



Innovent Biologics Clinical Data Update

Mazdutide (IBI362) Higher Dose 9mg

Phase 2 Clinical Update in Obesity (48 Weeks)

October 30, 2023

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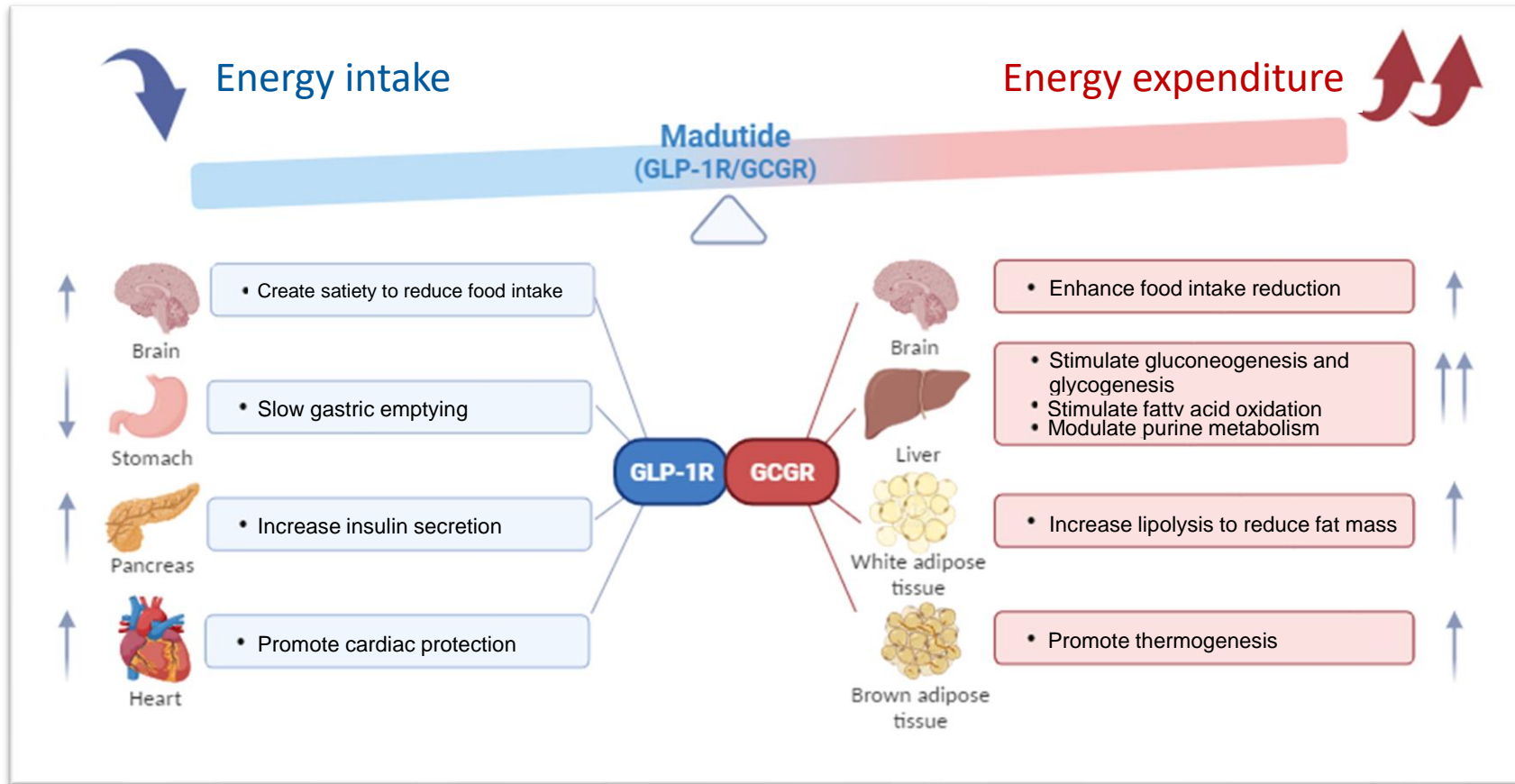


**Mazdutide Higher Dose 9mg
Phase 2 Clinical Update in Obesity**

Differentiated Mechanism of Mazdutide as a Novel GLP-1R/GCGR Dual Agonist

GCGR agonism may provide additional benefits in treating obesity and metabolic disorder

Targeting GLP-1R and GCGR may act on both sides of the energy balance equation



GCGR agonism may provide additional benefits in treating obesity and metabolic disorder

- GCGR agonism activates energy expenditure and increase metabolic rate to drive weight loss;
- GCGR is expressed in several key metabolic organs/tissues especially in liver, where the activation of GCGR could further enhance fat consumption and basal metabolism.

1. Conceição-Furber E, et al. Is glucagon receptor activation the thermogenic solution for treating obesity? *Front Endocrinol (Lausanne)* 2022;13:868037

2. Kleinert M, et al. Glucagon Regulation of Energy Expenditure. *Int J Mol Sci.* 2019 Oct 30;20(21):5407.

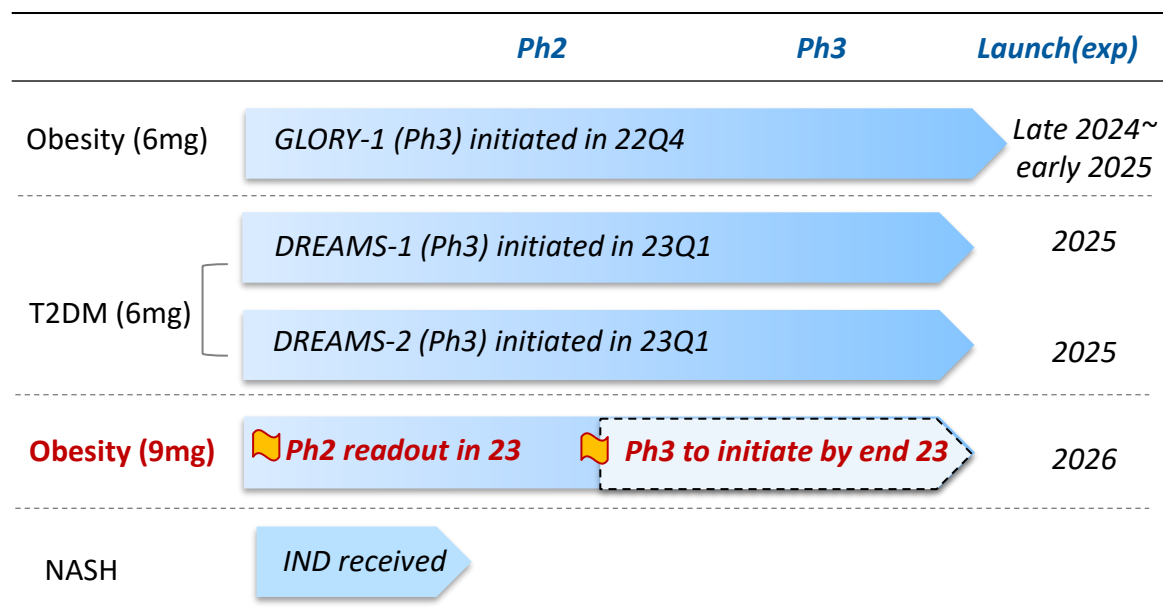
3. Jastreboff AM, et al. Retatrutide Phase 2 Obesity Trial Investigators. Triple-Hormone-Receptor Agonist Retatrutide for Obesity - A Phase 2 Trial. *N Engl J Med.* 2023 Aug 10;389(6):514-526.

