Madrigal

2Q25 Financial Results

Aug. 5, 2025

NASDAQ: MDGL

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; the expected benefit of Madrigal’s newly issued patent; the expected use of proceeds from Madrigal’s credit facility; Madrigal’s clinical development plans and timelines; Madrigal’s leadership position in the MASH sector; projections or objectives for obtaining approval from EMA for Rezdiffra and expected commercialization of Rezdiffra in Europe; 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 commercial launch of a new product, particularly for a company that did not have commercial experience prior to 2024; 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 Madrigal’s trials; any delays or failures in enrollment, and the occurrence of adverse safety events; risks related to the effects of Rezdiffra’s mechanism of action; 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 timing and outcomes of clinical trials of Rezdiffra; the uncertainties inherent in clinical testing; uncertainties concerning analyses or assessments outside of a controlled clinical trial; 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.

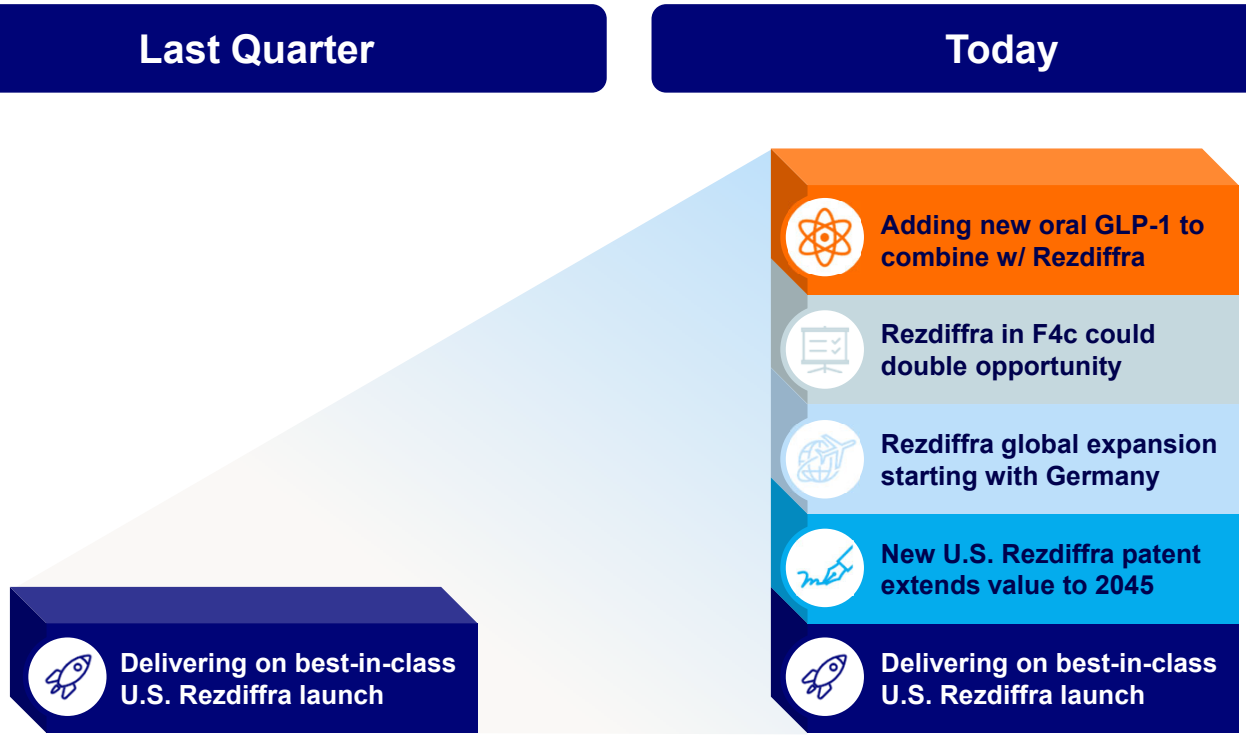
We've Made Significant Progress Toward Building Long-term Value and Global Leadership in MASH

1

Maximize the value of Rezdiffra

2

Expand pipeline to extend leadership



Non-dilutive financing of up to $500M accelerates our strategy to expand leadership in MASH

