Madrigal Pharmaceuticals

Corporate Presentation

August 2023

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).

See Appendix for a guide to acronyms and abbreviations used in this presentation.

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; statements concerning potential accelerated approval; and statements or references concerning - 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, objectives, timing and support for making for making a Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) submission to FDA, projections or objectives for obtaining accelerated or full approval for resmetirom, 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 and potential patient benefits with resmetirom, including future NASH resolution, safety, fibrosis treatment, cardiovascular effects, lipid treatment, and/or biomarker effects with resmetirom.

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; 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; and the uncertainties inherent in clinical testing. 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 section 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 as updated from time to time by Madrigal's other filings with the SEC.

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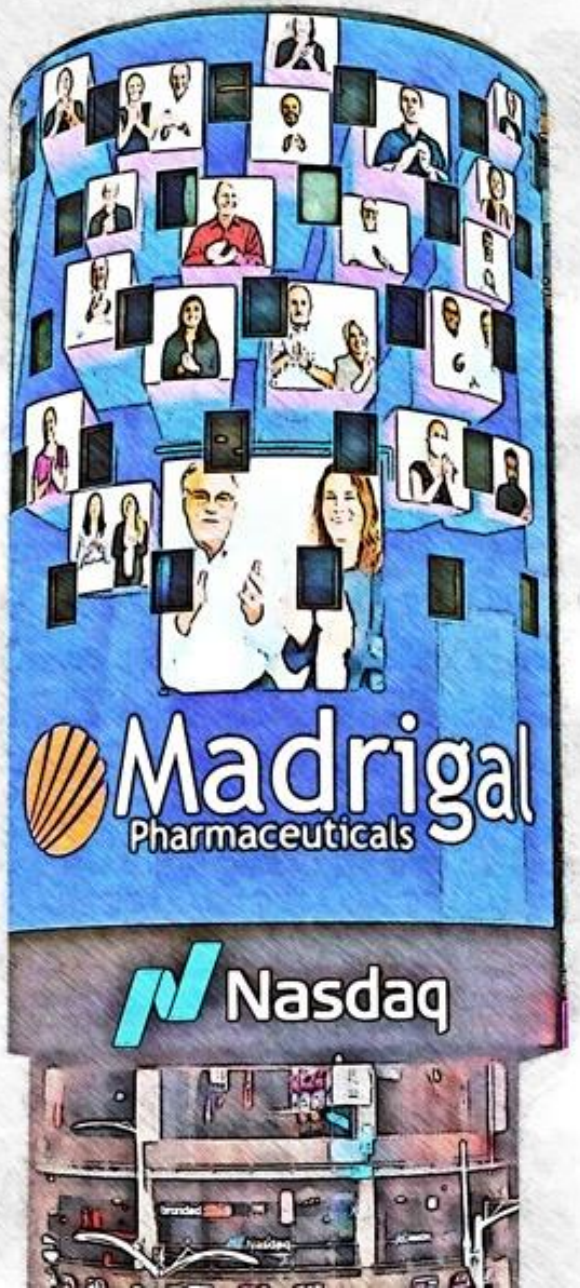

Madrigal is a clinical-stage biopharmaceutical company pursuing novel therapeutics for NASH, a liver disease with high unmet medical need

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Introduction to Madrigal

- **Nonalcoholic steatohepatitis (NASH)** is a prevalent liver disease with no approved therapy

- **Resmetirom**, Madrigal's lead product candidate, is designed to target key underlying causes of NASH in the liver
  - Resmetirom achieved both **NASH resolution and fibrosis improvement** primary endpoints* in a Phase 3 trial (MAESTRO-NASH)
  - Resmetirom was granted **Breakthrough Therapy** designation by FDA for the treatment of adults with NASH with liver fibrosis
  - The resmetirom **new drug application** was submitted to FDA in July 2023

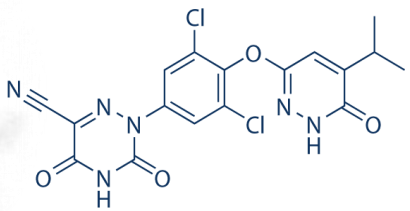
- **Our commercial strategy** focuses on launching resmetirom as a specialty medication for patients with at-risk NASH
  - Madrigal to commercialize in the U.S. and will partner in ex-U.S. territories

- **The Madrigal leadership team** has deep experience developing and commercializing successful pharmaceutical products

*The dual primary surrogate endpoints on biopsy are NASH resolution, with at least a 2-point reduction in NAS (NAFLD Activity Score), and with no worsening of fibrosis OR a one point decrease in fibrosis with no worsening of NAS.

The Madrigal Story

Origins



2004-2008: Madrigal founder Dr. Rebecca Taub studies THR-B agonism while working at Hoffmann-La Roche

2008: Madrigal predecessor company VIA Pharmaceuticals hires Dr. Taub and enters into a development agreement with Hoffmann-La Roche for resmetirom

Founding and Development

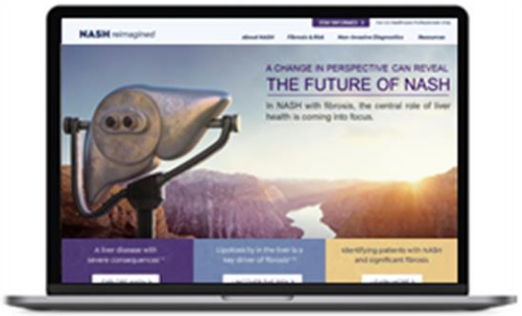
2011: Madrigal is incorporated in Delaware

2011: Ph 1 trial of resmetirom commences

2016: Ph 2 trial of resmetirom in NASH commences

2016: Madrigal merges with Synta Pharmaceuticals; is listed on NASDAQ

Growth



2016: Dr. Paul Friedman named CEO and Dr. Rebecca Taub named CMO of Madrigal

2017-2018: Positive Ph 2 results in NASH help accelerate Madrigal's growth

2019: Madrigal commences Ph 3 "MAESTRO" program for resmetirom

2020-2022: Madrigal expands its executive team with additional experienced leaders, begins building its commercial organization

2022: Positive Phase 3 MAESTRO data announced

2023: Resmetirom New Drug Application submitted to FDA

NASH is a Liver Disease with Severe Consequences

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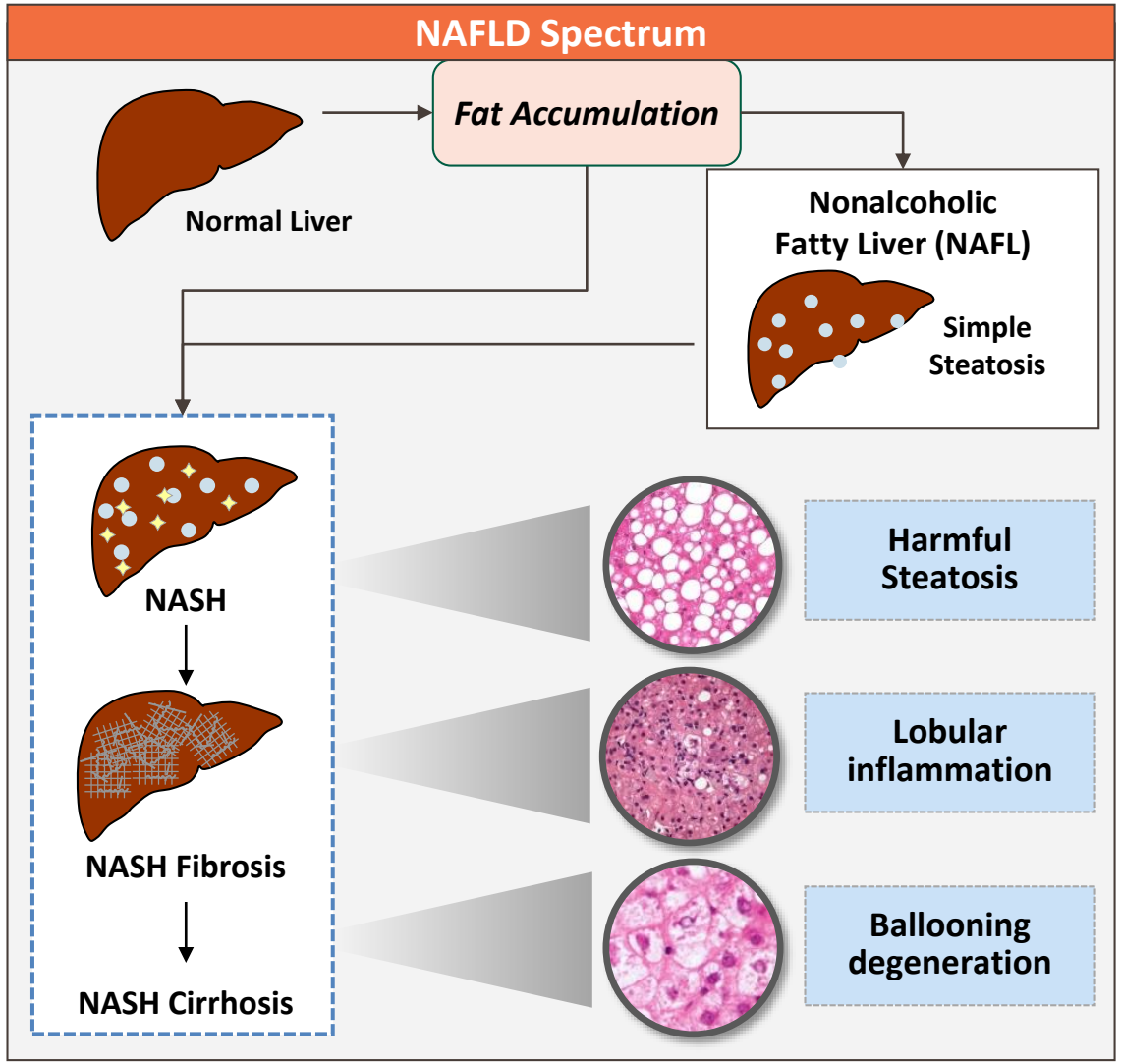
NASH – A Liver Disease with Severe Global Consequences



DISEASE

- Nonalcoholic steatohepatitis (NASH) is an advanced form of nonalcoholic fatty liver disease (NAFLD) defined by the development of inflammation and hepatocyte injury

PREVALENCE

- An estimated ~42 million people in the U.S., EU4/UK and Japan are living with NASH[1-3]
  - Of those, 15 million people are likely to have at-risk NASH (F2-F3)
    - ~7 million in the EU/UK and Japan alone
  - An estimated 4 million may have NASH cirrhosis

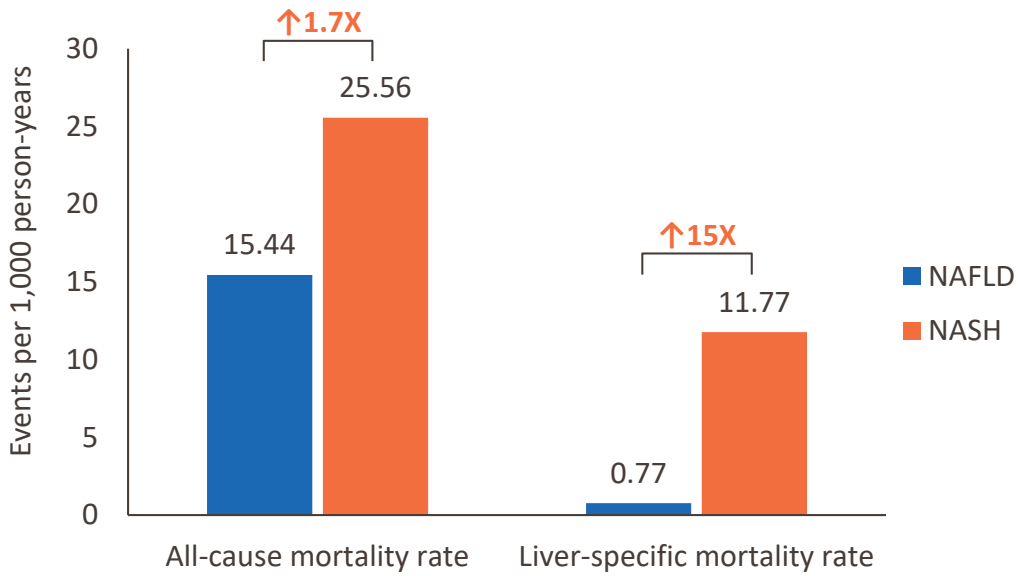
OUTCOME

- ~22% of NASH patients with stage 3 fibrosis progress to cirrhosis within 2 years[4]
- NASH is projected to soon become the leading cause for liver transplantation in the U.S.[5]

