Subject: MTSR1: Weekly Competitive Intelligence Newsletter (Feb 27 – Mar 4, 2024)
Date: Monday, March 4, 2024 at 11:23:01 AM Eastern Standard Time
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Attachments: image003.png, image002.wmz

Hi Metsera Team,

Please find below the weekly 'Competitive Intelligence Newsletter' for the week: Feb 27 – Mar 4, 2024

DASHBOARD

KEY TAKEAWAYS OF THE WEEK (Feb 27 – Mar 04, 2024)

- **Clinical –** Viking Therapeutics announced positive top-line results from Phase II clinical trial of VK2735, a dual agonist of GLP-1 and GIP receptors in development for the potential treatment of various metabolic disorders such as obesity [Global]
- **Regulatory –** NeuroBo Pharmaceuticals has received first site Institutional Review Board approval to proceed with the Phase 1 clinical trial of DA-1726, a novel dual oxyntomodulin analog agonist [U.S.]
- **Commercial –** Eli Lilly expects to launch MOUNJARO (tirzepatide) in India as early as next year [India]

DETAILED NEWS

CLINICAL

1 Viking Therapeutics announces positive top-line results from Phase II VENTURE Trial of Dual GLP-1/GIP receptor agonist VK2735 in patients with obesity [Global]
Feb 27, 2024

- Viking Therapeutics announced positive top-line results Phase II clinical trial of VK2735 (undisclosed), a dual agonist of GLP-1 and GIP receptors in development for the potential treatment of various metabolic disorders such as obesity
- The Phase II VENTURE trial successfully achieved its primary endpoint and all secondary endpoints, with patients receiving VK2735 demonstrating statistically significant reductions in body weight vs. placebo
  - Additionally, the study showed VK2735 treatment to be safe and well tolerated with the majority of treatment emergent adverse events (TEAEs) being categorized as mild or moderate
  - Based on these findings, Viking intends to meet with the U.S. FDA and discuss next steps in the development of VK2735
- Top-line study results include patients receiving weekly doses of VK2735 demonstrated statistically significant reductions in mean body weight after 13 weeks, ranging up to 14.7% from baseline
- VK2735 demonstrated encouraging safety and tolerability following 13 weeks of once-weekly dosing
- **Read more:** Viking Therapeutics Press Release, Endpoints News *(Subscription required)*
- **Implications:** Viking therapeutics showed data with patients on 15 mg dose of the treatment lost 13.1% of their body weight on average after 13 weeks. The majority of adverse side effects that patients experienced after starting Viking's drug were mild or moderate. The company is now an attractive deal target for larger companies like Merck and Sanofi trying to break into the space or expand their obesity treatment offering. Nevertheless, the current market cap of ~$9B would require significant capital for a M&A deal.

2 Trial update: A study of investigational tirzepatide (LY3298176) doses in participants with type 2 diabetes and obesity [Global]
Feb 29, 2024

- A Phase II trial sponsored by Eli Lilly titled, "*A study of investigational tirzepatide (LY3298176) doses in participants with type 2 diabetes and obesity"* has undergone changes
  - **PCD:** Updated from Jan 22, 2025 [Anticipated] to Dec 24, 2024 [Anticipated]

- **SCD:** Updated from Oct 29, 2025 [Anticipated] to Sep 30, 2025 [Anticipated]
- **Contacts/Locations:** Multiple sites were added and removed

- **Read more:** NCT06037252
- **Implications:** This phase 2 trial for tirzepatide is testing "high-dose" tirzepatide which indicates that Lilly might be testing higher doses for tirzepatide in order to demonstrate higher weight loss.

