Tuesday, May 14, 2024 at 12:21:37 Eastern Daylight Time

Subject: MTSR1: Weekly Competitive Intelligence Newsletter (Mar 12-18, 2024)
Date: Monday, March 18, 2024 at 2:37:17 PM Eastern Daylight Time
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Attachments: image002.png, image001.wmz

Hi Metsera Team,

Please find below the weekly 'Competitive Intelligence Newsletter' for the week: Mar 12-18, 2024

DASHBOARD

KEY TAKEAWAYS OF THE WEEK (Mar 12 - 18, 2024)

- **Clinical –** Kallyope initiated a Phase I trial to evaluate the safety, tolerability, PK, and PD of K-757 And K-833 in overweight/obese patients with type 2 diabetes mellitus [U.S.]
- **Regulatory –** Huadong Medicine received clinical trial approval from NMPA for the development of HDM1005 (undisclosed) for treatment of type 2 diabetes and obesity [China]
- **Regulatory –** Hanmi Pharmaceutical submitted an IND application for its obesity treatment candidate HM15275 (undisclosed) [South Korea]
- **Commercial –**Eli Lilly's ZEPBOUND (tirzepatide) hit 77,590 new prescriptions in the U.S., surpassing Novo Nordisk's WEGOVY (semaglutide) [U.S.]
- **Commercial –** Eli Lilly struck a deal with Amazon Pharmacy to deliver its obesity and diabetes medicines directly to patients [U.S.]

DETAILED NEWS

CLINICAL

1 **Trial Update: A study to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of AZD6234 (long-acting amylin analogue) after repeat dose administration in participants who are overweight or obese [Global]**
Mar 15, 2024

- A Phase I trial sponsored by AstraZeneca titled, *"A study to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of AZD6234 after repeat dose administration in participants who are overweight or obese"* has undergone changes
  - **PCD and SCD:** Updated from Oct 8, 2024 [Anticipated] to Apr 30, 2025 [Anticipated]
  - **Enrollment:** Updated from 68 [Anticipated] to 40 [Anticipated]
- **Read more:** NCT06132841
- **Implications:** AZD6234 (long-acting amylin analogue) development appears to be slower than expected, furthermore enrollment number decreased in their Ph1 trial.

2 **Trial Update: A research study to see how a new medicine NNC0487-0111 (similar to amylin and GLP-1) works in people with overweight or obesity when injected under the skin [U.S.]**
Mar 13, 2024

- A Phase I trial sponsored by Novo Nordisk titled, *"A research study to see how a new medicine NNC0487-0111 works in people with overweight or obesity when injected under the skin"* has undergone changes
  - **SCD:** Updated from Nov 13, 2024 [Anticipated] to Dec 12, 2024 [Anticipated]
- **Read more:** NCT06064006
- **Implications:** N/A

3 **New Trial: A study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of K-757 and K-833 in overweight/obese patients with type 2 diabetes [U.S.]**
Mar 12, 2024

- Kallyope initiated a Phase I trial to evaluate the safety, tolerability, PK, and PD of K-757 (undisclosed) and K-833 (undisclosed) in overweight/obese patients with type 2 diabetes mellitus
  - **Trial details:** N = 32; Status: Recruiting; Start date: Dec 7, 2023; PCD and SCD: Jul 2024; Location: U.S.

- **Read more:** NCT06305351

- **Implications:** N/A

4 **New research from Dario demonstrates ability to deliver improved health outcomes with integrated solution for members managing weight and blood glucose with or without GLP-1 medications [Italy]**
Mar 12, 2024

- DarioHealth presented two new clinical studies at the 17th International Conference on Advanced Technologies and Treatments for Diabetes (ATTD) 2024
- Examining evolving standards for metabolic health: Improving outcomes with or without medication
  - Study presented at ATTD 2024 is the first of a planned series examining the impact of Dario's integrated cardiometabolic solution to address weight and diabetes with or without a GLP-1
  - Dario is conducting a series of studies looking at the related clinical outcomes of those members taking a GLP-1 and those without the medication
  - Study presented at ATTD analyzed data from 6,963 members with pre-diabetes using Dario's solution, showing a 6.38% weight reduction and overall improvement in blood glucose levels over one year, particularly significant for those consistently engaging in meal tagging activities
- Additional research presented demonstrated Dario's ability to improve awareness of the importance of flu vaccines in member with type 2 diabetes

