Tuesday, May 14, 2024 at 12:23:45 Eastern Daylight Time

Subject: MTSR1: Weekly Business Intelligence Newsletter (Jan 22 – 29, 2024)
Date: Wednesday, January 31, 2024 at 7:29:19 AM Eastern Standard Time
From: Benjamin Kumpfmueller <bkumpfmueller@sai-med.com>
To: Metsera <Metsera@populationhp.com>
CC: Diksha Matta <dmatta@sai-med.com>, Nidhi Srivastava <nidhis@theratraq.com>, Ailen Thomas <AilenT@theratraq.com>, Diane Suchon <DSuchon@sai-med.com>
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Hi Metsera Team,

Please, find here the first weekly 'Competitive Intelligence Newsletter' for the week: Jan 22 – 29, 2024

DASHBOARD

KEY TAKEAWAYS OF THE WEEK (Jan 22 – 29, 2024)

- **Clinical –** Scholar Rock announces FDA clearance of IND application to initiate Phase II Proof-of-Concept trial with apitegromab to treat obesity [U.S.]
- **Regulatory –** The UK's Medicines and Healthcare products Regulatory Agency approved a four-dose version of Eli Lilly's MOUNJARO (tirzepatide) - MOUNJARO KwikPen
- **Commercial –** Eli Lilly is planning to launch its weight-loss treatment MOUNJARO in the Great Britain

DETAILED NEWS

CLINICAL

1 **Trial update: A study of LY3437943 (retatrutide) in postmenopausal female participants who are overweight or obese [U.S.]**
Jan 26, 2024

- A Phase I study sponsored by Eli Lilly titled, "*A study of LY3437943 (retatrutide) in postmenopausal female participants who are overweight or obese"* has undergone changes
  - **PCD and SCD:** Updated from Jan 2, 2025 to Jul 5, 2024 [Anticipated]

- **Read more:** NCT06039826
- **Implications:** *N/A*

2 **Trial update: A study of LY3298176 (tirzepatide) in participants with overweight or obesity and chronic kidney disease with or without type 2 diabetes (TREASURE-CKD) [Global]**
Jan 25, 2024

- A Phase II study sponsored by Eli Lilly titled, "*A study of LY3298176 (tirzepatide) in participants with overweight or obesity and chronic kidney disease with or without type 2 diabetes (TREASURE-CKD)"* has undergone changes
  - Changes made in eligibility for inclusion criteria
  - **Contacts/Locations:** Recruiting statuses have changed for various global locations

- **Read more:** NCT05536804
- **Implications:** The minimum eGFR requirement has been lowered from ≥30 ml/min/1.73 m² to ≥25 ml/min/1.73 m² I The upper limit for HbA1c has been lowered from ≤10.5% to ≤9.5% I The threshold for eGFR exclusion has been adjusted from <30

mL/min/1.73m² to <25 mL/min/1.73m²; Lowering eGFR boundaries broadens enrollment population, while lowering upper HbA1c threshold may be aiming to reduce the risk of adverse outcomes and complications associated with poor diabetes control

3 **Trial update: A study of LY3541105 in healthy and overweight participants [U.S.]**
Jan 24, 2024

- A Phase I study sponsored by Eli Lilly titled, *"A Study of LY3541105 (undisclosed) in healthy and overweight participants"* has undergone changes
  - **Overall Status:** Updated from 'Recruiting' to 'Active, not recruiting'
  - **Contacts/Locations:** Central Contact Person have been removed and sites were removed and added to the U.S. location

- **Read more:** NCT05380323
- **Implications:** *N/A*

4 **Trial update: A study to test whether BI 456906 (survodutide) helps Japanese people living with obesity disease (SYNCHRONIZE JP) [Japan]**
Jan 24, 2024

- A Phase III study sponsored by Boehringer Ingelheim titled, *"A study to test whether BI 456906 (survodutide) helps Japanese people living with obesity disease (SYNCHRONIZE JP)"* has undergone changes
  - **Contacts/Locations:** Seven new sites have been added to Japan location