4. Hope DCD, Vincent ML, Tan TMM. Striking the Balance: GLP-1/Glucagon Co-Agonism as a Treatment Strategy for Obesity. *Front Endocrinol (Lausanne).* 2021 Sep 8;12:735019.

Mazdutide: Globally First GLP-1R/GCGR Dual Agonist Entered Phase 3

Potentially BIC therapy for obesity and diabetes, the 4th Phase 3 trial to be initiated soon

Mazdutide Development Overview



- **T2DM (6mg):** both weight loss and glycemic control for long-term disease management benefits of diabetes;
- **Obesity/Overweight (6mg):** robust weight loss effect for broad obese and overweight population;
- **Obesity (9mg):** potentially bariatric surgery equivalent efficacy for moderate to severe obesity;
- Exploration for **more therapeutic areas** is underway.

Summary of Mazdutide 9mg Phase 2 in Obesity Clinical Update (48 week)

Mazdutide showed robust weight loss, differentiated cardiometabolic benefits and superior safety profile

Dual agonist to enhance metabolism and weight loss

**Mazdutide
(GLP-1R/GCGR)**

Balanced design to optimize safety and efficacy



Robust and rapid weight-loss efficacy further confirmed

- **Globally competitive weight loss data and the highest in Chinese population based studies:** mean percent change in body weight from baseline versus placebo of **-18.6% after 48 weeks** of treatment;
- Significantly more patients achieved $\geq 15\%/20\%$ weight loss at 48 weeks.



Differentiated metabolic benefits; 73.3% reduction in LFC

- Significant reduction in waist circumference, TG, TC, LDL-C, ALT and AST levels etc.; stable HDL-C throughout 48 weeks;
- **Differentiated benefits in significantly reducing liver fat content (LFC) and serum uric acid levels.**

*TG: Triglycerols; LDL-C: Low-density lipoprotein cholesterol; TC: Total cholesterol; ALT: Alanine transaminase; AST: Aspartate aminotransferase; HDL-C: High-density lipoprotein cholesterol



Favorable and superior safety profile

- **No SAE throughout 48 weeks treatment of mazdutide 9mg;**
- Similar heart rate increases between mazdutide and placebo at week 24, no further increase till week 48;
- **No signal of increased cardiovascular risk** throughout treatment period.



Good compliance and simple dose regimen

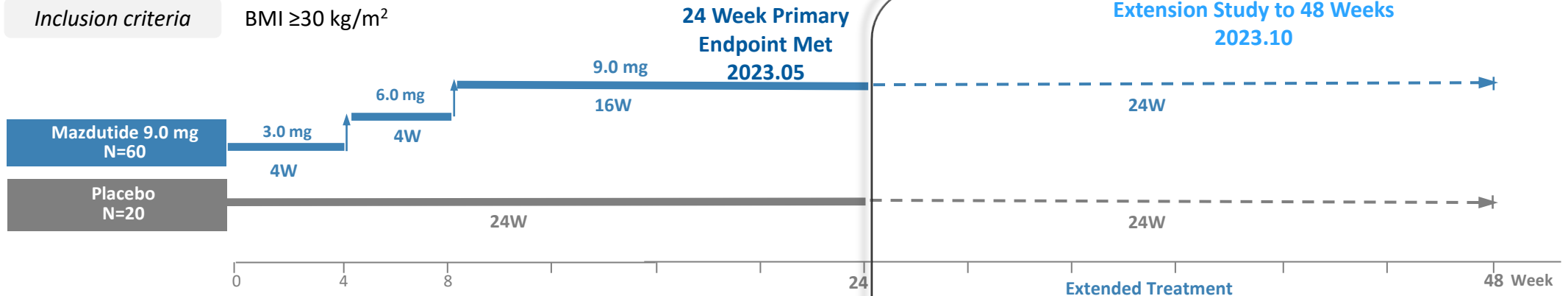
- **No AE leading to treatment discontinuation in mazdutide group;**
- **Simple and tolerable** two-step titration dose regimen to enter maintenance dose.

Mazdutide 9 mg Phase 2 in Chinese Adults with Obesity

An extension study to 48 weeks of treatment after 24-week primary endpoint was met

ClinicalTrials.gov ID NCT04904913

Inclusion criteria BMI ≥ 30 kg/m²



Baseline



Subjects
N=80



Mean Age
34 yrs



Mean Height
168.0 cm



Mean Weight
96.9 kg



Mean BMI
34.3 kg/m²



Subjects
N=59



Mean Age
34 yrs



Mean Height
168.4 cm



Mean Weight
98.4 kg



Mean BMI
34.7 kg/m²

- A total of 80 subjects were enrolled and randomized in a 3:1 ratio to mazdutide 9 mg group or placebo group.
- Primary endpoint achieved in May 2023: percentage change in body weight from baseline versus placebo after 24 weeks of treatment.

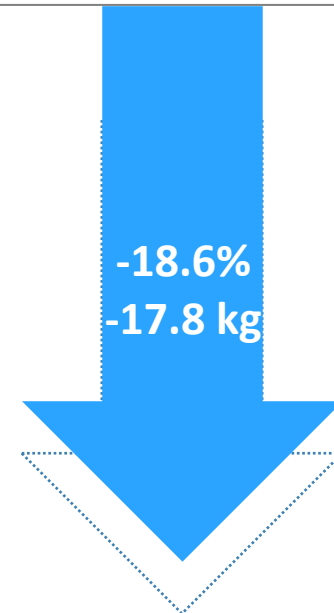
- Extend treatment to 48 weeks in subjects that agreed to receive additional 24 weeks of double blind extension treatment.
- 59 subjects (43 in the mazdutide 9.0mg group and 16 in the placebo group) accepted treatment till 48 weeks.

Mazdutide 9 mg Phase 2 in Chinese Adults with Obesity

Robust and rapid weight-loss efficacy with 18.6% mean weight loss versus placebo at 48 weeks

Placebo-adjusted mean body weight change from baseline at 48 weeks

Mean BMI 34.7kg/m²
Mean baseline weight 98.4 kg



**Mazdutide 9 mg
48 weeks**

Robust and durable weight reduction

- Long-lasting and robust weight reduction momentum, with mean percent change in body weight from baseline versus placebo of **-18.6% after 48 weeks** of treatment, and mean change in body weight from baseline versus placebo of **-17.8 kg**;
- A potential **superior treatment option than bariatric surgery*** for chronic weight management of moderate to severe obesity.

