
Madrigal
Fourth-Quarter and Full-Year 2024 Financial Results
Feb. 26, 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: Rezdiffra (resmetirom) and its expected use for treating MASH with moderate to advanced fibrosis; potential future growth of Rezdiffra sales; projections or objectives for obtaining approval from EMA for Rezdiffra (resmetirom) and expected commercialization of Rezdiffra (resmetirom) in Europe; the potential impact of positive results from the MAESTRO-NASH OUTCOMES trial; the competitive landscape and market dynamics; estimates of patients diagnosed with MASH and market opportunities; potential business development transactions; 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 of 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 does not have commercial experience; 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 (resmetirom’s) mechanism of action; enrollment and trial conclusion uncertainties; 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 (resmetirom); 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 the sections appearing in Part I, Item 1A of its Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on February 28, 2024, and Part II, Item 1A of its Quarterly Report on Form 10-Q for the quarter ended September 30, 2024, filed with the SEC on October 31, 2024, and as updated from time to time by Madrigal’s other filings with the SEC.

4Q24 Earnings Call Agenda

2024 Highlights and Accomplishments

Rezdiffra Launch Update

Geographic, Indication and Pipeline Expansion

New

2-year F4c data announced today[1]

1. Two-year data from the active-treatment open-label compensated MASH cirrhosis (F4c) arm of the Phase 3 MAESTRO-NAFLD-1 study; data are expected to be presented in their entirety at a future medical meeting.

2024 was an Incredible Year for Madrigal

Rezdiffra™
(resmetirom) tablets
60mg · 80mg · 100mg

Rezdiffra launch:

Establishing a foundational therapy

Maximizing value:

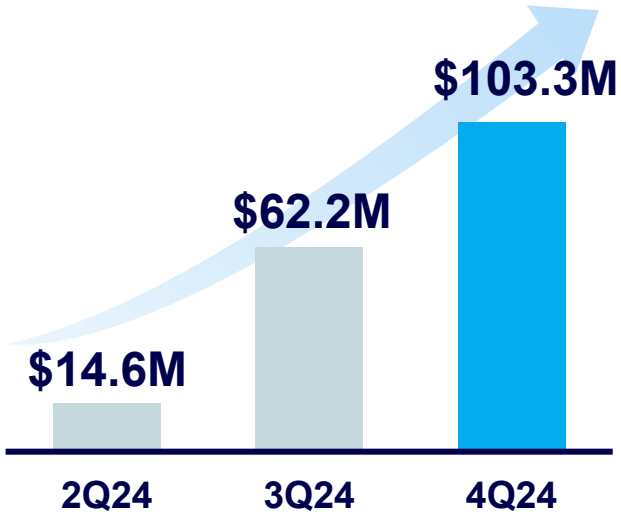
Expanding via geography, indication and pipeline

- Built expert leadership and commercial teams
- Phase 3 data in *New England Journal of Medicine*
- **Landmark FDA approval of Rezdiffra on March 14, 2024**
- Guidelines updated to include Rezdiffra as first-line therapy
- Expanding to Europe in 2025, pending EMA approval
- MAESTRO-NASH OUTCOMES trial in F4c MASH fully enrolled

