UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 3, 2024

Structure Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Cayman Islands	**001-41608**	**98-1480821**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

601 Gateway Blvd., Suite 900	
South San Francisco, California	**94080**
(Address of principal executive offices)	**(Zip Code)**

(Registrant's telephone number, including area code): (628) 229-9277

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name Of Each Exchange Trading Symbol(s)**	**On Which Registered**
American Depositary Shares (ADSs), each representing three ordinary shares, par value $0.0001 per ordinary share	GPCR	Nasdaq Global Market
Ordinary shares, par value $0.0001 per share*		Nasdaq Global Market*

* Not for trading, but only in connection with the registration of the American Depositary Shares

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On June 3, 2024, Structure Therapeutics Inc. (the Company) issued a press release and will be hosting a conference call and webcast to discuss 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.

Copies of the press release and investor presentation the Company intends to use during the conference call and webcast are attached as Exhibits 99.1 and 99.2 to this Current Report on Form 8-K, respectively.

The information set forth in this Item 7.01 and in the press release and investor presentation attached hereto as Exhibits 99.1 and 99.2, respectively, is deemed to be "furnished" and shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the Exchange Act), or otherwise subject to the liabilities of that Section. The information set forth in this Item 7.01, including Exhibits 99.1 and 99.2, shall not be deemed incorporated by reference into any filing under the Exchange Act or the Securities Act of 1933, as amended, except to the extent that the Company specifically incorporates it by reference.

Item 8.01 Other Events.

GSBR-1290 – Phase 2a 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% ($p<0.0001$, using least-squares means (LSM) and analyzed based on the primary efficacy estimand using a mixed model for repeated measures) 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% ($p<0.0001$, using LSM and analyzed based on the primary efficacy estimand using a mixed model for repeated measures) 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.

GSBR-1290 Phase 2b Obesity Study Expected to Begin in Fourth Quarter 2024

The Company 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.

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.

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.

Forward Looking Statements

This Current Report on Form 8-K 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 LSM 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release, dated June 3, 2024.
99.2	Investor Presentation, dated June 3, 2024.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Structure Therapeutics Inc.

Date: June 3, 2024

By: /s/ Raymond Stevens
Raymond Stevens, Ph.D.
Chief Executive Officer

Exhibit 99.1

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

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 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 3, 2024 – 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.

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

“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

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CONTACTS

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STRUCTURE THERAPEUTICS

GSBR-1290
Obesity Topline Data Presentation

June 2024

Disclaimers and Forward Looking Statements

This presentation contains "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. All statements o
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prospects, any expectations regarding the safety, efficacy, tolerability and chemistry, manufacturing and controls and scalability of GSBR-1290 under development based on the to
clinical data from the Phase 2a study of GSBR-1290 in patients with type 2 diabetes mellitus (T2DM) and obesity, including the potential for maintained or increased efficacy results
longer duration of treatment, the ability of GSBR-1290 to treat T2DM, obesity, chronic weight management or related indications, the planned initiation and study design of the Co
Phase 2b study for GSBR-1290 in patients with obesity and the timing thereof; the update from the capsule to tablet formulation bridging optimization study of GSBR-1290; the pla
timing to submit an investigational new drug application to support a Phase 2b study for chronic weight management for GSBR-1290; the planned timing of the Company's data res
continued development of GSBR-1290 and next generation combination GLP-1R candidates; the Company's anticipated milestones; the anticipated market opportunity for GSBR-1
oral small molecules and the Company's expected cash runway until 2026. In addition, when or if used in this presentation, the words "may," "could," "should," "anticipate," "believ
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impact of any data collection omissions at any of our clinical trial sites, the Company's ability to fund development activities and achieve development goals, the Company's reliance
third parties, including clinical research organizations , manufacturers, suppliers and collaborators, over which it may not always have full control, the impact of any global pandemic
inflation and 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 th
Securities and Exchange Commission (SEC), including the Company's Annual Report on Form 10-K for the year ended December 31, 2023 filed with the SEC on March 8, 2024, Quart
Report on Form 10-Q for the quarter ended March 31, 2024 filed with the SEC on May 9, 2024, and future reports the Company may file with the SEC from time to time. All forward
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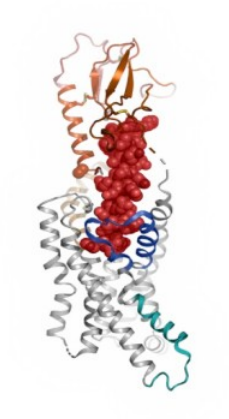
Agenda

Opening Remarks and Overview	**Raymond Stevens, Ph.D.** *Chief Executive Officer*
GSBR-1290 Obesity Topline Data • Efficacy Summary • Safety and Tolerability Summary • Pharmacokinetic (PK) summary	**Blai Coll, M.D., Ph.D.** *VP Clinical Development*
GSBR-1290 Planned Next Steps • Phase 2b 36-week Obesity study	**Blai Coll, M.D., Ph.D.**
GSBR-1290 Opportunity & **Building a Leading Oral Small Molecule Portfolio**	**Raymond Stevens, Ph.D.**
Q&A	**Raymond Stevens, Ph.D.,** *CEO* **Blai Coll, M.D., Ph.D.,** *VP Clinical Development* **Mark Bach, M.D., Ph.D.,** *Chief Medical Officer* **Xichen Lin, Ph.D.,** *Chief Scientific Officer* **Jun Yoon**, *Chief Financial Officer*

Our Mission is to Make Medicines More Accessible to All

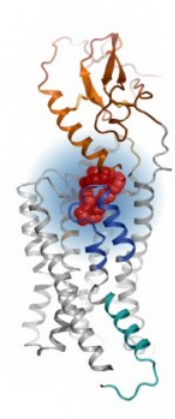


PEPTIDE OR BIOLOGIC

MEDICINES ACCESSIBLE FOR ALL

STRUCTURE THERAPEUTICS
Oral Small Molecules

Programs/ Targets
- GLP-1R Selective
- Amylin
- GIPR
- GCGR
- Apelin/APJR
- LPA1R



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We believe GSBR-1290 Obesity Data Position for Potential Best-in-Class Oral GLP-1