**Note: metabolic surgery is recommended for Chinese population with a BMI of 32.5 kg/m² or above.*

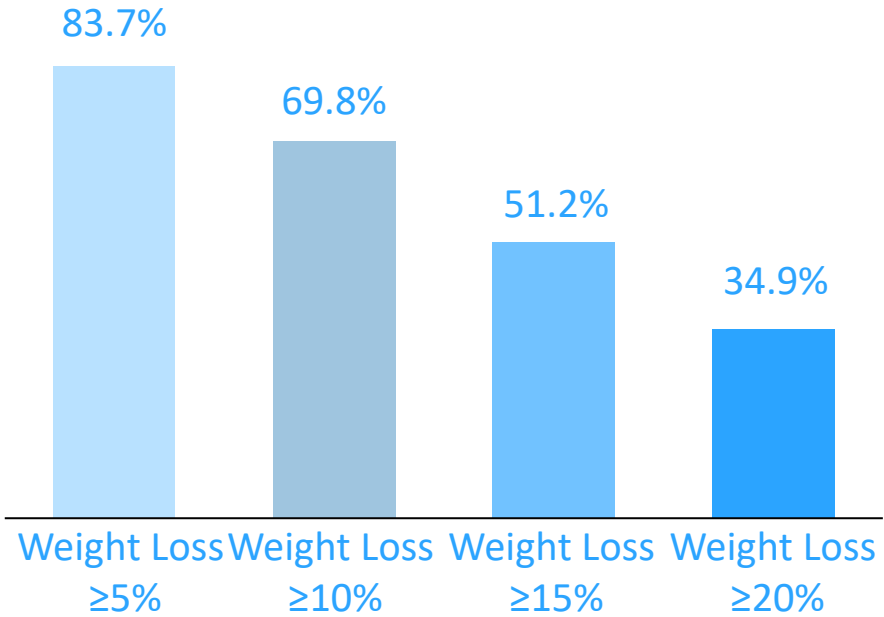
Rapid onset weight-loss with simple regimen

- Mazdutide has induced **rapid onset of weight-loss** effect with its **simple and tolerable two-step titration regimen**.

Mazdutide 9 mg Phase 2 in Chinese Adults with Obesity

Significantly proportion of patients achieved $\geq 15\%$ and $\geq 20\%$ weight loss

Proportion of participants achieved $\geq 5\%$ weight loss from baseline at 48 weeks



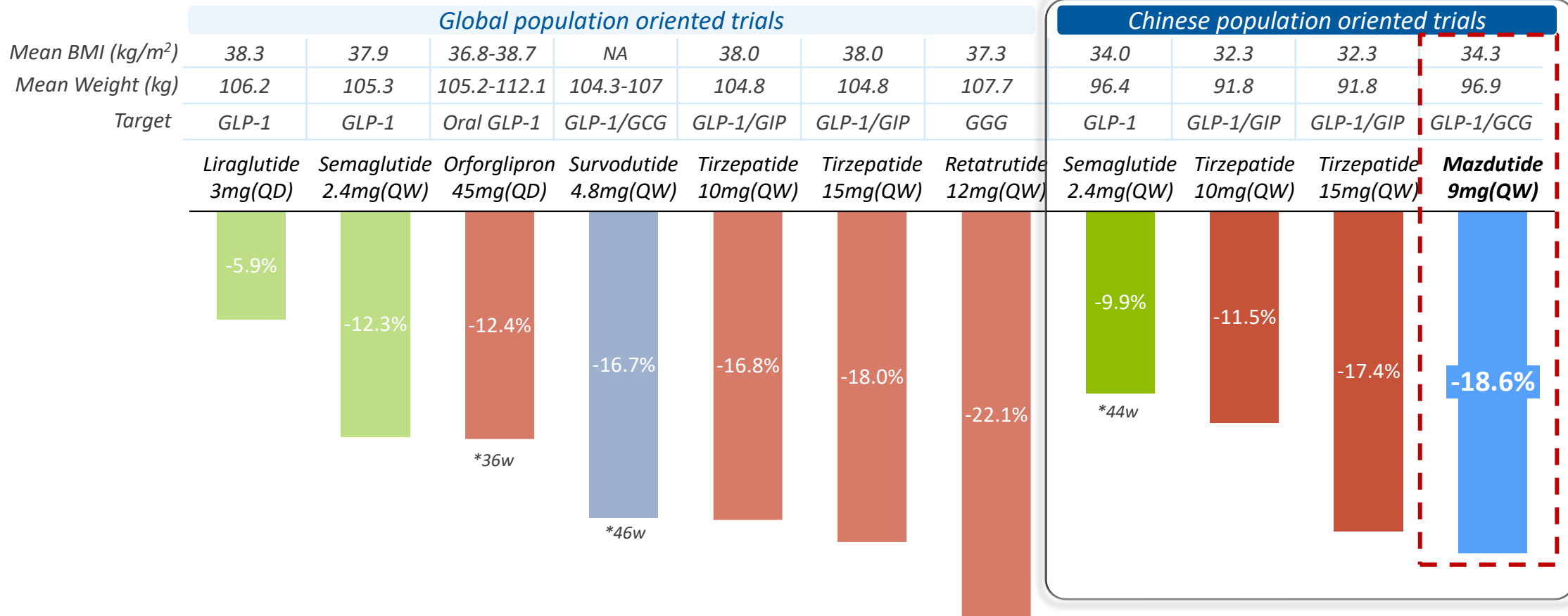
Mazdutide 9 mg 48 weeks

- 51.2% and 34.9% of the subjects in the mazdutide 9 mg group achieved 15% or more and 20% or more weight loss from baseline;
- **Significantly more subjects achieved $\geq 15\%$ and $\geq 20\%$ weight loss when extended to 48 weeks of mazdutide 9mg treatment;**
- No subject in placebo group lost 5% or more of body weight.