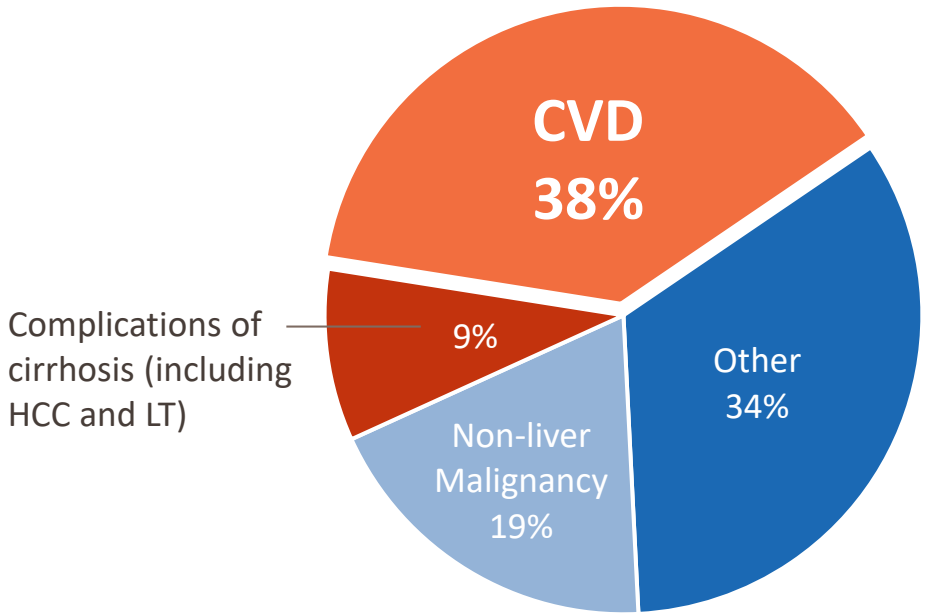
1. Estes C, Razavi H, Loomba R, Younossi Z, Sanyal AJ. Hepatology. 2018;67(1):123-133. 2. Hardy T, Oakley F, Anstee QM, Day CP. Annu Rev Pathol. 2016;11:451-496. 3. Rinella MA, Lominadze Z, Loomba R, et al. Ther Adv Gastroenterol. 2016;9(1):4-12. 4. Loomba R, Adams L. Hepatology. 2019;70(6):1885-1888. 5. Younossi ZM, et al. Clin Gastroenterol Hepatol. 2021;19(3):580-589.

NASH is Associated with Significant Morbidity and Mortality

The mortality rate among patients with NASH is substantially higher than patients with NAFLD[1]



Cardiovascular disease is a leading cause of death in patients with NASH/NAFLD[2]



1. Younossi Y, et al. Hepatology. 2016;64(1):73-84. 2. Angulo, et al. Gastroenterology. 2015;149:389-97

Leading the Way in NASH

The Resmetirom Clinical Development Program

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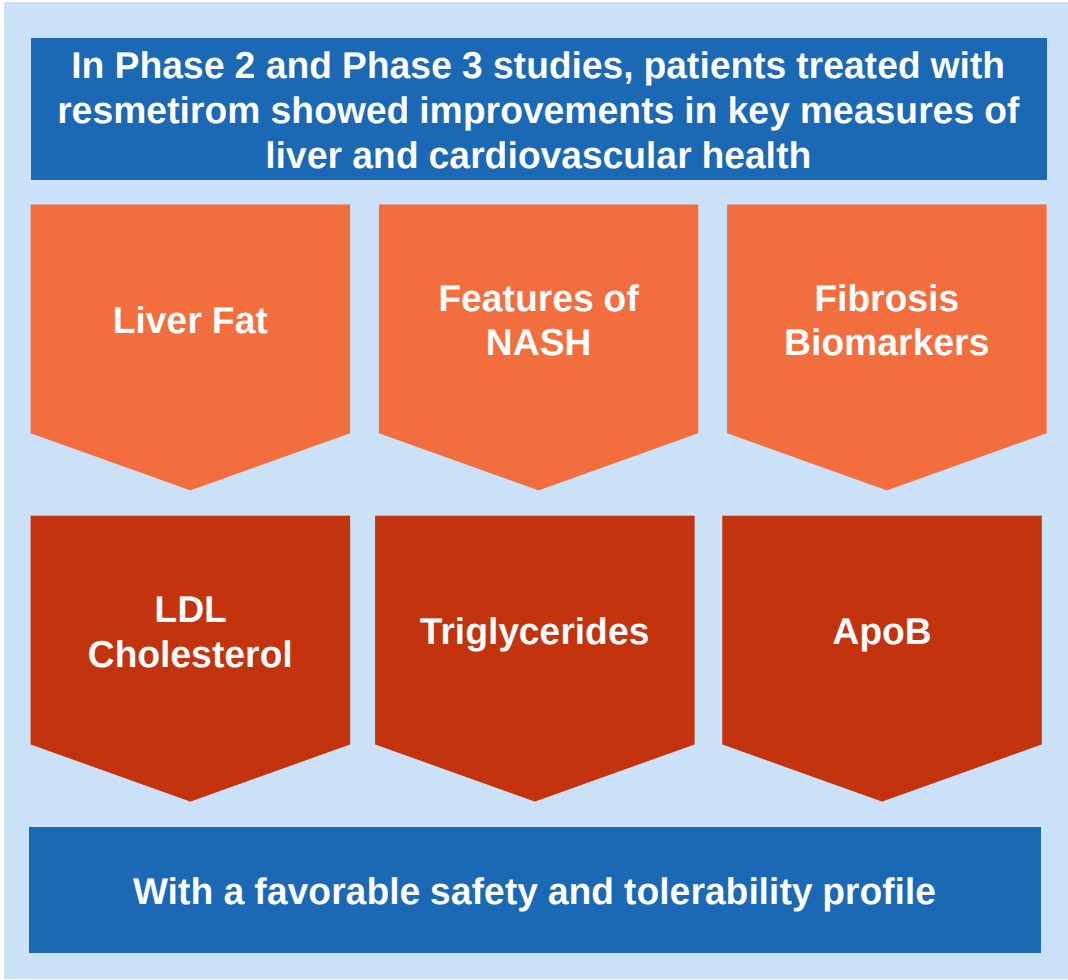
Resmetirom for the Treatment of At-Risk NASH

Madrigal's lead product candidate is **resmetirom**, a thyroid hormone receptor (THR) β-selective agonist

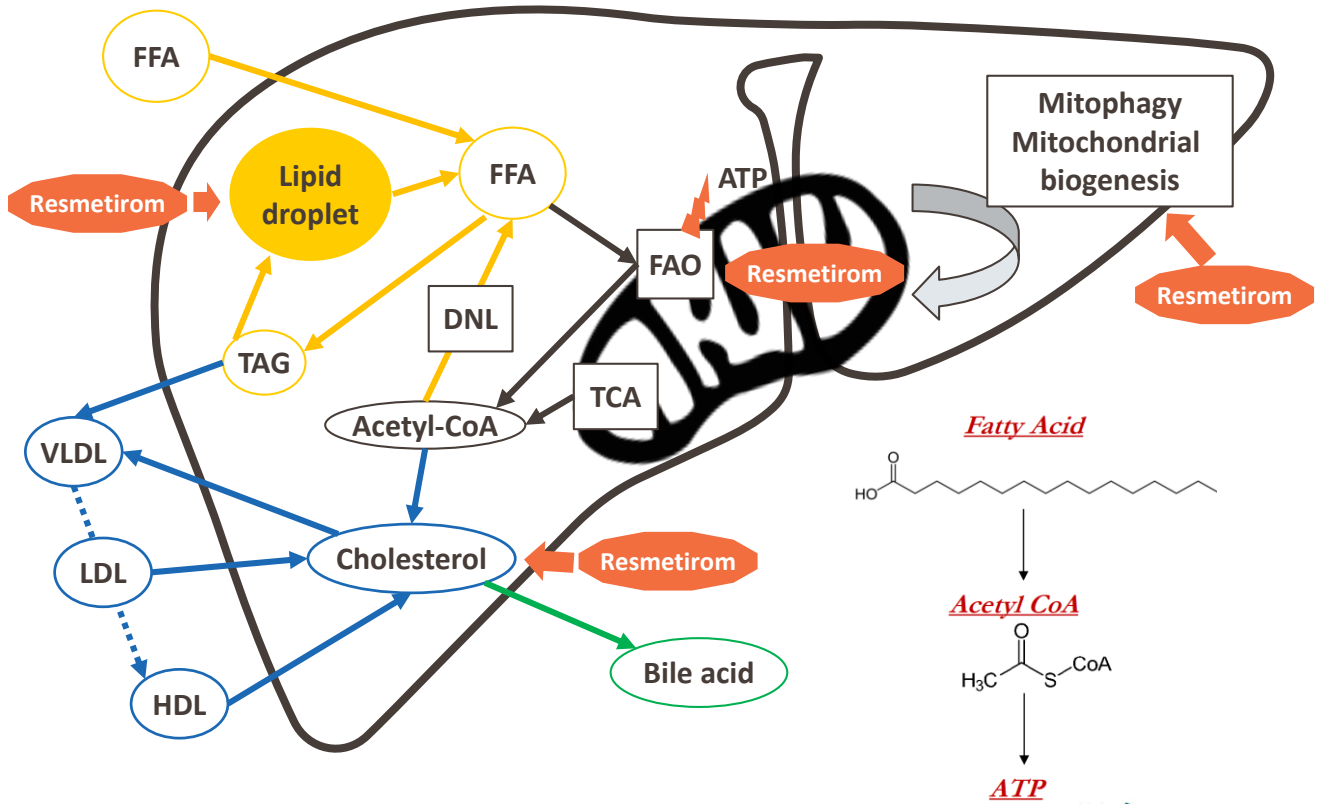
- Designed to target key underlying causes of NASH in the liver
- An oral, once-daily treatment
- Currently being evaluated in multiple Phase 3 trials, with positive efficacy and safety data reported in 2022

Resmetirom has the potential to become the first foundational therapy for patients with NASH



THR-β Pathway Plays a Key Role in Liver Health

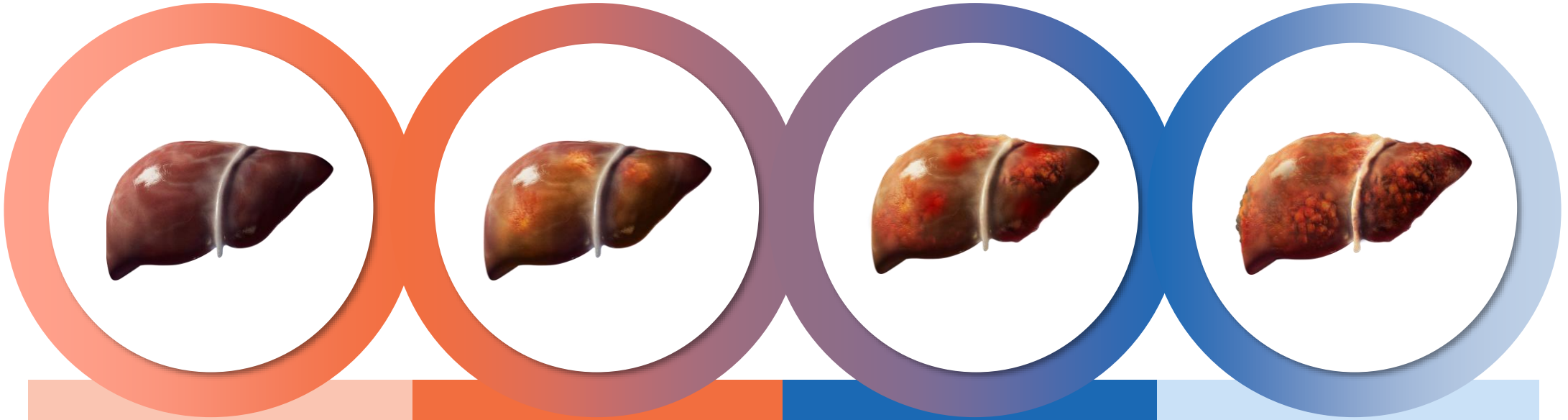
- **Selective THR-β agonists without extrahepatic effects**
- THR-β agonists act on multiple hepatic pathways to maintain liver health by controlling[1]:
  - De novo lipogenesis
  - Fatty acid oxidation
  - Mitophagy & mitochondrial biogenesis
  - Cholesterol metabolism
  - Direct anti-inflammatory & anti-fibrotic effects
- In human NASH, the liver has relatively low THR-β activity, exacerbating mitochondrial dysfunction & lipotoxicity
- Potential for hepatic and CV benefits in patients with NASH and liver fibrosis



See Appendix for a guide to acronyms and abbreviations used in this presentation.

