Madrigal Pharmaceuticals

Corporate Presentation

January 2024

Resmetirom is an investigational therapy and has not been approved by the FDA (or any other regulatory authority). Resmetirom is only available for use in a clinical trial setting (ClinicalTrials.gov NCT03900429, NCT04197479, NCT05500222).

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, including the examples in the paragraph below; resmetirom's potential to be the first specialty therapy for NASH patients with significant liver fibrosis; projections or objectives for obtaining accelerated or full approval for resmetirom, including all statements concerning potential clinical benefit to support accelerated approval and/or potential approval; and statements or references concerning - the relationship between NASH progression and adverse patient outcomes; the estimated clinical burden of uncontrolled NASH; analyses for patients with NASH with significant fibrosis concerning potential progression to cirrhosis, decompensated cirrhosis, liver transplant or death, and cardiovascular risks, comorbidities and outcomes; health economics assessments or projections, the potential efficacy and safety of resmetirom for noncirrhotic NASH patients and cirrhotic NASH patients, possible or assumed future results of operations and expenses, business strategies and plans (including ex-US. Launch/partnering plans), research and development activities, and the timing and results associated with the future development of resmetirom, the timing and completion of projected future clinical milestone events, including enrollment, additional studies, top-line data and open label projections, plans, Madrigal's primary and key secondary study endpoints for resmetirom and the potential for achieving such endpoints and projections, demonstrating clinical benefit to support accelerated approval, the potential to support an additional indication for resmetirom in patients with well-compensated NASH cirrhosis, optimal dosing levels for resmetirom and projections regarding potential NASH or NAFLD patient populations, our launch focus on patients, pricing for resmetirom, and potential patient benefits with resmetirom, including future NASH resolution, safety, fibrosis treatment, cardiovascular effects, lipid treatment, and/or biomarker effects with resmetirom 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," inform," "intended," "intends," "may," "might," "on track," "planned," "planning," "plans," "positions," "potential," "powers," "predicts," "predictive," "projects," "seeks," "should," "will," "will achieve," "will be," "would" 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; risks associated with meeting the objectives of Madrigal's clinical studies, 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 studies; any delays or failures in enrollment, and the occurrence of adverse safety events; risks related to the effects of resmetirom's mechanism of action; the achievement of enrollment objectives concerning patient number, safety database and/or timing for Madrigal's studies; enrollment and trial conclusion uncertainties; market demand for and acceptance of our products; the potential inability to raise sufficient capital to fund ongoing operations as currently planned or to obtain financings on terms similar to those arranged in the past; the ability to service indebtedness and otherwise comply with debt covenants; outcomes or trends from competitive studies; future topline data timing or results; our ability to prevent and/or mitigate cyber-attacks, unauthorized exfiltration of data or other security incidents; the risks of achieving potential benefits in studies that includes substantially more patients, and patients with different disease states, than prior studies; the timing and outcomes of clinical studies of resmetirom; the uncertainties inherent in clinical testing; the uncertainties inherent in clinical testing; and uncertainties concerning analyses or assessments outside of a controlled clinical trial. 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, or 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, 2022, filed with the SEC on February 23, 2023, as amended by our Form 10-K/A filed with the SEC on March 3, 2023, and Part II, Item 1A of its Quarterly Reports on Form 10-Q for the quarters ended June 30, 2023 and September 30, 2023, and as updated from time to time by Madrigal's other filings with the SEC.

