

#### Revolutionizing Weight Management The Impact of GLP-1 Drugs on The Natural Products Industry

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## **Revolutionizing Weight Management**

The Impact of GLP-1 Drugs on The Natural Products Industry

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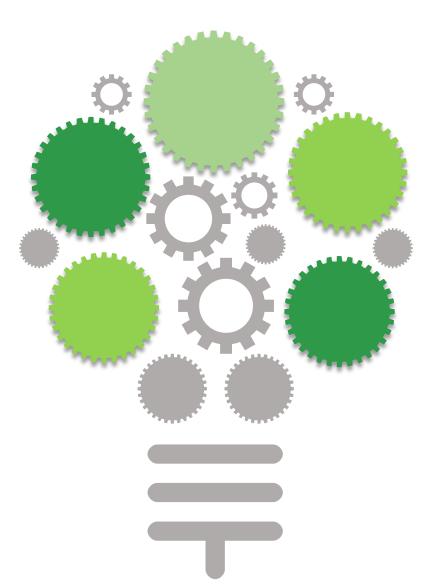
#### Introduction

#### Nature's Way

#### 01

#### Why do GLP-1's exist and how did we get here?





#### 02

#### What is a GLP-1?



#### Nature Finds A Way The First GLP-1 Drug





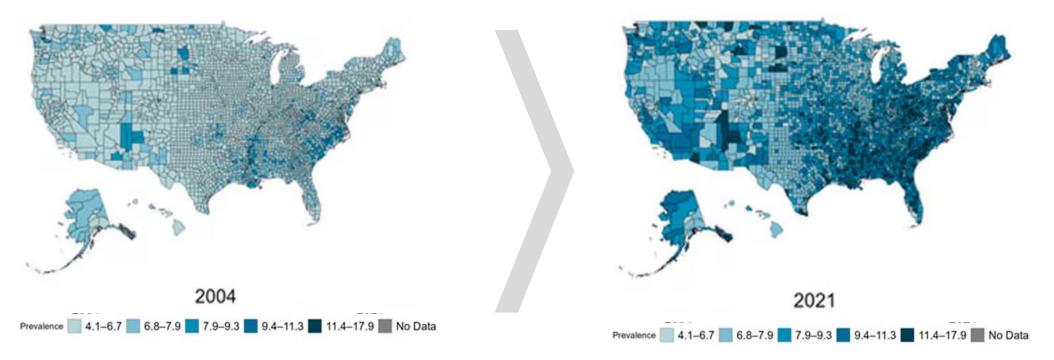
- The Gila Monster is able to slow down its metabolism and maintain constant blood sugar levels
- Venom from the Gila Monster's bite causes enlargement of the pancreas
- A peptide in the venom similar in structure to a human's natural GLP-1 was identified and named Exendin-4
- Similar to GLP-1, Exendin-4 overstimulates the pancreas to **produce insulin**
- While GLP-1 is only active in the body for 2 minutes, Exendin-4 is active for hours
- Exendin-4 (from Amylin) was approved as a diabetes GLP-1 drug in 2005

# Why Do GLP-1 Drugs Exist & How Did We Get Here?

## Type II Diabetes: Prevalence



Age-adjusted, county-level prevalence of diagnosed diabetes among adults aged 20 years or older, United States, 2004 and 2021



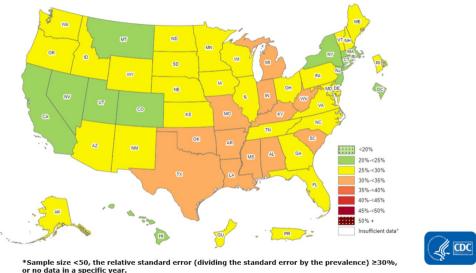
- About 1 in 6 adults have diabetes, prevalence has doubled over 20 years
- Diabetes-related costs were **over \$410 billion** in 2022, estimated to be over \$600 billion by 2030

#### **Obesity: Prevalence**



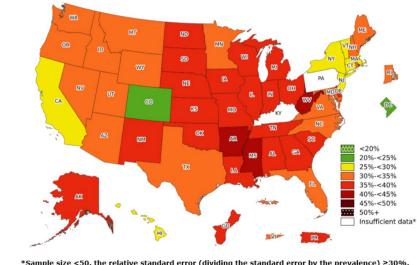
#### Prevalence<sup>¶</sup> of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2011

<sup>1</sup> Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.