1. Sinha RA, et al. *Nat Rev Endocrinol*. 2018;14(5):259-269.

The Phase 3 MAESTRO Development Program is Intended to Provide a Comprehensive Data Set in Patients with NASH



MAESTRO NAFLD-1	MAESTRO NAFLD-OLE	MAESTRO NASH	MAESTRO NASH OUTCOMES
Safety & tolerability as measured by incidence of Adverse Events (AE)	Safety & tolerability as measured by incidence of AEs (Extension to MAESTRO-NAFLD-1)	NASH resolution and/or fibrosis improvement on liver biopsy and composite clinical events	Event-driven trial evaluating progression to hepatic decompensation in patients with well-compensated NASH cirrhosis
52 weeks	52 weeks	52 weeks biopsy (completed) 54 months clinical outcomes	~36 months
~1200 patients (Completed)	~700 patients (Ongoing)	~1700 patients (Ongoing)	~700 patients (Recruiting)

NDA Submitted to FDA July 2023 Following Two Positive Phase 3 MAESTRO Study Readouts

MAESTRO-NASH Biopsy Study

December 2022

Resmetirom achieved both primary endpoints with both daily oral doses, 80 mg and 100 mg, relative to placebo:

- NASH resolution (ballooning of 0, inflammation of 0-1) and ≥2-point NAS reduction with no worsening of fibrosis ($p<0.0001$ at both doses)
- Fibrosis improvement by at least one stage with no worsening of NAS ($p=0.0002$ and <0.0001 at 80 and 100 mg, respectively)

MAESTRO-NAFLD-1 Safety Study

January 2022

Primary and key secondary endpoints from the MAESTRO-NAFLD-1 safety study were achieved. In this study, resmetirom:

- Was safe and well-tolerated at 80 and 100 mg in patients treated for 52 weeks
- Provided significant and clinically relevant reductions in liver fat
- Significantly reduced atherogenic lipids, including LDLc, apolipoprotein B and triglycerides

Based on these positive Phase 3 results, Madrigal has submitted a New Drug Application Seeking Accelerated Approval of Resmetirom

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Pivotal Phase 3 MAESTRO-NASH Study Results

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MAESTRO-NASH Trial Design

KEY ELIGIBILITY CRITERIA

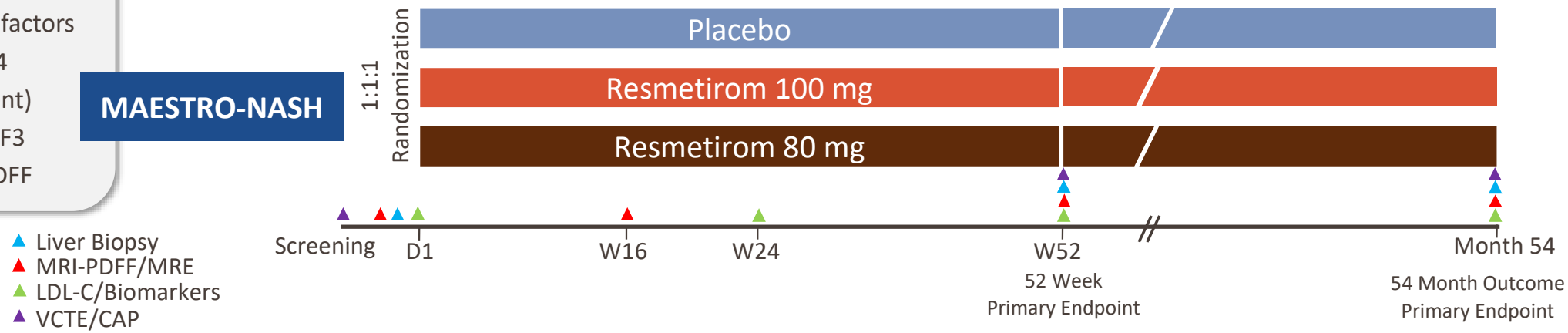
Presence of ≥3 metabolic risk factors

NASH on biopsy: NAS ≥4
(with ≥1 in each component)

Fibrosis stage F1B, F2, or F3

≥8% hepatic fat by MRI-PDFF

MAESTRO-NASH



DUAL PRIMARY ENDPOINT AT WEEK 52

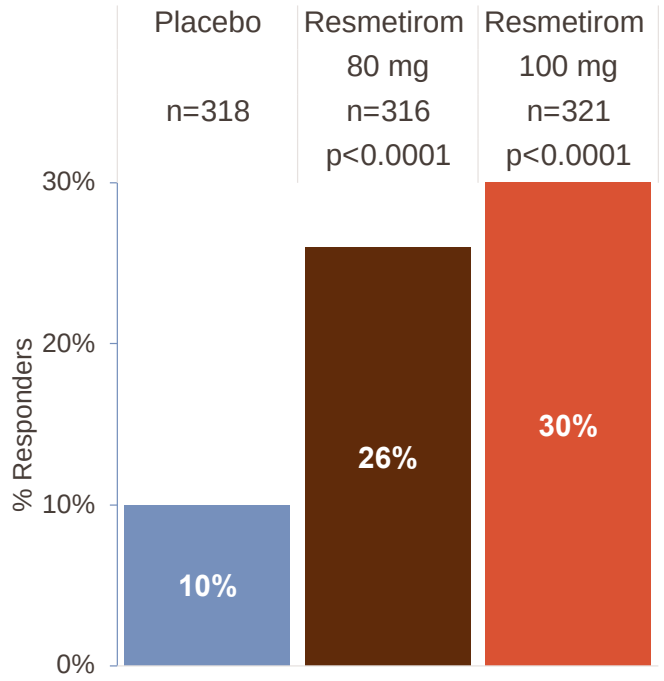
NASH resolution (ballooning score=0, inflammation score=0/1, & ≥2-point reduction in NAS) with no worsening of fibrosis

≥1-stage improvement in fibrosis with no worsening of NAS

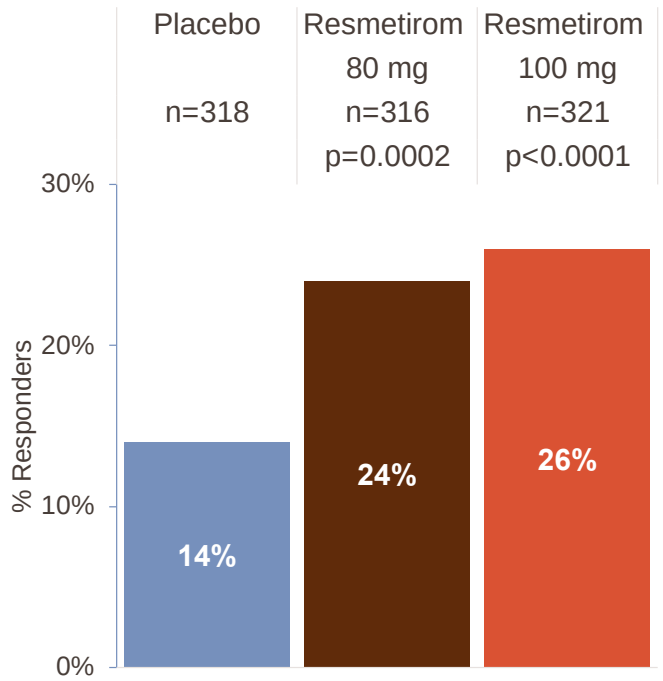
See Appendix for a guide to acronyms and abbreviations used in this presentation.

Dual Primary Endpoints (Week 52): Primary Analysis

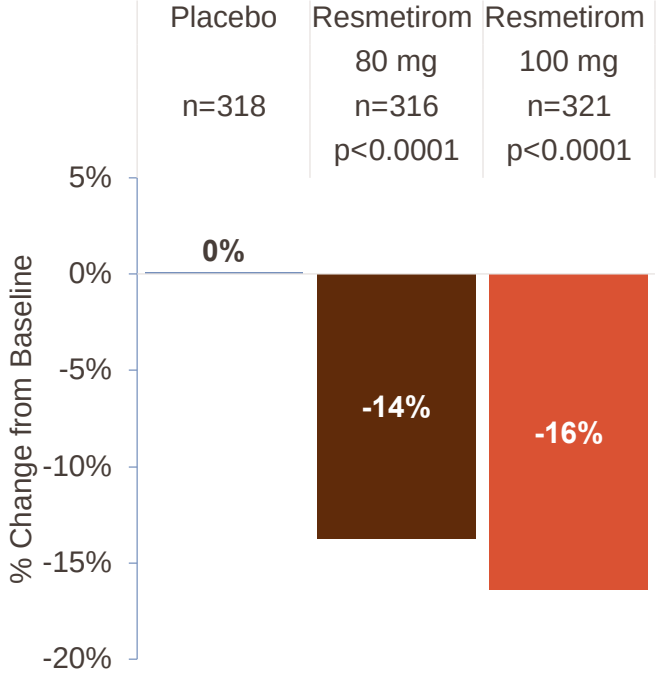
NASH Resolution*



≥1 Stage Fibrosis Improvement*



LDL Cholesterol



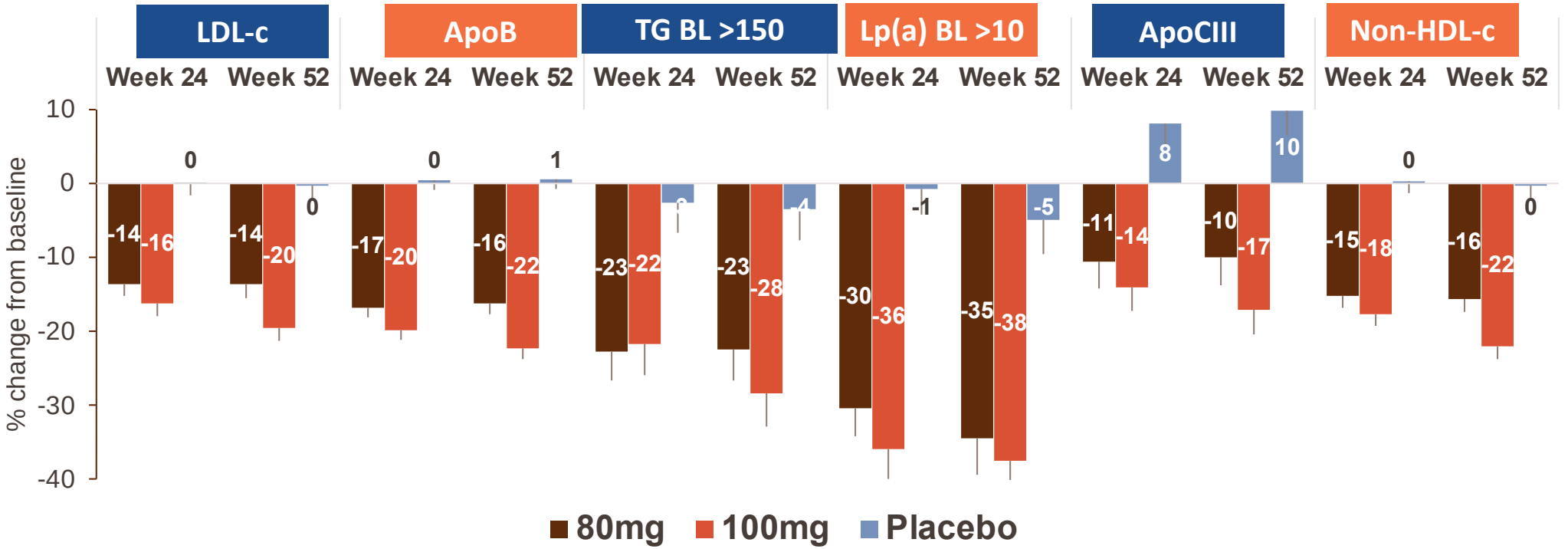
Both primary liver biopsy endpoints and the key secondary endpoint of LDL cholesterol lowering were met

