Madrigal Pharmaceuticals

Corporate Presentation

August 2022

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).

NASDAQ: MDGL

Forward Looking Statement

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 our beliefs and assumptions and on information currently available to us, but are subject to factors beyond our control. Forward-looking statements include but are not limited to statements or references concerning: anticipated or estimated future results, including the risks and uncertainties associated with our future operating performance and financial position; our possible or assumed future results of operations and expenses, business strategies and plan (including ex-US. Launch/partnering plans), including incurrence of indebtedness and compliance with debt covenants under the Loan and Security Agreement with Hercules Capital, Inc., as agent and lender, market trends, market sizing, competitive position, industry environment and potential growth opportunities, among other things; our ability to delay certain research activities and related clinical expenses as necessary; our clinical trials, including the anticipated timing of disclosure, presentations of data from, or outcomes from our trials; research and development activities, and the timing and results associated with the future development of our lead product candidate, resmetirom (formerly known as MGL-3196), including projected market size, sector leadership, and patient treatment estimates for NASH and NAFLD patients; the timing and completion of projected future clinical milestone events, including enrollment, additional studies, top-line data and open label projections; plans, objectives and timing 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 for noncirrhotic NASH patients with compensated cirrhosis; our primary and key secondary study endpoints for resmetirom and the potential for achieving such endpoints and projections, including NASH resolution, safety, fibrosis treatment, cardiovascular effects, and lipid treatment with resmetirom; 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; the potential efficacy and safety of resmetirom for noncirrhotic NASH patients and cirrhotic NASH patients; the potential for resmetirom to become the best-in-class and/or first-to-market treatment option for patients with NASH and liver fibrosis; anticipated or estimated future results of operations and expenses as we expand our resmetirom clinical development program and our commercial development program; ex-U.S. launch/partnering plans; the ability to develop clinical evidence demonstrating the utility of noninvasive tools and techniques to screen and diagnose NASH and/or NAFLD patients; the predictive power of liver fat reduction with resmetirom, as measured by noninvasive tests, on NASH resolution and/or fibrosis reduction or improvement, and potential NASH or NAFLD patient risk profile benefits with resmetirom; the predictive power of liver fat, liver volume changes or MAST scores for NASH and/or NAFLD patients; the predictive power of NASH resolution and/or liver fibrosis reduction or improvement with resmetirom using noninvasive tests, including the use of ELF, FibroScan, MRE and/or MRI-PDFF; the predictive power of noninvasive tests generally, including for purposes of diagnosing NASH, monitoring patient response to resmetirom, or recruiting and conducting a NASH clinical trial; market demand for and acceptance of our products; research, development and commercialization of new products; obtaining and maintaining regulatory approvals, including, but not limited to, potential regulatory delays or rejections; risks associated with meeting the objectives of our clinical studies, including, but not limited to our ability to achieve enrollment objectives concerning patient numbers (including an adequate safety database), outcomes objectives and/or timing objectives for our studies, any delays or failures in enrollment, the occurrence of adverse safety events, and the risks of successfully conducting trials that are substantially larger, and have patients with different disease states, than our past trials; risks related to the effects of resmetirom’ s mechanism of action and our ability to accomplish our business and business development objectives and realize the anticipated benefit of any such transactions; the achievement of enrollment objectives concerning patient number, safety database and/or timing for our studies; and assumptions underlying any of the foregoing.

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Forward Looking Statement (cont'd)

Forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events; include all statements that are not historical facts; and can be identified by terms such as "accelerate," "achieve," "allow," "anticipates," "appear," "be," "believes," "can," "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: our clinical development of resmetirom; enrollment and trial conclusion uncertainties, generally and in relation to COVID-19 related measures and individual precautionary measures that may be implemented or continued for an uncertain period of time; our potential inability to raise sufficient capital to fund our ongoing operations as currently planned or to obtain financings on terms similar to those we have arranged in the past; our ability to service our indebtedness and otherwise comply with our 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 our prior studies; limitations associated with early stage or non-placebo controlled study data; 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 or furnished with the U.S. Securities and Exchange Commission 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. We specifically discuss these risks and uncertainties in greater detail in the section appearing in Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on February 25, 2022, as updated by the risk factors discussed in Part II, Item 1A of the Quarterly Report on Form 10-Q filed with the SEC on May 9, 2022, as well as in our other filings with the SEC.

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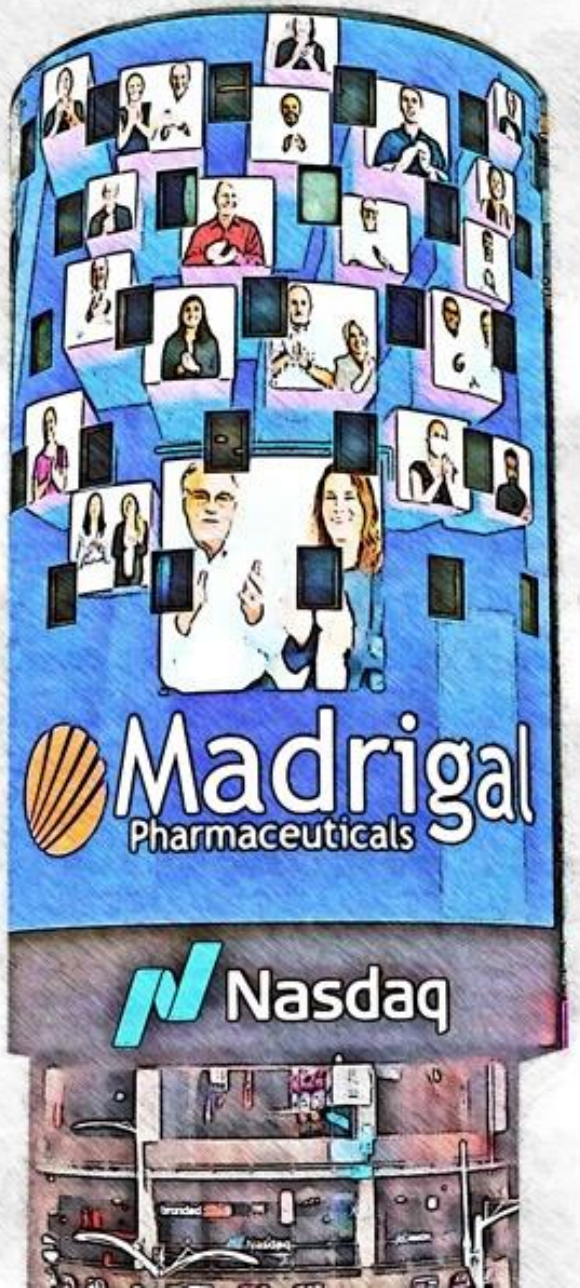

Madrigal is a clinical-stage biopharmaceutical company pursuing novel therapeutics for NASH, a liver disease with high unmet medical need

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Pharmaceuticals

Introduction to Madrigal

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

- **Resmetirom**, Madrigal's lead product candidate, is designed to target key underlying causes of NASH in the liver
  - Positive Phase 3 safety data and secondary endpoints were announced in January 2022
  - Topline data from pivotal Phase 3 trial expected in Q4 2022

- **Our commercial strategy** focuses on launching resmetirom as a specialty medication for NASH patients with significant liver fibrosis
  - Madrigal to commercialize in the US and will partner in ex-US territories

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

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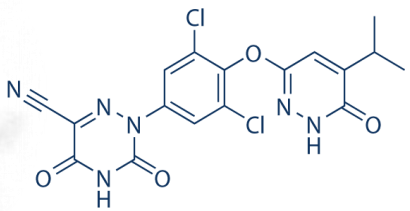
The Madrigal Story

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

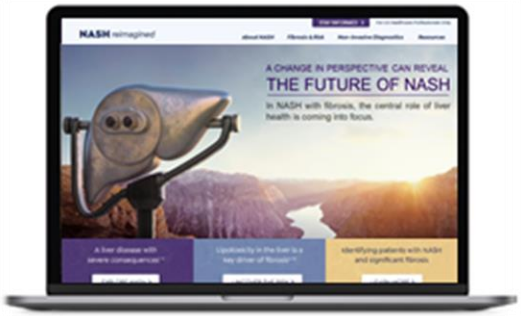
2011: Madrigal is incorporated in Delaware

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: Madrigal hires Remy Sukhija as Chief Commercial Officer and begins building its commercial organization

2021: Madrigal expands executive team with additional experienced leaders

2022: Positive Phase 3 MAESTRO-NAFLD-1 resmetirom data announced

NASH is a Liver Disease with Severe Consequences

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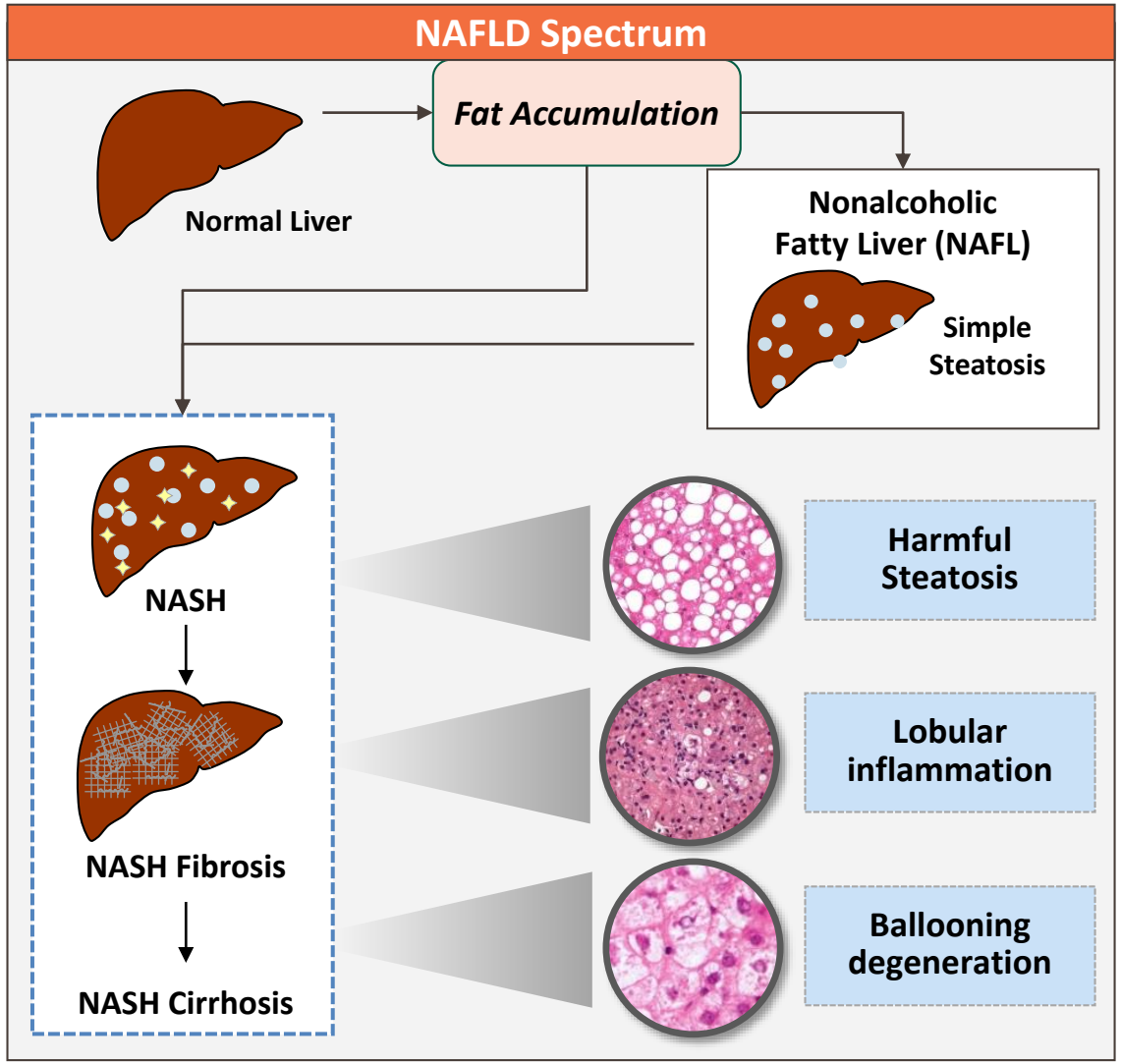
NASH – A Liver Disease with Severe Consequences