- **Read more:** DarioHealth Press Release

- **Implications:** Demonstrates the effectiveness of DarioHealth's digital therapeutics platform in managing weight and blood glucose. Shows digital solutions can lead to significant health behavior changes, emphasizing the importance of DTx in chronic disease management to support pharmacological interventions.

5 **Spanish press highlights efficacy of Lilly's MOUNJARO for weight loss [Spain]**
Mar 15, 2024

- Daily newspapers El Español, ABC, news agency Europa Press and financial newspaper El Economista, reported stories about the efficacy of Eli Lilly's MOUNJARO (tirzepatide) in obese patients
- According to El Español, tirzepatide is set to be the driver of a second revolution in the field of obesity treatments following Novo Nordisk's OZEMPIC (semaglutide)
  - OZEMPIC has helped lose weight to those who can afford it
  - In Spain, unless one has type 2 diabetes, it costs €130 monthly

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

- **Implications:** N/A

6 **Trial Update: A research study to look at how CagriSema influences food intake, appetite and emptying of the stomach in people with excess body weight [Germany]**
Mar 15, 2024

- A Phase I trial sponsored by Novo Nordisk titled, *"A research study to look at how CagriSema influences food intake, appetite and emptying of the stomach in people with excess body weight"* has undergone changes
  - **Overall Status:** Updated from 'Not yet recruiting' to 'Recruiting'
  - **SSD:** Updated from Mar 23, 2024 to Feb 23, 2024
  - **SCD:** Updated from Jan 1, 2025 [Anticipated] to Dec 8, 2024 [Anticipated]

- **Read more:** NCT06207877

- **Implications:** N/A

7 **Trial Update: Phase I/Ib study of TLC-6740 in healthy subjects and subjects with obesity [New Zealand]**
Mar 13, 2024

- A Phase I trial sponsored by OrsoBio titled, *"Phase I/Ib study of TLC-6740 in healthy subjects and subjects with obesity"* has undergone changes
  - **Brief Title:** Updated from "*A study to evaluate single and multiple doses of TLC-6740 in healthy subjects*" to "*Phase I/Ib study of TLC-6740 in healthy subjects and subjects with obesity*"
  - **Official Title:** Updated from *"A Phase I study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of single and multiple ascending doses of TLC-6740 in healthy subjects and an open-label assessment of the relative bioavailability of, and effect of food on, a tablet formulation of TLC-6740* to "*A Phase 1/1b study of single and multiple ascending doses of TLC 6740 in healthy subjects, including evaluation of food effect and potential drug-drug interactions, and preliminary safety and efficacy in subjects with obesity"*
  - **PCD:** Updated from Jan 2024 [Anticipated] to Jan 2025 [Anticipated]
  - **SCD:** Updated from Mar 2024 [Anticipated] to Mar 2025 [Anticipated]
  - **Number of arms:** Updated from 3 to 4
  - **Enrollment:** Updated from 156 [Anticipated] to 236 [Anticipated]
  - **Brief Summary, Detailed Description, Arms and Interventions, Outcome Measures, Eligibility and Contacts/Locations:** Updated

- **Read more:** NCT05822544

- **Implications:** The timeline for the Phase 1 trial of TLC-6740, a mitochondrial protonophore being developed by OrsoBio, has been delayed by one year.