3 **Trial update: A study of tirzepatide (LY3298176) in participants with overweight or obesity and chronic kidney disease with or without type 2 diabetes (TREASURE-CKD) [Global]**
Feb 29, 2024

- A Phase II trial sponsored by Eli Lilly titled, "*A study of tirzepatide (LY3298176) in participants with overweight or obesity and chronic kidney disease with or without type 2 diabetes (TREASURE-CKD)"* has undergone changes
  - **Contacts/Locations:** Multiple sites were added and removed
- **Read more:** NCT05536804
- **Implications:** N/A

4 **Trial update: A research study to see how semaglutide helps people with excess weight, lose weight (STEP UP) (STEP UP) [Global]**
Feb 29, 2024

- A Phase III trial sponsored by Novo Nordisk titled, "*A research study to see how semaglutide helps people with excess weight, lose weight (STEP UP)"* has undergone changes
  - **PCD:** Updated from Sep 13, 2024 [Anticipated] to Sep 20, 2024 [Anticipated]
  - **SCD:** Updated from Nov 15, 2024 [Anticipated] to Nov 22, 2024 [Anticipated]
  - **Contacts/Locations:** Multiple sites were added and removed
- **Read more:** NCT05646706
- **Implications:** N/A

5 **Trial update: A study of tirzepatide (LY3298176) once weekly in adolescent participants who have obesity or overweight with weight-related comorbidities [Global]**
Feb 29, 2024

- A Phase III trial sponsored by Eli Lilly titled, "*A study of tirzepatide (LY3298176) once weekly in adolescent participants who have obesity or overweight with weight-related comorbidities"* has undergone changes
  - **Brief Title:** Updated from 'A Study of Tirzepatide (LY3298176) Once Weekly in Adolescent Participants Who Have Obesity, or Are Overweight With Weight-Related Comorbidities' to 'A Study of Tirzepatide (LY3298176) Once Weekly in Adolescent Participants Who Have Obesity or Overweight With Weight-Related Comorbidities'
  - **Contacts/Locations:** Multiple sites were added and removed
- **Read more:** NCT06075667
- **Implications:** N/A

6 **New Trial: A study of RGT001-075 (undisclosed) in adult patients with obesity [U.S.]**
Feb 28, 2024

- Regor Pharmaceuticals initiated a Phase II trial to compare RGT001-075 (oral GLP-1 RA) with placebo in adult patients with obesity or overweight
  - **Trial details:** N = 60; Status: Not Yet Recruiting; Start date: Mar 2024; PCD: Jun 2024; SCD: Jul 2024; Location: U.S.
- **Read more:** NCT06277934
- **Implications:** N/A

7 **Trial update: Effect of administration of itraconazole on the pharmacokinetics of S-309309 (MGAT2 inhibitor) in healthy participants [U.S.]**
Feb 29, 2024

- A Phase I trial sponsored by Shionogi titled, "*Effect of administration of itraconazole on the pharmacokinetics of S-309309 (undisclosed) in healthy participants"* has undergone changes
  - **Overall Status:** Updated from 'Active, not recruiting' to 'Completed'
  - **SCD:** Updated from Feb 16, 2024 [Anticipated] to Feb 14, 2024 [Actual]
- **Read more:** NCT06106334

- **Implications:** N/A

8 **Trial update: Ph 2 study of the safety and efficacy of three HU6 dose levels and placebo in obese subjects with type 2 diabetes at risk of nonalcoholic steatohepatitis [U.S.]**

Feb 29, 2024

- A Phase II trial sponsored by Rivus Pharmaceuticals titled, "*Ph 2 study of the safety and efficacy of three HU6 dose levels and placebo in obese subjects with type 2 diabetes at risk of nonalcoholic steatohepatitis"* has undergone changes
  - **Contacts/Locations:** Multiple sites were added and removed
- **Read more:** NCT05979779
- **Implications:** N/A

9 **Trial update: A study of how CagriSema works on appetite in people with excess body weight [Germany]**

Feb 28, 2024

- A Phase I study sponsored by Novo Nordisk titled, "*A study of how CagriSema works on appetite in people with excess body weight"* has undergone changes
  - **Overall Status:** Updated from 'Not yet recruiting' to 'Recruiting'
- **Read more:** NCT06267092
- **Implications:** N/A