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 ~22 million people in the U.S. are living with NASH[1-3]
  - Of those, 8 million people are likely to have significant fibrosis (F2-F3)[1]
  - An estimated 2 million people in the U.S. may have NASH cirrhosis[1]

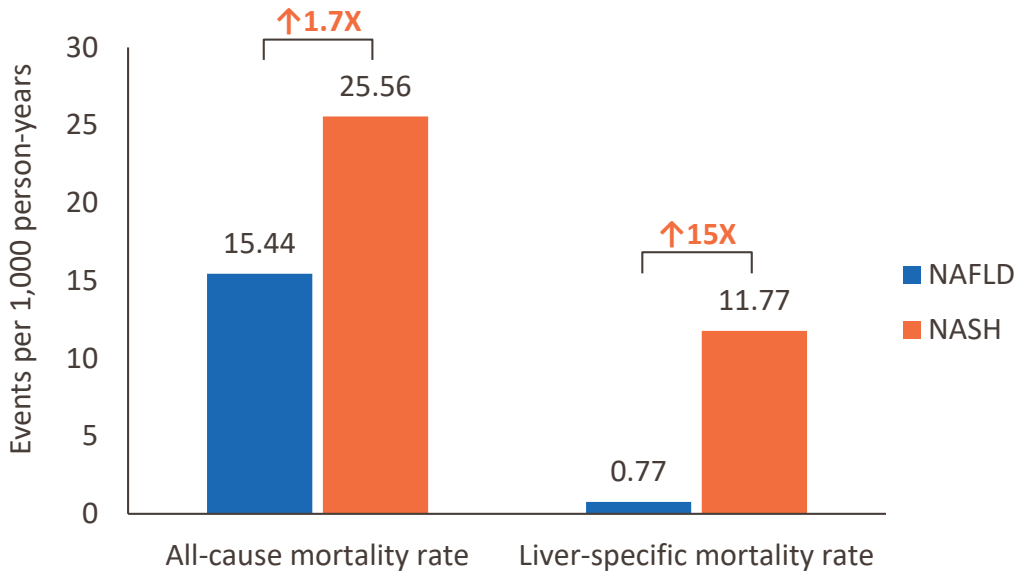
OUTCOME

- ~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]

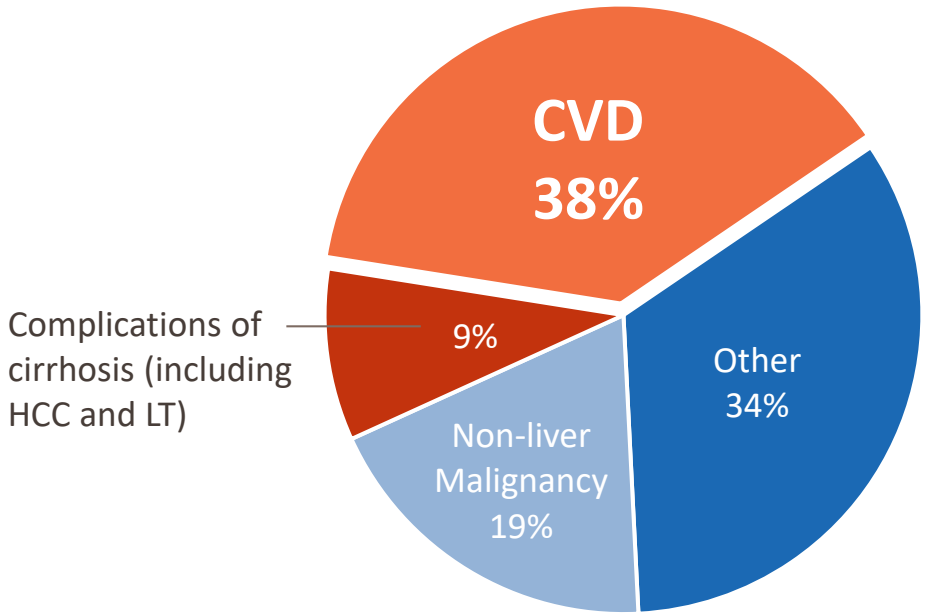
1. Estes C, Razavi H, Loomba R, Younossi Z, Sanyal AJ. Hepatology. 2018;67(1):123-133. 2. Hardy T, Oakley F, Anstee QM, Day CP. Annu Rev Pathol. 2016;11:451-496. 3. Rinella MA, Lominadze Z, Loomba R, et al. Ther Adv Gastroenterol. 2016;9(1):4-12. 4. Loomba R, Adams L. Hepatology. 2019;70(6):1885-1888.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



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



CV, cardiovascular; CVD, cardiovascular disease; HCC, hepatocellular carcinoma; LT, liver transplantations

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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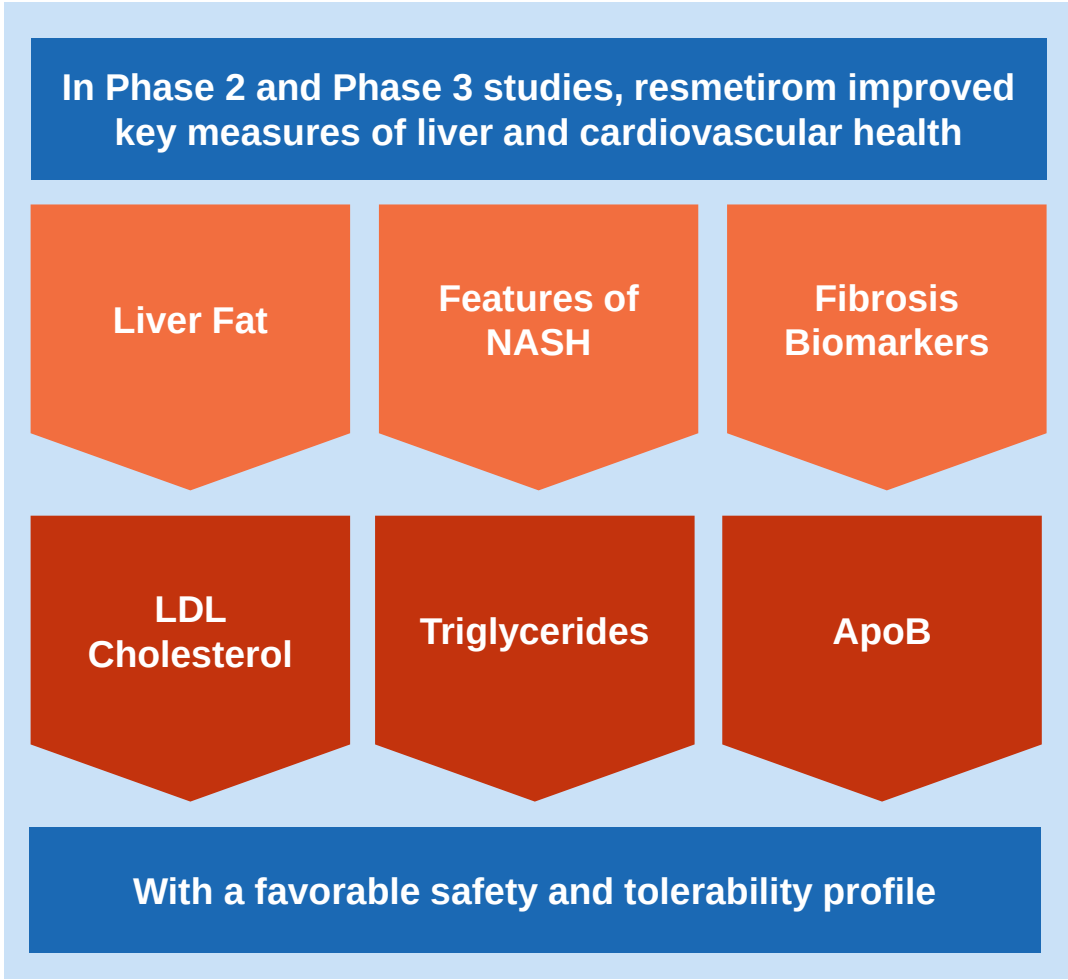
Resmetirom for the Treatment of NASH with Significant Fibrosis

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 two Phase 3 trials[1], with a pivotal biopsy readout in Q4 2022

Resmetirom has the potential to become the first medication approved for the treatment of patients with NASH

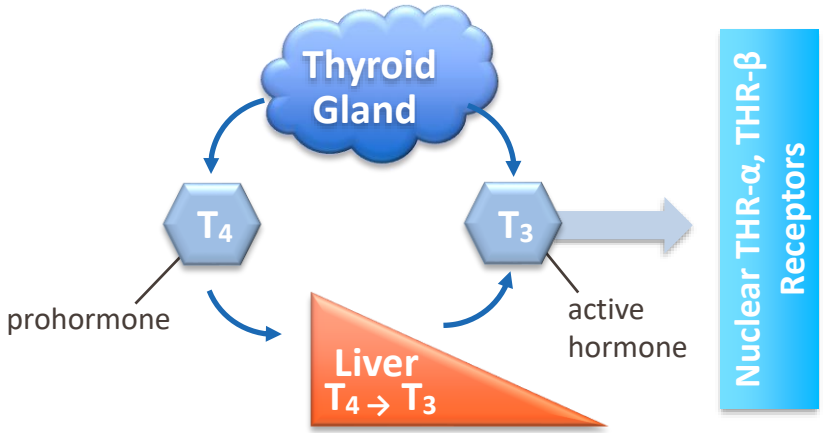


LDL, low-density lipoprotein; ApoB, Apolipoprotein B

1. ClinicalTrials.gov NCT03900429, NCT04197479

The Mechanism of Action of Resmetirom Targets Key Features of NASH

MoA: importance of liver THR_β in NASH[1-3]



Thyroid hormone pathway

In humans, THR_β agonism:[3,4]

- Lowers liver fat, potentially reducing lipotoxicity, NASH
- Reduces fibrosis biomarkers
- Lowers triglycerides, LDL, ApoB
- *No thyrotoxicosis (**THR_α effect**)*

Resmetirom is a liver-directed, THR_β selective agonist[3,5,6]

THR_β selective liver targeted molecule, administered once a day

No exposure outside the liver or activity at the systemic THR_α

Resmetirom decreases rT3 levels and increases the fT3/rT3 ratio

Patients treated with resmetirom showed a correction of endogenous hepatic thyroid hormone activity

Pleiotropic effects with potential for addressing the underlying metabolic syndrome and hallmark features of NASH: steatosis/lipotoxicity, inflammation, ballooning, and fibrosis (both directly and indirectly)