#### Prevalence<sup>1</sup> of Obesity Based on Self-Reported Weight and Height Among US Adults by State and Territory, BRFSS, 2023

<sup>1</sup> Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.



\*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30% or no data in a specific year.

- United States: 1 in 5 children & 2 in 5 adults have obesity.
- Currently 40% of adults are obese, and 73% are either overweight or obese
- Obesity costs the US healthcare system almost **\$173 billion** a year.

CDC

## **Changing Diet Patterns**

#### Not just what & how much we eat, but also when and where

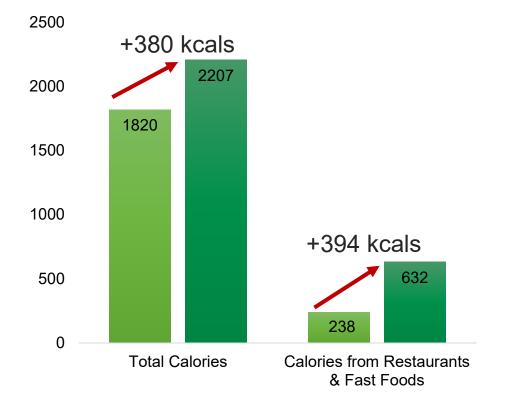


**More Calories, Away from Home:** Adults eat more calories than they did 50 years ago, mainly from foods prepared away from home:

- +380 calories more on a typical day since 1977
- Main increase is from Restaurant & Fast Foods with higher calories/lower nutrient density

**The 4<sup>th</sup> Meal:** Almost 25% of daily calories now come from "Snacking" - Adults snack 2.3x per day

**Still Lacking Greens:** 9 out of 10 adults continue to not meet guidelines for Fruit & Vegetable intake



**1977-78 2017-18** 

#### For educational purposes only.

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USDA, Agricultural Research Service, 2021. Usual Nutrient Intake from Food and Beverages, by Gender and Age, What We Eat in America, NHANES 2015-2018 Disparities in Snacking Trends in US Adults over a 35 Year Period from 1977 to 2012 (nih.gov) Dietary Quality by Food Source and Demographics in the United States, 1977-2018 (usda.gov); Adults 20-64 years

#### Low Diet Quality Leads to Low Nutrient Intake

Maintaining nutrient adequacy is the foundation of any diet



#### Most Adults Do Not Meet Nutrient Recommendations Through Foods Alone

Essential Nutrient	Daily Requirement for Adults <sup>*</sup> Female Male	Adults <sup>*</sup> <u>Not</u> Meeting Requirement Female Male	Health Benefits
Vitamin D	10 ug 10 ug	<b>97%</b> 95%	Bone & Immune
Dietary Fiber	25 g 38 g	<b>94% 97%</b>	Heart & Digestive
Vitamin E	12 mg 12 mg	<b>85% 71%</b>	Heart & Antioxidant
Magnesium	265 mg 350 mg	<b>48% 55%</b>	Bone & Heart
Vitamin C	60 mg 75 mg	<b>45% 53%</b>	Immune & Antioxidant
Calcium	800 mg 800 mg	<b>42% 28%</b>	Bone Health
Potassium	2600 mg 3400 mg	<b>29% 31%</b>	Heart & Hydration

\*Based on Estimated Average Requirements for Ages 19-50 years; Dietary Fiber values based on Adequate Intake

USDA, Agricultural Research Service, 2021. Usual Nutrient Intake from Food and Beverages, by Gender and Age, What We Eat in America, NHANES 2015-2018

#### For educational purposes only.

USDA, Agricultural Research Service, 2021. Usual Nutrient Intake from Food and Beverages, by Gender and Age, What We Eat in America, NHANES 2015-2018 Astrup, A. and Bügel, S. Overfed but undernourished: recognizing nutritional inadequacies/deficiencies in patients with overweight or obesity. Int J Obes. 2019 Feb;43(2):219-232 Blumberg, et al. Contribution of Dietary Supplements to Nutritional Adequacy in Various Adult Age Groups. Nutrients 2017, 9, 1325.

