

Leading the Fight Against MASH

January 12, 2026

J.P. Morgan 44th Annual Healthcare Conference

Bill Sibold, Chief Executive Officer

Dave Soergel, M.D., Chief Medical Officer

Forward-looking Statements

This presentation includes “forward-looking statements” made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, that are based on Madrigal’s beliefs and assumptions and on information currently available to it but are subject to factors beyond its control. Forward-looking statements reflect management’s current knowledge, assumptions, judgment and expectations regarding future performance or events. Forward-looking statements include all statements that are not historical facts; statements referenced by forward-looking statement identifiers; and statements regarding: potential future growth of Rezdiffra (resmetirom) sales; expected commercial insurance coverage for Rezdiffra; the expected benefit of Madrigal’s intellectual property; Madrigal’s ability to obtain full approval for Rezdiffra in the United States and Europe; expectations regarding Madrigal’s clinical development plans and related timelines; Madrigal’s leadership position in the MASH sector; the potential impact of positive results from the MAESTRO-NASH OUTCOMES trial; the potential benefit of Rezdiffra in patients with compensated MASH cirrhosis; the competitive landscape and market dynamics; estimates of patients diagnosed with MASH and market opportunities; and strategies, objectives and commercial opportunities, including potential prospects or results.

Forward-looking statements can be identified by terms such as “accelerate,” “achieve,” “allow,” “anticipates,” “appear,” “be,” “believes,” “can,” “confidence,” “continue,” “could,” “demonstrates,” “design,” “estimates,” “expectation,” “expects,” “forecasts,” “future,” “goal,” “help,” “hopeful,” “inform,” “intended,” “intends,” “may,” “might,” “on track,” “planned,” “planning,” “plans,” “positions,” “potential,” “powers,” “predicts,” “predictive,” “projects,” “seeks,” “should,” “will,” “will achieve,” “will be,” “would,” “future” or similar expressions and the negatives of those terms.

Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to: the assumptions underlying the forward-looking statements; risks related to obtaining and maintaining regulatory approvals, including, but not limited to, potential regulatory delays or rejections; the challenges with the commercialization of a new product; our history of operating losses and the possibility that we may never achieve or maintain profitability; risks associated with meeting the objectives of Madrigal’s clinical trials, including, but not limited to Madrigal’s ability to achieve enrollment objectives concerning patient numbers (including an adequate safety database), outcomes objectives and/or timing objectives for trials for any product candidate; any delays or failures in enrollment, and the occurrence of adverse safety events; risks related to the effects of Rezdiffra’s mechanism of action or any other product candidate; market demand for and acceptance of Rezdiffra; the potential inability to raise sufficient capital to fund ongoing operations as currently planned or to obtain financing on acceptable terms; our ability to service indebtedness and otherwise comply with debt covenants; outcomes or trends from competitive trials; future topline data timing or results; our ability to prevent and/or mitigate cyber-attacks; the uncertainties inherent in clinical testing; uncertainties concerning analyses or assessments outside of a controlled clinical trial; our ability to enter into strategic transactions and realize the benefits of any such transaction; our ability to obtain, maintain and protect our intellectual property; and changes in laws and regulations applicable to our business and our ability to comply with such laws and regulations. Undue reliance should not be placed on forward looking statements, which speak only as of the date they are made. Madrigal undertakes no obligation to update any forward-looking statements to reflect new information, events, or circumstances after the date they are made, or to reflect the occurrence of unanticipated events. Please refer to Madrigal’s submissions filed with the U.S. Securities and Exchange Commission (“SEC”) for more detailed information regarding these risks and uncertainties and other factors that may cause actual results to differ materially from those expressed or implied. Madrigal specifically discusses these risks and uncertainties in greater detail in Part I, Item 1A of its Annual Report on Form 10-K for the year ended December 31, 2024, filed with the SEC on February 26, 2025, and as updated from time to time by Madrigal’s other filings with the SEC.

Executing on Our Strategic Growth Priorities

Maximizing the Value of Rezdiffra

**Delivering on
best-in-industry
drug launch**

Annualizing at
>\$1B net sales

**Progressing toward
F4c indication
expansion**

Potential to double
Rezdiffra opportunity¹

Building Our Pipeline

**Extending
leadership through
pipeline expansion**

Adding new MOAs
and new modalities

1. Pending successful completion of MAESTRO-NASH OUTCOMES trial and FDA approval; **F4c**: Compensated MASH cirrhosis; **MOA**: Mechanism of action.

