

NASDAQ: HRTS

# Tema Cardiovascular and Metabolic ETF

Addressing the "Diabesity" epidemic

Q4 2023

For inquiries: info@temaetfs.com



### Disclosure



Carefully consider the Fund's investment objectives, risk factors, charges and expenses before investing. This and additional information can be found in the Fund's prospectus or summary prospectus, which may be obtained by visiting <a href="https://www.temaetfs.com">www.temaetfs.com</a>.

Read the prospectus carefully before investing.

#### **Risk Information**

Investing involves risk including possible loss of principal. There is no guarantee the adviser's investment strategy will be successful.

Sector Focus Risk: Obesity and Cardiology companies are highly dependent on the development, procurement and marketing of drugs and the protection and exploitation of intellectual property rights. A company's valuation can also be greatly affected if one of its products is proven or alleged to be unsafe, ineffective or unprofitable. The stock prices of oncology companies have been and will likely continue to be very volatile. The costs associated with developing new drugs can be significant, and the results are unpredictable. Newly developed drugs may be susceptible to product obsolescence due to intense competition from new products and less costly generic products. Moreover, the process for obtaining regulatory approval by the U.S. Food and Drug Administration or other governmental regulatory authorities is long and costly and there can be no assurance that the necessary approvals will be obtained or maintained. Companies in the medical equipment industry group may be affected by the expiration of patents, litigation based on product liability, industry competition, product obsolescence and regulatory approvals, among other factors.

Tema Global Limited serves as the investment adviser to Tema Cardiovascular and Metabolic ETF (the "Fund"), and NEOS Investments, LLC serves as a sub adviser to the Fund. The Fund is distributed by Foreside Fund Services LLC, which is not affiliated with Tema Global Limited nor NEOS Investments, LLC. Check the background of Foreside on FINRA's BrokerCheck.

**Distributor**: Foreside Fund Services LLC

For inquiries: info@temaetfs.com

# Tema: thematic ETFs managed differently



# Our name is our mission

Tema (noun) Latin for Theme

**Our mission** is to democratize access to institutionally-focused<sup>1</sup> thematic investing through risk-managed, active ETF strategies.

### Backed by top-tier<sup>2</sup> investors & led with expertise<sup>3</sup>

























### Management team



**Maurits Pot**Founder and CEO



**Yuri Khodjamirian, CFA** 



A David K. Song
MD, PhD, CFA
Cardiovascular and Metabolic PM

# Tema ETFs product sample



Luxury



American Reshoring



Monopolies and Oligopolies

# The "Diabesity" crisis is at a breaking point



Diabetes doubles the risk

of cardiovascular disease<sup>5</sup>

Over 80% of patients with coronary heart disease (CHD) are overweight or obese<sup>4</sup>



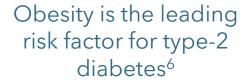
# CARDIOVASCULAR DISEASES

#1 cause of death<sup>1</sup>



#### **OBESITY**

42%<sup>1</sup> of US adults are obese<sup>2</sup>



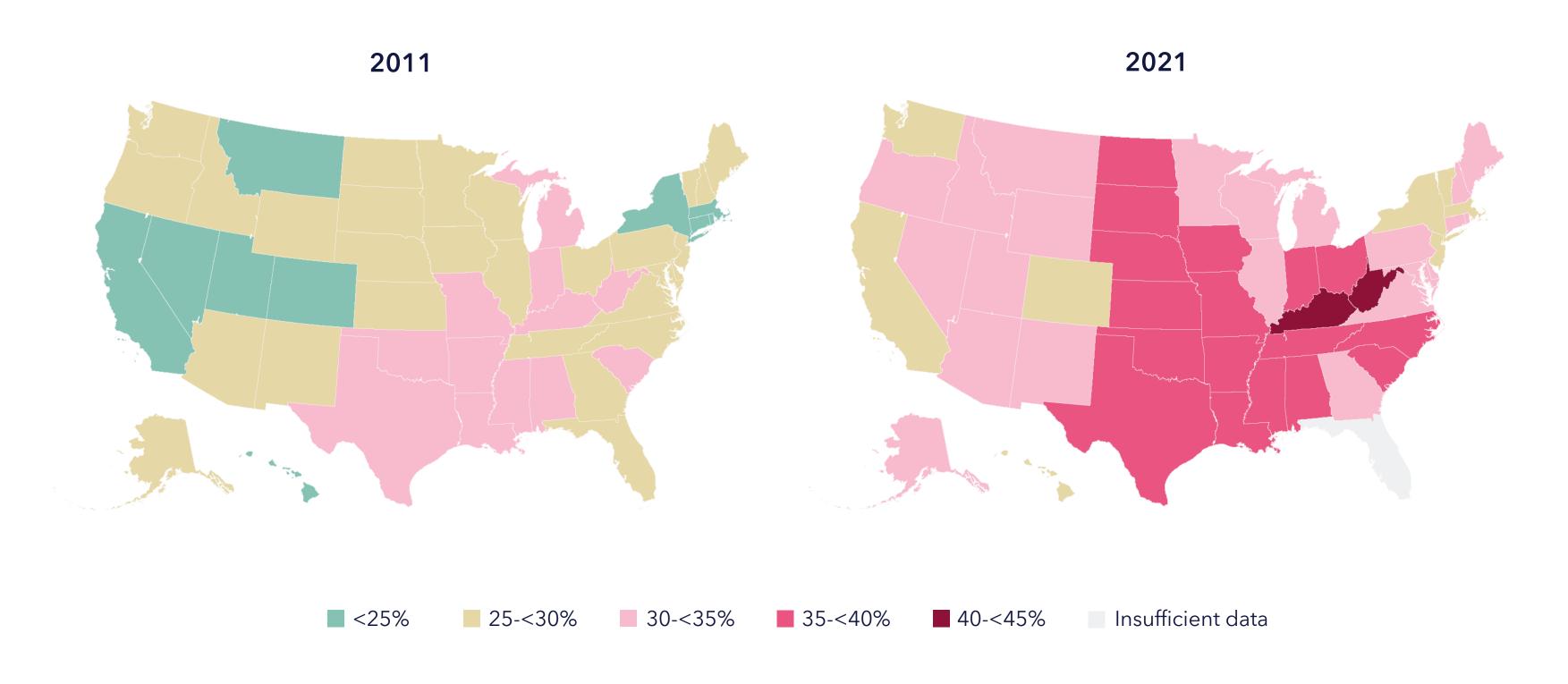


#### **DIABETES**

Half a billion adults affected globally<sup>3</sup>

# Obesity is getting worse: 42% of US adults are obese

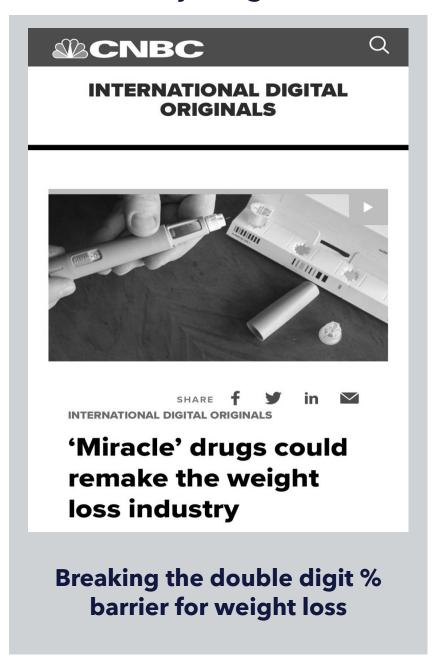




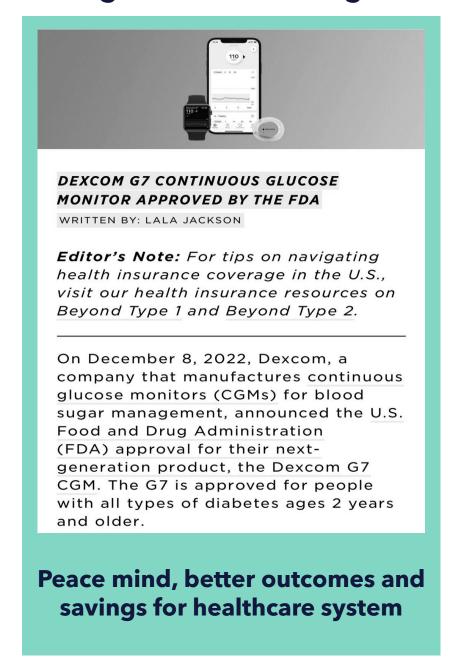
# New breakthroughs in metabolics are turning the tide



