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Subject: MTSR1: Weekly Competitive Intelligence Newsletter (Feb 20 – 26, 2024)
Date: Monday, February 26, 2024 at 9:15:06 AM Eastern Standard Time
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Attachments: image003.png, image001.wmz

Hi Metsera Team,

Please find below the weekly 'Competitive Intelligence Newsletter' for the week: Feb 20 – 26, 2024

DASHBOARD

KEY TAKEAWAYS OF THE WEEK (Feb 20 – 26, 2024)

- **Clinical –** Novo Nordisk initiated a Phase I trial to investigate the effect of CagriSema on appetite and functional brain activity in people with overweight or obesity [Germany]
- **Regulatory –** The EMA's CHMP is scheduled to deliberate on extending the market authorization for Eli Lilly's MOUNJARO (tirzepatide) to include its multi-dose, pre-filled KwikPen [EU]
- **Commercial –** Novo Nordisk launched WEGOVY (semaglutide) as the first obesity drug in over three decades [Japan]

DETAILED NEWS

CLINICAL

1 Trial update: Trial to learn about the study medicine PF-07081532 (lotiglipron tromethamine) and rybelsus in people with Type 2 Diabetes and separately PF-07081532 in people with obesity [Global]
Feb 20, 2024

- A Phase II study sponsored by Pfizer titled, "*Trial to learn about the study medicine PF-07081532 (lotiglipron tromethamine) and rybelsus in people with Type 2 Diabetes and separately PF-07081532 in people with obesity"* has undergone changes
  - **PCD:** Updated from Sep 22, 2023 [Actual] to Jul 14, 2023 [Actual]
  - **Contacts/Locations:** Multiple sites were added
- **Read more:** NCT05579977
- **Implications:** N/A

2 Trial update: Phase Ib/IIa study of GSBR-1290 (undisclosed) in adult overweight or obese healthy subjects and subjects with Type 2 Diabetes Mellitus [U.S.]
Feb 23, 2024

- A Phase Ib/IIa study sponsored by Gasherbrum titled, *"Phase Ib/IIa study of GSBR-1290 (undisclosed) in adult overweight or obese healthy subjects and subjects with Type 2 Diabetes Mellitus"* has undergone changes
  - **Overall Status:** Updated from 'Recruiting' to 'Active, not recruiting'
  - **PCD and SCD:** Updated from Mar 22, 2024 [Anticipated] to Apr 14, 2024 [Anticipated]
  - **Enrolment:** Updated from 118 [Anticipated] to 144 [Actual]
  - **Contacts/Locations:** Multiple sites were removed and added
- **Read more:** NCT05762471
- **Implications:** N/A

3 **New Trial: A study of how CagriSema works on appetite in people with excess body weight [Germany]**
Feb 20, 2024

- Novo Nordisk initiated a Phase I trial to investigate the effect of cagrilintide and semaglutide combination treatment (CagriSema) on appetite and functional brain activity in people with overweight or obesity
    - **Trial details:** N = 150; Status: Not Yet Recruiting; Start date: Feb 15, 2024; PCD: Jan 19, 2026; SCD: Jan 19, 2026; Location: Germany
- **Read more:** NCT06267092
- **Implications:** Cagrilintide is a long-acting amylin analog. Phase 2 data published in June showed that once-weekly CagriSema led to an average 15.6% bodyweight reduction at week 32 among Type 2 diabetes patients who were overweight or obese. This trial is seeking answers to know more about the mechanism of action for CagriSema

4 **Trial update: Study exploring the supportive effect of acarbose in weight management [Sweden]**
Feb 15, 2024

- A Phase II study sponsored by Empros Pharma titled, *"Study exploring the supportive effect of acarbose in weight management"* has undergone changes
    - **Overall Status:** Updated from 'Recruiting' to 'Active, not recruiting'
    - **Primary Completion Date:** Updated from Dec 11, 2023 [Anticipated] to Nov 21, 2023 [Actual]
    - **Study Completion Date:** Updated from Dec 11 March 15, 2023 to Dec 11 March 15, 2024 [Anticipated]
- **Read more:** NCT05934110
- **Implications:** N/A