As the Market Leader, We are Shaping Our Future and the Future of MASH

2024

FDA Approval for First MASH Medicine

Landmark FDA approval of Rezdiffra on March 14, 2024

2025

Building the Foundational Therapy

Rezdiffra + oral GLP-1

Rezdiffra global expansion starting with Germany

New U.S. Rezdiffra patent extends value to 2045

Rezdiffra annualizing at >\$1B in 6th quarter of launch

2026+

Shaping Our Future

Continue to build pipeline through BD

Rezdiffra + DGAT-2 inhibitor

Accelerate Rezdiffra evidence generation

F4c indication could double opportunity (2027 readout)¹

Drive and shape MASH market

Strong first-line access supports Rezdiffra's growth

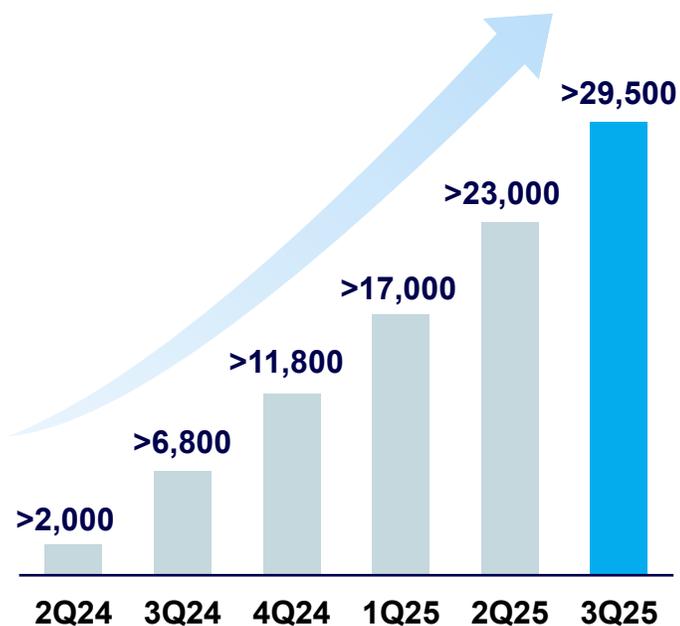
- Building our pipeline
- Maximizing Rezdiffra

1. Pending successful completion of MAESTRO-NASH OUTCOMES trial and FDA approval.

Rezdiffra: One of the Best Specialty Medicine Launches of the Last Decade

Rezdiffra Launch Performance Through 3Q25

Active Patients on Therapy

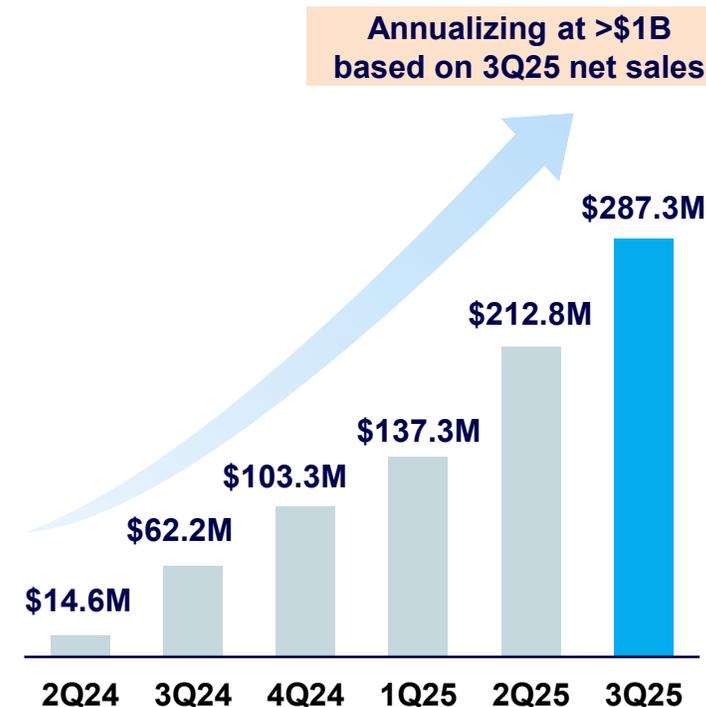


Total Rezdiffra Prescribers

>10,000

Total number of healthcare providers that have prescribed Rezdiffra as of 3Q25

Net Sales



Strong Execution on Rezdifra Access Objectives for 2026

National Payer Contracts Recognize Rezdifra's Value



Broad first-line access to Rezdifra



No step edit requirements



Improvements in utilization management criteria

Less than 10% Penetrated in a Market with a 10% Diagnosis Rate; Addressable Patient Population Poised for Significant Expansion



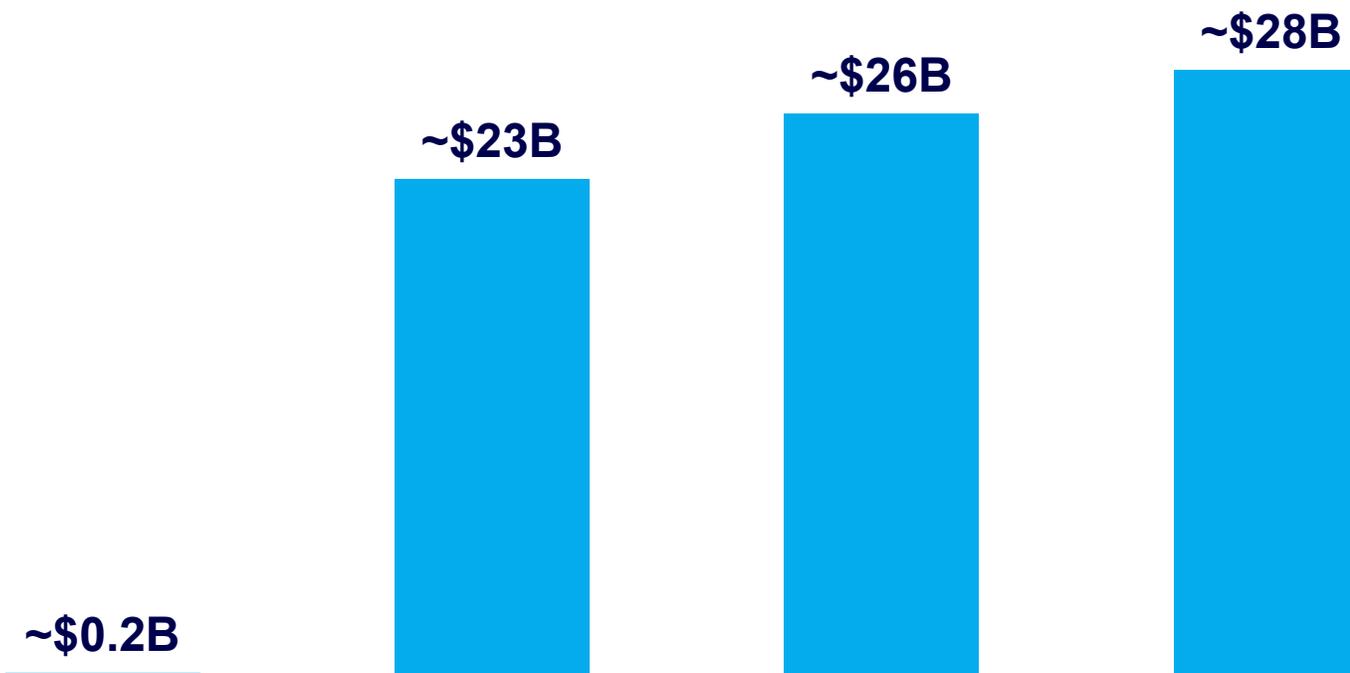
**Significant opportunity
for market growth and
Rezdifra penetration**

