Structure Therapeutics Reports Positive Topline Data from its Phase 2a Obesity Study and Capsule to Tablet PK Study for its Oral Non-Peptide Small Molecule GLP-1 Receptor Agonist GSBR-1290

June 3, 2024

GSBR-1290 achieved a clinically meaningful and statistically significant placebo-adjusted mean weight loss of 6.2% (p<0.0001) in the Phase 2a obesity study and up to 6.9% (p<0.0001) in the capsule to tablet PK study, in both cases at 12 weeks

GSBR-1290 demonstrated generally favorable safety and tolerability results with low AE-related study discontinuations

Pharmacokinetic data support dose proportional exposure and once-daily oral dosing of GSBR-1290

36-week Phase 2b study in obesity on track to begin in the fourth quarter of 2024

Company to host conference call today at 8:30 a.m. ET

SAN FRANCISCO, June 03, 2024 (GLOBE NEWSWIRE) -- Structure Therapeutics Inc. (NASDAQ: GPCR), a clinical-stage global biopharmaceutical company developing novel oral small molecule therapeutics for metabolic and cardiopulmonary diseases, today announced positive 12-week topline obesity data from its Phase 2a study of GSBR-1290, along with positive topline results from its capsule to tablet PK study. Both studies achieved their primary and secondary objectives.

Topline Results Summary

- **In the Phase 2a obesity study, GSBR-1290 demonstrated a clinically meaningful and statistically significant placebo-adjusted mean decrease in weight of 6.2%[1] (p<0.0001) at 12 weeks.** At Week 12, 67% of GSBR-1290 treated participants achieved ≥6% weight loss and 33% achieved ≥ 10% weight loss, compared to 0% for placebo.

- **A capsule to tablet PK study designed to explore a new tablet formulation of GSBR-1290 demonstrated a placebo-adjusted mean weight loss of up to 6.9%[1] (p<0.0001) with the tablet formulation at 12 weeks.** In addition, the tablet formulation demonstrated comparable exposure to the prior capsule formulation and pharmacokinetic data support dose proportional exposure and a once-daily dose profile of GSBR-1290.

- **GSBR-1290 demonstrated generally favorable safety and tolerability results following repeated, daily dosing up to 120mg.** As expected for the GLP1-RA drug class, leading adverse events (AEs) were gastrointestinal (GI)-related and the two most common AEs were nausea and vomiting. GI-related adverse events were generally observed early in treatment and attenuated after titration was completed. AE-related study discontinuations ranged from 5% in the Phase 2a obesity study to 11% in the capsule to tablet PK study. There were zero cases of drug-induced liver injury or persistent liver enzyme elevations reported across the two studies.

“These topline results demonstrate the substantial weight loss effect of GSBR-1290 and its potential to become a best-in-class oral small molecule GLP-1RA as well as an ideal backbone for future combination therapeutics for the treatment of obesity and related diseases,” said Raymond Stevens, Ph.D., Founder and CEO of Structure. “We designed GSBR-1290 to be dosed once-a-day, and are pleased to see the competitive treatment effect at 12 weeks, dose proportional exposure and target engagement over 24 hours.”

Dr. Stevens continued: “We are pleased that our new tablet performed well and that a start low and go-slow titration strategy proved beneficial and we will carry these observations into our planned Phase 2b study. As previously reported, we believe our large safety window will allow us the option to explore higher doses in future studies. As a non-peptide small molecule, our large-scale manufacturing process is expected to be more than capable of meeting the anticipated global demand of a product with the profile of GSBR-1290. We are excited to move into a Phase 2b study in overweight and obese individuals. ”

“By 2030, the global prevalence of obesity is expected to reach 1 billion. There is a need for oral treatments, including small molecules, which are easier to make at scale, more stable thus easier to transport and store, and more cost-effective,” said Ania Jastreboff, M.D., Ph.D., Associate Professor of Medicine and Pediatrics at Yale School of Medicine; Director, Yale Obesity Research Center (Y-Weight), and co-Director of the Yale Center for Weight Management. “All these factors may enable greater treatment reach for this worldwide disease. The phase 2 data with GSBR-1290 demonstrate safety to date and clinically meaningful weight reduction with 12 weeks of treatment and are encouraging for its development as a potential future therapeutic for obesity.”

GSBR-1290 Phase 2b Obesity Study Expected to Begin in Fourth Quarter 2024
Structure plans to submit an IND to the FDA in the third quarter of 2024 to support initiation of trials in chronic weight management and thereafter initiate a Phase 2b obesity study of GSBR-1290 in the fourth quarter of 2024. The 36-week global study is expected to use the tablet formulation of GSBR-1290 and include approximately 300 participants to be treated with multiple doses and dose titration regimens.

About the Phase 2a Study of GSBR-1290 in Obesity
The double-blind, 12-week placebo-controlled Phase 2a clinical trial enrolled 64 healthy overweight or obese participants that were randomized to

GSBR-1290 120mg (n=37) or placebo (n=27), dosed once daily with weekly dose titrations.

About the GSBR-1290 capsule to tablet PK study
The 12-week placebo-controlled capsule to tablet PK study (n=54) was designed to evaluate the tolerability, safety and pharmacokinetics of a new tablet formulation of GSBR-1290 and assess three different dosing and titration regimens, while exploring changes in weight during the 12-week duration. Based on the results with the new tablet formulation, Structure anticipates using the tablet formulation for future studies starting with the planned 36-week Phase 2b obesity study.