- **Read more:** NCT06176365
- **Implications:** Japanese PhII trial with BI 456906, a glucagon receptor/GLP-1 receptor dual agonist, started in December 2023 and is currently expanding recruitment sites. Trial including patients with BMI of 35 or more and at least one health problem related to their weight, or a BMI of 27 kg/m² or more and at least two health problems related to their weight

5 **Trial update: A study of LY3298176 (tirzepatide) once weekly in adolescent participants who have obesity, or are overweight with weight-related comorbidities [Global]**
Jan 24, 2024

- A Phase III study sponsored by Eli Lilly titled, *"A study of LY3298176 (tirzepatide) once weekly in adolescent participants who have obesity, or are overweight with weight-related comorbidities"* has undergone changes
  - **Overall Status:** Updated from 'Not yet recruiting' to 'Recruiting'
  - **Study Start Date:** Updated from Oct 15, 2023 to Oct 16, 2023
  - **Primary Completion Date (PCD):** Updated from Feb 14, 2026 to Oct 1, 2026 [Anticipated]
  - **Study Completion Date (SCD):** Updated from Dec 2026 to Oct 1, 2026 [Anticipated]
  - **Contacts/Locations:** Recruiting statuses have changed for various global locations

- **Read more:** NCT06075667
- **Implications:** *N/A*

6 **Scholar Rock announces FDA clearance of IND application to initiate Phase II Proof-of-Concept trial with apitegromab to treat obesity [U.S.]**
Jan 23, 2024

- The Phase II trial is a randomized, double-blind, placebo-controlled, multi-center study to evaluate the effect of apitegromab, a highly selective myostatin inhibitor, to safely preserve lean muscle mass as an adjunctive therapy in overweight and obese adults who are taking a GLP-1 RA
- Trial initiation is on track for mid-2024, and data from the apitegromab Phase II trial are expected in mid-2025
- In parallel, Scholar Rock is developing SRK-439, a novel investigational selective myostatin inhibitor, optimized for the treatment of obesity
  - The company plans to file an IND for SRK-439 in 2025

- **Read more:** Scholar Rock Press Release
- **Implications:** The initiation of the Phase 2 trial for apitegromab will test the efficacy of targeting specific forms of myostatin to maintain muscle mass, a key factor in metabolic health, during weight loss. Because GLP-1 agonists cause more rapid and sustainable weight loss compared with intensive behavioral lifestyle therapy, there has been more attention recently about possible muscle mass loss with GLP-1 agonist use.

REGULATORY

7 **Four-dose MOUNJARO "KwikPen" approved by MHRA for diabetes and weight management [UK]**
Jan 25, 2024

- The UK's Medicines and Healthcare products Regulatory Agency (MHRA) approved a four-dose version (covering a month's treatment) of the diabetes and weight management medicine MOUNJARO (tirzepatide) - MOUNJARO KwikPen
  - MOUNJARO KwikPen is approved to treat adults with type-2 diabetes and for weight management in adult patients with a BMI of 30kg/m² or more (obesity), as well as those with a BMI between 27 – 30kg/m² (overweight) who also have weight-related health problems such as prediabetes, high blood pressure, high cholesterol, or heart problems
  - The medicine is to be used together with a reduced-calorie diet and increased physical activity
- MOUNJARO KwikPen is available as a four-dose pre-filled injection pen containing 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, and 15 mg of tirzepatide per dose, injected under the skin of a patient's stomach area, thigh, or upper arm
- Starting dose is 2.5 mg once a week for four weeks, increasing to 5 mg once a week
  - The dose may then be increased in at least 4-week intervals up to the maximum dose of 15 mg once weekly, if recommended by the patient's doctor

- **Read more:** UK MHRA Press Release
- **Implications:** In the United States, Lilly offers a single-use device specifically designed for administering Mounjaro. In contrast, for markets outside of the U.S., Lilly has introduced a multi-use device. Additionally, the KwikPen, an established device from Lilly's portfolio, has a history of being utilized for insulin delivery.