Summary of Weight Reduction in Major GLP-1 Class Drugs in 48 weeks

Forefront weight loss efficacy of mazdutide as a GLP-1R and GCGR dual agonist

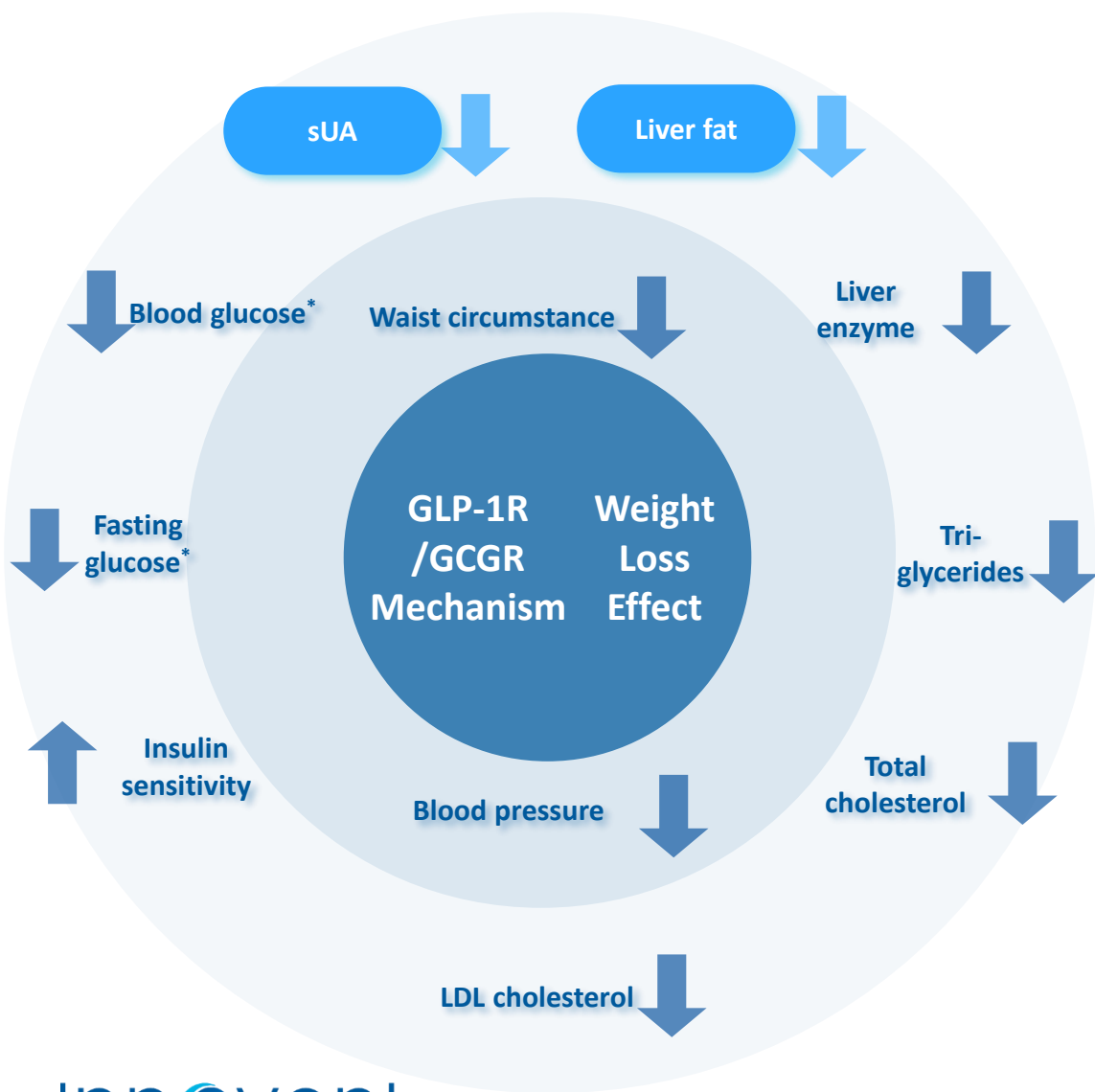
48-week mean body weight reduction% (indirect comparison, placebo-adjusted)



48-week weight loss data of liraglutide 3 mg, semaglutide 2.4 mg, tirzepatide 10/15 mg and retatrutide 12mg were estimated from published results of SCALE¹, STEP-1², SURMOUNT-1³, SURMOUNT-CN⁴ and a Phase II (NCT04881760)⁵ studies, respectively; while <48-week weight loss data of orforglipron 45mg, survodutide 4.8mg and semaglutide 2.4mg(CN) were published results of a Phase II (NCT05051579)⁶, a Phase II (NCT04667377)⁷ and STEP-7⁸ studies, respectively.

Metabolic Benefits Summary of Mazdutide

Multiple and differentiated benefits observed as a GLP-1R/GCGR dual agonist



- Corresponding to changes in body weight, the mean **waist circumference** and **blood pressure** of subjects in the mazdutide group decreased.
- After 24-week treatment, mazdutide 9 mg significantly reduced **TG, TC, LDL-C, ALT/AST** levels and improved insulin sensitivity, the effects were maintained during the extended treatment period. **HDL-C level** was stable throughout the treatment period.

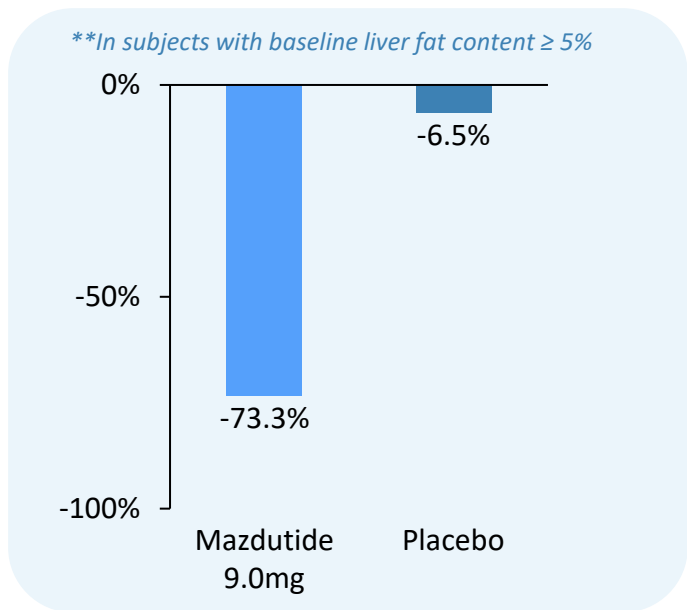
- Mazdutide showed differentiated benefits in significantly reducing liver fat content (LFC) and uric acid levels, with innovative mechanism of action (MoA) as a GLP-1R/GCGR dual agonist .

Metabolic Benefits Highlights of Mazdutide

Significantly reduced liver fat content, ALT, AST and sUA levels

73% liver fat content reduction

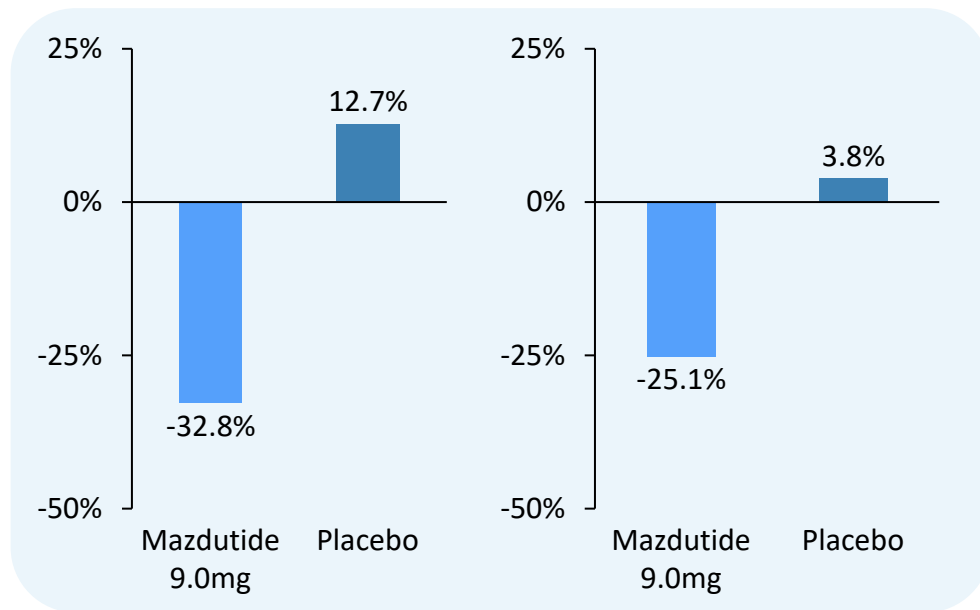
Mean liver fat content change (%) from baseline by MRI-PDFF at 24 weeks*