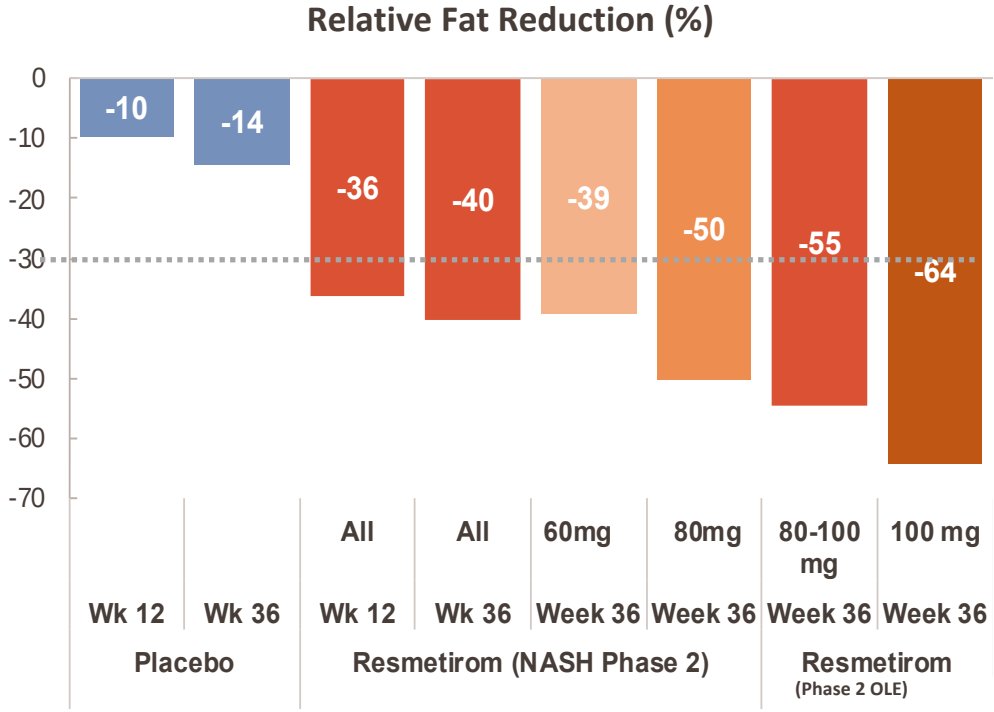
Reduction of liver fat through breakdown of fatty acids, and normalization of mitochondrial and liver function

fT3, free T3 (active); MoA, mechanism of action; rT3, reverse T3 (inactive); T3, triiodothyronine; T4, thyroxine; THRα/β, thyroid hormone receptor α/β.

1. Sinha RA, et al. *Autophagy*. 2015;11(8):1341-57; 2. Sinha RA, Yen PM. *Cell Biosci*. 2016;6:46; 3. Taub R, et al. Poster presented at NASH-TAG, January 9-11 2020; 4. Loomba, et al. Oral presentation AS077. Presented at ILC 2020; 5. Taub R, et al. Poster #1969 presented at AASLD 2017; 6. Harrison SA, et al. *Hepatol Commun*. 2021;0:1-16. Figure adapted from Taub R, et al. Poster presented at NASH-TAG, January 9-11 2020.

Successful Proof-of-Concept in Phase 2 Guided Madrigal's Strategy for the Phase 3 MAESTRO Program

- **Primary endpoint achieved:** Relative reduction in hepatic fat on MRI-PDFF at Week 12[1]
  - Dose dependent 50% reduction of hepatic fat at 80 mg dose
- **Key secondary and exploratory endpoints achieved:** Significant reductions in resolution of NASH, fibrosis biomarkers, liver enzymes, LDLc, ApoB, triglycerides and lipoprotein(a)[2]
- **Safety:** No change in Grade 2 or higher AEs and no safety signals related to mechanism of action
- **Fat reduction correlated with histologic improvement:** Resmetirom PDFF response correlated with NASH resolution and fibrosis reduction as measured by biopsy
- **Health-related quality of life:** Improved in patients who achieved reductions in PDFF and/or NAFLD Activity Score[3]



Resmetirom responders with ≥ 30% PDFF reduction had higher rates of NASH resolution (37%) on Week 36 liver biopsy compared to non-responders (4%)—hypothesis generating

MRI-PDFF, magnetic resonance imaging proton density fat fraction; OLE, open label active extension study; AE, adverse event

1. Harrison SA et al. Lancet. 2019 Nov 30;394(10213):2012-2024. 2. Harrison SA et al. Hepatol Commun. 2021 Jan 4;5(4):573-588. 3. Younossi ZM et al. Clin Gastroenterol Hepatol. 2021 Jul 27;S1542-3565(21)00821-1.

Overview of the MAESTRO Phase 3 Program

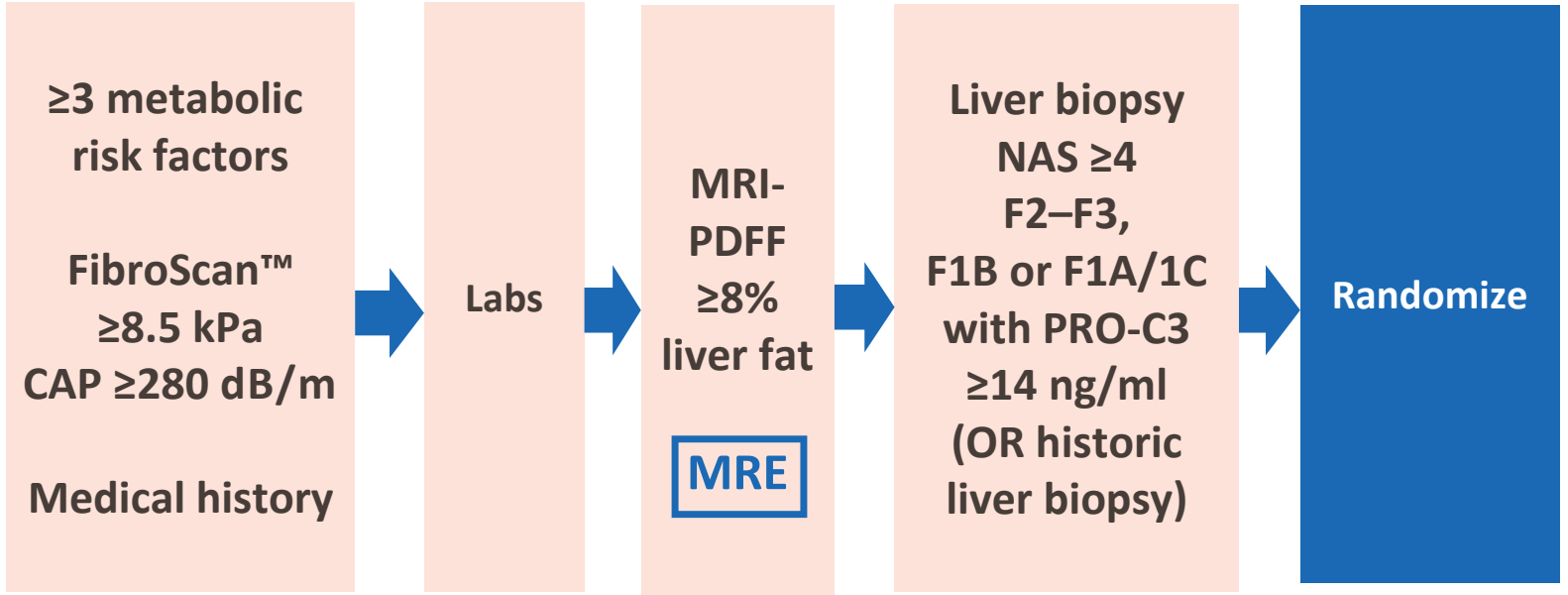
	MAESTRO-NAFLD-1 Safety Study	MAESTRO-NASH Biopsy Study	MAESTRO-NASH Outcomes Study
Primary Objective	To evaluate **safety and tolerability** as measured by incidence of adverse events at 52 weeks	To evaluate **improvement in histology*** at 52 weeks; study continues on to measure outcomes	To evaluate **progression to decompensation** events noninvasively
Patient Population	Over 1,200 patients with **presumed NASH**, identified noninvasively	~2,000 patients with NASH with **significant fibrosis** (Subpart H population = ~900)	~700 patients with NASH with **compensated cirrhosis**
Timeline	Positive results announced in **January 2022** Open-label extension ongoing	Biopsy results for Subpart H population expected **Q4 2022** Outcomes portion of trial is event-driven (est. 2026-27)	Trial is **event-driven** Estimated to reach outcomes 2025-26 (likely before MAESTRO-NASH Biopsy study)

*The dual primary surrogate endpoints on biopsy are NASH resolution, with at least a 2-point reduction in NAS (NASH Activity Score), and with no worsening of fibrosis OR a one point decrease in fibrosis with no worsening of NASH. Either primary endpoint can be achieved for a successful trial outcome.

The Phase 3 MAESTRO Screening Algorithm Successfully Identified Patients with NASH with Significant Fibrosis

Risk factors for NASH
Age >50
BMI >30
T2DM
Hypertension
Dyslipidemia
Metabolic syndrome
FibroScan VCTE ≥8.5 kPa CAP >280 dB/m

MAESTRO, 8 Week screening process



Metabolic risk factors and screening FibroScans were used to identify patients for both MAESTRO trials

- A lower VCTE threshold was used for MAESTRO-NAFLD-1 compared to MAESTRO-NASH with no liver biopsy
- An MRE was obtained in more than half of the patients, and was not used as an eligibility criterion

Using this screening paradigm, about 80% of screened MAESTRO-NASH patients have had NASH with significant fibrosis on liver biopsy

BMI, body mass index; T2DM, type 2 diabetes mellitus; VCTE, vibration-controlled transient elastography; CAP, controlled attenuation parameter; MRE, magnetic resonance elastography; NAS, NAFLD Activity Score; PRO-C3, the pro-peptide of type lll collagen

MAESTRO-NAFLD-1
Study Results

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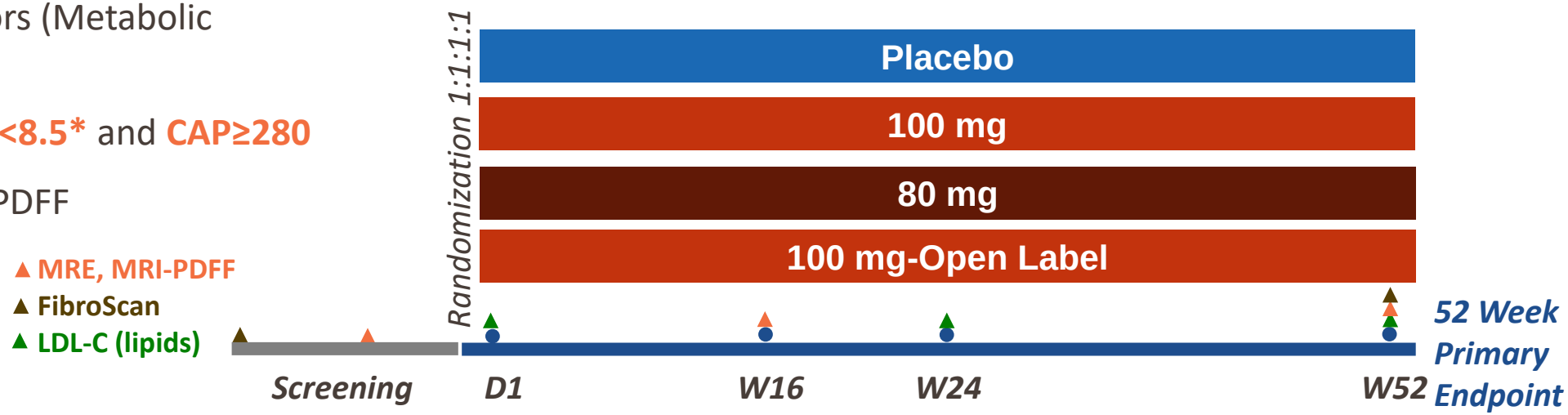
Phase 3 MAESTRO-NAFLD-1 (presumed NASH) Study Design: Randomized, Double-Blind, PBO Controlled with 100 mg Open Label Arm