2Q25 Earnings Call Agenda

New U.S. Rezdiffra IP to 2045

Rezdiffra U.S. Launch

Oral GLP-1 License Agreement

Expansion to Europe

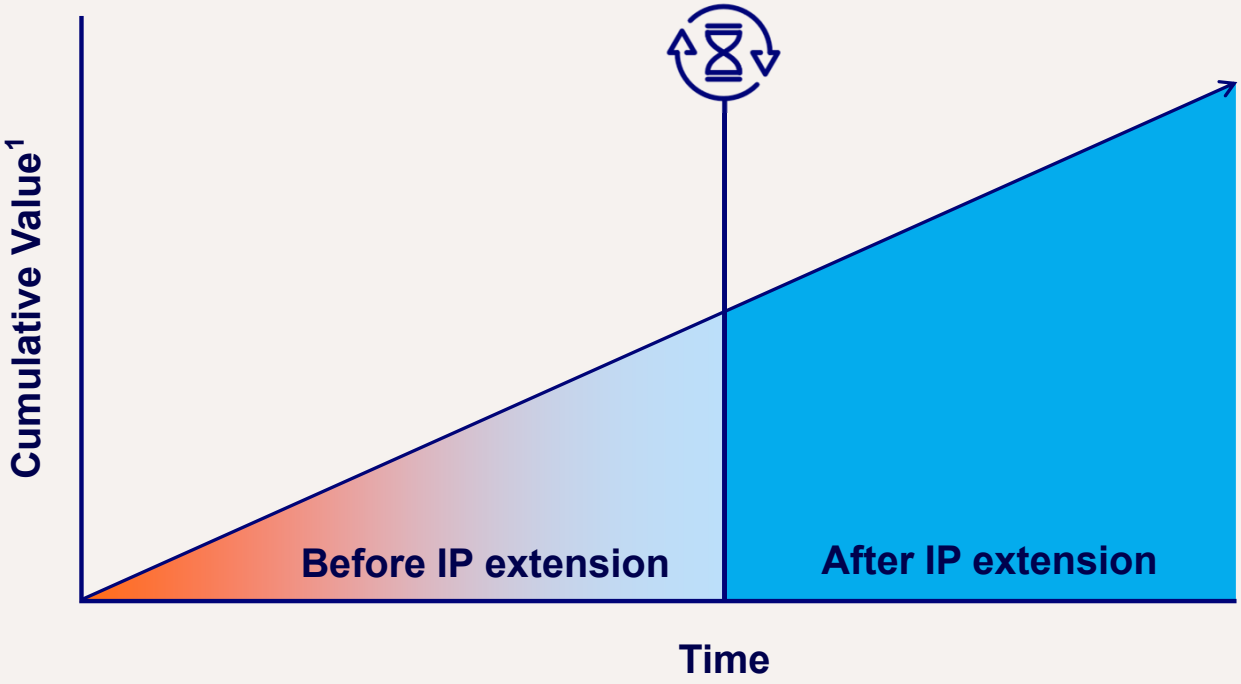
Progress in F4c Indication

Madrigal

New U.S. Rezdiffra Patent Extends Strategic Runway and Adds Significant Additional Revenue to 2045

New Rezdiffra Patent: Methods for Treating a Fatty Liver Disease (U.S. 12,377,104)

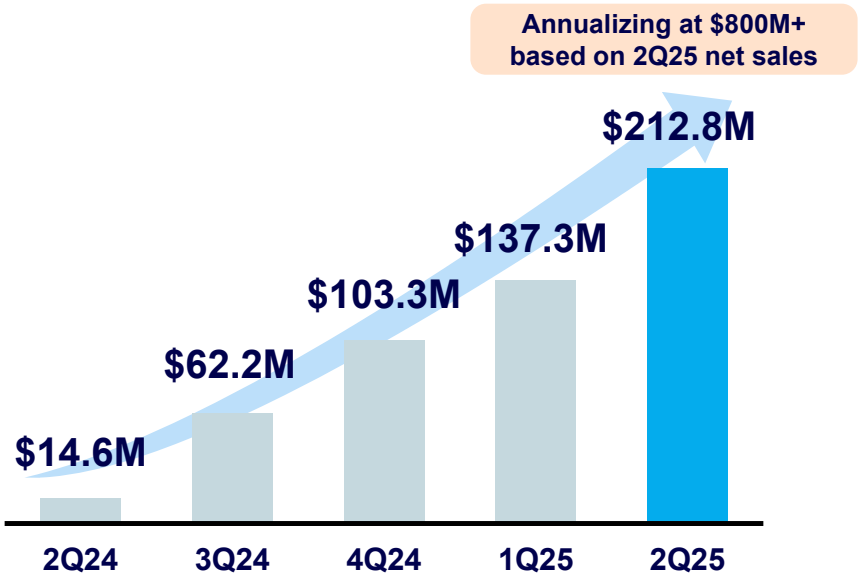
1. Weight-threshold dosing regimen patent with protection to Feb. 4, 2045
2. Clear and compelling finding that patented dosage regimen led to better patient outcomes; adopted by FDA and incorporated into label
3. Supported by precedent U.S. case law