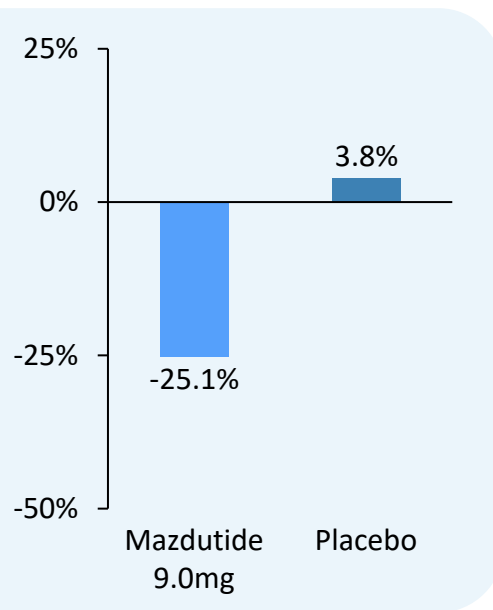
**Histologic fat fraction $\geq 5\%$ as the reference standard for diagnosing hepatic steatosis

Significant ALT and AST levels reduction

Mean ALT change (%) from baseline at 24 weeks*

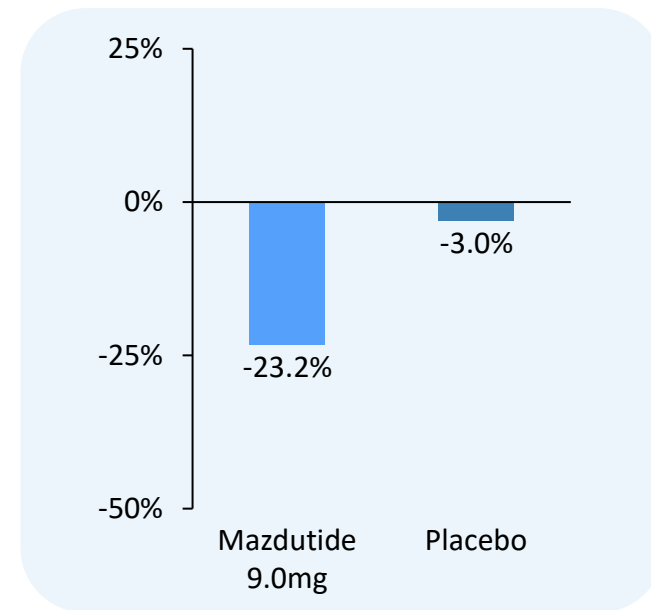


Mean AST change (%) from baseline at 24 weeks*



Significant sUA level reduction

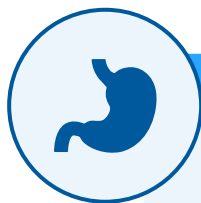
Mean sUA change (%) from baseline at 24 weeks*



*Note: The above benefits were maintained during extended treatment period to 48 weeks.

Key Safety Profile of Mazdutide

Favorable and superior tolerability and safety profile of mazdutide



Overall AE Profile

- Gastrointestinal adverse reactions (nausea, vomiting and diarrhea) were the most common adverse events, most of **mild or moderate** severity. The incidence of gastrointestinal adverse reactions reduced during the extended treatment period, and most are mild.
- The profile of adverse events was **consistent with** that observed in previous studies of mazdutide and other **GLP-1 drugs**, with no new safety signals observed.



No SAE

- **No subject** in the mazdutide group **discontinued treatment due to adverse events**.
- **No serious adverse events** occurred.



Cardiovascular Profile

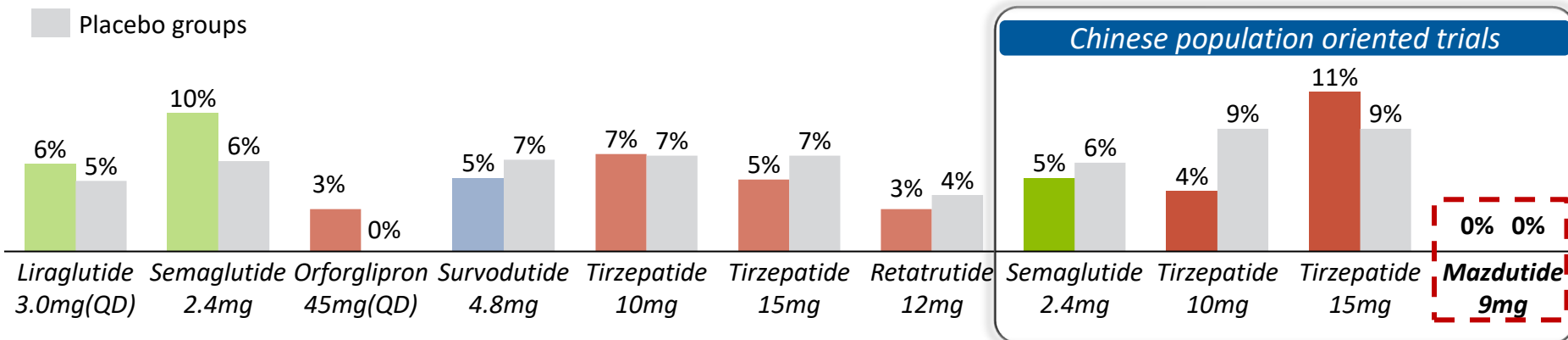
- The increase in **heart rate in the mazdutide group was similar** to that in the placebo group after 24 weeks of treatment, **with no further increase** in heart rate being observed during the extended treatment period.
- **No signal of increased cardiovascular risk** was observed throughout the treatment period.

Note: After the completion of the study, the 24-week primary endpoint and the 48-week extended treatment period, other secondary and exploratory endpoints, and safety profile will be further analyzed and fully disclosed at academic conferences and journals.