Inclusion/Exclusion

- ≥3 metabolic risk factors (Metabolic Syndrome)
- FibroScan **kPa ≥ 5.5 & <8.5*** and **CAP≥280**
- **≥8 % liver fat** on MRI-PDFF



- 1143 presumed NASH patients enrolled in the U.S. (~80 sites)
  - 972 randomized to double-blind arms
  - 171 open label patients (recruitment completed July 1, 2020)

A "Real-life" NASH Study with Noninvasive Monitoring of Patient Response

*except at sites not participating in MAESTRO-NASH where FibroScans ≥ 5.5 kPa (no upper limit) were allowed; includes MAESTRO-NASH patients who screen fail at the biopsy stage

Positive Phase 3 MAESTRO-NAFLD-1 Results Announced in January 2022

Primary and key secondary endpoints from the double-blind placebo-controlled Phase 3 MAESTRO-NAFLD-1 safety study were achieved:

- ✓ Resmetirom met the primary safety endpoint and was well-tolerated in patients treated for 52 weeks
- ✓ Resmetirom met key secondary endpoints by providing significant and clinically relevant reductions in liver fat and significantly reducing atherogenic lipids, including LDLc, ApoB and triglycerides

Stephen Harrison, M.D., Principal Investigator of the MAESTRO studies

*"**This positive readout from MAESTRO-NAFLD-1 is a significant milestone for the field.** As the first Phase 3 study in NASH that does not rely on liver biopsy to identify patients and measure treatment response, MAESTRO-NAFLD-1 will help accelerate the role of noninvasive imaging and biomarkers in NASH drug development. We see a safety and tolerability profile for resmetirom in this study of nearly one thousand patients treated for 52 weeks that, similar to earlier studies, leads to very low adverse event discontinuation rates."*

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Safety Double-Blind Arms

Safety population	Resmetirom 80 mg n=327	Resmetirom 100 mg n=324	Placebo n=318
At least one TEAE	**289 (88.4)**	**279 (86.1)**	**260 (81.8)**
Grade 1	99 (30.3)	99 (30.6)	92 (28.9)
Grade 2	164 (50.2)	151 (46.6)	139 (43.7)
TEAE ≥ Grade 3 Severity	25 (7.6)	29 (9.0)	29 (9.1)
Related TEAE >= Grade 3 Severity	1(0.3)	1(0.3)	2 (0.6)
At least one Serious TEAE	**20 (6.1)**	**24 (7.4)**	**20 (6.3)**
AE discontinuations from study	**8 (2.4)**	**9 (2.8)**	**4 (1.3)**
Related AE discontinuations from study	**5 (1.5)**	**6 (1.9)**	**3 (0.9)**
GI AE discontinuations from study	5 (1.5)	6 (1.9)	2 (0.6)

- In the 100 mg resmetirom open-label arm, 94% & 89% completed key efficacy endpoints at Weeks 24 & 52, respectively
- Drop-out rate due to AEs was 1.2%

TEAE (treatment-emergent adverse event)

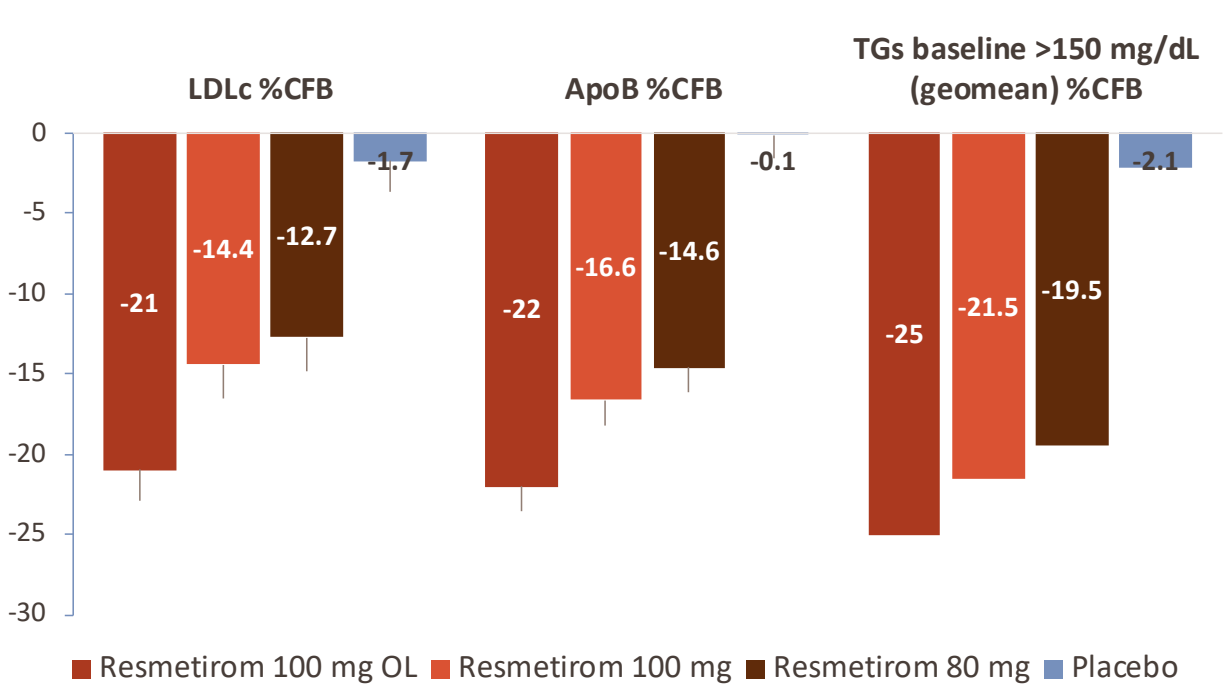
AEs ≥5% MAESTRO-NAFLD-1 Double-blind

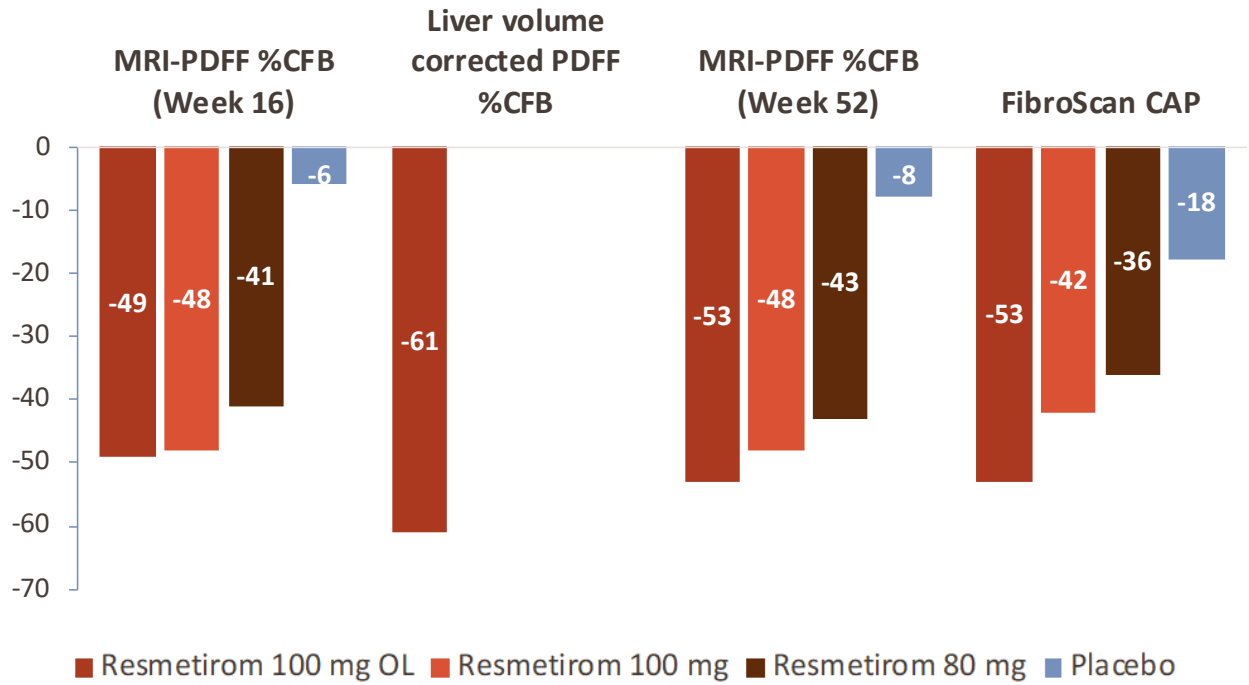
Preferred Term	80 mg N = 327	100 mg N = 324	Placebo N = 318	All N = 969
Diarrhea	77 (23.5)	101 (31.2)	44 (13.8)	222 (22.9)
Nausea	39 (11.9)	59 (18.2)	25 (7.9)	123 (12.7)
Abdominal pain	14 (4.3)	23 (7.1)	14 (4.4)	51 (5.3)
COVID-19	27 (8.3)	27 (8.3)	27 (8.5)	81 (8.4)
Urinary tract infection	21 (6.4)	20 (6.2)	23 (7.2)	64 (6.6)
Arthralgia	24 (7.3)	27 (8.3)	21 (6.6)	72 (7.4)
Pain in extremity	16 (4.9)	18 (5.6)	16 (5.0)	50 (5.2)
Back pain	17 (5.2)	18 (5.6)	14 (4.4)	49 (5.1)
Headache	22 (6.7)	27 (8.3)	24 (7.5)	73 (7.5)
Fatigue	21 (6.4)	15 (4.6)	13 (4.1)	49 (5.1)

- Most frequent AEs – GI Related (Diarrhea and Nausea) – Consistent with the Phase 2 study & MAESTRO-NAFLD-1 open-label arm, no increase in incidence of GI-related AEs after first 12 weeks of resmetirom treatment. Females had higher incidence of early nausea
- Consistent with Phase 2 data, minimal reduction in prohormone free T4 (due to liver effect) & no effect on active hormone free T3 or TSH; no increase in AEs associated with hyper or hypothyroidism