*NASH Resolution with no worsening of fibrosis; ≥1 Stage Fibrosis Improvement with no worsening of NAS

Additional Secondary Biopsy Endpoints (Week 52)

	Resmetirom 80mg (n=316)	Resmetirom 100mg (n=321)	Placebo (n=318)
≥2-point reduction in NAS (with ≥1-point reduction in ballooning or inflammation) with no worsening of fibrosis			
Response rate, %	**41.3**	**44.9**	**21.2**
Difference from placebo (95% CI)	20.2 (13.8, 26.5)	23.8 (17.4, 30.2)	
p-value	<0.0001	<0.0001	
2-stage fibrosis improvement (F2-F3 patients with ≥2-point reduction in fibrosis) with no worsening of NAS			
Response rate, %	**8.3**	**10.1**	**2.8**
Difference from placebo (95% CI)	5.6 (2.5, 8.7)	7.4 (3.9, 10.8)	
p-value	0.0001	<0.0001	
NASH resolution & ≥1-stage improvement in fibrosis			
Response rate, %	**14.2**	**16.0**	**4.9**
Difference from placebo (95% CI)	9.5 (5.4, 13.6)	11.6 (7.5, 15.8)	
p-value	<0.0001	<0.0001	
NASH resolution (with ≥2 pt reduction in NAS and no worsening of fibrosis), Observed Data (both baseline and week 52 biopsy pair)			
Response rate, %	**31.8**	**38.7**	**11.2**
Difference from placebo (95% CI)	20.9 (14.6,27.1)	28.5 (22.1,34.9)	
p-value	<0.0001	<0.0001	
≥1-stage Fibrosis Improvement with no Worsening of NAS, Observed Data (both baseline and week 52 biopsy pair)			
Response rate, %	**29.7**	**33.5**	**16.3**
Difference from placebo (95% CI)	13.6 (7.3,19.9)	17.2 (10.8,23.6)	
p-value	<0.0001	<0.0001	
NASH Resolution OR Fibrosis Improvement	**42%**	**50%**	**19%**

Percent Change from Baseline in Lipids/Lipoproteins (Weeks 24 & 52)



Key secondary endpoint met (LDL-C lowering)

Significant effect of resmetirom 80 & 100 mg on multiple atherogenic lipids/lipoproteins at Week 24 and 52

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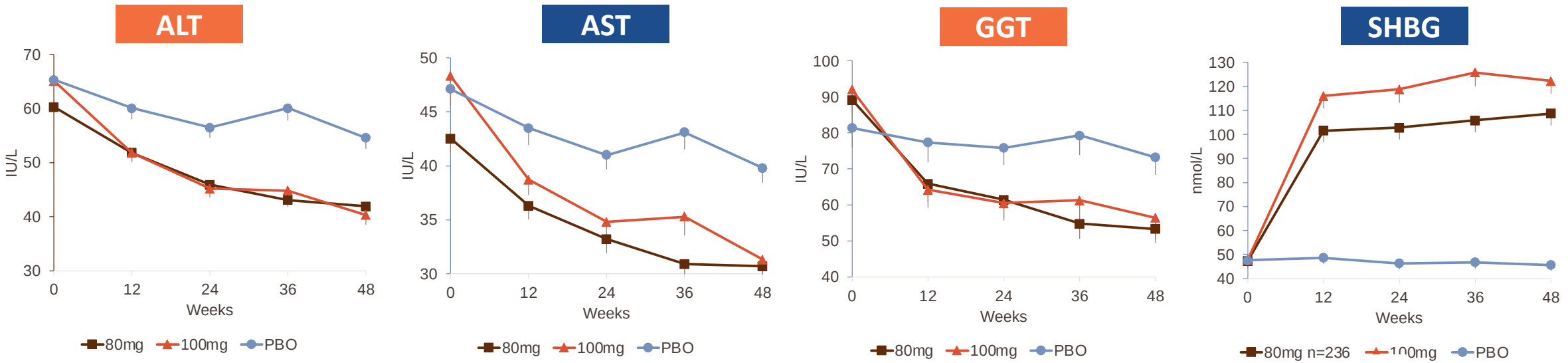
Change from Baseline in Liver Enzymes* & SHBG

- Significant reduction of liver enzymes relative to placebo, both percentage change and absolute reduction
- Associated with the neutral biomarker SHBG that increases in proportion to resmetirom target engagement (exposure)

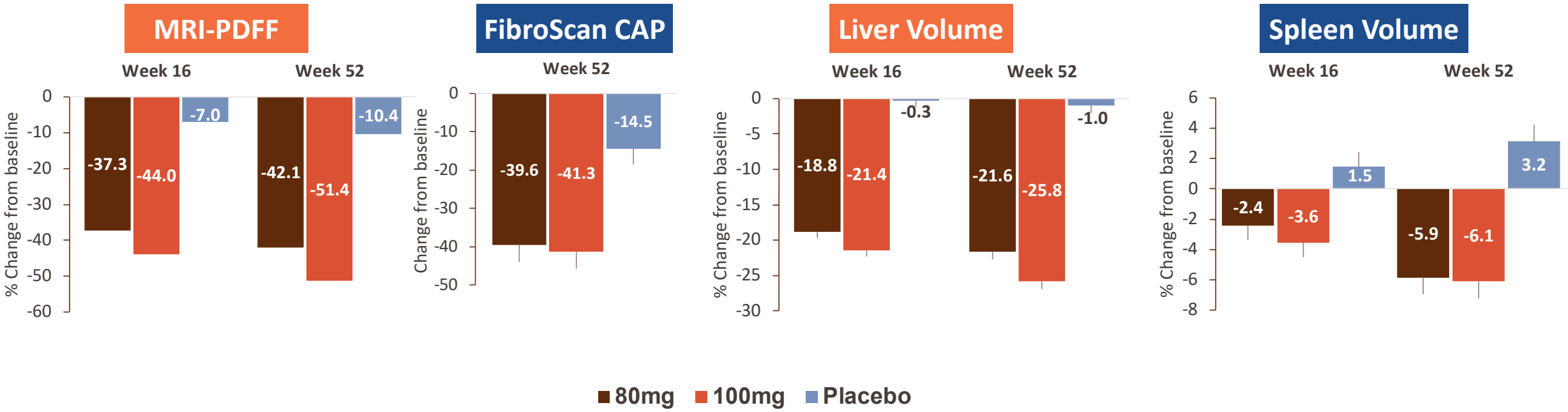


80mg **100mg** **Placebo**

*Evaluated in patients with baseline ALT ≥30 IU/L.

Change from Baseline in MRI-PDFF & FibroScan CAP

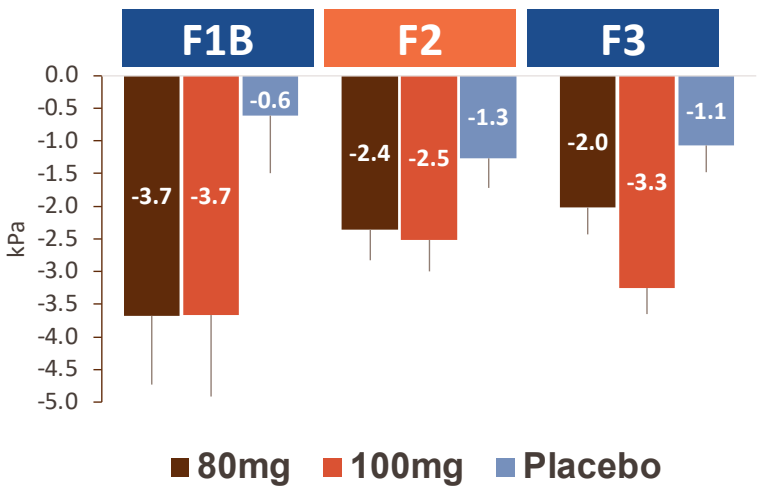
- Significant effect of resmetirom 80 & 100 mg on both MRI-PDFF & FibroScan CAP
- Significant effect of resmetirom to reduce liver and spleen volume as assessed on serial MRI-PDFF
  - Liver volume corrected MRI-PDFF reduction is a mean of 60% at the 100 mg dose



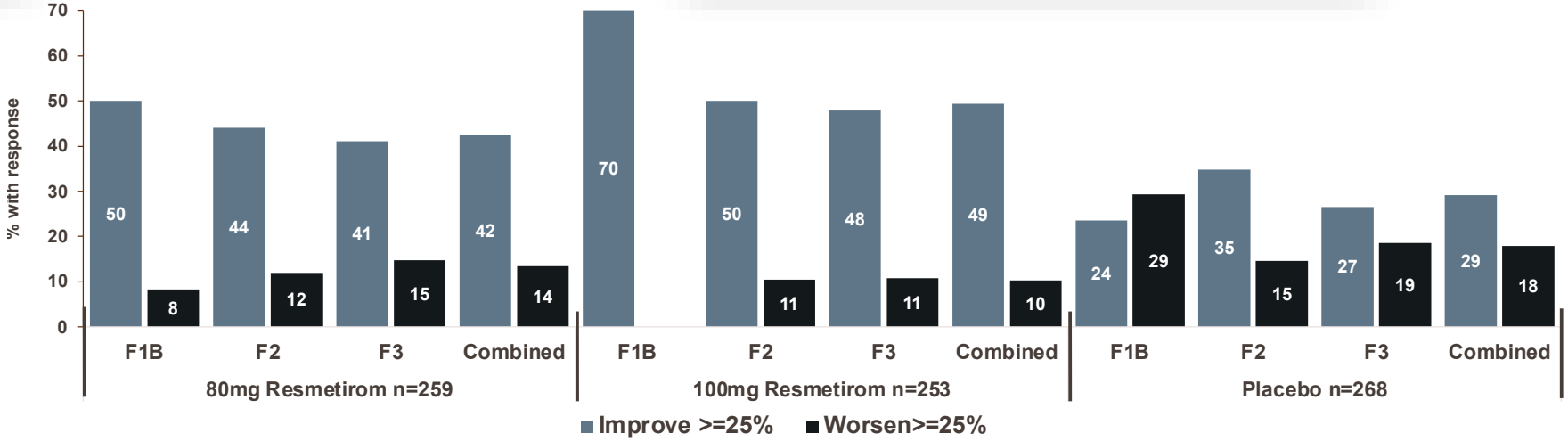
Change from Baseline in FibroScan VCTE/LSM (Week 52)

Significant effect of resmetirom 80 & 100mg on liver stiffness measured by FibroScan VCTE, mean change from baseline (A) & responder analysis (B)
Other fibrosis endpoints achieved: Reduction in MRE, ELF

A - FibroScan VCTE Mean Change



B - FibroScan VCTE Responder Analysis



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Safety Overview

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 DILI events (adjudicated)

*Nonfatal stroke, nonfatal myocardial infarction, & cardiovascular death.

