



PureTech Founded Entity Seaport Therapeutics Announces Publication in *Science Translational Medicine* Featuring GlyphAllo™ (SPT-300) as the First Triglyceride-Mimetic Prodrug to Achieve Therapeutically Relevant Drug Levels in Humans

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[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, notes that its Founded Entity, Seaport Therapeutics, today announced the publication of first-in-human clinical and preclinical data for GlyphAllo™ (SPT-300 or Glyph Allopregnanolone) in *Science Translational Medicine*.

The GlyphAllo program and the underlying Glyph platform were initially advanced at PureTech, applying the Company's strategy of identifying clinically validated pharmacology and overcoming key limitations through targeted innovation. The Glyph platform and related programs are now being advanced by PureTech's Founded Entity, Seaport Therapeutics.

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

Seaport Therapeutics Announces *Science Translational Medicine* Peer-Reviewed Publication Featuring GlyphAllo™ (SPT-300) as the First Triglyceride-Mimetic Prodrug to Achieve Therapeutically Relevant Drug Levels in Humans

Newly published findings further support clinical validation of Seaport's proprietary Glyph™ platform to enable oral dosing

Data supported advancement of ongoing Phase 2b clinical trial of GlyphAllo in major depressive disorder (MDD)

BOSTON, March 25, 2026 - [Seaport Therapeutics](#) ("Seaport" or the "Company"), a clinical-stage therapeutics company focused on inventing and developing new medicines for patients with depression, anxiety, and other debilitating neuropsychiatric disorders with a proven strategy and team, today announced the first comprehensive disclosure of first-in-human clinical and preclinical data for GlyphAllo™ (SPT-300 or Glyph Allopregnanolone), a novel, Glyphed oral prodrug of allopregnanolone, published in *Science Translational Medicine*, tracing the program's pathway from discovery through initial proof-of-concept. The peer-reviewed article, titled "An oral allopregnanolone prodrug bypasses liver metabolism via lymphatic transport enabling bioavailability in animals and humans," details the design, optimization, and clinical translation of GlyphAllo, and further supports clinical validation of Seaport's proprietary Glyph™ platform.

"Allopregnanolone is an endogenous molecule with a rapid onset of action and well established, clinically validated antidepressant, anxiolytic, and sleep-promoting effects, as demonstrated in third-party clinical trials for the treatment of postpartum depression, a form of depression that shares symptomatology with MDD," said Steven Paul, M.D., Co-Founder and Board Chair at Seaport Therapeutics, and author on the paper. "GlyphAllo is our lead investigational product candidate designed to overcome the bioavailability limitations of allopregnanolone and deliver rapid and durable clinical effects. With the now optimized pharmaceutical properties of GlyphAllo, we can now study an oral prodrug of allopregnanolone as a potential new treatment for MDD."

The newly published research details the discovery process driving the creation of GlyphAllo, in which simple triglyceride-mimetic (TG-mimetic) allopregnanolone prodrug candidates with direct conjugation of a desired drug with lipophilic moieties were synthesized, screened, and evaluated across preclinical models. Multiple prodrug candidates demonstrated robust lymphatic transport and plasma release profiles consistent with achieving therapeutically relevant allopregnanolone exposure after oral dosing. The data further demonstrated that Glyph enabled and enhanced the oral administration of molecules historically limited by high first-pass metabolism. The paper describes how Seaport used the Glyph platform to optimize GlyphAllo, demonstrating enhanced oral bioavailability in preclinical models, with oral dosing resulting in robust lymphatic transport and systemic exposure. These data supported the selection and advancement of GlyphAllo into Phase 1 and Phase 2a clinical development.

Translation of these findings into humans was confirmed in Phase 1/2a clinical development, which demonstrated dose-dependent, therapeutically relevant allopregnanolone levels and pharmacodynamic effects in healthy volunteers. In Phase 1, GlyphAllo was generally well-tolerated following single- and multiple-ascending oral doses ranging from 70-1000 mg and provided therapeutically relevant plasma exposures of allopregnanolone. In the Phase 2a initial proof-of-concept trial using the Trier Social Stress Test (TSST), a validated clinical model of anxiety, a single 375 mg dose of

GlyphAllo significantly reduced levels of salivary cortisol versus placebo ($p=0.0001$), demonstrating that GlyphAllo potently blunted the acute physiological stress response.

"This pioneering work, published in *Science Translational Medicine*, a premier, high-impact journal, positions GlyphAllo as a compelling drug candidate and supports further investigation of its potential to address MDD, including in patients with or without anxious distress," said Michael Chen, Ph.D., Co-Founder and Chief Scientific Officer at Seaport Therapeutics, and senior author of the paper. "Importantly, these findings also further support the broad compatibility of the Glyph platform to transform promising small molecules with pharmacokinetic limitations into prodrugs with the right properties."

Collectively, the results support the continued development of GlyphAllo as a potential differentiated therapy for MDD. In July 2025, Seaport initiated BUOY-1, a global, randomized, double-blind, placebo-controlled Phase 2b trial evaluating the efficacy, safety, and tolerability of GlyphAllo in adults with MDD, with or without anxious distress. Beyond GlyphAllo, the publication highlights the broad translatability of the Glyph platform, demonstrating an efficient, repeatable approach to creating and validating Glyph molecules that can overcome pharmacokinetic barriers, with potential applications extending beyond neuropsychiatry into oncology, immunology and inflammation, metabolic disease, and obesity.

In addition to Dr. Paul and Dr. Chen, the research was led by Seaport authors Jamie Simpson, Ph.D., lead author of the publication, original co-inventor of the Glyph technology and Head of Chemistry, and Daniel Bonner, Ph.D., Co-Founder, Senior Vice President, Platform. The research was conducted in collaboration with Monash University under the direction of Christopher Porter, Ph.D., an original co-inventor of the Glyph technology and Director of the Monash Institute of Pharmaceutical Sciences.

Read the paper here: www.science.org/doi/10.1126/scitranslmed.adu2352

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](#), [Molecular Pharmaceutics](#), and [Science Translational Medicine](#) supporting the Glyph platform's capabilities. See Glyph in action [here](#).

About Seaport Therapeutics

Seaport Therapeutics is a clinical-stage therapeutics company advancing the development of novel neuropsychiatric medicines in areas of high unmet patient needs. The Company's experienced team of industry leaders has a proven track record of building successful companies that have developed and commercialized innovative neuropsychiatric medicines. The Company has focused its strategy on 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 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 [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 GlyphAllo™ (SPT-300) and the Glyph platform, the design and expected safety and efficacy outcomes of the Phase 2b 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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