Only **10%**
of MASH patients diagnosed

<10% Rezdifra
penetration

MASH is Similar to Other Large Therapeutic Categories Where Additional Therapies Grow the Market Over Time

Total Global Sales by Therapeutic Category in 2024



Therapeutic Category	MASH	IBD	RA	Psoriasis
# of approved therapies in 2025	2	19	13	14
Year first therapy was approved	2024	1998	1999	2004

IBD: Inflammatory bowel disease; RA: Rheumatoid arthritis.

Rezdiffra is the Foundational Therapy in MASH

Driven by its Compelling Profile

			Rezdiffra
	Mechanism of Action	Liver-directed	✓
	MASH Efficacy	Consistent across patient subtypes (e.g., T2D) ¹	✓
	Tolerability	Well-tolerated ¹	✓
	Adherence	High ¹	✓
	Route of Administration	Once-daily pill; no titration	✓

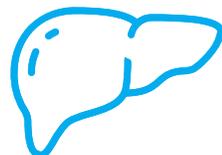
1. Harrison SA, et al. A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis. *N Engl J Med.* 2024;390(6):497-509.

Expansion into F4c has the Potential to Double the Opportunity for Rezdiffra¹

Significant Unmet Need in Compensated MASH Cirrhosis (F4c)

Estimated addressable U.S. patient population
~245,000

Higher urgency to treat given **42x** higher risk of liver-related mortality



Rezdiffra tracking to be **first to market**



No treatments available today

F4c outcomes trial data estimated in
2027



2-year OLE data provides confidence in MAESTRO-NASH OUTCOMES²

1. Pending successful completion of MAESTRO-NASH OUTCOMES trial and FDA approval; 2. 2-year OLE data are from the F4c cohort of the Phase 3 MAESTRO-NAFLD-1 trial; **OLE**: open-label extension.

Madrigal is Shaping the Future of MASH

MASH is a complex, heterogeneous disease with a broad spectrum of comorbidities. Its future will include multiple therapies, combinations and personalized regimens.

MASH Treatment Today

- Treatment available in F2/F3
- Combination therapy strategies undefined
- 10% patients diagnosed
- <10% patients treated

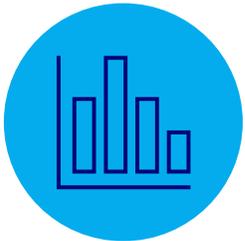
Rezdiffra[®]
resmetirom tablets
is the foundational therapy

MASH Treatment in the Future

- Treatment available in **F2-F4c**
- **Combination therapies** to drive better outcomes and tailored treatment approaches
- **Awareness and screening** expand diagnosed and treated patient population

Madrigal is Uniquely Positioned to Extend its Leadership in MASH

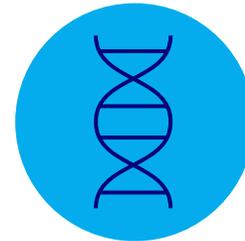
Our R&D strategy is to build the **industry-leading MASH pipeline** through targeted business development and internal innovation, **leveraging Rezdifra as the foundational therapy**



Deliver transformational **outcomes** data, securing full approval from F2-F4c



Advance **combination therapies** anchored by Rezdifra



Invest in **new modalities**, including those that enable patient-specific care



Execute **disciplined, capital-efficient** clinical development (quick go / no-go)