5 **Rhythm Pharmaceuticals announces clinical development plan of setmelanotide for hypothalamic obesity in Japan [Japan]**
Feb 22, 2024

- Rhythm Pharmaceuticals announced plans to add a cohort of patients with hypothalamic obesity in Japan to its ongoing global Phase III clinical trial of setmelanotide, with dosing expected to begin in Q3 2024
- The Company and Japan's PMDA agreed to add a cohort of 12 Japanese patients to the ongoing trial and, pending completion of the trial, to use these data as part of the company's registration package to seek approval from Japan's Ministry of Health, Labour and Welfare (MHLW)
    - In addition to efficacy data, Rhythm will collect and submit PK data from Japanese patients, expediting the typical pathway of collecting such data from an earlier-stage trial in Japanese subjects
- Rhythm also announced that it completed enrollment in the 120-patient cohort in its global Phase III trial of setmelanotide in hypothalamic obesity with patients, aged four years or older with hypothalamic obesity randomized 2:1 to setmelanotide therapy or placebo for a total of 60 weeks, including up to eight weeks for dose titration
    - Rhythm's regulatory submissions would be based on data from this cohort as agreed with both the U.S. FDA and the EMA
    - The additional 12 patient Japanese cohort will not affect timing for regulatory submissions in the U.S. or EU
    - The company remains on track to obtain top-line study results in the H1 2025
- **Read more:** Rhythm Pharmaceuticals press release
- **Implications:** N/A

6 **NodThera touts potential weight loss effect of NLRP3 inhibitors**
Feb 20, 2024

- NodThera is moving its NLRP3 inhibitors into the clinic after preclinical data showed it reversed obesity and inflammation in mice in a study that compared it against Novo Nordisk's WEGOVY (semaglutide)
- In the trial, mice receiving NT-0796 (undisclosed), lost 19% of their starting body weight by 28 days vs. mice who took semaglutide, which lost 21.5% of weight over the same time period
- According to data published in the *Journal of Pharmacology and Experimental Therapeutics*, NT-0796 and another NLRP3 inhibitor also showed reduction in cardiovascular inflammation, pointing to a potential risk reduction in cardiovascular problems. It could suggest an effect similar to WEGOVY, which was shown to have reduced cardiovascular risk by 20% in a large study in 2023
- Based on the early data, NodThera is recruiting patients with obesity for a small Phase Ib/IIa study testing out NT-0796
    - While the primary endpoint will be reducing inflammation, the company is also looking for weight reduction. Data from the trial are expected in May 2024
- The company mentioned that there are additional data not released in the study that could hit on another issue associated with the GLP-1s currently dominating the market weight gain after patients stop the drug
    - The mice on NodThera's inhibitor maintained their weight loss even after stopping the drug, in contrast to mice that gained the weight back after being taken off the GLP-1
- **Read more:** Endpoints News *(Subscription required)*, NodThera Press Release

- **Implications:** NodThera assets NT-0796 and NT-0249 were evaluated against Wegovy and calorie restriction in mice with obesity. NT-0796 induced weight loss at a rate comparable to Wegovy, whereas NT-0249 led to a reduction in inflammatory markers linked to cardiovascular disease. While the pre-clinical results look promising, we will have to wait for Phase Ib/IIa results to understand the effectiveness of this molecule further.