COMMERCIAL

8 **Eli Lilly to launch MOUNJARO for weight-loss in UK 'within weeks' [UK]**
Jan 26, 2024

- The Financial Times reported that Eli Lilly is to make its weight-loss treatment MOUNJARO (tirzepatide) available in the Great Britain
  - MOUNJARO is currently approved for type-2 diabetes, received its label expansion to include weight loss in Nov 2023, however not enough of the regular format of the drug was available to supply the UK
  - The UK's MHRA announced the approval of Lilly's "KwikPen", a format that provides four doses in one device, allowing the company to be able to supply the drug to England, Scotland, and Wales
- The Financial Times also specified that patients in Northern Ireland will not have access to the pen, and said it is unlikely that Lilly will provide enough doses of the drug to Britain to meet the demand for weight-loss treatments

- **Read more:** APM Health *(Subscription required)*
- **Implications:** Lilly is progressively launching MOUNJARO in various countries, with the rollout being conducted sequentially due to constraints in supply

9 **Cipla plans to launch diabetes and obesity drugs [Global]**
Jan 25, 2024

- According to a top official at Cipla, the company is preparing to launch drugs for diabetes and obesity in India, other emerging markets, and the U.S., as it sees a huge opportunity for these formulations
  - The company is also reported to be in dialogue with multinational corporation Eli Lilly for its GLP-1 class of drugs

- **Read more:** Live Mint
- **Implications:** *N/A*

10 **EraCal Therapeutics enters into a collaboration and license agreement with Novo Nordisk [Global]**
Jan 23, 2024

- EraCal Therapeutics entered into a collaboration and license agreement with Novo Nordisk to develop and commercialize EraCal's oral, small molecule program
  - The asset was discovered with EraCal's platform technology and is believed to target a novel mechanism of action controlling appetite and body weight to treat obesity
- Novo Nordisk obtained the exclusive rights to develop and commercialize the program under the agreement
  - EraCal is eligible to receive upfront, development, and commercial milestones of up to €235 Mn and further royalties on sales of a marketed product

- **Read more:** EraCal Therapeutics Press Release
- **Implications:** Novo Nordisk is expanding its investment in obesity research and assets, with a focus on developing treatments that

can be administered orally

11 **The Hill publishes opinion article arguing for Medicare Part D obesity drug coverage [U.S.] [Opinion Article]**
Jan 22, 2024

- The Centers for Medicare and Medicare Services (CMS) must expand obesity care and provide coverage of anti-obesity medications in Medicare Part D in order to address the obesity epidemic among senior populations and recognize obesity as the disease it is
- In 2022, direct medical costs of diabetes reached over $300 Bn
    - Groundbreaking research published in *The New England Journal of Medicine*, demonstrated that these treatments can reduce the risk of heart attacks and strokes by 20 percent in adults with heart disease and obesity
- The CMS lags evidence and progress of states and other federal agencies, failing to cover anti-obesity drugs in Medicare Part D
    - Yet CMS has previously altered its interpretation of the law to allow coverage of drugs that treat cachexia, causing weight gain
    - By simply applying this same legal interpretation to medications used to treat obesity, CMS could instantly remove its self-imposed prohibition
- **Read more:** The Hill
- **Implications:** Manufacturers and stakeholders, citing GLP-1s' significant weight loss benefits and potential health improvements for those with weight-related conditions, are advocating for legal changes to enable Medicare coverage. Bipartisan lawmakers have proposed the Treat and Reduce Obesity Act to permit Part D coverage for obesity treatment and weight management medications in individuals with related comorbidities.