We're Building Our Pipeline with the Most Promising Targets

MASH Disease Pathways and Potential Mechanisms

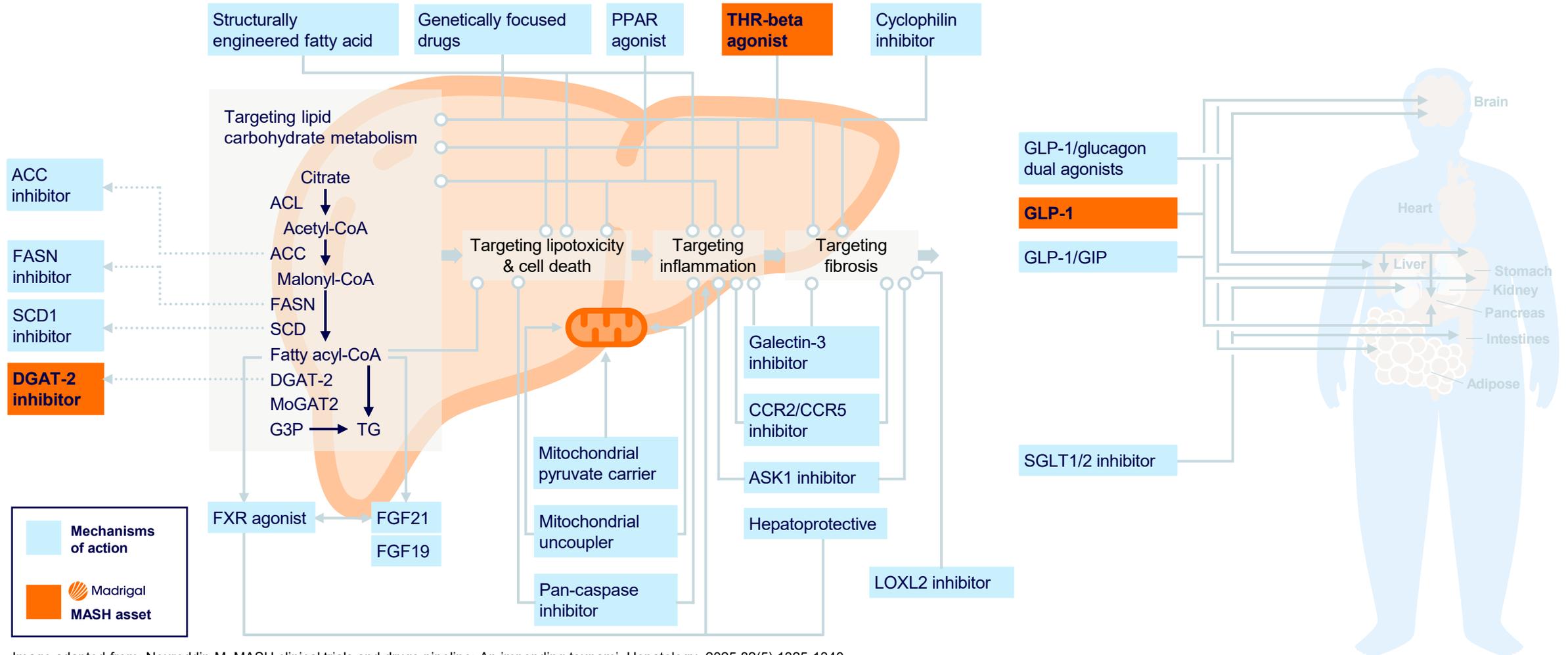
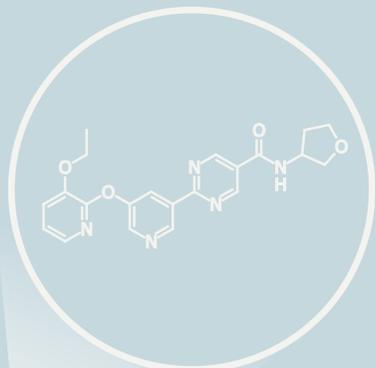


Image adapted from: Nouredin M. MASH clinical trials and drugs pipeline: An impending tsunami. Hepatology. 2025;82(5):1325-1340.

We Have Added a Promising New Mechanism to Our Pipeline

DGAT-2 Inhibitor (ervogastat)



Development Stage

Completed Phase 2b

Route of Administration

Oral

Mechanism of Action

Blocks final step of triglyceride assembly to reduce steatosis

Rationale

Phase 2b data demonstrate impressive MRI-PDFF reduction

Complementary; combo with Rezdiffra could result in additive efficacy/compelling real-world profile