#### **Populations with Higher Nutrient Needs**

Supplementation can help fill nutrient gaps

#### Obese Adults May Have Even Greater Nutrient Gaps

Compared to normal weight adults, **obese adults** had lower:

- Overall diet quality
- Intakes of **key nutrients**
- Were less likely to meet daily nutrient requirements

Obesity associated with **higher risk** of clinical deficiency: **iron, zinc, vitamin D, vitamin B12, others** 

#### Reducing Calories Increases Risk of Nutrient Inadequacy

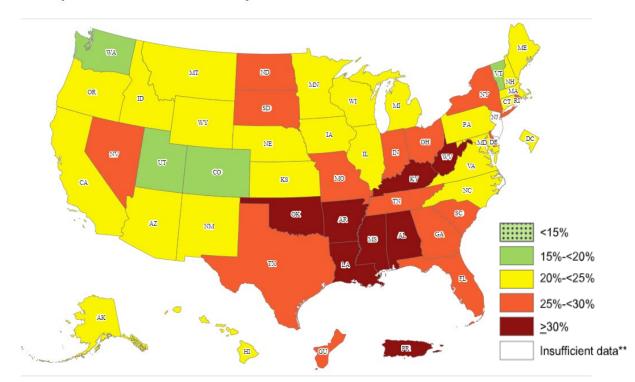
- Foods come first, but **reducing calories** for weight loss or from using GLP-1s makes it **challenging to meet nutrient needs** from diet alone
- Dietary **supplementation increases nutrient density** of the diet and can help meet nutrient requirements **within calorie limits**



## **High Rates of Inactivity**



Prevalence of Self-Reported Physical Inactivity\* Among U.S. Adults by State and Territory, BRFSS, 2017–2020



- 25% of adults say they do **no physical activity**
- Most adults spend about 9.5 hours a day being sedentary
- Less then 5% of adults get 30 minutes of leisure activity each day
- Only 1 in 4 adults meet guidelines for aerobic and muscle strengthening activity (>150 minutes moderate intensity + 2 muscle training sessions/week)

"During the past month, other than your regular job, did you participate in any physical activities or exercises such as running, calisthenics, golf, gardening, or walking for exercise?" https://www.cdc.gov/physical-activity/php/data/inactivity-maps.html - Behavioral Risk Factor Surveillance System https://www.hhs.gov/sites/default/files/call-to-action-walking-and-walkable-communites.pdf Sedentary Behavior in United States Adults: Fall 2019 (nih.gov)

#### **Technology, Lifespan & Obesity** 90 Chemotherapy Human genome 80 Penacillin (3) 70 70 Insulin OW

1960

1950

Year

1970

1980

WWW

1990

2000

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90

80

60

50

40

30

20

10

Life expectancy

۲

2021: The Evolution of Technology and Physical Inactivity: The Good, the Bad, and the Way Forward - PMC (nih.gov)

0

-R 60

-4500 -2000

Vaccines

developed

1900

1930

first

1770

1860

Bacteria

60

50

40

30

**Food delivery** 0

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2010

8

C

%

Nature's way

## What is a GLP-1?

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#### **GLP-1** Executive summary



#### What is a GLP-1?

**Glucagon like peptide-1 aka GLP-1** <u>The hormone:</u> a gastrointestinal peptide hormone the body secretes naturally in response to food intake in the intestinal tract that stimulates insulin release.

**GLP-1 receptor agonists (GLP-1 RA) aka <u>The drug:</u> Injectable or oral drugs that mimics the action of GLP-1 used to treat type II diabetes and obesity.** 

Branded Examples: Ozempic, Wegovy, Rybelsus, Mounjaro, Zepabound

**Uses:** depending on type & brand they are used for diabetes glycemic control management, cardiovascular risk reduction and weight management in specific populations.

**Common Side Effects:** gastrointestinal related, eg nausea, vomiting, diarrhea

## The Drug



#### Semaglutide Common Side Effects

	Placebo N = 1,261 %	WEGOVY 2.4 mg N = 2,116 %
Nausea	16	44
Diarrhea	16	30
Vomiting	6	24
Constipation	11	24
Abdominal Pain <sup>a</sup>	10	20
Headache	10	14
Fatigue <sup>b</sup>	5	© 11

#### Tips for managing nausea

If you experience nausea, be sure to contact your health care professional. He or she will offer guidance on ways to manage it, which may include:

Wegovy Website



Eat bland, low-fat foods, likeEat foods that contain water, Avoid lying down after you eat<br/>like soups and gelatin





