



Innovent Biologics Clinical Data Update

Mazdutide @ 2024 ADA

June 25, 2024

Agenda

01 Introduction

02 ADA Highlights

03 Q&A

Introduction

Prof. Linong Ji *Leading PI; Peking University People's Hospital*

Dr. Lei Qian *Vice President of General Biomedicine Development*

Opening remarks by invited guest



Prof. Linong Ji, MD

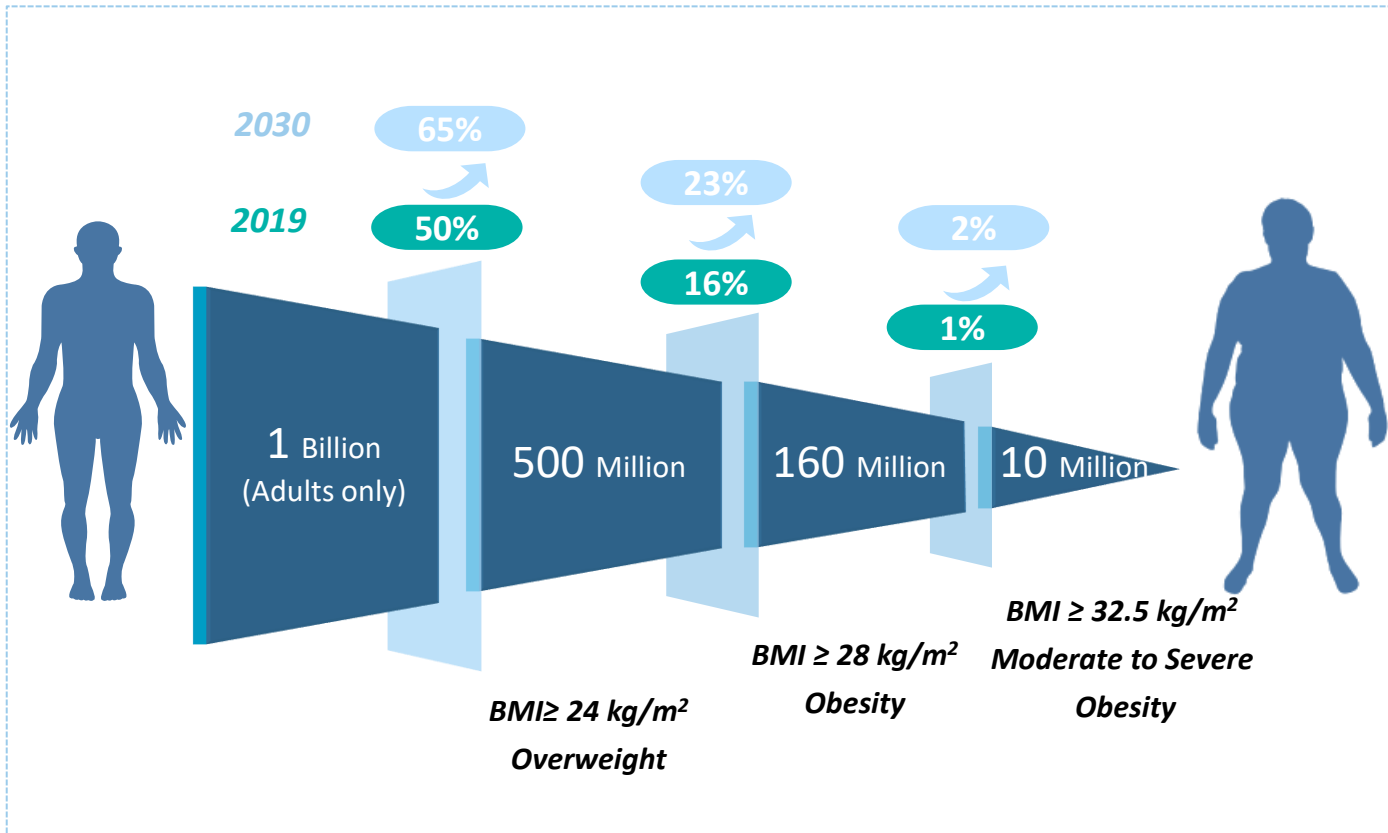
Leading Principal Investigator; Peking University People's Hospital

- **Director of Peking University Diabetes Center and Director of the Department of Endocrinology and Metabolism, Peking University People's Hospital, Beijing, China.**
- **President of Specialty Committee of Clinical Research on Diabetes and Metabolic Drugs of China Pharmaceutical Innovation and Research Development Association (PhIRDA), Former Vice President of International Diabetes Federation (IDF), Former Chair of International Diabetes Federation Western Pacific Region (IDF-WPR), Former President of the Chinese Diabetes Society (CDS), Vice President of the Chinese Endocrinologist Association (CEA), President of Chinese Geriatric Endocrine and Metabolism Society, Executive board member of Asia Association for the Study of Diabetes (AASD).**
- **Chief Editor of Chinese Diabetes Journal and an editorial board member of Journal of Diabetes, Diabetes Research and Clinical Practice, Diabetes Technology & Therapeutics, Metabolism, International Journal of Diabetes.**
- **Principal investigator of 60+ clinical studies. Published 500+ articles in peer-reviewed journals.**

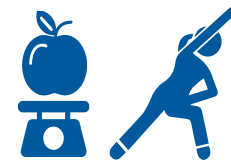
Key facts of obesity/overweight in China

China has the largest obese and overweight population, with <1% on medication

500m adults in China live with obesity or overweight



Weight management options are limited



Lifestyle Intervention

Low compliance
Non-ideal outcome



Bariatric Surgery

Very limited usage
Various obstacles



Pharmacotherapy

Limited efficacy and
serious adverse effects
before GLP-1 class

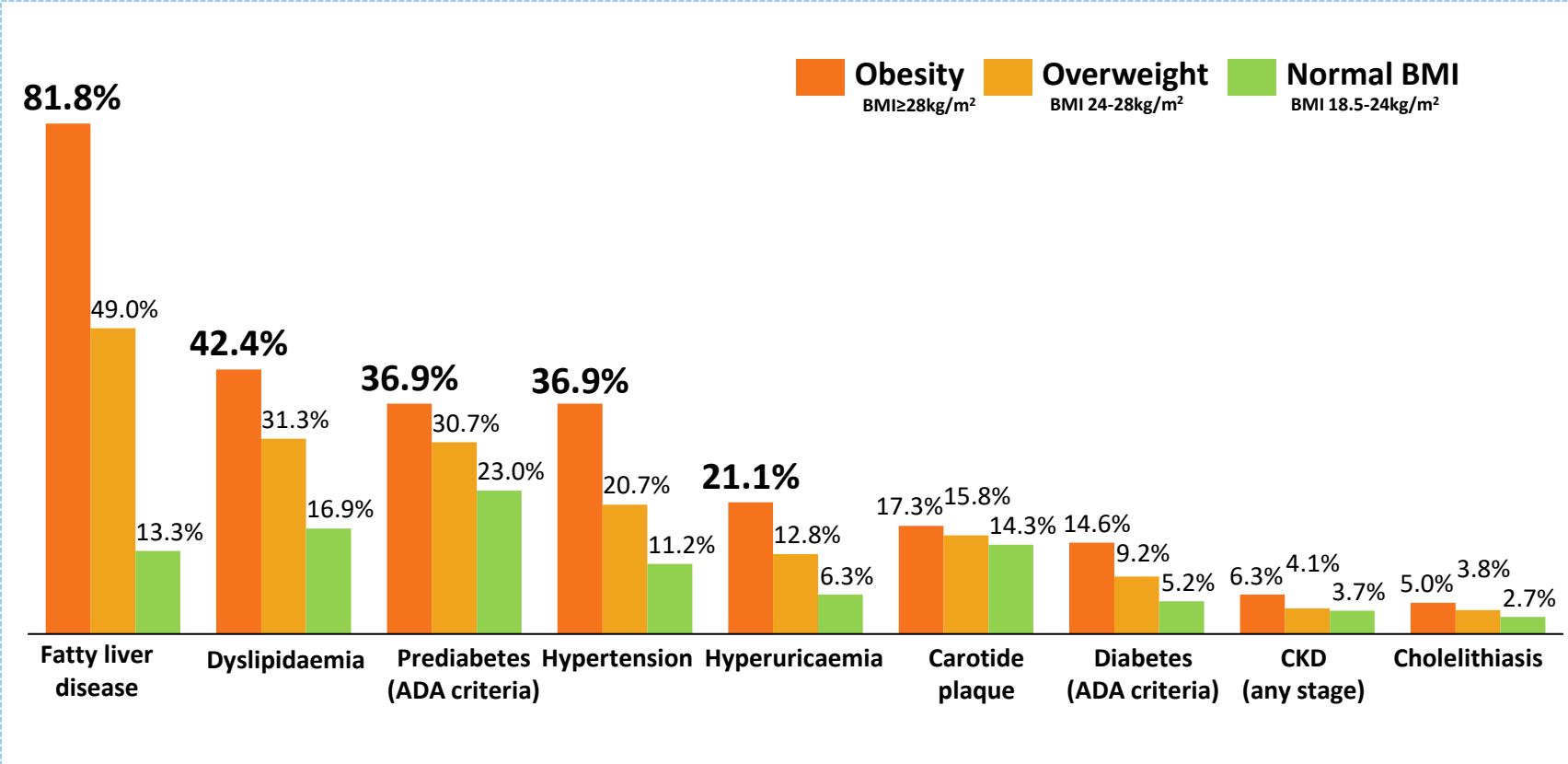
1. Pan XF, Wang L, Pan A. Epidemiology and determinants of obesity in China. *Lancet Diabetes Endocrinol.* 2021 Jun;9(6):373-392. doi: 10.1016/S2213-8587(21)00045-0. Erratum in: *Lancet Diabetes Endocrinol.* 2021 Jul;9(7):e2. PMID: 34022156.
2. Wang Y, Zhao L, Gao L, Pan A, Xue H. Health policy and public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

Key facts of obesity/overweight in China

High burden of comorbidities with overweight/obesity

Prevalence of comorbidities in normal BMI, overweight or obesity in China

- Top 5 weight-related comorbidities**
- Fatty Liver Disease
 - Pre-diabetes
 - Dyslipidaemia
 - Hypertension
 - Hyperuricaemia



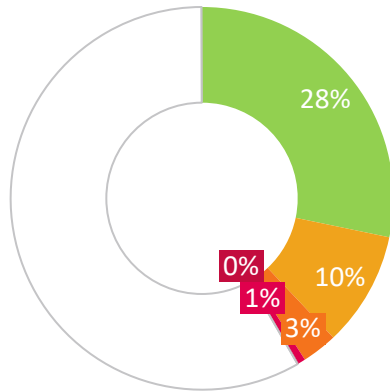
Chen K, Shen Z, Gu W, Lyu Z, Qi X, Mu Y, Ning Y; Meinian Investigator Group. Prevalence of obesity and associated complications in China: A cross-sectional, real-world study in 15.8 million adults. *Diabetes Obes Metab.* 2023 Nov;25(11):3390-3399. doi: 10.1111/dom.15238. Data were obtained from 519 Meinian health check-up centres across 243 cities. Eligible participants were aged ≥18 years, with a routine check-up in 2019 (N = 21 771 683)