7 **Trial update: A study in people with obesity to test the effects of BI 456906 (survodutide) compared with semaglutide on glucagon receptor activity in the liver**
Feb 20, 2024

- A Phase I study sponsored by Boehringer Ingelheim titled "*A study in people with obesity to test the effects of BI 456906 (survodutide) compared with semaglutide on glucagon receptor activity in the liver"* has undergone changes
    - **Brief Title:** Updated from "A study in people with obesity to test the effects of different doses of BI 456906 compared with semaglutide on glucagon receptor activity in the liver" to "A study in people with obesity to test the effects of BI 456906 compared with semaglutide on glucagon receptor activity in the liver"
    - **Official Title:** Updated from "Open-label , , Randomised, 3 Parallel-group, Phase I Clinical Trial to Investigate BI 456906occupancy of Glucagon Receptorsin Liver and Glucagon-like Peptide 1receptors in Pancreas in Comparison With Semaglutide After Administration of Radiolabeled Tracer in Male and Female Subjectswith Obesityusing PET and MRI" to "Open-label , , Randomised, 4 Parallel-group, Phase I Clinical Trial to Investigate 456906 Occupancy of Glucagon Receptors in Liver and Glucagon-like Peptide 1 Receptors in Pancreas in Comparison With Semaglutide After Administration of Radiolabeled Tracer in Male and Female Subjects With Obesity Using PET and MRI"
    - **Study Completion Date:** Updated from "Oct 6, 2025 [Anticipated] to Nov 3, 2025 [Anticipated]
    - **Number of arms:** Updated from 3 to 4
    - **Enrollment:** Updated from 21 [Anticipated] to 30 [Anticipated]
    - Brief Summary, Arms and Interventions, Outcome Measures were also updated
- **Read more:** NCT05202353
- **Implications:** N/A

REGULATORY

8 **EU to review Lilly's multi-dose pen for MOUNJARO on heels of UK launch [EU]**
Feb 20, 2024

- According to the draft agenda published on Feb 19, 2024, the EMA's CHMP is scheduled to deliberate on extending the market authorization for Eli Lilly's MOUNJARO (tirzepatide) to include its multi-dose, pre-filled KwikPen
- Lilly's extension application seeks to add six new strengths of MOUNJARO —including its 2.5, 5, 7.5, 10, 12.5 and 15 mg doses each to be used with the KwikPen, which can deliver four weekly SC injections
- According to Reuters, the EMA's review comes a week after MOUNJARO launched in Britain, making it Lilly's fourth European launch of the top-selling diabetes drug, following Germany, Switzerland, and Poland
    - British pharmacies have already started fulfilling orders for MOUNJARO, with some reporting tens of thousands of patients on their waitlists
- **Read more:** BioSpace
- **Implications:** In the United States, Eli Lilly has introduced a single-use auto-injector, while in the EU, Lilly opted to release an older version of its auto-injector, which is designed for multiple uses. Like Novo Nordisk, Lilly has been actively addressing the high demand for Mounjaro in the U.S. market. It's important to highlight that some supply issues may stem from limited auto-injector production capacity, which was probably one of the factors hat influenced their decision to offer the KwikPen in the EU.

COMMERCIAL

9 **Stock Watch: Novo Edges ahead of Lilly in GLP-1 agonist battle [U.S.]**
Feb 20, 2024

- Novo Nordisk and Eli Lilly, are the major players in the GLP-1 agonist market for diabetes and obesity, have consistently reported quarterly results in the same period, with Novo Nordisk usually preceding Eli Lilly's reports
    - This strategic timing impacts market perception and stock performance
- In Q4 2023, Novo Nordisk's results showcased significant growth, with sales increasing by 37% vs. Q4 2022. OZEMPIC (semaglutide) and WEGOVY (semaglutide), played a pivotal role, with OZEMPIC sales soaring by 77% and WEGOVY by 293%
    - Novo Nordisk experienced cannibalization of its first-generation GLP-1 products by newer, more advanced offerings like OZEMPIC and WEGOVY. VICTOZA and SAXENDA sales declined sharply, reflecting a shift in consumer preference towards newer treatments
- Despite challenges in its insulin franchise due to market dynamics like the Inflation Reduction Act, Novo Nordisk managed to maintain resilience, with insulin sales surpassing analysts' estimates by 1%. The rise of GLP-1 agonists mitigated potential losses for insulin manufacturers
- In Q4 2023, Eli Lilly's results were notable, with strong growth in MOUNJARO (tirzepatide), which witnessed a staggering 690%

sales increase

- However, concerns arose over sales guidance falling below analysts' expectations, possibly due to supply constraints and cautious outlook regarding GLP-1 agonist markets

