Structure Therapeutics Announces Positive Results from Phase 1b Clinical Study of Oral GLP-1 Receptor Agonist GSBR-1290 and Provides Program Update

September 29, 2023

GSBR-1290 shown to be generally well-tolerated with no adverse event-related discontinuations in Phase 1b multiple ascending dose study

Significant weight loss at 28 days supporting once-daily dosing

Topline data from Phase 2a type 2 diabetes cohort expected in latter half of fourth quarter 2023; topline data from obesity cohort now expected in the first half 2024

Phase 2b studies in type 2 diabetes and obesity planned for initiation in 2024

Company to host conference call today, September 29 at 8:30 a.m. ET

SAN FRANCISCO, Sept. 29, 2023 (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 results from the Phase 1b multiple ascending dose (MAD) study of its highly selective oral GLP-1 receptor agonist, GSBR-1290, in healthy overweight or obese individuals. In the 28-day study, GSBR-1290 demonstrated significant weight loss supporting once-daily (QD) dosing and an encouraging safety and tolerability profile.

“These positive Phase 1b results support GSBR-1290 as a promising, differentiated oral GLP-1 receptor agonist with once-daily dosing,” said Raymond Stevens, Ph.D., Founder and CEO of Structure. “GSBR-1290 demonstrated an encouraging safety and tolerability profile with no adverse event-related discontinuations and we are encouraged by the weight loss observed following four weeks of treatment. We look forward to sharing results of GSBR-1290 over a longer 12-week period in the Phase 2a study, and we continue to move forward with all activities in order to begin Phase 2b clinical trials in both type 2 diabetes and obesity as planned in 2024.”

Phase 1b Study Results

The Phase 1b MAD study focused on the safety and tolerability of GSBR-1290 in 24 healthy overweight or obese individuals. Participants were randomized 3:1 to GSBR-1290 or placebo across three dose cohorts with target doses of 30mg, 60mg or 90mg.

GSBR-1290 demonstrated reductions in mean body weight ranging up to 4.9 kg compared to baseline, and up to 4.9% placebo-adjusted.

Table 1: Percent weight change from baseline to day 28

	Placebo (n=5)	GSBR-1290 30 mg (n=6)	GSBR-1290 60 mg (n=6)	GSBR-1290 90 mg (n=5)
% weight change from baseline	-0.5%	-1.6%	-5.2%	-5.4%
% weight change placebo-adjusted (90% CI)	-	-1.1% (-3.8 to 1.7)	-4.6% (-6.6 to -2.7)	-4.9% (-7.8 to -1.9)
Exploratory p-value vs. placebo	-	0.494	0.002	0.013

GSBR-1290 demonstrated an encouraging safety and tolerability profile following once-daily dosing. No participants discontinued the study drug due to adverse events. The majority of adverse events reported were mild, with no severe or serious adverse events observed. As expected for this class, leading adverse events were gastrointestinal-related, with the two most common adverse events being nausea and vomiting, with higher incidences observed in the 60 and 90 mg dose cohorts compared to placebo. There were no clinically meaningful changes in liver function tests.

Table 2: Summary of Treatment Emergent Adverse Events (TEAEs)

Event, N (%)	GSBR-1290 30 mg (n=6)	GSBR-1290 60 mg (n=6)	GSBR-1290 90 mg (n=6)	Placebo pooled (n=6)
Any TEAE	5 (83)	6 (100)	6 (100)	4 (66)
Any TEAE by maximum severity				
Mild	4 (66)	4 (66)	3 (50)	4 (66)
Moderate	1 (16)	2 (33)	3 (50)	0
Severe	0	0	0	0
Any Serious Adverse Events	0	0	0	0

Phase 2a Program Update

A data collection omission occurred at a clinical site that impacted the obesity cohort (120 mg dose level) of the Phase 2a study, where weight was not collected at the final (week 12) visit for 24 of the 40 enrolled participants. Other safety and laboratory assessments were measured at all visits, including the week 12 visit as per protocol. Structure will enroll additional participants in the Phase 2a obesity cohort to replace those for whom 12-week weight data was not collected. The replacement participants will follow the same study protocol, without changes in the titration schema or target dose (120 mg/QD). As a result, Structure now plans to report topline data from the obesity cohort in the first half of 2024. While Structure remains blinded to data from the Phase 2a obesity cohort, there were no adverse-event related discontinuations through the end of the study at 12 weeks for any of the 40 participants in the Phase 2a obesity cohort.

Structure remains on track to report topline data from the type 2 diabetes cohort of the Phase 2a study in the latter half of the fourth quarter of 2023 as planned, along with results from the Japanese ethno-bridging study of GSBR-1290.

Phase 2b Studies Planned to Initiate in 2024

Structure continues to plan to initiate two Phase 2b studies of GSBR-1290 in 2024. The type 2 diabetes study is expected to include approximately 500 individuals across the United States, Europe and Japan. The obesity study is expected to include approximately 275 individuals across the United States and Europe.

In preparation for the Phase 2b studies, Structure is also planning a separate formulation bridging PK study to support the planned transition from capsules to tablets, which is expected to initiate in the fourth quarter of 2023 and complete in the second quarter of 2024. Pending supportive data from this bridging study, the tablet formulation would be used in future GSBR-1290 studies starting with the planned Phase 2b studies.

Conference Call and Webcast Information

Structure will host a conference call and webcast today, September 29, 2023 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 the Oral Incretin 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 and obesity. GSBR-1290 was designed through the company's structure-based drug discovery platform and is designed to be a biased GPCR agonist, which selectively activates the G-protein signaling pathway. Beyond GSBR-1290, Structure is developing next generation combination GLP-1R candidates, including dual GLP-1R/GIPR agonists and amylin agonists, each designed with customized properties to achieve additional benefits.

About Structure Therapeutics

Structure Therapeutics is a leading clinical-stage biopharmaceutical company focused on discovering and developing innovative oral 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 scientifically-driven, GPCR-targeted pipeline, featuring two wholly-owned proprietary clinical-stage small molecule compounds designed to surpass the 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 clinical data from Structure's Phase 1b MAD study for GSBR-1290, the clinical update from Structure's Phase 2a study, for GSBR-1290 in patients with type 2 diabetes and obesity, any expectations regarding the safety, efficacy or tolerability of GSBR-1290 and other candidates under development, the ability of GSBR-1290 to treat type 2 diabetes, obesity or related indications, the planned initiation and study design of Structure's Phase 2b studies for GSBR-1290 in patients with type 2 diabetes and obesity and the timing thereof; the planned timing of the Company's data results and continued development of GSBR-1290 and next generation combination GLP-1R candidates and expectations regarding an oral development candidate targeting GLP-1R. 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, 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 the preliminary nature of the results due to length of the study and sample size, the risks that unblinded data is not consistent with blinded data, 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, 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 Annual Report on Form 10-K filed with the SEC on March 30, 2023, Quarterly Report on Form 10-Q filed with the SEC on August 10, 2023, 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.

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