1. Illustrative depiction.

Rezdiffra Launch: Impressive Quarter; Continued Strong Momentum

Net Sales: Continuing to Generate Strong Uptake



55%

QoQ growth from 1Q25 to 2Q25

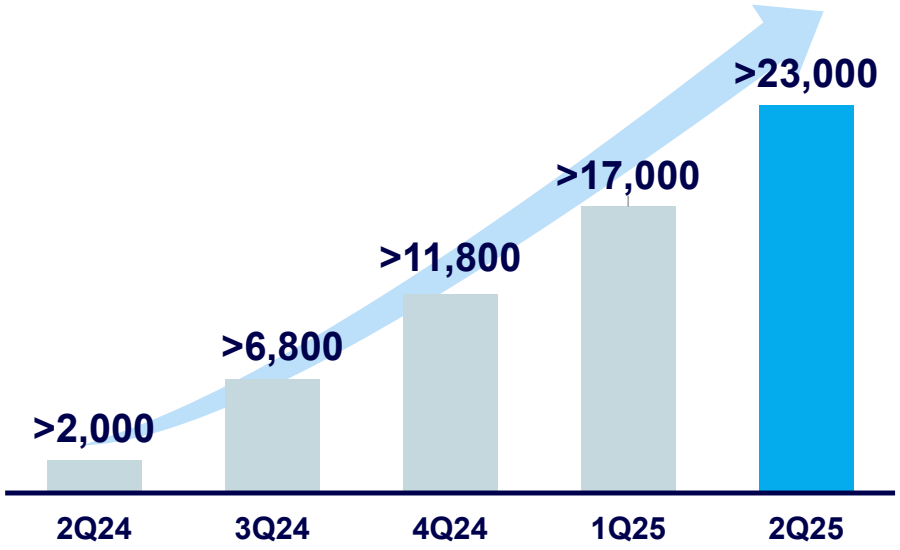
$212.8M

2Q25 net sales

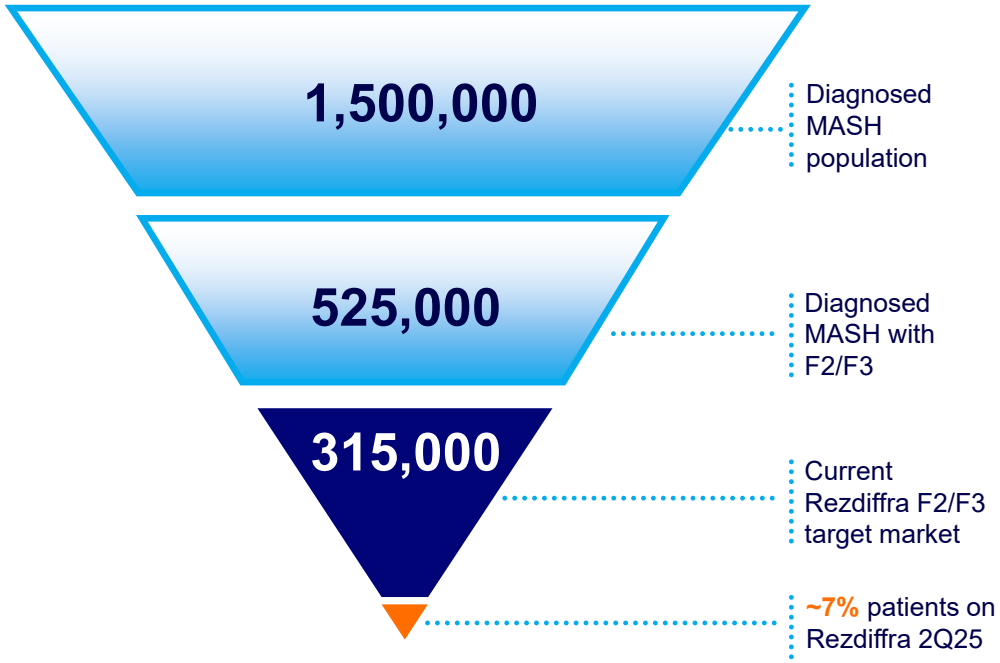
Rezdiffra Launch: Tracking in line with other best-in-class specialty blockbuster launches

Steadily Adding Patients in a Market Positioned for Significant Expansion

Patients on Rezdiffra:
Steadily Adding New Patients



Significant Opportunity in 315,000 Target Market[1]



1. Forian Claims Data; Clearview Analysis; Fishman J, et al. Poster presented at: ISPOR 2023; May 7-10, 2023; Boston, MA. Data on file: REF-00571.

