Tuesday, May 14, 2024 at 12:17:59 Eastern Daylight Time

Subject: MTSR1: Weekly Competitive Intelligence Newsletter (Apr 23-29, 2024)
Date: Monday, April 29, 2024 at 6:25:18 AM Eastern Daylight Time
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Attachments: image002.png

Hi Metsera Team,

Please find below the weekly 'Competitive Intelligence Newsletter' for the week: Apr 23-29, 2024

DASHBOARD

KEY TAKEAWAYS OF THE WEEK (Apr 23-29, 2024)

- **Regulatory –** ANSM is expecting a progressive improvement in stocks of Novo Nordisk's OZEMPIC (semaglutide) from Sep 2024 [France]
- **Commercial –** Novo Nordisk announced that from May 1, 2024, WEGOVY (semaglutide) will be available but not reimbursed for obesity in Spain [Spain]
- **Miscellaneous –** A U.S. Senate committee launched an investigation into the prices of Novo Nordisk's diabetes and weight loss drugs OZEMPIC (semaglutide) and WEGOVY (semaglutide) in the U.S. [U.S.]

DETAILED NEWS

CLINICAL

1 Trial Update: A study of tirzepatide (LY3298176) compared with dulaglutide on major cardiovascular events in participants with type 2 diabetes (SURPASS-CVOT) [Global]
Apr 26, 2024

- A Phase III trial sponsored by Eli Lilly titled, "*A study of tirzepatide (LY3298176) compared with dulaglutide on major cardiovascular events in participants with type 2 diabetes (SURPASS-CVOT)"* has undergone the following changes
  - **PCD and SCD:** Updated from Oct 17, 2024 [Anticipated] to Jun 2025 [Anticipated]
  - **Contacts/Locations:** Multiple sites were added and removed
- **Read more:** NCT04255433
- **Implications:** SURPASS-CVOT appears to complete about 8 months later than to previous CT.gov timelines, suggesting that events might come in slower than expected. SURPASS-CVOT is an important trial for tirzepatide comparing its efficacy H2H vs. dulaglutide

2 New Trial: The effect of retatrutide once weekly on cardiovascular outcomes and renal function in adults living with obesity (TRIUMPH-OUTCOMES) [Global]
Apr 25, 2024

- Eli Lilly initiated a Phase III trial to investigate the effect of retatrutide on the incidence of major adverse cardiovascular events and the decline in kidney function in participants with body mass index >27 kg/m^2 and atherosclerotic cardiovascular disease and/or chronic kidney disease
  - **Trial details:** N = 10,000; Status: Not yet recruiting; Start date: May 2024; PCD and SCD: Feb 2029; Location: Global
- **Read more:** NCT06383390
- **Implications:** In Phase 2 trials, participants who received retatrutide experienced weight reductions along with improvements in cardiometabolic indicators, such as waist circumference, systolic and diastolic blood pressure, glycated hemoglobin, fasting glucose, insulin, and lipid levels. It will be interesting to observe the cardiovascular and renal outcomes in this trial

3 Trial Update: DAYBREAK: A study of setmelanotide in patients with specific gene variants in the MC4R pathway [Global]
Apr 22, 2024

- A Phase II trial sponsored by Rhythm Pharmaceuticals titled, "*DAYBREAK: A study of setmelanotide in patients with specific gene variants in the MC4R pathway"* has undergone the following changes
  - **PCD:** Updated from Apr 2024 [Anticipated] to Feb 14, 2024 [Actual]

- **SCD:** Updated from Apr 2024 [Anticipated] to Jul 17, 2024 [Anticipated]

- **Read more:** NCT04963231

- **Implications:** N/A

4 **Trial Update: Phase Ib/IIa study of GSBR-1290 in adult overweight or obese healthy subjects and subjects with type 2 diabetes mellitus [U.S.]**
Apr 25, 2024

- A Phase I/II trial sponsored by Gasherbrum Bio titled, "*Phase Ib/IIa study of GSBR-1290 in adult overweight or obese healthy subjects and subjects with type 2 diabetes mellitus"* has undergone following changes
  - **Overall Status:** Updated from 'Active, not recruiting' to 'Completed'
  - **PCD and SCD:** Updated from Apr 14, 2024 [Anticipated] to Apr 11, 2024 [Actual]
  - **Enrollment:** Updated from 144 [Anticipated] to 142 [Actual]

- **Read more:** NCT05762471

- **Implications:** N/A

5 **Trial Update: First in human study in subjects with obesity, but otherwise healthy [U.S.]**
Apr 22, 2024