For educational purposes only. Wegovy® Side Effects | Wegovy® (semaglutide) Injection 2.4 mg Go outdoors for fresh air

Eat more slowly

## What is the Impact of GLP-1s on Calorie Intake?



Eating less on GLP-1s can also increase risk of low nutrient intake

2969 -726 -24% Mean Kcals Consumed kcals 2243\* Fewer Daily Calories 1093 1007 869 847\* 827\* 568\* LUNCH DINNER **PM SNACK** TOTAL Semaglutide (n = 30) ■ Placebo (n = 28)

Calorie Intake at Buffet-style Meal Challenge after 12 weeks Semaglutide 1.0 mg vs. Placebo Treatment

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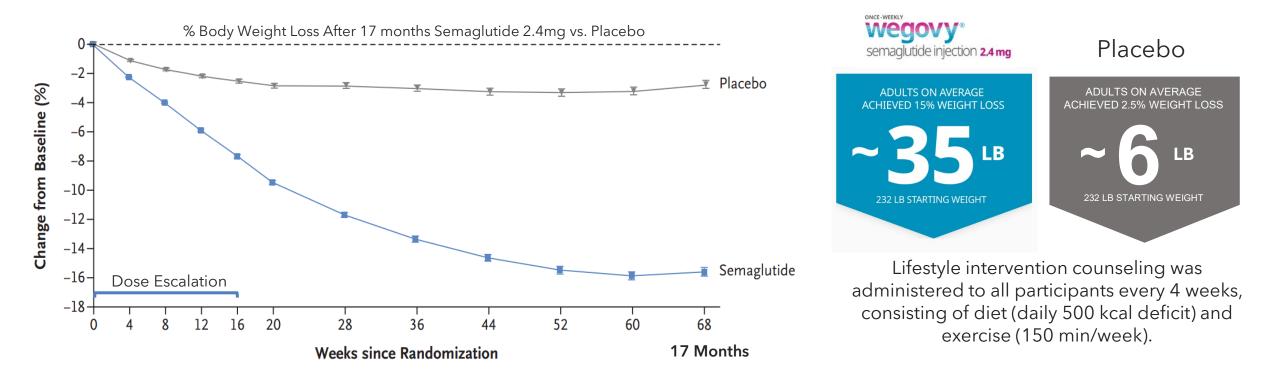
p<0.05 vs. placebo

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Adapted from Friedrichsen et al., The effect of semaglutide 2.4 mg once weekly on energy intake, appetite, control of eating, and gastric emptying in adults with obesity, Diabetes Obes Metab. 2021;23:754-762.

### **GLP-1 Drug Impacts on Weight Loss**

Significant effects beyond diet and exercise alone



Nature's

#### Body weight (kg) Body weight (%) – change from baseline -2 -ADULTS ON AVERAGE HAD 12% ADULTS ON AVERAGE HAD 2% WEIGHT REGAIN WEIGHT REGAIN -4 . 1 Year After -6 Discontinuing change from baseline -8 . 12% 232 LB STARTING WEIGHT 232 LB STARTING WEIGHT -10Weight -10 . Regain -12 **Post-Semaglutide Weight Loss Maintenance:** -14~10 LB Loss -15-16 -5% Body Weight Semaglutide 2.4 mg arm Placebo arm -180 4 8 12 16 20 28 36 52 60 68 75 80 104 120 44 Time since randomization (wk)

**GLP-1** Drug Weight Loss Maintenance Weight regain is likely, but overall results can be clinically meaningful

C

ONCE-WEEKLY

semaglutide injection 2.4 mg

For educational purposes only.

2 -

0

68-week treatment phase

Nature's Vol

Placebo

LB

Adapted from: Wilding, et al. Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. Diabetes Obes Metab. 2022;24:1553-1564.

52-week off-treatment

extension phase

## **GLP-1** Drugs in the Real World

Growing understanding of consumer weight management behaviors, including usage of GLP-1s

New Weight Management Cycle with GLP-1 Drugs?



