Tuesday, May 14, 2024 at 12:20:58 Eastern Daylight Time

Subject: MTSR1: Weekly Competitive Intelligence Newsletter (Mar 27- Apr 1, 2024)
Date: Monday, April 1, 2024 at 11:27:23 AM Eastern Daylight Time
From: Diksha Matta <dmatta@sai-med.com>
To: Metsera <metsera@populationhp.com>
CC: Benjamin Kumpfmueller <bkumpfmueller@sai-med.com>, Diane Suchon <DSuchon@sai-med.com>, Nidhi Srivastava <nidhis@theratraq.com>, Ailen Thomas <AilenT@theratraq.com>
Attachments: image002.png, image001.wmz

Hi Metsera Team,

Please find below the weekly 'Competitive Intelligence Newsletter' for the week: Mar 27-Apr 1, 2024

DASHBOARD

KEY TAKEAWAYS OF THE WEEK (Mar 27 – Apr 1, 2024)

- **Clinical –** During Q4 and FY 2023 earnings call, Altimmune reported pemvidutide saw patients lose about 75% fat and only 25% muscle in results of a Phase II clinical trial [Global]
- **Clinical –** Viking Therapeutics announced positive results from Phase I multiple ascending dose clinical trial of VK2735 (undisclosed) [U.S.]
- **Regulatory –** CinFina Pharma announced the U.S. FDA clearance of its Investigational New Drug Application for CIN-110 (undisclosed) [U.S.]
- **Regulatory –** The UK's MHRA approved Biocon/Zentiva's gSAXENDA (liraglutide) in a 6mg/ml solution for injection in pre-filled pen for the treatment of weight management as an adjunct to a reduced-calorie diet and increased physical activity [UK]
- **Commercial –** According to Eli Lilly some patients may have trouble getting its new weight loss drug ZEPBOUND as complaints of backorders and delays mount across the U.S. [U.S.]

DETAILED NEWS

CLINICAL

1 A new OZEMPIC rival helps patients lose fat, but keep their muscle — the holy grail for a weight-loss drug [Global]
Mar 29, 2024

- During Q4 and FY 2023 earnings call, Altimmune reported its new weekly injectable, pemvidutide, saw patients lose about 75% fat and only 25% muscle in results of a Phase II clinical trial
  - When compared to existing GLP-1 drugs, patients can lose as much as 40% of their muscle mass. Their muscle-to-fat ratio usually still improves, but in particularly vulnerable populations, such as older adults, rapid and significant muscle loss can be a dangerous issu
  - This is why doctors recommend patients on weight-loss drugs do some strength training in tandem with taking their medication
- Pemvidutide is a two-part drug that combines a GLP-1 drug with another in a single shot
  - In this case, it's boosting glucagon, a key blood-sugar-regulating hormone
  - While the GLP-1 reduces a person's appetite, the glucagon is thought to mimic the effects of exercise
- **Read more:** Yahoo News
- **Implications:** Altimmune's experimental drug, pemvidutide, reduced muscle loss targeting obesity and showing promise for treating MASH with a GLP-1 and glucagon combination; results for the MASH study are expected in early 2025

2 Viking Therapeutics announces results from Phase I clinical trial of oral tablet formulation of dual GLP-1/GIP receptor agonist VK2735 [U.S.]
Mar 26, 2024

- Viking Therapeutics announced positive results from Phase I multiple ascending dose (MAD) clinical trial of an oral tablet formulation of VK2735 (undisclosed), a dual agonist of the GLP-1 and GIP receptors
- Based on these Phase I results, the company plans to initiate a Phase II trial with the oral formulation of VK2735 in obesity later in 2024
  - The 28-day MAD study results highlight positive signs of clinical activity following treatment with oral VK2735
  - Overall, no clinically meaningful differences were reported for GI-related AEs among subjects treated with VK2735 vs. placebo. In addition, no serious adverse events have been reported to date

- The Phase I MAD study of oral VK2735 is an extension of the company's Phase I single ascending dose (SAD)/MAD trial of VK2735 administered subcutaneously

