Seaport Therapeutics Announces the Publication of New Research Demonstrating Increased Lymphatic Transport with up to 55 Percent Drug Absorption via Lymphatics with GlyphTM Platform

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Published data shows new site of Glyph prodrug attachment demonstrated highest reported level of lymphatic transport to date of the studied immunomodulatory drug

New linkers display up to two-fold higher release in lymph nodes compared to top-performing previously reported linkers

Research builds on prior evidence supporting the versatility of Glyph platform

BOSTON, February 12, 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 the publication of new data showcasing the Glyph™ platform's unique ability to enhance drug transport through the lymphatic system for increased therapeutic exposure. The paper, published in *Molecular Pharmaceutics*, is the first to show the impact of changing the drug attachment point of a lymph-directed prodrug on lymphatic drug transport and targeted drug exposure. It also deepens the evidence supporting Glyph's ability to render a wide variety of molecules, including immunomodulators, more amenable to lymphatic transport and thus providing them with direct access to the immune system.

The study evaluated ways of modifying mycophenolic acid (MPA), an immunomodulatory drug, to improve its absorption through the lymphatic system, and increase its concentration in lymph nodes, shown in preclinical models. Specifically, a comparison between distinct attachment points on the same drug molecule was made. A newly examined phenol attachment point showed the highest lymphatic transport of MPA reported to date – approximately 55 percent – and up to two-fold higher release in lymph nodes compared to the previously reported acid attachment point. The research demonstrated the impact of linker characteristics on the extent of lymphatic transport and release in the lymph nodes. Overall, these results help to underscore the benefits of a tailored lymphatic-targeting prodrug design approach.

"This research expands our understanding of lymphatic delivery and offers new insights for more effectively designing drugs with higher exposures at their intended targets, including immunomodulatory drugs used to treat a wide range of diseases," said Christopher Porter, Ph.D., an original Co-inventor of the Glyph technology and Director of the Monash Institute of Pharmaceutical Sciences at Monash University in Melbourne. "This study highlights the importance of integrating a careful and individualized balance of intestinal stability, transport efficiency and release in the mesenteric lymph nodes to maximize therapeutic exposures as part of a tailored prodrug design approach."

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 leading to low bioavailability and/or side effects, including liver enzyme elevations or hepatotoxicity. Seaport exclusively licensed this technology from Monash University based on the pioneering research of the Porter Research Group, including co-inventors Professor Porter and Jamie Simpson, Ph.D., who is now Head of Chemistry at Seaport Therapeutics.

"Our Glyph platform allows for a bespoke design approach, and this research reinforces the significance of the innovation behind our prodrug chemistry technology," said Daniel Bonner, Ph.D., Co-founder, Senior Vice President, Platform, at Seaport Therapeutics. "Most importantly, Glyph has been clinically validated with demonstrated proof-of-concept data in humans and is being applied across Seaport's pipeline of novel neuropsychiatric medicines, with enormous potential across a broad range of applications beyond CNS and neuropsychiatry."

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 leading to low bioavailability and/or side effects, including liver enzyme elevations or hepatotoxicity. 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 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 are guided by an extensive network of renowned scientists, clinicians and key opinion leaders. For more information, please visit www.seaporttx.com.