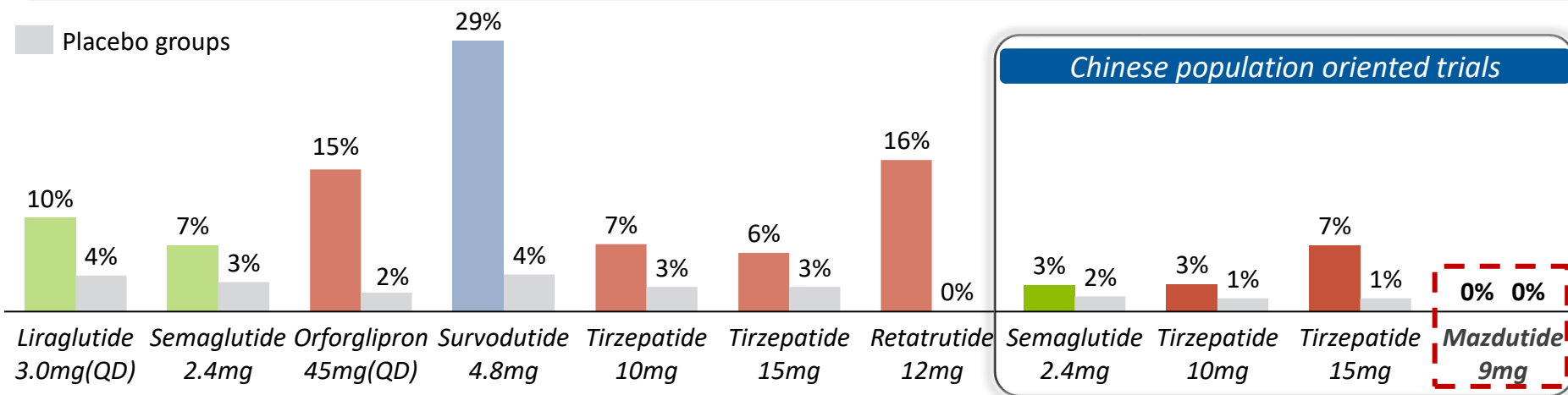
SAE and AE-led Drop-out in Major GLP-1 Class Drugs

Favorable and superior tolerability and safety profile of mazdutide

Serious adverse events % during treatment (indirect comparison)



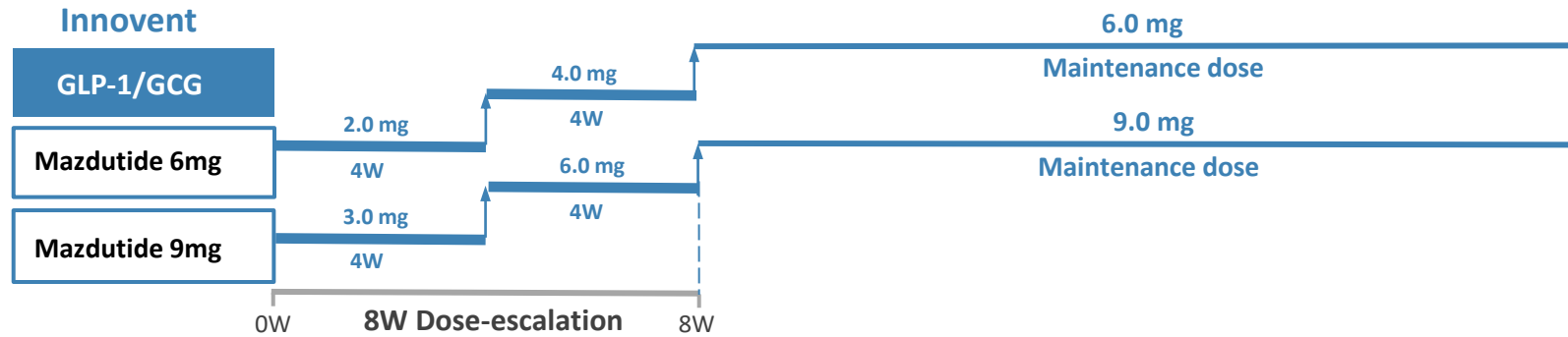
Adverse events leading to withdrawal/discontinuation % (indirect comparison)



Mazdutide 9mg demonstrated superior safety profile under leading weight loss efficacy and simple two-step titration dose regimen.

Mazdutide Simplified Dose-Escalation Regimen

Only two steps to enter maintenance dose



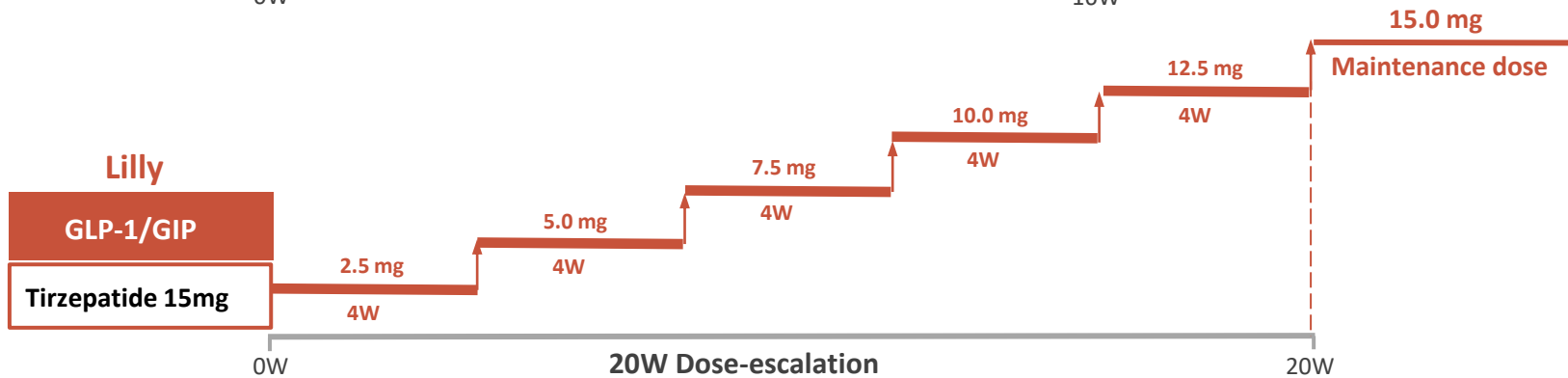
Mazdutide 6mg/9mg

- 3 strengths (pens)
- 8-week dose-escalation



Semaglutide 2.4mg

- 5 strengths (pens)
- 16-week dose-escalation



Tirzepatide 15mg

- 6 strengths (pens)
- 20-week dose-escalation

Mazdutide Near-term Catalysts

Obesity/Overweight (6mg)

- **NDA submission in late 2023 to early 2024**
- Phase 2 results will have full manuscript publication by the end of 2023

Obesity (9mg)

- **Phase 3 to be initiated by the end of 2023**
- Phase 2 results further publication at future academic conferences or journals

T2DM (6mg)

- **NDA submission in 2024**
- Phase 2 results will have full manuscript publication in late 2023 to early 2024

More indications

- More indication opportunities are under exploration

Innovent's Strategy in CVM: Build Strong Franchise and Expand Next-generation Pipeline

Next Wave Innovation



• Oral CVM projects



• Other novel modalities



• Pediatric and aging diseases

Expanding Pipeline of Blockbusters

Approved Product



SINTBILO® (tafolecimab injection)

Mid-to-Late Stage Assets

Mazdutide (6mg)

- Ph3 – Overweight/Obesity
- Ph3 – T2DM

Mazdutide (9mg)

- Ph2 – Obesity (moderate-to-severe)

IBI128 (Tigulixostat)

- MRCT Ph3 – Gout
(overseas, LG Chem)