Key facts of obesity/overweight in China

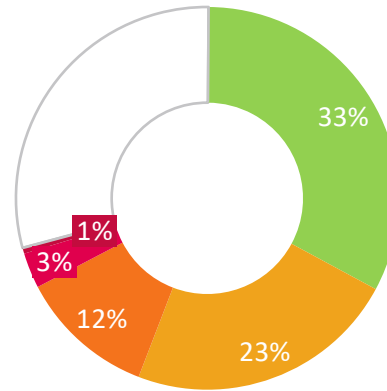
Most people with overweight/obesity have one or more comorbidities

Number of comorbidities in adults with normal BMI, overweight or obesity in China

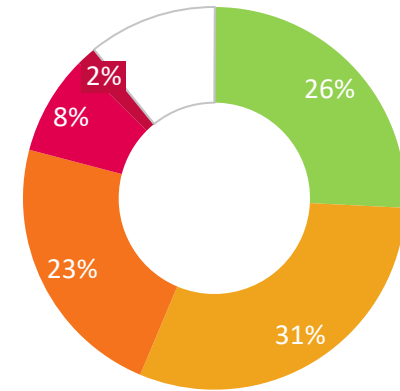
42% of normal BMI population have ≥ 1 comorbidities



71% of overweight population have ≥ 1 comorbidities



89% of obese population have ≥ 1 comorbidities



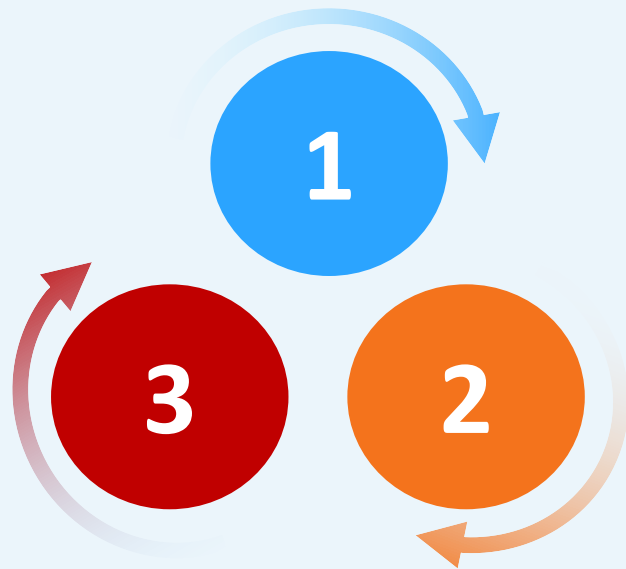
Overweight and obesity were associated with a high prevalence of cardiometabolic diseases, emphasizing the need for weight management efforts that address both excess body weight and associated comorbidities.

Chen K, Shen Z, Gu W, Lyu Z, Qi X, Mu Y, Ning Y; Meinian Investigator Group. Prevalence of obesity and associated complications in China: A cross-sectional, real-world study in 15.8 million adults. *Diabetes Obes Metab.* 2023 Nov;25(11):3390-3399. doi: 10.1111/dom.15238. Data were obtained from 519 Meinian health check-up centres across 243 cities. Eligible participants were aged ≥ 18 years, with a routine check-up in 2019 (N = 21 771 683)

Key advantages of mazdutide in weight management

Aids obese/overweight population to achieve better weight management

Mazdutide confers robust weight loss, special liver benefits and improvements on multiple cardiometabolic risk factors.



1

Robust Weight Loss

Rapid and strong **weight loss**

Reduce **waist, hip and neck circumferences**

2

Special Liver Benefits

Reduce **liver fat content**

Reduce **transaminase and serum uric acid**

3

Address Obesity-related Comorbidities

Reduce key cardiometabolic risk factors including **blood pressure, lipids and glucose** etc.

Mazdutide key mechanisms of action in weight management

Dual agonism of GLP-1R/GCGR induces robust weight loss and additional benefits

GLP-1/GCG's key mechanisms on weight loss (vs. GLP-1 and GLP-1/GIP)



- Mazdutide is an analogue of oxyntomodulin (OXM), a natural peptide hormone existing in humans that activates **both GLP-1R and GCGR**.
- Mazdutide can promote weight loss through various regulatory mechanisms across multiple organs (shown left).
- By additionally targeting GCGR in the liver and brown adipose tissues, mazdutide may offer metabolic benefits by enhancing energy expenditure and promoting lipolysis.

GLP-1= glucagon-like peptide-1, GIP= glucose-dependent insulin releasing peptide, GCG=glucagon, GLP-1R= glucagon-like peptide-1 receptor, GCGR=glucagon receptor

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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. Sanyal, A.J., et al. Triple hormone receptor agonist retatrutide for metabolic dysfunction-associated steatotic liver disease: a randomized phase 2a trial. *Nat Med* (2024). <https://doi.org/10.1038/s41591-024-03018-2>

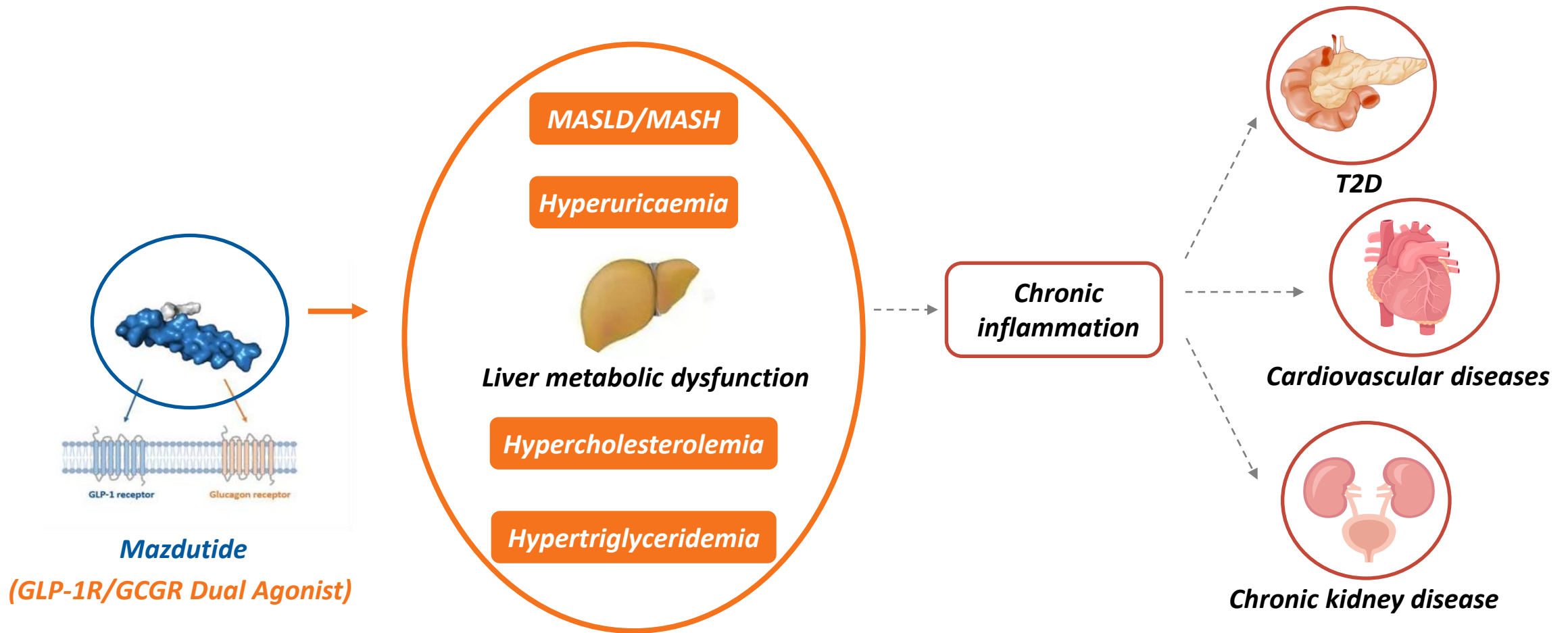
4. Hope DD, Vincent ML, Tan TMM. Striking the Balance: GLP-1/Glucagon Co-Agonism as a Treatment Strategy for Obesity. *Front Endocrinol (Lausanne)*. 2021 Sep 8;12:735019.

5. Pocai A. Action and therapeutic potential of oxyntomodulin. *Mol Metab.* 2014;3 (3) :241-251. doi:10.1016/j.molmet.2013.12.001

