Seaport Therapeutics Presents New Meta-Analysis Examining Correlations Between Clinical Trial Design Factors and Placebo Response in Major Depressive Disorder Studies

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A key finding is that the number and frequency of clinician-administered assessments in MDD trials were positively correlated with an increased placebo response

Meta-analysis was presented at the International Society for CNS Clinical Trials and Methodology (ISCTM) Conference

BOSTON, February 21, 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 presentation of a new meta-analysis exploring the impact of clinical trial design factors on the magnitude of placebo response in major depressive disorder (MDD) clinical trials. A poster highlighting this research was presented at the International Society for CNS Clinical Trials and Methodology (ISCTM) Conference held February 19 – 21, 2025, in Washington, D.C.

"CNS clinical trials present unique challenges, including high placebo responses. Analyzing past studies in a systematic way can help propel the entire field forward," said Tony Loebel, M.D., Chief Medical Officer and President of Clinical Development at Seaport Therapeutics. "At Seaport, as we progress our pipeline of investigational antidepressants and anxiolytics, we believe our experience in the field, combined with our focus on clinically validated mechanisms, positions us to run better designed and informed trials that minimize placebo effects. Through sharing analyses such as these, we hope to contribute to broader knowledge in the field."

Approximately 50-70 percent of MDD trials fail to meet their primary endpoint[1]. Participants in randomized, placebo-controlled trials often exhibit a high placebo response on clinical endpoints, making it difficult to assess the true effect of antidepressants[2]. The meta-analysis examined 27 industry-sponsored Phase 2-4, placebo-controlled MDD trials conducted in the past 10 years, all of which met strict inclusion criteria, including the use of the gold-standard Hamilton Depression Rating Scale (HAM-D) or Montgomery–Åsberg Depression Rating Scale (MADRS) primary endpoints.

In the meta-analysis, a higher number and frequency of clinician-administered assessments (CAAs) were associated with an increased placebo response even after accounting for factors like the number of trial sites, patient in-clinic visits, and treatment type. Other factors investigated include the number of trial sites and study duration, with neither showing a significant association with placebo effects. Higher baseline depression severity, as measured by HAM-D scores, appeared to have a modest association with a greater placebo change, though a limited subset of studies included baseline HAM-D scores.

This research provides new insights into factors potentially influencing the placebo effect and highlights the need for further investigation into the impact of design factors in MDD clinical trials.

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.

Footnotes

1.Turner, E. H., Matthews, A. M., Linardatos, E., Tell, R. A., & Rosenthal, R. (2008). Selective publication of antidepressant trials and its influence on apparent efficacy. *NEJM, 358*(3), 252–260.

2. Walsh, B. T., Seidman, S. N., Sysko, R., & Gould, M. (2002).