Subject: CI update
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From: Robert Stoekenbroek <robert.stoekenbroek@metsera.com>
To: Metsera <Metsera@populationhp.com>
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Metsera Reports

February 6, 2024

Investor Updates

Key insights from Lilly's quarterly call

Summary and Implications

- Strong sales growth in Q4 (28% YoY) driven by Mounjaro and Zepbound (as well as Verzenio and Jardiance). Q4 Mounjaro revenue was $2.11 billion, representing a 30% organic growth quarter-over-quarter.
- Continues to invest heavily in new manufacturing capacity, including a $2.5 billion site in Germany, to increase global injectable and device manufacturing network.
- Positive topline results from the Phase 2 SYNERGY-NASH study, showing up to 74% of participants taking tirzepatide achieved an absence of MASH with no worsening of fibrosis at 52 weeks, compared to nearly 13% of participants on placebo.

Context

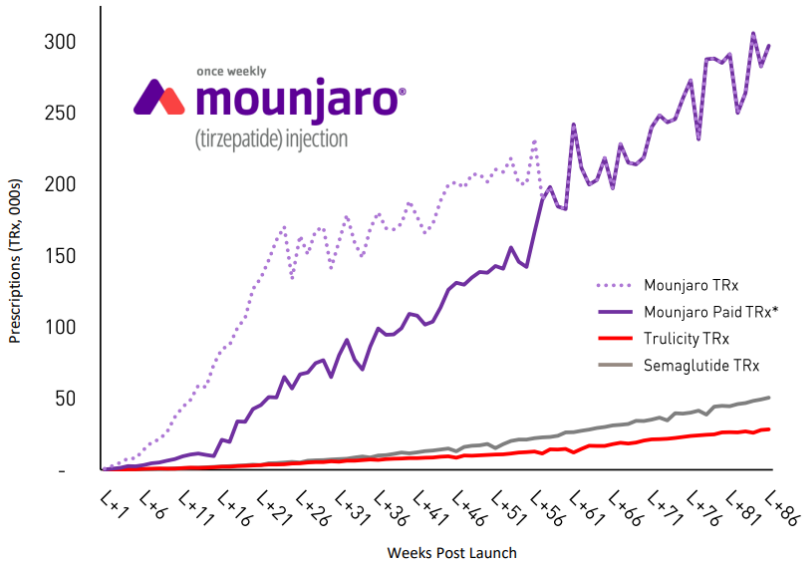
Aside from market performance – particularly uptake of Mounjaro and early indications of the uptake of Zepbound (approved Nov 8th, 2023) – areas of specific interest going into this quarterly call were 1) manufacturing updates, 2) pipeline and trial updates, and 3) 2024 outlook.

Content

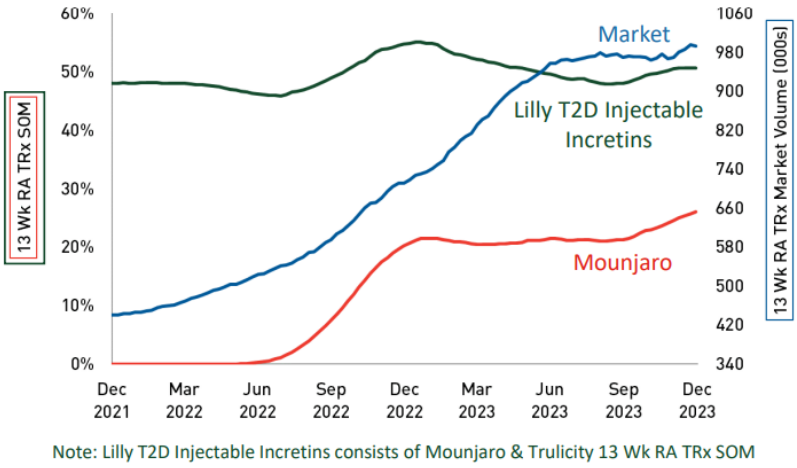
Performance and market developments

Lilly reported 4Q results ahead of expectations on top-line (28% revenue growth) and in line with expectations on bottom-line (13% net income growth). Mounjaro sales of $2.2 billion (+$476mm vs cons) came in ahead of expectations, largely on a one-time favorable change in estimates for rebates and discounts (~$450mm benefit in the quarter). Without this one-time adjustment, quarter-to-quarter growth in sales would have been 30%. Of this $2.2 billion, $2.1 billion was US revenue. On Zepbound, sales of $176mm also came in above expectations – note that Zepbound was only approved in November of 2023 and became available in early December. Three-fourths of that revenue came from initial channel stocking, while Lilly indicated encouraging prescription trends.

Lilly's share of market in T2DM incretins remained relatively stable as Mounjaro's share grew at the expense of Trulicity's share, while the overall market grew rapidly.



U.S. TRx SOM and Market Volume



Note: Lilly T2D Injectable Incretins consists of Mounjaro & Trulicity 13 Wk RA TRx SOM

On market access, Lilly indicated that Mounjaro access for patients with type 2 diabetes in the US was 90% in aggregate across commercial and Part D, including 92% access for commercial patients, while Lilly also indicated that it expects Zepbound access to take more time as the company is building on employer opt-ins.