6. Habegger, Kirk M et al. Nature reviews. *Endocrinology* vol. 6, 12 (2010): 689-97.

Mazdutide special liver benefits

Directly targets liver, which plays a central role in metabolic diseases

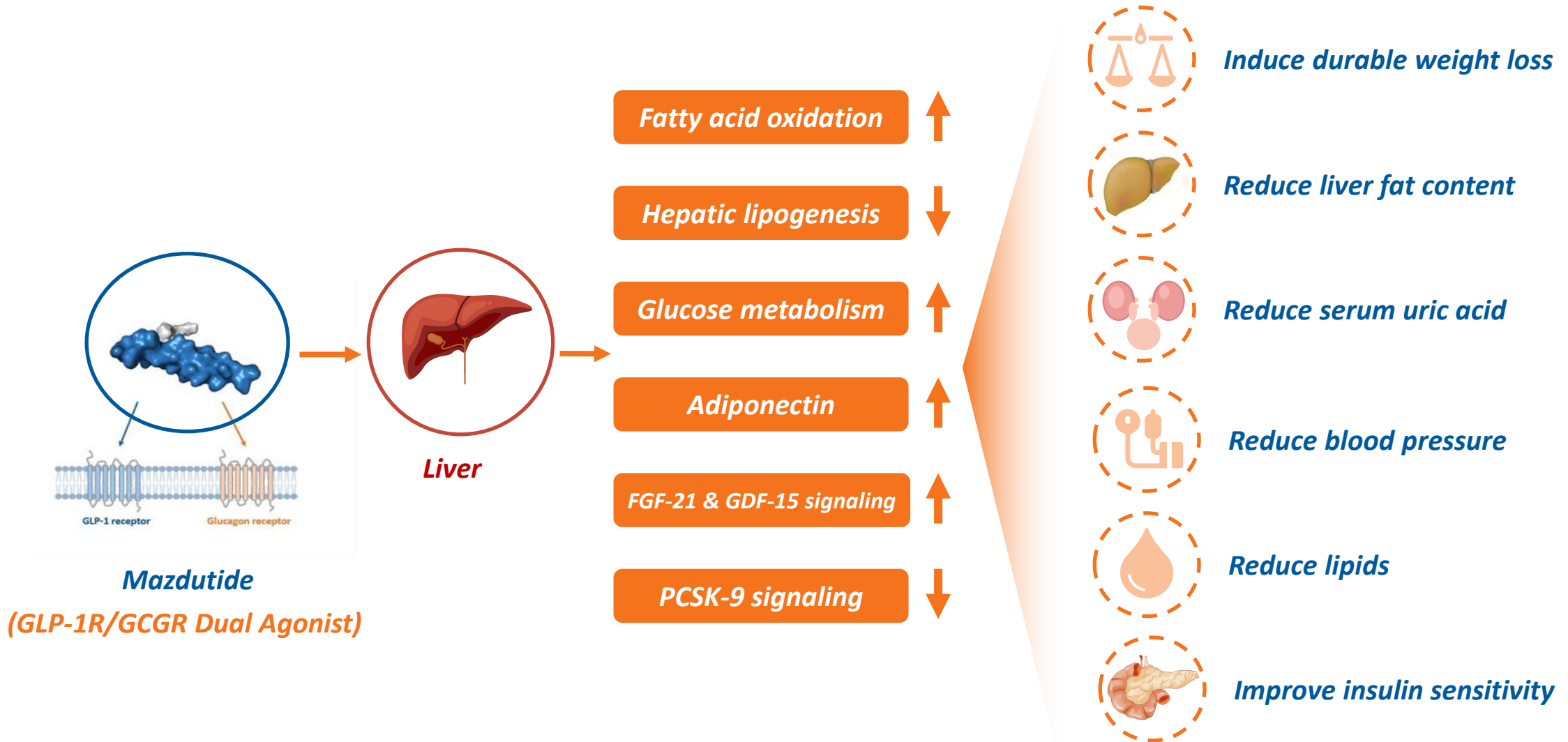


Liver plays a central role in human metabolism. Its dysfunction can lead to chronic inflammation, which underlies the pathogenesis of various metabolic diseases such as **T2D, cardiovascular diseases, chronic kidney diseases.**

MASLD=metabolic dysfunction-associated steatotic liver disease; MASH=metabolic dysfunction-associated steatohepatitis; T2D= type 2 diabetes

Mazdutide special liver benefits

Improves liver metabolism and reduces factors of liver metabolic dysfunction



Mazdutide
(GLP-1R/GCGR Dual Agonist)

FGF-21=Fibroblast growth factor 21; GDF-15=Growth differentiation factor 15; PCSK-9=Proprotein convertase subtilisin/kexin type 9 serine protease.

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1. Pocai A. Action and therapeutic potential of oxyntomodulin. *Mol Metab.* 2014;3 (3) :241-251. doi:10.1016/j.molmet.2013.12.001
2. Habegger, Kirk M et al. *Nature reviews. Endocrinology* vol. 6,12 (2010): 689-97.
3. Yanyun Chen, et al. *Diabetes* 2021;70(Supplement 1):682-P. <https://doi.org/10.2337/db21-682-P>

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GLORY-1 Phase 3 Results and Insights

Dr. Lei Qian *Vice President of General Biomedicine Development*

Mazdutide development programs

GLORY-1: the first and successful Phase 3 study of GLP-1/GCG dual target in weight management

Mazdutide Development Programs and Publications

| Indications | Trial | Ph3 | NDA | Approval |
|--|----------------|-----|--------------|------------|
| Weight Management | | | | |
| Obesity/overweight 4mg/6mg vs. placebo | GLORY-1 (Ph3) | | ✓ 2024.02 | 1H 2025 |
| Obesity 9mg vs. placebo | GLORY-2 (Ph3) | | | |
| Obesity Adolescent | Ph1 in plan | | | |
| Type 2 Diabetes | | | | |
| T2D 4mg/6mg vs. placebo | DREAMS-1 (Ph3) | | 2024 | 2025 |
| T2D 4mg/6mg vs. dulaglutide | DREAMS-2 (Ph3) | | 2024 | 2025 |
| T2D 6mg vs. semaglutide | DREAMS-3 (Ph3) | | | |
| Others | | | | |
| MASH | IND approved | | | |

| | | |
|--|---------|-----------------------------------|
| eClinicalMedicine Part of THE LANCET Discovery Science | 2021.09 | Phase 1b in obesity or overweight |
| nature COMMUNICATIONS | 2022.06 | Phase 1b in T2D |
| eClinicalMedicine Part of THE LANCET Discovery Science | 2022.10 | Phase 1b (higher dose) in obesity |
| American Diabetes Association. 83 rd SCIENTIFIC SESSIONS | 2023.06 | Preclinical research |
| Diabetes Care. American Diabetes Association. | 2023.11 | Phase 2 in T2D |
| nature COMMUNICATIONS | 2023.12 | Phase 2 in obesity |
| American Diabetes Association. 84 th SCIENTIFIC SESSIONS | 2024.06 | GLORY-1 Ph3 & 9mg Obesity Ph2 |

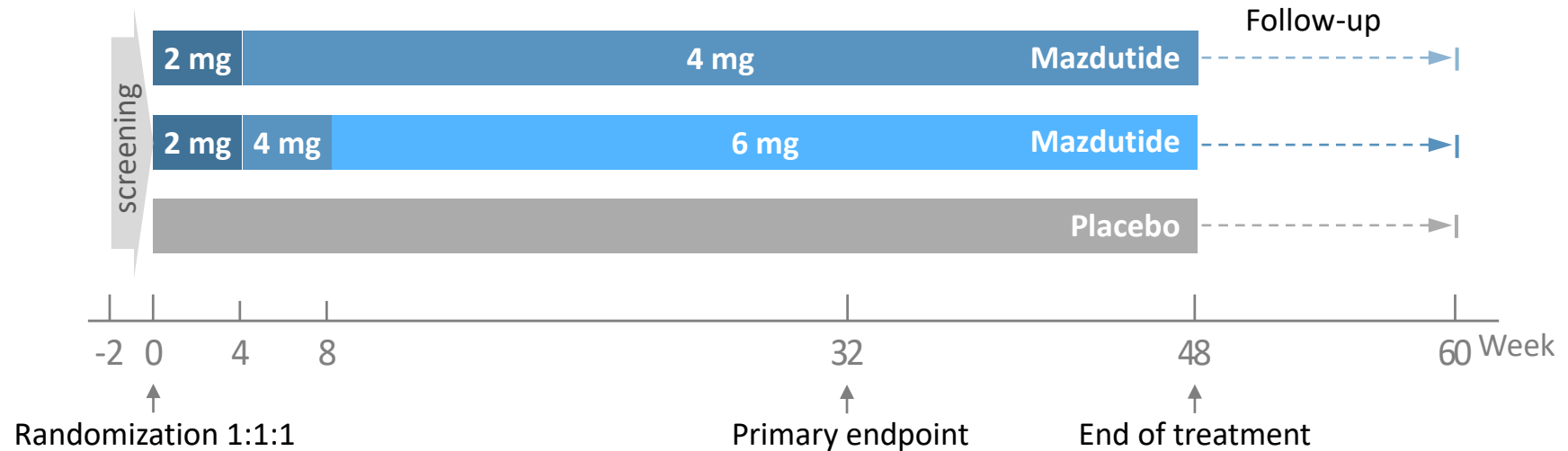
GLORY-1: trial design and baseline characteristics

Evaluating weight loss efficacy and safety in Chinese adults with obesity/overweight

ClinicalTrials.gov ID NCT05607680

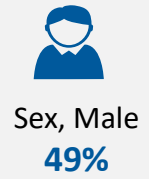
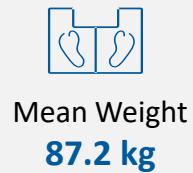
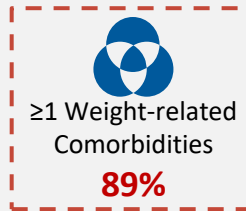
Inclusion criteria BMI ≥ 28 kg/m² or BMI ≥ 24 kg/m² plus ≥ 1 weight-related comorbidity. Excluding diabetes.

Dose regimen



Baseline
(N=610)

Baseline characteristics were essentially balanced across treatment groups

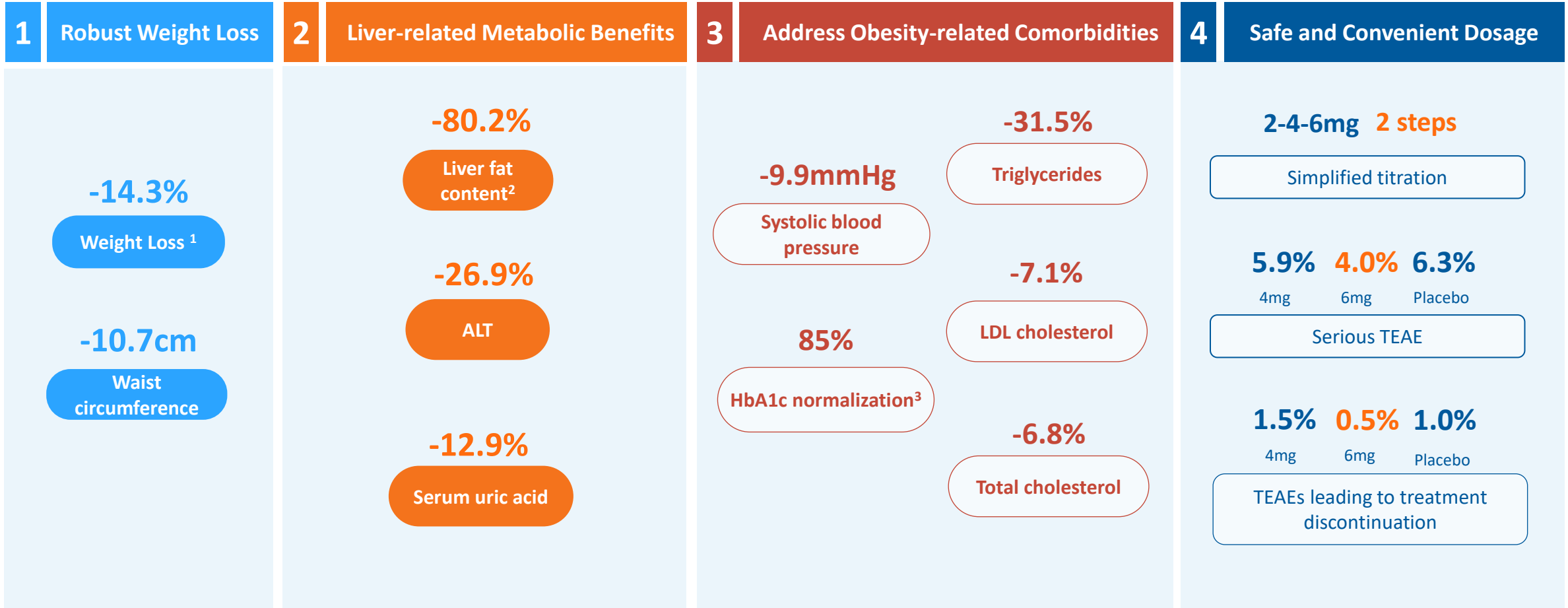


63.6% participants have ≥ 2 weight-related comorbidities, and 35.6% participants have ≥ 3 weight-related comorbidities.

