Seaport Therapeutics Launches with $100 Million Oversubscribed Series A Financing Round to Advance Novel Neuropsychiatric Medicines

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Seaport Therapeutics Announces Management Appointments

Daphne Zohar, Founding CEO of PureTech Health and Co-Founder of Karuna Therapeutics, is Founder, Chief Executive Officer and Member of the Board of Directors of Seaport

Steven M. Paul, M.D., former CEO and Chair of Karuna Therapeutics, President of Lilly Research Laboratories, is Founder and Chair of the Board of Directors of Seaport

BOSTON, April 9, 2024 – Seaport Therapeutics, a clinical-stage biopharmaceutical company that is charting a proven path in neuropsychiatry, today announced the closing of a $100 million oversubscribed Series A financing round. The round was co-led by ARCH Venture Partners and Sofinnova Investments along with Third Rock Ventures and Seaport founder PureTech Health. Seaport also announced the appointment of Daphne Zohar as Founder, Chief Executive Officer and a member of the Board of Directors, and Steven M. Paul, M.D., as Founder and Chair of the Board of Directors.

Seaport is advancing a clinical-stage pipeline of novel neuropsychiatric medicines powered by its proprietary Glyph™ Technology Platform, which leverages the lymphatic system to create new medicines building on clinically validated mechanisms. The financing will support the rapid advancement of Seaport's clinical-stage pipeline of first and best-in-class medicines as well as further development of the Glyph platform, which has demonstrated clinical proof-of-concept.

The company is built on a proven development strategy and is led by the team that created and advanced the groundbreaking drug candidate KarXT (xanomeline-trospium), which is now poised to be the first new class of medicine in over 50 years for patients living with schizophrenia. Daphne Zohar, the Chief Executive Officer of Seaport, is the founder and former CEO of PureTech Health where she also co-founded Karuna Therapeutics. Under Ms. Zohar's leadership, PureTech's R&D engine led to 28 new medicines, including two that received U.S. FDA clearance and a third (KarXT) that has been filed for FDA approval.

Dr. Paul, Founder and Chair of the Seaport Board of Directors, is the former CEO and Chair of the Board of Directors of Karuna Therapeutics, which was recently acquired by Bristol Myers Squibb. Dr. Paul is also the former President of Research and Development at Eli Lilly, where he oversaw the development of CNS drugs such as Zyprexa® and Cymbalta® as well as xanomeline, where its anti-psychotic and pre-cognitive properties were initially demonstrated.

"Major depression and anxiety disorders are among the most common, disabling and potentially fatal of all medical conditions. Current standard-of-care treatments provide inadequate relief for far too many patients. Seaport's pipeline of investigational antidepressants and anxiolytics are well positioned to more effectively treat these disorders and to help millions of people and their families," said Steven M. Paul M.D. "Given the historically low success rates within neuropsychiatric drug development, precisely solving the previous limitations of clinically validated mechanisms improves the probability of success and enables us to significantly accelerate development."

"We are dedicated to bringing first and best-in-class medicines to those that are suffering from depression, anxiety and other neuropsychiatric disorders," said Daphne Zohar, Founder and CEO of Seaport Therapeutics. "I'm excited to deliver on this mission along with a stellar team of senior leaders and investors."

All of the programs in Seaport's pipeline are based on the Glyph platform, which is designed to enable and enhance oral bioavailability, avoid first-pass metabolism and reduce hepatotoxicity and other side effects to advance active drugs that were previously held back by those limitations. Seaport's most advanced therapeutic candidate is SPT-300 [1], which is an oral prodrug of allopregnanolone, an endogenous neurosteroid, in development for the treatment of anxious depression. Allopregnanolone has demonstrated therapeutic benefit in a range of neuropsychiatric conditions, but it is only approved as an intravenous infusion, which has limited the scope of its clinical use. Using the Glyph platform, SPT-300 retains the activity and potency of endogenous allopregnanolone in an oral form and has the potential to capture the breadth of the natural biological response. In a Phase 2a clinical trial, SPT-300 demonstrated proof-of-concept in a validated clinical model of anxiety in healthy volunteers.

Seaport's pipeline also includes SPT-320 [2], a novel prodrug of agomelatine being advanced for the treatment of Generalized Anxiety Disorder, which uses the Glyph platform to bypass first-pass metabolism by the liver and thus has the potential to lower its effective dose, reduce liver exposure and eliminate the need for liver function monitoring that has held back agomelatine. SPT-348, a prodrug of a non-hallucinogenic neuroplastogen in development for the treatment of mood and other neuropsychiatric disorders, leverages Glyph to create a potential first-in-class treatment with improved pharmacokinetics and tolerability compared to conventional psychedelics. Beyond these programs, Seaport has multiple discovery and preclinical programs underway.

The additional members joining the Seaport Board of Directors are Robert Nelsen (Managing Partner and Co-founder of ARCH Venture Partners), James Healy, M.D., Ph.D. (Managing Partner of Sofinnova Investments), Eric Elenko, Ph.D. (Co-founder and President of PureTech and Co-inventor of KarXT), and Bharatt Chowrira Ph.D., (newly appointed Chief Executive Officer of PureTech). Courtney Wallace (Venture Partner at Third Rock Ventures) is joining as Board Observer.

"I'm thrilled to be partnering again with this outstanding team, led by Daphne and Steve, to change the lives of people with neuropsychiatric disorders," said Robert Nelsen, Co-founder and Managing Director of ARCH Venture Partners. "We were the lead investors in Karuna's Series A and Series B financing rounds, and I'm excited to partner with these strong leaders again to deliver on Seaport's proven strategy and robust pipeline and bring important new medicines to patients."

"Seaport has the potential to meaningfully change the lives of patients with neuropsychiatric disorders," said James Healy, M.D., Ph.D., Managing Partner at Sofinnova Investments. "We've had the pleasure of knowing Steve and Daphne for a number of years, as one of the investors in Karuna, and we believe this team has the unique expertise to help solve the challenges of treating serious mental health conditions. I am eager to support Seaport as an investor and board member as the team continues to advance its clinical-stage pipeline of novel therapeutics."

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. Seaport believes the Glyph technology 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 hepatotoxicity. The Glyph platform has been refined at Seaport to efficiently generate multiple therapeutic candidates within the company's pipeline. Seaport has exclusively licensed this technology from Monash University based on the pioneering research of the Porter research group, along with the co-inventors from PureTech Health and Seaport. The group and its collaborators have published research in *Nature Metabolism*, *Frontiers in Pharmacology* and the *Journal of Controlled Release* supporting the Glyph platform's capabilities.

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. We have a proven strategy of advancing clinically validated mechanisms previously held back by limitations we overcome with our proprietary Glyph^{TM} technology platform. All the therapeutic candidates in our 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 hepatotoxicity and other side effects. We are led by an experienced team that was involved in inventing and advancing KarXT and other neuropsychiatric medicines and are guided by an extensive network of renowned scientists, clinicians and key opinion leaders across neurological specialties. For more information, please visit www.seaporttx.com.

Footnotes

[1] SPT-300, formerly known as LYT-300

[2] SPT-320, formerly known as LYT-320