- **Read more:** Viking Therapeutics Press Release

- **Implications:** Viking's VK2735 drug achieved a 3.3% weight loss at its 40-mg dose and 1.1% at half strength in 28 days, aligning with market expectations and comparable to Novo Nordisk's oral amycretin's 4% efficacy at similar time point

3 **Lepu Medical Technology (Beijing) doses first patient in phase II clinical trials of GLP-1/GCGR/GIP-Fc fusion protein MWN101 (undisclosed) in type 2 diabetes and obesity or overweight [China]**
Mar 29, 2024

- Lepu Medical Technology announced that, first subjects have been dosed in Phase II clinical trials of MWN101 (undisclosed) in type 2 diabetes (CTR20240817) and obesity or overweight (CTR20240802)
- MWN101 injection is an innovative drug developed by Shanghai Minwei Biotechnology in partnership with Lepu Medical Technology
  - It is the first GLP1/GCGR/GIP-Fc fusion protein drug in China
  - It can regulate human metabolism and control blood sugar through mechanisms such as blood sugar-dependent stimulation of insulin secretion, delaying gastric emptying, and mildly improving metabolism. It is expected to be used to lower blood sugar and lose weight
- The Phase II trials were conducted to evaluate the effectiveness, safety, and PK of MWN101 injection in the treatment of type 2 diabetes and overweight or obesity

- **Read more:** *No link available*

- **Implications:** Lepu Medical's MWN101, a novel GLP-1/GCGR/GIP-Fc fusion protein targeting type 2 diabetes and obesity, enters Phase II trials in China, promising metabolic regulation and weight loss

4 **Trial Update: A study comparing IBI362 (mazdutide) vs semaglutide in Chinese adults with early type 2 diabetes and obesity [China]**
Mar 28, 2024

- A Phase III trial sponsored by Innovent Biologics titled, *"A study comparing IBI362 (mazdutide) vs semaglutide in Chinese adults with early type 2 diabetes and obesity"* has undergone changes
  - **Overall Status:** Updated from 'Not yet recruiting' to 'Recruiting'
  - **SSD:** Updated from Jan 31, 2024 to Feb 29, 2024
  - **PCD:** Updated from May 31, 2024 [Anticipated] to May 31, 2025 [Anticipated]
  - **Condition:** Updated from 'Type 2 Diabetes and Obesity (Chinese Classification Criteria)' to 'Obesity'
  - **Arms and Interventions:** Changes made in assigned interventions

- **Read more:** NCT06184568

- **Implications:** N/A

5 **Trial Update: A study of LY3502970 (orforglipron) in Chinese participants with obesity or are overweight with weight-related comorbidities [China]**
Mar 26, 2024

- A Phase I trial sponsored by Eli Lilly titled, *"A study of LY3502970 (orforglipron) in Chinese participants with obesity or are overweight with weight-related comorbidities"* has undergone changes
  - **Overall Status:** Updated from 'Recruiting' to 'Active, not recruiting'
  - **PCD:** Updated from Nov 29, 2024 [Anticipated] to Jul 2024 [Anticipated]
  - **SCD:** Updated from Nov 29, 2024 [Anticipated] to Jul 2024 [Anticipated]
  - **Location:** Sites were removed and added to location

- **Read more:** NCT06023095

- **Implications:** N/A

6 **Eli Lilly launches Phase III trials for new oral weight-loss pill in India [India]**
Mar 29, 2024

- Eli Lilly has initiated phase three clinical trials in India for its innovative oral weight-loss drug, orforglipron
  - This move marks a significant advancement in the realm of weight management, particularly for individuals with type-two diabetes and those who are overweight or obese with an increased risk of cardiovascular complications
- The trials, aimed at evaluating the safety and efficacy of orforglipron compared to insulin glargine, are underway at 12 sites across India, with a sample size of 120 participants, as per India's clinical trial registry
  - Previous research from Phase II trials unveiled promising results, demonstrating that orforglipron led to notable weight loss ranging from 8.6% to 12.6% after 26 weeks of follow-up, significantly surpassing the effects of a placebo
- Eli Lilly's spokesperson in India highlighted ongoing clinical studies on novel products, including orforglipron, which is positioned as an oral non-peptide GLP-1 receptor agonist. This drug is poised to offer an alternative to injectable weight-loss medications like semaglutide and liraglutide, which have demonstrated effectiveness but pose challenges related to administration