- A Phase I trial sponsored by NeuroBo Pharmaceuticals titled, "*First in human study in subjects with obesity, but otherwise healthy"* has undergone following changes
  - **Overall Status:** Updated from 'Not yet recruiting' to 'Recruiting'
  - **SSD:** Updated from Mar 2024 to Mar 25, 2024
  - **PCD:** Updated from Aug 2025 [Anticipated] to Dec 14, 2024 [Anticipated]
  - **SCD:** Updated from Jan 2026 [Anticipated] to Jun 2025 [Anticipated]
  - **Outcome Measures/Eligibility:** Updated
  - **Contacts/Locations:** Sites updated

- **Read more:** NCT06252220

- **Implications:** N/A

6 **Aphaia Pharma provides enrollment and protocol update for Phase II trial [Germany/Puerto Rico]**
Apr 25, 2024

- Aphaia Pharma announced the completion of enrollment in its Phase II trial evaluating the safety and efficacy of a once-daily 12g dose of its APHD-012 (oral glucose formulation) to induce weight loss in individuals with obesity
- The company also announced that the U.S. FDA has approved the expansion of the trial's protocol to further explore the contribution of circadian effects in weight loss treatment
  - The new protocol will include four additional cohorts, which will be dosed with either 6g (APHD-006) or 8g (APHD-008) of Aphaia's formulation or their respective placebos twice per day
- Aphaia Pharma aims to leverage the beneficial effects of circadian timing, which are known to improve metabolic diseases and weight control
  - Part of the strategy is to readjust the patient's internal clock and metabolism to optimize long-term therapeutic outcomes for patients

- **Read more:** Aphaia Pharma Press Release

- **Implications:** N/A

REGULATORY

7 **French drug regulator anticipates improvement in supplies of GLP-1 analogues, including OZEMPIC [France]**
Apr 26, 2024

- France's drug regulator ANSM is expecting a progressive improvement in stocks of Novo Nordisk's OZEMPIC (semaglutide) from Sep 2024, and suggested treatment initiations could "progressively restart" once stocks have been partially restored
  - This committee interviewed Novo Nordisk and Eli Lilly mid-Mar and asked them about supply replenishment, especially of doses used to initiate diabetes type 2 treatment – add as sub-bullet to the above
  - According to Novo Nordisk, progressive supplies of OZEMPIC 0.25 mg should arrive over the next few months, which would partially cover the expected needs - same comment as above
  - However, Eli Lilly's supply tensions for TRULICITY will last beyond the end of 2024 - same comment as above
- Given the therapeutic need, the committee suggested a progressive restart of treatment initiations with OZEMPIC or VICTOZA in certain situations as soon as stocks are partially replenished
  - It recommended that the prescription of GLP-1 analogues as first-time treatment be reserved for "type 2 diabetes patients with severe artheromatic disease, namely with a previous vascular event or a significant artheromatic lesion
  - For patients with no previous ischemic cardiovascular event, the use of another diabetes drug is preferred
- These new recommendations however will only apply "once the progressive replenishment of low dose OZEMPIC and VICTOZA is confirmed

- **Read more:** APM Health *(Subscription required)*

- **Implications:** Ozempic supply shortages expected to improve from Sep 2024 onwards in France

COMMERCIAL

8

Novo Nordisk's WEGOVY rejected for reimbursement in Spain [Spain]
Apr 25, 2024

- Novo Nordisk announced that from May 1, 2024, WEGOVY (semaglutide) will be available but not reimbursed for obesity in Spain
  - WEGOVY has been rejected for reimbursement in Spain by drug pricing commission CIPM
  - Physicians will be authorised to prescribe it for obesity starting next week and patients will have to pay for the drug
- The drug will be used together with diet and physical activity to lose weight and keep weight under control in adults with:
  - A BMI of 30 kg/m² or greater (obesity) or
  - A BMI of at least 27 kg/m² but less than 30 kg/m² (overweight) who have weight-related comorbidities (such as diabetes, high blood pressure, abnormal levels of fats in the blood, breathing problems during sleep called 'obstructive sleep apnoea' or a history of heart attack, stroke, or blood vessel problems)
- It will also be reimbursed in adolescents from 12 years of age whose BMI is at or above the 95th percentile for their age and gender (obesity) and who weigh more than 60 kg
  - The maintenance dose will be 2.4 mg once a week escalating from 0.25 mg
  - The approval is based on the results of the Phase IIIa/IIIb Semaglutide Treatment Effect in People with Obesity (STEP) trial. The development programme includes 17 trials comprising 8,700 patients who are overweight or obese with and without comorbities
- A total of nine of these studies have already been completed