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TEAEs Reported in >5% of Patients Overall

n (%)	Resmetirom 80mg (n=322)	Resmetirom 100mg (n=323)	Placebo (n=321)
Diarrhea	89 (27.6)	109 (33.7)	50 (15.6)
COVID-19	78 (24.2)	56 (17.3)	68 (21.2)
Nausea	70 (21.7)	62 (19.2)	40 (12.5)
Arthralgia	46 (14.3)	34 (10.5)	40 (12.5)
Back pain	36 (11.2)	27 (8.4)	38 (11.8)
Urinary tract infection	33 (10.2)	26 (8.0)	29 (9.0)
Fatigue	32 (9.9)	26 (8.0)	27 (8.4)
Pruritus	26 (8.1)	37 (11.5)	22 (6.9)
Abdominal pain upper	25 (7.8)	27 (8.4)	29 (9.0)
Headache	30 (9.3)	24 (7.4)	27 (8.4)
Vomiting	28 (8.7)	35 (10.8)	17 (5.3)
Type 2 diabetes	25 (7.8)	27 (8.4)	25 (7.8)
Abdominal pain	27 (8.4)	30 (9.3)	18 (5.6)
Constipation	21 (6.5)	27 (8.4)	18 (5.6)
Muscle spasms	14 (4.3)	22 (6.8)	21 (6.5)
Hypertension	16 (5.0)	13 (4.0)	25 (7.8)
Dizziness	21 (6.5)	19 (5.9)	11 (3.4)

Conclusions

- Resmetirom is the **first treatment to achieve meaningful effects on both primary liver biopsy endpoints** that are reasonably likely to predict clinical benefit in a **Phase 3** trial in patients with NASH
- Both 80 and 100 mg doses were effective offering optionality for patients
- **Multiple supportive analyses and additional data** using non-invasive measures increase the confidence in the liver biopsy data.
- The safety profile of resmetirom in MAESTRO-NASH was consistent with previous Phase 2/3 trials in which the most common AEs were diarrhea & nausea at treatment initiation
- A limitation of these data are:
  - Lack of clinical outcomes data to correlate with the biopsy data; however, the MAESTRO-NASH trial will continue for 54 months to accrue & evaluate clinical outcomes
- These data from the MAESTRO-NASH trial **support the potential for resmetirom to provide benefit to patients with NASH**

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Phase 3 MAESTRO-NAFLD-1 Safety Study Results

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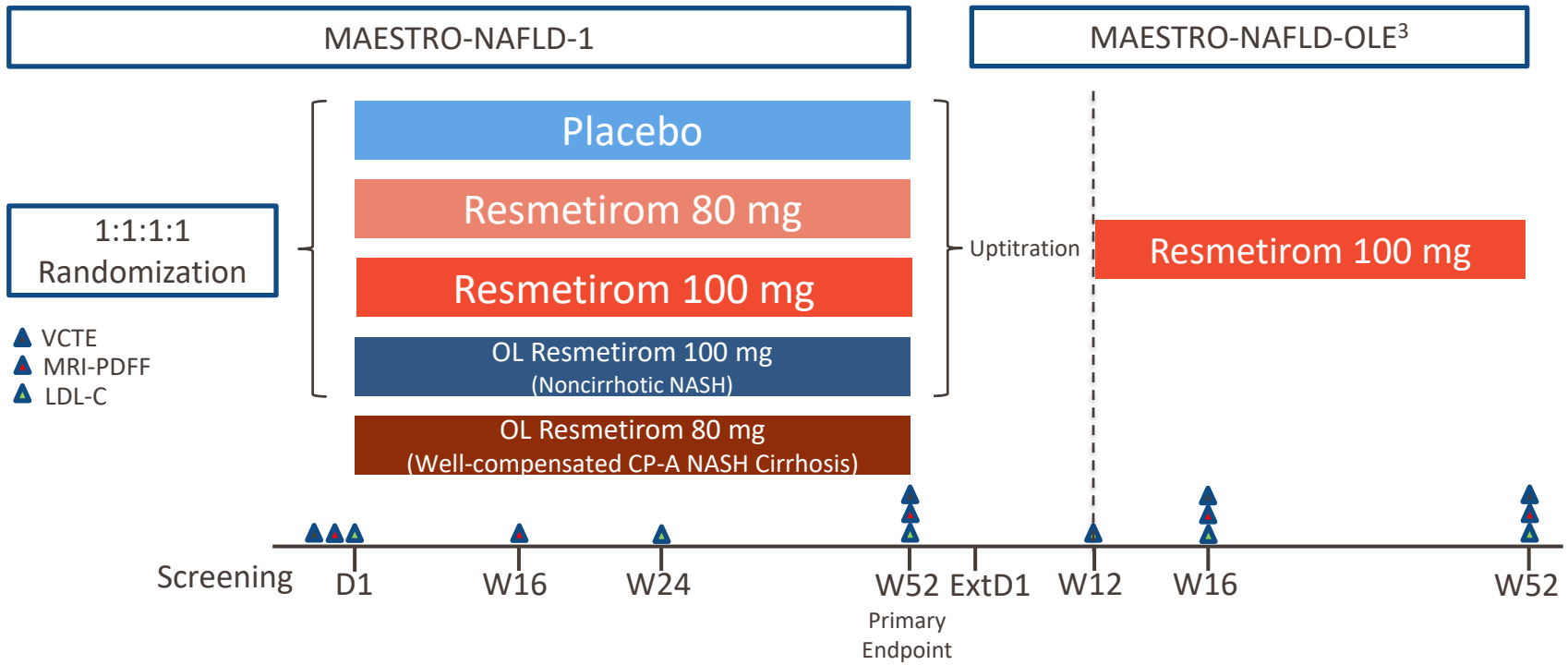
MAESTRO-NAFLD-1 Study Design:

Randomized, Double-Blind, Placebo-Controlled With Open-Label Resmetirom 100 mg Arm



Key Inclusion/Exclusion Criteria

- ≥3 metabolic risk factors (Metabolic Syndrome)
- FibroScan VCTE ≥5.5 & ≤8.5 kPa & CAP ≥280 dB/m
- ≥8% liver fat on MRI-PDFF

Enrollment

- 1143 presumed NASH patients enrolled in the USA (~80 sites)
  - 972 randomized to DB arms
  - 171 OL patients (recruitment completed July 1, 2020)

See Appendix for a guide to acronyms and abbreviations used in this presentation.

MAESTRO-NAFLD-1 Safety Summary: Double-Blind Population

	Resmetirom 100 mg DB (n=324)*	Resmetirom 80 mg DB (n=327)*	Placebo DB (n=318)*
≥1 TEAE, n (%)	279 (86.1)	289 (88.4)	260 (81.8)
Grade 1	99 (30.6)	99 (30.3)	92 (28.9)
Grade 2	151 (46.6)	164 (50.2)	139 (43.7)
≥ Grade 3 Severity	29 (9.0)	25 (7.6)	29 (9.1)
Drug-related TEAE ≥ Grade 3 Severity	1 (0.3)	1 (0.3)	2 (0.6)
≥1 Serious TEAE, n (%)	24 (7.4)	20 (6.1)	20 (6.3)
Study Discontinuations Due to AE, n (%)	9 (2.8)	8 (2.4)	4 (1.3)
Study Discontinuations Due to Drug-Related AE	6 (1.9)	5 (1.5)	3 (0.9)
Study Discontinuations Due to GI AE	6 (1.9)	5 (1.5)	2 (0.6)

*Safety population.

Harrison S, et al. *J Hepatol.* 2022;77(S1):S14.

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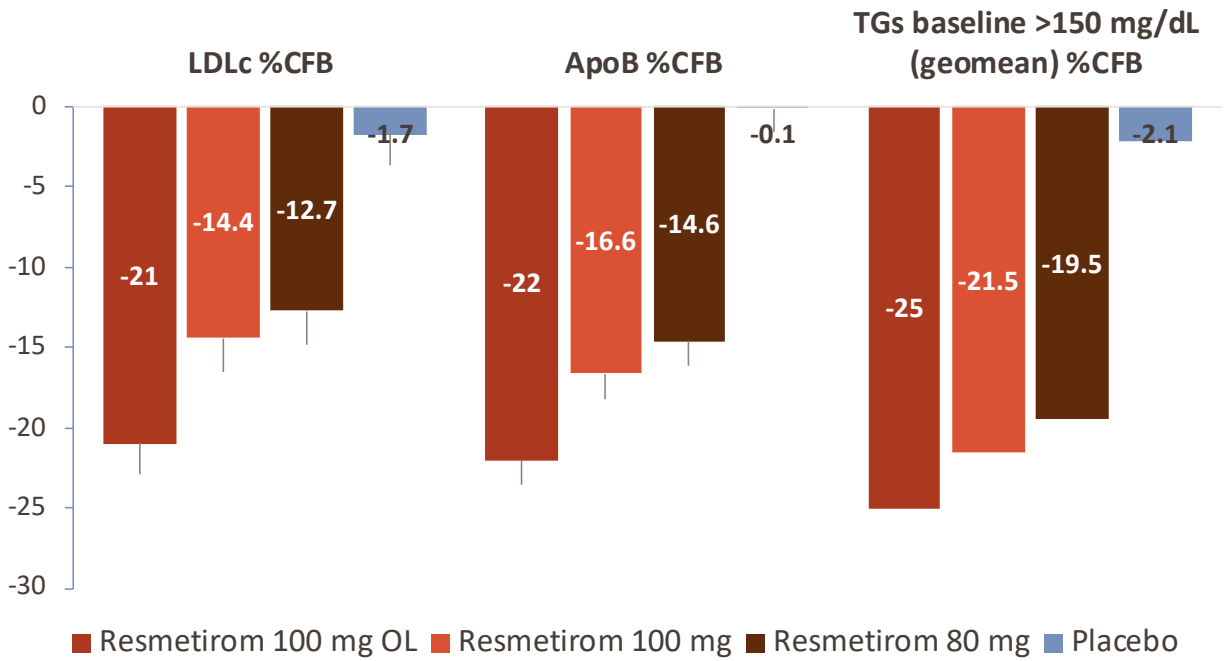
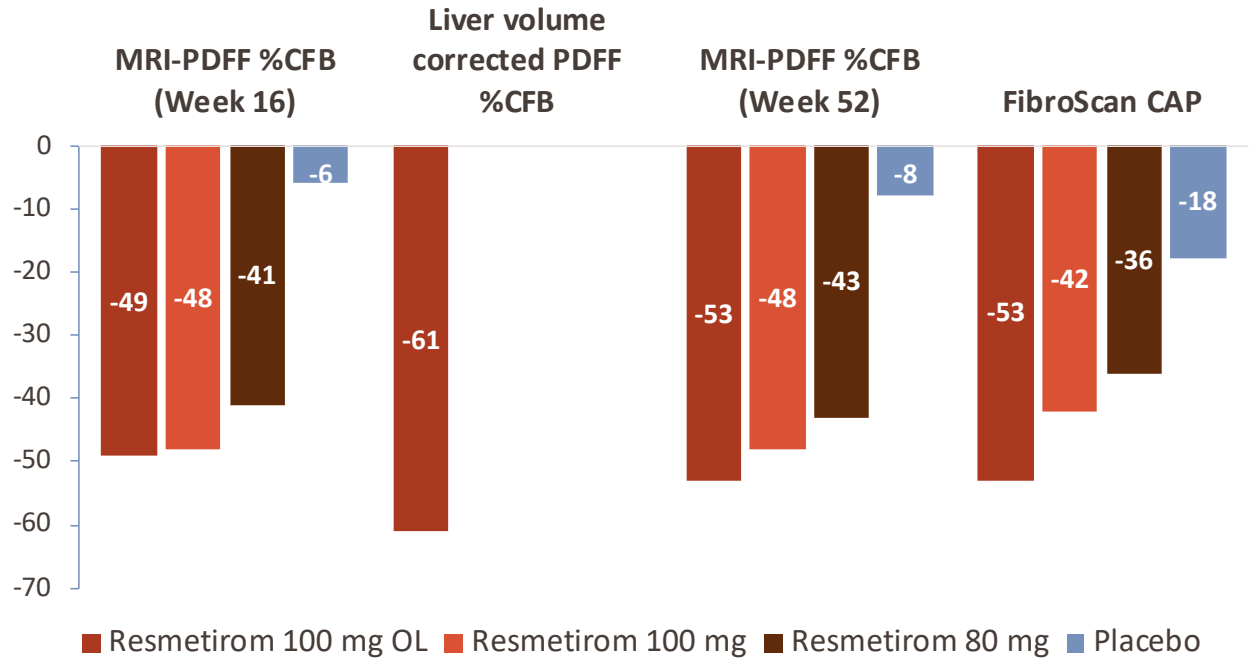
MAESTRO-NAFLD-1 Key Secondary Endpoints





- Key secondary endpoints were achieved for both 80 & 100 mg groups ($p<0.0001$ for LDL-C, apoB, TG, MRI-PDFF, & CAP)
  - Lipid reductions were numerically greater in the 100 mg OL arm vs 100 mg DB arm
    - Patients in the 100 mg OL arm were less impacted by COVID-related dose interruptions than DB patients
- MRI-PDFF reductions occurred compared to placebo even though some DB patients had COVID-related treatment interruptions prior to Week 16 or 52 MRI-PDFF

Harrison S, et al. *J Hepatol.* 2022;77(S1):S14.