Weight-related comorbidities include dyslipidemia, fatty liver, hyperuricemia, hypertension, abnormal liver function, prediabetes, kidney disease, and weight-bearing joint pain.

GLORY-1: 48-week treatment results summary

A safe medication that brings robust weight loss and reduces cardiometabolic risk factors



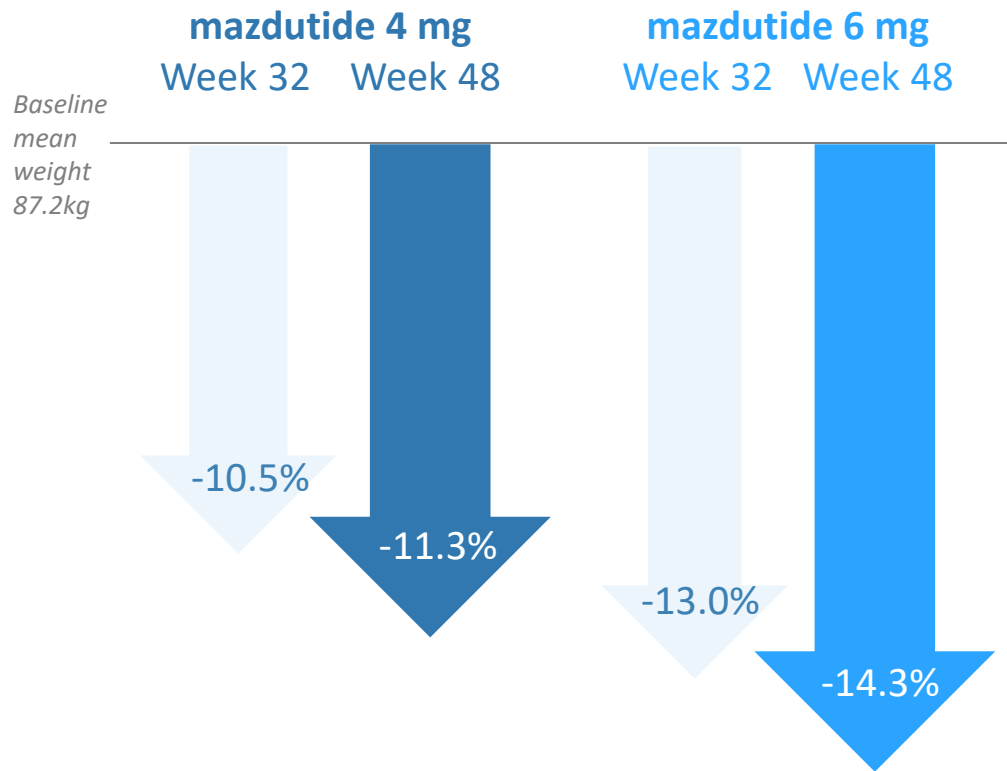
All above efficacy endpoints are 48-week results of mazdutide 6mg group (treatment-policy estimand), more data presented at 2024 ADA (1856-LB) and will be published at peer-reviewed academic journals

1. Placebo-adjusted mean body weight percentage change from baseline; 2. Evaluated in participants with baseline LFC ≥ 10%; 3. Evaluated in participants with baseline A1c ≥ 5.7%

GLORY-1: weight loss efficacy

Robust weight-loss efficacy achieved in mazdutide treatment groups

Placebo-adjusted mean body weight percentage change from baseline at week 48



Robust and durable weight reduction with simple regimen

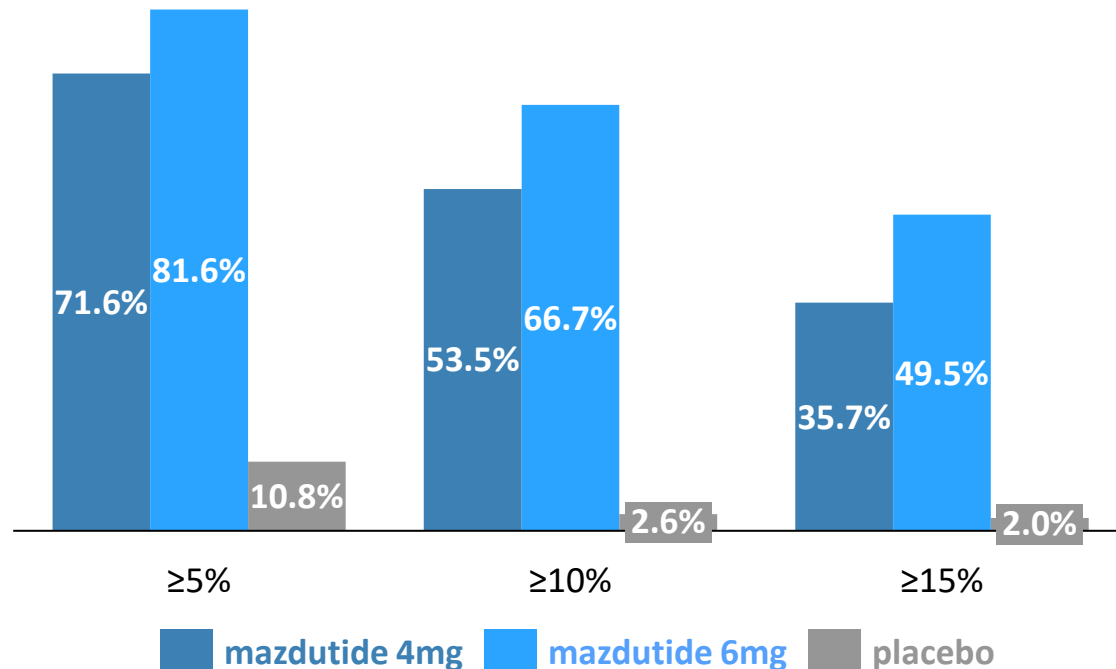
- Placebo-adjusted mean body weight reduction of -14.3% in mazdutide 6mg after 48-week treatment.
- Mazdutide has induced robust and durable weight-loss effect with its simple and tolerable two-step titration regimen.

*The treatment-policy estimand results

GLORY-1: weight loss efficacy

Half of participants receiving mazdutide 6mg achieved $\geq 15\%$ weight loss

Proportion of participants achieved $\geq 5\%/10\%/15\%$ weight loss from baseline at 48 weeks



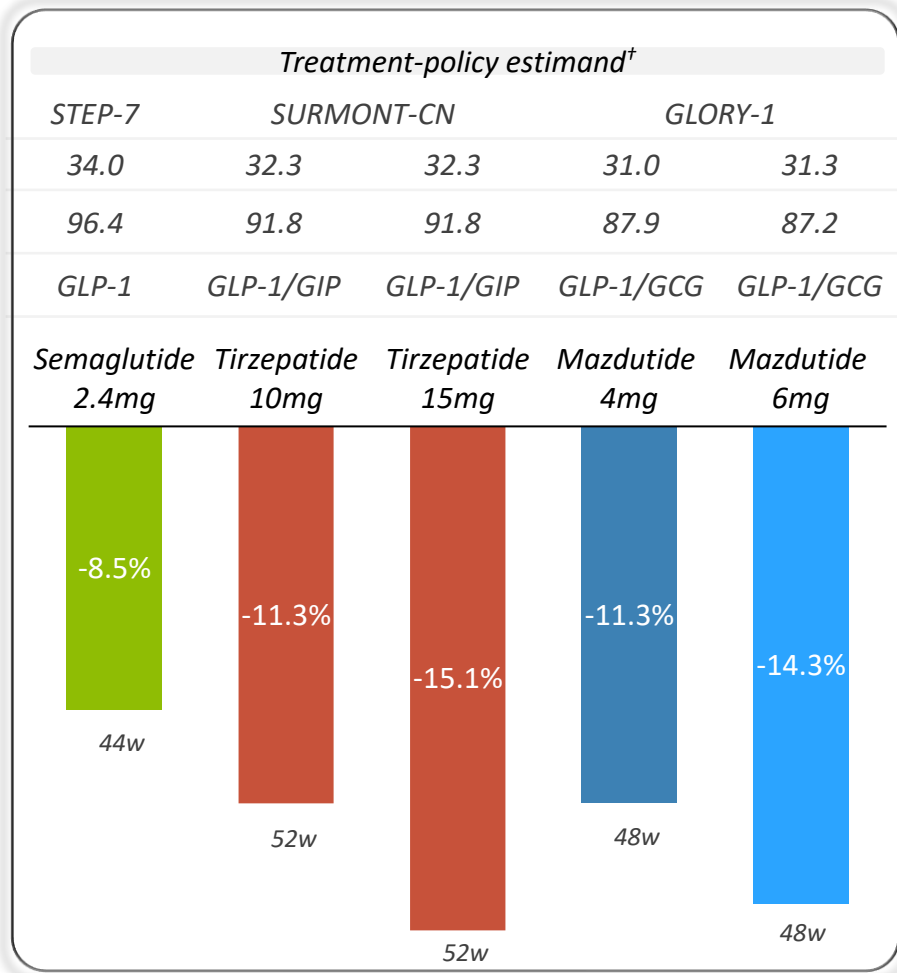
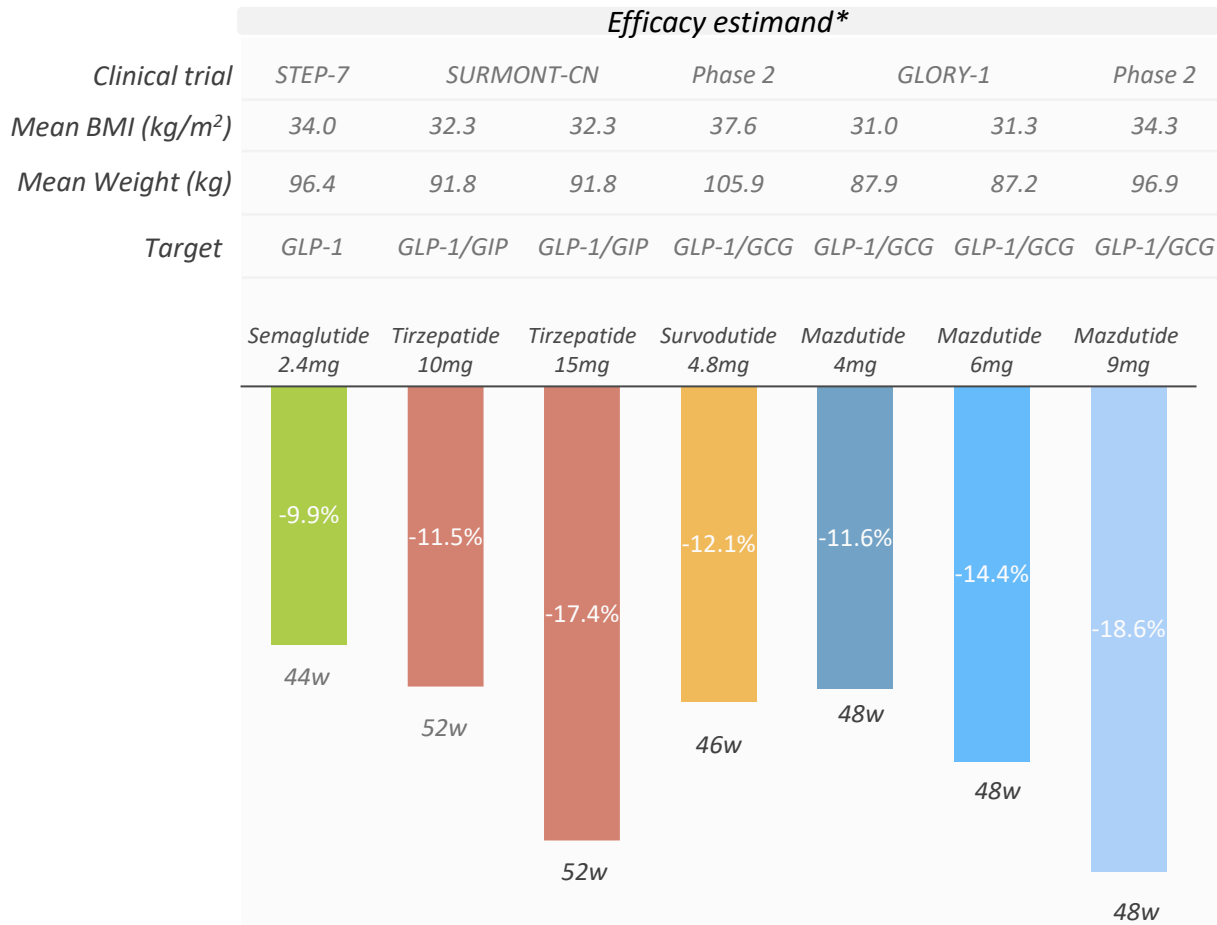
- At week 48, 81.6% and 71.6% of the participants in the mazdutide 4 mg and 6 mg group achieved 5% or more weight loss from baseline;
- **49.5% participants achieved $\geq 15\%$ weight loss in mazdutide 6 mg group after 48 weeks of treatment.**