TSH, thyroid stimulating hormone

Key Secondary Endpoints

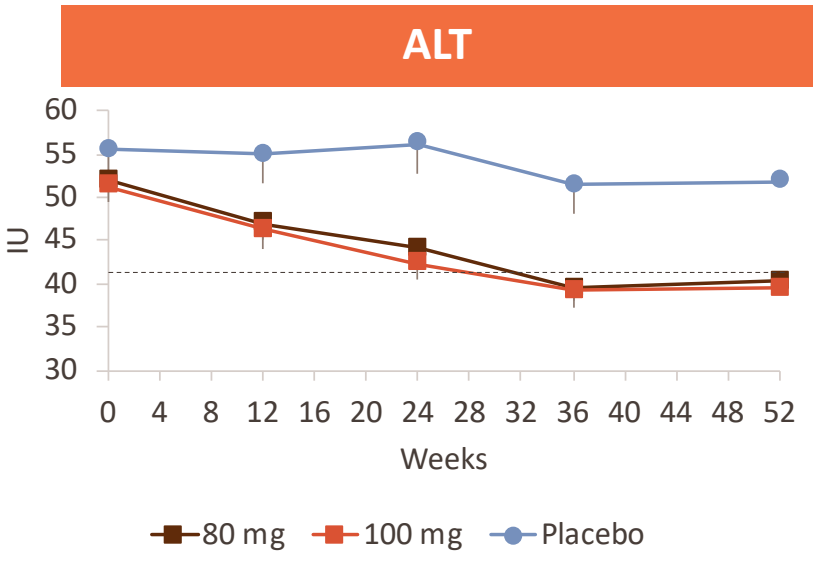


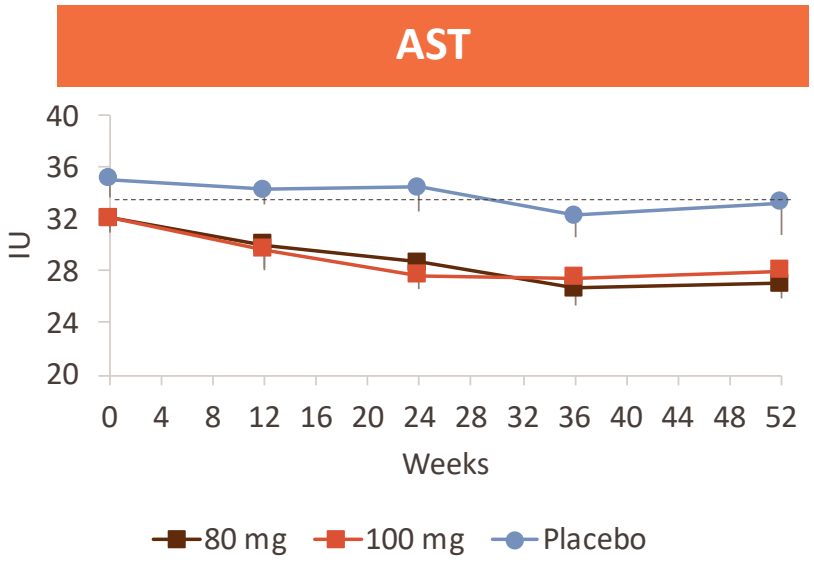


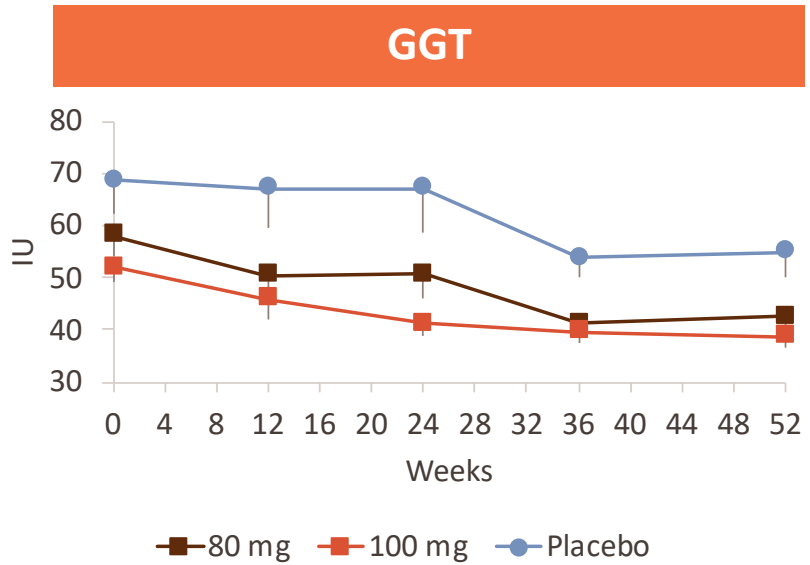
- Key secondary endpoints were achieved for both 80 and 100 mg dose groups ($p<0.0001$ for LDLc, ApoB, TGs, MRI-PDFF and CAP)
  - Lipid reductions were numerically greater in the 100 mg open label treatment arm compared to the 100 mg double-blind arm. Patients in the open-label active 100 mg treatment arm were not impacted by COVID-related dose interruptions (due to blister pack shortages) compared to double-blind patients
- MRI-PDFF reductions were robust even though some double-blind patients had COVID-related treatment interruptions prior to the Week 16 or 52 MRI-PDFFs

TGs, triglycerides; CFB, change from baseline

Liver Enzymes in the subgroup of patients with baseline ALT ≥30
80 mg (n=172) - 100 mg (n=164) - placebo (n=159)





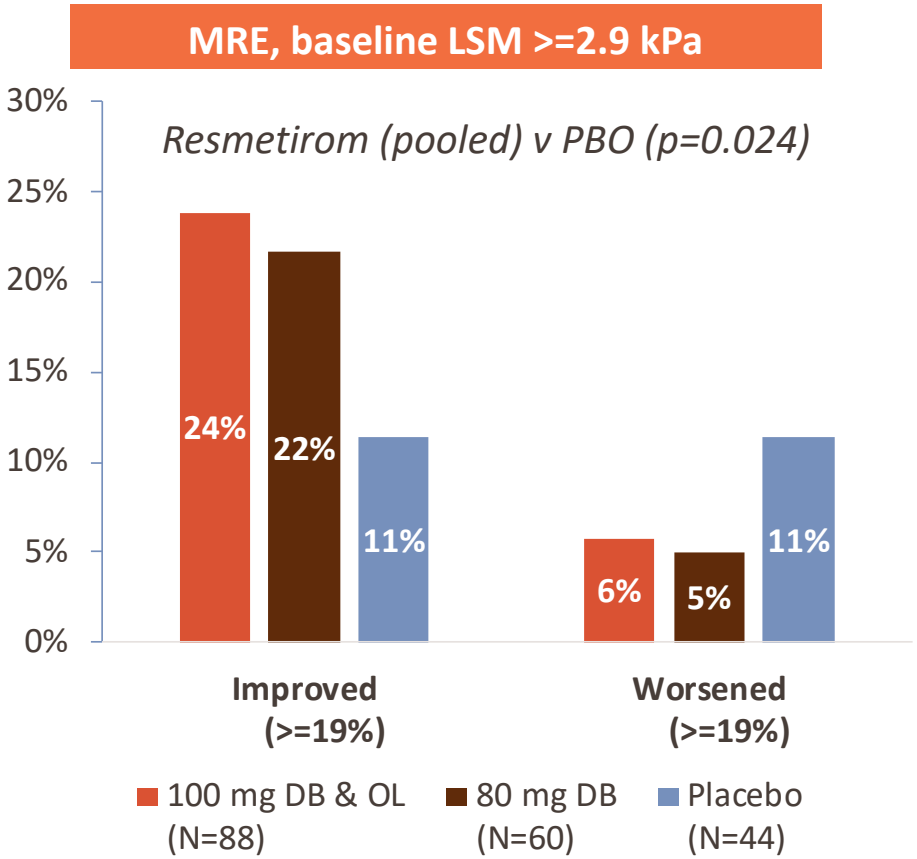


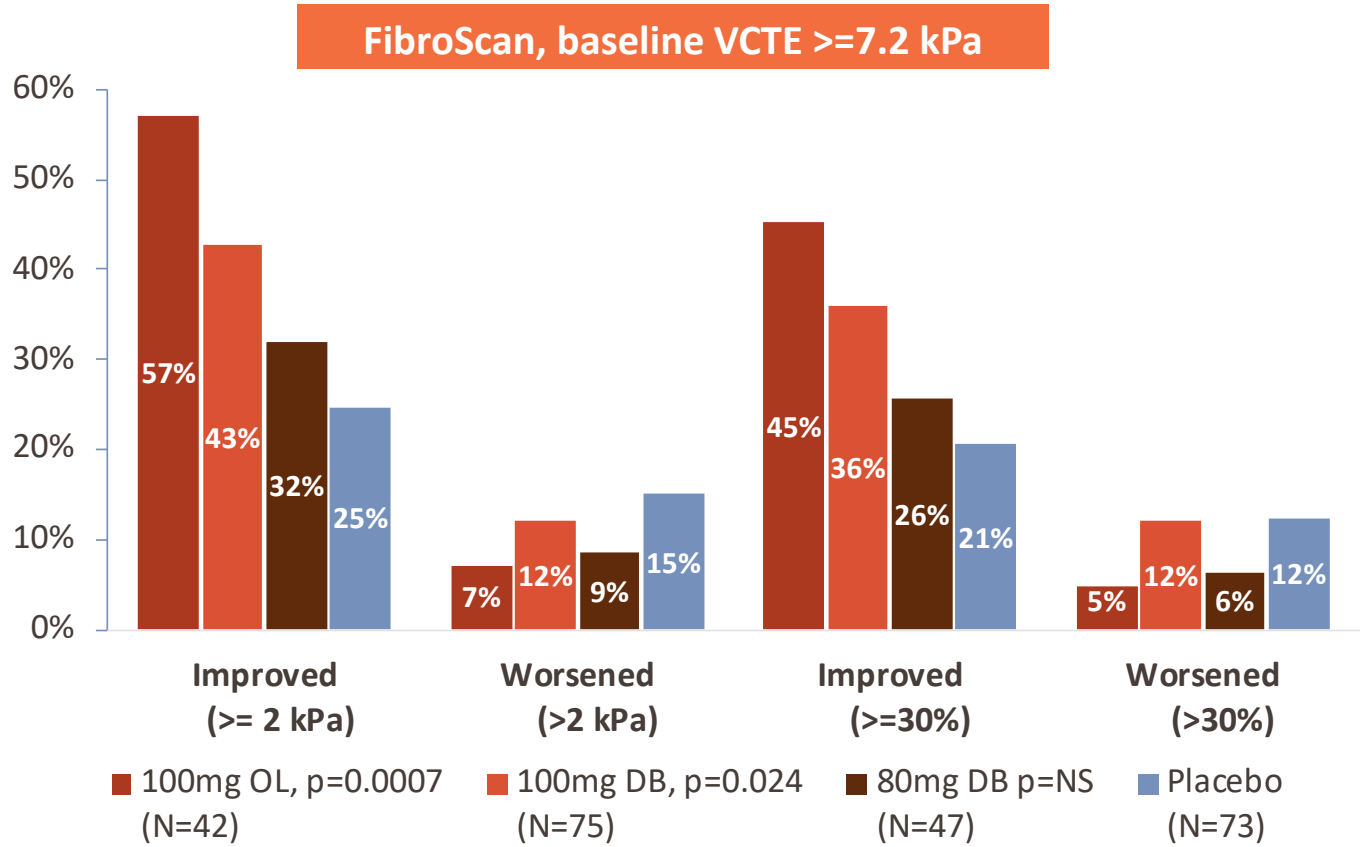
- Patients in the resmetirom 80 mg and 100 mg (double-blind) achieved reductions relative to placebo in:
  - ALT (p=0.002; <0.0001)
  - AST (p=0.028; 0.074)
  - GGT (p=0.039;0.021)
    - This was consistent with the 100 mg OL arm