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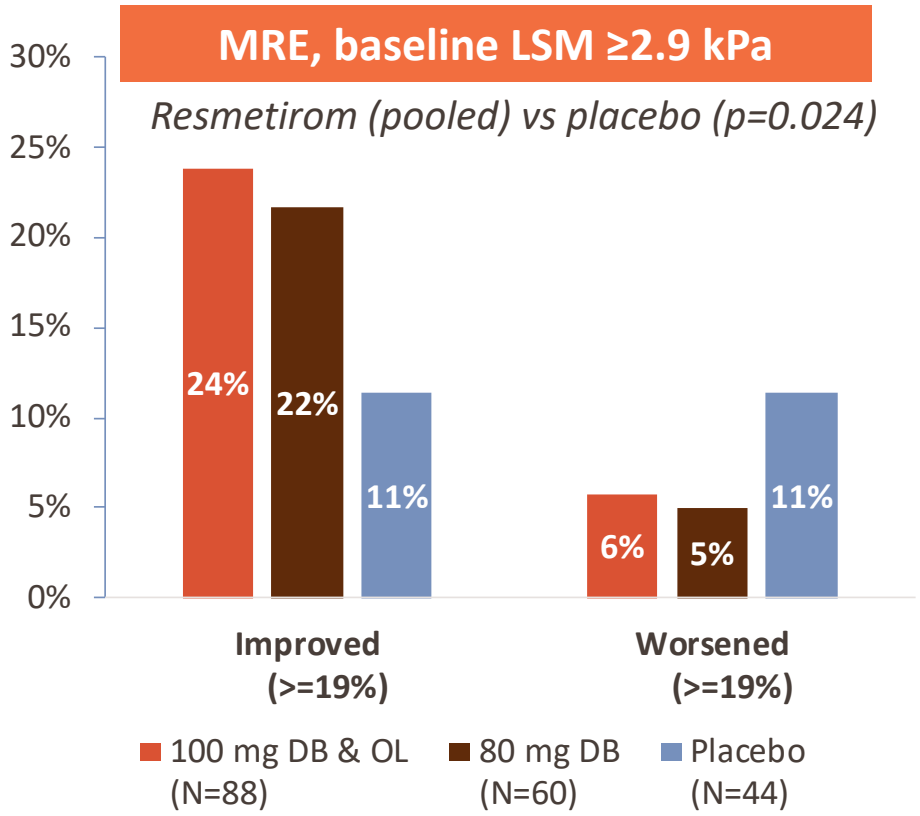
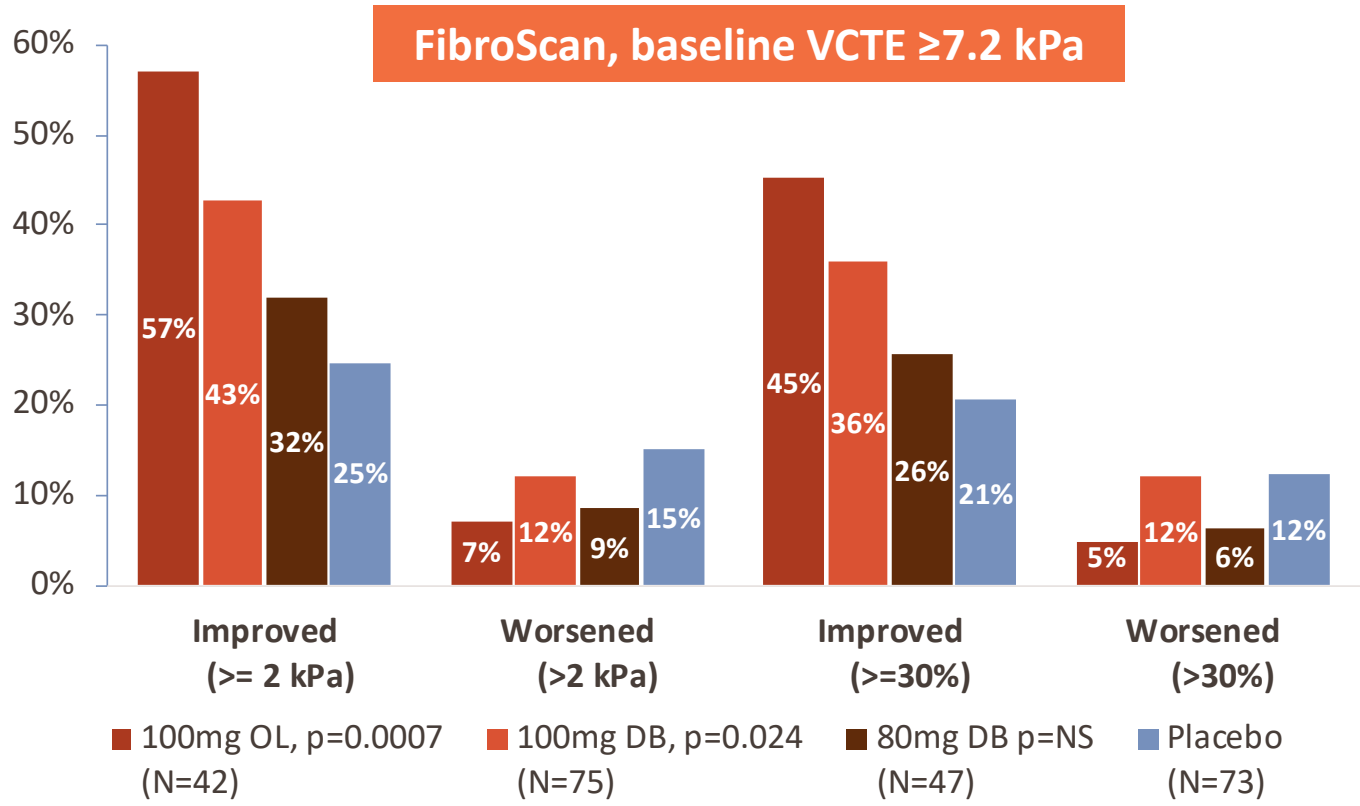
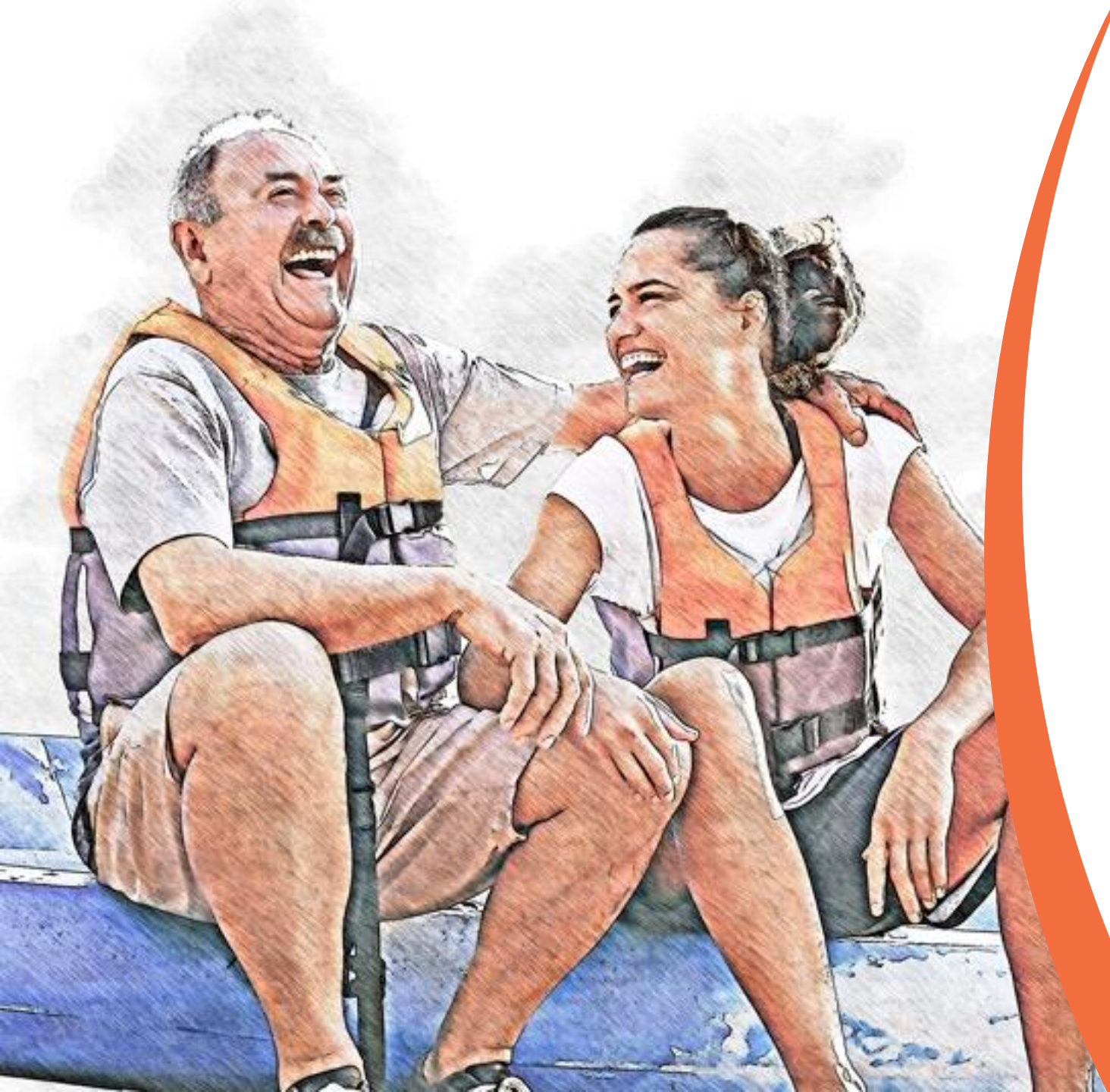
MAESTRO-NAFLD-1 MRE & FibroScan VCTE: Change at Week 52





- Responder analyses were conducted to reduce the influence of highly variable measurements & showed statistically significant response in resmetirom compared with placebo
  - In this study, most patients did not have baseline VCTE on FibroScan or MRE that met criteria for analysis
  - Mean change was not significantly different for FibroScan VCTE LSM

Harrison S, et al. *J Hepatol.* 2022;77(S1):S14.