**GLP-1:** first effective obesity drugs ever



### **Diabetes: continuous** glucose monitoring



### Gene editing: treating the root cause of heart disease



#### CRISPR-Cas9 In Vivo Gene Editing for Transthyretin Amyloidosis

Julian D. Gillmore, M.D., Ph.D., Ed Gane, M.B., Ch.B., Jorg Taubel, M.D., Justin Kao, M.B., Ch.B., nna Fontana, M.D., Ph.D., Michael L. Maitland, M.D., Ph.D., Jessica Seitzer, B.S., Daniel O'Connell, Ph. Kathryn R. Walsh, Ph.D., Kristy Wood, Ph.D., Jonathan Phillips, Ph.D., Yuanxin Xu, M.D., Ph.D., Adam Amaral, B.A., Adam P. Boyd, Ph.D., Jeffrey E. Cehelsky, M.B.A., Mark D. McKee, M.D., Andrew Schiermeier, Ph.D., er Harari, M.B., B.Chir., Ph.D., Andrew Murphy, Ph.D., Christos A. Kyratsous, Ph.D., Brian Zambrowicz, Ph.D., Randy Soltys, Ph.D., David E. Gutstein, M.D., John Leonard, M.D., Laura Sepp-Lorenzino, Ph.D.,

and David Lebwohl M.D. ABSTRACT

ansthyretin amyloidosis, also called ATTR amyloidosis, is a life-threatening sease characterized by progressive accumulation of misfolded transthyretin by Division of Medicine, London, Royal Free disease characterized by progressive accumulation of misfolded transthyretin (TTR) protein in tissues, predominantly the nerves and heart. NTLA-2001 is an in vivo gene-editing therapeutic agent that is designed to treat ATTR amyloidosis by reducing the concentration of TTR in serum. It is based on the clustered regularly interspaced short palindromic repeats and associated Cas9 endonuclease (CRISPR-Cas9) system and comprises a lipid nanoparticle encapsulating messenge RNA for Cas9 protein and a single guide RNA targeting TTR.

After conducting preclinical in vitro and in vivo studies, we evaluated the safety and pharmacodynamic effects of single escalating doses of NTLA-2001 in six patients with hereditary ATTR amyloidosis with polyneuropathy, three in each of the two initial dose groups (0.1 mg per kilogram and 0.3 mg per kilogram), within an

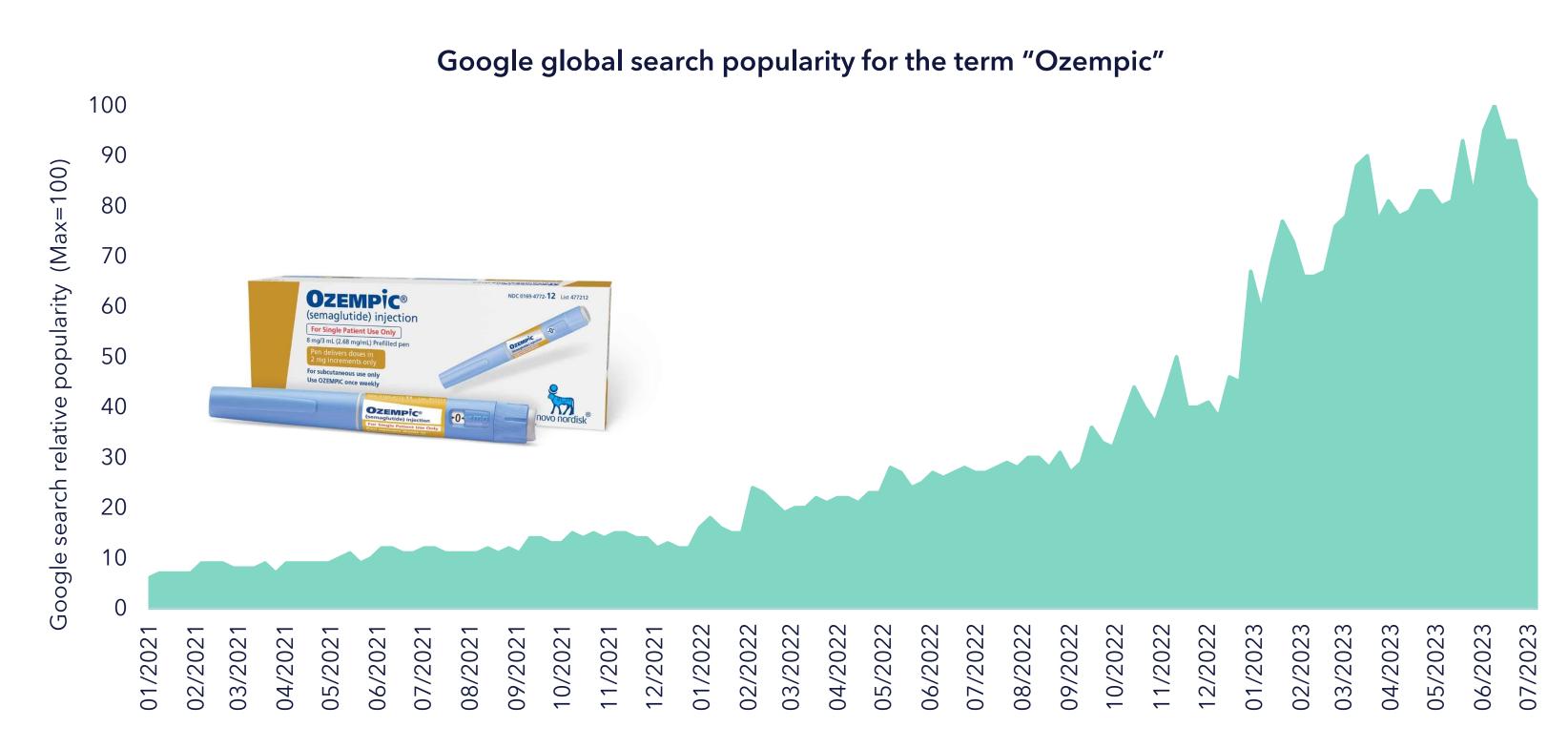
Preclinical studies showed durable knockout of TTR after a single dose. Serial assessments of safety during the first 28 days after infusion in patients revealed few This article was publish 2021, at NEJM.org. dverse events, and those that did occur were mild in grade. Dose-dependent pharmacodynamic effects were observed. At day 28, the mean reduction from N Engl J Med 2021;385:493-502 baseline in serum TTR protein concentration was 52% (range, 47 to 56) in the group that received a dose of 0.1 mg per kilogram and was 87% (range, 80 to 96) n the group that received a dose of 0.3 mg per kilogram.

thy, administration of NTLA-2001 was associated with only mild adverse events and led to decreases in serum TTR protein concentrations through targeted knockout of TTR. (Funded by Intellia Therapeutics and Regeneron Pharmaceuticals; ClinicalTrials.gov number, NCT04601051.)

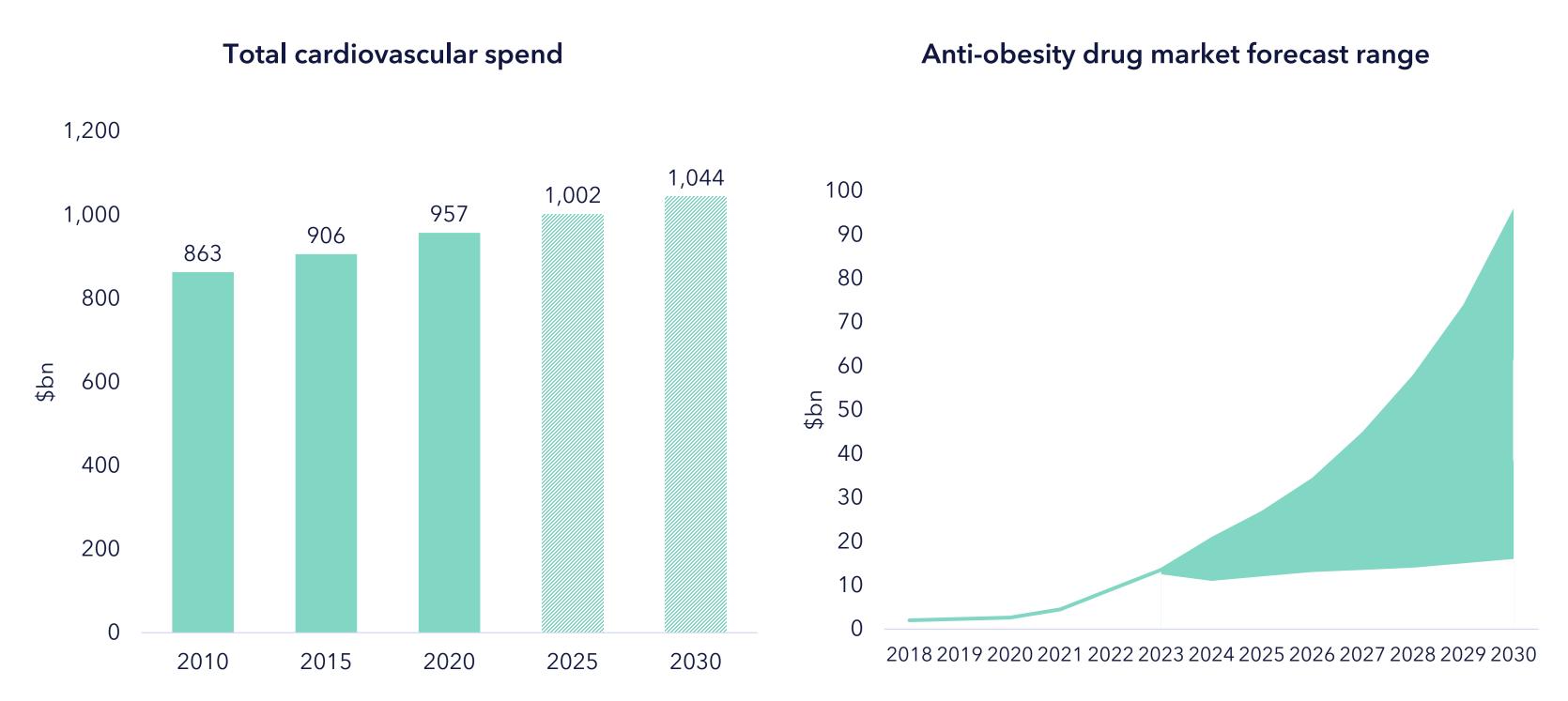
One of the first in-vivo gene therapies in development