Best-in-Class Criteria	GSBR-1290 Performance through Phase 2a
Competitive Efficacy	**6.2 – 6.9% placebo-adjusted weight loss at 12 weel**
Safety	**No liver liability** Large safety window – potential to go higher in dose
Tolerability	**5 – 11% AE-related study discontinuations**
Once-Daily Dosing	**PK supports QD dosing** No fasting requirement
Manufacturable at Scale and Low COGS	**Scalable to potentially serve >120 million patients** GMP batches for Phase 2b studies completed

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GSBR-1290 Obesity Topline Results

Efficacy Summary

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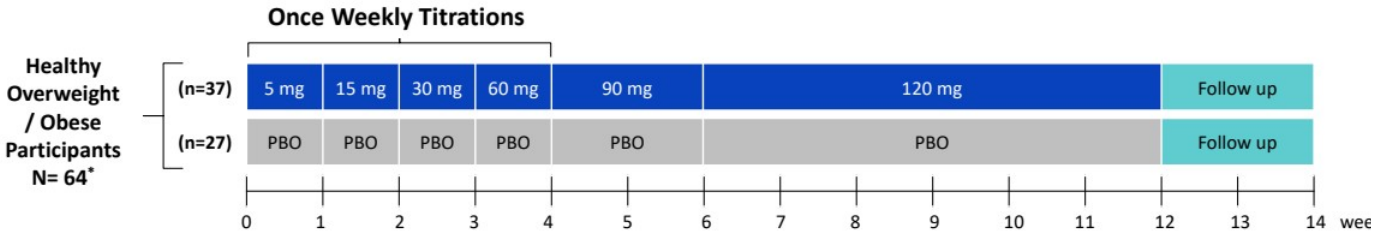
GSBR-1290 Phase 2a Study Design in Overweight or Obese Participan



Key Eligibility Criteria:

- Healthy overweight/obese adult men and women
- BMI ≥27.0 and ≤40.0 kg/m2
- HbA1c ≤6.5%
- Age ≥18 and ≤75 years

Primary Endpoint:

- Safety and tolerability

Secondary Endpoint:

- Change in body weight (%) from baseline to Week 12**

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** Cohort of 24 participants added as replacements*
*** Analysis based on the primary efficacy estimand*

GSBR-1290 Phase 2a Study Baseline Characteristics

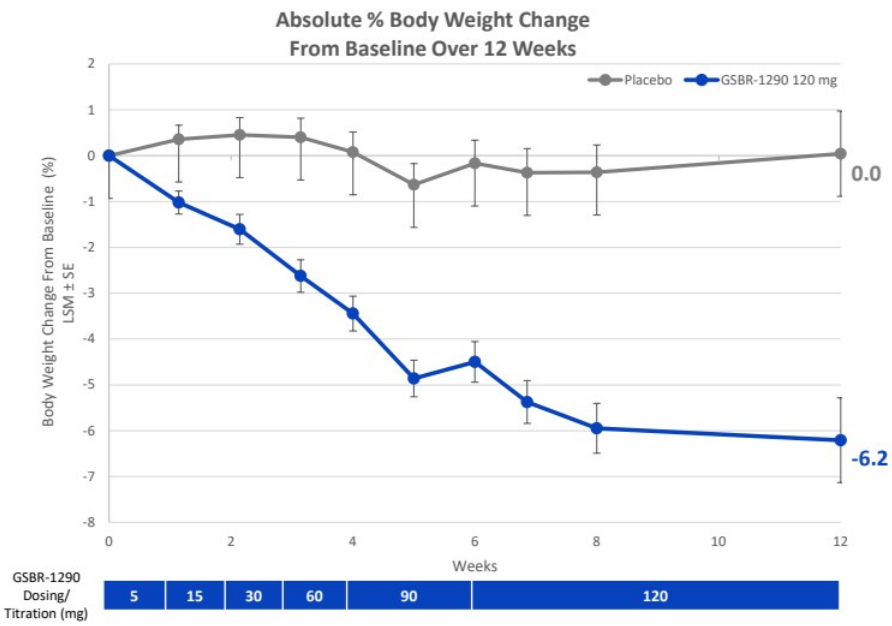
Phase 2a Obesity Study (12 week)
N=64, Randomized
GSBR-1290 capsule

Characteristics Mean (SD) or N (%)	120 mg (N=37)	Placebo (N=27)
Age, years	45.1 (14.3)	44.7 (12.0)
Sex, female, N (%)	20 (54.1)	11 (40.7)
Hispanic or Latino, N (%)	16 (43.2)	13 (48.1)
Weight, kg	90.2 (14.3)	91.5 (14.4)
BMI, kg/m^2	31.5 (3.2)	31.6 (3.0)
HbA1c, %	5.5 (0.3)	5.5 (0.4)

No significant differences in baseline characteristics between original and replacement cohorts

STRUCTURE THERAPEUTICS

GSBR-1290 Phase 2a Results:
Significant Weight Loss Observed at 12 Weeks



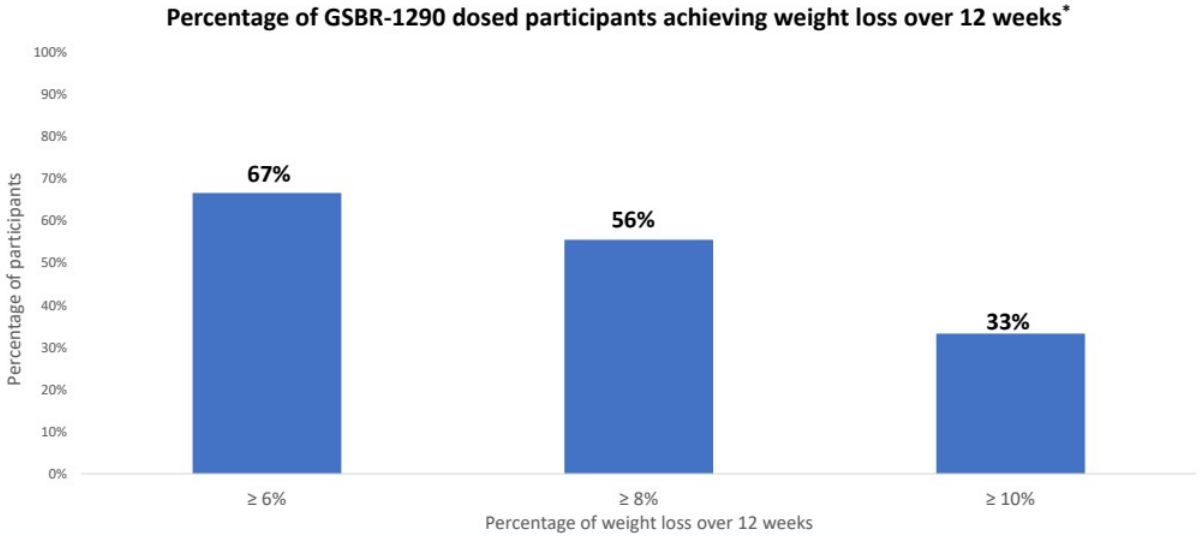
- **6.2% placebo-adjusted weight loss observed after 12 weeks**
- **Statistically significant weight reductio over 12 weeks with a clear separation compared to placebo**