- **Read more:** APM Health *(Subscription required)*

- **Implications:** Wegovy's rejection for reimbursement by Spain's CIPM could be influenced by factors such as cost concerns, perceived cost-effectiveness, or budgetary constraints within the national healthcare system.This decision limits broader access to Wegovy for obesity treatment in Spain, potentially affecting Novo Nordisk's market penetration

MISCELLANEOUS

9 **U.S. Senate Committee investigates pricing of Novo's OZEMPIC and WEGOVY [U.S.]**
Apr 25, 2024

- The U.S. Senate Committee launched an investigation into the prices of Novo Nordisk's diabetes and weight loss drugs OZEMPIC (semaglutide) and WEGOVY (semaglutide) in the U.S.
  - Senator Bernie Sanders, Chair of the Senate Committee on Health, Education, Labor and Pensions, sent a letter to Novo Nordisk's CEO seeking more information on the U.S. prices for the two drugs, which are higher than the prices in other countries
  - The committee also asked the compnay if it will substantially reduce both the list price and the net price of both the drugs, and why the company was charging a higher price for the weight loss drug WEGOVY than OZEMPIC, which contains the same compound
- Novo Nordisk remains committed to working with policymakers to advance solutions to support access and affordability for all patients, and we reiterated this commitment in our conversation with Chairman Sanders

- **Read more:** Reuters

- **Implications:** The finding from Yale University that these medications can be profitably produced for less than $5 a month, alongside their considerably lower retail prices in countries like Canada, Germany, and the UK, suggests room for substantial price adjustments. This discrepancy may prompt calls for policy reform and could drive market pressure on Novo Nordisk and other manufacturers

10 **3.6 Mn Medicare enrollees may now be eligible for WEGOVY coverage [U.S.]**
Apr 24, 2024

- According to an analysis published by KFF, about 3.6 Mn Medicare enrollees may qualify for coverage of the anti-obesity drug WEGOVY (semaglutide)
  - But it could wind up costing Medicare nearly $3 Bn a year and contribute to higher Part D premiums for all beneficiaries
- According to KFF, an estimated 7% of Medicare enrollees – including just over a quarter of those diagnosed as overweight or obese – fit the criteria for WEGOVY coverage in 2020
  - Of the 3.6 Mn beneficiaries, 1.9 Mn of them had diabetes and may have been already eligible for Medicare coverage of GLP-1 drugs for that disease
- The price tag for Medicare could approach $3 Bn for one year, assuming just 10% of eligible beneficiaries use WEGOVY and if Part D plans receive a 50% rebate on the list price of $1,300 a month
  - But it will probably result in higher Part D premiums for enrollees, though the exact impact is difficult to pin down

- **Read more:** CNN, Reuters

- **Implications:** Approximately 3.6 million Medicare enrollees could now be eligible for coverage of the anti-obesity drug Wegovy following FDA approval for cardiovascular benefits, potentially increasing Medicare spending by nearly $3 billion annually and raising Part D premiums. Lilly's Mounjaro could be the next obesity drug added for Medicare coverage once it receives the sleep apnea indication

11 **Zealand Pharma partners with Benchling to advance R&D of engineered peptide medicines [U.S./ Switzerland**
Apr 23, 2024

- Benchling announced Zealand Pharma has selected the Benchling R&D Cloud as its central source of truth for scientific data, collaboration, and insights
- Teams across Zealand will use the Benchling R&D Cloud to capture, analyze, and share stability data internally and with their external contract manufacturing organization partners, in compliance with GxP

- **Read more:** PR Newswire

- **Implications:** Zealand Pharma's integration of Benchling's R&D Cloud positions the company to accelerate its market presence in developing advanced peptide treatments for obesity

12 **Mayo Clinic diet survey spotlights important correlation between weight loss medication and behavioral support programs [U.S.]**
Apr 23, 2024

- In a recent survey conducted by the Mayo Clinic Diet, a staggering 59% of respondents identified not finding the right weight loss program as the primary barrier to shedding pounds effectively
- This revelation, coupled with the increasing use of weight loss medications like OZEMPIC (semaglutide) alone, without physician guidance or comprehensive lifestyle program, has sparked concerns among experts

- **Read more:** PR Newswire

- **Implications:** Mayo Clinic Diet Survey reveals the critical need for holistic support in weight loss strategies, showing that reliance solely on GLP-1 medications without behavioral programs can hinder effective weight management and health outcomes

13 **MyFitnessPal announces tools and content to support the health and wellness of members on GLP-1 medications [U.S.]**
Apr 23, 2024