Rapidly Built a Strong Prescriber Base, a Key Indicator of Long-term Success

Breadth: Penetration of Top Targets (%)

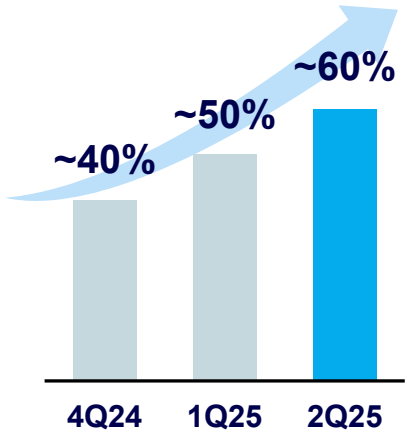
Top targets ~6,000

~80%

of ~6,000 top target prescribers have prescribed Rezdiffra as of 2Q25

Breadth: Penetration of Total Targets (%)

Total targets ~14,000



Prescriber Experience

My patients on Rezdiffra are doing even better than I anticipated they would; my real-world experience with the therapy has surpassed my expectations. I have about 40 patients on Rezdiffra for over a year who have been retested with NITs, and the vast majority of them have not only stabilized but are actually improving.

– Pierre Gholam, M.D.; Hepatologist

Prescriber depth in-line with top-tier specialty medicine launches

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	✓

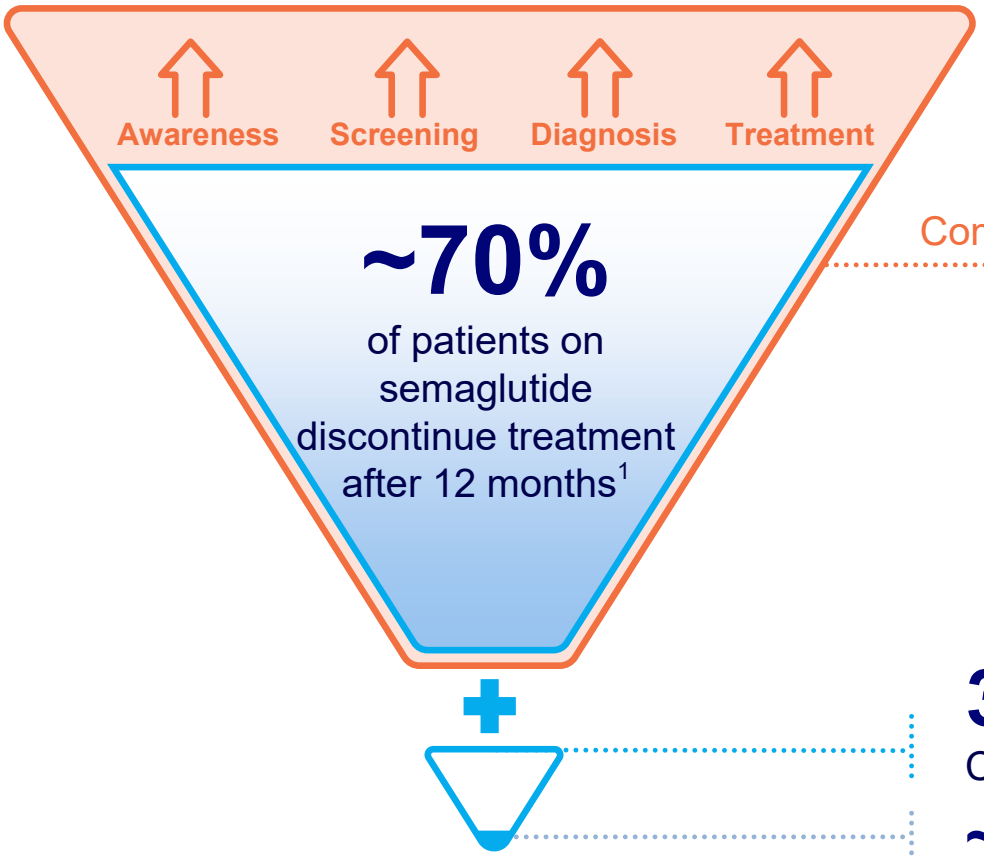
1. Harrison SA, et al. A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis. *N Engl J Med*. 2024;390(6):497-509.

Rezdiffra's Real-world Profile Is a Competitive Advantage

		Rezdiffra	Injectable GLP-1 (semaglutide)
Mechanism of Action	Liver-directed	✓	✗
MASH Efficacy	Consistent across patient subtypes (e.g., T2D)	✓	TBD
Tolerability	Well-tolerated	✓	✗
Adherence	High[1,2]	✓	✗
Route of Administration	Once-daily pill; no titration	✓	✗
Weight Loss	Meaningful weight reduction	✗	✓
Combination use	Used alone or in combination with complementary MOAs	✓	✓

1. Early indicators suggest Rezdiffra adherence is in line with other well-tolerated, oral medicines; 2. Novo Nordisk: Investor presentation, 1Q25, "Patient persistency on anti-obesity medications after 12 months," slide 63.