#### Many Consumers Stop GLP-1s Before Experiencing Full Clinical Benefit

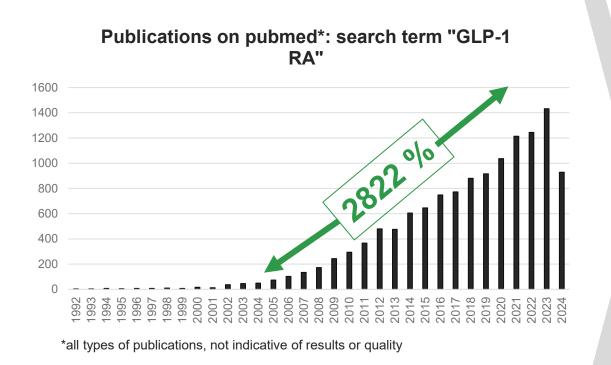
Time Since Starting Drug Treatment	GLP-1 Users Discontinuing Drug*
0 to <4 weeks	1%
4 to <8 Weeks	41%
8-12 Weeks	15%
>12 Weeks	42%

\*Prescribed clinical treatment of >12 weeks to achieve ≥5% loss of body weight; Based on BCBS submitted insurance claims 2014-2023 Nature

## GLP-1, What's Next

#### Future Research Areas





#### Clinicaltrial.gov

- Total studies related to "GLP-1": 2025
  - Active studies: ~ 594
- Topics for research (beyond the current):
  - Alcohol use
  - Mental health
  - Kidney disease
  - Inflammation
  - Pregnancy
  - PCOS
  - Alzheimers
  - Parkinsons
  - Cancer



# The Impact of GLP-1 Drugs on the Natural Products Industry

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## Introduction to GLP-1 Drugs

- GLP-1, short for Glucagon-Like Peptide-1, is a hormone produced in the intestine that plays a pivotal role in regulating blood sugar (glucose) levels and appetite. When you consume foods, especially carbohydrates, GLP-1 is released to stimulate insulin secretion, promoting glucose uptake by cells, and thus reducing your blood glucose levels.
- Glucagon-like peptide-1 receptor agonists (GLP-1 RA) are a class of medications that mainly help manage blood sugar (glucose) levels in people with type 2 diabetes. Some GLP-1 RA drugs can also help with obesity. They mimic the action of the natural hormone GLP-1.
- These medications are relatively new. The U.S. Food and Drug Administration (FDA) approved the first GLP-1 RA drug (exenatide) in 2005.
- GLP-1 RA drugs alone can't treat type 2 diabetes or obesity. Both conditions require other treatment strategies, including lifestyle and dietary changes.
- GLP-1 RA drugs are most often injectable medications, meaning you inject a liquid medication with a needle and syringe. Other names for this medication class include: Glucagon-like peptide-1 agonists, GLP-1 receptor agonists, Incretin mimetics, GLP-1 analogs, or GLP-1 drugs.

Sources:

Exposure-response analyses of liraglutide 3.0 mg for weight management - PubMed (nih.gov)

Efficacy of Liraglutide for Weight Loss Among Patients With Type 2 Diabetes: The SCALE Diabetes Randomized Clinical Trial - PubMed (nih.gov)

3 years of liraglutide versus placebo for type 2 diabetes risk reduction and weight management in individuals with prediabetes: a randomised, double-blind trial - PubMed (nih.gov)

## How Do GLP-1 Drugs Work?

- GLP-1 hormone (and GLP-1 drugs in this case) plays several roles in glucose control and body weight management.
- Stimulates insulin release from your pancreas: Insulin is an essential hormone that helps your body use the food you eat for energy. It lowers the amount of glucose (sugar) in your blood. If you don't have enough insulin, your blood sugar increases, potentially leading to diabetes.
- Inhibits glucagon secretion: Glucagon is a hormone your body uses to raise your blood sugar levels when necessary. GLP-1 prevents more glucose from going into your bloodstream.
- Slows stomach emptying: Slower digestion often means that your body absorbs less nutrients and releases less glucose (sugar) from the food you eat into your bloodstream.
- Suppresses appetite and increases satiety: GLP-1 affects areas of your brain that processes hunger and satiety. You feel fuller, so you eat less, and thus you lose weight.

Sources:

Biology of incretins: GLP-1 and GIP - PubMed (nih.gov)

Weight Loss and Maintenance Related to the Mechanism of Action of Glucagon-Like Peptide 1 Receptor Agonists - PMC (nih.gov)

## Side Effects of GLP-1 drugs

The most common side effects of GLP-1 receptor agonists are **digestive issues**: Loss of appetite, Nausea, Vomiting, Diarrhea, Constipation.