10 **Trial update: Study of INV-202 (CB1r Blocker) in patients with obesity and metabolic syndrome [Canada]**

Feb 26, 2024

- A Phase II study sponsored by Inversago Pharma (now Novo Nordisk) titled, "*Study of INV-202 in patients with obesity and metabolic syndrome"* has undergone changes
  - **Overall Status:** Updated from 'Recruiting' to 'Active, not recruiting'
  - **Enrollment:** Updated from 240 [Anticipated] to 243 [Actual]
  - **Contacts/Locations:** Multiple sites were removed and added
- **Read more:** NCT05891834
- **Implications:** N/A

11 **New Trial: Dose-finding study evaluating effect on body composition of enobosarm in patients taking a GLP-1 for chronic weight mgmt**

Feb 28, 2024

- Veru initiated Phase II trial to evaluate the effect on body composition and safety of enobosarm in patients treated with GLP-1 receptor agonists for chronic weight management
  - **Aim:** Dose-finding study evaluating effect on body composition of enobosarm in patients taking a GLP-1 for chronic weight mgmt
  - **Trial details:** N= 90; Status: Not Yet Recruiting; Start date: Apr 29, 2024; PCD: Dec 20, 2024; SCD: Apr 30, 2025; Location: Undisclosed
- **Read more:** NCT06282458
- **Implications:** Enobosarm, tested in 27 clinical trials with 1,581 participants for up to three years, was well-tolerated without increasing gastrointestinal side effects, unlike GLP-1 RA treatments. It's expected to enhance fat reduction and total weight loss without muscle loss when combined with a GLP-1 RA.

12 **Trial update: A study to test whether multiple doses of BI 456906 have an effect on cardiac safety in people with overweight or obesity**

Mar 01, 2024

- A Phase I study sponsored by Boehringer Ingelheim titled, "*A study to test whether multiple doses of BI 456906 have an effect on cardiac safety in people with overweight or obesity"* has undergone changes
  - **PCD and SCD:** Updated from Mar 24, 2025 [Anticipated] to May 30, 2025 [Anticipated]
  - **Eligibility:** Inclusion Criteria updated from 'Body mass index (BMI) of 27.0 to 34.9 kg/m2 (inclusive) and body weight > 70 kg' to 'Body mass index (BMI) of 27.0 to 39.9 kg/m2 (inclusive) and body weight > 70 kg'
- **Read more:** NCT06200467
- **Implications:** N/A

REGULATORY

13 **Neurobo Pharmaceuticals receives first site IRB approval for its Phase I clinical trial evaluating DA-1726 for the treatment of obesity [U.S.]**
Feb 29, 2024

- NeuroBo Pharmaceuticals received first site Institutional Review Board (IRB) approval for the Phase I clinical trial of DA-1726, a novel dual oxyntomodulin analog agonist that functions as a GLP1R and GCGR, for the treatment of obesity
- The company expects to randomize the first patient in Q2 2024
- The Phase I trial is designed to be a randomized, placebo-controlled, double-blind, two-part study to investigate the safety, tolerability, PK, and PD of single and multiple ascending doses of DA-1726 in obese, otherwise healthy subjects
    - Part 1 will be a single ascending dose study, expected to enroll approximately 45 participants, randomized into one of five planned cohorts. Each cohort will be randomized in a 6:3 ratio of DA-1726 or placebo
    - Part 2 will be a multiple ascending dose study, expected to enroll approximately 36 participants, who will be randomized at the same 6:3 ratio into four planned cohorts, each to receive four weekly administrations of DA-1726 or placebo
- The primary endpoint will assess the safety and tolerability of DA-1726 by monitoring AEs, SAEs, TEAEs and AEs leading to treatment discontinuation
    - Secondary endpoints include the PK of DA-1726, assessed via serum concentrations over time and metabolite profiling at the highest doses of DA-1726
    - Exploratory endpoints will include the effect of DA-1726 on metabolic parameters, cardiac parameters, fasting lipid levels, body weight, waist circumference and body mass index, among others