	GSBR-1290 120 mg
% Change in Body Weight, placebo-adjusted	-6.2
95% Confidence Interval (CI)	-8.9, -3.6
P-value vs placebo*	<0.0001

STRUCTURE THERAPEUTICS

* *Least-Squares Means, CI and p value from Mixed Model for Repeated Meas*

GSBR-1290 Phase 2a Results:
Two Thirds of Participants Reported at least 6% Weight Loss



- **67% participants receiving GSBR-1290 achieved at least a 6% weight loss**
- **33% achieved at least a 10% weight loss**
- **0% of participants receiving placebo achieved at least a 5% weight loss**

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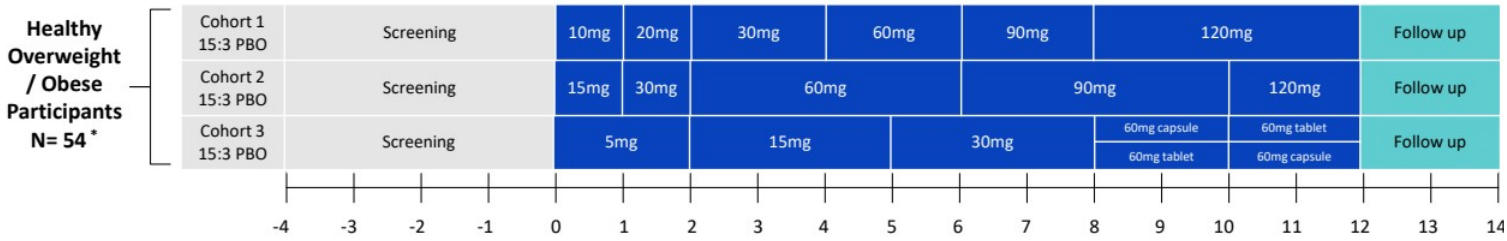
**Analysis based on the primary efficacy estiman*

GSBR-1290 Capsule to Tablet PK Study Design



Key Eligibility Criteria:

- Healthy overweight/obese adult men and women
- BMI ≥27.0 and ≤40.0 kg/m^2
- Age ≥18 and ≤75 years

Objectives:

- Safety and tolerability of the tablet formulation, with different starting doses and titration schemes
- Assess comparability of capsule and tablet at 60 mg
- Exploratory effects of GSBR-1290 on change from baseline in body weight **

Key baseline demographics similar across cohorts

Mean baseline BMI of 30 kg/m^2

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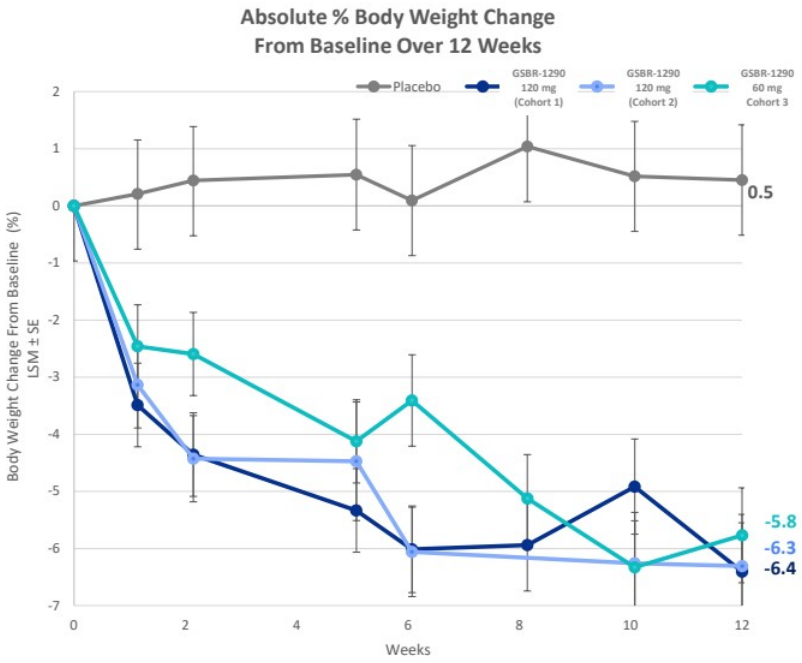
** Tablet formulation used with the exception of Cohort 3 crossover Weeks 8*

*** Analysis based on the primary efficacy estimand*

GSBR-1290 Capsule to Tablet PK Study Results:
Significant Weight Loss Observed with Tablet Formulation



- **<u>6.2% to 6.9% placebo-adjusted</u> weight loss observed after 12 weeks**
- **Statistically significant weight reduction at 12 weeks for both 60 mg and 120 mg dos**

	GSBR-1290 120 mg (C1)	GSBR-1290 120 mg (C2)	GSBR-1 60 mg
% Change in Body Weight, placebo-adjusted	-6.9	-6.8	-6.2
95% CI	-9.4, -4.3	-9.4, -4.2	-8.8, -
P-value vs placebo*	<0.0001	<0.0001	<0.00