We are Building Toward a Blockbuster Medicine

Net Sales: Generating Strong Uptake Early in the Launch

FY24 Net Sales: $180.1M



66%

QoQ growth from 3Q24 to 4Q24

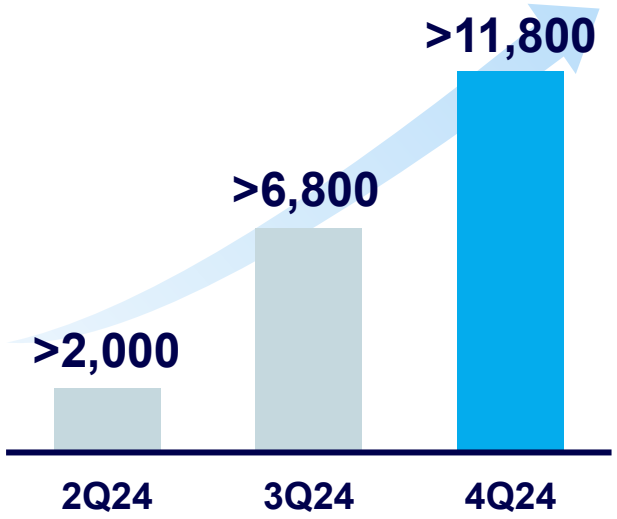
$180.1M

FY24 net sales in just 9 months

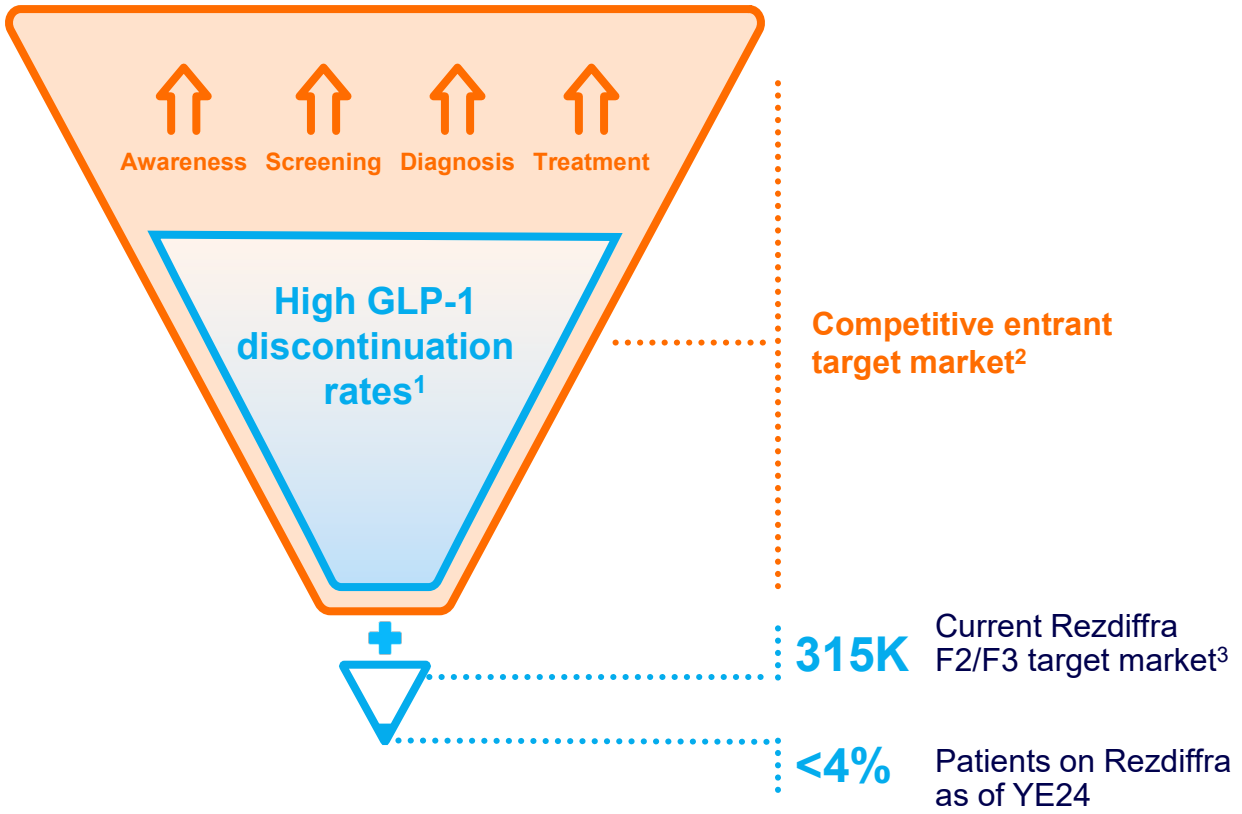
Rezdiffra launch is tracking in line with other best-in-class specialty blockbuster launches

Steadily Adding Patients in a Market Positioned for Significant Expansion

Patients on Rezdiffra: Steadily Adding New Patients



Rezdiffra Potential: 315K Patients Today with Potential for Significant Expansion with Competition