8 **New Trial: A study to measure calorie consumption and usage in participants with obesity using LY3437943 (retatrutide)**
Mar 15, 2024

- Eli Lilly initiated Phase I trial to investigate the effect of LY3437943 (retatrutide) vs. placebo on calorie intake and energy expenditure in participants with obesity under calorie restriction
  - **Trial details:** N = 74; Status: Not Yet Recruiting; Start date: Mar 18, 2024; PCD: Jul 15, 2025; SCD: Jul 15, 2025; Location: Undisclosed
- **Read more:** NCT06313528
- **Implications:** N/A

9 **New Trial: A study to test whether survodutide helps people living with obesity or overweight and with a confirmed or presumed liver disease called non-alcoholic steatohepatitis (NASH) to reduce liver fat and to lose weight**
Mar 13, 2024

- Boehringer Ingelheim initiated a Phase III trial to evaluate the efficacy and safety of survodutide administered subcutaneously in participants with overweight or obesity and presumed or confirmed nonalcoholic steatohepatitis (NASH)
  - **Trial details:** N = 160; Status: Not Yet Recruiting; Start date: Mar 20, 2024; PCD: Feb 16, 2026; SCD: Mar 9, 2026; Location: Undisclosed
- **Read more:** NCT06309992
- **Implications:** Boehringer Ingelheim is advancing its dual agonist, survodutide, targeting both glucagon and GLP-1 receptors, to Phase 3 trials for treating NASH, with a scheduled completion date in 2026.

10 **Fractyl Health announces new results from its Rejuva platform demonstrating potent and durable effects of a single dose of a human GLP-1 pancreatic gene therapy transgene compared to semaglutide in the db/db mouse model of diabetes**
Mar 12, 2024

- Fractyl Health announced new preclinical findings for the first clinical candidate in its Rejuva pancreatic gene therapy platform
- RJVA-001 is the company's first GLP-1 gene therapy candidate to emerge from the platform, setting the stage for a potentially transformative approach to treating metabolic diseases, including obesity and T2D
- Results show that the human GLP-1 coding sequence of RJVA-001 demonstrates potency on both glucose lowering and weight loss in db/db mice, the standard rodent T2D efficacy model used for clinical development
- The company has reached alignment with European regulators on the use of this efficacy model to support the submission of a Clinical Trial Application in Europe
- Fractyl Health anticipates progressing RJVA-001 through IND-enabling toxicity studies in 2024 and initiating First-in-Human clinical studies in 2025
- **Read more:** Fractyl Health Press Release
- **Implications:** N/A

REGULATORY

11 **NMPA approves Huadong Medicine's clinical trial of HDM1005 for treatment of type II diabetes and obesity [China]**
Mar 11, 2024

- Huadong Medicine received clinical trial approval in China for the development of a new GLP-1/GIP dual agonist, HDM1005 for treatment of type 2 diabetes and obesity
- Preclinical data of HDM1005 show the ability to promote the release of insulin, suppress appetite, improve glucose tolerance, cut back blood sugar levels, and trigger weight loss
- **Read more:** Navlin Daily
- **Implications:** N/A

12 **Hanmi Pharmaceutical, submission of IND for Phase I clinical trial of next-generation obesity treatment triple agonist [South Korea]**
Mar 8, 2024

- Hanmi Pharmaceutical submitted an IND application for a Phase I clinical trial of its obesity treatment candidate HM15275 to the Korean Ministry of Food and Drug Safety
  - The company also plans to submit the IND application to the U.S. FDA in Mar 2024
- Hanmi Pharmaceutical's next-generation obesity treatment HM15275 is a triple agonist (LA-GLP/GIP/GCG) which is expected to minimize muscle loss and weight loss of more than 25%
- HM15275 is an innovative new drug candidate included in Hanmi's full-cycle obesity treatment drug project 'H.O.P' (Hanmi Obesity Pipeline) and is a next-generation new drug that will continue the innovation of 'Efpeglenatide', which is currently under Phase III clinical development
- Hanmi Pharmaceutical will present the results of HM15275 at the 2024 American Diabetes Association meeting in Jun 2024
- **Read more:** Hanmi Pharmaceutical Press Release *(Translated from Korean)*, Korea Biomedical Review
- **Implications:** Hanmi Pharmaceutical is advancing a drug similar to retratrutide into Phase 1 trials, showcasing its commitment to

developing innovative combination therapies for metabolic diseases.