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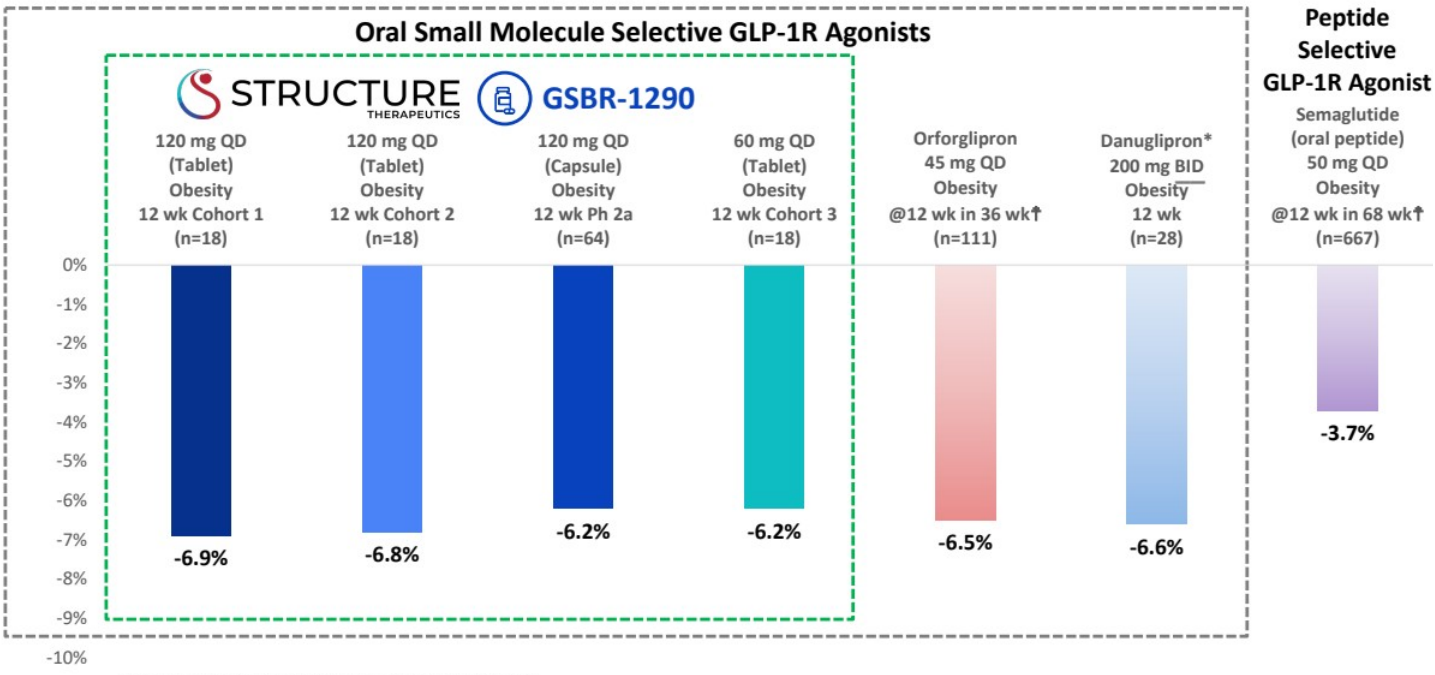
* LSM, CI and p value from Mixed Model for Repeated Me

GSBR-1290 Obesity Data Compare Favorably to for Other Oral Selective GLP-1

Cross trial comparison of 12 Week Placebo-adjusted % Change in Body Weight



Sample size indicate total number of subjects enrolled study drug and placebo

*†Indicates approximate 12 week weight loss, extrapolated by the Company using data from 36 week study (Orforglipron, NEJM 2023) and 68 week study (Semaglutide, The Lancet 2023). * EASD 2022: OP#588*

***No head-to-head study has been conducted evaluating GSBR-1290 against the other product candidates included herein. Differences exist between study designs and conditions, and caution should be exercised when comparing data across st*

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GSBR-1290 Obesity Topline Results

Safety and Tolerability

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GSBR-1290 Phase 2a Study Participant Disposition

Phase 2a Obesity Study (12 week)
N=64, Randomized
GSBR-1290 capsule

Number of Participants Reporting N (%)	120mg (N=37)	Placebo (N=27)
Discontinued study not due to AEs	**5 (13.5)**	**1 (3.7)**
Discontinued study due to AEs related to treatment	**2 (5.4)***	**0**
Dose discontinuation, down titrated or hold due to AEs		
Dose discontinuation	2 (5.4)*	0
Dose reduced	15 (40.5)	0
Dose temporarily on hold	2 (5.4)	0
Completed study	**30 (81.1)**	**26 (96.3)**

- **Low (5.4%) AE-related study discontinuations**

*Same two participants, both with GI-related AEs

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GSBR-1290 Phase 2a Study: Safety and Tolerability

Gastrointestinal-related AEs Most Common in Rapid 12 Week Titration

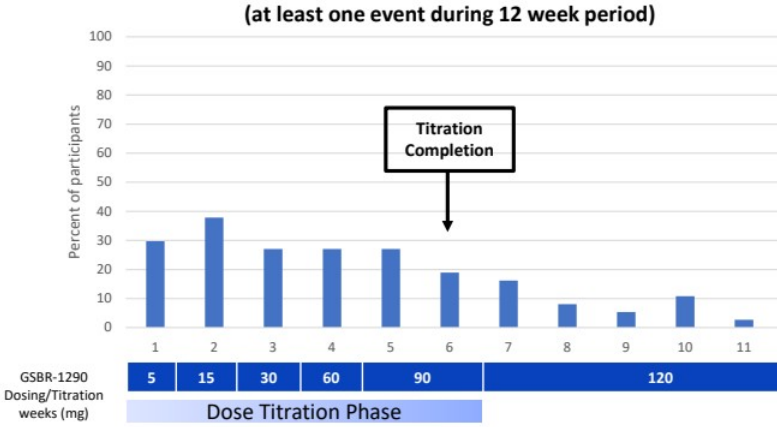
GI Tolerability Summary

Participants with at least one event during 12 week period, N (%)	120 mg (N=37)	Placebo (N=27)
Serious Adverse Events	0	0
Nausea	33 (89.2)	3 (11.1)
Mild	15 (40.5)	3 (11.1)
Moderate	18 (48.6)	0
Severe	0	0
Vomiting	23 (62.2)	1 (3.7)
Constipation	16 (43.2)	4 (14.8)
Decreased appetite	15 (40.5)	3 (11.1)

- **All AEs mild or moderate**
- **No serious adverse events**

Incidence of Nausea Over Time

(at least one event during 12 week period)