IBI311

- Ph3 - TED

Huge Market Potential

~500M patients
Impacted



~RMB 100B
CVM Market in China



**Supplemental Slides:
Obesity and Overweight in China**

Obesity — a Growing Public Health Issue in China



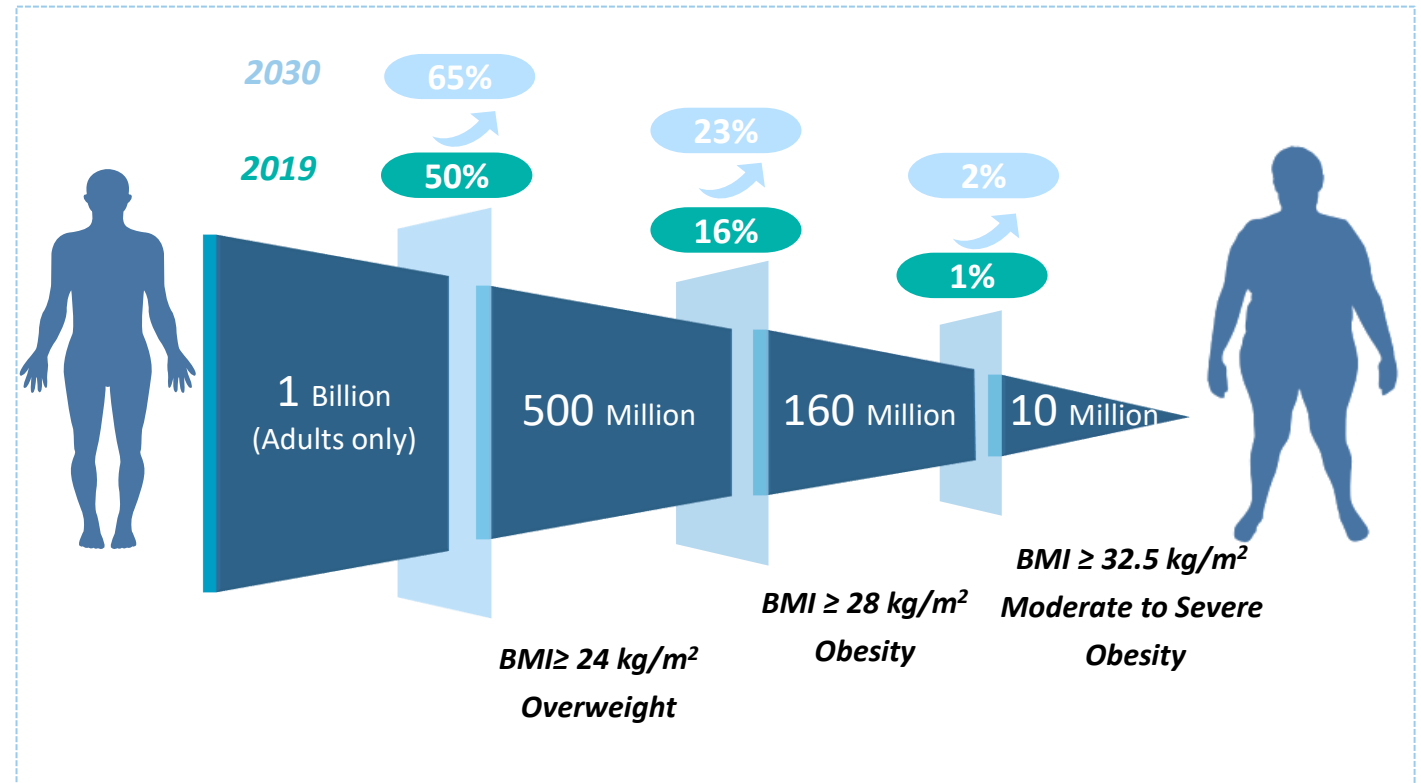
1. Pan XF, Wang L, Pan A. Epidemiology and determinants of obesity in China. *Lancet Diabetes Endocrinol.* 2021 Jun;9(6):373-392. doi: 10.1016/S2213-8587(21)00045-0. Erratum in: *Lancet Diabetes Endocrinol.* 2021 Jul;9(7):e2. PMID: 34022156.
2. Wang Y, Zhao L, Gao L, Pan A, Xue H. Health policy and public health implications of obesity in China. *Lancet Diabetes Endocrinol.* 2021 Jul;9(7):446-461. doi: 10.1016/S2213-8587(21)00118-2. Epub 2021 Jun 4. PMID: 34097869.
3. Institute for Health Metrics and Evaluation. Global Health Data Exchange. GBD results tool. <http://ghdx.healthdata.org/gbd-results-tool> (accessed Jan 10, 2021).

China Has the Largest Obese and Overweight Population

~500M adults in China are living with obesity or overweight, **potentially the largest in the world**^{i,1}.

- Overweight (BMI 24-27.9kg/m²): 340M
- Obesity (BMI ≥ 28kg/m²): 160M
- Moderate to severe obesity (BMI ≥ 32.5kg/m²): 10M

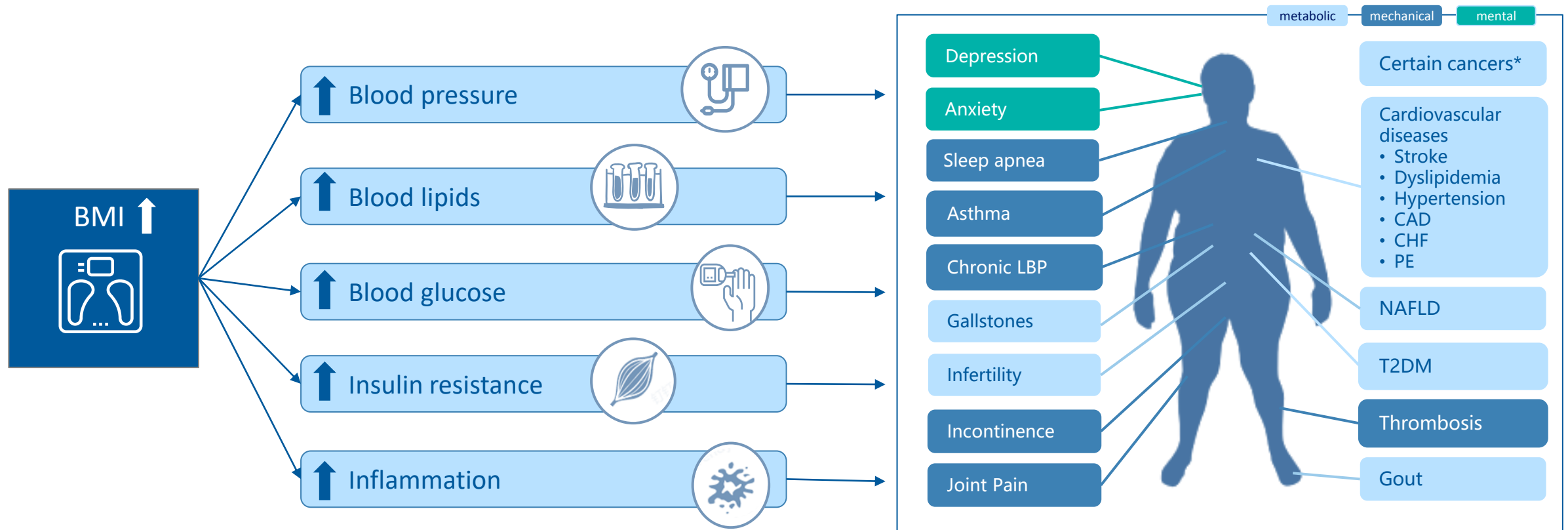
ⁱ: WHO criteria define overweight in adults as a BMI of 25.0–29.9 kg/m² and obesity as a BMI of 30.0 kg/m² or higher. However, accumulated evidence has shown that Chinese people are likely to have higher percentages of body fat (as shown via imaging techniques) and higher rates of cardiovascular risk factors and all-cause mortality than White people at given BMI levels.