COMMERCIAL

13 **Lilly weight-loss drug ZEPBOUND new U.S. prescriptions surpass WEGOVY for first time [U.S.]**
Mar 15, 2024

- According to data from IQVIA, Eli Lilly's ZEPBOUND (tirzepatide) hit 77,590 new prescriptions in the U.S. for the week ending on Mar 8, 2024, surpassing Novo Nordisk's WEGOVY (semaglutide) for the first time
- According to the data published by JPMorgan, some 6,000 fewer WEGOVY prescriptions were filled in the U.S. for the week ending on Mar 8, 2024, but Novo Nordisk maintained its lead for total weekly prescriptions over ZEPBOUND by 25,307
- At stake in the competition for new patients looking to lose weight is a market analysts' see reaching at least $100 Bn by the end of the decade
  - Demand so far has well outpaced supplies, as consumers flock to new treatments that have been shown to reduce weight by as much as 20%

- **Read more:** Reuters

- **Implications:** ZEPBOUND could surpass WEGOVY as the leading treatment in the obesity market. Furthermore, Lilly, with its robust pipeline in obesity treatments, could challenge Novo Nordisk's dominance in this therapeutic area.

14 **Eli Lilly taps Amazon Pharmacy to dispense its prescription medicines [U.S.]**
Mar 13, 2024

- Eli Lilly struck a deal with Amazon Pharmacy to deliver its obesity, diabetes and migraine medicines directly to patients
- Amazon will work through Eli Lilly's LillyDirect, telehealth platform which was launched in Jan 2024
  - Lilly began LillyDirect with Form Health as a telehealth provider, and keeps Truepill as a dispensing partner, making Amazon Pharmacy its second
  - Lilly also uses Eversana pharmacy services for benefits verification, manufacturer savings and prescription routing
- The Amazon deal is not an exclusive agreement and Lilly is continuing to evaluate other telehealth, pharmacy, and service provider partners for LillyDirect
- Neither Lilly nor Amazon is promising MOUNJARO (tirzepatide) and ZEPBOUND (tirzepatide) now available through LillyDirect won't face shortages
- Amazon's customer service page about GLP-1s says it is now accepting prescriptions for MOUNJARO and ZEPBOUND on Amazon Pharmacy, but due to ongoing challenges in the marketplace for WEGOVY (semaglutide) and OZEMPIC (semaglutide), it is prioritizing existing customers and those patients with insurance plans where Amazon Pharmacy is the exclusive online pharmacy provider

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

- **Implications:** Expands access to Eli Lilly's medications through Amazon's distribution network and highlights the evolving landscape of pharmaceutical distribution and patient access.

15 **CBO hints that Medicare may soon cover obesity drugs for their cardiovascular benefits [U.S.]**
Mar 12, 2024

- According to Congressional Budget Office (CBO), Medicare could have billions of dollars in future expenses if it begins covering obesity drugs such as Novo Nordisk's WEGOVY and Eli Lilly's ZEPBOUND
- In written questions, Rep. Buddy Carter asked the CBO how it is considering the costs of GLP-1s now that the U.S. FDA expanded the label for WEGOVY (semaglutide) to include cardiovascular risk reduction benefits
- The CBO said in its written response on Mar 08, 2024, that if the U.S. FDA approves GLP-1s for cardiovascular indications, which it did for WEGOVY, "*Then Medicare will cover those drugs for the treatment of cardiovascular conditions among people with obesity*"
  - In that case, CBO mentioned it would incorporate the costs of covering GLP-1 agonists for Medicare patients with the newly approved indication to its baseline, and then the cost of broadening Medicare coverage to include obesity drugs would likely fall
- Currently, CMS does not cover any drugs for weight loss
- According to an article published in *The New England Journal of Medicine*, if only 10% of Medicare beneficiaries who are obese used WEGOVY, the estimated cost to Medicare Part D would be $26.8 billion

- **Read more:** Endpoints News *(Subscription required),* Daily Maverick

- **Implications:** Medicare may cover obesity drugs like WEGOVY and ZEPBOUND due to their cardiovascular benefits. A substantial cost impact is anticipated if a fraction of Medicare beneficiaries use these drugs.