- **Incidence of nausea decreased over time**
- **Similar attenuation with other GI-AEs**

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GSBR-1290 Obesity Studies: Safety and Tolerability

Liver Profile

Number of Participants Reporting N (%)	Phase 2a Obesity Study (GSBR-1290 capsule) 120 mg (N=37)	Phase 2a Obesity Study (GSBR-1290 capsule) Placebo (N=27)	Capsule to Tablet PK Study (GSBR-1290 tablet) 120 mg (C1, C2) (N=30)	Capsule to Tablet PK Study (GSBR-1290 tablet) 60 mg (C3) (N=15)	Capsule to Tablet PK Study (GSBR-1290 tablet) Placebo (N=9)
Serious Adverse Events	0	0	0	0	0
Drug Induced Liver Injury (DILI)	0	0	0	0	0
Hepatic enzymes increased*	0	0	0	0	0
Mean Change from Baseline to Week 12					
ALT**, (U/L) Mean (SD)	-2.2 (11.7)	-1.4 (8.1)	-0.9 to 2.6	1.6 (11.2)	-3.0 (5.2)
AST**, (U/L) Mean (SD)	-1.4 (7.2)	-3.0 (11.5)	1.1 to 2.5	-1.4 (5.7)	-1.7 (3.4)
3 or > ULN in ALT or AST	1 (2.7)[1]	1 (3.7) [2]	1 (3.3)[3]	0	0
5 or > ULN in ALT or AST	0	0	0	0	0
10 or > ULN in ALT or AST	0	0	0	0	0

- **No DILI or permanent elevations in liver enzymes**
- **No study discontinuations related to liver function**

[1] Female participant with a sporadic increase in ALT (3.9xULN) and AST (2xULN) at day 44, and returned to normal at day 48 without stopping study drug
[2] Male participant with fluctuations in ALT/AST throughout the study with a peak at day 30 (both ALT and AST @3xULN) associated with an increase in creatinine kinase in the context of a viral syndrome
[3] Male participant with an isolated increase in AST (4XULN) at day 84 associated with an increase in creatinine kinase

Preferred term in the TEAE reported in the safety database
** Alanine aminotransferase (ALT) and Aspartate aminotransfera*

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GSBR-1290

PK Summary and Comparability of Capsule to Tablet Formulation

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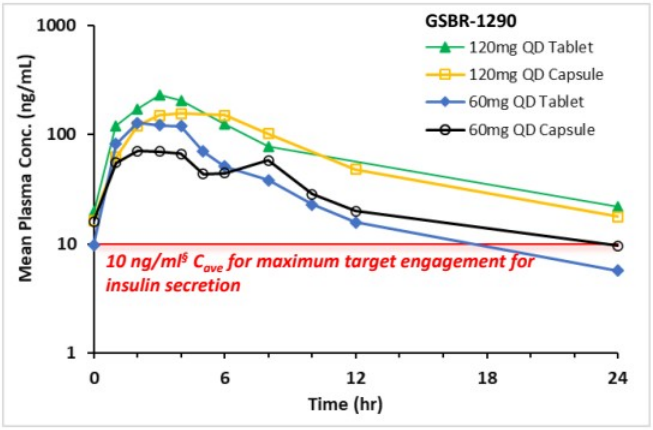
GSBR-1290 Overall Properties Confirm Once Daily (QD) Dosing



Geometric mean (% CV) plasma PK parameters across stud

	Phase 2a Study Obesity	Capsule to Tablet PK Study (GSBR-1290 capsule to tablet)		
	120 mg Capsule	120 mg (C1, C2) Tablet	60 mg (C3) Tablet	60 m Caps
AUC0-tau (ng*h/mL)	1370 (60.0)	1500 (60.6)	654 (93.8)	624 (6
$C_{max,ss}$ (ng/mL)	190 (92.8)	192 (104)	101 (170)	79.2 (
$T_{max,\ ss}$* (h)	6.0 (2.0–23.9)	3.5 (0.9 – 24.1)	3.5 (2.0-24.0)	8.0 (2.0
C_{Trough} (ng/mL)**	11.0 (128)	14.1 (120)	3.8 (134)	5.4 (1
$T_{½}$ el (h)	5.3 (36.8) ***	8.5 (24.5)	4.7 (28.8)	6.5 (4

** Median (min-max) ** At 24h post-dose *** The $T_{1/2}$ at Day 49 in the capsule study @120 mg does not capture samp beyond 24h (half-life value might be underestimated)*

Molecular and Pharmacokinetic Properties

Efficacy

- ✓ **Full agonist** and **minimal β-arrestin** signal
- ✓ **AUC driven efficacy** and favorable free drug concentration
- ✓ **Generally proportional exposure** between 60 and 120 mg doses
- ✓ Plasma concentration at **24 hours above 10 ng/mL§** for 120 mg

Safety and Tolerability

- ✓ **Large safety window** with minimal tissue accumulation based non-clinical data
- ✓ Different **formulations** underway to modulate PK characterist

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§ 10 ng/mL C_{ave} correlated with maximum insulin secretion in NHP studies

GSBR-1290 Next Steps and Summary

Phase 2b Obesity Study (36 week)

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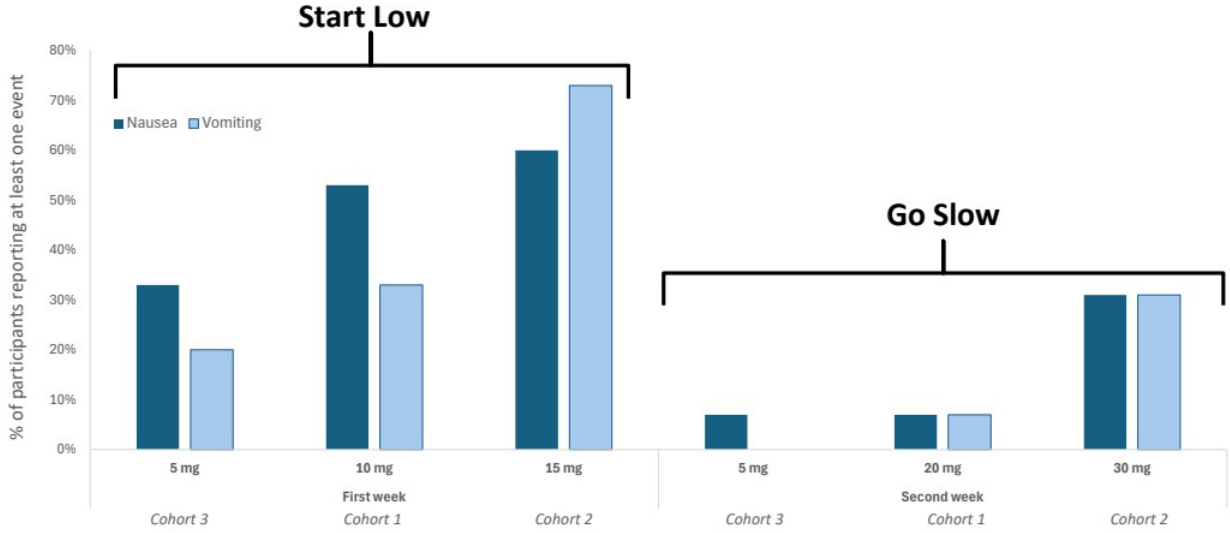
Capsule to Tablet PK Study Key Learnings Inform Phase 2b Study Design