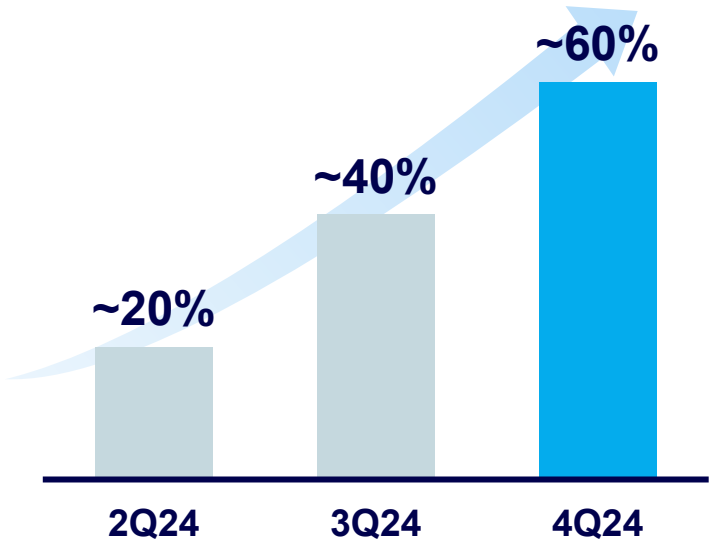
1. Novo Nordisk: Investor presentation, 1H24, "Patient persistency on anti-obesity medications after 12 months," slide 60 states that approximately 70 percent of patients on semaglutide discontinue after 12 months; 2. Novo Nordisk Capital Markets Day presentation 2024, "~22 million people are expected to live with MASH F2-F4c by 2030," slide 16; 3. An estimated 315,000 patients in the U.S. are diagnosed with moderate to advanced fibrosis (F2/F3) and seen by ~14K target specialists.

Increased Breadth of Rezdiffra Prescribers Sets a Strong Foundation to Build a Blockbuster Medicine

Penetration of Top Targets (%)

Top targets = ~6,000

~60% top target penetration in only 9 months



Productivity of Top Targets

>75%

of prescriptions written by top targets

Penetration of Total Targets (%)

Total targets = ~14,000

~40%

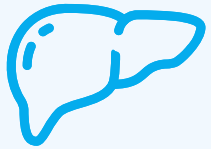
of 14,000 total target prescribers as of 4Q24

Steadily increasing penetration of Rezdiffra prescribers is a leading indicator for continued strong growth

Rezdiffra: Foundational Therapy in MASH with Exceptional Profile

> Living with MASH felt like having a time bomb in my body. Rezdiffra gave me hope — and my life back.
>
> – Jennifer, patient with F2 MASH on Rezdiffra

> For decades, MASH had no viable treatment. Rezdiffra changed that. Our practice is now implementing screening and treatment protocols to better manage MASH— a major step forward for patient care.
>
> – Reed B. Hogan, M.D.; GI physician treating MASH



Liver-directed MOA

THR-β agonist targets underlying causes of MASH

Highly effective

Halts/improves liver stiffness in 91% of patients at 3 years[1]

Once daily oral pill

Differentiated ease of administration

Well tolerated

Positive real-world impact

1. Assessment of Resmetirom Efficacy (80 mg vs. 100 mg) Stratified by Baseline Body Mass Index and Weight in Patients from the MAESTRO-NASH trial presented at the EASL Congress Milan, Italy June 5-8, 2024.

Expanding Madrigal's MASH Leadership Position and Total Addressable Market Opportunity

Geographic Expansion

- Expecting mid-2025 CHMP opinion[1]
- EU launch on schedule for 2H25, pending EMA approval[2]