16 **Novo Nordisk looks to invest share of WEGOVY windfall in UK – press [UK]**
Mar 15, 2024

- The head of Novo Nordisk's controlling shareholder plans to invest a portion of the company's windfall from obesity drug WEGOVY (semaglutide) in the UK, considering it a highly attractive investment destination
- Kasim Kutay, Chief Executive of Novo Holdings which manages $150 billion of assets, said "The UK will see strong inflows from the investment company in the biotechnology and life sciences sectors"
- Kutay's remarks, will be seen as a boost to attempts to attract overseas investment and to turn UK into a life sciences superpower
- Novo Holdings, which manages the assets of the Novo Nordisk Foundation philanthropic organisation, owns about 28% of the shares in Novo Nordisk and 77% of the voting rights

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

- **Implications:** N/A

17 **OZEMPIC for weight loss now 'fashionable' in Italy despite side effect risks, shortages – press [Italy]**
Mar 15, 2024

- According to an Italian daily newspaper, Il Messaggero, using Novo Nordisk's OZEMPIC (semaglutide) for weight loss has become fashionable in Italy despite the risk of side effects and growing problems of shortages for diabetes patients
  - The paper suggested the trend is being fuelled by celebrities, actors and other high-profile people who have started using it
- It was noted by Il Messaggero that a programme on the public broadcaster RAI Tre included a discussion by a panel of scientists and other experts. A woman from the capital, stated in an interview that, "*It is the fashion here in Roma Nord, everyone is using it, at least eight out of 10 women, even though they won't admit it*"
- The paper stressed that, with the increase in demand, the drug has become difficult to find, especially for those who suffer from diabetes and need it

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

- **Implications:** N/A

18 **Italy's HTA of Rhythm's obesity drug IMCIVREE finds significant added value in area of unmet need [Italy]**
Mar 14, 2024

- Italy's health technology assessment (HTA) of Rhythm Pharmaceuticals' orphan drug IMCIVREE (setmelanotide) found it provides significant added value in an area of unmet need
- Medicines agency AIFA approved reimbursement of IMCIVREE in Feb 2024 for the treatment of obesity and the control of hunger associated with genetically confirmed Bardet-Biedl syndrome (BBS) in adults and children aged six years or older
- A report was published in Mar 2024, on the HTA conducted by the regulator's technical-scientific commission (CTS)
  - In the analysis of the need for new therapies, it was noted that current therapies for BBS are limited to diet and exercise, lacking long-term effectiveness due to intense hunger
  - IMCIVREE targets the specific pathogenetic mechanism of insatiable hunger in BBS, offering a new therapeutic option
- Phase III study showed 32.3% weight loss (primary endpoint) at 52 weeks, with 43% response rate in BBS patients
  - Concerns were raised about the small number of patients aged 6-12, but efficacy and safety data were comparable to older patients
  - Secondary endpoints and additional analyses confirmed IMCIVREE's efficacy in BBS, leading to a considerable clinical benefit rating
- This allows for it to be paid for through special funding outside ordinary reimbursement budgets

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

- **Implications:** N/A

19 **PegBio plans Hong Kong IPO to support long acting GLP-1 for diabetes/obesity [Hong Kong]**
Mar 14, 2024

- PegBio filed for a Hong Kong IPO to support commercialization of its long-acting pegylated GLP-1 receptor agonist, PB-119 for type 2 diabetes and obesity
  - The company has filed for NMDA approval of the drug, which has completed two China Phase III trials in T2DM patients, one as a monotherapy and the other in combination with metformin
- The company anticipates launch of PB-119 in early 2025