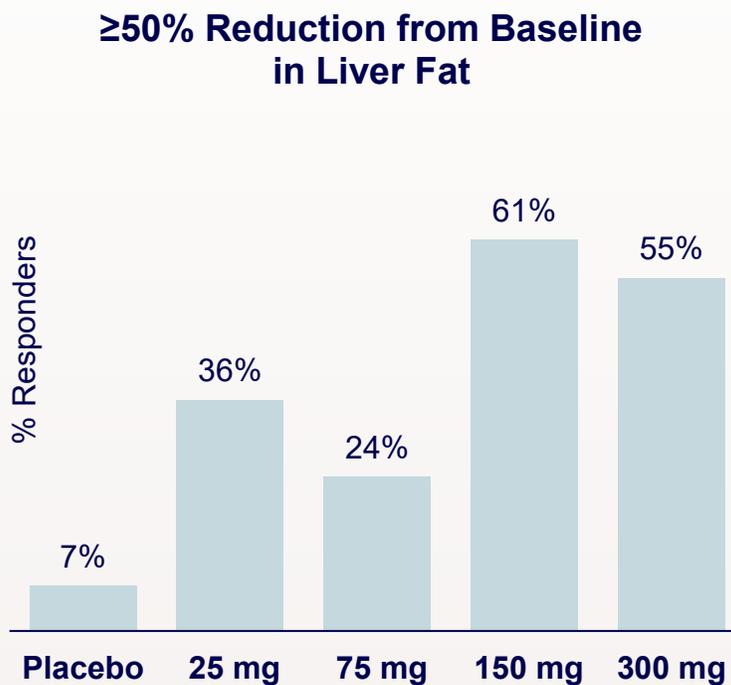
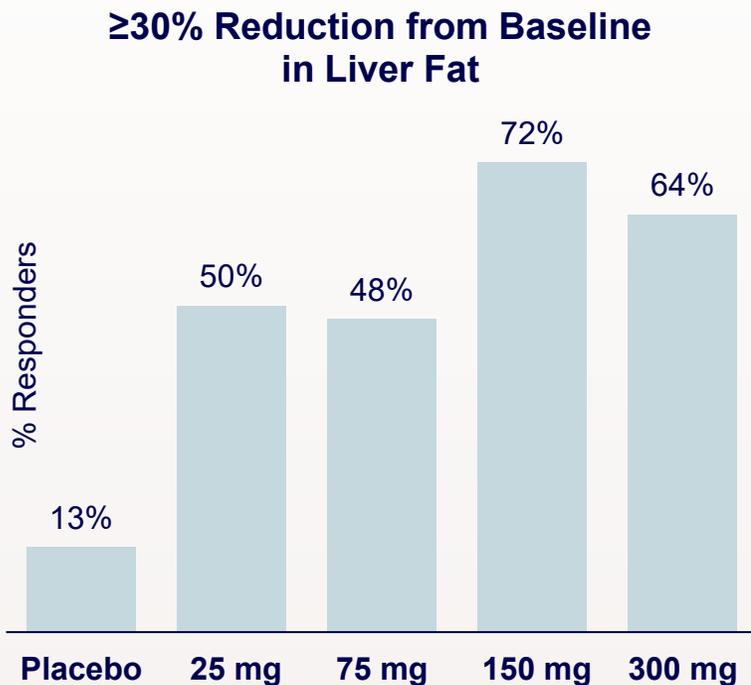
Clean safety and tolerability profile

Next Steps: DDI study in 2026; Phase 2 combination study anticipated to start in 2027 following regulatory discussions

DGAT-2: Diacylglycerol O-acyltransferase 2; DDI: Drug-drug interaction

A Closer Look at Ervogastat: Impressive Liver Fat Reduction with Up to 61% of Patients Considered “Super-Responders”

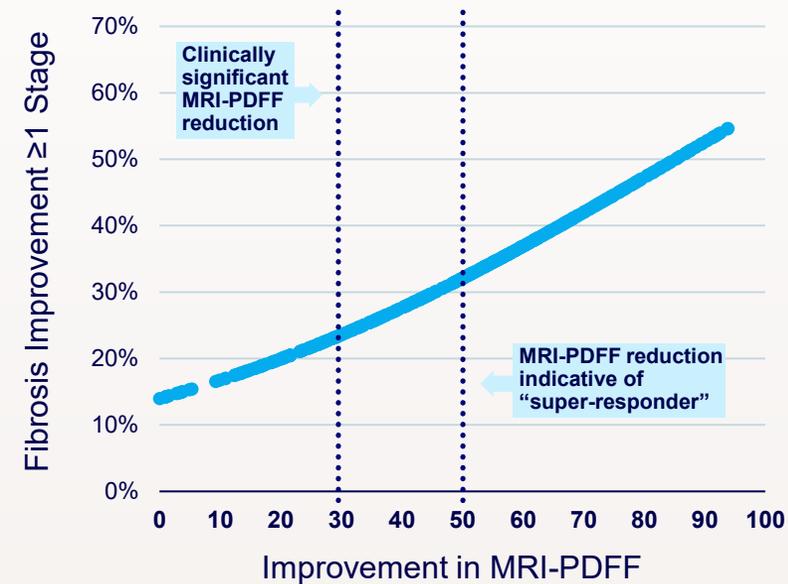
MRI-PDFF Phase 2 Ervogastat Results¹



In addition to MRI-PDFF reduction, reassuring trends on reductions in liver stiffness measurements (LSM) and liver enzymes and improvements in histology

Rezdiffra Phase 3 Fibrosis/MRI-PDFF Data

MRI-PDFF Reduction Correlates with Fibrosis Reduction in MAESTRO NASH²



1. Wong VW, Amin NB, Takahashi H, et al. Efficacy and safety of ervogastat alone and in combination with clesacostat in patients with biopsy-confirmed metabolic dysfunction-associated steatohepatitis and F2-F3 fibrosis (MIRNA): results from a phase 2, randomised, double-blind, double-dummy study. *Lancet Gastroenterol Hepatol.* 2025;10(10):924-940; 2. Alkouri, N et al. Use of non-invasive tests to diagnose and follow NASH with liver fibrosis patients treated with resmetirom, [Poster presentation], AASLD, Nov. 15-19, 2024, San Diego, CA.