- **Read more:** eHealth Network, The Economic Times

- **Implications:** Eli Lilly has begun Phase III clinical trials in India for orforglipron. Conducted across 12 sites with 120 participants, these trials will assess orforglipron's safety and efficacy against insulin glargine. Preliminary Phase II results showed significant weight loss of 8.6% to 12.6% over 26 weeks, outperforming placebo and indicating the potential of orforglipron as a convenient

alternative to injectable treatments like semaglutide and liraglutide

REGULATORY

7 **Fractyl Health receives FDA IDE approval for the Revita Remain-1 pivotal study of weight maintenance in obesity after discontinuation of GLP-1 based drugs [U.S.]**

Apr 1, 2024

- Fractyl Health announced the U.S. FDA approval of an Investigational Device Exemption (IDE) to study Revita's efficacy in maintaining weight loss following the discontinuation of GLP-1 receptor agonist) drug therapy
- The IDE approval launches the Remain-1 study, set to begin in H2 of 2024
  - Remain-1 is a randomized, double-blind trial of Revita vs. sham procedure in patients who have lost at least 15% total body weight on tirzepatide therapy. It is designed to be a pivotal study to potentially enable registrational filing for Revita for weight maintenance after GLP-1RA discontinuation
  - In parallel with the randomized portion of the Remain-1 study, Fractyl Health also announced Reveal-1, an open-label cohort that will follow a similar patient population and management protocol with anticipated open-label data updates as the study progresses
- The patient population for Remain-1 will consist of obese individuals with a BMI ≥ 30 kg/m^2. These GLP-1RA-naïve individuals will initiate tirzepatide therapy, titrated to achieve at least a 15% total body weight loss, followed by discontinuation of tirzepatide and randomization to either Revita treatment or a sham procedure. At least 315 subjects will be randomized 2:1 to Revita or sham
- The primary objectives of the study are
  - To demonstrate that Revita is superior to sham in percent change in body weight from baseline to week 24, and
  - To demonstrate that a majority of Revita participants maintain clinically significant weight loss after discontinuing tirzepatide therapy

- **Read more:** GlobeNewswire

- **Implications:** Revita, is an endoscopic procedure targeting the duodenal lining to improve metabolic disease management. Fractyl Health's is positioning Revita to maintain weight loss after GLP-1 receptor agonist therapy cessation

8 **CinFina Pharma announces FDA clearance of investigational new drug application and first participants dosed in Phase I trial of CIN-110 (undisclosed) for the treatment of obesity [U.S.]**

Mar 26, 2024

- CinFina Pharma announced the U.S. FDA clearance of its Investigational New Drug Application for CIN-110 (undisclosed), a PYY3-36 analog, allowing the first in-human clinical study to proceed
  - CinFina also announced the first cohort of participants has been dosed
- The trial will evaluate the safety, tolerability, PK, PD, and immunogenicity of CIN-110 in a randomized, double-blind, placebo-controlled, single ascending dose study in otherwise healthy subjects with obesity
- CIN-110 is a stable and long-acting analog of PYY3-36 being developed both as a monotherapy and co-administration agent for obesity
- PD evaluation of CIN-110 demonstrated that repeat SC dosing leads to significant reduction of food intake and body weight in obese, non-human primates and rodents

- **Read more:** BioSpace, Yahoo Finance

- **Implications:** CinFina Pharma's CIN-110, a PYY3-36 analog targeting obesity, enters Phase I trials after FDA clearance, focusing on safety and efficacy in reducing food intake and body weight

9 **Biocon gains after receiving MHRA UK approval for Liraglutide injection [UK]**

Apr 1, 2024

- Biocon through its European partner, Zentiva, has received approval from the UK's MHRA, for its complex formulation gSAXENDA (liraglutide) in a 6mg/ml solution for injection in pre-filled pen, used in the treatment of weight management as an adjunct to a reduced-calorie diet and increased physical activity
  - On Mar 27, 2024, the UK's MHRA approved gVICOTZA (liraglutide) for the treatment of Type 2 Diabetes Mellitus, filed through Zentiva
  - The approvals will further strengthen Biocon's portfolio of vertically integrated, complex drug products