Indication Expansion

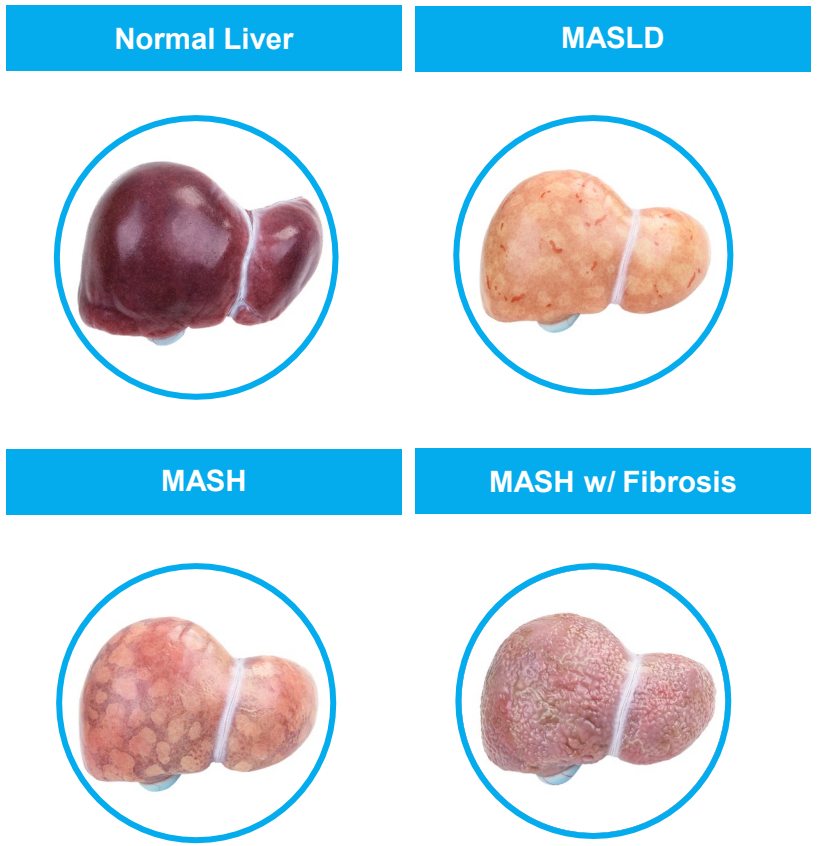
- Completed enrollment in MAESTRO-NASH OUTCOMES trial
- Rezdiffra has potential to be first medicine approved for F4c MASH

Pipeline

- Committed to leadership position in MASH
- Strategically assessing BD opportunities

1. CHMP: Committee for Medicinal Products for Human Use; 2. EMA: European Medicines Agency

Unmet Need in Compensated MASH Cirrhosis (F4c)



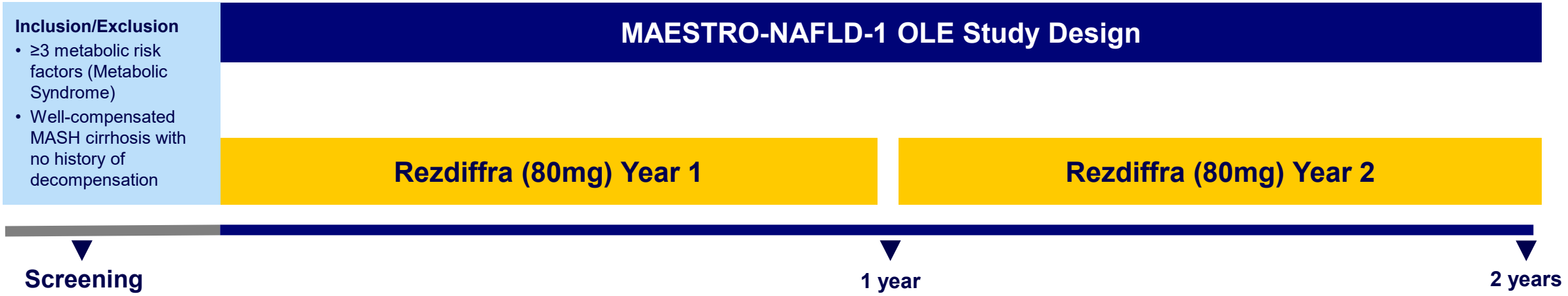
Cirrhosis (F4)

Cirrhosis is a chronic, progressive liver disease characterized by fibrosis and loss of liver function. It can lead to liver failure and portal hypertension which can result in complications like ascites, variceal bleeding and hepatic encephalopathy. Cirrhosis can also lead to liver transplant, liver cancer and death.

There is a **higher urgency to treat patients with cirrhosis** because of 42x higher risk of liver-related mortality.

Ascites: abnormal accumulation of fluid in the abdominal cavity; **Hepatic encephalopathy:** brain disorder caused by liver dysfunction; **MASH:** Metabolic Dysfunction Associated Steatohepatitis**; MASLD:** Metabolic Dysfunction-associated Steatotic Liver Disease; **Variceal bleeding:** bleeding from enlarged veins, usually in the esophagus or stomach; **Portal hypertension:** increased pressure in the portal vein, which carries blood from the intestines, stomach, pancreas, and spleen to the liver.