# Ozempic is a watershed moment for Obesity, seeing enormous demand





# Why now? Cardiovascular disease spend forecast to crest \$1 trillion annually **'iema** while anti-obesity drug market alone could cross \$100bn by 2030

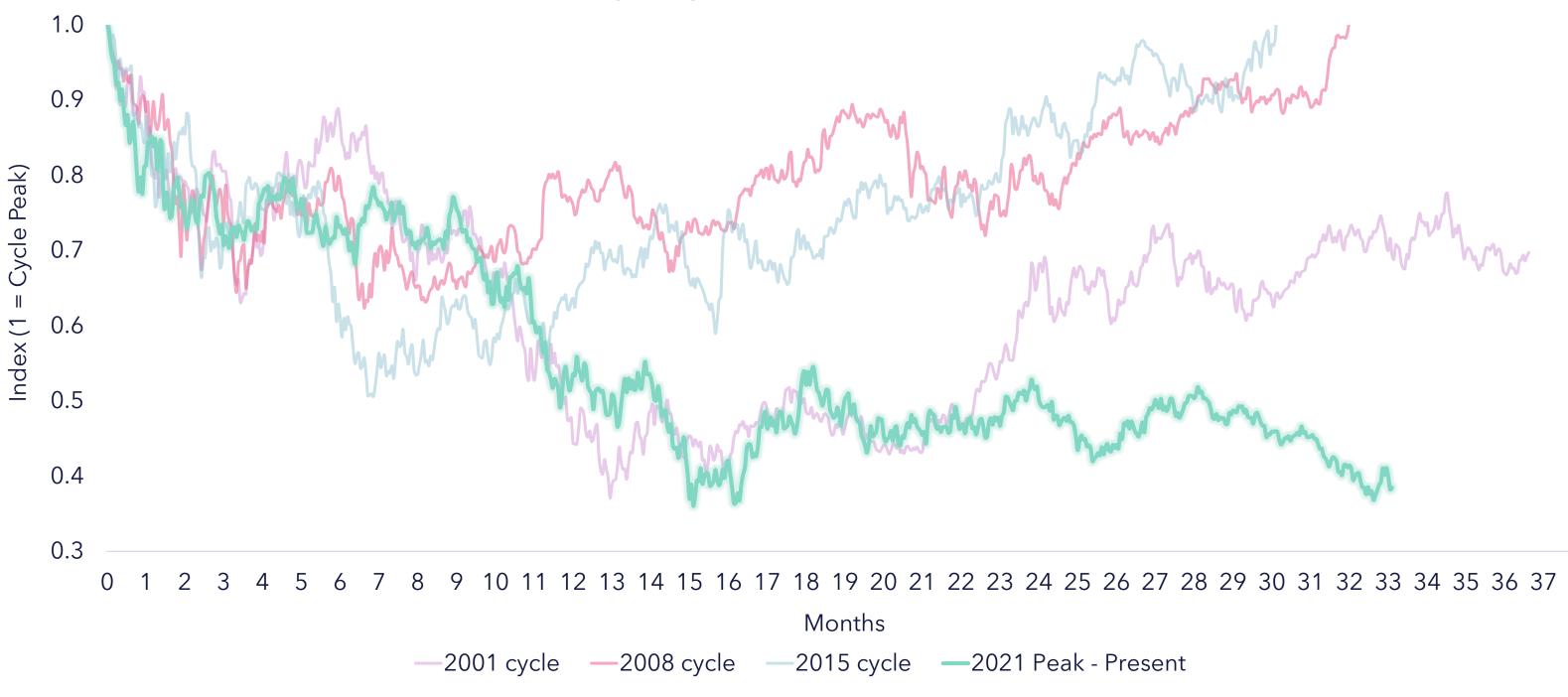


Source: LHS - World Economic Forum and the Harvard School of Public Health. "The Global Economic Burden of Non-communicable Diseases", 2011. Bloom, D.E., Cafiero, E.T., Jané-Llopis, E., Abrahams-Gessel, S., Bloom, L.R., Fathima, S., Feigl, A.B., Gaziano, T., Mowafi, M., Pandya, A., Prettner, K., Rosenberg, L., Seligman, B., Stein, A.Z., & Weinstein, C. (2011). RHS – IQVIA Forecast Link, May 2023. Forecasts are inherently limited and should not be relied upon when making investment decisions. There is no guarantee projected growth will occur. See Glossary in appendix for full definition.

# Why now? Worst biotech downcycle in decades, nearly 29% of small biotech trade below net cash value<sup>1</sup>

# Tema





Source: Bloomberg. S&P Biotechnology Select Industry Index used for 2008, 2015, 2021 cycles. Cycles start dates are defined by index price peaks for each year. Nasdaq Biotech Index used for 2001 cycle. Past performance is not indicative of future results. ¹Bloomberg as of October 2023, biotech defined by GICS definition of the biotechnology sub-industry, small cap defined by North American companies under \$2 billion mkt cap. The referenced index is shown for informational purposes only and is not meant to represent the Fund. You cannot invest directly in an index. The measures are representative of the indexes underlying holdings and are not indicative of future performance. See Glossary in appendix for full definition.

# Cardiovascular and metabolics are attractive healthcare sub-segment



Characteristics	Tema HRTS ETF	General Healthcare Index	
Growth	Secular growth (top drugs e.g., Ozempic / Mounjaro reported high double-digit growth <sup>1</sup> )	GDP+ growth (as represents 20% of GDP)	
Chronic vs. Acute	Life-long diseases	Diluted with acute illnesses	
Barriers to Entry	High barriers to entry: Clinically - requires '000s patient outcome trials Commercially - primary care salesforce	High but lower in some sub-segments	
Dynamisms	Large degree of technological change	Diluted (e.g., managed care, generic drugs)	
Pricing risk	Mitigation due to large healthcare system savings (Obesity alone directly costs health systems \$150bn²)	High risk (due to IRA reforms)	
Complexity of analysis	Requires detailed technology & commercial analysis given pace of change	Weak	