Competitive Entrants Focused on Market Expansion



Competitive entrant target market

315K

Current Rezdiffra F2/F3 target market

~7% patients on Rezdiffra 2Q25

> "The commercial potential we expect is around **22 million people from F2 to F4**… So, when we are thinking about how we commercially prepare for this market, it's all about awareness."
>
> - Novo Nordisk Capital Markets Day 7 March 2024[2]

1. Novo Nordisk: Investor presentation, 1Q25, "Patient persistency on anti-obesity medications after 12 months," slide 63 states that approximately 70 percent of patients on semaglutide discontinue after 12 months;
2. Novo Nordisk Capital Markets Day presentation 2024, "~22 million people are expected to live with MASH F2-F4c by 2030," slide 16.

Global License Agreement for an Oral GLP-1: Advancing Pipeline and Extending Leadership Position

Expands our pipeline

- Expands Madrigal's pipeline in an attractive market
- Supports strategy to develop innovative combination treatments for MASH, anchored by Rezdiffra

With the right asset

- SYH2086 is an orforglipron derivative
- Favorable stability/PK profile; amenable to combo
- Expected to enter clinic in 1H26

To develop a best-in-disease oral combo

- Uniquely positioned to combine Rezdiffra with SYH2086 to potentially achieve a best-in-disease MASH treatment in a once-a-day, well-tolerated pill
- Rezdiffra data suggests modest weight loss (≥5%) can increase its anti-fibrotic effect

Deal Terms

- Global rights to SYH2086
- Upfront payment of $120M with up to $2B in milestones and royalties

Positive CHMP Opinion Supports European Approval and Country-by-Country Launch Approach

Positive CHMP opinion received in June 2025 based on robust data from pivotal Phase 3 MAESTRO-NASH trial

European Commission decision expected in August; expect German launch in 2H25

Leveraging our U.S. blueprint; strong anticipation and early guideline inclusion

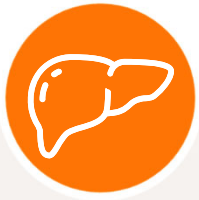
~370,000 F2/F3 MASH patients diagnosed and under the care of a liver specialist across Europe[1]

1. Not including UK.

Rezdiffra Has Strong Potential in F4c

Unmet Need in F4c

- No FDA-approved treatments
- F4c represents a significant unmet need



Liver-directed MoA

- Rezdiffra directly targets the liver to reduce fibrosis via THR-β agonism
- THR-β: Master regulator of liver metabolism

Open-label Data and Outcomes Trial

- Promising 2-year OLE data in F4c[1]
- MAESTRO-NASH OUTCOMES Phase 3 placebo-controlled trial in F4c

