Subject: CI update
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Metsera Reports

March 26, 2024

Trial Update

Viking Therapeutics releases oral GLP-1RA/GIP data

Summary and Implications

- Viking Therapeutics released 4-week Phase 1 data for the oral version of GLP-1RA/GIP VK2735 (13-week data for the subcutaneous version of the same molecule were released one month ago – refer to the 2/27/2024 update)
- Efficacy was roughly in line with orforglipron and oral semaglutide 50 mg (after adjusting for more rapid titration), and tolerability was remarkably clean (no vomiting, 14% nausea)
- High doses (40 mg) were required for efficacy comparable to orforglipron and oral semaglutide 50 mg, suggesting that large required peptide quantities may be an issue for commercial scale-up
- Viking plans to initiate a Phase 2 trial for the oral formulation later this year
- Investors received the data positively – Viking share price +17% today

Context

VK2735 is a GLP-1RA/GIP and is being developed in a subcutaneous and an oral formulation. Data released in February for the subcutaneous formulation suggested Zepbound®-like performance, with ~13% weight loss in the 15 mg group at Week 13 (with fast titration). As a result, Viking's market cap has roughly doubled reflecting a $~4B increase. Data on the oral

formulation has been anticipated.

Content

Design

This was a 28-day MAD in obese subjects without T2DM with 5 dose arms ranging between 2.5 mg and 40 mg (n=6 to 8 per arm) and a 10-subject placebo arm. Rapid titration was applied, e.g., subjects in the 40 mg arm received 20 mg QD for 1 week, followed by 40 mg QD for the remaining 3 weeks.

Efficacy

In the 40 mg arm, subjects lost 5.3% from baseline (3.3% PBO-adjusted) from a baseline weight of 90.0 kg. The body weight loss was dose-dependent – the 10 mg group had barely any weight loss (-1.1% from baseline; +1.0% vs. PBO) and the 20 mg group was intermediate between the 40 mg and the 10 mg groups (-3.2% from baseline, -1.1% vs. PBO). This body weight loss compares to roughly -3.5% from baseline for orforglipron, although the latter was titrated much less aggressively.

Tolerability

There were no instances of vomiting in the study and only 2 subjects experienced nausea in the 40 mg group (25%), suggesting that the compound was well tolerated. Based on the favorable tolerability, Viking is continuing further dose escalation in this study.

Pharmacokinetics and formulation

Viking did not disclose information on the formulation of the peptide (i.e., the technology enabling oral bioavailability), and did not release data on pharmacokinetics (including bioavailability). Based on the high doses used, it could be speculated that the oral bioavailability is comparable to oral semaglutide which would mean that large required API quantities could be an issue for commercial scale-up.

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