MAESTRO-NAFLD-1 Open-Label Extension (OLE) F4c Study Design



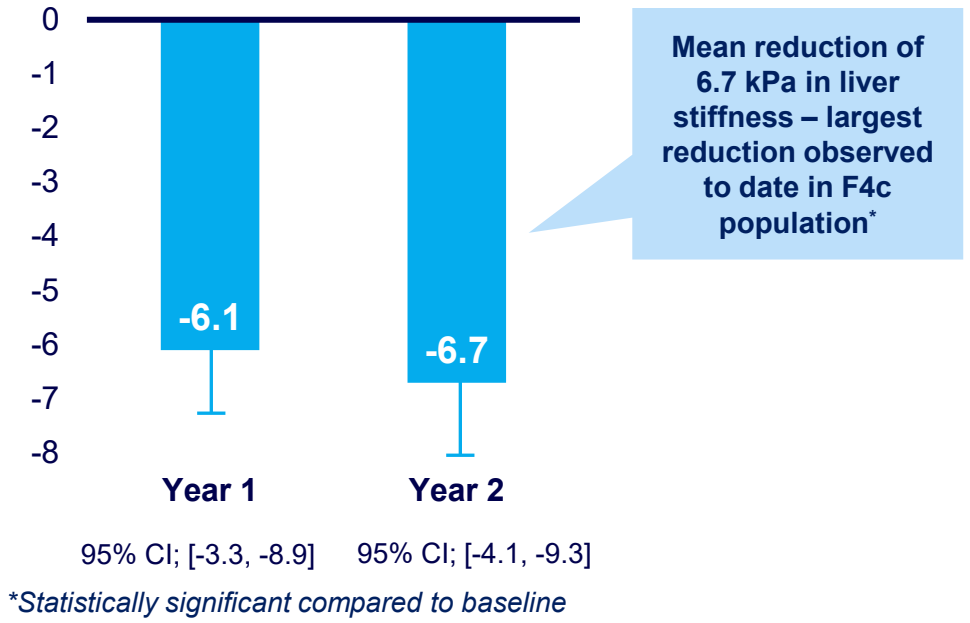
Study Overview

- MAESTRO-NAFLD-1: Double-blind placebo-controlled, randomized Phase 3 trial that evaluated the safety and tolerability of Rezdiffra to support regulatory approval
- MAESTRO-NAFLD-OLE (F4c): Active-treatment arm of the open-label extension of MAESTRO-NAFLD-1 that specifically followed F4c patients
- 1-year data were previously presented and demonstrated Rezdiffra improved key markers of fibrosis, reduced liver and spleen volume, and lowered lipid levels
- After 1 year, the study offered extended open-label dosing with Rezdiffra for continued treatment
- New 2-year results presented today include VCTE data from 101 patients with F4c

1. VCTE: vibration-controlled transient elastography

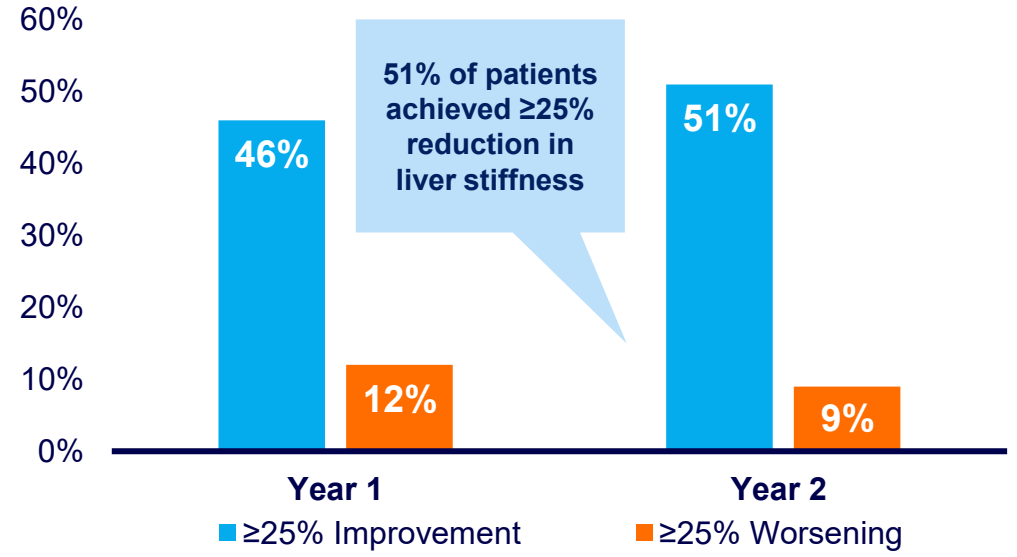
New Two-Year Data from MAESTRO-NAFLD-1 OLE (n = 101) Demonstrate Potential Benefit of Rezdiffra in F4c Patients[1]