- **Read more:** NeuroBo Pharmaceuticals Press Release

- **Implications:** DA-1726 functions as a dual oxyntomodulin analog agonist that targets both GLP1R and glucagon receptors. This mechanism suggests a potential for improved weight loss outcomes and tolerability compared to current therapies

14 **Determination of regulatory review period for purposes of patent extension; MOUNJARO [U.S.]**
Feb 29, 2024

- The U.S. FDA determined the regulatory review period for MOUNJARO (tirzepatide) and is publishing this notice as required by law due to a patent extension application submitted to the U.S. Patent and Trademark Office (USPTO)
    - Anyone who believes the published dates regarding this determination are incorrect must submit comments for a redetermination by Apr 29, 2024
    - Additionally, interested individuals can petition the U.S. FDA to determine if the applicant for the extension acted diligently during the review period by Aug 27, 2024
    - Comments can be submitted electronically through the regulations.gov website until 11:59 p.m. ET at the end of Apr 29, 2024, or via mail/hand delivery/courier, with timely submissions considered if received by that date

- **Read more:** Federal Register

- **Implications:** Lilly is attempting to extend the patent protection for MOUNJARO, pending a decision from the regulatory agency.

15 **Judge rules against AstraZeneca in suit over IRA price negotiations [U.S.]**
Mar 01, 2024

- A federal judge in Delaware ruled in favor of the Biden administration in a case brought by AstraZeneca seeking to overturn parts of the drug price negotiations established by the Inflation Reduction Act
    - The opinion makes clear that AstraZeneca's constitutional challenge against the IRA should not move forward because the company "has no legitimate claim of entitlement to sell its drugs to the Government at any price other than what the Government is willing to pay," meaning "its due process claim fails as a matter of law
- Beginning in 2026, CMS selected AstraZeneca's diabetes drug FARXIGA (dapagliflozin) as one of the first ten drugs to be negotiated
    - AstraZeneca and almost a dozen of its peers filed suit over the negotiations for a variety of Constitutional and other reasons, but so far the suits have struggled to muster momentum as PhRMA has also had its suit thrown out
    - Four other companies will present their cases before a New Jersey federal judge next week
- In the AstraZeneca case, the judge makes clear that AstraZeneca's participation in Medicare is voluntary, so the company does not have a protected interest in selling drugs to the government at prices the government will not agree to pay
    - AstraZeneca's "desire" or even "expectation" to sell its drugs to the government "at the higher prices it once enjoyed does not create a protected property interest," Friday's opinion makes clear

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

- **Implications:** The decision underscores the difficulty of challenging the IRA on constitutional grounds, particularly regarding due process claims related to drug pricing negotiations with the government.

16 **Consultation to remove glucagon-like-peptide-1 (GLP-1) receptor agonist analogues from the pharmacist extemporaneous**

compounding exemption [Australia]
Feb 29, 2024

- The Therapeutic Goods Administration (TGA) has begun a targeted consultation process as part of a proposal to change the Therapeutic Goods Regulations 1990 to remove all medicines containing GLP-1 receptor agonist, including semaglutide-like medicines, from the pharmacist extemporaneous compounding exemptions
- The current proposal aims to mitigate safety risks that may be present in the compounding of GLP-1 receptor agonists. These risks may include:
    - The unknown nature and safety of the ingredients used in manufacture
    - Compounding outside of the current exemptions that specify manufacture only on an individual patient basis and only after receipt of a valid prescription, and
    - The absence of evaluation of these medicines for safety and quality that is a feature of other drugs, that are evaluated by the TGA and entered onto the Australian Register of Therapeutic Goods (ARTG)
- The TGA notes the well-established role of pharmacist compounding, including in preparing medicines for individual patients in a community pharmacy or hospital settings. Such medicines are prepared using formulations from established formularies such as the Australian Pharmaceutical Formulary, and address patient need where commercially available medicine formulations are not clinically appropriate
- The TGA met with state and territory Chief Health Officers and Chief Pharmacists and the Australian Health Practitioner Regulation Agency in Jan 2024 to discuss the issue
- The consultation is an opportunity for identified stakeholders to provide their views on the proposed amendments and advise of any potential unintended consequences. The TGA will consider all responses in determining its next steps. A final decision will be progressed by Jun 2024
    - For further information, refer to the TGA published a statement regarding the compounding of GLP-1 RAs, including semaglutide-like medicines, available at Compounding safety information: semaglutide-like products