Combination Hypothesis: Resmetirom and Ervogastat Work in Complementary Ways to Reduce Fat Build-Up in the Liver

Resmetirom + Oral DGAT-2

1

Reduces STEATOSIS in two distinct but complementary ways:

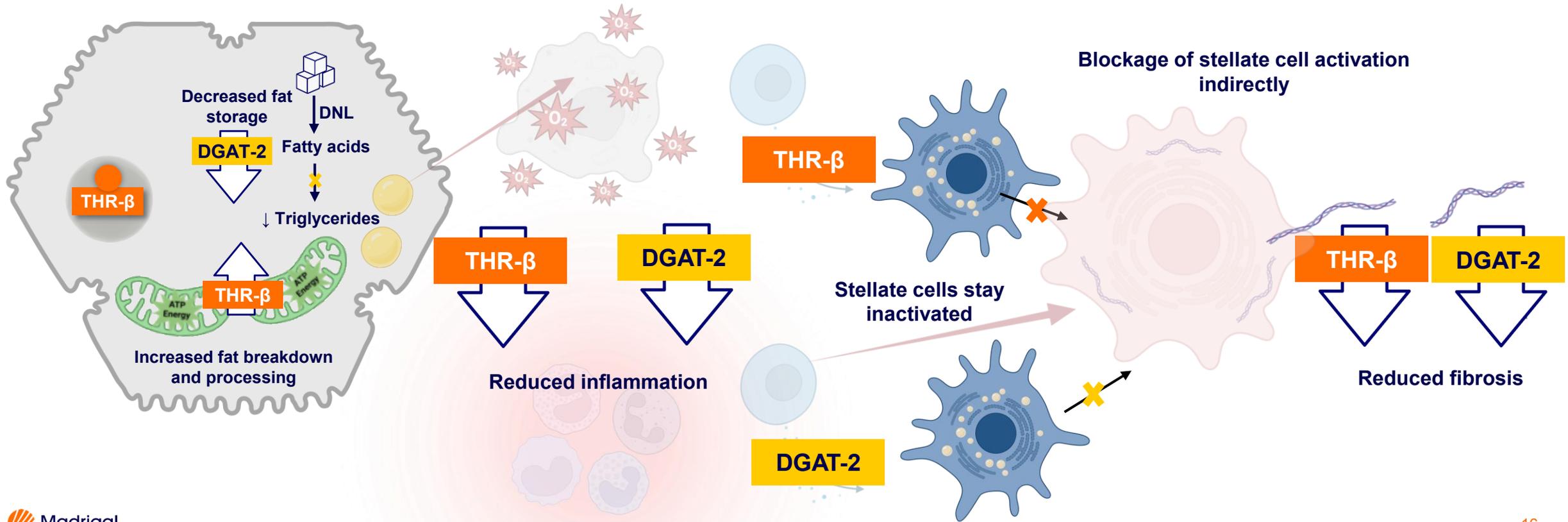
- Resmetirom increases fat processing
- DGAT-2 inhibition blocks hepatic triglyceride assembly

