicated structures backed by external capital, we accelerate their path to patients while creating sustainable value for shareholders.

For more information, visit www.puretechhealth.com or connect with us on [LinkedIn](#) and 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 those related to Seaport's development plans for its pipeline of neuropsychiatric therapeutics based on the Glyph™ Platform, the potential of GlyphAgo™ (SPT-320 or Glyph Agomelatine) and the Glyph platform, the broader applicability of the platform, the addressable market for Seaport's product candidates, if approved, 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, 2025, 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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¹ Stein, D.J., et al. (2008). Efficacy of agomelatine in generalized anxiety disorder: a randomized, double-blind, placebo-controlled study. *J Clin Psychopharmacol*, 28(5), 561-566.; Stein, D.J., et al. (2012). Agomelatine prevents relapse in generalized anxiety disorder: a 6-month randomized, double-blind, placebo-controlled discontinuation study. *J Clin Psychiatry*, 73(7), 1002-1008.; Stein, D.J., et al. (2014). Agomelatine in generalized anxiety disorder: an active comparator and placebo-controlled study. *J Clin Psychiatry*, 75(4), 362-368. Stein, D.J., et al. (2017). Efficacy and safety of agomelatine (10 or 25 mg/day) in non-depressed out-patients with generalized anxiety disorder: A 12-week, double-blind.

² Slee, A., et al. (2019). Pharmacological treatments for generalized anxiety disorder: a systematic review and network meta-analysis. *The Lancet*, 393(10173), 768-777.; Hood, S.D., et al. (2025). Systematic review and network meta-analysis of agomelatine for the treatment of generalized anxiety disorder in adult patients. *Int Clin Psychopharmacol*, 40(2), 62-74.

³ World Health Organization, 2025.

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