- **Read more:** TGA Press Release

- **Implications:** The TGA is considering regulatory changes to exclude GLP-1 receptor agonists, like semaglutide, from pharmacist compounding exemptions due to safety concerns, including the use of unapproved ingredients and non-compliant compounding practices. This proposal, under consultation with healthcare authorities and stakeholders, aims to ensure drug safety while maintaining access to necessary compounded medicines. A decision is expected by June 2024

COMMERCIAL

17 **Eli Lilly could launch obesity drug in India next year, CEO says [India]**
Feb 29, 2024

- Eli Lilly expects to launch MOUNJARO (tirzepatide) in India as early as next year after it clears an ongoing regulatory review
- The market opportunity is huge in the world's most populous country, which has high obesity rates, especially among women, and the second-highest number of people with type-2 diabetes globally
- Indian drugmakers are testing their own versions of weight-loss drugs, while illegal versions are also sold online

- **Read more:** The Economic Times

- **Implications:** The anticipated launch taps into a critical healthcare need, potentially setting a new standard for diabetes and obesity treatment in a country facing these growing health concern

GENERAL

18 **One in eight people are now living with obesity [Global]**
Mar 01, 2024

- According to new study released by *The Lancet*, in 2022, more than one billion people in the world are now living with obesity
    - Worldwide, obesity among adults has more than doubled since 1990, and has quadrupled among children and adolescents. The data also show that 43% of adults were overweight in 2022
- The study also shows that even though the rates of undernutrition have dropped, it is still a public health challenge in many places, particularly in South-East Asia and sub-Saharan Africa
    - Countries with the highest combined rates of underweight and obesity in 2022 were island nations in the Pacific and the Caribbean and those in the Middle East and North Africa
- WHO has contributed to the data collection and analysis of this study. The full dataset is now also disseminated through the Global Health Observatory

- **Read more:** WHO Press Release, *The Lancet*

- **Implications:** Governments and public health organizations will need to prioritize the development and implementation of comprehensive strategies and policies aimed at combating obesity.

19 **Lawsuit over MOUNJARO intestinal obstructions, gastroparesis diagnosis filed against Eli Lilly [U.S.]**
Feb 26, 2024

- Eli Lilly faced a product liability lawsuit brought by a New York woman, which indicates that the gastroparesis side effects of

MOUNJARO (tirzepatide) caused her to develop intestinal obstructions, severe sepsis and other complications, which resulted in the need for multiple surgeries and left her with permanent injuries

- On Feb 01, 2024, Melissa Wrubel filed a complaint in the U.S. District Court for the Southern District of New York, indicating that Eli Lilly failed to provide adequate warnings, for users or the medical community, about the risk that MOUNJARO may cause gastroparesis, also known as stomach paralysis, which led to a cascade of injuries
- Although advertisements promote the drugs as safe and effective, with few long-term side effects, former users are now pursuing MOUNJARO lawsuits, OZEMPIC lawsuits and WEGOVY lawsuits against the manufacturers, each raising similar allegations that the widespread use of the drugs has made it clear that the drug label fails to adequately warn about the risk of severe and long-lasting gastroparesis side effects