Advancing Drug Development in Compensated NASH Cirrhosis

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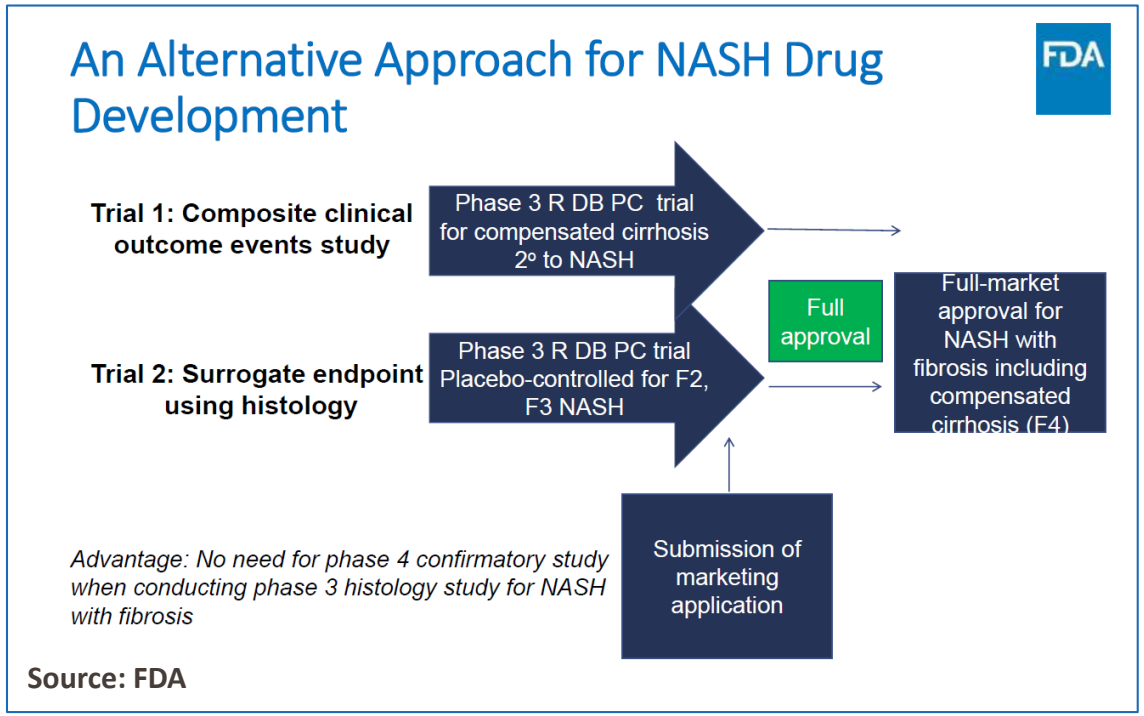
MAESTRO-NASH OUTCOMES: Leveraging An Alternative Approach to NASH Drug Development Proposed by FDA

- MAESTRO-NASH OUTCOMES was designed to leverage an "alternative approach" to NASH drug development outlined by FDA in a 2021 public webcast[1]
  - FDA stated that an outcome study in NASH cirrhosis patients can support full approval in noncirrhotic NASH
  - Madrigal met with FDA to confirm the strategy and study design

- The alternative approach has several advantages:
  - ✓ Enhances the **statistical power** of MAESTRO to assess clinical benefit, improving potential for success
  - ✓ May create a faster **path to full approval** since patients with cirrhosis are likely to reach outcomes faster
  - ✓ Could **expand the future resmetirom label** to include patients with compensated NASH cirrhosis, a substantial population with very high unmet need

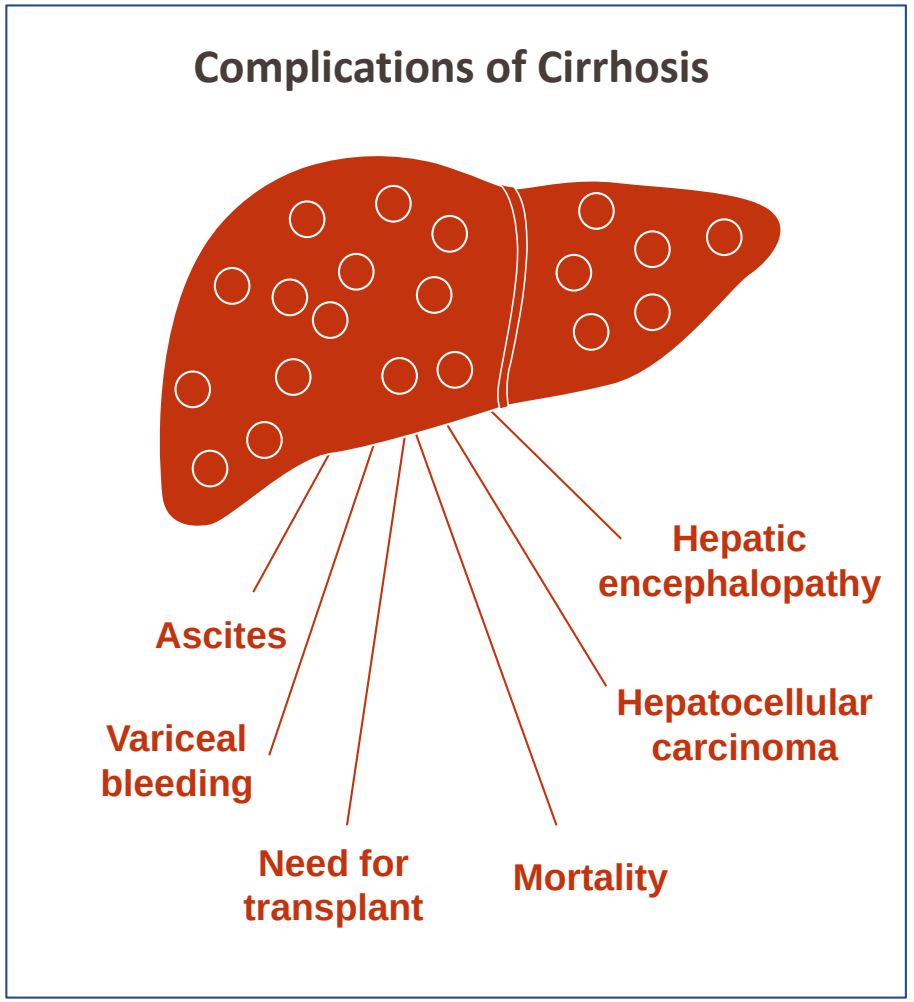
FDA Webcast: Regulatory Perspectives for Development of Drugs for Treatment of NASH



1. FDA Webcast. "Regulatory Perspectives for Development of Drugs for Treatment of NASH." January 29, 2021. Available at https://www.fda.gov/drugs/news-events-human-drugs/regulatory-perspectives-development-drugs-treatment-nash-01292021-01292021.

MAESTRO-NASH OUTCOMES Carries Potential to Unlock Opportunity in Compensated NASH Cirrhosis

- If successful, MAESTRO-NASH OUTCOMES carries the potential to expand the eligible population for resmetirom to include patients with compensated NASH cirrhosis
  - Of the estimated 2 million patients with NASH cirrhosis in the U.S., 85% are believed to be compensated[1,2]
- There is a higher urgency to treat patients with cirrhosis because of their elevated risk of developing serious and costly liver-related complications
  - Patients with cirrhosis are at 105x higher risk of liver-related morbidity compared to those without fibrosis[3]
  - Patients with cirrhosis account for >80% of annual direct medical costs in NASH[4]
- We believe the first NASH medication to demonstrate benefit in preventing or delaying complications of cirrhosis will have a substantial competitive advantage



1. Estes C et al. Hepatology. 2018;67(1):123-133. 2. GBD 2017 Cirrhosis Collaborators. Lancet Gastroenterol Hepatol. 2020 Mar;5(3):245-266. 3. Hagström H et al. Journal of Hepatology. 2017;67:1265-1273.
4. Younossi ZM et al. Hepatology. 2016;64(5):1577-1586.

Establishing Resmetirom as a Foundational Therapy for NASH

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Madrigal is Working to Establish Resmetirom as a Foundational Therapy for Patients with NASH

NASH: An Attractive Therapeutic Market with No Approved Treatment

- High and growing prevalence; sizable patient population already identified
- Providers, patients and payers see high unmet medical need

Resmetirom: Potential to Become a Foundational Treatment for NASH

- Positive interim Phase 3 results indicate potential for resmetirom to address key goals for treatment
- Resmetirom development program is supported by two ongoing outcomes studies

Madrigal: Well Positioned for Long-Term Growth

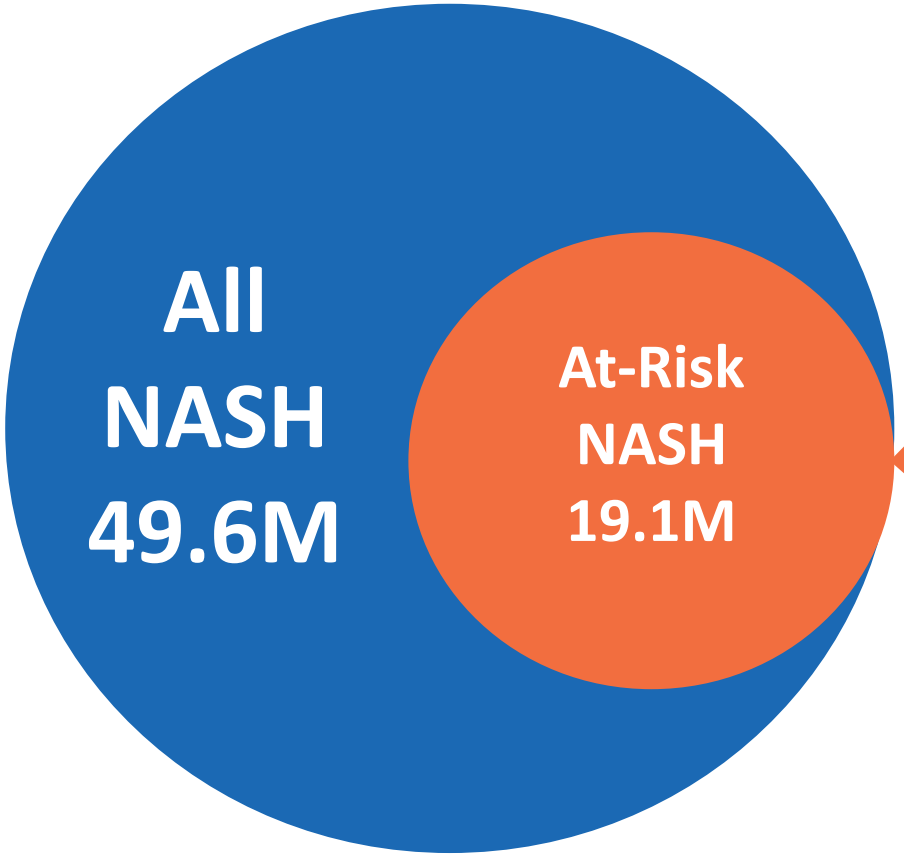
- Compelling opportunity for resmetirom in Europe and key international markets beyond the US, if approved
- Market can grow with improved awareness, education and screening
- Potential future label expansion in NASH with compensated cirrhosis*

*If the ongoing MAESTRO-NASH OUTCOMES study demonstrates resmetirom can improve outcomes in patients with compensated NASH cirrhosis

The Long-Term Global Market Opportunity for Resmetirom is Driven By Unmet Need for Therapies that Address At-Risk NASH

2030: Projected NASH Prevalence in Key Markets[1]

U.S., Germany, France, U.K., Italy, Spain, Japan



Patients with At-Risk NASH Represent the Intended Population for Rx Treatment

- **Clinician urgency-to-treat** is higher because patients are at elevated risk of progressing to cirrhosis
- **Treatment guidelines** recommend referral of patients with at-risk NASH to specialists[2]
- **Regulatory guidance** documents from FDA and EMA focus on patients with at-risk NASH[3,4]
- **The MAESTRO-NASH trial** recruited patients with at-risk NASH (F3 ~60%, F2 ~35%)

1. Estes C, et al. Hepatology. 2018:67(1):123-33. 2. Kanwal F et al. Gastroenterology. 2021 Nov;161(5):1657-1669. 3. FDA Draft Guidance. 2018. 4. EMA Draft Reflection Paper. 2018.