- ALT increases ≥3 times the upper limit of normal occurred in 0.61% in the resmetirom 80 mg group, 0.31% in the 100 mg group and 1.6% of patients in the placebo group

ALT, alanine transaminase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase

FibroScan and MRE, Liver Stiffness Measure Change at Week 52





- In this study most patients did not have baseline LSM on FibroScan or MRE that met criteria for analysis
- Although directionally showing a resmetirom treatment effect at 100 mg, mean change was not significantly different for FibroScan LSM
- Responder analyses were conducted to reduce the influence of highly variable (inaccurate) measurements and showed statistically significant response in resmetirom compared with placebo

LSM, liver stiffness measure

Conclusions

- **Resmetirom was safe and well-tolerated** at the top dose of 100 mg as well as 80 mg in MAESTRO-NAFLD-1; MAESTRO-NAFLD-1 achieved the primary endpoint
- **Key secondary endpoints were achieved in MAESTRO-NAFLD-1 at both dose groups**
- Safety and efficacy are in line with expectations from Phase 2 liver biopsy study and randomized parallel open label 100 mg arm of MAESTRO-NAFLD-1
- Limitation of the study was the early fibrosis stage of MAESTRO-NAFLD-1 patients
- Positive results from this trial support our conviction that resmetirom has the potential to be the first medication approved for treatment of patients with NASH and liver fibrosis

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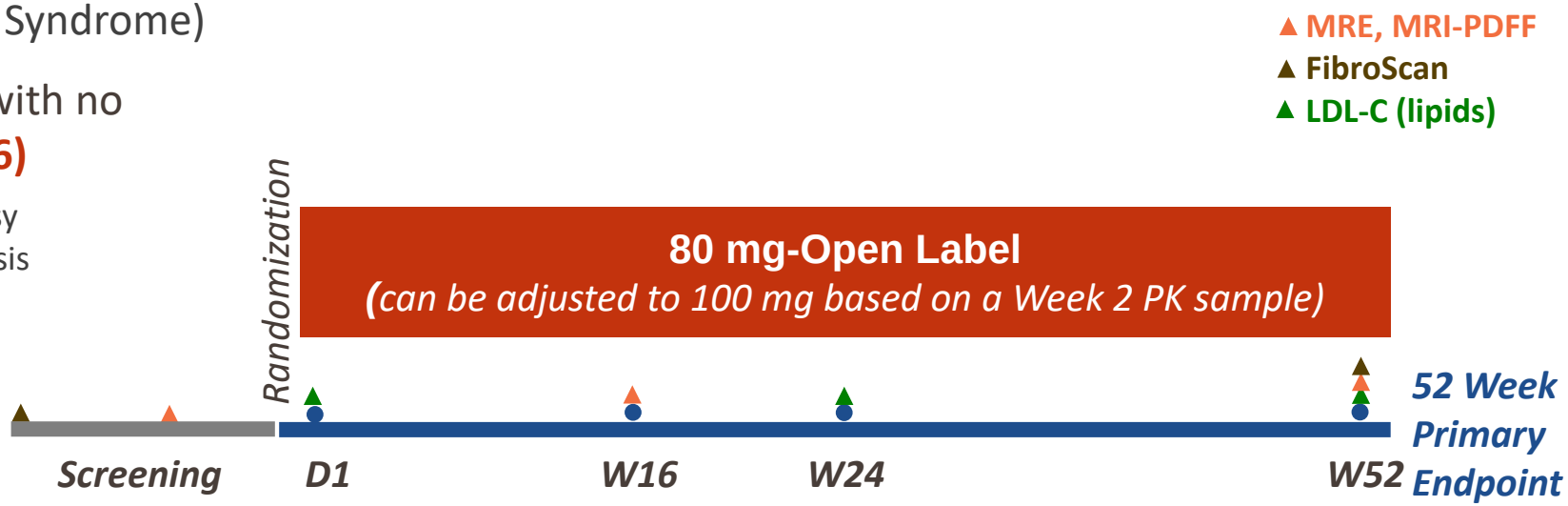
Phase 3 MAESTRO-NAFLD-1 Study Design: Well-compensated NASH Cirrhosis Open-Label Active Treatment Arm (n=180)

Inclusion/Exclusion

- ≥3 metabolic risk factors (Metabolic Syndrome)
- **Well-compensated NASH cirrhosis** with no history of decompensation **(CP-A 5-6)**
  - F4 fibrosis either historic or recent biopsy
  - or historic biopsy with NASH F2-F3 fibrosis & subsequent progression to cirrhosis
  - Clinical evidence NASH cirrhosis (few)

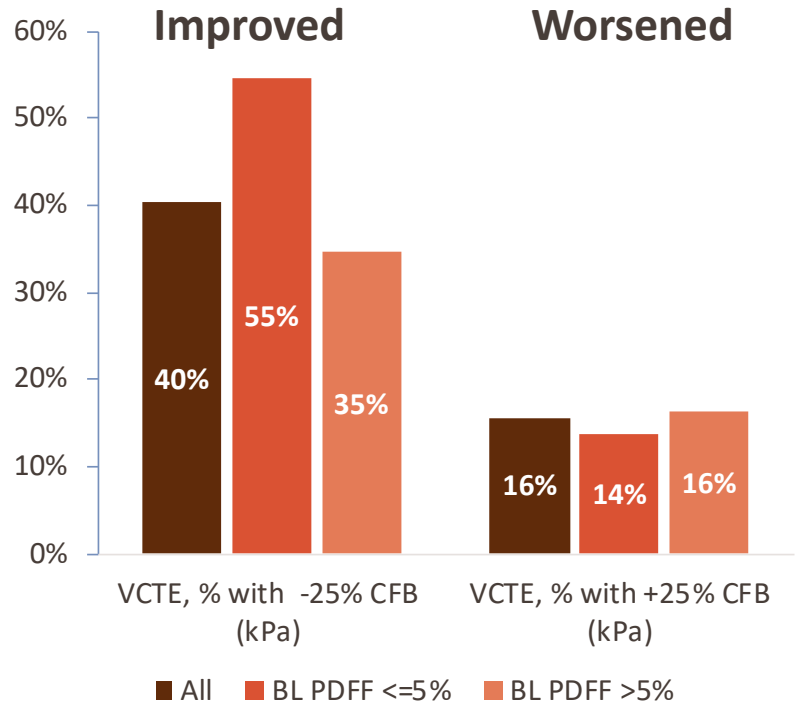


- Cohort 1 (n=105) has completed 52 weeks
- Cohort 2 (n=75) is ongoing
- Other than the addition of a Week 2 visit, the NASH cirrhotic 52-week protocol is identical to MAESTRO-NAFLD-1 non-cirrhotic protocol

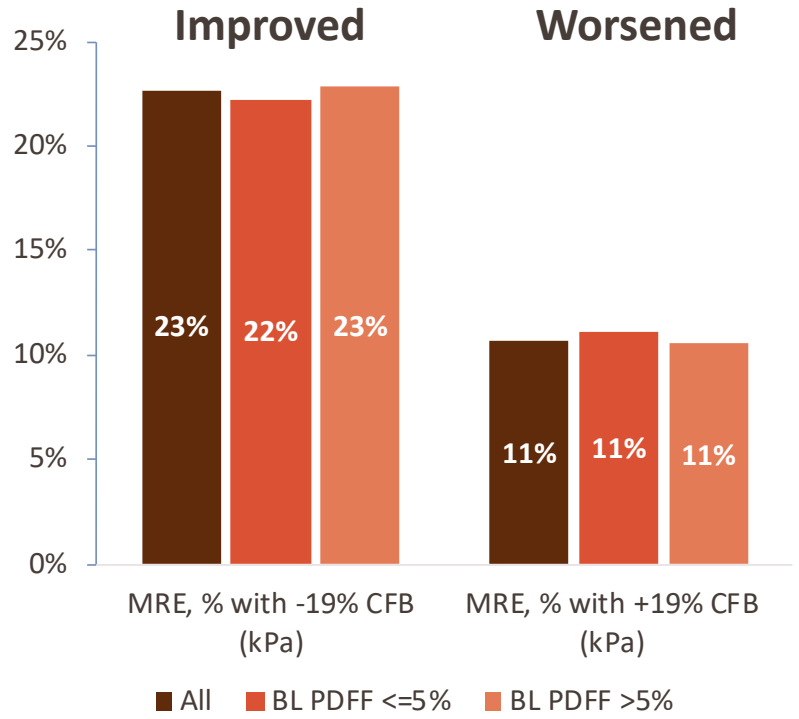
CP-A, Child–Pugh A; PK, pharmacokinetic
ClinicalTrials.gov (NCT04197479): https://clinicaltrials.gov/ct2/show/NCT04197479?term=MAESTRO-NAFLD-1&draw=2&rank=1

Resmetirom-mediated Changes to Fibrosis Imaging (Week 52)

FibroScan



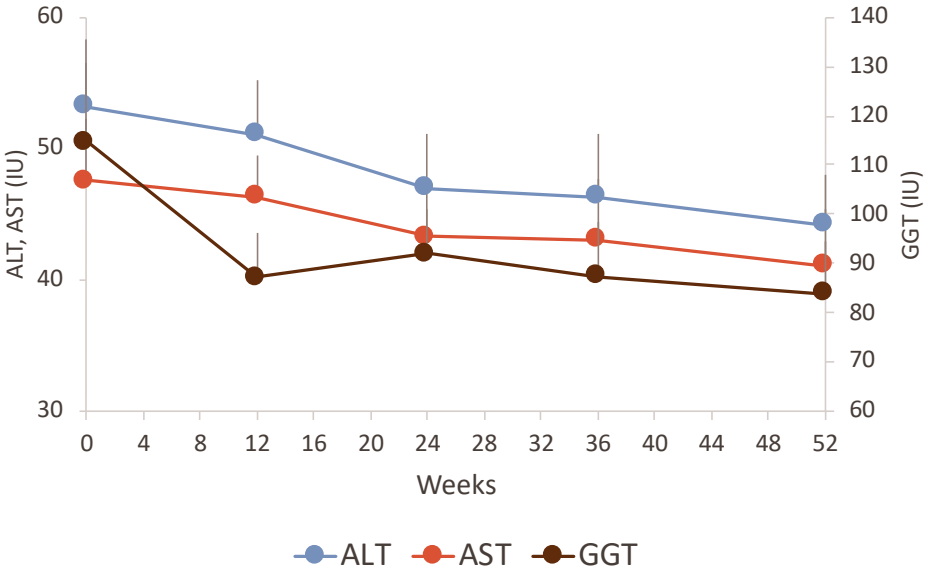
MRE



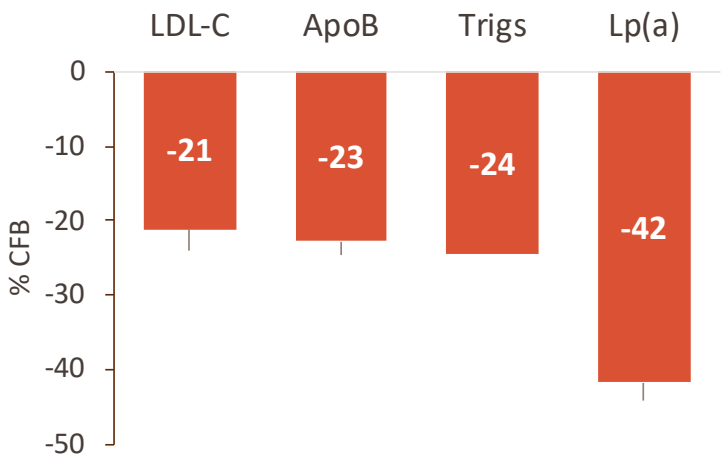
- Largest reduction in VCTE (mean, 9 kPa) in the most advanced group (BL PDFF ≤5%)
- Similar improvements were observed in MRE

