

PureTech Founded Entity Seaport Therapeutics Advances Second Therapeutic Candidate into Clinical Development with Dosing of First Participant in Phase 1 Study of GlyphAgo™ (SPT-320) in Healthy Volunteers

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GlyphAgo is an oral prodrug of agomelatine, a medicine with established clinical efficacy in generalized anxiety disorder (GAD)

GlyphAgo is designed to overcome a key limitation of agomelatine by shifting absorption toward the intestinal lymphatics, avoiding first-pass liver metabolism, and increasing systemic exposure of the drug

Phase 1 proof-of-concept study will evaluate the safety, tolerability, and pharmacokinetics of GlyphAgo and is designed to demonstrate therapeutic levels of agomelatine at lower doses that reduce liver exposure

[PureTech Health plc](#) (Nasdaq: PRTC, LSE: PRTC) ("PureTech" or the "Company"), a hub-and-spoke biotherapeutics company dedicated to giving life to science and transforming innovation into value, 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 that the first participant has been dosed in the Phase 1 study of GlyphAgo™ (SPT-320 or Glyph Agomelatine).

GlyphAgo is being developed to treat generalized anxiety disorder (GAD), one of the most common mental health conditions worldwide. It is a "Glyphed" oral prodrug of agomelatine, a medicine that has already shown clinical benefit in multiple third-party studies of GAD, but whose use has been limited by liver-related side effects. Using Seaport's proprietary Glyph™ platform, GlyphAgo is designed to improve how the drug is absorbed in the body so that people living with GAD may potentially achieve a therapeutic benefit at lower doses with reduced liver exposure.

The study marks the second therapeutic candidate from Seaport's pipeline to advance into clinical-stage development.

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

Seaport Therapeutics Advances Second Therapeutic Candidate into Clinical Development with Dosing of First Participant in Phase 1 Study of GlyphAgo™ (SPT-320) in Healthy Volunteers

GlyphAgo is an oral prodrug of agomelatine, a medicine with established clinical efficacy in four out of four previous third-party randomized, placebo-controlled studies in

generalized anxiety disorder (GAD)

Building on agomelatine's proven clinical efficacy, GlyphAgo is designed to overcome a key limitation of agomelatine by shifting absorption toward the intestinal lymphatics, avoiding first-pass liver metabolism, and increasing systemic exposure of the drug

Phase 1 proof-of-concept study will evaluate the safety, tolerability, and pharmacokinetics of GlyphAgo and is designed to demonstrate therapeutic levels of agomelatine at lower doses that reduce liver exposure

Boston, MA - September 11, 2025 - [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 that the first participant has been dosed in the Phase 1 study of GlyphAgo™ (SPT-320 or Glyph Agomelatine), a "Glyphed" oral prodrug of agomelatine in development for the treatment of generalized anxiety disorder (GAD). The study will evaluate the safety, tolerability, and pharmacokinetics of GlyphAgo in healthy adult volunteers. This marks the second therapeutic candidate in Seaport's pipeline in clinical development.

Agomelatine, a clinically validated melatonin receptor agonist and serotonin 2C receptor antagonist, is an effective anxiolytic and antidepressant approved for the treatment of GAD in Australia and major depressive disorder (MDD) in Australia and the European Union (EU). In GAD, agomelatine has demonstrated statistically significant separation from placebo in four out of four third-party placebo-controlled studies and has better efficacy and tolerability - including reduced risk of abuse potential, sexual dysfunction, and weight gain - than standard of care drugs, like selective serotonin reuptake inhibitors (SSRIs) or benzodiazepines. However, over 90 percent of unmodified agomelatine is lost to first-pass liver metabolism and its use has been limited by dose-dependent liver enzyme elevations and the need for frequent liver monitoring.

Using Seaport's proprietary Glyph™ platform, GlyphAgo is designed to overcome this limitation by shifting absorption toward the intestinal lymphatics, avoiding first-pass liver metabolism, and increasing systemic exposure of agomelatine. As a result, GlyphAgo has the potential to achieve exposure levels that have demonstrated efficacy in GAD at a lower dose that does not cause an increase in liver enzymes and reduces or eliminates the need for liver function testing.