- **Read more:** Scrip *(Subscription required)*

- **Implications:** The strategic timing of Novo Nordisk's earnings report, usually released before Eli Lilly's, can influence investor sentiment and stock valuation in the short term. Both companies show impressive growth momentum driven by T2D/obesity assets, reflecting the high demand.

10 **CVS executive criticizes obesity drugs over 'egregious' pricing [U.S.] [Article]**
Feb 21, 2024

- According to Sree Chaguturu, CVS Health, Chief Medical Officer, the cost of new medicines for weight loss and diabetes has gotten out of control
- Sree Chaguturu stated that, "*The prices are $1,000 a month. It's egregious pricing that's outside of the needs of normal, regular, everyday Americans"*
- In Dec 2023, CVS executives warned that OZEMPIC (semaglutide), ZEPBOUND (tirzepatide) and other drugs known as GLP-1s are generating billions of dollars in revenue for their manufacturers but their skyrocketing popularity is also contributing to increased pharmacy costs

- **Read more:** BNN Press Release

- **Implications:** Employers and commercial insurers generally cover GLP-1 medications like Ozempic and Mounjaro for diabetes management but frequently do not extend coverage for weight loss, a policy also reflected by Medicare and most state Medicaid programs. This limited coverage significantly restricts access to these treatments for weight management

11 **Weight-loss drugs could boost U.S. GDP by 1% in coming years, Goldman says [U.S.]**
Feb 22, 2024

- According to Goldman Sachs, the widespread use of powerful new weight-loss drugs in the U.S. could boost gross domestic product by 1% in the coming years as lower obesity-related complications are likely to boost workplace efficiency
- Some analysts have predicted the market for weight-loss drugs could reach $100 Bn a year by the end of the decade, with OZEMPIC maker Novo Nordisk and MOUNJARO producer Eli Lilly leading the race

  - GLP-1 agonists, are being keenly pursued by several companies and more could enter the market depending on clinical trials
- The brokerage estimated weight-loss drugs could bolster U.S. GDP by 0.4% in a scenario with 30 Mn users, and could rise to 1% with 60 Mn users

  - The current wave of healthcare innovation such as AI-powered drug discovery coupled with GLP-1s could raise the level of the U.S. GDP by 1.3% in the coming years, equivalent to $360 Bn per year in current exchange rates, with potential for an increase ranging from 0.6% to 3.2%

- **Read more:** Reuters

- **Implications:** The potential rise in GDP highlights the significant economic benefits of reducing obesity-related health complications.

12 **OZEMPIC and WEGOVY sales are so hot they're powering Denmark's GDP [Denmark]**
Feb 20, 2024

- Denmark's gross domestic product increased by 2% in Q4 2023 due to soaring demand for OZEMPIC (semaglutide) and WEGOVY (semaglutide), used to treat diabetes and obesity

  - Statistics Denmark reported in a preliminary reading that that the pharmaceutical industry was a driving force for the nation's growing economy in Q4 and FY 2023
- Skyrocketing sales of OZEMPIC and WEGOVY have made Novo Nordisk the most valuable company in the EU

- **Read more:** Quartz

- **Implications:** The surge in demand for weight-loss drugs like Ozempic and Wegovy has significantly contributed to Denmark's economic growth, with Novo Nordisk's booming sales driving a 2% increase in the country's GDP last quarter. This pharmaceutical success not only underscores the industry's impact on national economies but also positions Novo Nordisk on a path toward becoming one of the first pharma companies to reach a $1 trillion market cap