# Balanced portfolio across technologies and modalities













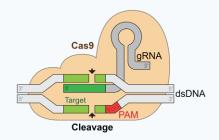








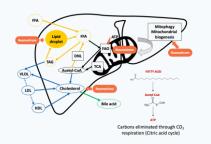




**CRISPR** editing







Resmetirom

Small molecule

approaches



Sapien 3 valve

& vascular devices

Interventional Diabetes cardiology devices



Gene editing & gene therapy

Amvuttra

RNA-based modalities

Ozempic

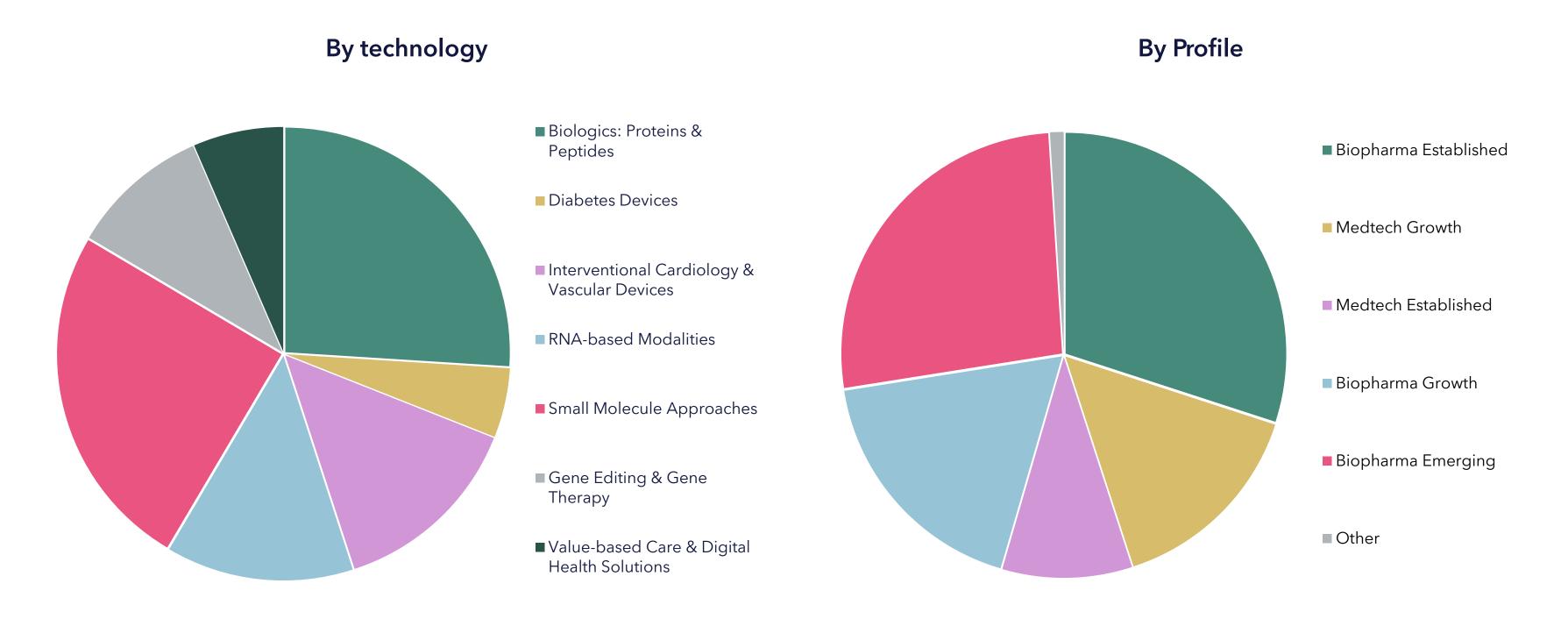
Biologics: proteins & peptides

Masimo SET pulse oximeter

Value-based care & digital health solutions

# Balanced portfolio across key technologies and risk profiles

# **Tema**



Source: Tema HRTS ETF Portfolio as of 11/21/2023, subject to change. Tema classification based on main business and company drivers. Risk profile is subjective categorization by Tema. Established refers to maturing growth businesses with a long-term history of profitable operations. Growth businesses refer to recently commercialized companies or companies in early stages of rapid growth from a material product cycle, with not yet at scale profit margins. Emerging Biopharma refer to pre-revenue companies. For a full list of fund holdings <u>click here.</u>

# Managed by a veteran stock picker





David K. Song, MD, PhD, CFA
Fund manager

Over 25 years of combined investment and life sciences industry experience.

David holds a medical degree from the University of Pennsylvania and a PhD in health economics from Wharton.

19 years of investment experience

Lead healthcare investment teams at Rockefeller, Millenium and Balyasny

Vast domain experience and expertise in healthcare

Managed Rockefeller Capital's Healthcare Fund Strategy for a decade

Academic publications in both biochemistry and health economics fields

Advised CEOs of private and public companies

# Why Tema?





**Process** 

Bottom-up research led by a team of **experienced** professionals



**Product** 

Own businesses that deliver breakthrough solutions to the metabolics epidemic, at reasonable valuations

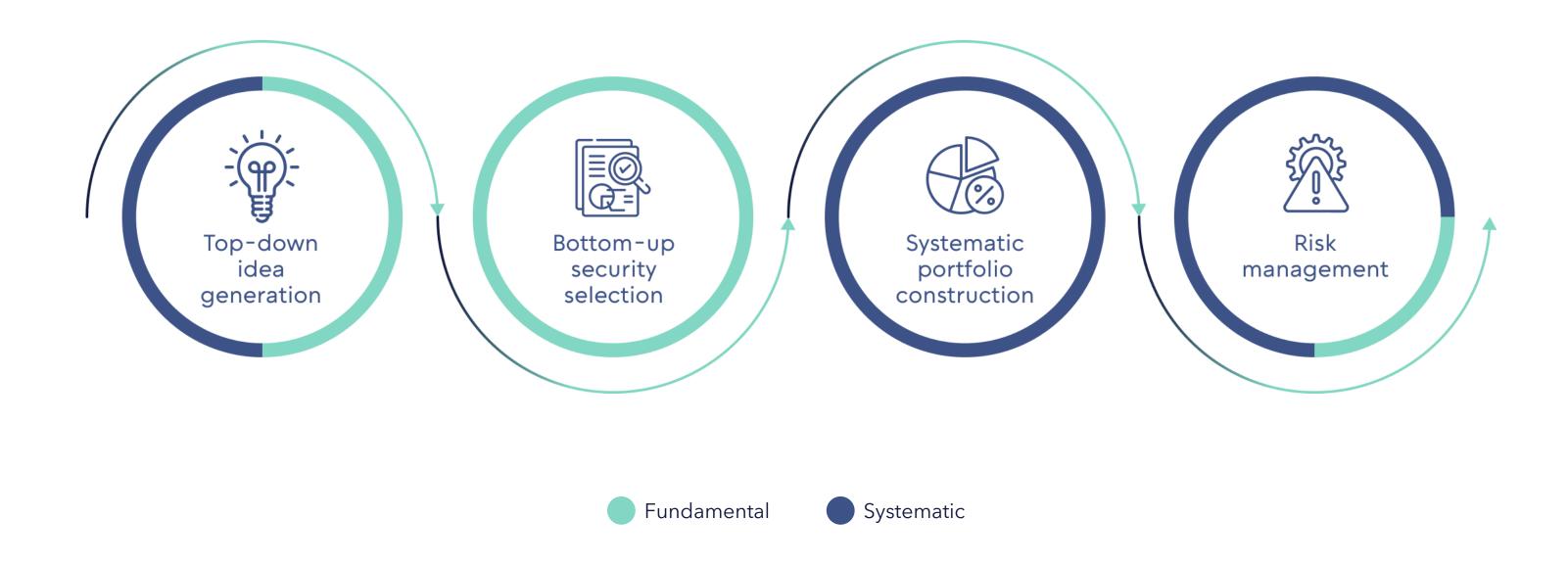


Firm

Supported by large operational and funding partners

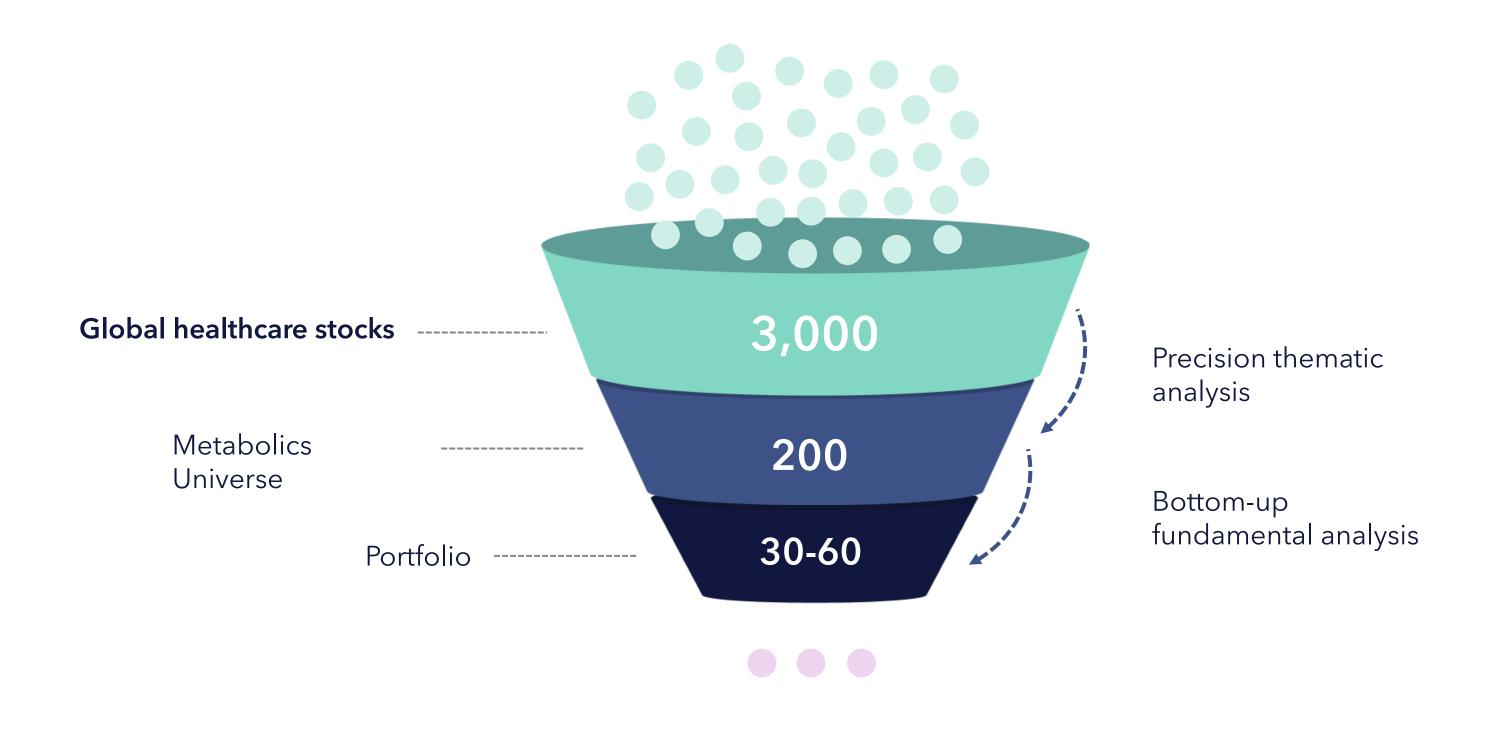
# Investment process: top-down idea generation, bottom-up fundamental security selection and systematic portfolio construction