Week 1	Week 2
Participants receiving 5 mg associated with lowest incidence of GI events	Improved tolerability with slower titration

Low (11%) AE-related study discontinuations in Capsule to Tablet PK Study

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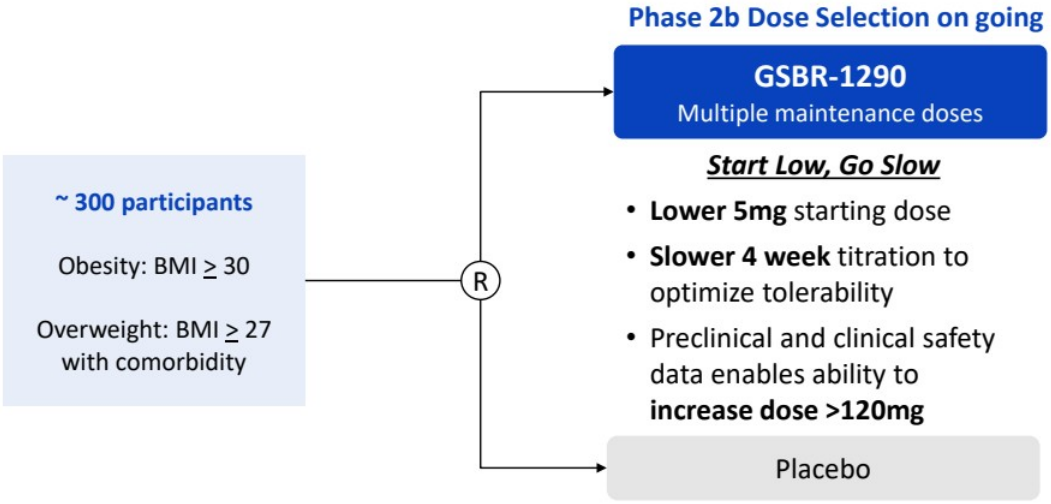
GSBR-1290 Phase 2b Obesity Study (36 weeks) Anticipated to Initiate in Q4 2(



- **On track to submit IND to FDA to support study for chronic weight management in Q3 2024**
- **On track to initiate Phase 2b study (36 week) in Q4 2024**

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New GSBR-1290 Obesity Data Demonstrate Potential Best-in-Class Profil

Competitive Efficacy Results and Once Daily Dosing as an Oral Small Molecule

EFFICACY RESULTS	SAFETY RESULTS	TOLERABILITY RESULTS
✓ **6.2%** placebo-adjusted weight loss at **12 weeks** in Phase 2a Obesity	✓ More than **200** participants exposed to **GSBR-1290**, up to **12 weeks**	✓ **Low (5 – 11%)** AE-related stuc **discontinuations**
✓ **6.2 to 6.9%** placebo-adjusted weight loss at **12 weeks** with new **tablet** formulation	✓ Safety profile consistent with the large **safety margin** seen in GLP-tox studies	✓ **Attenuation** of GI-related AEs time
✓ Proportional PK exposure and **once daily dosing**	✓ **No DILI or discontinuations** due to liver function	

- ***Key Learnings: Lower starting dose, monthly titration, tablet formulation***
- ***Potential to go higher in dosing for the 36-week Phase 2b Obesity Study; Expected to Start in Q4 2024***

Foundational Backbone Asset in Oral Small Molecule Metabolic Portfolio

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GSBR-1290 Opportunity

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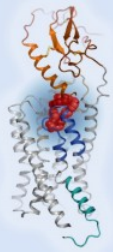
12-week Data Positions GSBR-1290 as Potential Best-in-Class Oral GLP-1RA

Original GLP-1RA Oral Small Molecule Aspirational Target Product Profile

- ✓ Highly potent, non-peptide, full GLP-1R agonist with minimal β-arrestin signaling engagement
- ✓ Weight loss comparable to injectable GLP-1R peptides
- ✓ Designed for ~24 hour drug exposure to enable QD dosing in a large patient population
- ✓ Clean 6 and 9 month GLP-tox studies with high safety margin, rat NOAEL 1000 mg/kg
- ✓ Ability to modulate C_{max} and tolerability with formulation technologies
- ✓ Scalability in commercial manufacturing



More than 800 million patients globally can benefit with GLP-1RAs

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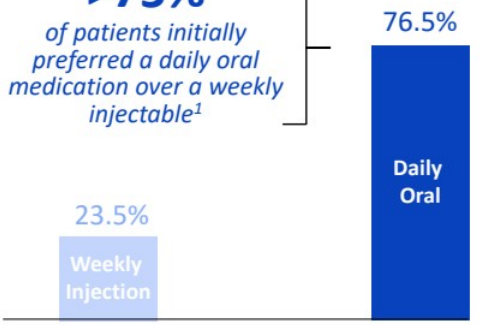
GSBR-1290

>75%

of patients initially preferred a daily oral medication over a weekly injectable[1]



Boye et al, 2021 Diabetes Obesity Metabolism https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7839441/

Oral small molecules could potentially help unl
a > $100 billion GLP-1RA market opportunit

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We are Committed to Developing Oral Small Molecules to Meet the Unmet Needs of a Very Large Global Obesity Patient Population