2

Reduces INFLAMMATION by reducing liver fat and oxidative stress

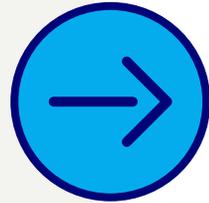
3

Reduces FIBROSIS by indirectly blocking stellate cells

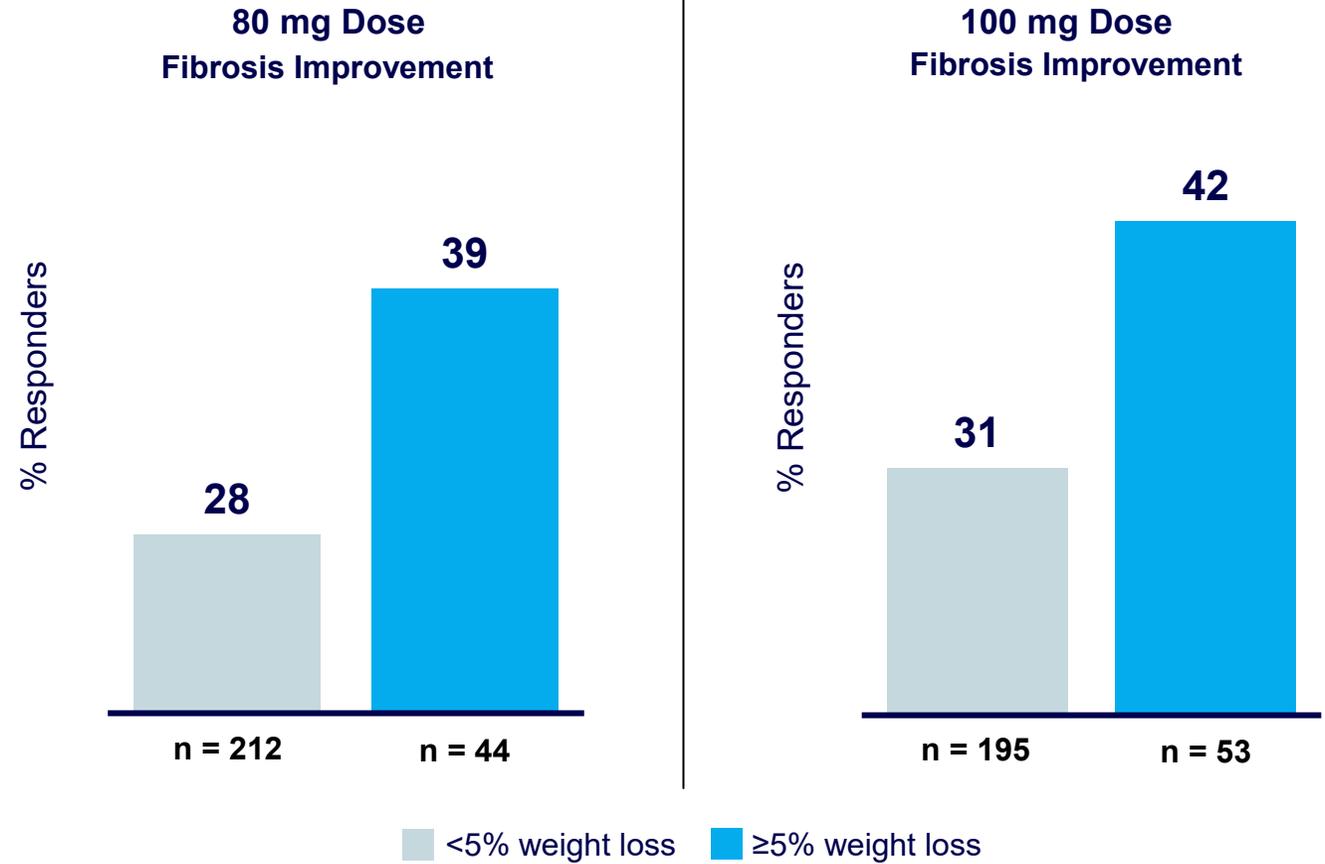


A Closer Look at Oral GLP-1: Advancing MGL-2086 and Resmetirom in Combination

- Rezdiffra patients with $\geq 5\%$ weight loss (WL) see enhanced antifibrotic effect
- 22% of Phase 3 trial patients on Rezdiffra achieved $\geq 5\%$ WL; goal to increase percentage with Rezdiffra/GLP-1 combo
- **Development goal:** Balance moderate weight loss from MGL-2086 with Rezdiffra's antifibrotic effect in a once daily oral combo with good tolerability
- **Next steps:** MGL-2086 Phase 1 SAD study to begin 2Q26



Weight Loss $\geq 5\%$ Improves Rezdiffra's Efficacy¹



1. Nouredin, M., Effect of Resmetirom or Placebo in NASH Fibrosis Patients with <5% or $\geq 5\%$ Weight Loss and/or on Baseline GLP-1 Therapy in the MAESTRO NASH 52-Week Serial Biopsy Study [Conference presentation] AASLD Nov. 15-19, 2024, San Diego, CA; **SAD:** single ascending dose.

Combination Hypothesis: Resmetirom's Antifibrotic Effect has Potential to be Amplified by Modest Weight Loss from MGL-2086

Resmetirom + Oral GLP-1

1

Reduces STEATOSIS in two distinct but complementary ways:

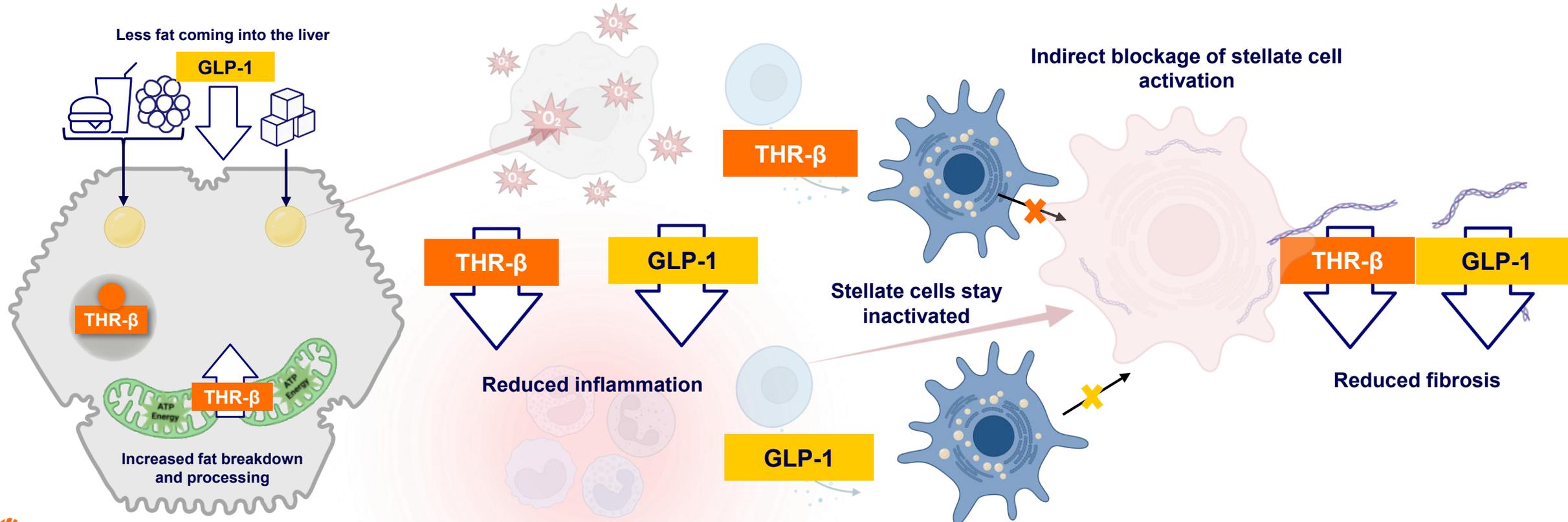
- Resmetirom increases fat processing
- GLP-1 decreases fat accumulation