# Idea generation: using expert led insights and quantitative tools to narrow down research set





# Security analysis: our fundamental research assesses stocks based on four key pillars



1

### Operating base

Solid R&D leadership or platform

Competitive advantage

Predictable cash flows

2

# Balance sheet and cash flow

Strong balance sheet

Strong cash generation

Access to non-dilutive capital

3

#### **Valuation**

Compelling asymmetric upside

Inexpensive vs. peers, history, or fundamentals

4

### Tema's edge

Deep understanding of clinical product profile and fundamental R&D drivers

See Glossary in appendix for full definition

# Portfolio construction: active systematic principles have the potential to drive considerable benefits to investors



### Three tiers of positions size

Conviction based sizing

Active systematic guidelines and rebalancing

Risk managed approach

Highest conviction position

Higher conviction position

Foundation position

#### **Benefits**



Risk managed conviction portfolios



Focus on stock-picking alpha



Limited trading activity, long-term focus



Mitigates human biases

# Risk oversight: we monitor risk from multiple viewpoints



Risk factor	Risk assessment	Mitigations
Drug pricing	Monitor developments in healthcare policy through policy expert contacts, conferences, and trade journals	Recent pricing provisions provide long-term clarity for industry. Invest in breakthrough drugs, as well as areas (e.g., medical devices) somewhat insulated from policy risks
Product risk - scientific and commercial	Medical publications, scientific conferences, calls with key opinion leaders, and third-party commercial product data sources	Avoid unfavorable risk-reward events, expert led analysis of clinical data, and models of patient populations and market sizes using third-party commercial data sources
Funding risk	Company financial reports and calls with management teams and peers	Portfolio construction and balance sheet analysis

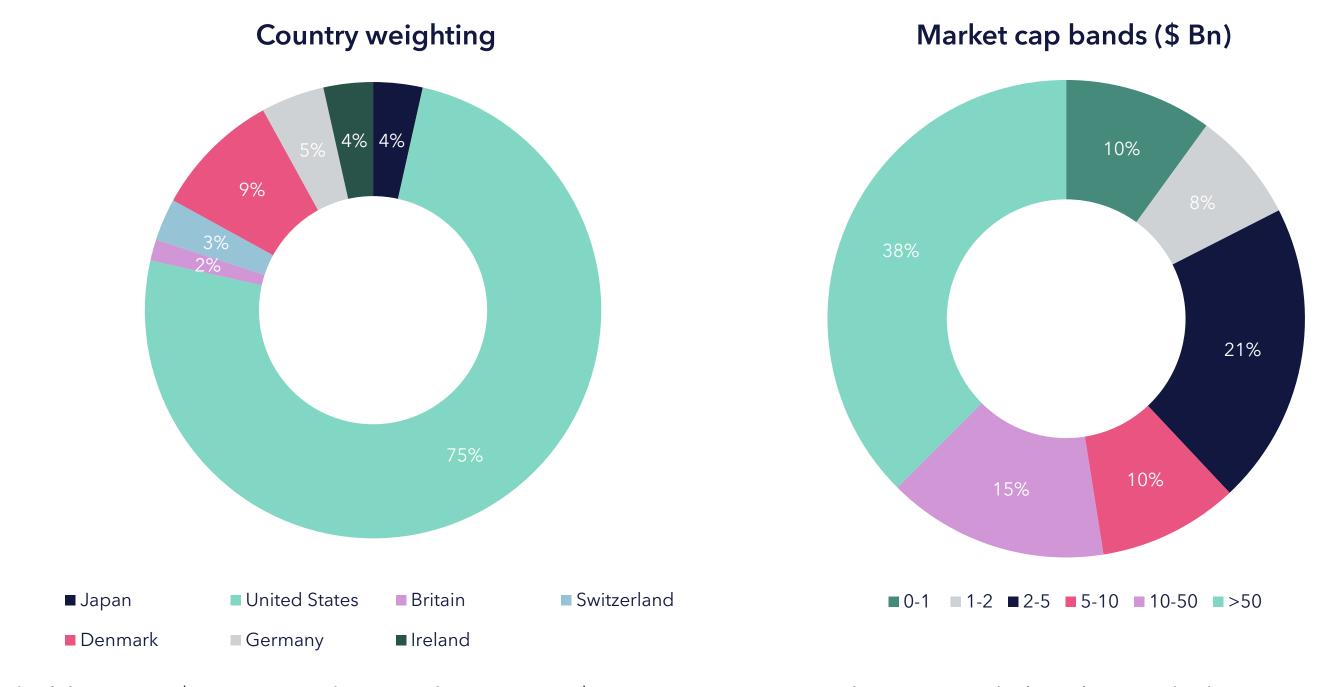
See Glossary in appendix for full definition.

Strictly for distribution outside the EU/UK

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# Current portfolio positioning





42 holdings • c\$3.3 Bn median market cap • c\$151 M mean 6-month average daily value traded (ADVT) per holding

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# Appendix

# Case study: Madrigal



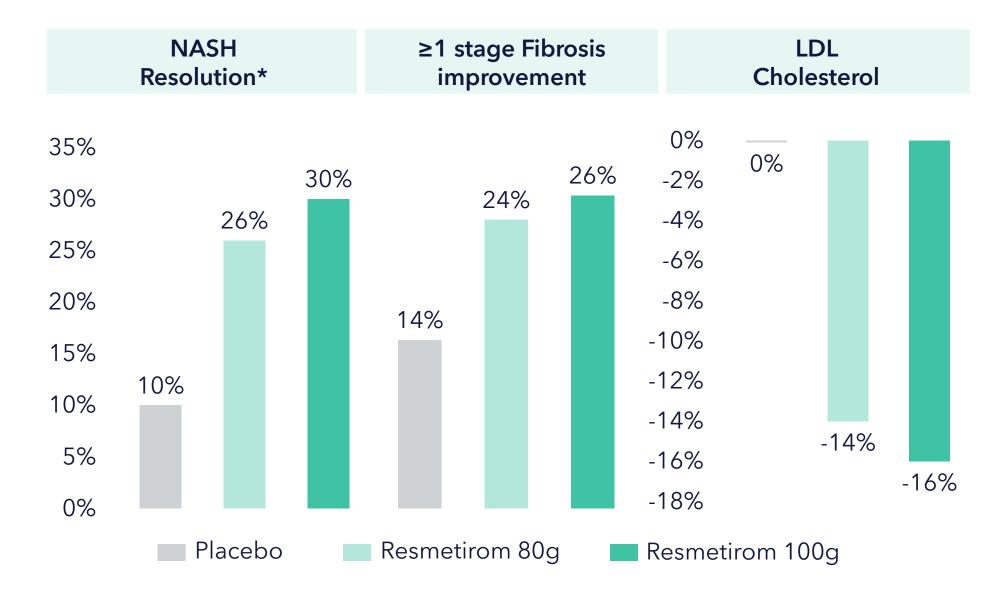


- First-in-class therapy for the treatment of NASH (non-alcoholic steatohepatitis)
- 20-30 million people have NASH in US, representing a significant unmet need with few treatment alternatives
- Expect accelerated approval of Resmetirom, based on robust Phase 3 data