GLP-1RA Peptides
Challenging to Scale

> $30 billion Sales[4]

>5 million in US

OZEMPIC semaglutide injection · wegovy semaglutide injection · RYBELSUS semaglutide tablets · mounjaro · zepbound

Shortage and supply chain constraints[3]

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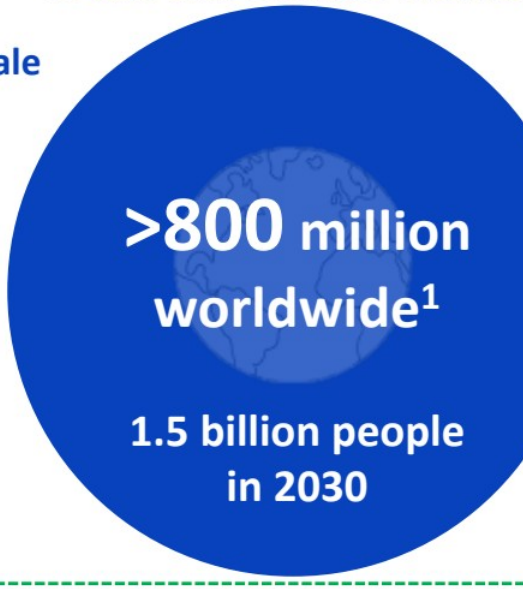
Oral Small Molecules – Ability to Scale

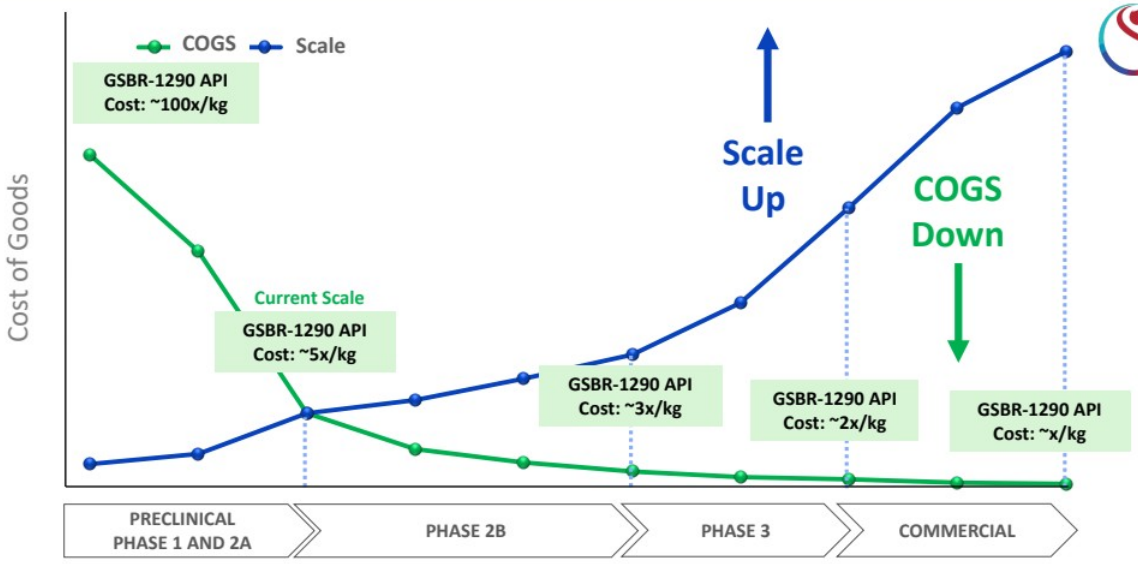
>$100 billion Total Addressable Marke



1. 2022 World Health Organization https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
2. Trust for America's Health Report https://www.tfah.org/report-details/stateofobesity2019/#:~:text=Obesity%20is%20a%20growing%20epidemic,100%20million%20people%20%E2%80%93%20have%20obesity.
3. https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages
4. 2023 Sales, GlobalData, Drugs database https://www.globaldata.com/media/pharma/glp1-agonists-set-to-become-the-best-selling-drugs-in-2024-says-globaldata/

We Believe GSBR-1290 can be Commercially Manufactured at Scale

- Synthetic route locked and ready for planned batches
- Manufacturing of Phase 2b GMP supply completed[1]
- Current manufacturing capacity of 6,000 tons/year to supply >120M patients



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120 million patients/yea

~6,000 tons

1. Based on current clinical study design

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We believe GSBR-1290 Obesity Data Position for Potential Best-in-Class Oral GLP-1

Best-in-Class Criteria	GSBR-1290 Performance through Phase 2a
Competitive Efficacy	**6.2 – 6.9% placebo-adjusted weight loss at 12 weel**
Safety	**No liver liability** Large safety window – potential to go higher in dose
Tolerability	**5 – 11% AE-related study discontinuations**
Once-Daily Dosing	**PK supports QD dosing** No fasting requirement
Manufacturable at Scale and Low COGS	**Scalable to potentially serve >120 million patients** GMP batches for Phase 2b studies completed