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The Madrigal Opportunity

Building the Leading Biopharmaceutical Company in NASH

NASH is a disease with significant unmet need, and no approved therapies

Resmetirom is a **liver-directed** oral THR-β agonist therapy targeting the underlying causes of NASH

Unprecedented Phase 3 results - first therapy to achieve NASH resolution and fibrosis improvement primary endpoints

First-to-market opportunity in NASH with significant fibrosis (consistent with F2/F3)

Specialty launch focused on patients who are most in need of therapy

Experienced **leadership** team

NASH, nonalcoholic steatohepatitis; THR-β, thyroid hormone receptor-β

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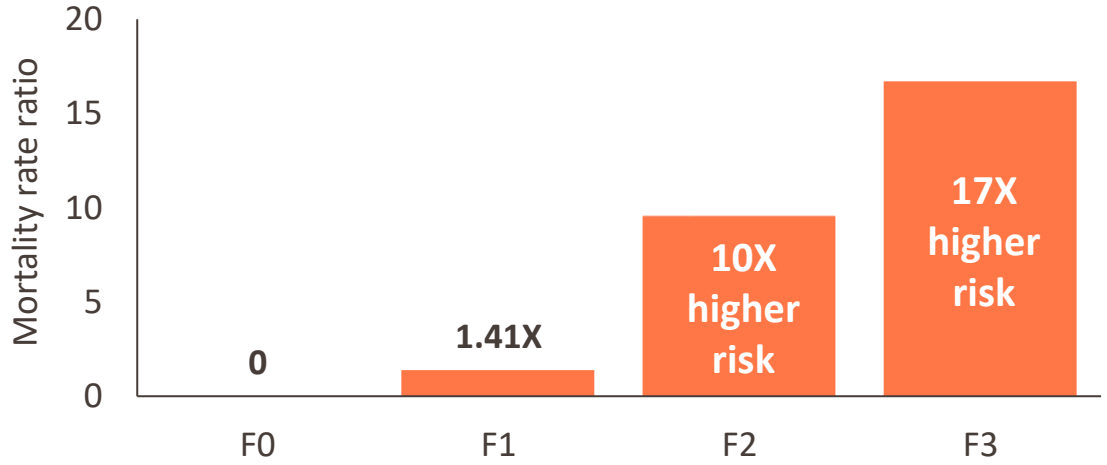
Taking on a Serious Liver Disease

NASH with Significant Fibrosis Carries a High Burden for Patients

NASH increases risk of cirrhosis, liver failure, liver cancer, and premature mortality

- Risk of liver-related mortality increases substantially once significant fibrosis develops[1,2]
- Incidence of associated HCC expected to double between 2015 and 2030[3]
- Leading cause of liver transplants in the U.S. for women, soon to be overall[4]

Patients with NASH with Significant Fibrosis have ~10-17x Higher Risk of Liver-Related Mortality vs. Patients with No Fibrosis[1]