1. Pan XF, Wang L, Pan A. Epidemiology and determinants of obesity in China. *Lancet Diabetes Endocrinol.* 2021 Jun;9(6):373-392. doi: 10.1016/S2213-8587(21)00045-0. Erratum in: *Lancet Diabetes Endocrinol.* 2021 Jul;9(7):e2. PMID: 34022156.

2. Wang Y, Zhao L, Gao L, Pan A, Xue H. Health policy and public health implications of obesity in China. *Lancet Diabetes Endocrinol.* 2021 Jul;9(7):446-461. doi: 10.1016/S2213-8587(21)00118-2. Epub 2021 Jun 4. PMID: 34097869.

Raised BMI is a Major Risk Factor for >200 Non-communicable Diseases



*Including breast cancer, colorectal cancer, ovarian cancer, cervical cancer, esophageal cancer, renal cancer, prostate cancer, etc.
 CAD: coronary artery disease CHF: congestive heart failure PE: pulmonary embolism LBP: Low Back Pain
 NAFLD: nonalcoholic fatty liver disease

- Overweight and obesity contribute to **11.1% of deaths** associated with non-communicable diseases;
- Overweight and obesity are also associated with **significantly increased morbidity**, which can affect almost every organ system. The organs affected by obesity can be broadly grouped into three classes: metabolic, mechanical, and mental.

Obesity Management Could Reverse Disease Trajectory

5%
~15%

- 5%-15% weight loss within 6 months is recommended for patients with obesity or overweight with complications.
- Increased weight loss percentage is associated with increased improvements in obesity-related risk factors and comorbidities, and could be of significant benefit for patients.

- ✓ Hypertension
- ✓ Hyperglycemia

- ✓ T2DM Prevention
- ✓ NAFLD
- ✓ Dyslipidemia
- ✓ PCOS

- ✓ T2DM Remission
- ✓ Incontinence
- ✓ GERD
- ✓ NASH
- ✓ Sleep Apnea
- ✓ CV diseases
- ✓ Joint Pain

- ✓ T2DM Remission
- ✓ CHF
- ✓ CV death rate

Weight Loss (%)

0-5%

5-10%

10-15%

≥15%

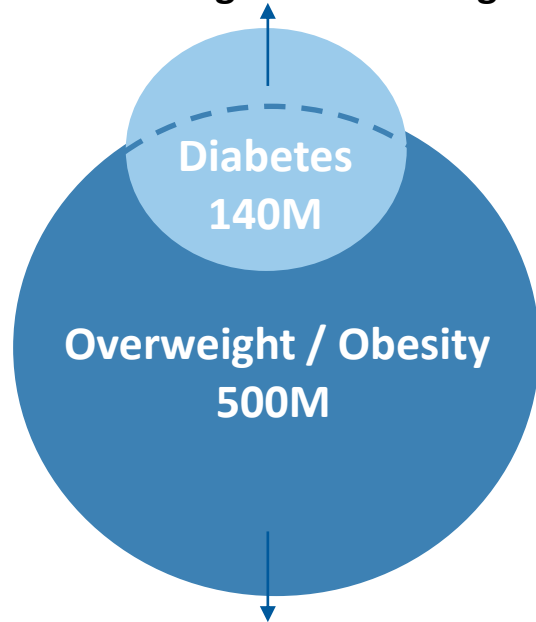
1. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY COMPREHENSIVE CLINICAL PRACTICE GUIDELINES FOR MEDICAL CARE OF PATIENTS WITH OBESITY; Endocr Pract. 2016 Jul;22 Suppl 3:1-203. doi: 10.4158/EP161365.GL. Epub 2016 May 24 .

PCOS: polycystic ovary syndrome NASH: Non-alcoholic steatohepatitis
GERD: gastroesophageal reflux disease

Obesity Management is Highly Beneficial in T2DM Treatment

Two digit or more significant weight loss may lead to the remission of T2DM

~50% T2DM adult patients
in China are living with overweight or obesity



T2DM incidence rates in Chinese population:

- 8.8% in BMI < 25 group;
- 13.8% in 25 ≤ BMI < 30 group;
- 20.1% in BMI ≥ 30 group.



- **T2DM prevention:** There is strong and consistent evidence that **obesity management can delay the progression from prediabetes to T2DM.**
- **Beneficial in T2DM treatment:** In patients with T2DM who also have overweight or obesity, modest and sustained weight loss (>5%) has been shown to **improve glycemic control, reduce the need for glucose-lowering medications and result in metabolic benefits** including lowering of blood pressure and blood lipids, improving insulin resistant and β -cell function.
- **Potential of T2DM remission:** Increased weight loss percentage was associated with increased odds of T2DM remission, starting with 10–15%.

1. JAMA. 2021 Dec 28;326(24):2498-2506. doi: 10.1001/jama.2021.22208. Prevalence and Treatment of Diabetes in China, 2013-2018

2. Chinese Diabetes Society, Guideline for the prevention and treatment of type 2 diabetes mellitus in China(2020 edition)

3. American Diabetes Association; 8. Obesity Management for the Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes—2021. Diabetes Care 1 January 2021; 44 (Supplement_1): S100–S110.

4. Hou X, Lu J, Weng J, Ji L, Shan Z, Liu J, et al. (2013) Impact of Waist Circumference and Body Mass Index on Risk of Cardiometabolic Disorder and Cardiovascular Disease in Chinese Adults: A National Diabetes and Metabolic Disorders Survey. PLoS ONE 8(3): e57319.

5. Ameena Meerasa, Satya Dash; Weighing in on Type 2 Diabetes Remission. Diabetes Care 5 January 2022; 45 (1): 28–30.

Lack of Satisfactory Measures Calls for Breakthrough in Obesity Management for Huge Population in China



Lifestyle Intervention

Low Compliance

Lack of established approach

Intensive time commitment

Self-management disparities

Non-ideal outcome

China is in lack of established and comprehensive lifestyle intervention approach for widespread use



Pharmacotherapy

<1% treated

Lack of effective medicines

Insufficient response

Safety and tolerability issues of current therapy

Concomitant medications limit

Only Orlistat is approved for weight loss use in China. It is difficult to meet various clinical needs and has limited efficacy and serious adverse effects.



Bariatric Surgery

~0.25% treated

Psychological resistance

Considerable cost

Weight rebound

Short / long term complications

The adoption of bariatric surgery in China faces many obstacles, such as a series of serious postoperative complications

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