Mean Change in VCTE (kPa); Mean Baseline: 25 kPa[2]



Statistically significant compared to baseline

% of Patients Achieving ≥25% Reduction in Liver Stiffness[3]

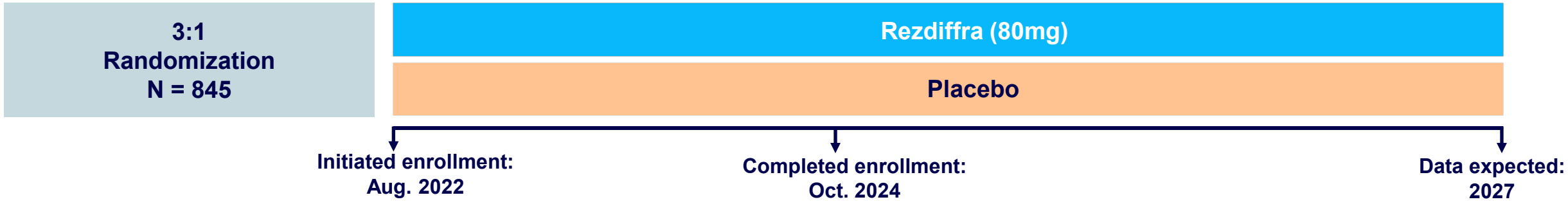


> These data demonstrating Rezdiffra helped patients with compensated MASH cirrhosis achieve marked reductions in VCTE are highly encouraging…The results are particularly meaningful in light of recently published, multi-center, longitudinal studies demonstrating VCTE is a strong predictor of clinical outcomes and may be more predictive of clinical outcomes than fibrosis stage assessed by liver biopsy.
>
> – Mazen Noureddin, M.D., MHSc; Professor of Medicine, Director Houston Research Institute [4,5]

1. Two-year data from the active-treatment open-label compensated MASH cirrhosis arm of the Phase 3 MAESTRO-NAFLD-1 study; data are expected to be presented in their entirety at a future medical meeting; 2. VCTE: vibration-controlled transient elastography; 3. As measured by VCTE; 4. Lin H, Lee HW, Yip TC, et al. Vibration-Controlled Transient Elastography Scores to Predict Liver-Related Events in Steatotic Liver Disease. *JAMA*. 2024;331(15):1287–1297; 5. Gawrieh, S, et al. Increases and Decreases in Liver Stiffness Measurement are Independently Associated with the Risk of Liver-Related Events in NAFLD. *Journal of Hepatology*. 2024;81(4):600–608.

Positive Results from MAESTRO-NASH OUTCOMES in F4c Patients Could Expand Rezdiffra Patient Population

MAESTRO-NASH OUTCOMES Trial Design



Summary

- Event-driven trial evaluating progression to liver decompensation
- Designed to expand the eligible patient population to include patients with compensated MASH cirrhosis (F4c) and support full approval
- 845 patients enrolled

Primary Outcome Measure[1]

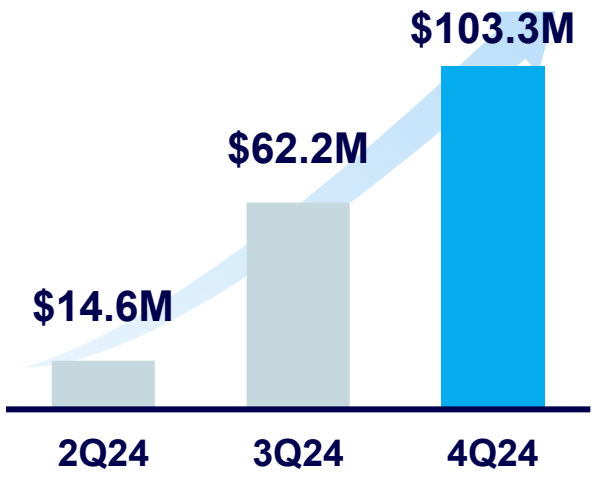
- Time to adjudicated Composite Clinical Outcomes: Mortality, liver transplant, ascites, hepatic encephalopathy, gastroesophageal variceal hemorrhage, and confirmed increase of MELD score from <12 to ≥15 due to liver disease[2]