Goal: Treat NASH with significant fibrosis prior to negative patient outcomes

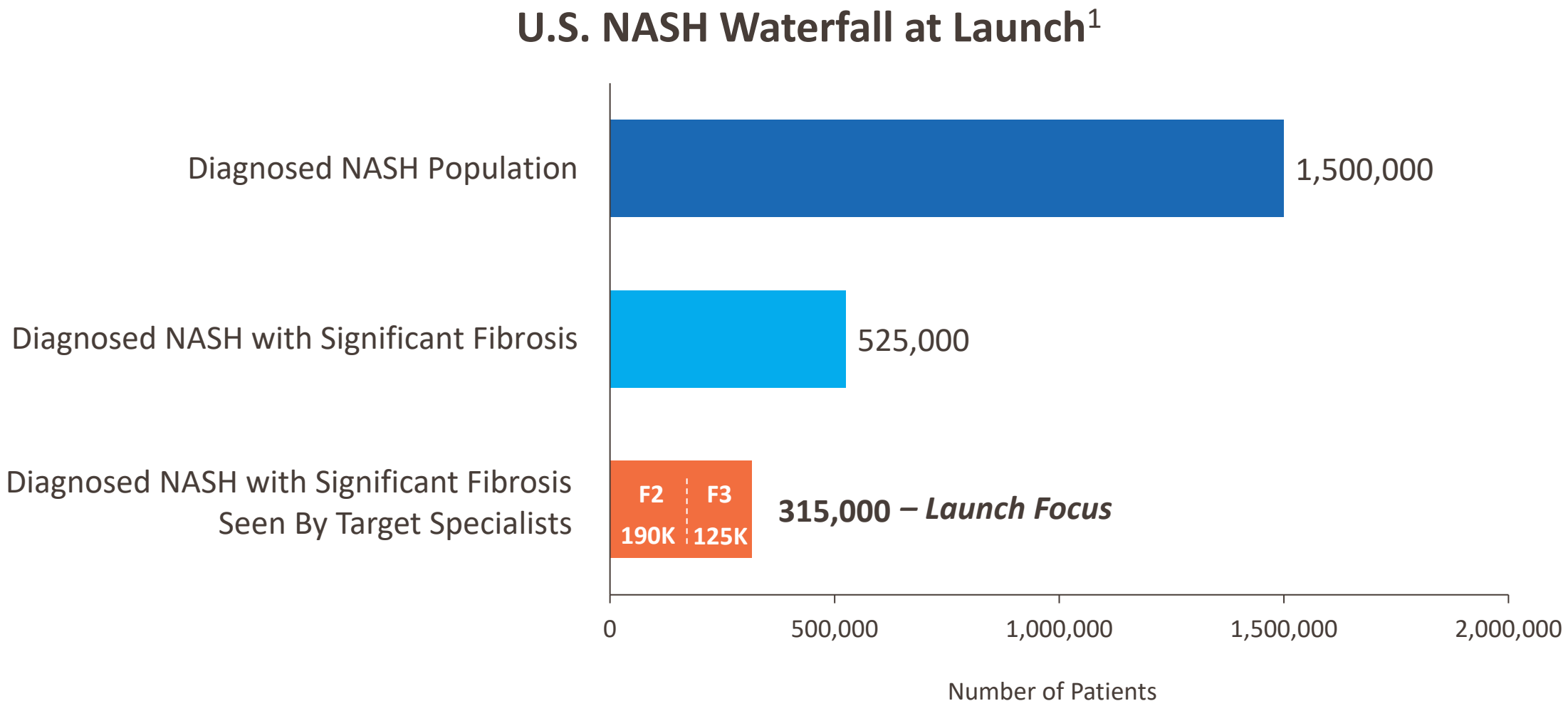
~22% of patients with stage 3 fibrosis progress to cirrhosis within 2 years[5]

HCC, hepatocellular carcinoma

1. Angulo P, et al. *Gastroenterology*. 2015;149:389-397. 2. Dulai PS, et al. *Hepatology*. 2017;65:1557-1565. 3. Estes C, et al. *Hepatology*. 2018 Jan;67(1):123-133. 4. Noureddin M, et al. *Am J Gastroenterol*. 2018 Nov;113(11):1649-1659. 5. Loomba R, Adams L. *Hepatology*. 2019;70(6):1885-1888.

Focusing on Patients Who are Most in Need

Specialty Launch Will Focus on Patients With Significant Fibrosis (Consistent with F2/F3) Seen by Heps/GIs



Heps, hepatologists; GIs, gastroenterologists

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

A Liver-directed Oral Therapy

Resmetirom to Become the FIRST Foundational Therapy for NASH with Significant Fibrosis

Differentiated Mode of Action

THR-ß selective agonist that normalizes the liver's critical role in fat metabolism

MOA differentiated vs. injectable therapies that treat NASH indirectly

Compelling Product Profile

Liver-directed oral therapy

Efficacy in resolving NASH and **improving fibrosis**

Favorable emerging **safety and tolerability** profile

Robust Evidence to Support Value

Health economics outcomes research supports resmetirom value

ICER cost-effectiveness range of **$39,600 – $50,100** per year[1]