Manufacturing updates

Similar to Novo Nordisk, Lilly has faced supply shortages for its incretins. Lilly indicated that it plans to construct a new $2.5 billion manufacturing site Germany to further expand the company's global injectable product and device manufacturing network, and recognized $3.4 billion in capital investments in 2023 (roughly similar to Novo Nordisk's 2023 capital investments). It expects demand to continue to outpace supply in 2024, and suggested that sellable doses in the second half of 2024 will be at least one-and-a-half times the production in the second half of 2023.

Pipeline and trial updates

Topline results for the Phase 2 tirzepatide MASH study were reported. The study included 196 patients with biopsy-proven MASH (F2 and F3), and Lilly reported that after 52 weeks, 73.9% of patients treated with tirzepatide 15 mg met the endpoint of absence of MASH without worsening of fibrosis vs. 12.6% in the PBO group (this compares to 59% in a prior semaglutide Phase 2 study). In addition, it was reported that there was a "clinically meaningful" difference in the secondary endpoint of decrease of fibrosis by at least one stage without worsening of MASH. Note that in the prior trial with semaglutide in MASH, there was also a numerical reduction in fibrosis which was not statistically significant – it remains unclear if the difference in the tirzepatide trial was statistically significant.

In 2023, Lilly has started Phase 3 trials for orforglipron and retatrutide, as well as the Phase 3 SURMOUNT-5 study which is a head-to-head study of tirzepatide vs. semaglutide in obesity. Lilly also advanced mazdutide (GLP-1/GCGR) into Phase 2 for obesity, despite suggestions in the past that it had prioritized retatrutide over mazdutide. In 2024, we can expect read-outs of SURMOUNT-5, the SUMMIT trial of tirzepatide in HFpEF, and a Phase 3 trial of tirzepatide in obstructive sleep apnea. The Phase 3 trials for orforglipron and retatrutide (as well as the CVOT for tirzepatide) will read out in 2025 and 2026. Lilly also expects to complete two Phase 1 trials with an amylin agonist and a DACRA in the second half of 2024.

2024 outlook

Lilly provided 2024 guidance that was ahead of expectations on the top line. The 2024 EPS outlook is in line with expectations despite the top-line beat as LLY continues to invest aggressively in its pipeline.

Analyst questions

Almost all analyst questions were about Lilly's incretin franchise, and covered a broad range of topics including manufacturing, uptake, access and coverage, and trial specifics. Key points:

- Since almost all Mounjaro revenue was incurred in the US, one question focused on ex-US. Lilly seemed to indicate that ex-US launches and roll-out may occur "[as] we monitor our ramp-up in capacity for supply".
- On coverage, Lilly reinforced that 1) it is positive about Mounjaro coverage, while 2) Zepbound coverage efforts will focus on expanding formulary inclusion and employer opt-ins, although this is expected to take time, and 3) that it expects that evidence in obesity complications (sleep apnea, HFpEF, CV) will unlock Medicare Part D coverage.
- Lilly did not unequivocally indicate it will be pursuing a MASH indication for tirzepatide – and seemed to suggest that one variable is that it may have a better MASH drug in the form of retatrutide. Lilly also emphasized that is sees moving away "as much as we can from liver biopsies and replace them with non-invasive testing" as a priority regardless of the drug.
- On manufacturing, Lilly indicated it is building out both the injectable peptide manufacturing capacity and the small molecule capacity for orforglipron – the latter requires at-risk pending Ph3 outcomes. Lilly also highlighted that it will continue to work with third-party manufacturer in addition to internal capacity, that it will "hold Catalent accountable to their contract" regardless of the Novo deal, and that "the reality is there just isn't built capacity that's available" – both for GLP-1RA manufacturing and for "the machines that make the products".
- On lean body mass loss, Lilly indicated that as a consequence of the 1:3 ratio of lean body mass loss vs. fat mass loss, tirzepatide overall improves body composition. However,

bimagrumab (and other portfolio assets?) are explored as opportunities to further improve body composition.

- Lilly seemed to position the opportunity for orforglipron as both addressing supply constraints (for peptides / injectables) and a suitable drug for the 20% of patients who do not want an injectable.
- On competitive positioning of tirzepatide vs. AMG133, Lilly was quite aggressive in their response to questions about AMG133. It suggested that GIP antagonism may have a negative impact on triglycerides vs. GIP agonism, and highlighted the sheer size of the evidence supporting GIP agonism. Lilly also suggested that the AMG133 sustainability data was “a bit underwhelming” and that the doses that were tolerated did not cause that much weight loss.
- On genericization of GLP-1RAs, Lilly commented that it seeks to “bring something into the market that provides a meaningfully improved outcome for patients” and gave retatrutide as an example, and emphasized the capital outlays that would be required by generic / biosimilar entrants.

Robert Stoekenbroek | +1-908-206-6357
www.populationhp.com