- MyFitnessPal, global food and nutrition tracking app, introduced a variety of new tools and content developed to support the health and wellness of their members on GLP-1 medications (e.g., MOUNJARO, OZEMPIC, WEGOVY, ZEPBOUND) to ensure they are offered a holistic approach that optimizes success
  - In addition to tracking their weight loss, the new updates and tools offered by MyFitnessPal empower members to develop and maintain consistency and proper nutrition while on these medications
  - Members will have access to a library of exercise videos to help maintain muscle, along with encouragement to eat and log high quality, nutrient-dense food to support the development of consistency and lasting healthy behaviors
  - Along with medication tracking, MyFitnessPal launched a free recipe collection and in-app Nutrition Plan developed by their team of registered dietitians with the guidance of MyFitnessPal's Scientific Advisory Council

- **Read more:** PR Newswire

- **Implications:** MyFitnessPal introduces specialized tools and content to support members on GLP-1 medications, including medication logging, a GLP-1 Nutrition Plan, and resources to manage diet and exercise effectively, aiming for sustainable health improvements and comprehensive wellness support

14 **Lilly acquires new injectable medicine manufacturing facility from Nexus Pharmaceuticals [U.S.]**
Apr 22, 2024

- Eli Lilly and Nexus Pharmaceuticals announced a definitive agreement for Eli Lilly to acquire a manufacturing facility from Nexus, a leading sterile manufacturer in the pharmaceutical industry
- The acquisition of the U.S. FDA approved facility in Pleasant Prairie, Wisconsin will further expand Eli Lilly's global parenteral (injectable) product manufacturing network and support increased demand for the company's medicines
  - Eli Lilly estimates that production at this facility could begin at the end of 2025
- The Pleasant Prairie facility does not provide contract manufacturing services, allowing the facility to be solely dedicated to Eli Lilly's manufacturing mission to deliver medicines to patients with safety first and quality always

- **Read more:** Eli Lilly Press Release, Nexus Pharmaceuticals Press Release

- **Implications:** Lilly's acquisition indicates its willingness to expand production among high demand and shortages. Currently four of Lilly's drug are listed on FDA's shortage database. This acquisition in another step in enhancing its global parenteral product network to meet growing medicine demand, with production expected by end of 2025

15 **GLP-1 coverage restrictions in medicare Part D surge as demand for obesity drugs grows [U.S.]**
Apr 19, 2024

- A major shift from unfettered coverage to prior authorizations was recorded by MMIT over the past year for the leading GLP-1/GIP agonist diabetes drugs. Public interest in using the drugs off label for weight loss drove the change
- The introduction of obesity products in the GLP-1/GIP agonst drug class has jolted Medicare Part D plans even though the program does not cover weight loss drugs
- A major shift from preferred coverage without restrictions to prior authorization requirements began in 2023
- The trend is sure to continue as drugs approved for obesity (WEGOVY and ZEPBOUND) gain additional indications that Part D does cover

- **Read more:** Pink Sheet *(Subscription required)*

- **Implications:** Prevalence of obesity in the US is estimated to be around 40% due to which Medicare and commercial payers are facing increased financial pressures, prompting them to introduce tighter coverage restrictions such as prior authorizations for GLP-1/GIP agonists. This trend, driven by the drugs' off-label use for weight loss and the introduction of new obesity medications, reflects a strategic effort to manage costs and refine eligibility criteria within healthcare coverage policies, directly impacting drug access and market dynamics for obesity treatment

16 **Africa's biggest drug manufacturer, Aspen, eyes role in easing global obesity medication supply [South Africa]**
Apr 22, 2024

- According to Stephen Saad, CEO, Aspen, the company is set to play a pivotal role in alleviating the supply shortage of the world's

most sought-after obesity medications
- In an interview, Saad disclosed Aspen's capacity to bolster the availability of highly demanded medications, including Eli Lilly's blockbuster diabetes drug, MOUNJARO (tirzepatide), across Southern Africa
- Aspen aims to contribute through "fill and finish" services, involving the packaging of drugs for distribution

- **Read more:** Nairametrics

- **Implications:** Aspen Pharmacare, Africa's largest drug manufacturer, could alleviate the global shortage of obesity medications by expanding its production roles, particularly in "fill and finish" services for GLP-1s

KEY UPCOMING EVENTS

Q1 2024 Earnings Call:
- **Eli Lilly:** Apr 30, 2024 (Eli Lilly Investor update)
- **Pfizer:** May 1, 2024 (Pfizer Investor update)
- **Novo Nordisk:** May 2, 2024 (Novo Nordisk Investor update)

GLP-1-Based Therapeutics Summit:
- **Altimmune:** May 15, 2024 (Altimmune Investor update)

Thank you,
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