Liver Enzymes & CV Effects of Resmetirom

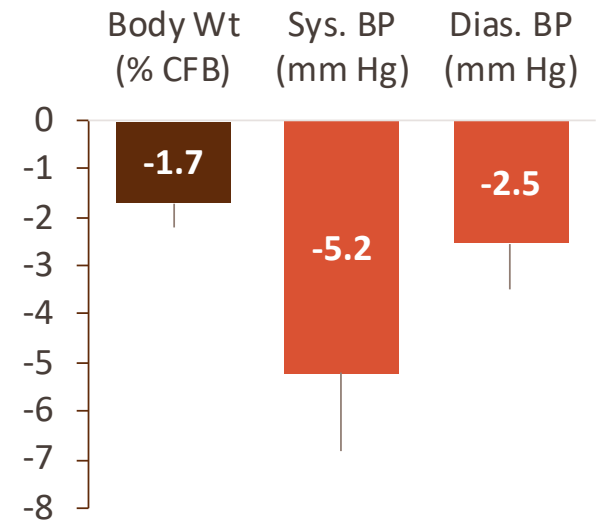
Liver Enzymes



Lipids



Vital Signs



- Reductions in liver enzymes & atherogenic lipids were similar across all patient subgroups
- Decreases in SBP & DBP, consistent with effects in non-cirrhotic NASH patients, independent of cirrhosis severity

Baseline ALT>=30 IU

Safety Summary

	% of Patients
Any TEAE	**94**
Severity	
Grade 1	23.1
Grade 2	56.5
≥ Grade 3	11.4
Preferred Term	
Diarrhea	33.3
Nausea	25.0
UTI	16.7
COVID-19	12
Arthralgia	10.2
Fatigue	12.3
TEAE Leading to Study Discontinuation	**2.8**
Drug-related TEAE Leading to Study Discontinuation	**0**

- **No difference between cirrhosis severity groups or compared with non-cirrhotic NASH patients**
  - Most common AEs were mild, intermittent loose stools or nausea at initiation of resmetirom therapy
  - Low percentage (~15%) primarily GI AEs were considered related
- **No central thyroid axis changes**
  - Small decreases (~10%) in prohormone FT4 consistent with previous studies, no changes in active hormone FT3 or TSH
  - No hyper- or hypothyroid symptoms
  - Similar PD changes in euthyroid patients compared with patients with pre-existing hypothyroidism on thyroxine treatment

Database is not locked; AE results are preliminary.
FT3, free triiodothyronine; FT4, free thyroxine; GI, gastrointestinal; PD, pharmacodynamic; UTI, urinary tract infection

Conclusions

- In patients with CP-A NASH cirrhosis, **resmetirom 80-100 mg daily for 52 weeks**:
  - was **safe and well tolerated** (mostly mild GI AEs at the beginning of resmetirom treatment)
  - **reduced MRI-PDFF, LDL-C, & other atherogenic lipids**
  - **reduced FibroScan CAP & VCTE as well as MRE (kPa)**
  - **statistically significantly reduced liver volume by an average of ~20%**

- Limitations of the study include lack of placebo control group
- This study provides foundation for MAESTRO-NASH Outcomes, a Phase 3 trial in well-compensated CP-A NASH cirrhosis patients that will initiate in the next few months

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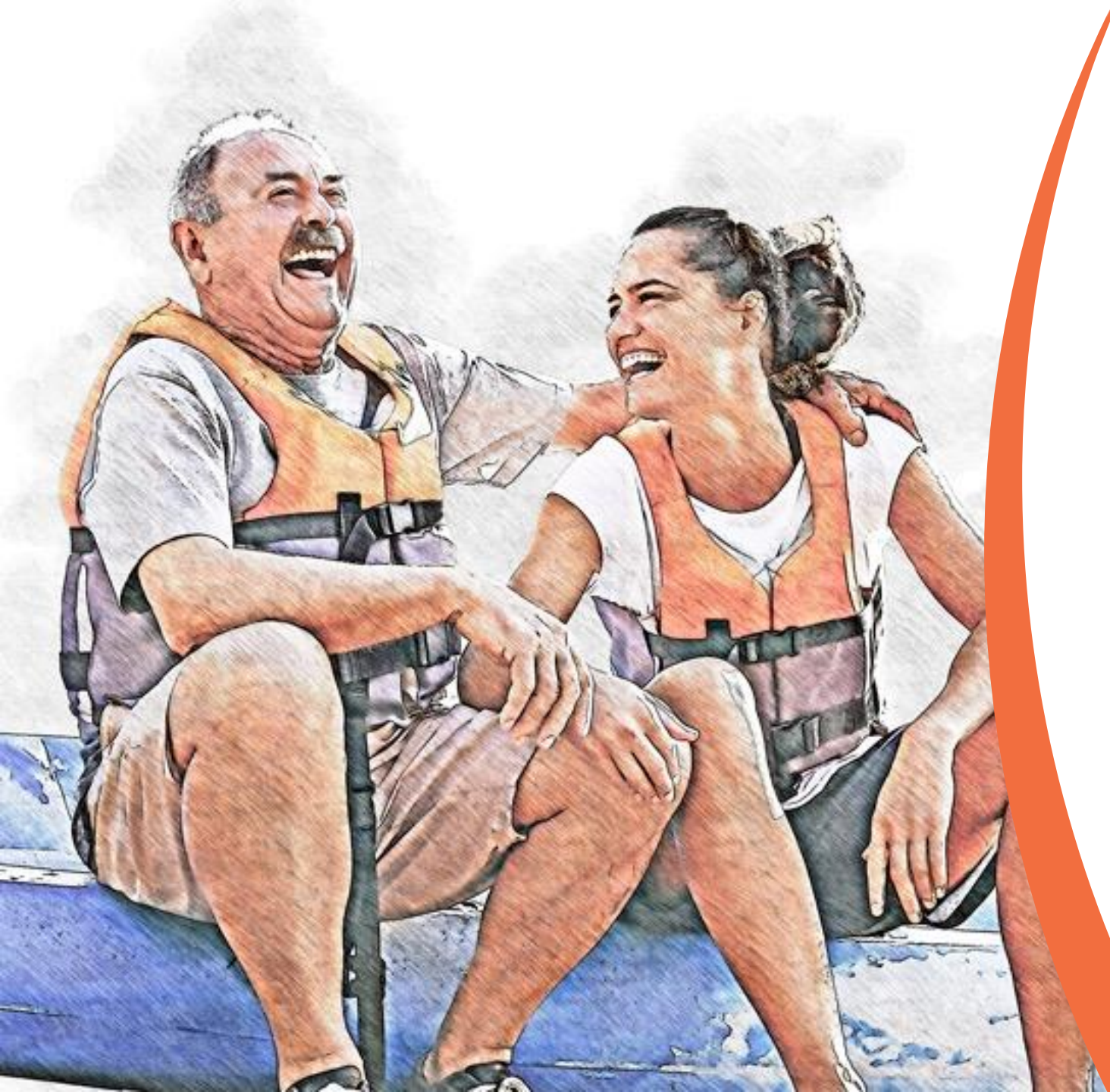

Advancing NASH Drug Development and Patient Care

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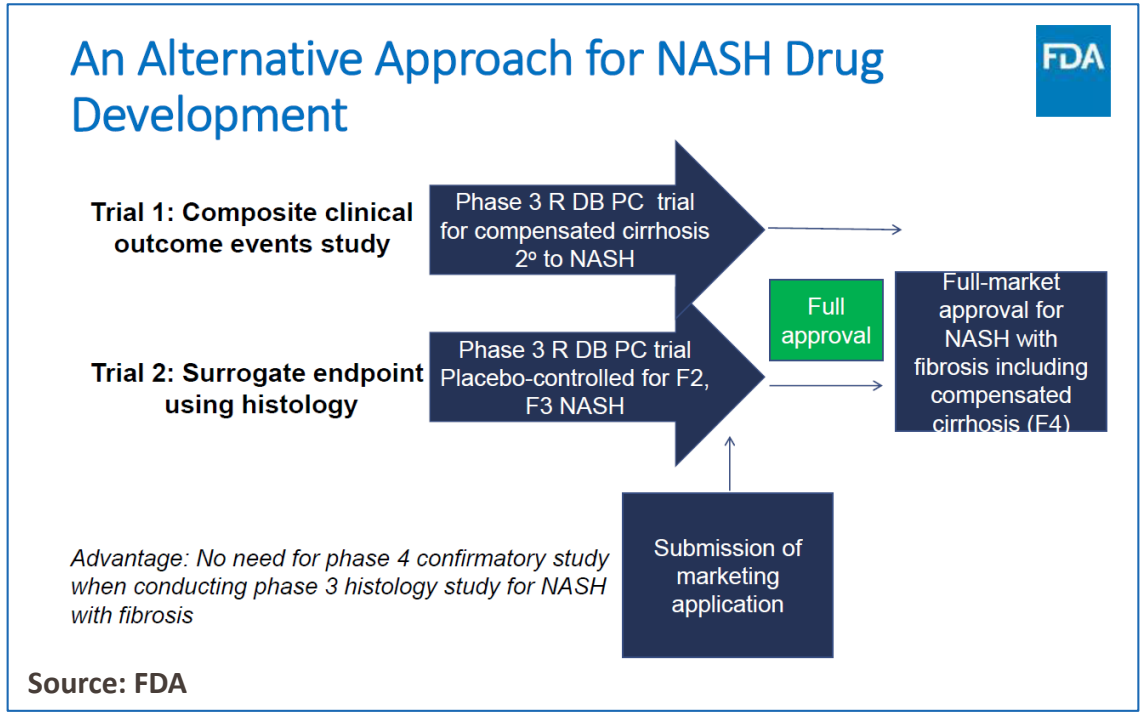
MAESTRO-NASH Outcomes

- MAESTRO-NASH Outcomes is a randomized double-blind placebo-controlled study in approximately 700 patients with early NASH cirrhosis to allow for noninvasive monitoring of progression to liver decompensation events
  - Designed to assess the rate of disease progression in early NASH cirrhosis patients and enhance the statistical power of MAESTRO to assess clinical benefit
  - Decompensation events are expected to occur at a rate that is higher than in MAESTRO-NASH
  - Liver biopsy is not an endpoint, the invasiveness and variability of liver biopsy is avoided
  - Several biomarker and imaging techniques will also be employed to assess correlates with disease progression