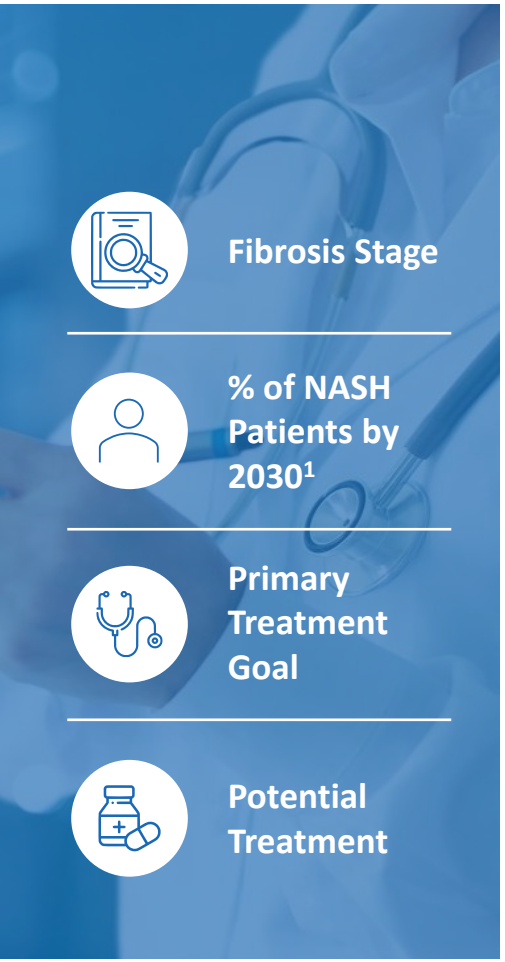
Resmetirom is an investigational therapy and has not been approved by the FDA (or any other regulatory authority)

MOA, mechanism of action

1. Institute for Clinical and Economic Review (ICER). Final Evidence Report and Meeting Summary. Last accessed December 4, 2023.

Resmetirom Position in the NASH Treatment Paradigm

Significant Opportunity for Resmetirom Where Unmet Need is Highest



	No or Mild Fibrosis		Significant Fibrosis		Cirrhosis	
Fibrosis Stage	F0	F1	F2	F3	F4C Compensated	F4D Decompensated
% of NASH Patients by 2030[1]	~10-15%	~30-35%	~20-25%	~15-20%	~10-15%	<5%
Primary Treatment Goal	Manage Cardiometabolic Risk		Halt or Improve Fibrosis; Resolve NASH		Prevent Liver Failure, HCC, Need for Transplant, Death	
Potential Treatment	Lifestyle change, GLP-1		Resmetirom (MAESTRO-NASH)		OUTCOMES trial in F4C	Liver Transplant

1. Estes C, et al. *Hepatology*. 2018 Jan;67(1):123-133.

The MAESTRO Phase 3 Program

The Most Advanced and Comprehensive Clinical Development Program in NASH

MAESTRO-NASH

Significant Fibrosis

Evaluates NASH resolution and/or fibrosis improvement on liver biopsy and composite clinical events

52 weeks biopsy (completed)
54 months clinical outcomes

~1700 patients (ongoing)

MAESTRO-NAFLD-1

Safety

Evaluates safety & tolerability as measured by incidence of adverse events

52 weeks (completed)

~1200 patients, including 200 with compensated cirrhosis

MAESTRO-NASH OUTCOMES

Compensated Cirrhosis

Event-driven trial evaluating progression to hepatic decompensation

~36 months

~700 patients (recruiting)