Conference Call and Webcast Information
Structure will host a conference call and webcast today, June 3, 2024 at 8:30 a.m. Eastern Time. A live webcast of the call will be available on the Investor Relations page of Structure's website at https://ir.structuretx.com/events-presentations/events. To access the call by phone, participants should visit this link (registration link) to receive dial-in details. The webcast will be made available for replay on the company's website beginning approximately two hours after the live event. The replay of the webcast will be available for 90 days.

About GSBR-1290 and Structure's Oral Metabolic Franchise
GSBR-1290 is an orally-available, small molecule agonist of the glucagon-like-peptide-1 (GLP-1) receptor, a validated drug target for the treatment of type 2 diabetes mellitus (T2DM) and obesity. Through the Company's structure-based drug discovery platform, GSBR-1290 was designed to be a biased GPCR agonist, which selectively activates the G-protein signaling pathway. Structure has completed a Phase 2a study of GSBR-1290 in participants with obesity or who are overweight and T2DM with high body mass index (BMI) ≥27. A Phase 2b study in obesity is expected to start in the fourth quarter of 2024, and the Phase 2 development plan in T2DM is expected to be determined in the second half of 2024. Beyond GSBR-1290, Structure is developing next generation combination GLP-1R candidates together with GIP, amylin, glucagon and apelin oral small molecules.

About Structure Therapeutics
Structure Therapeutics is a science-driven clinical-stage biopharmaceutical company focused on discovering and developing innovative oral small molecule treatments for chronic metabolic and cardiopulmonary conditions with significant unmet medical needs. Utilizing its next generation structure-based drug discovery platform, the Company has established a robust GPCR-targeted pipeline, featuring multiple wholly-owned proprietary clinical-stage small molecule compounds designed to surpass the manufacturing scalability limitations of traditional biologic and peptide therapies and be accessible to more patients around the world. For additional information, please visit www.structuretx.com.

Forward Looking Statements
This press release contains "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical fact are statements that could be deemed forward-looking statements, including, without limitation, statements concerning the Company's future plans and prospects, the potential to become a best-in-class oral small molecule GLP-1RA as well as an ideal backbone for future combination therapeutics for the treatment of obesity and related diseases, any expectations regarding the safety, efficacy, tolerability or once-daily dosing of GSBR-1290, including based on the clinical update from the Company's Phase 2a obesity study and capsule to tablet PK study, and other candidates under development, the ability of GSBR-1290 to treat T2DM, obesity or related indications, the planned IND submission and initiation and number of expected patients of the Company's Phase 2b obesity study and Phase 2 development plan in T2DM and the timing thereof, respectively and the planned timing of the continued development of GSBR-1290. In addition, when or if used in this press release, the words "may," "could," "should," "anticipate," "believe," "estimate," "expect," "intend," "plan," "predict" and similar expressions and their variants, as they relate to the Company may identify forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Although the Company believes the expectations reflected in such forward-looking statements are reasonable, the Company can give no assurance that such expectations will prove to be correct. Readers are cautioned that actual results, levels of activity, safety, efficacy, performance or events and circumstances could differ materially from those expressed or implied in the Company's forward-looking statements due to a variety of risks and uncertainties, which include, without limitation, risks and uncertainties related to topline results that the Company reports is based on a preliminary analysis of key efficacy and safety data, and such data may change following a more comprehensive review of the data related to the clinical trial and such topline data may not accurately reflect the complete results of a clinical trial, the preliminary nature of the results due to length of the study and sample size and results from earlier clinical trials not necessarily being predictive of future results, including the results using the least square means and mixed model for repeated measures which uses all available data, including data from patients who did not follow-up at 12 weeks, and estimates how patients with missing data would have responded based on patients who continued the study and had similar baseline characteristics (implicit imputation), potential delays in the IND submission or commencement, enrollment and completion of the Company's planned Phase 2 trials, including the Company will need to receive allowance from the FDA to proceed before initiating the planned Phase 2b trial, the Company's ability to advance GSBR-1290, LTSE-2578, ANPA-0073 and its other therapeutic candidates, obtain regulatory approval of and ultimately commercialize the Company's therapeutic candidates, competitive products or approaches limiting the commercial value of the Company's product candidates, the timing and results of preclinical and clinical trials, the Company's ability to fund development activities and achieve development goals, the impact of any global pandemics, inflation, supply chain issues, rising interest rates and future bank failures on the Company's business, its ability to protect its intellectual property and other risks and uncertainties described in the Company's filings with the Securities and Exchange Commission (SEC), including the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, as filed with the SEC on May 9, 2024, and future reports the Company may file with the SEC from time to time. All forward-looking statements contained in this press release speak only as of the date on which they were made and are based on management's assumptions and estimates as of such date. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

CONTACTS
Investors:
Danielle Keatley
Structure Therapeutics Inc.
ir@structuretx.com

Media:
Dan Budwick
1AB
Dan@1abmedia.com

[1] *Least-squares means and analyzed based on primary efficacy estimand using a Mixed Model for Repeated Measures*