*The treatment-policy estimand results

GLORY-1: weight loss efficacy

Mazdutide demonstrated robust weight reduction across dose levels

Summary of placebo-adjusted mean body weight reduction (%)



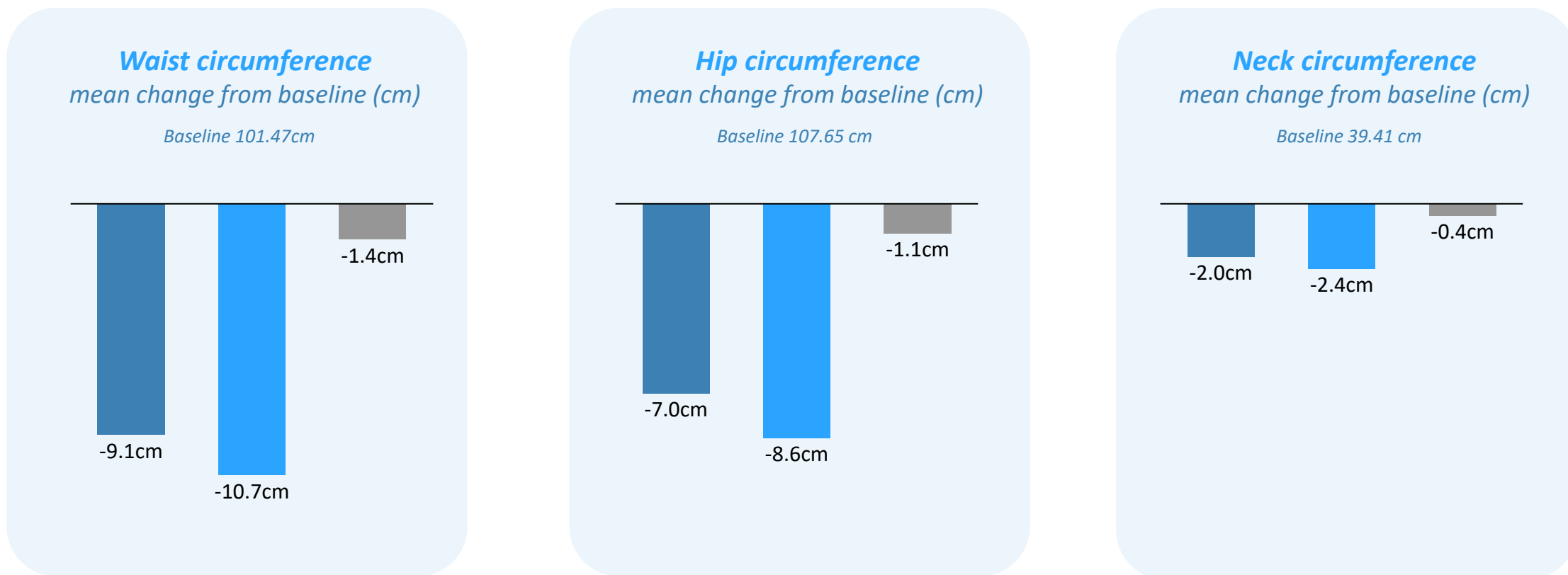
* The efficacy estimand represents the average treatment effect of mazdutide relative to placebo had participants remained on their randomized treatment for the entire planned 48 weeks treatment duration. Missing data were implicitly handled by using a mixed model for repeated measures (MMRM) under the assumption of missing at random.
 † The treatment policy estimand represents the average treatment effect of mazdutide relative to placebo regardless of the adherence to treatment. For analyses related to the treatment-regimen estimand, analysis of covariance (ANCOVA) was used for continuous endpoints and logistic regression was used for binary endpoints.



GLORY-1: weight loss efficacy

Significantly reduced waist, hip and neck circumferences, indicating body fat reduction

Significant reductions in waist/hip/neck circumferences at week 48



■ mazdutide 4 mg ■ mazdutide 6 mg ■ placebo

*The treatment policy-estimand results

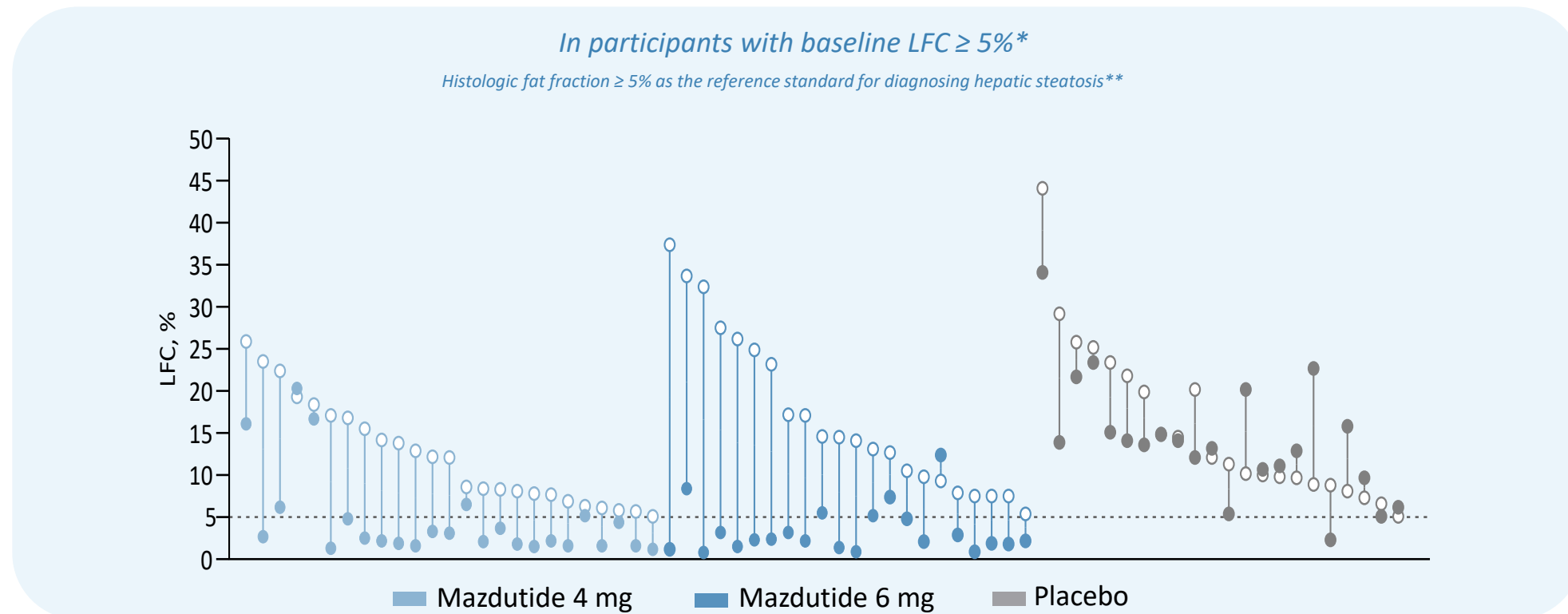
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GLORY-1: liver-related benefits

