Subject: Competitive Intelligence Update - Novo Q1 2024 Earnings
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Metsera Reports

May 3, 2024

Competitive Intelligence Update

Novo Reports Q1 2024 Earnings

Summary and Implications

- Ozempic US revenues grew 50% to $2.7B; Wegovy US revenues grew 100% to $1.2B
- Semaglutide Phase 3 data in NASH, PAD will read out in 2024; oral semaglutide Phase 3 data in CVD will read-out in H2 2024
- Once-monthly GLP1 / GIP Injectable Phase 1 data will be available by YE 2024
- Novo is pursuing multiple non-incretin mechanisms of action in MASH, including CB1, NLPR3, VAP1, and MARC1
- Novo capital expenditures are still expected to be around $6.5B in 2024

Commercial Content

Novo launched Ozempic and Rybelsus in Type 2 Diabetes (T2DM) in 2017 and 2019 respectively, and launched Wegovy in Obesity in 2021.

In Type 2 Diabetes, Ozempic did $2.7B in US revenues in Q1 2024, compared to $1.8B in Q1 2023 (50% YoY growth). Ex US contributed 32% of total Ozempic revenues. Ozempic did $4.0B in WW revenues in Q1 2024, compared to $2.8B in Q1 2023. Ozempic's US growth was powered by 15% YoY growth in prescription volume. But Ozempic US revenues were negatively

impacted by supply constraints and slight decrease in net price. Novo has 56% market share of GLP1 T2DM market, based on total prescriptions, and continues to take market share. Novo's share of the global T2DM 'value pool' is 34%. Interestingly, Rybelsus US revenues declined from $384M in Q1 2023 to $337M in Q1 2024. Total Rybelsus revenue slightly grew from $629M in Q1 2023 to $723M in Q1 2024, driven by ex US markets. Novo management may be prioritizing injectable semaglutide over oral semaglutide in US, based on Rybelsus financial performance.

In Obesity, Wegovy did $1.2B in US revenues in Q1 2024, compared to $639M in Q1 2023 (100% YoY Growth). Ex US is not a meaningful portion of Wegovy revenues yet. Wegovy run-rate weekly NBRx now exceeds 25,000; at the start of 2024, weekly NBRx was 5,000. After reducing lower dose supply in Q1 2023, Novo gradually increased the supply of lower dose strengths in Q1 2024. US Wegovy revenues were negatively impacted by slight net price decline in Q1 2024. 50M patients are currently 'covered' by Novo, but true coverage is a two-step process, requiring individual employers to opt-in to Obesity rider. Expansion of Medicare coverage for Chronic Weight Management with CVD expanded coverage by 4M patients, in-line with internal Metsera estimates of patients with BMI > 27 and CVD without T2DM.

Longer-term, Novo emphasized the Obesity market is still early. Today, Novo is only treating 1M out of 800M possible patients. Management explicitly said there is room for more than 2 companies. Management emphasized CagriSema will not cannibalize Wegovy revenues the way Wegovy cannibalized Saxenda. Novo refused to provide guidance on 2025 patient supply. Management is focused on single dose vials in near-term, but wants to deliver multiple doses in smarter way.

Development Content

Novo is developing many new compounds to address different market segments within Obesity, T2DM, and Metabolic Disease. Novo is also exploring many modalities preclinically.

Semaglutide + Insulin in T2DM (ICOSEMA)
Novo announced positive results from Phase 3 trial evaluating Insulin Icodec + Semaglutide 1.0 mg against Semaglutide monotherapy in T2DM patients inadequately controlled by GLP1. IcoSema once-weekly achieved HbA1C reduction of 1.35%, compared to 0.90% for Semaglutide 1.0 mg.

Semaglutide in CKD (FLOW)
In March 2024, Novo announced positive results from its Phase 2 FLOW trial evaluating semaglutide in CKD and submitted label expansion application in US. FLOW results will be

shared at the European Renal Association Congress in May 2024.