Other common side effects include:

- Muscle loss, Mild tachycardia (increased heart rate).
- Indigestion (stomach upset); Bowel obstruction
- Pancreatitis, Gastroparesis, Gallstone attacks and bile duct blockage.
- Medullary thyroid cancer.
- Acute (sudden) kidney injury.
- Worsening diabetes-related retinopathy.

Sources:

RYBELSUS® Results | RYBELSUS® (semaglutide) tablets 7 mg or 14 mg

Risk of Gastrointestinal Adverse Events Associated With Glucagon-Like Peptide-1 Receptor Agonists for Weight Loss | Gastroenterology | JAMA | JAMA Network

Adverse drug reactions of GLP-1 agonists: A systematic review of case reports - ScienceDirect

Once-Weekly Semaglutide in Adults with Overweight or Obesity | New England Journal of Medicine (nejm.org)



## Limitations of GLP-1 drugs

- Expensive Branded version typical cost up to \$1,300 /month before insurance; even compounded generic version costs up to \$300/month.
- Limited Access Rybelsus is only approved for glucose control for T2D, not weight loss. Wegovy (injectable) is only for obese people or those with BMI>27 AND weight-related medical problems. All need prescription.
- Moderate weight loss of oral form (Injectables work better) In the 6-month study, people on 14 mg/d lost only 4.1% of body weight, while people on 7 mg/d lost only 2.6%; vs people on placebo lost 1.5%.
- Weight rebound Majority of people regained weight after stopping, not sustainable. YoYo weight change can be more harmful than doing nothing
- Drug Dependence

Source:

https://www.rybelsus.com/why-rybelsus/rybelsus-results.html

## GLP-1 Drugs Market Size and Adoption Rate

- Market Size: Global GLP-1 drugs market expected to surpass \$100 billion by 2030, primarily driven by increasing consumer demand for weight loss.
- Adoption Rate:
- A 2024 KPMG report estimated that **3.5% of the US adult population**, approximately 13 million people, are currently using GLP-1 drugs, with numbers rising.
- A 2024 Mintel report estimated that **15% of US adult population** who are actively managing their weight use GLP-1 drugs.
- International markets including the UK, Australia, Middle East, Singapore, also foresee increasing demand of GLP-1 drugs.

Sources:

https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs

## GLP-1 Drugs Disrupt Weight Management

- Effectiveness: Clinical trials report effective weight loss for GLP-1 users within 12 months.
- Impact on Spending: GLP-1 users reduce food consumption by 21%, resulting in significant declines in grocery and dining expenses.
- Market Shift: Traditional weight management products, such as meal replacements and dietary supplements, have seen decreased demand.

Sources:

https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs

#### Impact on Conventional Weight Loss Supplements

- Declining Categories: Products like weight loss supplements and slimming teas are forecasted to decline by up to 13.5% by 2028.
- Why the Decline? GLP-1 drugs directly target appetite suppression, reducing the need for supplements like fat burners and appetite suppressants.
- Alternative Strategies: established brands should focus on repositioning supplements to address nutritional deficiencies and/or other side effects associated with GLP-1 use (e.g., vitamin B12, iron); e.g., GNC GLP-1 Support Program



Sources:

https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs

## Impact on Meal Replacement Products

- Category at Risk: Certain meal replacement products, which have historically been strong in weight loss markets, are forecasted to experience a -3.3% CAGR by 2028 due to GLP-1 substitution.
- Complementary Role: However, some GLP-1 users incorporate meal replacements as part of their nutritional regimen, especially products high in protein and low in calories, which can be positioned as companion to GLP-1 drugs.

Sources:

Euromonitor

https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs

#### Functional Foods and New Consumer Preferences

- Rising Demand for Functional Foods: GLP-1 users seek nutrientdense, high-fiber, and high-protein options to support satiety without excess calorie intake
- Projected Growth: Sales of functional foods tailored to weight management and metabolic health are expected to grow by 5 – 10% CAGR depending on region.
- Innovation Opportunities: Nestlé's "Vital Pursuit" line and Daily Harvest's GLP-1 companion meals are examples of functional foods tailored to GLP-1 users

Source:

**Euromonitor** 

https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs

#### Wellness Products: A Growth Segment

• Mental & Physical Wellness: GLP-1 users experience **muscle loss**, skin elasticity issues, or other mental and physical issues. This presents opportunities for wellness products that support these areas.