Substantially reduced liver fat content in participants with hepatic steatosis

Liver fat content (LFC) at baseline and week 48 by MRI-PDFF

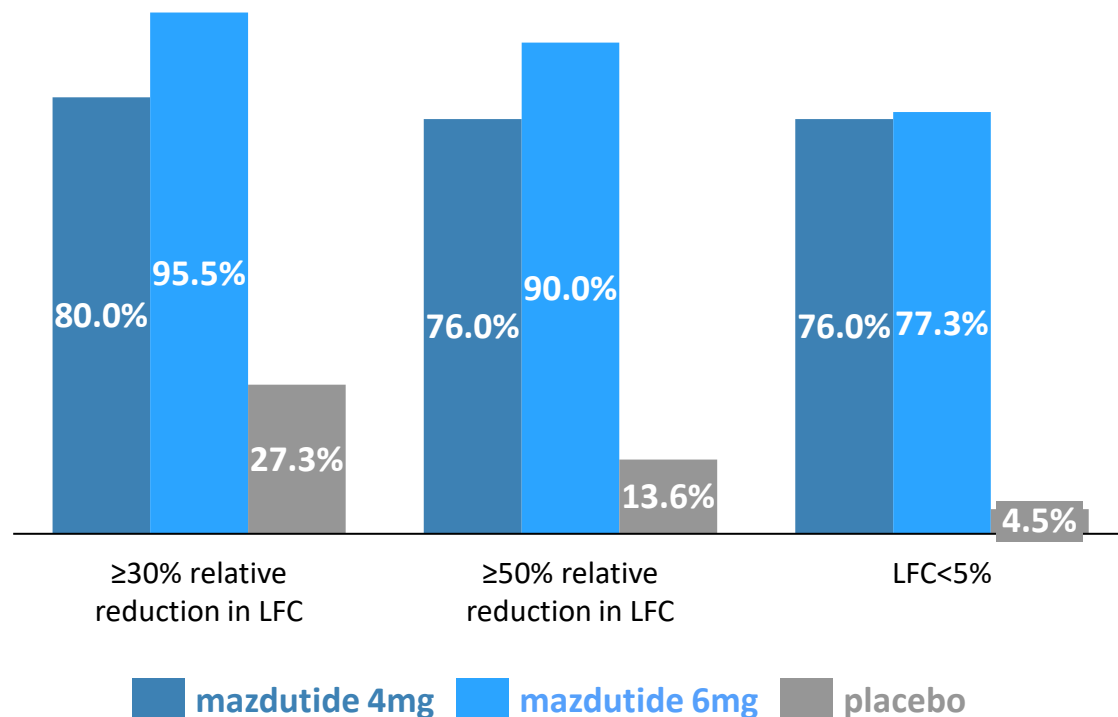


***A total of 69 participants (25 with mazdutide 4 mg, 22 with mazdutide 6 mg and 22 with placebo) had LFC $\geq 5\%$ at baseline and week 48 LFC assessment, and were included in this exploratory analysis of GLORY-1.**

GLORY-1: liver-related benefits

77.3% participants with mazdutide achieved normalization of LFC (< 5%)

Proportion of participants achieved $\geq 30\%/50\%$ LFC relative reduction or LFC < 5% at week 48



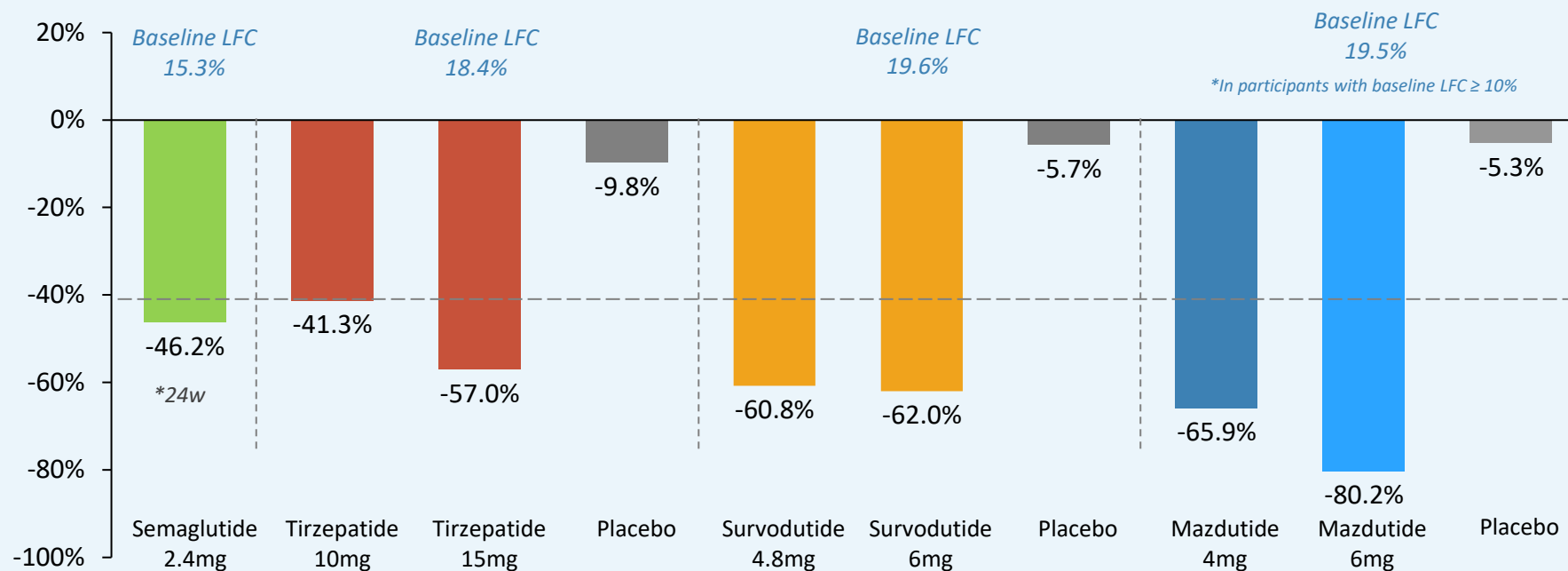
- In participants with baseline LFC $\geq 5\%$, compared to placebo, substantially more participants with mazdutide 4 mg or 6 mg treatment for 48 weeks achieved **clinically meaningful LFC reduction**.
- At week 48, normalization of LFC was achieved by 76.0% and 77.3% with mazdutide 4mg and 6mg while only 4.5% with placebo.

GLORY-1: liver-related benefits

Substantially reduced liver fat content in participants with hepatic steatosis

Up to 80.2% liver fat content reduction observed in mazdutide groups at week 48

Liver Fat Content
mean change (%) from baseline by MRI-PDFF



Semaglutide 2.4mg were published results of a Phase 2 trial¹; Tirzepatide 10mg & 15mg were published results of a Phase 2 trial²; survodutide 4.8mg were published results of a Phase 2 trial³

¹ Alkhoury N, et al. Safety and efficacy of combination therapy with semaglutide, cilofexor and firsocostat in patients with non-alcoholic steatohepatitis: A randomised, open-label phase II trial. *J Hepatol.* 2022 Sep;77(3):607-618. doi: 10.1016/j.jhep.2022.04.003. Epub 2022 Apr 16. PMID: 35439567.

² Loomba R, et al. SYNERGY-NASH Investigators. Tirzepatide for Metabolic Dysfunction-Associated Steatohepatitis with Liver Fibrosis. *N Engl J Med.* 2024 Jun 8. doi: 10.1056/NEJMoa2401943. Epub ahead of print. PMID: 38856224.

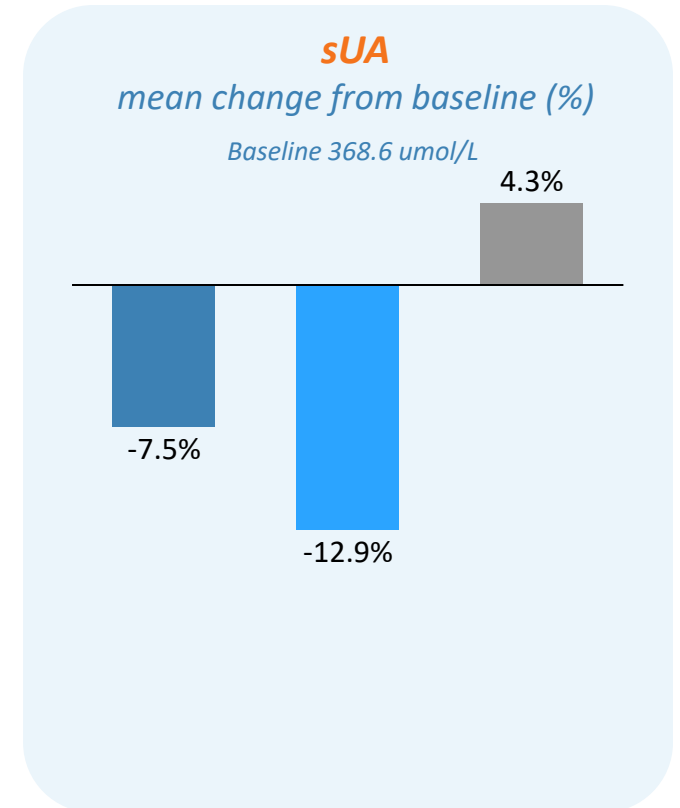
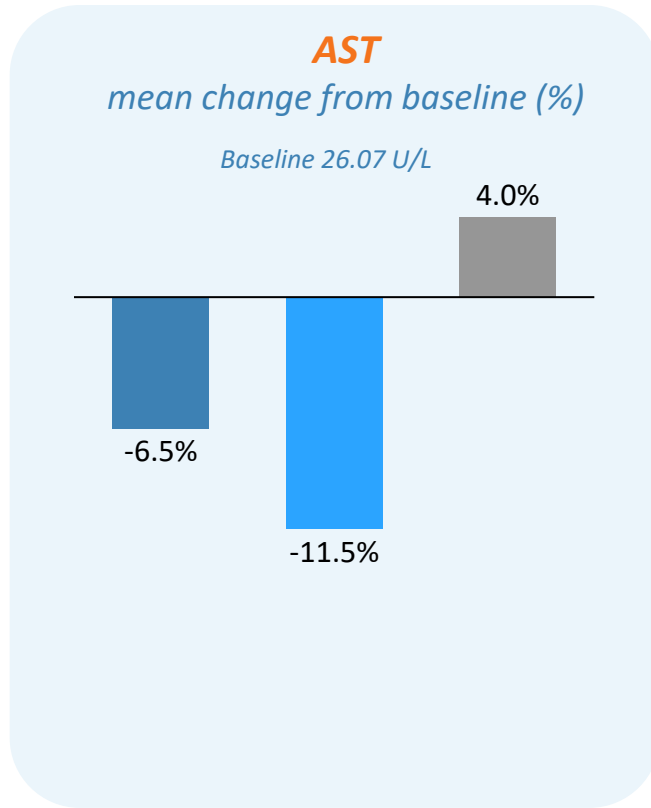
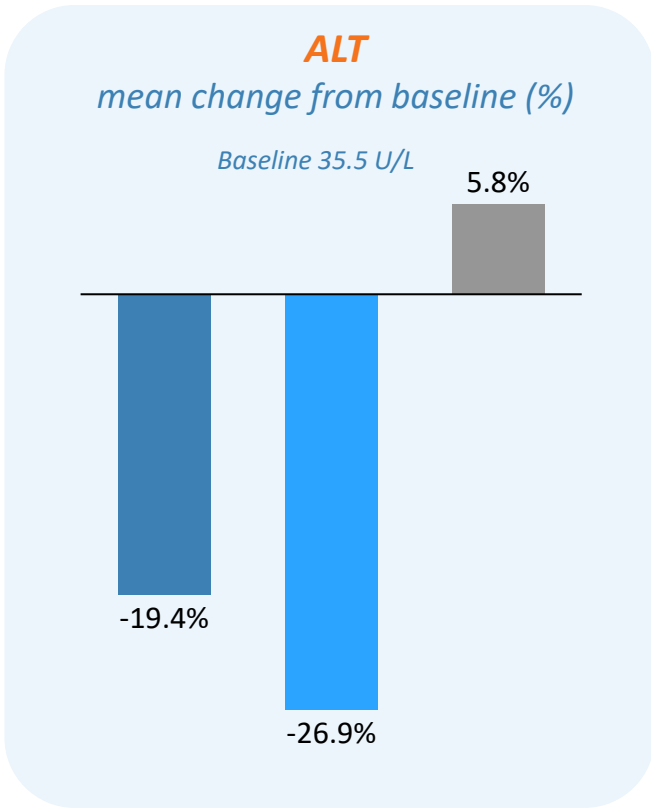
³ Sanyal AJ, et al. 1404-0043 Trial Investigators. A Phase 2 Randomized Trial of Survodutide in MASH and Fibrosis. *N Engl J Med.* 2024 Jun 7. doi: 10.1056/NEJMoa2401755. Epub ahead of print. PMID: 38847460.

