



## Seaport Therapeutics Reports Positive Multiple-Ascending Dose Data from Phase 1 Proof-of-Concept Trial of GlyphAgo™ in Healthy Volunteers

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*Repeat dosing of GlyphAgo confirms favorable safety, tolerability, and pharmacokinetics observed across the Phase 1 program, with no liver-related adverse events observed*

*New data demonstrate seven-day dosing of GlyphAgo achieved therapeutic exposures of agomelatine at doses projected to avoid liver enzyme elevations and reduce or eliminate the need for liver function testing*

*Results support dose selection and planned advancement into two parallel Phase 2 trials in patients with generalized anxiety disorder*

BOSTON--(BUSINESS WIRE)--Jun. 8, 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 positive data from the multiple-ascending dose (MAD) portion of its Phase 1 proof-of-concept clinical trial evaluating repeat dosing of GlyphAgo™ (SPT-320), a novel, Glyphed oral prodrug of agomelatine, in healthy volunteers. Repeat dosing of GlyphAgo demonstrated a safety, tolerability, and pharmacokinetic (PK) profile consistent with [previously reported](#) single-ascending dose (SAD) and crossover data, supporting its planned development in patients with generalized anxiety disorder (GAD).

The MAD data showed that seven-day dosing of GlyphAgo achieved therapeutic exposures of agomelatine at doses that reduce liver exposure and are projected to avoid liver enzyme elevations and reduce or eliminate the need for liver function testing that has previously limited agomelatine's clinical use. GlyphAgo AUC<sub>0-24</sub> and C<sub>max</sub> increased dose-dependently over the range of doses studied, and agomelatine exposures following GlyphAgo administration in the MAD portion were consistent with data from the SAD and crossover portions of the trial. There was no unmodified agomelatine arm in the MAD portion.

Across all dose levels evaluated, GlyphAgo was well tolerated, with no serious or severe adverse events, no liver-related adverse events, and no clinically significant changes in liver-related laboratory parameters observed, further supporting observations from the SAD and crossover cohorts.

"We are enthusiastic about the data from our Phase 1 program for GlyphAgo, where we've now observed consistent safety, tolerability, and PK across all cohorts," said Daphne Zohar, Co-Founder and Chief Executive Officer of Seaport Therapeutics. "We believe these results substantially derisk our future clinical development approach and strengthen the differentiated profile of GlyphAgo. The complete Phase 1 data package further validates our Glyph platform and supports the advancement of GlyphAgo into two parallel Phase 2 trials as we work to bring a new treatment option to patients with generalized anxiety disorder who have not had a new medicine approved in almost 20 years."

The Phase 1 proof-of-concept trial, which included 174 participants, was conducted in multiple parts to evaluate the safety, tolerability, and PK of GlyphAgo and to compare the PK of GlyphAgo to agomelatine alone. The trial included SAD and MAD cohorts, as well as a crossover portion (including both food-effect and within-participant comparison between GlyphAgo and agomelatine), using both open-label and placebo-controlled designs.

In the previously reported results from the head-to-head crossover portion of the trial, GlyphAgo demonstrated a 6.8-fold increase in bioavailability of agomelatine compared with orally administered unmodified agomelatine. GlyphAgo also showed significantly lower (10-fold) PK variability compared to unmodified agomelatine. The crossover portion included participants who were taking estrogen-containing oral contraceptives that are known to increase agomelatine exposure due to liver drug-drug interaction. In contrast, GlyphAgo exposure was unaffected by oral contraceptives, further supporting the ability of GlyphAgo to bypass first-pass liver metabolism. GlyphAgo demonstrated a 9.6 to 14.5-fold increase in dose-normalized exposure compared to agomelatine in a separate SAD portion of the trial in which no participants were on oral contraceptives.

Seaport expects to initiate a Phase 2a proof-of-pharmacology trial in the second half of 2026. This randomized, double-blind trial of two dose levels of GlyphAgo is designed to demonstrate proof-of-pharmacology by characterizing the potential benefits of GlyphAgo on sleep, including objective measures of sleep architecture, in patients with GAD and sleep disturbance. Topline data from this trial are expected in early 2028. Seaport also expects to initiate a Phase 2b trial of GlyphAgo in the first half of 2027. This randomized, double-blind, placebo-controlled, potentially registration-enabling trial is designed to evaluate the efficacy and safety of GlyphAgo in patients with GAD. Topline data from this trial are expected by the end of 2028. Seaport plans to present additional analyses from the Phase 1 trial at future upcoming scientific meetings.

### **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 of agomelatine that are effective in GAD but at a lower dose that reduces liver exposure and reduces or eliminates the need for liver function testing. 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](http://www.seaporttx.com).

### **Forward-Looking Statements**

This press release contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" 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, preclinical and clinical development activities and timelines, including projected data announcements, and our expectations for future operations and financial performance. These statements include, among other things, Seaport Therapeutics' expectations regarding the concurrent Phase 2 trials of GlyphAgo (SPT-320), including the expected trial design and the timing of topline data.

Forward-looking statements are based on management's current expectations and are subject to risks and uncertainties that could negatively affect Seaport Therapeutics' 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; Seaport Therapeutics' ability to execute on its strategy including obtaining the requisite regulatory approvals on the expected timeline, if at all; uncertainties relating to 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 Therapeutics' ability to attract, integrate and retain key personnel; risks related to the Company's financial condition and need for substantial additional funds in order 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 Therapeutics' intellectual property protections; and risks related to the competitive landscape for Seaport Therapeutics' product candidates; as well as other risks described in "Risk Factors," in Seaport Therapeutics' Registration Statement on Form S-1 filed with the Securities and Exchange Commission (SEC), as well as subsequent filings with the SEC. Seaport Therapeutics 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.

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