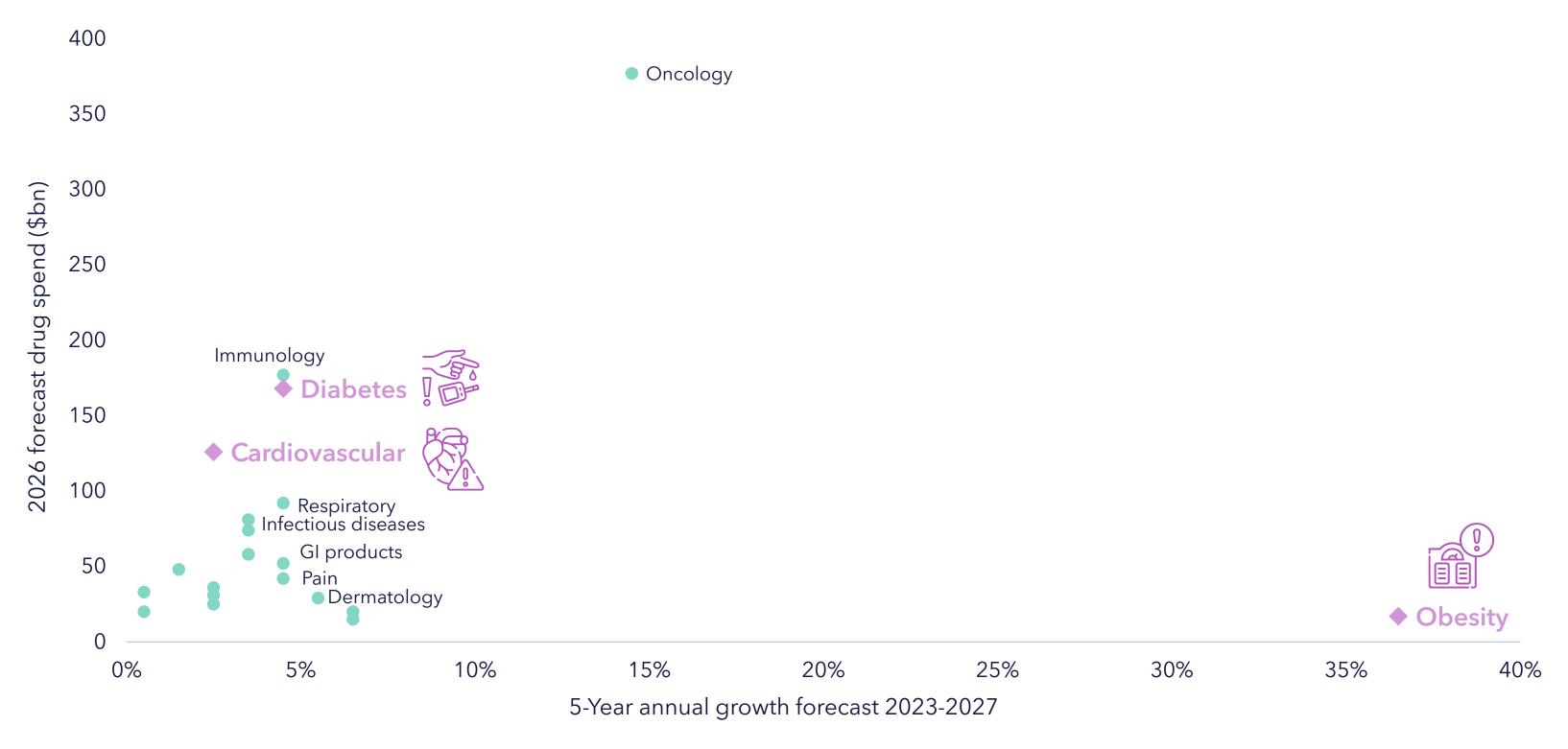


- Operating Base: Lengthy clinical trial timelines and significant market development in NASH give Madrigal, which already has completed clinical development, a competitive advantage
- Balance Sheet/Cash Flow: \$330m in cash, which provides Madrigal with ample runway through FDA approval
- Valuation: Current valuations are attractive as they reflect commercial uncertainties and residual concerns about regulatory approval
- What is our edge? View of the benefit in NASH is robust, and significant conviction in the vitality of the NASH commercial market





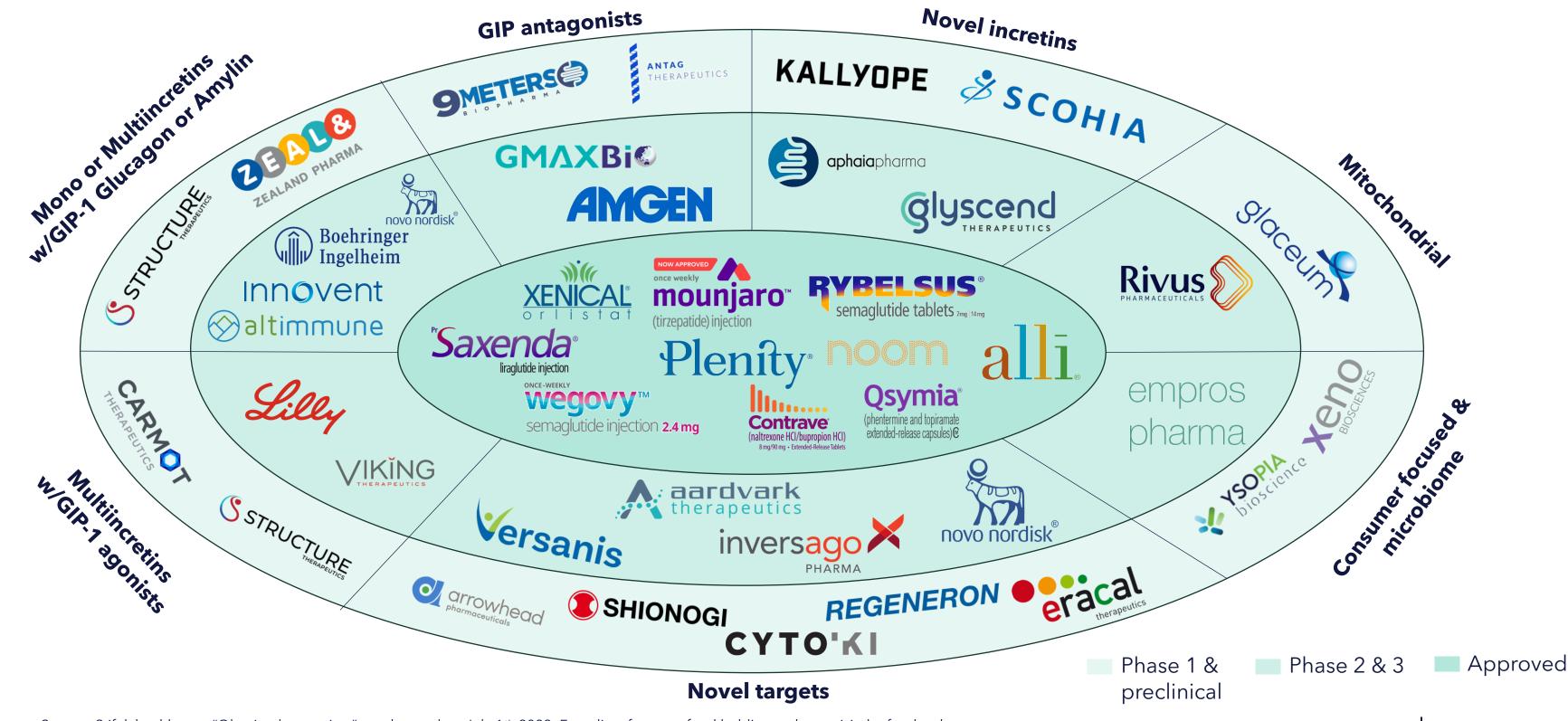
# Metabolics are a mix of large markets and young fast growing sub-sectors iema



Source: IQVIA Forecast Link, IQVIA Institute 2022. Report: The Global use of Medicines 2023: Outlook to 2027. IQVIA Institute for human data science, January 2023. See Glossary in appendix for full definitions. Forecasts are inherently limited and should not be relied upon when making investment decisions. There is no guarantee projected growth will occur.