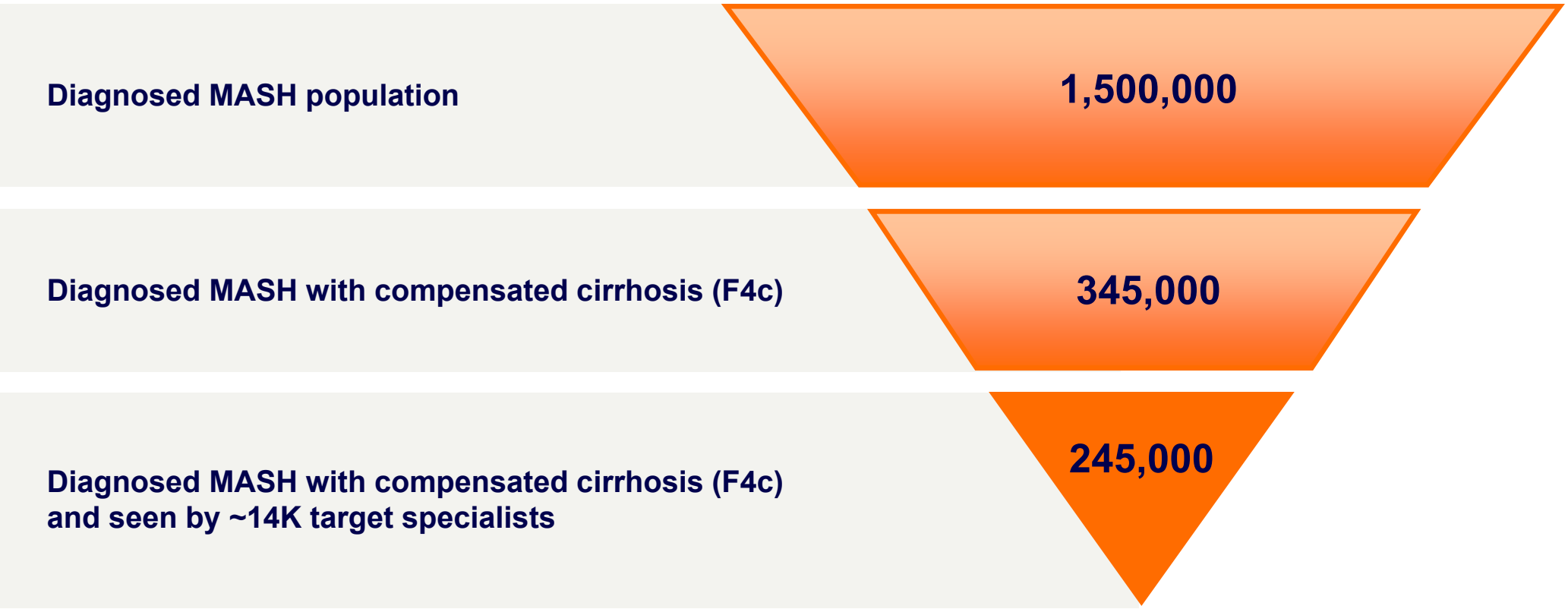
Real-world Use; First-mover Advantage

- Attractive profile
- Significant real-world use in F2/F3
- Potential first-mover advantage

1. OLE: Open-label extension.

F4c U.S. Opportunity: ~245K Diagnosed F4c Patients Under the Care of Liver Specialists

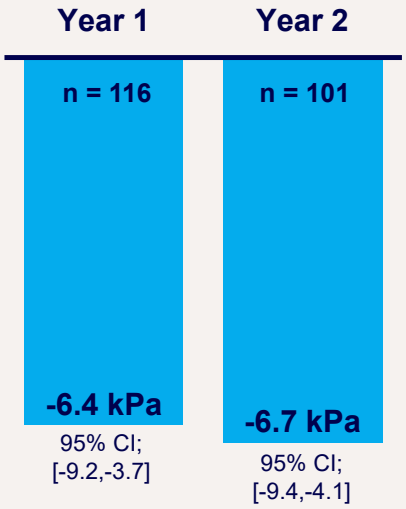
U.S. MASH Waterfall in F4c[1]



1. Forian Claims Data.

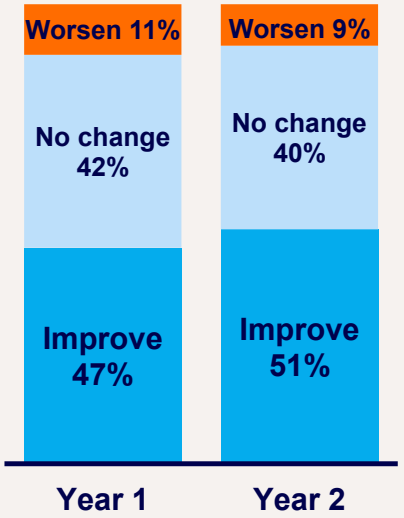
Data Supporting Potential Benefit of Rezdiffra in F4c for Liver Stiffness as Measured by VCTE

Mean Change from Baseline of 6.7 kPa

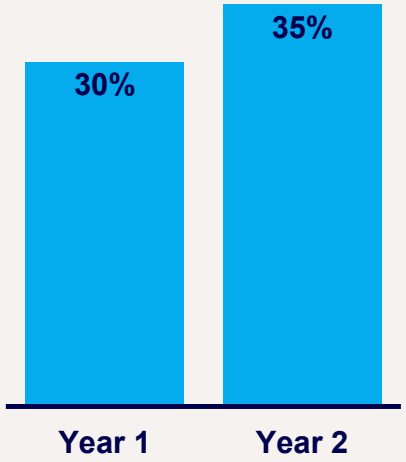


Statistically significant compared to baseline

>50% of Patients Achieved ≥25% Reduction in Liver Stiffness



35% of Patients Met Criteria for Regression from F4 to F3[1]