"Anxiety disorders are the most prevalent neuropsychiatric disorders, impacting nearly 30 percent of adults at some point in their lives, with GAD alone affecting approximately 100 million adults worldwide. Despite this, in the U.S., no new drugs or mechanisms have been approved for GAD in decades," said Antony Loebel, M.D., Chief Medical Officer, President of Clinical Development at Seaport Therapeutics. "Our Phase 1 proof-of-concept study could be highly derisking for the GlyphAgo program, as agomelatine's efficacy in GAD is already well established. The key question is whether we can achieve effective exposure at a lower dose, which would demonstrate GlyphAgo's ability to avoid agomelatine's dose-dependent liver issues. We believe GlyphAgo has the potential to redefine the treatment landscape for GAD and represents an important clinical advancement for patients."

The Phase 1 study will be conducted in multiple parts to evaluate the safety, tolerability, and pharmacokinetics of GlyphAgo compared to agomelatine. It will include single- and multiple-ascending dose phases, as well as a food-effect crossover portion, using both open-label and placebo-controlled designs.

In a series of preclinical proof-of-concept studies, GlyphAgo was shown to enhance lymphatic absorption and provide significantly higher systemic exposures of agomelatine compared to agomelatine alone. Specifically, oral dosing of GlyphAgo resulted in over 50 percent of agomelatine being transported through the mesenteric lymphatics versus less than one percent for orally dosed agomelatine alone. The [data](#), which were presented at the Society of Biological Psychiatry (SOBP) Annual Meeting 2025, also showed that oral dosing of GlyphAgo increased plasma exposure of agomelatine by over 10-fold versus agomelatine alone.

About the Glyph™ Platform

Glyph is Seaport's proprietary technology platform which uses the lymphatic system to enable and enhance the oral administration of drugs. With the Glyph platform, drugs are absorbed like dietary fats through the intestinal lymphatic system and transported into circulation. The Glyph platform has the potential to be widely applied to many therapeutic molecules that have high first-pass metabolism otherwise leading to low bioavailability and/or side effects, including liver enzyme elevations or hepatotoxicity. For each program, Seaport leverages its Glyph platform to create unique sets of prodrugs with differentiated profiles, including lymphatic transport and conversion characteristics, as potential candidates to advance into preclinical and clinical proof-of-concept studies. Seaport exclusively licensed this technology from Monash University based on the pioneering research of the Porter Research

Group . Advanced initially at PureTech Health and now at Seaport, Glyph has been applied to create therapeutic candidates for the Company's pipeline resulting in new intellectual property, including composition of matter. The group and its collaborators have published research in [Nature Metabolism](#), [Frontiers in Pharmacology](#), [Journal of Controlled Release](#) and [Molecular Pharmaceutics](#) supporting the Glyph platform's capabilities. See Glyph in action [here](#).

About GlyphAgo™ (SPT-320 or Glyph Agomelatine)

GlyphAgo (SPT-320 or Glyph Agomelatine), an oral prodrug of agomelatine, is in clinical stage development with the potential to be the first new treatment for generalized anxiety disorder (GAD) in decades. Using the Glyph™ platform, GlyphAgo was designed to bypass first-pass liver metabolism in order to lower the dose, reduce liver exposure, and reduce or eliminate the need for liver enzyme monitoring. Agomelatine is a clinically validated anxiolytic and antidepressant approved for GAD in Australia and major depressive disorder (MDD) in Australia and the European Union (EU). The use of agomelatine has been limited by high first-pass liver metabolism resulting in liver enzyme elevations in some patients and frequent, burdensome liver enzyme monitoring requirements. GlyphAgo is currently in a Phase 1 proof-of-concept study to evaluate the safety, tolerability, and pharmacokinetics in healthy adult volunteers.

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 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 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 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 neuropsychiatric therapeutics based on the Glyph™ Platform, the potential of GlyphAgo™ and the Glyph platform, the design and expected safety and efficacy outcomes of the Phase 1 study, 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, 2024, 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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Sources:

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