# We believe the vibrant universe of approved and pipeline obesity drugs calls for an active management approach



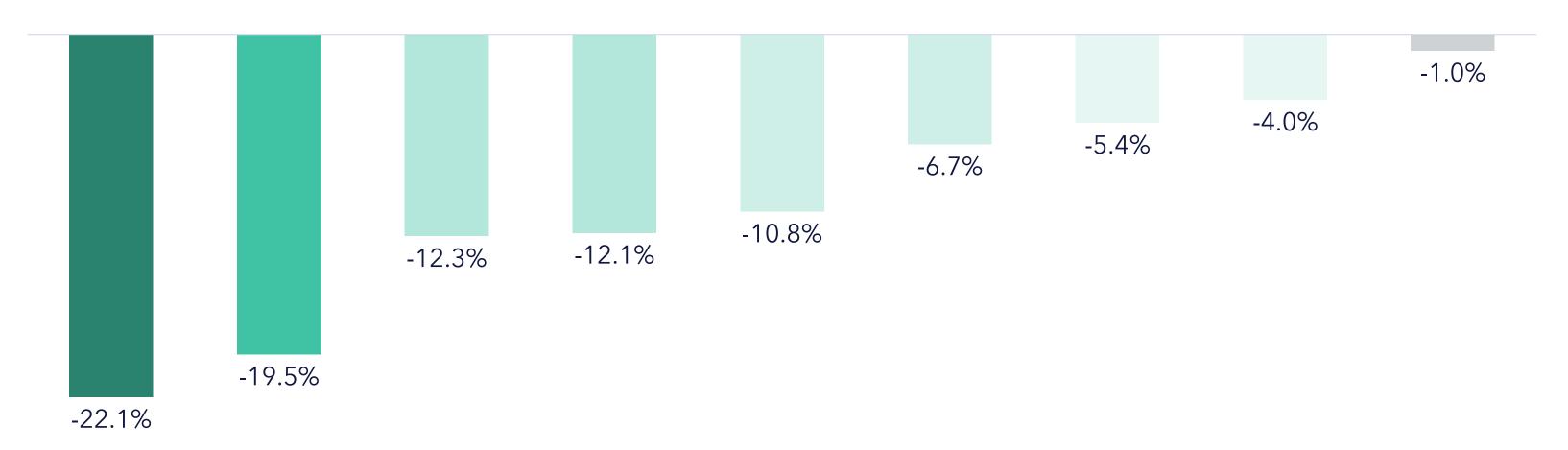


# Continual innovation in weight loss keeps pushing the boundary, especially in combination agents

### Tema

### Placebo adjusted weight loss among obese persons

(48 weeks, highest dose used)



Retatrutide

Tirzepatide

Semaglutide Survodutide

Qsymia

Nat / Buprop

Liraglutide Orlistat

Diet & exercise













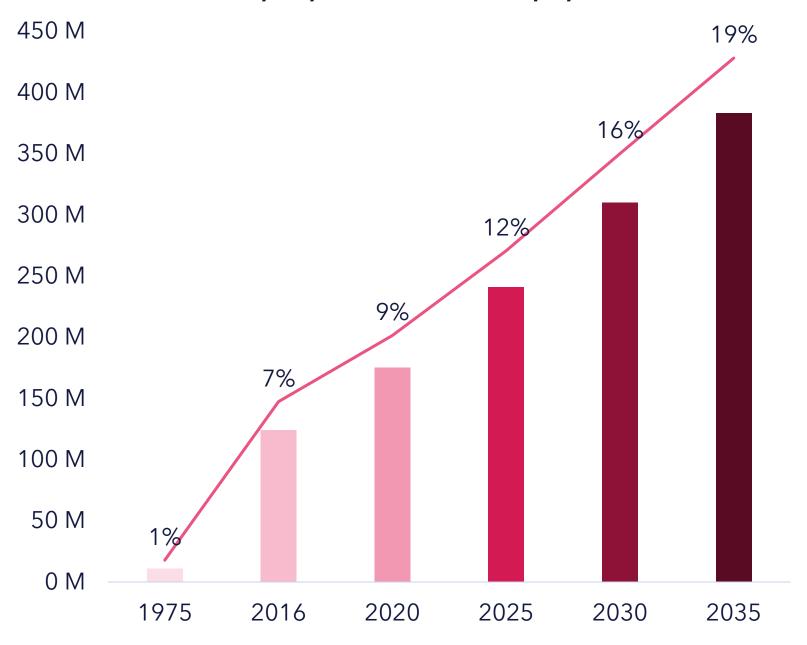




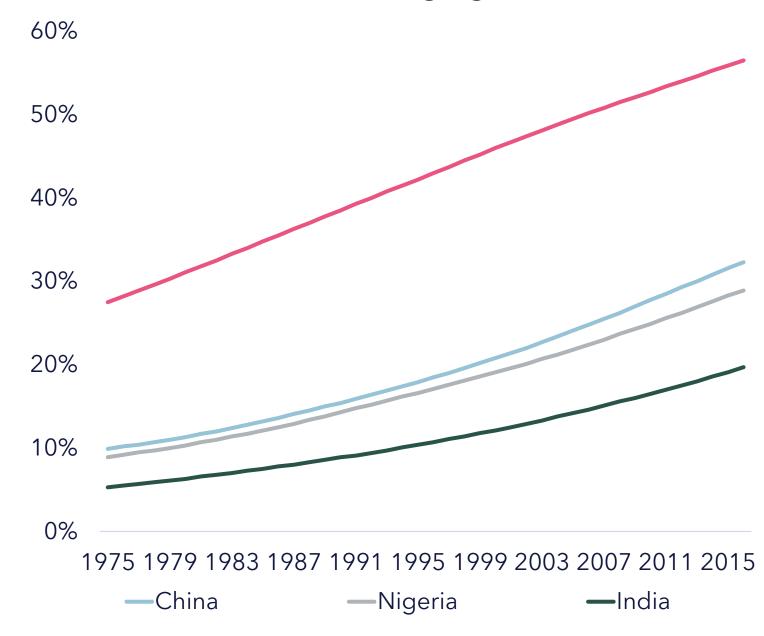
# Young people and many developing countries are afflicted with obesity

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# Obese children and adolescents (5-19 years old) (in M people and % of total population)



# % of adults obese or overweight<sup>2</sup> in selected emerging markets



# Patent expiries are set to intensify, yet M&A activity has not picked up

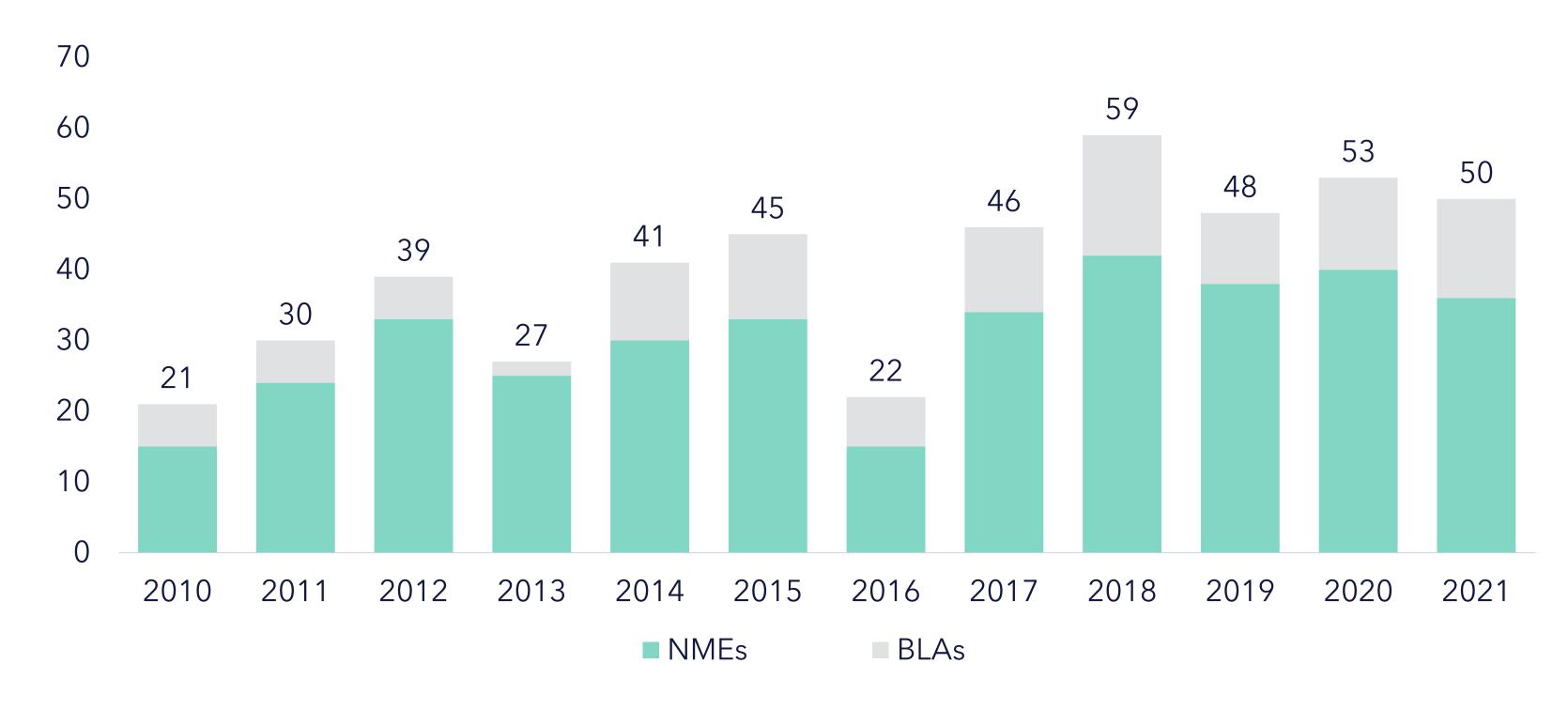




Source: Bioworld June 2023, Evaluate Pharma Aug 2022. Encompasses entire pharmaceutical industry, not just oncology. <sup>1</sup>Timelines are estimates based on key patent expirations or patent settlement agreements, and the life of a brand can be lengthened or shortened unexpectedly due to various factors. Forecasts are inherently limited and should not be relied upon when making investment decisions. There is no guarantee projected growth will occur. In addition, there is no guarantee it will translate to positive fund performance. M&A: merger and acquisitions. See Glossary in appendix for full definition.