- examples: Vital Proteins natural protein products, HMB ( $\beta$ -hydroxy  $\beta$ -methylbutyrate) and creatine from TSI Group

• Targeted Products: Supplements for mental health, skin health, collagen production, and muscle retention are gaining popularity among this consumer group.

Sources:

Euromonitor

https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs

#### Behavioral Changes in GLP-1 Consumers

- Calorie Reduction Without Sacrifice: GLP-1 consumers reduce their caloric intake but are not necessarily changing food types simply eating less of their favorite meals.
- Shift to Premium Products: High-income GLP-1 users often maintain or increase spending on premium, functional foods that complement their weight loss journey.
- Category Hoppers, a consumer segment, actively seek new and innovative products to support their weight loss journey.

Sources:

<u>Euromonitor</u>

https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs

#### **Regulatory and Market Challenges**

- Regulatory Scrutiny: The rise of GLP-1 medications has led to increased scrutiny of traditional weight loss supplements regarding their efficacy claims
- Regulations on Compounded Medications: FDA oversight is tightening around compounded versions of GLP-1 medications, creating challenges for alternative formulations
- Compliance Focus: Natural product brands need to ensure compliance with regulatory frameworks and focus on transparent claims

Sources:

**Euromonitor** 

https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs

#### **Innovations in Supplement Formulations**

- Supplements for GLP-1 Users: GLP-1 drugs often cause digestive and nutrient absorption issues, leading to opportunities for specialized multivitamins and protein supplements to support overall health.
- Safe, Natural, Effective Alternatives: Some consumers will choose not to engage with GLP-1 drugs for cost and lifestyle reasons, while others worry about the long-term risk of engaging with these drugs. Brands can appeal to these consumers by demonstrating that their products are both efficacious and cost-effective, while supplements offering natural alternatives can attract consumers reluctant to engage with chemical solutions.
- Ingredient Focus: probiotics are rising in popularity as they support metabolic health and gut health, addressing common side effects of GLP-1 drugs; berberine, along with other plant-based extracts are used as a safer, more natural option for those unable or unwilling to use GLP-1 drugs.
- Long-Term Health Solutions: Natural products that address blood sugar balance, gut health, and insulin sensitivity can offer additional benefits to GLP-1 consumers.

Sources:

Euromonitor

https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs

#### **Opportunities in Natural Products**

- Untapped Markets: Not all consumers can afford GLP-1 drugs (which cost between \$936-\$1,349 monthly without insurance). This opens opportunities for natural appetite suppressants and weight management solutions for the middle market.
- Alternative Solutions: Products such as high-fiber supplements, plant-based protein, and natural satiety aids (e.g., glucomannan) are seeing renewed interest.
- Leverage Personalization Health Solutions: The rise of AI and personalized nutrition is expected to grow, with companies integrating wearable technology to offer real-time dietary and fitness recommendations.

Sources:

**Euromonitor** 

https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs

https://kpmg.com/kpmg-us/content/dam/kpmg/pdf/2024/glp-1-meds-impact-on-food-and-bev-ind.pdf

#### **Consumer Demographics and Marketing Insights**

**Consumer Behavior Segments** 

- Premium Purchasers: These consumers reduce their food intake but shift spending toward premium brands offering functional health benefits
- Healthy Choice makers: They actively seek low-calorie, nutrient-rich foods, driving demand for clean-label, functional ingredients
- Category hoppers: they actively seek new products tailored to weight loss.
- Report shows higher-income consumers likely remain loyal to premium functional food brands even as they reduce overall calorie intake.
- Marketing Insights: Brands should focus on messaging around **health**, **convenience**, and **complementary benefits** to attract GLP-1 users

Sources:

<u>Euromonitor</u>

https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs

## Takeaways

- What? GLP-1 drugs are here to stay. Their impact on the natural products industry is profound.
- So What? Brands can adapt by innovating within complementary wellness products, functional foods, and personalized nutrition solutions.
- Now What? Strategic focus on premium ingredients, alternative offerings, compliance, and targeted marketing could help to remain competitive and capture new opportunities.

## Let's Connect!

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**Lawry Han** Founder/ Chief Science Officer Alpine Biotech



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