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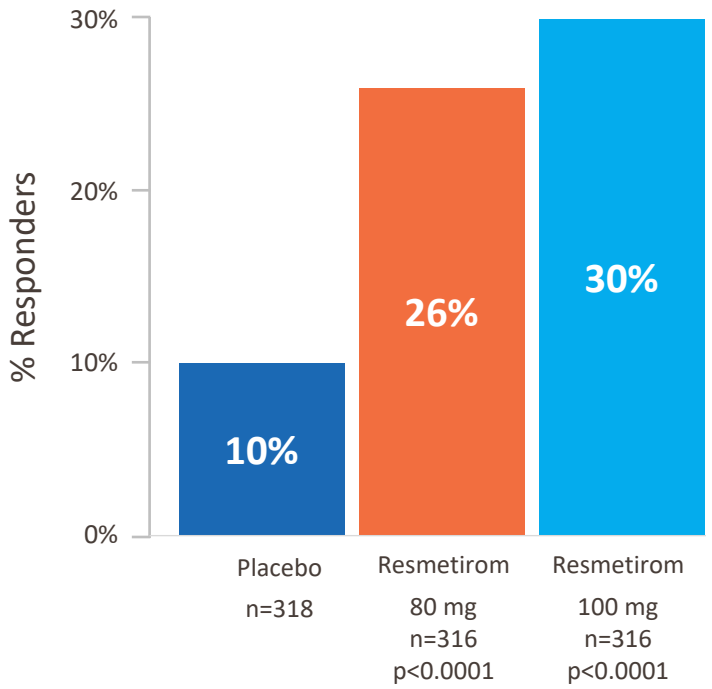
The Pivotal Phase 3 MAESTRO-NASH Trial

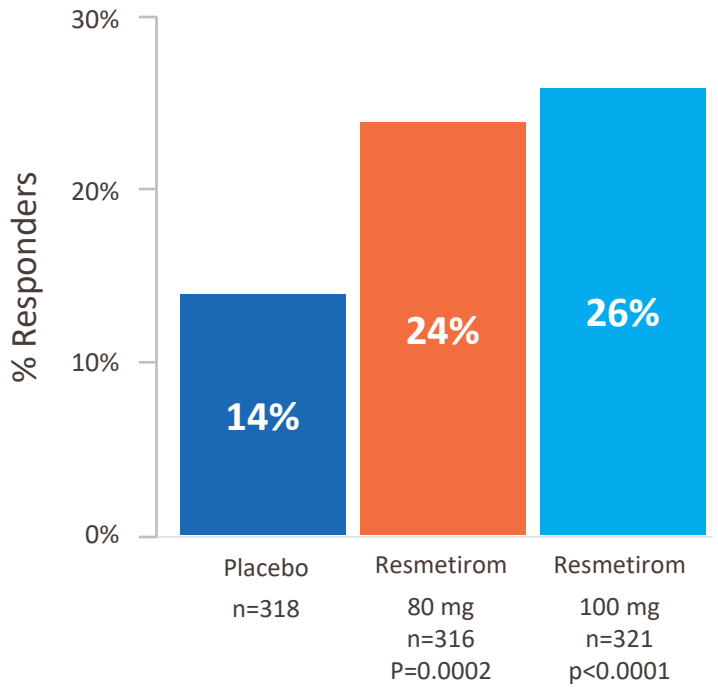
FIRST Phase 3 Trial to Achieve NASH Resolution and Fibrosis Improvement Primary Endpoints

Primary Endpoints

NASH Resolution[1]