# Number of new drug approvals has doubled in the last decade





# Glossary 1/2

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#### **Downcycle**

a time when there is less economic activity, or when prices or values of something are falling or low

#### MD

Medical doctor. MD is written after someone's name to indicate that they have been awarded a degree in medicine and are qualified to practice as a doctor.

#### PhD

degree awarded to people who have done advanced research into a particular subject. PhD is an abbreviation for 'Doctor of Philosophy'.

#### R&D

Research & development

#### **FDA**

The Food and Drug Administration is a government agency that regulates certain food, drugs, cosmetics, and medical products.

#### **S&P Biotechnology Select Industry Index**

S&P Select Industry Indices are designed to measure the performance of narrow GICS sub-industries. The Index comprises stocks in the S&P Total Market Index that are classified in the GICS biotechnology sub-industry.

#### Nasdaq Biotech Index

The NASDAQ Biotechnology Index contains securities of NASDAQ-listed companies classified according to the Industry Classification Benchmark as either Biotechnology or Pharmaceuticals which also meet other eligibility criteria. The NASDAQ Biotechnology Index is calculated under a modified capitalization-weighted methodology.

#### Patent cliff

potential sharp decline in revenues upon patent expiry of one or more leading products of a firm

#### NME

new molecular entity (NME): new drug whose active ingredient is a chemical substance that is marketed for the first time in the United States.

#### **BLA**

Biologics license application: a request for permission to introduce, or deliver for introduction, a biologic product into interstate commerce

#### PPP

Purchasing power parity: measurement of the price of specific goods in different countries and is used to compare the absolute purchasing power of the countries' currencies.

#### DDD

Defined Daily Dose (DDD): The assumed average maintenance dose per day for a drug used for its main indication in adults.

#### IQVIA

provider of biopharmaceutical development and commercial outsourcing services, focused primarily on Phase I-IV clinical trials and associated laboratory and analytical services, including consulting services.

#### **ADTV**

Average daily traded value - a measure of liquidity for individual stocks. Unless otherwise stated, this is calculated as the average daily volumes traded in the past 6 months x the most recent USD price.

#### **Alpha**

Alpha ( $\alpha$ ), used in finance as a measure of performance, is the excess return of an investment relative to the return of a benchmark index.

#### **AUM**

Assets Under Management

#### CAGR

Compounded annual growth rate between 2 points in time

#### **EBITDA**

EBITDA stands for Earnings Before Interest, Taxes, Depreciation, and Amortization. It is a financial metric used to assess a company's operating performance by focusing on its core profitability, excluding the impact of financing decisions, tax structures, and non-cash expenses such as depreciation and amortization.

#### **EPS**

Earnings per share (EPS) is a company's net profit divided by the number of common shares it has outstanding

#### **ESG**

Environmental, Social & Governance

#### ETF

Exchange-Traded Fund

#### Free Cash Flow or FcF

Free Cash Flow - calculated as cashflow from operations less capital expenditure (CAPEX)

#### Free Cash Flow conversion

Free cash flow conversion is calculated by taking free cash flow (FcF) and dividing it by net income, in order to assess what percentage of earnings convert to cash.

#### **GDP**

**Gross Domestic Product** 

#### P.a.

Per Annum

#### P/E

Price/Earning Ratio

#### ROCE

Return on Capital Employed- calculated by dividing the company's earnings before interest and taxes (EBIT) by its total capital employed, which includes both equity and debt

#### ROIC

Return on Invested Capital - calculated as net operating profit after taxes (NOPAT) / Invested capital (IC)

#### **Sharpe Ratio**

The Sharpe ratio is a measure of risk-adjusted return that compares the excess return of an investment to its volatility or risk, using the standard deviation of returns. It calculates how much additional return an investment generates for each unit of risk taken, relative to a risk-free investment. A higher Sharpe ratio indicates a better risk-adjusted performance

#### S&P 500

The Standard and Poor's 500, or simply the S&P 500, is a stock market index tracking the stock performance of 500 large companies listed on stock exchanges in the United States.

# Glossary 2/2

# Tema

#### **IQVIA**

provider of biopharmaceutical development and commercial outsourcing services, focused primarily on Phase I-IV clinical trials and associated laboratory and analytical services, including consulting services.

#### **Metabolics**

Refers to a group of medical conditions that result from disruptions in the normal metabolic processes within the body. These conditions often involve issues with the processing, storage, or utilization of energy sources like carbohydrates, fats, and proteins. Examples of metabolic disorders include obesity, diabetes, Gaucher's disease, and hemochromatosis.

#### Obesity

A medical condition involving an accumulation of excess body fat, usually defined as having a Body Mass Index (BMI) of 30 or higher. It's linked to increased risks of conditions like cardiovascular disease, type 2 diabetes, and certain cancers.

#### Overweight

Refers to having a Body Mass Index (BMI) between 25 and 29.9, indicating a higher body weight than considered optimal for health. It's associated with increased health risks, though to a lesser extent than obesity, including a higher likelihood of developing conditions like cardiovascular issues and type 2 diabetes.

#### BMI (Body Mass Index)

A numerical value derived from a person's weight and height. It's used as a rough indicator of whether a person has a healthy body weight. It's calculated by dividing a person's weight in kilograms by the square of their height in meters.

#### Cardiovascular

Relating to the heart and blood vessels, encompassing conditions and diseases that affect the circulatory system.

#### Diabesity

A term that combines "diabetes" and "obesity," highlighting the strong link between these two conditions, as obesity is a significant risk factor for developing type 2 diabetes.

#### Coronary Heart Disease (CHD)

A condition where the blood vessels supplying the heart muscle become narrowed or blocked due to atherosclerosis, leading to reduced blood flow and potential heart-related complications.

#### **CDC (Centers for Disease Control and Prevention)**

A national public health agency in the United States that is responsible for protecting and promoting public health through research, policy, and disease prevention.

#### **Type 2 Diabetes**

A chronic metabolic disorder where the body becomes resistant to the effects of insulin or doesn't produce enough insulin, leading to high blood sugar levels.

#### **GI** (Gastrointestinal) Products

Refers to products or substances that have an effect on the digestive system and its associated organs.

#### **GLP-1** (Glucagon-like Peptide-1)

A hormone released in the intestine after eating that stimulates insulin secretion, suppresses glucagon release, slows down stomach emptying, and promotes feelings of fullness.

#### In-vivo

Latin term meaning "within the living." In the context of research, it refers to experiments or studies conducted within a living organism.

#### Individual Retirement Account (IRA)

A financial account that provides individuals with a way to save for retirement while offering potential tax advantages. IRAs are offered by financial institutions and allow individuals to invest their savings in various financial instruments, such as stocks, bonds, and mutual funds, to grow their retirement funds over time.

#### Mounjaro

Mounjaro is an injectable prescription medicine that is used along with diet and exercise to improve blood sugar (glucose) in adults with type 2 diabetes mellitus.

#### Sapien 3 Valve

The Sapien 3 valve is a type of transcatheter heart valve used in transcatheter aortic valve replacement (TAVR) procedures to treat aortic valve stenosis.

#### Omnipod

A brand of wearable, tubeless insulin delivery devices for people with diabetes, allowing them to administer insulin without traditional injections.

#### **CRISPR Editing**

A revolutionary gene editing technology that allows scientists to precisely modify DNA within living organisms, holding potential for treating genetic disorders and other applications.

#### **Amvuttra**

AMVUTTRA is a prescription medicine that treats the polyneuropathy caused by an illness called hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis).

#### Resmetirom

A selective thyroid hormone receptor-beta agonist that has been investigated for its potential in treating metabolic and cardiovascular disorders.

#### Non-alcoholic Steatohepatitis (NASH)

A progressive liver disease characterized by inflammation and fat accumulation in the liver, not caused by excessive alcohol consumption.

#### **GIP Antagonists**

GIP (Glucose-dependent Insulinotropic Peptide) antagonists are compounds that block the effects of GIP, a hormone that stimulates insulin release after meals.

#### **Novel Incretins**

Refers to newly discovered or developed hormones that stimulate insulin secretion and regulate blood sugar levels.

#### Mitochondrial

Relating to mitochondria, which are organelles within cells responsible for energy production through cellular respiration.

#### Multiincretins w/GIP-1 Agonists

refers to a combination of multiple incretin hormones with GIP-1 (Glucose-dependent Insulinotropic Peptide) agonists, aiming to improve insulin secretion and glycemic control.

#### Mono or Multiincretins w/GIP-1 Glucagon or Amylin

Combinations of single or multiple incretin hormones with GIP-1, glucagon, or amylin, possibly for managing blood sugar levels.