- **Read more:** ChinaBio Today

- **Implications:** N/A

20 **Arecor and TRx biosciences establish research collaboration to develop oral GLP-1 with enhanced bioavailability**
Mar 12, 2024

- Arecor Therapeutics and TRx Biosciences announced a research collaboration for the formulation development of an oral GLP-1 receptor agonist product
- The only GLP-1 receptor agonist currently available to patients in pill form – Novo Nordisk's RYBELSUS (semaglutide) – has oral bioavailability of less than 1%
- Using TRx Biosciences' LipiCore oral delivery technology alongside Arecor's formulation platform, Arestat, the companies intend to jointly develop an oral GLP-1 receptor agonist product with enhanced physicochemical properties that can achieve higher oral bioavailability and stability
- The collaboration provides scope for expansion, following the initial oral GLP-1 receptor agonist program, to develop further oral peptide products
  - These include additional peptides and combination approaches which may be key in the treatment of obesity-related health conditions, as well as peptide products targeting multiple therapeutic areas

- **Read more:** GlobeNewswire, European Biotechnology

- **Implications:** Arecor Therapeutics and TRx Biosciences are partnering to create an oral GLP-1 receptor agonist with improved bioavailability, aiming to surpass the current oral option.

GENERAL

21 **Eli Lilly CEO David Ricks talks China, AI, and pharma's next 'golden era' after obesity [U.S.]**

Mar 13, 2024

- David Ricks, CEO, Eli Lilly, shared his view from the pharma industry's peak in an interview with the Economic Club of New York
- At the top of Ricks' mind is expanding supply for Eli Lilly's obesity and diabetes treatments, MOUNJARO and ZEPBOUND, the company is aggressively investing in manufacturing with six additional facilities now under production
  - Part of the challenge is focusing on the people who stand to benefit most from the drugs, as Lilly's recent advertising campaign put into focus. Ricks framed obesity as a life-shortening condition that now affects one in eight people worldwide
- According to Ricks, LillyDirect, the pharma's own direct-to-consumer website connecting patients and doctors for obesity, diabetes and migraine treatments, have been surprisingly successful
  - LillyDirect takes some of the chaos out of the U.S. healthcare process by giving clarity on elements like when a patient's next shipment will come

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

- **Implications:** N/A

22 **Novo gears up sustainability efforts by recycling injectors in Japan [Japan]**

Mar 13, 2024

- Novo Nordisk will launch a take-back and recycling program, dubbed ReMed, for the plastic parts of its used prefilled injection pens
- The drug maker will run a one-year pilot program in partner with major wholesaler and pharmacy operator Toho Holdings
  - It will be implemented at 15 pharmacy outlets of the Toho group in the greater Tokyo area, starting the same day through the end of Mar 2025
  - After assessing the pilot for improvements, Novo hopes to take this program to the national level
- Patients who wish to participate in this program will receive a return bag for the injectors at designated pharmacies
  - Patients will be asked to remove the needle after pen usage, place the used device in the bag, and then bring the bag to a pharmacy
  - The collected devices will be transported to recycling facilities in Japan to be recycled into new products and materials
- Injector pens are made of 77% plastic. In Japan, used pen devices have been incinerated and disposed in landfills thus far

- **Read more:** Pharma Japan *(Subscription required)*

- **Implications:** Novo Nordisk's ReMed program in Japan, aiming to recycle used injection pens, signals a strategic shift towards sustainability by reducing medical waste and promoting recycling, potentially setting a precedent for global healthcare environmental initiatives.

KEY UPCOMING EVENTS

Annual General Meeting 2024:
- **Zealand Pharma:** Mar 20, 2024 (Zealand Pharma Investor update)
- **Novo Nordisk:** Mar 21, 2024 (Novo Nordisk Investor update)

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)
- **Novo Nordisk:** May 2, 2024 (Novo Nordisk Investor update)

Obesity Summit on Future of Obesity Care Market:
- BMO Financial will host discussions with leading life sciences companies: Mar 20, 2024, (BMO Events)

Thank you,
Kind regards,
Diksha

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