- **Read more:** AboutLawsuits

- **Implications:** The lawsuit against Eli Lilly over Mounjaro's side effects could lead to increased scrutiny of drug safety and labeling practices, potentially affecting the company's reputation and financial standing. It highlights the need for comprehensive warnings about possible severe side effects and may influence future regulatory policies and litigation against pharmaceutical manufacturers. This case could also prompt healthcare providers to exercise greater caution in prescribing these medications, impacting patient trust and drug utilization trends

20 **Omada Health expands Insights Lab to advance industry learnings on long-term weight health [U.S.]**
Feb 26, 2024

- Omada Health announced an expansion of the Omada Insights Lab to leverage its over one million all-time enrolments with plans to study the impact of coupling behaviour change with GLP-1s for weight loss
    - As part of the expansion, Omada will establish the ANSWERS (ANalyzing Success of WEight medication with Real-world evidence and Stats) Initiative with plans to share research and insights specific to GLP-1s to complement the company's already robust library of 28 peer-reviewed publications
- As an extension of the Omada Insights Lab, the ANSWERS Initiative plans to evaluate factors associated with medication usage and the relationship between lifestyle program participation and both near- and long-term weight health, with and without GLP-1 use, at a population level
    - Omada's future findings may leverage the more than three billion health data points derived from member and care team interactions, cellular connected devices, tracked meals, and more

- **Read more:** Omada Health Press Release

- **Implications:** By studying the impact of combining behavior change with GLP-1 medications for weight loss, Omada Health aims to deepen the understanding of effective weight management strategies.

21 **CarelonRx launches digital-first weight management program to aid members in health journeys [U.S.]**
Feb 26, 2024

- CarelonRx will launch a weight management program this spring to provide members support on their weight loss journeys – including those who utilize GLP-1 medications
- CarelonRx's digital-first weight management program will provide access to digital coaching and wellness tools that will help participants manage and monitor their weight goals, with the ability to connect to live human support – both digitally and over the phone whenever needed. Behavioural health and social drivers of health screenings will also be incorporated to ensure whole health is at the heart of personalized wellness plans
- For those participants who are prescribed GLP-1 medications to aid in their weight management journeys, the program will feature a GLP-1 companion module that is designed to provide medication management support with a member's prescribing physician
- The weight management program will be available to ASO integrated clients

- **Read more:** CarelonRx Press Release

- **Implications:** CarelonRx's program could serve as a model for other healthcare providers and insurers looking to implement digital health solutions.

22 **National Alliance of Healthcare Purchaser Coalitions releases employer recommendations to address obesity coverage [U.S.]**
Feb 27, 2024

- The National Alliance of Healthcare Purchaser Coalitions (National Alliance) released a guidance from its National Obesity Advisory Council made up of employers, business coalitions, and medical experts to help employers and other purchasers make informed coverage decisions about comprehensive, holistic approaches to obesity care
- In support of its commitment to obesity management, the Council encourages:
    - Adoption of comprehensive guidelines that emphasize the importance of high-quality, interdisciplinary care, including prevention, treatment and maintenance
    - Plan and program design that reimburses providers for obesity care consistent with emerging standards of practice
    - Individualized treatment plans and the establishment of realistic expectations and goals
    - Inclusion of behavior modification programs to support mental and physical health and wellbeing
- Traditional approaches to weight management have fallen short with employers continuing to see rising obesity rates. The Council offered a series of recommendations that include:

- Promote education on the science of obesity
- Use person-first language in communications to reduce the bias, stigma and shame associated with the disease of obesity
- Implement clear conditions and qualifications for advance obesity management, targeting the medically eligible and those with the greatest need
- Ensure coaching supports each participant's unique demographics and lifestyle
- Work with health plans to make sure primary care physicians are trained and given incentives for the full spectrum of obesity care
- Provide coverage that enables physicians to consider appropriate anti-obesity medications where clinically warranted for individuals who are unresponsive to prior therapies and committed to lifestyle changes
- Consider environmental influences, mental health, biology, predisposition to metabolic syndrome, medication-induced weight gain, and other co-existing conditions
- Consider the long-term cost benefits of preventive obesity management to avoid the much higher costs and complexity of treating advanced obesity and ensuing co-existing conditions