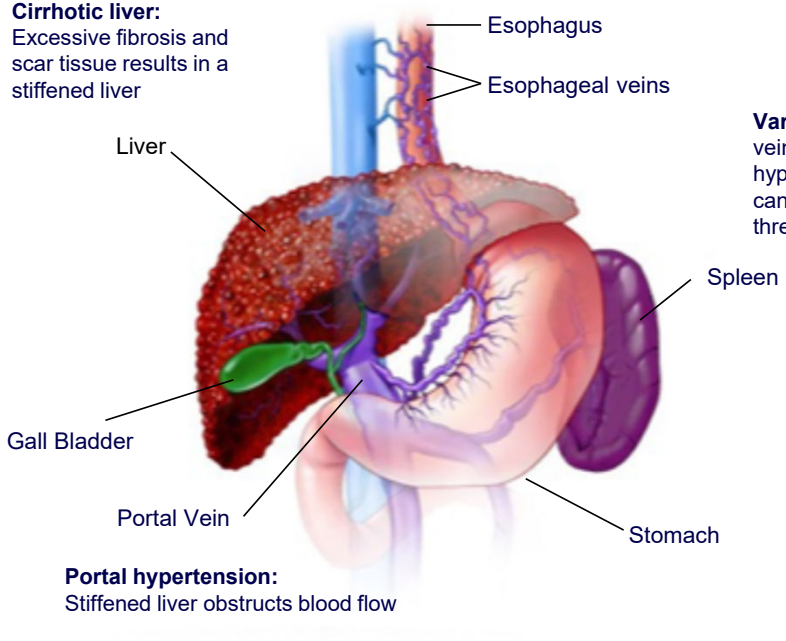


1. Patients with confirmed F4 at baseline (liver biopsy F4 and/or platelets <140 or MRE ≥5 with VCTE ≥15) showed a transition from F4 to potential F3 at year 2 (VCTE<15 and ≥25% decrease from baseline).

Data Supporting Potential Benefit of Rezdiffra in F4c for a Reduction in Clinically Significant Portal Hypertension (CSPH) Risk

CSPH is Responsible for the Most Severe and Fatal Complications of Cirrhosis[1]

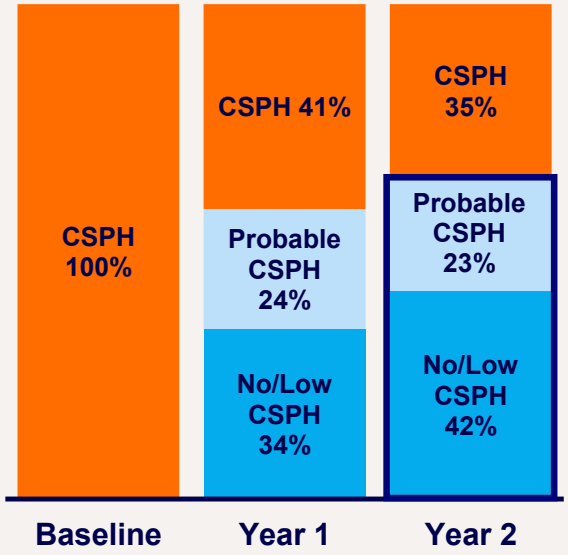
Cirrhotic liver:
Excessive fibrosis and scar tissue results in a stiffened liver



Varices: Enlarged veins due to portal hypertension; rupture can lead to life-threatening bleed

Portal hypertension:
Stiffened liver obstructs blood flow

65% of Patients with CSPH at Baseline Moved into Lower Risk Categories at Year 2



1. de Franchis R, et al. Baveno VII - Renewing consensus in portal hypertension. J Hepatol. 2022;76(4):959-974; image adapted from Mayo Clinic: Esophageal varices - Symptoms and causes - Mayo Clinic.

Consolidated Statement of Operations: 2Q25

Three Months Ended June 30 (in thousands)	2025	2024
Revenues:		
Product revenue, net	212,802	14,638
Operating expenses[1]:		
Cost of sales	9,065	636
Research and development	54,081	71,091
Selling, general and administrative	196,858	105,448
Total operating expenses	260,004	177,175
Loss from operations	(47,202)	(162,537)
Interest income	8,227	14,222
Interest expense	(3,264)	(3,656)
Other expense	(42)	--
Net loss	(42,281)	(151,971)
Basic and diluted net loss per common share	(1.90)	(7.10)
Basic and diluted weighted average number of common shares outstanding[2]	22,207,017	21,402,646

1. Operating expenses include $25.2 million and $24.4 million of non-cash stock-based compensation expense in 2Q25 and 2Q24, respectively;
2. Basic and diluted weighted average common shares outstanding not inclusive of: Preferred Stock (2,369,797) and Warrants (3,625,244).

Strong Balance Sheet

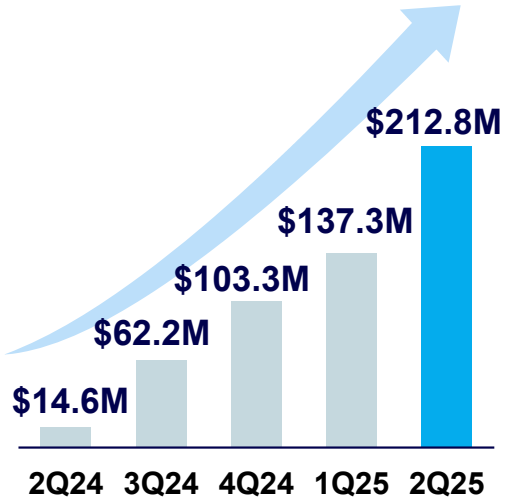
$802M in cash, cash equivalents, restricted cash and marketable securities as of June 30, 2025