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Market Research Indicates Healthcare Providers, Patients and Payers Understand the Potential of Resmetirom

Resmetirom Target* Product Profile

- ✓ Efficacy in resolving NASH and improving fibrosis
- ✓ Favorable emerging safety profile
- ✓ Well-tolerated
- ✓ Lowers LDL-C
- ✓ Once-daily oral medication

Healthcare Providers: ~85% of physicians see resmetirom as offering high clinical utility, based on the product profile[1]

Patients: ~75% of patients would be very to extremely likely to try resmetirom if approved and cost was not an issue[2]

Payers: ~90% of interviewed payers viewed the resmetirom profile favorably, identifying its success in meeting both FDA-approved endpoints, its safety and tolerability, and the high level of unmet need in NASH as key drivers of their enthusiasm[3]

* The Target Product Profile is consistent with results from the Phase 3 studies of resmetirom. but was used in market research and developed before the availability of the MAESTRO-NASH phase 3 biopsy study results. If resmetirom is approved by FDA, the approved product labeling may not be consistent with the Target Product Profile used in market research. Phase 3 studies of resmetirom in NASH are ongoing and the final results of these studies are not expected to be available until 2025-2026.

1. HCP Conjoint Research, US/EU5, n= 360 HCPs, Clearview Q4 2022. 2. NASH Patient Research, US, n= 140 patients, Clearview Q3 2021. 3. Payer Research, US, n= 24 payers, Clearview Q1 2023

The Resmetirom Launch Strategy Focuses on Patients with NASH with At-Risk NASH Who Are Managed by Liver Specialists

Identified Patient Population

~1,300,000 patients with NASH in the U.S. have already been identified and ICD-10 coded

- A subset of these coded patients – those with at-risk NASH – could be early candidates for resmetirom, if approved

NASH Specialist Audience

~15,000 – 20,000 NASH Specialists make up the target universe of healthcare providers for the initial launch of resmetirom in the U.S.

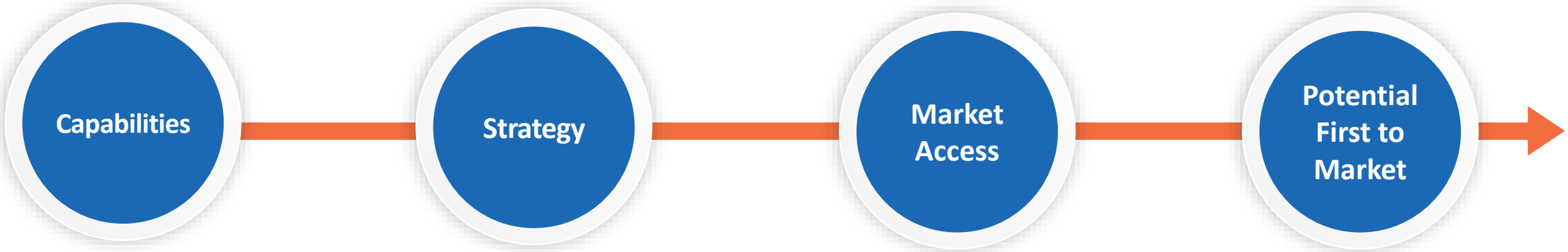
- Includes hepatologists, gastroenterologists and endocrinologists who manage patients with NASH

Specialty Field Team and Patient Services

~200 field team members are needed to reach NASH specialists in the U.S.

- Commercial infrastructure will include a specialty pharmacy network and extensive patient services to support access, medication initiation and adherence

U.S. Launch Preparation Is Expanding, with a Focus on Educating Healthcare Providers, Patients and Payers



- Commercial Leadership Team in Place
- Building infrastructure and organization in the U.S. with focus on Medical Affairs, Market Access, Data/Analytics, Marketing
- Field team to expand in H2 2023

- Clear product positioning and comprehensive launch strategy driven by extensive market research and secondary data analytics
- Support physicians in identification of priority patients via noninvasive tests

- Extensive payer education
- Health Economics evidence generation to support access for labeled patient population
- Specialty product distribution network with robust prescriber and patient support

PLANNED LAUNCH
2024

INITIALLY TARGET
15–20K Hepatologists/ Gastroenterologists, Endocrinologists, and their associated NPs/PAs

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MAESTRO-NASH OUTCOMES Has the Potential to Expand the Resmetirom Market Opportunity to Include Patients with Compensated NASH Cirrhosis

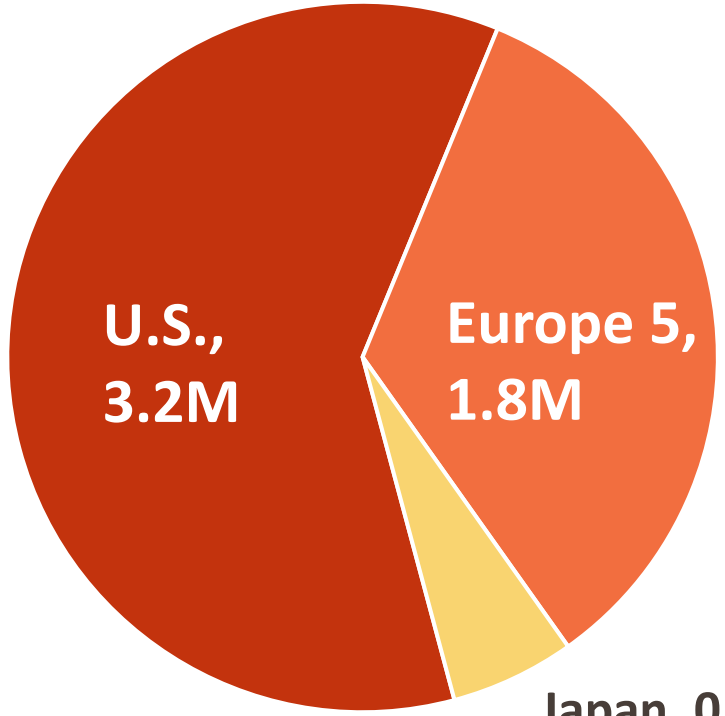
Unmet Need

- NASH Specialists recognize the high unmet need and potential for resmetirom in compensated NASH cirrhosis[1]
  - Unmet need is seen as higher because patients are on the edge of negative liver outcomes

MAESTRO-NASH OUTCOMES Opportunity

- If MAESTRO-NASH OUTCOMES is successful, the resmetirom label could expand to include patients with compensated NASH cirrhosis
  - Market research indicates the "halo effect" of positive outcomes data in compensated NASH cirrhosis could increase willingness to prescribe resmetirom in the precirrhotic at-risk NASH population[2]

2030: Projected Compensated NASH Cirrhosis Prevalence in Key Markets[3]



1. US HCP Compensated Cirrhosis Opportunity Primary Market Research (Hep/GI n=112); 2Q2022; 2. Compensated Cirrhosis Market Landscape Research, US, n=112 HCPs, n= 10 payers, Clearview Q3 2022. 3. Estes C, et al. Hepatology. 2018:67(1):123-33

Resmetirom is Well Positioned for Long-Term Growth as the Global Burden of NASH Increases

Madrigal believes the commercial opportunity for resmetirom will grow substantially in the years following launch, driven by outcomes data, increased disease awareness and the global prevalence of NASH

2024 2025 2026 2027 2028 2029 2030+

Specialty Launch

- U.S. launch will focus on 'NASH Specialists' who already manage patients with **at-risk NASH**
  - We estimate that a sizeable number of patients have already been identified and ICD-10 coded[1]
- Reimbursement in key European markets expected by mid-2020s

Potential Label Expansion

- Positive MAESTRO-NASH-OUTCOMES data could support label expansion into **compensated NASH cirrhosis**, a patient population with high unmet need
- If successful, Madrigal believes resmetirom could be the first NASH medication to demonstrate improvement in outcomes

Market Evolution

- By the end of the decade, NASH may become a **primary care category**, driven by:
  - Improved disease awareness
  - Evolution of NITs for screening and diagnosis
  - Growing global prevalence of NASH fueled by Western lifestyle

1. Forian Data; Madrigal and ClearView Analysis.

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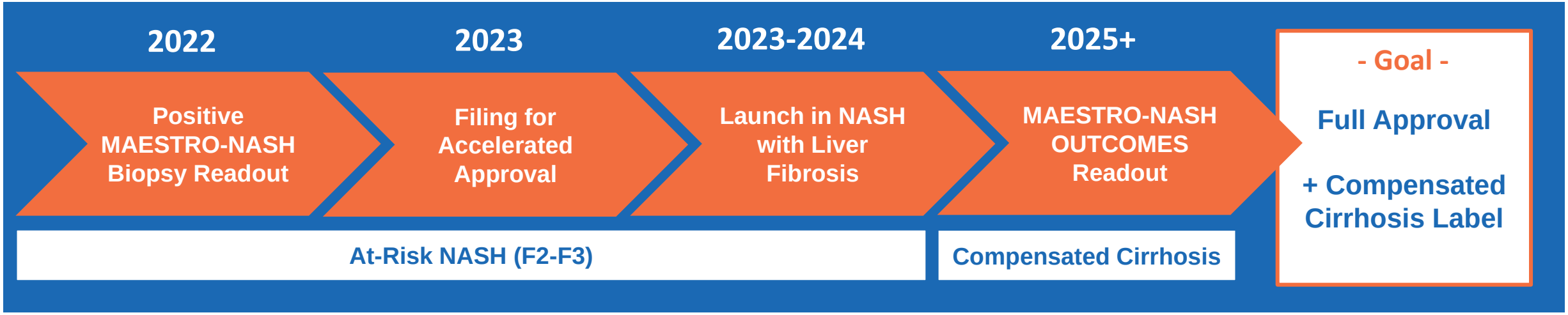
Based on Available Data, We Believe Resmetirom Has the Potential to Transform the Treatment of NASH

- ✓ **Meaningful efficacy** that targets key underlying causes of NASH in the liver
  - Resmetirom achieved both NASH resolution and fibrosis improvement primary endpoints in a Phase 3 trial
  - Resmetirom helped patients achieve improvements in noninvasive tests used to measure efficacy in real world clinical practice
- ✓ **Favorable safety profile** in studies conducted to date; large safety database to support regulatory review
- ✓ **Robust development program** with four Phase 3 studies designed to support accelerated approval and demonstrate long-term benefit on clinical outcomes



Appendix

Q2 2023 Financial Summary

Cash, cash equivalents and marketable securities at June 30, 2023	$298.4M
Operating expenses Q2 2023	$164.8M
R&D expenses Q2 2023	$130.8M
Cash burn[1] Q2 2023	$159.4M

	Total Facility	Available
ATM	$200.0M	$177.6M
Long Term Debt	$250.0M	$150.0M[2]

1. Cash burn represents net cash used in operating activities
2. Available in three defined tranches: $15M clinical tranche remains available and committed by Hercules, $75M tranche available upon FDA approval, $60M tranche available at Hercules discretion

Guide to Acronyms and Abbreviations

AE, adverse event
ALT, alanine transaminase
ApoB, apolipoprotein B
AST, aspartate aminotransferase
ATP, adenosine triphosphate
CAP, controlled attenuation parameter
CFB, change from baseline
CMH, Cochran-Mantel-Haenszel
CVD, cardiovascular disease
DB, double-blind
DILI, drug-induced liver injury
DNL, de novo lipogenesis
FAO, fatty acid oxidation
FFA, free fatty acid
GGT, gamma-glutamyl transferase
GI, gastrointestinal
GLP, glucagon-like peptide-1 receptor agonist
HCC, hepatocellular carcinoma
HCP, healthcare provider
HDL, high-density lipoprotein
ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
LDL, low-density lipoprotein
LT, liver transplantation
LSM, liver stiffness measurement
MACE, major adverse cardiovascular event
MELD, model for end-stage liver disease
MRE, magnetic resonance elastography
MRI-PDFF, magnetic resonance imaging-proton density fat fraction
NAFL, nonalcoholic fatty liver
NAFLD, nonalcoholic fatty liver disease
NAS, NAFLD activity score
NASH, nonalcoholic steatohepatitis
NP, nurse practitioner
OL, open-label
PA, physician assistant
PDFF, proton density fat fraction
SAE, serious adverse event
SD, standard deviation
TAG, triacylglycerol
TCA, tricarboxylic acid
TEAE, treatment-emergent adverse event
TG, triglycerides
THR, thyroid hormone receptor
VCTE, vibration-controlled transient elastography
VLDL, very low-density lipoprotein
WL, weigh loss

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