1. Nonalcoholic Steatohepatitis with Compensated Cirrhosis: Developing Drugs for Treatment Guidance for Industry, U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER), June 2019: *The FDA strongly recommends clinical outcome trials to support a marketing application. Histological improvements in fibrosis can be proposed and justified; however, at present the relationship between histological changes in cirrhosis and clinical outcomes has not been characterized, and further, reversal of cirrhosis (e.g., fibrosis stage F4) may not be feasible. Because currently there is insufficient evidence to support the use of histological improvements as a surrogate endpoint that is reasonably likely to predict clinical benefit to support accelerated approval, in general, the FDA expects to evaluate drugs for the treatment of compensated MASH cirrhosis under the traditional approval pathway;* 2. **Ascites**: abnormal accumulation of fluid in the abdominal cavity; **Gastroesophageal variceal hemorrhage**: bleeding from enlarged veins in the stomach; **Hepatic encephalopathy**: brain disorder caused by liver dysfunction; **MELD:** Model for End-stage Liver Disease.

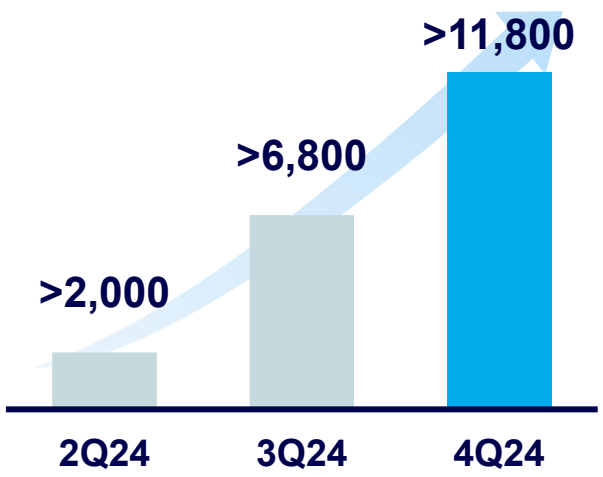
In Summary: Outstanding 2024 Builds a Strong Foundation for 2025 and Beyond

2024 Performance

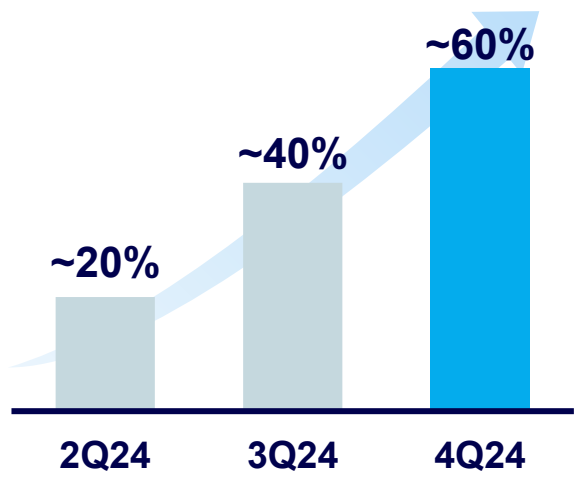
Net Sales



Active Patients on Therapy



Penetration of Top Prescribers



2025 and Beyond

- Expanding to EU[1]
- F4c MAESTRO-NASH OUTCOMES
- Building a Pipeline

1. Subject to regulatory approval

Financial Highlights: 4Q24

Three Months Ended December 31 (in millions)	2024	2023
Revenues:		
Total revenues	$103.3	$ -
Operating Expenses:		
Cost of sales	$3.4	$ -
Research and development	$25.6	$70.6
SG&A	$141.2	$46.5
Total operating expenses	$170.3	$117.2
Loss from operations	($67.0)	($117.2)
Interest income, net	$11.1	$9.0
Interest expenses	($3.5)	($4.0)
Net loss	($59.4)	($112.2)

Cash, Cash Equivalents, Restricted Cash and Marketable Securities of $931.3M as of 12/31/24

Rezdiffra FY24 net sales:
$180.1M

Higher level of SG&A expense related to Rezdiffra launch

Strong balance sheet fully resourced for Rezdiffra launch

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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