Additionally secured up to **$500M** in non-dilutive senior secured credit to advance MASH pipeline as of July 17, 2025

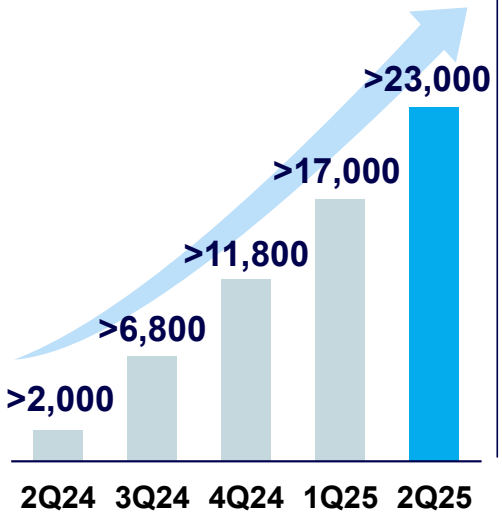
Strong 1H25; Rezdiffra Positioned for Continued Growth

Performance Since Launch

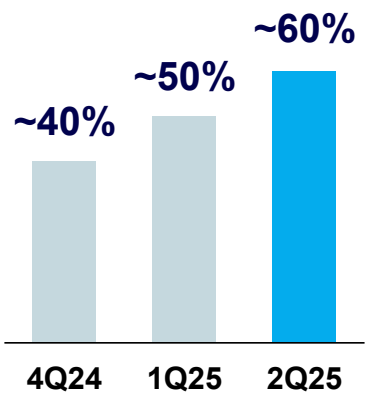
Net Sales



Active Patients on Therapy



Penetration of Total Prescribers



2025 and Beyond

- U.S. Patent Protection to 2045
- Expanding to EU[1]
- Expanding into F4c[1]
- Building a Pipeline

1. Subject to regulatory approval.

About Rezdiffra

What is Rezdiffra?

Rezdiffra is a prescribed medicine used along with diet and exercise to treat adults with nonalcoholic steatohepatitis (NASH) with moderate to advanced liver scarring (fibrosis), but not with cirrhosis of the liver.
It is not known if Rezdiffra is safe and effective in children (under 18 years old).
This indication is approved based on improvement of NASH and liver scarring (fibrosis). There are ongoing studies to confirm the clinical benefit of Rezdiffra.

Before you take Rezdiffra, tell your healthcare provider about all of your medical conditions, including if you:

- have any liver problems other than NASH.
- have gallbladder problems or have been told you have gallbladder problems, including gallstones.
- are pregnant or plan to become pregnant. It is not known if Rezdiffra will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Rezdiffra passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take Rezdiffra.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

- Rezdiffra and other medicines may affect each other, causing side effects. Rezdiffra may affect the way other medicines work, and other medicines may affect how Rezdiffra works.
- Especially tell your healthcare provider if you take medicines that contain gemfibrozil to help lower your triglycerides, or cyclosporine to suppress your immune system, because Rezdiffra is not recommended in patients taking these medicines.
- Tell your healthcare provider if you are taking medicines such as clopidogrel to thin your blood or statin medicines to help lower your cholesterol.
- Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

What are the possible side effects of Rezdiffra?

Rezdiffra may cause serious side effects, including:

- liver injury (hepatotoxicity). Stop taking Rezdiffra and call your healthcare provider right away if you develop the following signs or symptoms of hepatotoxicity: tiredness, nausea, vomiting, fever, rash, your skin or the white part of your eyes turns yellow (jaundice), pain or tenderness in the upper middle or upper right area of your stomach (abdomen).
- gallbladder problems. Gallbladder problems such as gallstones, inflammation of the gallbladder, or inflammation of the pancreas from gallstones can occur with NASH and may occur if you take Rezdiffra. Call your healthcare provider right away if you develop any signs or symptoms of these conditions including nausea, vomiting, fever, or pain in your stomach area (abdomen) that is severe and will not go away. The pain may be felt going from your abdomen to your back and the pain may happen with or without vomiting.

The most common side effects of Rezdiffra include: diarrhea, nausea, itching, stomach (abdominal) pain, vomiting, dizziness, constipation.
These are not all the possible side effects of Rezdiffra. For more information, ask your healthcare provider or pharmacist.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
You may also report side effects to Madrigal at 1-800-905-0324.

Please see the full Prescribing Information, including Patient Information, for Rezdiffra.

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2Q25 Financial Results

Aug. 5, 2025

NASDAQ: MDGL