- **Read more:** Biocon Stock Exchange Disclosure, Business Standard

- **Implications:** The approval boosts Biocon's generics business, focusing on GLPs. In partnership with Zentiva, Biocon aims to commercialize Liraglutide in the UK addressing a substantial market opportunity in diabetes and weight loss

10 **Substandard semaglutide vials [Australia]**

Mar 28, 2024

- The Therapeutic Goods Administration (TGA) has tested a product, labelled 'Semaglutide 2.64mg/mL, L-carnitine 100mg/mL B12 .05mg/mL solution for SC injection 3', and found that:
  - The vials contain ten times the amount of vitamin B12 (cyanocablamin) labelled
  - The content of L-carnatine, was estimated at 0.5-0.7mg/mL, well below the labelled 100mg/mL
- Consumers are advised that semaglutide is a prescription-only medicine in Australia
- The medicine, which purported to be compounded had solution within blue capped vials which was a distinctive red colour which is not the expected appearance, and was supplied to patients via regular mail, not purchased and dispensed from an Australian pharmacy
  - SC injection of this compounded semaglutide like product is alleged to have resulted in the hospitalisation of a patient for peripheral neuropathy

- The product tested is not listed in the Australian Register of Therapeutic Goods and has not been assessed by the TGA for quality, safety or efficacy as required under Australian legislation. The place of manufacture has not been determined
- The TGA has published specific compounding safety information for semaglutide-like products. Consumers should be aware that medicines manufactured by compounding pharmacists are not assessed by the TGA for safety, quality, or efficacy

- **Read more:** TGA Press Release

- **Implications:** N/A

COMMERCIAL

11 **Demand for weight-loss drug ZEPBOUND is so strong that Eli Lilly is warning patients may leave pharmacies empty-handed [U.S.]**
Mar 30, 2024

- According to Eli Lilly some patients may have trouble getting its new weight loss drug ZEPBOUND (tirzepatide) as complaints of backorders and delays mount across the U.S.
- A Eli Lilly spokesperson said, *"Due to the unprecedented demand for these medicines, some patients may experience difficulty when trying to fill their prescription at their pharmacy"*
- The U.S. FDA doesn't currently consider the obesity shot in shortage and the company continues to manufacture and ship all doses of ZEPBOUND
- Rite Aid and Amazon Pharmacy said that the drug was in short supply, and multiple pharmacists across the U.S. told Bloomberg News that some or all the doses of the drug were on backorder

- **Read more:** Fortune

- **Implications:** Eli Lilly's Zepbound is already facing supply constraints due to exceptionally high demand since its launch less than six months ago. Despite efforts to maintain production across all doses, pharmacies, including Amazon Pharmacy, are experiencing shortages, reflecting the challenge in meeting nationwide demand for this popular weight loss treatment.

12 **The IRA, medicare and the high costs of GLP-1 drugs Like WEGOVY [U.S.]**
Mar 29, 2024

- On Mar 27, 2024, Sen. Bernie Sanders, Chairman, Senate Health, Education, Labor, and Pensions Committee, called on Novo Nordisk for the "outrageous" cost of its OZEMPIC (semaglutide) type 2 diabetes medication and weight-loss drug WEGOVY (semaglutide), after a study was published in the *Journal of the American Medical Association*
- Sanders mentioned that Novo Nordisk is charging Americans nearly $1,000 a month for OZEMPIC, while the same exact product can be purchased for just $155 a month in Canada and $59 in Germany
- The high costs of GLP-1 drugs is an issue that will continue to fester amid surging demand for these blockbusters
- Sanders wants Novo Nordisk to lower the U.S. prices for OZEMPIC and WEGOVY like it did with insulin products by some 75% in the U.S.

