Structure Therapeutics Provides Comprehensive GSBR-1290 Program Update Including Clinically Meaningful Proof-of-Concept Data From Phase 2a Clinical Study

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GSBR-1290 was generally well-tolerated with no treatment-related serious adverse events over 12 weeks; 2.8% study discontinuation rate due to adverse events related to study drug in diabetes and 0% study discontinuation rate due to adverse events in obesity

Topline Phase 2a data from first study in type 2 diabetes mellitus (T2DM) demonstrate significant reductions in hemoglobin A1c (HbA1c) and weight at 12 weeks

Interim Phase 2a data from obesity cohort demonstrate significant reduction in weight at 8 weeks; full 12-week obesity data expected in second quarter 2024 with Phase 2b study initiation on track for second half 2024

Program update includes results from Japanese bridging study and findings from 6- and 9-month toxicology studies demonstrating encouraging safety to support advancing into Phase 2b development

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

SAN FRANCISCO, Dec. 18, 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 provided a comprehensive development program update for its highly selective oral GLP-1 receptor agonist, GSBR-1290.

“We are pleased that we have achieved the objectives of our first Phase 2a clinical trial of GSBR-1290 in T2DM patients which were to demonstrate favorable safety, tolerability and efficacy results and guide our plans to further optimize the already encouraging performance of GSBR-1290,” said Raymond Stevens, Ph.D., Founder and CEO of Structure. “Our data demonstrated that once-daily GSBR-1290 has the potential to be a best-in-class compound and a backbone for future combinations that could address large cardiometabolic indications.”

“GSBR-1290 has demonstrated proof of concept in individuals with both obesity and T2DM, with clear effects on both weight loss and HbA1c that has the potential to increase with longer duration of treatment,” said David D’Alessio, M.D., Chief of the Division of Endocrinology and Metabolism at Duke University. “The unmet medical need for both T2DM and chronic weight management continues to be very large, and the GLP-1 receptor is a target with considerable potential. Safe and effective oral small molecule GLP-1 receptor agonists would be a significant advance in that they could expand access for many patients for whom this is not now possible.”

Phase 2a Study in Diabetes and Obesity

The randomized, double-blind, 12-week placebo-controlled Phase 2a clinical trial has enrolled a total of 94 participants to date, including 60 participants randomized to GSBR-1290. The T2DM cohort enrolled 54 participants, randomized to GSBR-1290 45 mg (n=10) or 90 mg (n=26), or placebo (n=18), dosed once daily. The obesity cohort initially enrolled 40 individuals randomized to GSBR-1290 120 mg (n=24) or placebo (n=16), once-daily. An additional 24 participants are currently being enrolled in the obesity arm as previously announced and will also be randomized 3:2 to GSBR-1290 or placebo.

The primary endpoint of the Phase 2a study is safety and tolerability of GSBR-1290. Key secondary endpoints include reduction in weight for both cohorts, as well as reduction in HbA1c for the T2DM cohort.

Safety and Tolerability Results

GSBR-1290 demonstrated encouraging safety and tolerability following repeated, daily dosing for all doses studied (up to 120 mg) in the obesity and T2DM cohorts.

- The majority (88 to 96%, depending on study arm) of adverse events (AEs) reported were mild to moderate.
- There were no serious adverse events (SAEs) related to study drug.
- As expected for this mechanism of action, leading AEs were gastrointestinal-related. The two most common AEs were nausea and vomiting.
- There were no cases of elevated liver enzymes in the obesity cohort. One participant in the T2DM treatment group experienced an event of elevated liver enzymes without an increase in bilirubin initially at day 8 while receiving 5 mg of study drug. This participant was diagnosed with fatty liver disease while in the study.
- Of the 60 participants dosed with GSBR-1290, only one participant discontinued the study due to AEs related to study drug (none in the obesity cohort and one (2.8%) in the T2DM cohort).

Table 1: Summary of Treatment Emergent Adverse Events (TEAEs)

	Phase 2a TDM Cohort	**Phase 2a Obesity Cohort**

	(12-week data)			(12-week interim data)	
Event, N (%)	GSBR-1290 45 mg (n=10)	GSBR-1290 90 mg (n=26)	Placebo (n=18)	GSBR-1290 120 mg (n=24)	Placebo (n=16)
Any TEAE	10 (100)	25 (96.2)	8 (44.4)	23 (95.8)	11 (68.8)
Any TEAE by maximum severity					
Mild	2 (20)	6 (23.1)	6 (33.3)	6 (25)	9 (56.3)
Moderate	7 (70)	17 (65.4)	2 (11.1)	17 (70.8)	2 (12.5)
Severe	0	2 (7.7)	0	0	0
Any SAEs	1 (10)	1 (3.8)	0	0	0
Any SAEs related to study drug	0	0	0	0	0

Efficacy Results

GSBR-1290 demonstrated clinically meaningful activity in both T2DM and obesity cohorts.