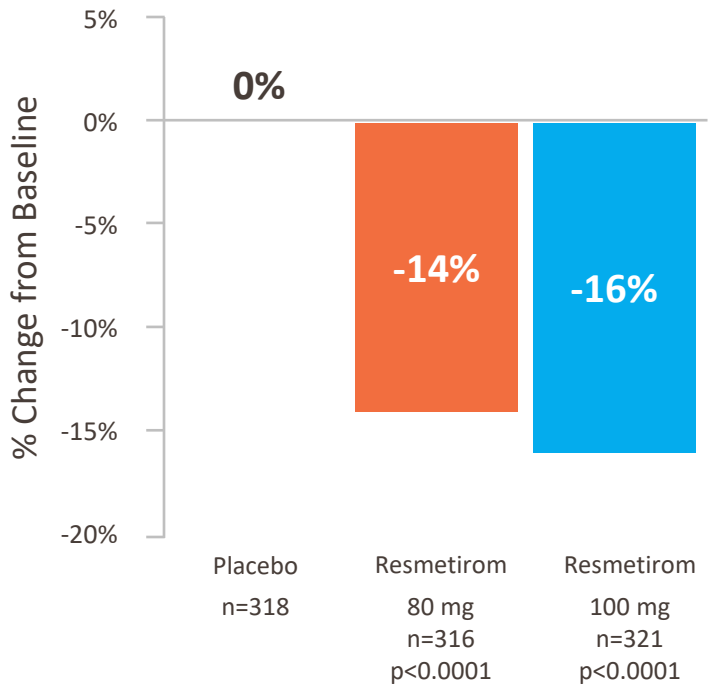


≥1 Stage Fibrosis Improvement[1]



Secondary Endpoint[2]

LDL Cholesterol



Both primary liver biopsy endpoints and the key secondary endpoint of LDL cholesterol lowering were met

1. NASH Resolution (ballooning score=0, inflammation score=0/1, & ≥2-point reduction in NAFLD Activity Score (NAS)) with no worsening of fibrosis; ≥1 Stage Fibrosis Improvement with no worsening of NAS.
2. LDL cholesterol secondary endpoint measured at Week 24

The Pivotal Phase 3 MAESTRO-NASH Trial

Favorable Emerging Safety and Tolerability Profile

n (%)	Resmetirom 80mg (n=322)	Resmetirom 100mg (n=323)	Placebo (n=321)
≥1 TEAEs	**296 (91.9)**	**296 (91.6)**	**269 (92.2)**
Grade 1 (mild)	71 (22.0)	65 (20.1)	77 (24.0)
Grade 2 (moderate)	180 (55.9)	183 (56.7)	167 (52.0)
≥ Grade 3 (severe)	45 (14.0)	48 (14.9)	52 (16.2)
≥1 drug-related TEAEs	122 (37.9)	134 (41.5)	86 (26.8)
≥1 serious TEAEs	**38 (11.8)**	**41 (12.7)**	**39 (12.1)**
≥1 drug-related serious TEAEs	2 (0.6)	0	1 (0.3)
TEAEs leading to study discontinuation (in 52 Weeks)	**6 (1.9)**	**22 (6.8)**	**8 (2.5)**
Fatal TEAE	**1 (0.3)**	**1 (0.3)**	**1 (0.3)**
3-pt MACE* (adjudicated)	**1 (0.3)**	**1 (0.3)**	**1 (0.3)**
Other cardiovascular events (adjudicated)	**0**	**1 (0.3)**	**3 (0.9)**

Study discontinuations in the 100 mg arm were increased relative to placebo only during the first 12 weeks and were similar in all treatment groups for the remaining period of the first 52 weeks; after 52 weeks, placebo discontinuations were higher than drug treatment arms

Most AE discontinuations in the 100 mg arm were **GI-related.** No increase in the incidence of diarrhea and nausea in resmetirom- relative to placebo-treated patients after the first few weeks. Diarrhea lasted on average 2-3 weeks often characterized as loose stools or worsening of underlying diarrhea

No drug-induced liver injury (DILI) events

*Nonfatal stroke, nonfatal myocardial infarction, & cardiovascular death or other cardiovascular events were adjudicated by cardiac committee. Potential DILI events were adjudicated by hepatic committee.

Building for the Future

First-to-Market Advantage Provides a Long-Term NASH Leadership Opportunity

Complete	2024	Future
Positive Phase 3 MAESTRO-NASH Data *Breakthrough Therapy & Priority Review*	**Specialty Launch of Resmetirom** *PDUFA: March 14*	**Full Approval + Compensated Cirrhosis Label**

Build Organization

- Hire, train and deploy teams

Develop Market

- Educate stakeholders, establish path from Dx to Rx fulfillment, secure market access

Execute Specialty Launch

- Target specialists (Heps, GIs) + Patients with NASH with significant fibrosis (315,000)