- **Read more:** Biospace, USA Today

- **Implications:** The rising cost of GLP-1 medications is increasingly scrutinized. Expectations are high that CMS could use the IRA to negotiate lower prices for expensive treatments like Wegovy soon, focusing on cost reduction

13 **Weight-loss drug deals to drive around 4% of Gerresheimer yearly growth, CEO says [Germany]**
Mar 29, 2024

- Dietmar Siemssen, CEO, Gerresheimer, expects about 4% of the company's revenue growth per year from deals to supply makers of drugs for weight loss and diabetes with vials, cartridges, syringes and autoinjectors
- The company reported in Feb 2024, that it expects to grow an average of 10% per year. Nearly half of that will come from its association with drugs in the GLP-1 class

- **Read more:** XM, The Economic Times

- **Implications:** Gerresheimer, known for manufacturing injection pens for companies like Novo and Lilly, anticipates that contracts for weight-loss drugs will contribute to around 4% of its annual growth. This projection underscores the significant impact of the growing demand for obesity treatments on the supply chain and manufacturing sectors within the pharmaceutical industry

14 **Novo Nordisk's $1,000 diabetes drug Ozempic can be made for less than $5 a month, study suggests [U.S.]**
Mar 27, 2024

- A study 'Estimated Sustainable Cost-Based Prices for Diabetes Medicines' published in *JAMA Network Open* suggested, the blockbuster diabetes drug Ozempic could be manufactured for less than $5 a month, even as Novo Nordisk charges close to $1,000 per month for the injection in the U.S. before insurance
- The study, from researchers at Yale University, King's College Hospital in London and the nonprofit Doctors Without Borders, raised more questions about the hefty price tag of the top-selling diabetes treatment and similar drugs for weight loss
  - Ozempic can generally be produced for less than various forms of insulin, according to the study
- Researchers found that a month's supply of the treatment could be made for an estimated 89 cents to $4.73, figures that include a profit margin
  - They evaluated manufacturing costs for the weekly injection along with a profit margin with an allowance for tax to produce those estimates, which they call "cost-based prices."
- The researchers concluded, Novo Nordisk's list price for a monthly package of Ozempic is $935.77 before insurance and other rebates. The findings suggest that GLP-1s "can likely be manufactured for prices far below current prices, enabling wider access

- Novo Nordisk declined to provide production costs for Ozempic and its weight loss drug counterpart Wegovy

- **Read more:** CNBC

- **Implications:** The study showed that Novo Nordisk's Ozempic costs less than $5 to produce, with almost a 20,000% markup, prompting swift backlash. Lawmakers and advocates are urging Novo Nordisk to lower its list price, currently at $935.77 for a month's supply. Senator Bernie Sanders plans to meet with the company's CEO to discuss possible solutions, amid calls for legislative action and potential hearings on drug pricing

GENERAL

15 **With GIP, obesity research is at odds [Global]**
Mar 27, 2024

- Over a decade ago, researchers discovered a new approach to treating obesity and diabetes in mice by activating gut hormone receptors GLP-1 and GIP, leading to the development of Eli Lilly's MOUNJARO (tirzepatide) and ZEPBOUND (tirzepatide)
- Amgen's research initially focused on GIP receptor antagonism for weight loss but Yie and Lloyd, scientists at Amgen, were supportive of the GIP antagonist project because genetic studies in humans had suggested lower levels of the GIP receptor were associated with lower body mass index
- Amgen published an early-stage study in *Nature Metabolism* that showed its GLP-1 agonist and GIP antagonist known as MariTide could elicit up to 14% weight loss in humans
  - GIP receptor agonism and antagonism can lead to weight loss is a paradox, and researchers have no solid explanations
- But over the last 10 years, scientific interest in GIP has reignited, in part from the success of incretin therapies
  - The market for incretin-based therapies generated billions of dollars in sales and it turned Lilly and Novo Nordisk into two of the most valuable companies in the world
  - With the obesity drug market projected to reach $100 billion by 2030, companies like Amgen and Lilly are fiercely defending their approaches to incretin-based therapies, emphasizing the importance of side effects in determining success

- **Read more:** Endpoints News *(Subscription required)*

- **Implications:** GIP receptor agonism and antagonism can lead to weight loss remains to be a paradox. However, it is not stopping the incretin-based therapy market's success which is expected to hit $100 billion by 2030