12 **EMA considers cardiovascular indication & extra market protection for WEGOVY [EU]**
Jan 23, 2024

- The EMA is discussing whether Novo Nordisk should be granted approval to extend the EU indication of WEGOVY (semaglutide) to include its use for reducing the risk of major adverse cardiovascular events (MACE), and also be awarded an extra year of market protection.
    - Novo Nordisk's application for approval of the new indication and extended market protection is listed on the CHMP's draft meeting agenda and is based on data from the SELECT CVOT trial
    - As part of the application, Novo Nordisk is also requesting a one-year extension to the 10-year period market protection period that WEGOVY received when it was approved in the EU on Jan 6, 2022 for treating patients with obesity or who are overweight
- **Read more:** Pink Sheet *(Subscription required)*
- **Implications:** Novo Nordisk is seeking to broaden the approved use of WEGOVY, based on the results of the SELECT CVOT. This expansion aims to provide prescribers with additional evidence supporting WEGOVY's role in preventing CVD and could help to get one year patent extension in the EU

GENERAL

13 **Motion to consolidate lawsuits against OZEMPIC, WEGOVY, other GLP-1 receptor agonists manufacturers to be reviewed by MDL panel [U.S.]**
Jan 23, 2024

- The U.S. Judicial Panel on Multidistrict Litigation announced it will hear arguments on a motion to centralize all pretrial proceedings, and determine whether any multidistrict litigation (MDL) should also include similar claims against the makers of other glucagon-like peptide-1 (GLP-1) receptor agonist medications, including MOUNJARO (tirzepatide) and ZEPBOUND (tirzepatide)
    - Originally approved for the treatment of type 2 diabetes, OZEMPIC (semaglutide), WEGOVY (semaglutide), MOUNJARO and other GLP-1 drugs have more recently been identified as breakthrough weight loss treatments
    - This has led them to quickly become blockbuster medications used by individuals throughout the U.S.
- However, evidence has emerged over the past year that certain users experienced gastroparesis, which lawsuits allege was not fully disclosed on the drug labels
- Each of the complaints filed throughout the federal court system involve nearly identical allegations, indicating that drug manufacturers knew or should have known about the potential the potential GLP-1 gastroparesis side effects, but withheld information from consumers and the medical community to increase profits
- **Read more:** About Lawsuits, Scrip *(Subscription required)*
- **Implications:** A panel of judges will review a motion to consolidate lawsuits against GLP-1 receptor agonists manufacturers, including OZEMPIC and WEGOVY, focusing on whether the multidistrict litigation should encompass similar claims against other drugs in this class. The consolidation would significantly impact the manufacturers of these drugs. It could lead to increased scrutiny of their products and practices, and potentially result in substantial legal and financial ramifications

14 **Noom enters digital fitness to fight muscle loss from obesity drugs [U.S.]**
Jan 25, 2024

- Noom is expanding into online fitness to address the decline of muscle mass seen in some patients taking popular new obesity treatments
- The company has teamed up with online-fitness company FitOn, to add “Muscle Defense,” a program aimed at helping patients keep muscle as they shed pounds using GLP-1 drugs
    - With the program, Noom is increasing its involvement in the use of GLP-1 weight-loss treatments from Novo Nordisk and Eli Lilly
- Members of Noom’s program will receive access to exercise videos designed by obesity specialists along with educational materials geared toward minimizing muscle loss. Some studies indicate that people taking GLP-1s are at risk of losing muscle without making dietary changes and increasing exercise
    - The rollout of the program will begin in Mar 2024, and follows Noom’s pivot to tailoring other services for people taking weight-loss drugs, including the broader GLP-1 Companion program that launched earlier in 2024

- **Read more:** The Seattle Times, Bloomberg
- **Implications:** This program could influence how healthcare providers recommend and manage obesity treatments, integrating fitness and nutrition guidance with medication

KEY UPCOMING EVENTS

Q4 and FY2023 Earnings Call:

- **Pfizer:** Jan 30, 2024 (Pfizer Investor update)
- **Novo Nordisk:** Jan 31, 2024 (Novo Nordisk Investor update)
- **Roche:** Feb 1, 2024 (Roche Investor update)
- **Eli Lilly:** Feb 6, 2024 (Eli Lilly Investor update)
- **Amgen:** Feb 6, 2024 (Amgen Investor update)
- **AstraZeneca:** Feb 8, 2024 (AstraZeneca Investor update)