Semaglutide in MASH (ESSENCE)
Novo will announce Phase 3 MASH results in H2 2024. The Phase 3 study includes 800 patients treated over 72 weeks, with primary endpoint of liver biopsy assessment of steatosis and fibrosis. Novo's Phase 2 MASH study was not powered to show a statistically significant reduction in fibrosis. However, Novo's Phase 2 can serve as a label-enabling registrational study, so it only needs to conduct a single Phase 3 study.

Semaglutide in PAD (STRIDE)
Novo will announce Phase 2 data evaluating semaglutide in peripheral arterial disease (PAD) in H1 2024.

Semaglutide in Heart Failure (STEP HFpEF)
In August 2023, Novo announced positive results from its Phase 3 STEP HFpEF trial evaluating semaglutide in patients with Heart Failure with Preserved Ejection Fraction. Based on this data, Novo submitted label expansion application in US. The FDA gave a priority review designation and will convene an advisory committee in H2 2024 to discuss this label expansion.

High-Dose Semaglutide (8 and 16 mg once-weekly)
Novo completed a Phase 2 study evaluating 8 and 16 mg semaglutide once-weekly in T2DM patients. Safety and tolerability was in-line with previous semaglutide trials. Novo may develop higher doses of semaglutide in T2DM.

Next Generation Obesity Products
Amycretin is being evaluated in T2DM and Obesity. In T2DM, the Phase 2 is underway. In Obesity, Novo is finalizing subcutaneous formulation and will decide whether to progress oral or subcutaneous formulation forward.

Novo's new prodrug GLP1 / GIP dosed once-monthly is being evaluated in T2DM. In prior presentations, Novo said Phase 1 data is expected in 2025. However, in the Q1 2024 earnings call, Novo hinted at an earlier read-out before 2024 year-end. Management said efficacy is the most important product attribute, not dose interval.

Monlunabant, Novo's CB1 inverse agonist acquired from Inversago, is being evaluated in a large Phase 2 study. This Phase 2 will carefully examine CNS penetrance and psychiatric adverse events. Novo is confident Monlunabant's CNS penetrance is less than that of other CB1 inverse agonists.

Lean Mass Preservation Discussion

Martin Lange, Novo's Development Chief, was asked if he was concerned that lean mass loss contributed to 40% of total weight loss for semaglutide. Dr. Lange emphasized that during any type of weight loss, such as calorie restriction, 25-45% of the weight loss can be attributed to lean mass. The speed of weight loss determines whether lean mass accounts for 25% or 45%; faster weight loss typically results in greater % contribution of lean mass loss. Dr. Lange is more concerned about functional improvements and CV risk reduction than loss of lean mass. Furthermore, Dr. Lange suggested Amylin biology may address this concern and improve the lean to fat mass ratio during weight loss.

Current Novo clinical-stage assets in Obesity, T2DM and MASH, besides insulin, include:

Phase 1

- Prodrug GLP1 / GIP Once-Monthly (T2DM)
- Amycretin SC (Obesity)
- Oral Amycretin (Obesity)
- Dual Amylin and Calcitonin Receptor (every 2 weeks)
- NLRP3 Inhibitor (MASH)
- LXR Inhibitor (MASH)
- VAP1 Inhibitor (MASH)
- MARC1 Inhibitor (MASH)

Phase 2

- Once-weekly GLP1 / GIP (T2DM)
- Oral Amycretin (T2DM)
- Semaglutide 8 mg or 16 mg Once-Weekly (T2DM)
- Monlunabant CB1 Inverse Agonist (Obesity, CKD)
- Unnamed FGF21 (MASH)
- Ultrasound Therapy with GE Healthcare (T2DM, Obesity)

Phase 3

- CagriSema (T2DM, Obesity)
- Semaglutide (MASH, PAD, AD)
- IcoSema Insulin + Semaglutide 1.0 mg (T2DM)
- Semaglutide 7.2 mg (Obesity)
- Oral Semaglutide 25 mg and 50mg (T2DM, Obesity)

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