16 **OZEMPIC, weight-loss drugs force a change of focus on health**
Mar 30, 2024

- During an interview with The Street, Sabrena Jo, Senior Director, science, and research at the American Council on Exercise (ACE) mentioned that GLP-1 medications, like OZEMPIC, are highlighting the necessity for fitness coaches to recalibrate their focus towards comprehensive lifestyle factors, including physical activity, for individuals using these treatments by
  - Amplifying the role of physical activity
  - Addressing side effects with lifestyle modifications
  - Education on sustainable health behaviors
  - Personalized coaching strategies
  - Collaborative care approach

- **Read more:** The Street

- **Implications:** N/A

17 **Popular obesity drugs may lead to medical procedure complications [U.S.]**
Mar 27, 2024

- According to population-based study is published in the *Gastroenterology* journal, Cedars-Sinai investigators found GLP-1 receptor agonists medications like OZEMPIC (semaglutide) and WEGOVY (semaglutide) that are used to treat diabetes and obesity are associated with an increased risk of aspiration pneumonia following endoscopy
  - The study analyzed data from nearly 1 million de-identified U.S. patients who underwent upper or lower endoscopy procedures between Jan 2018 - Dec 2020
  - Patients who were prescribed GLP-1RA medications had a 33% higher chance of experiencing aspiration pneumonia than those who did not take these medications before the procedure
- This comparison also considered other variables that could influence the outcome to ensure a fair comparison between the two groups

- **Read more:** Cedars Sinai Press Release, U.S. News

- **Implications:** The study's findings on surgery risks for patients taking GLP-1 receptor agonists like Ozempic and Wegovy could impact Novo's market positioning. Highlighting the need for careful pre-surgical planning and potentially pausing medication to prevent aspiration pneumonia underscores a critical consideration in their use for weight loss.

18 **iBio partners with AstralBio to develop obesity treatments using AI-driven platform [U.S.]**
Mar 27, 2024

- iBio entered into a collaboration agreement with AstralBio to discover, engineer and develop novel antibodies to treat obesity and other cardiometabolic conditions
  - The company will use a portion of the net proceeds to support new partnerships, such as this collaboration with AstralBio
- As a result of this collaboration, iBio and AstralBio have agreed to initiate the development of a novel lead program focused on targeting the transforming growth factor beta (TGFb) superfamily for the treatment of muscle wasting and obesity
  - Upon mutual consent, the parties may also expand the collaboration to include additional targets in other fields

- **Read more:** iBio Press Release

- **Implications:** The collaboration between iBio and AstralBio targets the transforming growth factor beta (TGFb) superfamily for the treatment of muscle wasting and obesity. This approach harnesses AI-powered technology to develop antibodies against challenging targets, potentially offering a transformative solution to address these conditions

19 **Hoth Therapeutics' wholly owned subsidiary Merveille.ai, advances AI-driven discovery for obesity treatment [U.S.]**
Mar 27, 2024

- Hoth Therapeutics announced a significant breakthrough by its subsidiary, Merveille.ai, in the field of obesity treatment
  - Utilizing advanced AI, Merveille.ai has identified a promising new therapeutic candidate, culminating in a strategic patent filing
- Capitalizing on Hoth Therapeutics' diverse portfolio, Merveille.ai employed a sophisticated large language model to analyze and identify synergies within existing compounds
- This innovative approach has led to the discovery of a potential obesity therapeutic that complements Hoth's existing lineup

- **Read more:** PR Newswire

- **Implications:** Leveraging advanced artificial intelligence, Merveille.ai is identifying synergies within existing compounds to uncover a potential obesity therapeutic, complementing Hoth's portfolio. With plans for a pre-clinical study in 2024 and collaboration with the Nvidia Developer Program, Merveille.ai is poised to advance its research to the next milestone

KEY UPCOMING EVENTS

Q1 2024 Earnings Call:

- **Roche:** Apr 24, 2024 (Roche Investor update)
- **AstraZeneca:** Apr 25, 2024 (AstraZeneca Investor update)
- **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)
- **Amgen:** May 5, 2024 (Amgen Investor update)

Thank you!
Kind regards,
Diksha

Diksha Matta
Project Manager

SAI MedPartners LLC
4970 DeMoss Blvd Suite 300
Reading, PA 19606
t: +1 (484) 877-0698
e: dmatta@sai-med.com

www.sai-med.com