- In the T2DM cohort, there was a statistically significant HbA1c reduction (- 1.01 to -1.02%, placebo-adjusted) at Week 12 (Table 2). The study demonstrated a statistically significant and clinically meaningful reduction in weight at Week 12 (-3.26% to -3.51%, placebo-adjusted) (Table 3). Weight loss continued to decrease through Week 12.
- Results of the interim analysis in the obesity cohort, showed a statistically significant and clinically meaningful decrease in weight at Week 8 (-4.74%, placebo-adjusted) (table 4). Weight loss continued to decrease throughout the eight weeks of treatment.

Table 2: Diabetes cohort least square means difference (LSM) change in HbA1C from baseline to 12 weeks (%)

	GSBR-1290 45 mg (n=10)	GSBR-1290 90 mg (n=26)	Placebo (n=18)
LSM HbA1C change from baseline (%)	-0.79	-0.84	0.18
% HbA1C change placebo-adjusted (LSM, 95% confidence interval (CI))	-1.01 (-1.73, -0.29)	-1.02 (-1.59, -0.44)	
P-value vs. placebo	p= 0.008	p= 0.001	

[*] *LSM, CI and p value from Mixed Model for Repeated Measures*

Table 3: Diabetes cohort LSM change in weight from baseline (%)

	GSBR-1290 45 mg (n=10)	GSBR-1290 90 mg (n=26)	Placebo (n=18)
LSM weight change from baseline (%)	-3.32	-3.22	0.04
% weight change placebo-adjusted (LSM, 95% CI)	-3.51 (-5.58, -1.43)	-3.26 (-5.17, -1.36)	-
P-value vs. placebo	p= 0.0019	p= 0.0013	-

[*] *LSM, CI and p value from Mixed Model for Repeated Measures*

Table 4: Obesity Cohort LSM change in weight from baseline (%) 8-week interim results

	GSBR-1290 120 mg (n=24)	Placebo (n=16)
LSM weight change from baseline (%)	-5.55	-0.82
% weight change placebo-adjusted (LSM, 90% CI)	-4.74 (-6.74, -3.10)	
P-value vs. placebo	p< 0.0001	

[*] *LSM, CI and p value from Mixed Model for Repeated Measures*

Results from Phase 1 Japanese Bridging Study

The 4-week Phase 1 Japanese ethnobridging study included healthy lean Japanese participants randomized to GSBR-1290 (n=9) and placebo (n=3), and healthy lean non-Japanese participants receiving GSBR-1290 (n=6). GSBR-1290 demonstrated a substantial weight reduction in Japanese participants (-3.91% on GSBR-1290 vs -1.67% placebo) and in non-Japanese participants (-5.13% not placebo-adjusted), with no discontinuations or dose reductions, and no SAEs. These data will be used for regulatory interactions in Japan in preparation for potential future global studies of GSBR-1290.

Results from 6- and 9-Month Toxicology Studies

In preparation for Phase 2b development with longer durations of treatment, Structure has completed 6-month (rodent) and 9-month (non-human primate) toxicology studies to evaluate the safety of GSBR-1290. No major findings were observed in either study, with no test article-related changes observed in the liver, including ALT/AST, at all doses, and a >100 fold safety window at the 120 mg therapeutic dose.

GSBR-1290 Next Steps

Full 12-week results from the Phase 2a obesity cohort (n=64), including data from the additional 24 participants currently being enrolled, are expected in the second quarter of 2024.

Structure plans to initiate a Phase 2b obesity study of GSBR-1290 in the second half of 2024. The study is planned to include at least 275 individuals across the United States and Europe and will include multiple modified dose titration regimens to optimize efficacy and tolerability. An additional Phase 2 study in T2DM is also planned for the second half of 2024 to optimize the efficacy and tolerability of GSBR-1290 in this patient population.

The ongoing formulation bridging and titration optimization study is evaluating capsule versus tablet pharmacokinetics (PK) and exploring different titration regimens. This study has completed enrollment (n=54), and data are expected 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 Phase 2b studies.

Conference Call and Webcast Information

Structure will host a conference call and webcast today, December 18, 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 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 and obesity. GSBR-1290 was designed through the company's structure-based drug discovery platform 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 together with GIP, amylin, glucagon and apelin.

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. These compounds are 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; any expectations regarding the safety, efficacy or tolerability of GSBR-1290 and other candidates under development based on the topline and interim clinical data from the Phase 2a study of GSBR-1290 in patients with T2DM and obesity, including the potential for increased efficacy with longer duration of treatment, the ability of GSBR-1290 to treat T2DM, obesity or related indications, , the planned initiation and study design of the Company's Phase 2b studies for GSBR-1290 in patients with T2DM and obesity and the timing thereof, the update from the PK/formulation study of GSBR-1290 and the planned 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 a new tablet formulation 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 risk that interim results of a clinical trial do not predict final results and that one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, as follow-up on the outcome of any particular patient continues, and as more patient data become available; 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 impact of any data collection omissions at any of its' clinical sites, the Company's ability to fund development activities and achieve development goals, the Company's reliance on third parties, including clinical research organizations , manufacturers, suppliers and collaborators, over which it may not always have full control, the impact of any global pandemics, inflation, or supply chain issues 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 November 17, 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.

CONTACTS

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

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