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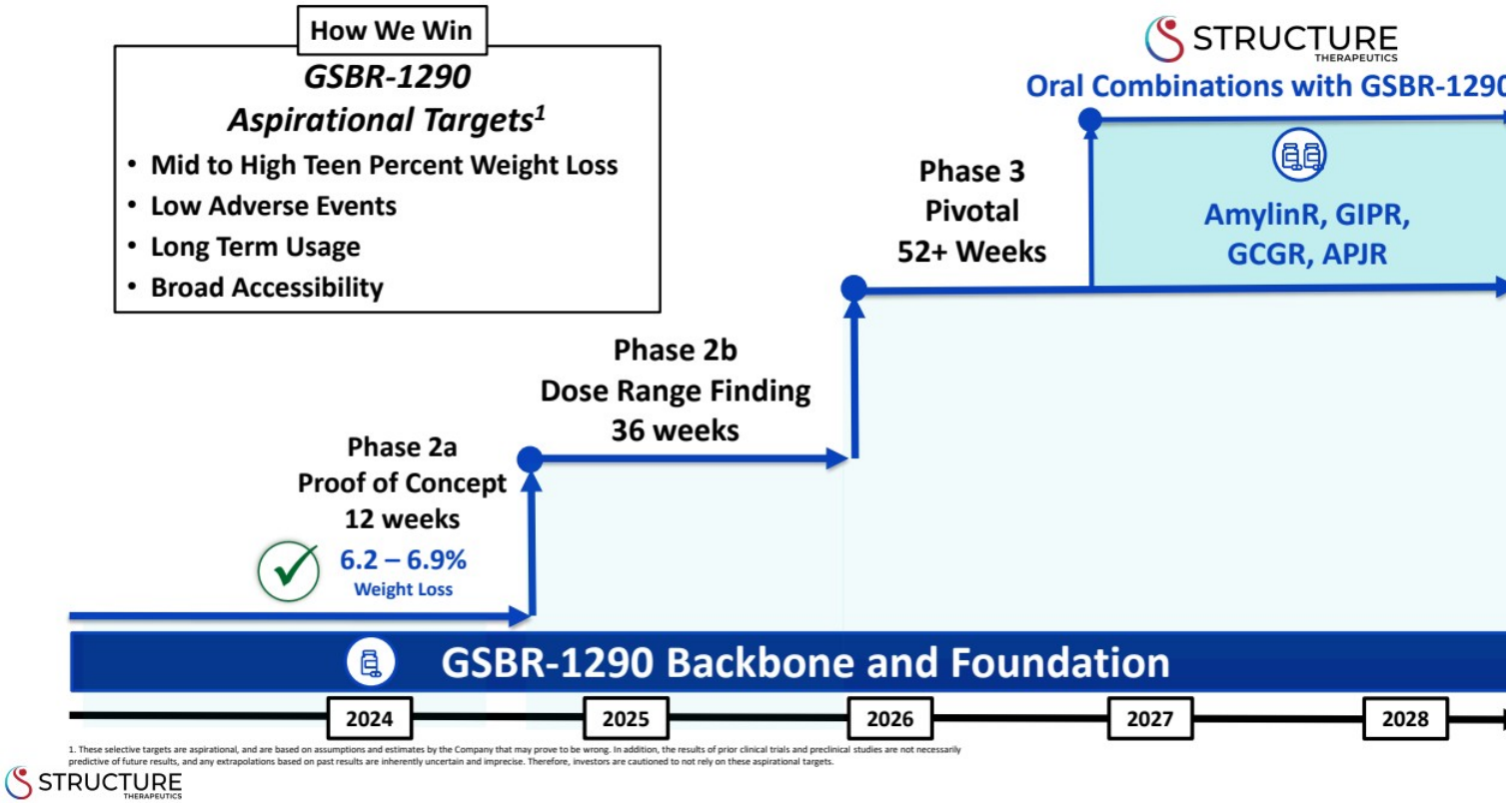
Where does GSBR-1290 fit in the GLP-1RA landscape?



1. These selective targets are aspirational, and are based on assumptions and estimates by the Company that may prove to be wrong. In addition, the results of prior clinical trials and preclinical studies are not necessarily predictive of future results, and any extrapolations based on past results are inherently uncertain and imprecise. Therefore, investors are cautioned to not rely on these aspirational targets.

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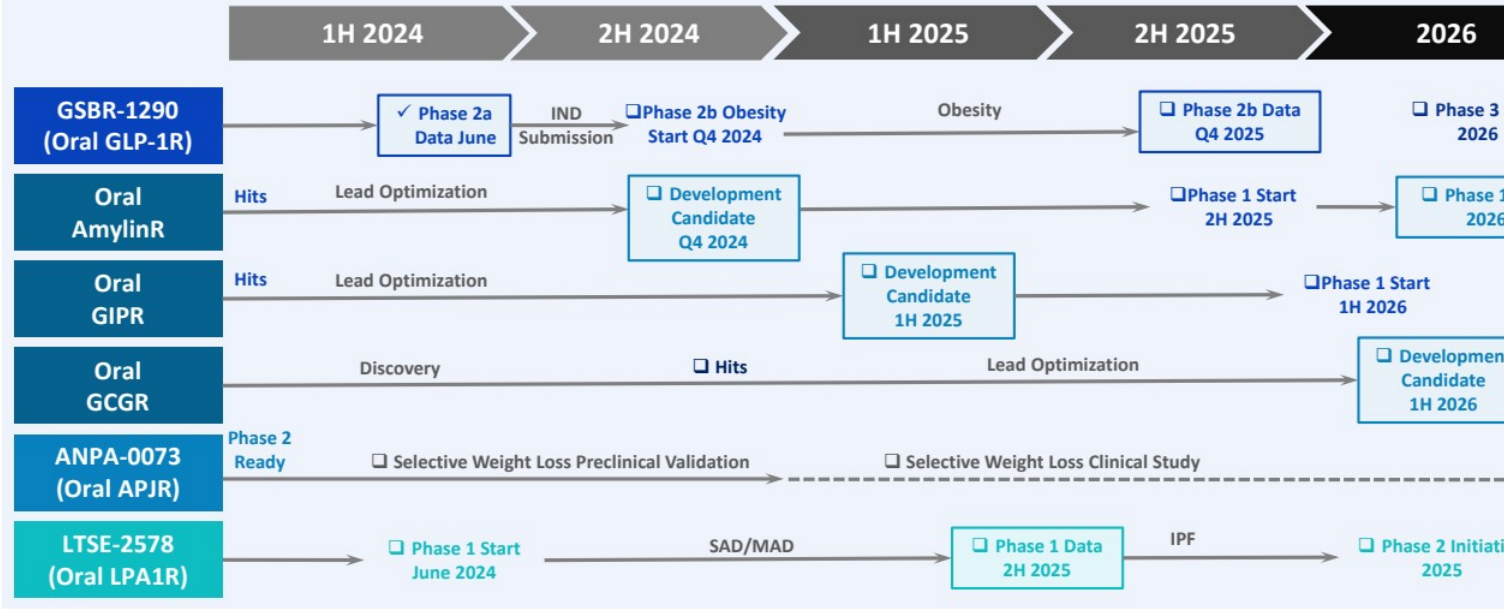
Strong Momentum with Multiple Potential Catalysts in 2024 – 202

~$436.4 million in cash[1] as of 3/31/2024 expected to fund operations through 2026

Anticipated Milestones – Entire Oral Small Molecule Portfolio



1. Cash includes cash, cash equivalents and short-term investments

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Thank you

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