13 **Eli Lilly and Company discloses Form 10-K including orforglipron related information [Japan]**
Feb 22, 2024

- Chugai issued a press release regarding Eli Lilly disclosing a form 10-K, including economic conditions of orforglipron
- The Form 10-K includes following description:

  - *"We have a license agreement with Chugai Pharmaceutical which provides us with the worldwide development and commercialization rights to orforglipron. Chugai has the right to receive tiered royalty payments on future worldwide net sales from mid-single digits to low teens if the product is successfully commercialized. As of December 31, 2023, Chugai is eligible to receive up to $140.0 million contingent upon the achievement of success-based regulatory milestones and up to $250.0 million in a series of sales-based milestones, contingent upon the commercial success of orforglipron. During the years*

ended December 31, 2023, 2022, and 2021, milestone payments to Chugai were not material"

- **Read more:** Chugai Press Release; Eli Lilly Form 10-K, Pharma Japan *(Subscription required)*
- **Implications:** Chugai Pharmaceutical, a subsidiary controlled by Hoffmann-La Roche, is eligible to receive tiered royalty payments on future worldwide net sales from mid-single digits to low teens if orforglipron is successfully commercialized.

14 **As WEGOVY hits Japan market, Novo re-stresses need for proper use [Japan]**
Feb 26, 2024

- On Feb 22, 2024, Novo Nordisk launched WEGOVY (semaglutide) in Japan as the first obesity drug in over three decades
  - Upon the rollout, the company vowed to ensure its proper use and endeavor to address inappropriate off-label administration
- According to data presented to the Central Social Insurance Medical Council, peak sales are projected at ¥32.8 Bn in the fifth year on the market, with the drug expected to treat 100,000 patients
- Mariko Shimizu, Head of the Obesity Business, Novo Nordisk Japan, mentioned that, "*Novo will make sure that the medicine will be distributed to wholesalers with cooperative relationships with medical institutions that comply with the drug's optimal use guidelines compiled by the MHLW. "Not all wholesalers are subject to (its distribution)"*
- Shimizu stressed that although manufacturers cannot impose binding transaction rules on distributors, the company will strive to provide information and thorough explanations on proper use
  - Novo Nordisk sales representatives will meticulously detail the drug to doctors and pharmacists as well
- Kasper Bødker Mejlvang, President, Novo Nordisk Japan, emphasized that as demand for WEGOVY grows globally, the company is investigating its API manufacturing capacity to ensure a stable supply regime

- **Read more:** Pharma Japan *(Subscription required),* NKH World Japan
- **Implications:** N/A

15 **India pharma companies develop versions of WEGOVY to get in on weight-loss windfall [India]**
Feb 22, 2024

- Indian drugmakers are developing their own versions of Novo Nordisk's wildly in demand WEGOVY (semaglutide)
- With some analysts predicting a weight-loss market reaching $100 Bn a year or more by the end of the decade, executives at Sun Pharma, Cipla, Dr Reddy's and Lupin mentioned they started work on WEGOVY versions
- Novo Nordisk has been unable to produce enough WEGOVY to meet demand in more than half a dozen countries where it has already launched, amid record global obesity rates and people looking for easier alternatives to diet and exercise

- **Read more:** The Economic Times, Business Today
- **Implications:** Indian pharmaceutical companies, including Sun Pharma, Cipla, Dr. Reddy's, and Lupin, are creating their own versions of the weight-loss drug WEGOVY, aiming to tap into a market potentially worth over $100 billion by the end of the decade.