GLORY-1: liver-related benefits

Robust reductions in transaminase and serum uric acid

Robust reduction in ALT and AST at week 48

Unique reduction in sUA at week 48

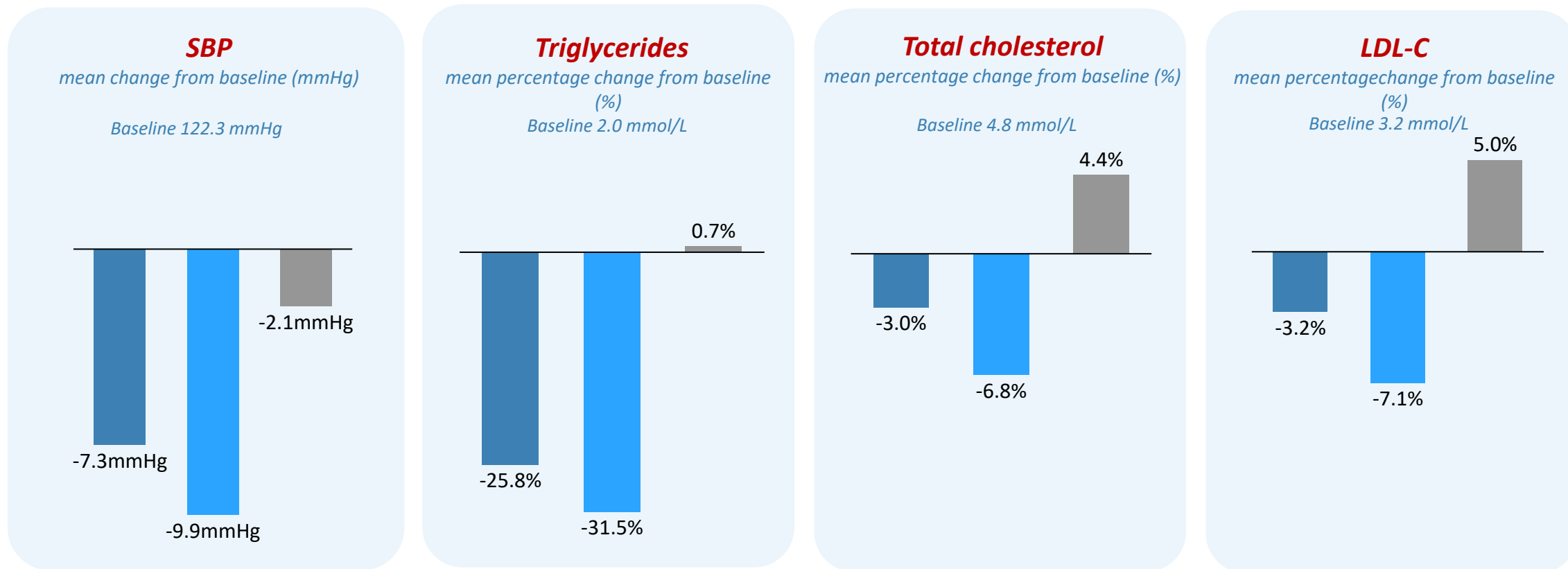


■ mazdutide 4 mg ■ mazdutide 6 mg ■ placebo

GLORY-1: cardio-metabolic benefits

Significantly reduced cardiometabolic risk factors, alleviating comorbidity burden

Significant reductions in blood pressure and lipids at week 48



■ mazdutide 4 mg ■ mazdutide 6 mg ■ placebo

*The treatment-policy estimand results

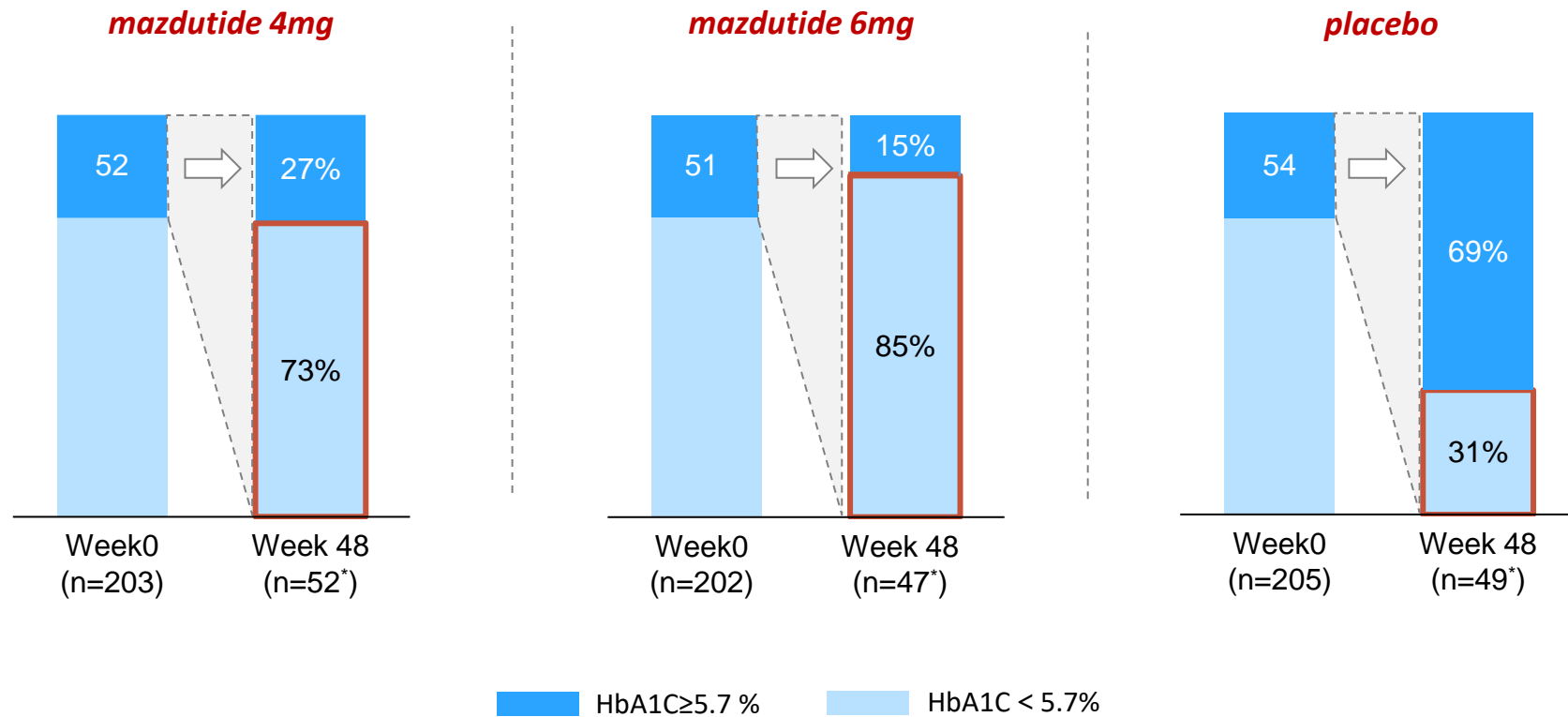
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GLORY-1: glycemic benefit

Significantly normalized blood sugar level for participants with HbA1C $\geq 5.7\%$

Proportion of participants with baseline HbA1c $\geq 5.7\%$ achieved A1c normalization at week 48

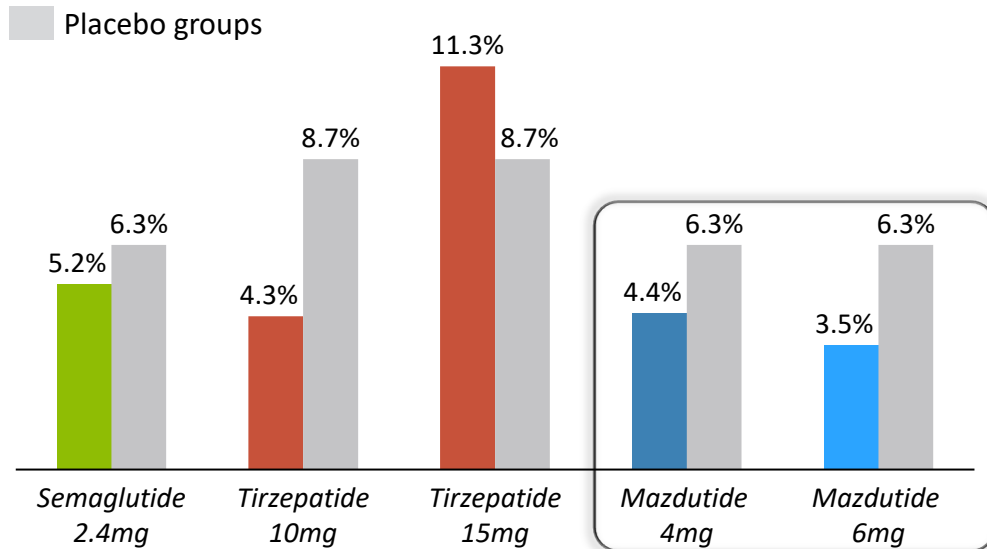


*Number of participants with baseline A1c $\geq 5.7\%$ and evaluable data at week 48.