2

Reduces INFLAMMATION by reducing liver fat and oxidative stress

3

Reduces FIBROSIS by indirectly blocking stellate cells



Advancing an Industry-Leading MASH Pipeline to Transform Patient Care



Rezdiffra[®]
resmetirom tablets

MOA Indication Preclinical Phase 1 Phase 2 Phase 3 Launched

THR-β agonist MASH F2/F3 [Progress bar: Preclinical to Phase 3]

THR-β agonist MASH F4c [Progress bar: Preclinical to Phase 2]

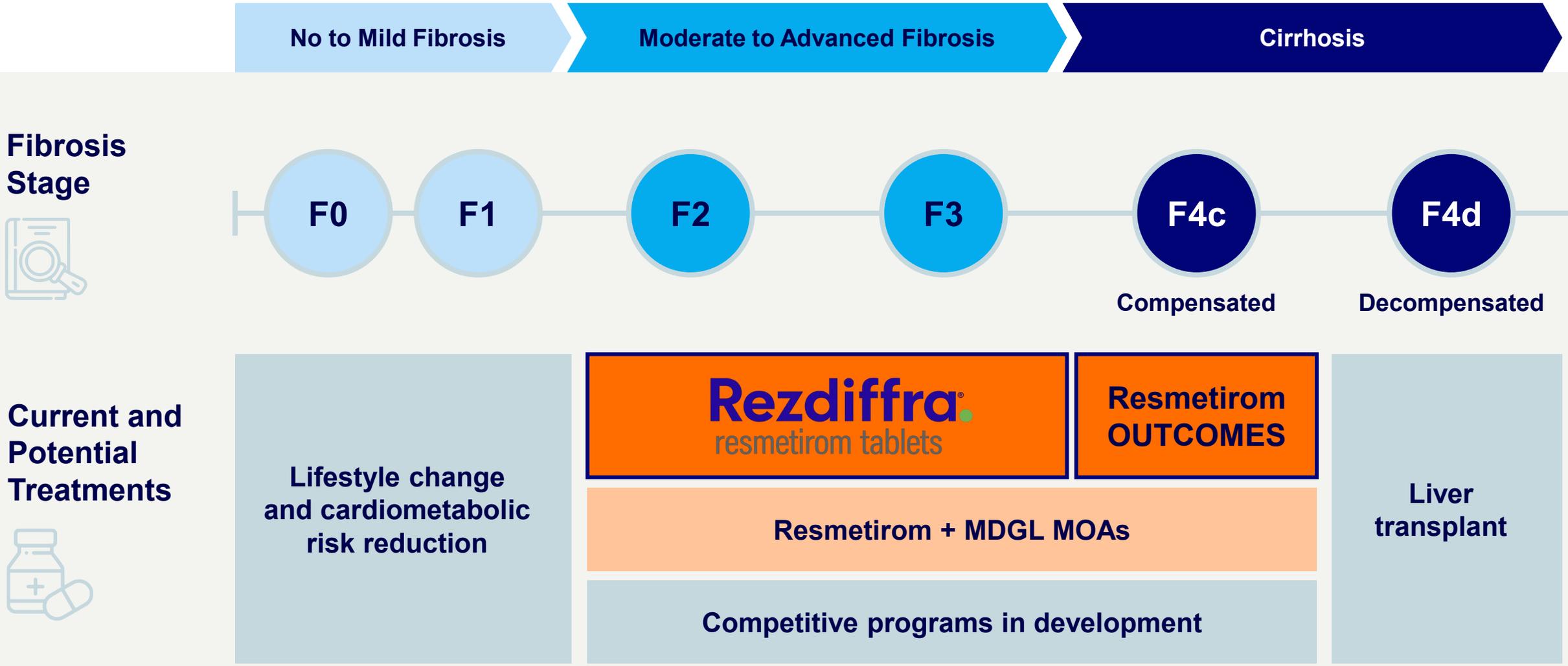
Ervogastat/resmetirom combo¹ Oral DGAT-2 inhibitor MASH [Progress bar: Preclinical to Phase 1]

MGL-2086/resmetirom combo² Oral GLP-1 receptor agonist MASH [Progress bar: Preclinical to Phase 1]

Additional MASH Assets
in varying stages of development Exploratory oral assets (2) MASH

1. Ervogastat monotherapy Phase 2b study completed by Pfizer; drug-drug (resmetirom/ervogastat) interaction (DDI) study expected to initiate in 2026; Phase 2 combination study expected to initiate in 2027 following regulatory discussions; 2. MGL-2086 Phase 1 single ascending dose (SAD) study expected to initiate in 2Q26; **MOA**: mechanism of action.

With Rezdiffra as the Foundational Therapy, Madrigal is Shaping the Future of MASH in F2 to F4c



Madrigal is Well-Positioned for Continued Value Creation in 2026 and Beyond

Rezdiffra F2/F3 Launch

**Annualizing
at >\$1B**

In just the 6th quarter of launch

Indication Expansion

**F4c
Outcomes**

Data anticipated in 2027 could
double the opportunity¹

Building Our Pipeline

1

New Phase 2 trial²

2

Ongoing Phase 3 trials³

3

Clinical-stage assets

Leading the Fight Against MASH

1. Pending successful completion of MAESTRO-NASH OUTCOMES trial and FDA approval; 2. Phase 2 combination (resmetirom/ervogastat) study expected to initiate in 2027 following regulatory discussions;
3. MAESTRO-NASH F2/F3; MAESTRO-NASH OUTCOMES F4c.

Leading the Fight Against MASH

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