- The resource also offers guidance on coverage benefit decision approaches for anti-obesity medications to help employers decide how and when to cover or not cover these drugs. The coverage guidance and full report, Addressing Obesity through Holistic Design for Affordability and Sustainability, can be downloaded here

· **Read more:** National Alliance of Healthcare Purchaser Coalition Press Release

· **Implications:** The emphasis on comprehensive, holistic approaches marks a significant shift in how employers and healthcare purchasers view obesity management. This approach recognizes obesity as a complex, chronic condition that requires interdisciplinary care.

23 **Bariatric surgery provides long-term blood glucose control, type 2 diabetes remission [U.S.]**
Feb 27, 2024

- A study funded by the National Institutes of Health found that individuals with type 2 diabetes who underwent bariatric surgery experienced better long-term blood glucose control and higher rates of diabetes remission compared to those who received medical management and lifestyle interventions alone
- The study published in *JAMA*, combined data from four independent trials conducted in the U.S. between 2007 and 2013, evaluating the effectiveness of bariatric surgery vs. intensive lifestyle and medication therapy for overweight or obese adults with type 2 diabetes
- At seven-years, participants who underwent surgery achieved a 20% weight loss compared to 8% in the medical/lifestyle group
  - Moreover, 54% of surgery participants achieved an HbA1c less than 7%, whereas only 27% of those in the medical/lifestyle group reached this target
- Bariatric surgery showed beneficial effects even for participants with a BMI between 27 and 34, highlighting its potential for individuals who don't meet the traditional BMI threshold for surgery
  - Though AEs were similar between groups, the surgery group experienced more fractures, anaemia, low iron, and gastrointestinal events, underscoring the need for continued monitoring and addressing nutritional deficiencies post-surgery

· **Read more:** National Institutes of Health Press Release

· **Implications:** Bariatric surgery remains a valid treatment option for overweight or obese adults with type 2 diabetes. However, more potent pharmacological interventions could reduce the market share of bariatric surgery.

24 **Novo Nordisk plans for life after WEGOVY, setting up roots in Boston to try and find its future**
Feb 28, 2024

- Novo Nordisk unveiled its new R&D facility just outside the city, pitching it as a U.S. flagship to match its headquarters in Denmark, and an important step towards life after its blockbuster GLP-1 drugs
- According to Jacob Sten Petersen, Senior Vice President of global nucleic acid therapies, Novo Nordisk, the company is putting its OZEMPIC (semaglutide) and WEGOVY (semaglutide) profits into research on genetic medicines treatments that achieve even greater weight loss
  - By blocking, editing or fine-tuning the output of genes, Novo hopes to develop therapies that trick our bodies into burning fat, as well as treatments to counteract the muscle loss caused by its existing drugs
- In total, Novo has 450 employees around Boston and plans to hire 75 more in 2024
- The company's current RNAi efforts have grown to more than 50 programs, and he plans to advance at least three new ones into early clinical studies each year
  - The company is interested in targeting other parts of the body, including the blood, fat, heart, muscle and even the brain — due to growing evidence that the nervous system plays a vital role in hunger and obesity

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

· **Implications:** Novo Nordisk continues its dedication to addressing obesity beyond the scope of WEGOVY, committing substantial

resources to the research and development of genetic medicines.