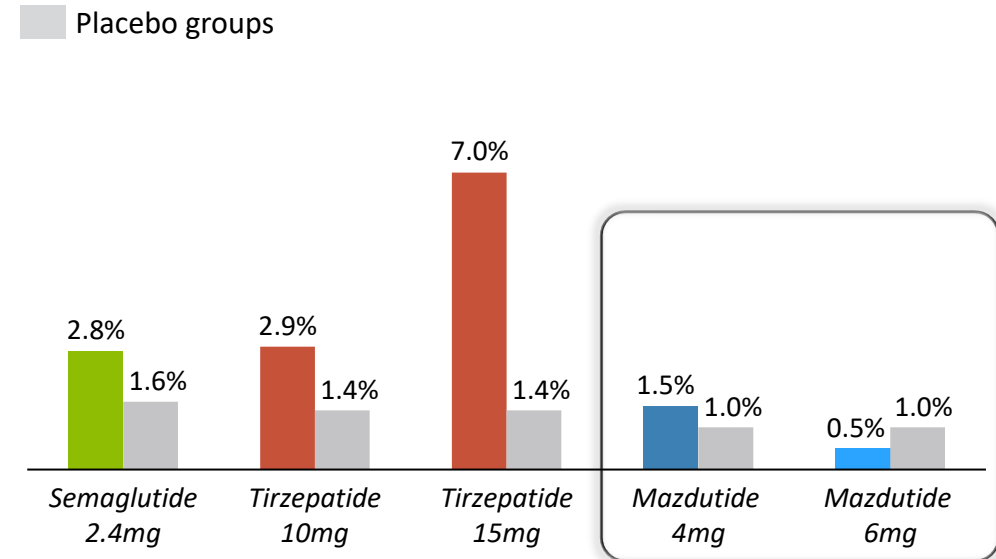
GLORY-1: safety profile

Favorable tolerability and safety profile of mazdutide

Serious adverse events %



Adverse events leading to discontinuation %



- Gastrointestinal symptoms (nausea, vomiting and diarrhea) were the most common adverse events, **mostly mild or moderate severity**.
- Most gastrointestinal adverse events occurred during the dose escalation period.

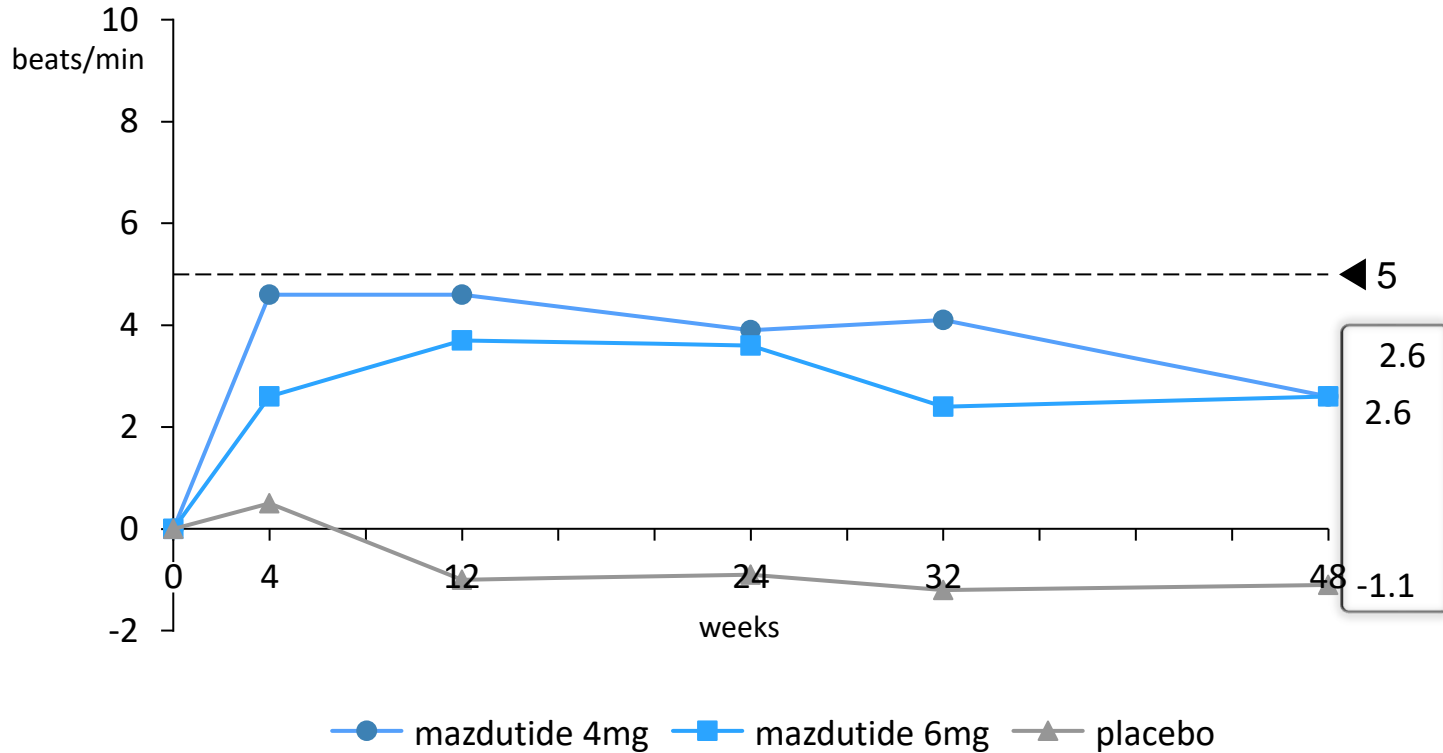
Safety data of semaglutide 2.4 mg, tirzepatide 10/15 mg were from published results of SURMOUNT-CN¹ and STEP-7² studies, respectively.

¹ Zhao L, Cheng Z, et al. JAMA. Published online May 31, 2024. doi:10.1001/jama.2024.9217 ² Prof Yiming Mu, MD, et al. The Lancet Diabetes & Endocrinology. Published online February 05, 2024. doi:10.1016/S2213-8587(23)00388-1

GLORY-1: safety profile

No signal of increased cardiovascular risk was observed throughout the 48-week treatment

Mean heart rate change from baseline over 48-week treatment (beats/min)



- The increase in **heart rate in the mazdutide groups was mild and mainly in dose-escalation stage**. Mean changes from baseline were no more than 5 beats/min throughout the 48-week treatment period for both mazdutide groups.
- **No safety signal of increased cardiovascular risk** was observed throughout the treatment period.

Summary and takeaway 1:

GLORY-1 reinforces mazdutide's advantage as a potent medication for weight management



Robust and rapid weight-loss efficacy

- Mean weight loss from baseline of -14.3%
- Half patients achieved $\geq 15\%$ weight loss

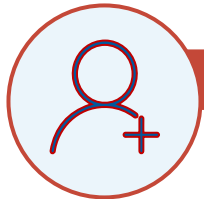
Competitive weight loss effect and strong clinical evidence in Chinese population



80% LFC reduction and liver benefits

- Differentiated benefits in significantly reducing LFC, ALT and serum uric acid levels

Implication of the additional benefit of GCGR agonism through direct activation on liver



Improvements in related comorbidities indicators

- Significant reduction in waist circumference, SBP, TG, TC, LDL-C levels etc.

Potential to improve healthy outcomes for people living with obesity and associated comorbidities



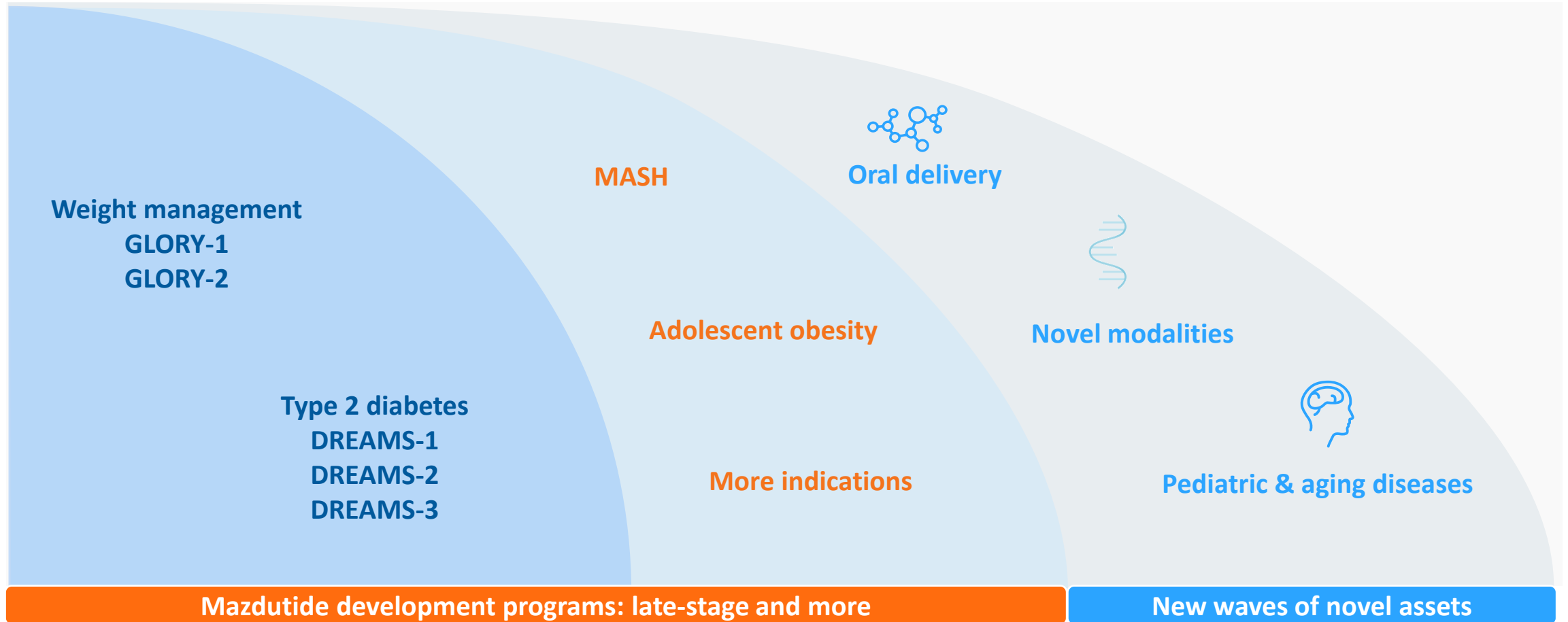
Favorable and superior safety and tolerability

- Most GI AEs are of mild or moderate severity
- Relatively low SAEs and drop-out rate
- Heart rate increase was mild and stable, no increased cardiovascular risk observed

Facilitate treatment compliance and quality of life under convenient, safe and tolerable two-step dose regimen

Summary and takeaway 2:

Expand indication exploration of mazdutide and innovate in early-stage pipeline



- Evaluate and advance mazdutide to address significant unmet medical needs in other key metabolic diseases
- Continue to innovate in more early-stage metabolic pipeline

Q&A

All management

Disclaimer

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