GENERAL

16 **Opinion: I see patients every day who need OZEMPIC and can't get it [U.S.]**
Feb 19, 2024

- According to Jody Dushay, top shelf medications for weight loss are out of reach for many. Millions have access only to medications approved decades ago
- Dushay discussed that for many people, the most powerful tools for medical weight management are the GLP1 agonist
- As of 2024, insurance, not body weight or BMI, has become the most important vital sign for doctors who see patients for medical weight management
  - Insurance now determines the practitioners can use Stanley or Playskool tools to construct a medical treatment plan for patients with obesity. Often for Medicare patients, the toolbox is flimsy
- Since Medicare will not pay for any medications with the U.S. FDA indication for weight loss, prior ability to prescribe GLP1 agents approved for type 2 diabetes for some patients gave me access to those more powerful tools, which Dushay tried to use for certain people with high body weight and several weight-associated comorbidities

- **Read more:** CNN
- **Implications:** Insurance limitations, not clinical need, increasingly dictate access to advanced GLP-1 medications for weight loss, leaving many patients, especially those on Medicare, reliant on outdated treatments. This shift compromises the ability to effectively manage obesity and its comorbidities, underscoring a pressing need for policy changes to expand access to these transformative drugs

17 **Veru announces new scientific advisory board for its enobosarm program for high quality weight loss [U.S.]**
Feb 20, 2024

- Veru announced the formation of a new Scientific Advisory Board to support the advancement of enobosarm, an oral novel selective androgen receptor modulator, to avoid muscle loss and augment fat loss when combined with a GLP-1 RA drugs for potentially higher quality weight loss
- The members of Veru's new Scientific Advisory Board are:
  - Dr. Caroline M. Apovian, Co-Director of the Center for Weight Management and Wellness in the Division of Endocrinology, Diabetes, and Hypertension at Brigham and Women's Hospital and Professor of Medicine at Harvard Medical School

- Dr. Shalender Bhasin, Professor of Medicine at the Harvard Medical School, and Director of the Research Program for Men's Health and Aging at the Brigham and Women's Hospital in Boston, Mass
- Dr. Adrian Dobs, Professor of Medicine and Oncology and Director of the Johns Hopkins Clinical Research Network of the Johns Hopkins Institute for Clinical and Translational Research
- Dr. William J. Evans, Adjunct Professor of Medicine in the Division of Geriatrics at the Duke University Medical Center and Human Nutrition in the Department of Nutritional Sciences at the University of California, Berkeley

· **Read more:** Veru Press Release

· **Implications:** Veru Inc. establisheed a Scientific Advisory Board for enobosarm, focusing on obesity treatment by promoting fat loss while preserving muscle, signaling a pioneering approach to high-quality weight management with clinical trials beginning in April 2024

18 **Dario acquires Twill Creating one of the most comprehensive digital health platform across the most prevalent chronic conditions [U.S.]**

Feb 21, 2024

- DarioHealth acquired Twill, the combination enables Dario to create one of the most comprehensive digital offerings in the market for chronic conditions, spanning a wide spectrum of health and well-being needs from emotional health to the costliest chronic conditions
  - The transaction created immediate scale, with three of the top eight national health plans, multiple fortune 100 employers and several major pharmaceutical companies as customers

· **Read more:** DarioHealth Press Release

· **Implications:** Twill partners with employers, health plans, and pharma companies to improve outcomes and deliver measurable value through one unified care platform

KEY UPCOMING EVENTS

UBS European Healthcare Conference

· **Roche:** Feb 27, 2024 (Roche Investor update)

· **Astrazeneca:** Feb 27, 2024 (Astrazeneca Investor update)

Cowen 44th Annual Health Care Conference

· **Astrazeneca:** Mar 4, 2024 (Astrazeneca Investor update)

· **Roche:** Mar 6, 2024 (Roche Investor update)

Barclays 26th Annual Global Healthcare Conference

· **Astrazeneca:** Mar 12, 2024 (Astrazeneca Investor update)

· **Roche:** Mar 12, 2024 (Roche Investor update)

Capital Markets Day 2024:

· **Novo Nordisk:** Mar 7, 2024 (Novo Nordisk Investor update)

Annual General Meeting 2024:

· **Roche:** Mar 12, 2024 (Roche Investor update)

· **Novo Nordisk:** Mar 21, 2024 (Novo Nordisk Investor update)

Have a great week!
Ben

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