25 **Vivani Medical announces positive NPM-115 preclinical weight loss data comparable to OZEMPIC/WEGOVY and discloses NPM-139 as semaglutide as strategy shifts to prioritize obesity portfolio**

Feb 28, 2024

- Vivani Medical announced positive preclinical data on weight loss effects for NPM-115 (exenatide), the company's miniature, twice-yearly, exenatide implant under development for the treatment of chronic weight management
- The Company also disclosed the active pharmaceutical ingredient in NPM-139 (semaglutide), a miniature, subdermal GLP-1 RA implant in development for chronic weight management, with the added potential benefit of once-yearly administration
- These developments are part of a strategic shift to prioritize the company's obesity implants based on emerging data regarding the potential for high-dose GLP-1 products to improve health outcomes for obese and overweight patients
    - In a study in high-fat diet-induced obese mice, NPM-115 generated weight loss of approximately 20% vs. a sham implant control after a 28-day treatment duration, comparable to weight loss observed in mice treated with semaglutide injections in the same study
    - In a second study in healthy rats, a single administration of the Company's exenatide implant NPM-119, in development for the treatment of type 2 diabetes, resulted in body weights that were approximately 25% lower than a vehicle implant control after 15 weeks of treatment with an expected duration of effect of six months
- These preclinical data provide further evidence that the weight loss potential of exenatide treatment in humans may be comparable to other GLP-1 molecules such as semaglutide assuming adequate exposure levels are achieved and maintained
    - It is designed to improve adherence by enabling patients to receive continuous dosing over a six-month interval from a single administration. NPM-115 is planned to maximize exenatide's weight loss effect in humans, pending further development and regulatory clearance, by evaluating exenatide exposure levels higher than previously explored
    - Dr. Mendelsohn will present study results on May 17, 2024, at the TIDES USA 2024 conference in Boston

· **Read more:** Vivani Medical Press Release

- **Implications:** Vivani Medical appears to leverage a strategy similar to Intarcia Therapeutics's ITCA 650 implantable device for T2D, which has failed FDA approval. If approved, this technology is expected to be utilized primarily in niche settings, catering specifically to patients with severe cases of the condition who face challenges in adhering to their medication.

26 **ZyVersa Therapeutics highlights data from review article published in Nature Reinforcing IC 100's rationale for inhibiting ASC and ASC Specks to attenuate damaging inflammation associated with various conditions, including obesity and its complications**

Feb 28, 2024

- ZyVersa Therapeutics highlighted data published in *Nature* reinforcing IC 100's rationale for inhibiting ASC and ASC Specks to attenuate damaging inflammation associated with various conditions, including obesity and its complications
- Studies dating back to 2011 have implicated a pathogenic role for inflammasome activation in initiation of obesity and its metabolic complications
- Authors of the review paper published in *Nature* titled, "*Cell death and inflammation during obesity: Know my methods, WAT(son),*" reviewed 111 papers, which demonstrated that the state of low-grade chronic inflammation in obesity combined with activated macrophages in adipose tissue result in a vicious cycle of inflammation, cell death, and metabolic disbalance that together cause metabolic syndromes. This also promotes a pro-tumorigenic microenvironment that induces or supports tumour growth in cancers linked to obesity such as breast, liver, and colon carcinomas
    - The authors concluded, "*There is no question that macrophage-inflammasome activation triggers systemic inflammation during obesity and it is one of the main culprits of metabolic syndromes"*
- Stephen C. Glover, Co-founder, Chairman, CEO and President, ZyVersa stated that, *"Obesity, a well-established risk factor for array of different metabolic disorders, including insulin resistance, type 2 Diabetes, hypertension, cardiovascular disease, and cancer, has reached pandemic proportions, and may affect up to two-thirds of the adult population in developed countries"*

· **Read more:** ZyVersa Therapeutics Press Release

· **Implications:** N/A

KEY UPCOMING EVENTS

Cowen 44th Annual Health Care Conference

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

· **Amgen:** Mar 5, 2024 (Amgen 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)
- **Zealand Pharma:** Mar 20, 2024 (Zealand Pharma Investor update)
- **Novo Nordisk:** Mar 21, 2024 (Novo Nordisk Investor update)

Have a great week!
Ben

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