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**From:** Robert Stoekenbroek
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Metsera Reports

SEPTEMBER 29, 2023

CLINICAL TRIAL UPDATES

# Oral GLP-1RA GSBR1290 Phase 1b data

**Summary and Implications**

- Structure Therapeutics today reported Phase 1b data on its oral small molecule GLP-1RA GSBR1290
- Key results: weight loss up to 5.4% in healthy overweight/obese men and women; acceptable safety and tolerability (particularly relevant: no clinically meaningful changes in liver function tests); confirmation of once-daily dosing profile

**Context**

The oral GLP-1RA pipeline can be broadly divided into small molecules and peptides. Leading oral small molecule candidates are Structure Therapeutics' GSBR1290 (Ph2), Carmot Therapeutics' CT-996 (Ph1), Lilly's orforglipron (Ph3), and Pfizer's danuglipron (Ph2). In the oral peptide field, the leading candidate is Novo Nordisk's oral semaglutide 50 mg (Phase 3 completed) – 14 mg dose for T2DM approved (Rybelsus).

Structure Therapeutics today announced Phase 1b results for its GSBR1290. Ahead of the trial, there was keen interest in its liver safety considering the discontinuation of Pfizer's oral small molecule GLP-1RA due to observations of elevated LFTs, and its PK profile (considering some questions about the relatively short t1/2 in the previously announced Phase 1a data).

**Content**

Today's data covers a 28-day, 24-subject Phase 1b trial with 3 dosing groups (30 mg, 60 mg, and 90 mg). At 28 days, weight loss was 5.4% (4.9% PBO-adjusted) which is similar to (perhaps slightly better than) orforglipron in the Phase 1 and 2 trials (i.e., orforglipron had 3.6% PBO-adjusted weight loss in Phase 1, albeit at a slightly lower dose than was subsequently chosen for Phase 2).

No patients down-titrated or discontinued due to adverse events (AEs). AEs were primarily GI-related (in line with the class) and were all mild-moderate in severity – 5/6 patients in the highest dosing group (90 mg) reported nausea and 3/6 reported vomiting. Nausea and vomiting primarily occurred upon initiation (particularly at the higher 10 mg dose vs. 5 mg) and upon reaching the highest dose (90 mg) – note that this Phase 1b trial used weekly titration (Q2W in the lower 30 mg arm). The Phase 2a trial also employs weekly titration, with a 5 mg starting dose, and titrates slightly slower to the 90 mg dose (one week extra to reach the 90 mg dose).

It was also stated that the larger Ph 2a obesity study had a clinical trial conduct issue: 24/40 patients on 120 mg dose (i.e., highest dose) did not get final visit data at week 12. These 24 patients still completed the trial, but an additional 24 patients were enrolled to maintain the trial's power and data integrity. The Ph2a trial in T2D patients is expected to readout in 4Q23. GSBR1290's Phase 2a obesity trial results are expected in 1H2024.

Please find the company presentation attached.



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