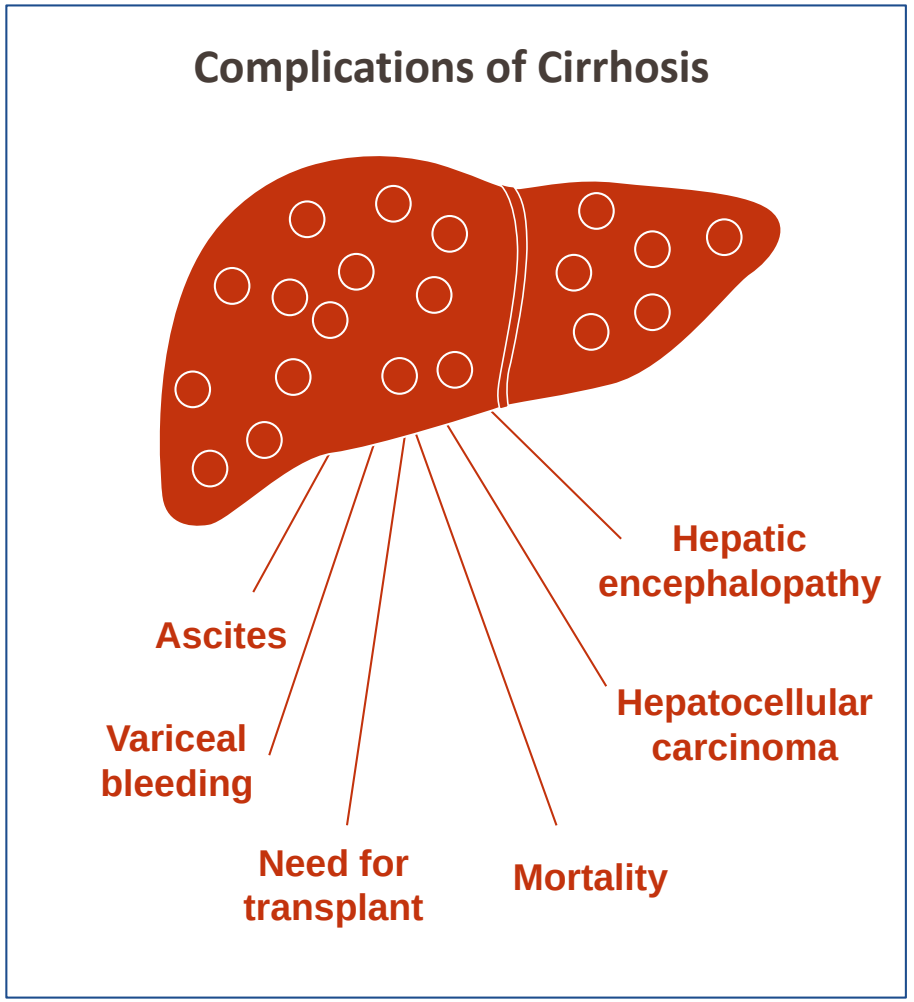


FDA has publicly stated[1] that an outcome study in NASH cirrhosis patients can support full approval in non-cirrhotic NASH; Madrigal met with FDA to confirm the strategy and study design

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 Cirrhosis Due to NASH

- If successful, MAESTRO-NASH Outcomes carries the potential to expand the eligible population for resmetirom to include patients with compensated cirrhosis due to NASH
  - Of the estimated 2 million NASH patients with 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.

The Resmetirom Development Program is Driving Advances in Noninvasive Diagnosis and Monitoring of NASH

- Biopsy is a requirement for registrational studies in NASH, but rarely performed in "real world" clinical practice
- The resmetirom clinical development program is designed to accelerate validation of noninvasive tests (NITs) in NASH drug development and provide clinicians with valuable data to inform patient care
  - **Phase 2** data demonstrated MRI-PDFF response predicts NASH resolution and fibrosis improvement on biopsy
  - **MAESTRO-NAFLD-1** is the first fully noninvasive Phase 3 study in NASH
  - **MAESTRO-NASH** includes multiple NITs that will further validate alternatives to biopsy
- Madrigal is committed to helping patients and healthcare providers move *Beyond the Biopsy*

Patient Advocates and Other NASH Stakeholders are Calling for Noninvasive Alternatives to Biopsy

GLI GLOBAL LIVER INSTITUTE

Beyond the Biopsy

"Noninvasive alternatives are necessary to respond to the growing incidence of NAFLD, NASH, and other liver diseases… Newer noninvasive screening and diagnostic tools are now being used, offering a safer and more thorough examination of the liver."

Source: Global Liver Institute

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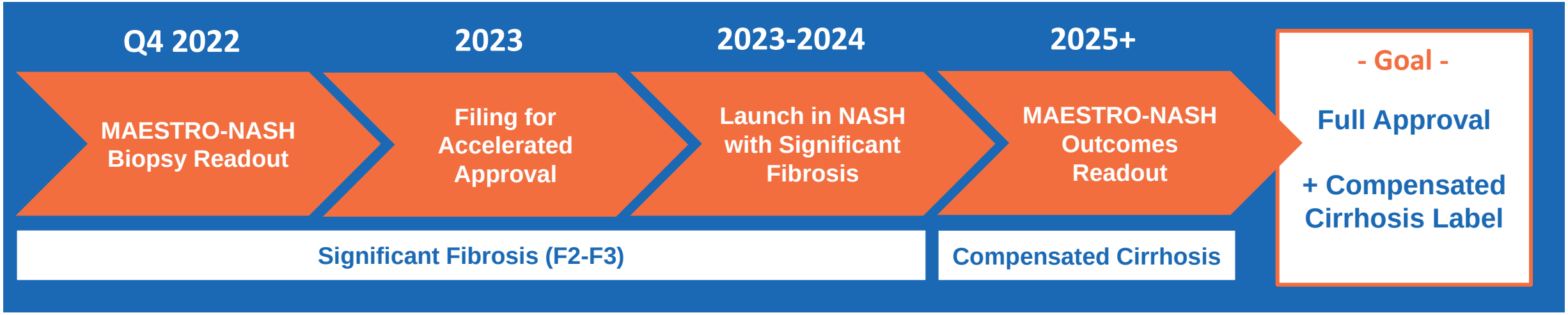
Based on Available Data, We Believe Resmetirom Has the Potential to Transform the Treatment of NASH

- ✓ **Meaningful efficacy** that targets key underlying causes of NASH in the liver
  - In Phase 2, resmetirom achieved marked reductions in liver fat and resolved NASH on biopsy
  - In Phase 3 (MAESTRO-NAFLD-1), resmetirom improved noninvasive measures of efficacy used in "real world" clinical practice to manage patients with NASH
- ✓ **Favorable safety profile** in studies conducted to date; large safety database to support regulatory review
- ✓ **Robust development program** with three Phase 3 studies designed to support accelerated approval and demonstrate long-term benefit on clinical outcomes



The NASH Market Opportunity for Resmetirom

Madrigal

Potential First-to-Market Opportunity to Transform the Treatment of NASH

Sizeable Market Opportunity

First-to-market opportunity in a prevalent disease that that is expected to grow meaningfully over the next decade

Attractive Product Profile

Resmetirom Target Profile* is highly attractive to 'NASH Specialists' based on primary market research

Specialty Launch Strategy

Resmetirom launch will focus on the 'NASH Specialists' who already manage a substantial number of patients with NASH in the U.S.

*Target Profile assumes resmetirom achieves NASH Resolution and Fibrosis Improvement endpoints; reduces LDL, and has favorable safety/tolerability profile with QD oral dosing in Phase 3. Information shown represents market research; not clinical data. Source: Madrigal US primary market research, Heps/GIs/Endos (n=127), Q4 2020

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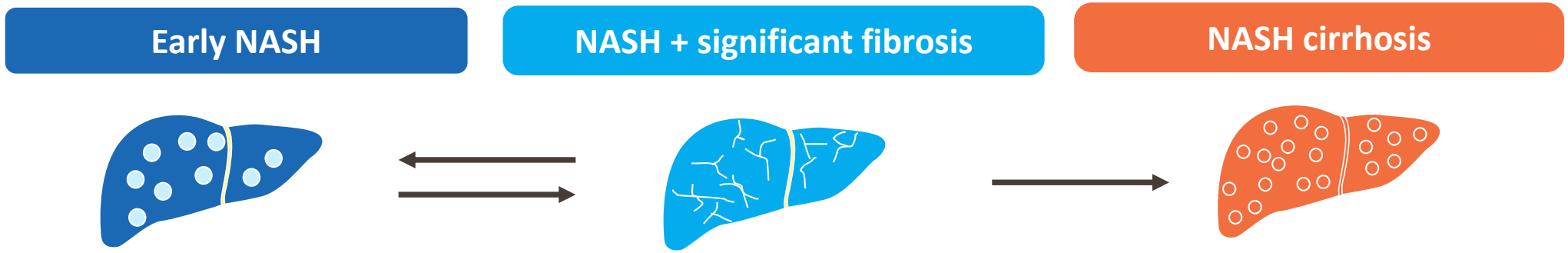
Resmetirom Clinical Development Program Focuses on NASH Patients with Significant Fibrosis (stage F2/F3) and on NASH Patients we Compensated Cirrhosis



Epidemiology estimates (US 2022[1]):	**~11M** F0=~3.5M, F1=~7.5M	**~7.5M** F2=~4.5M, F3=~3M	**~2M** Compensated cirrhosis=1.8M[2]
Commercial Opportunity	**Not a commercial target** Patients managed with diet and exercise	**Initial target opportunity** based on MAESTRO-NASH subpart H readout (Q4 2022)	**Expanded opportunity** based on MAESTRO-NASH Outcomes readout (est. 2025-26)

Roughly ~1M patients have been identified and ICD-10 coded as NASH patients in the community setting.[3]
This provides solid footing for resmetirom launch, post FDA approval

1. Estes C, et al. Hepatology. 2018:67(1):123-33; 2. GBD 2017 Cirrhosis Collaborators. Lancet Gastroenterol Hepatol. 2020 Mar;5(3):245-266. 3. Forian Data; Madrigal and ClearView Analysis.

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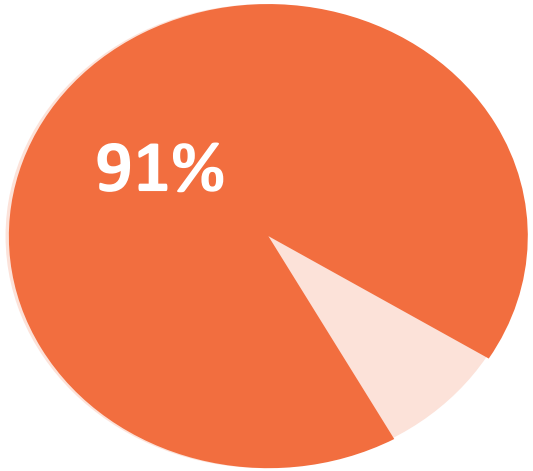
Resmetirom Target Profile is Highly Attractive to NASH Specialists Based on Primary Market Research

91% of NASH Specialists* Report Resmetirom Target Profile has "Extremely High" Utility in NASH with Significant Fibrosis[1]



49% of NASH specialists **expect to prescribe** resmetirom immediately at launch[1]

- Exceeds more typical response of 15–20%

NASH Specialists Recognize the High Unmet Need and Potential for Resmetirom in NASH with Compensated Cirrhosis[2]

Unmet need is seen as higher in compensated cirrhosis vs. significant fibrosis because patients are on the edge of negative liver outcomes

Clinical utility of resmetirom in compensated cirrhosis perceived to be equivalent to clinical utility in significant fibrosis

- Biggest driver of utility would be the ability to reduce decompensation events

*Term 'NASH specialist' describes subset of Heps, GIs and Endos who manage at least 20-30 NASH patients per month.

1. Madrigal US primary market research, Heps/GIs/Endos (n=127), Q4 2020. Target Profile assumes resmetirom achieves NASH Resolution and Fibrosis Improvement endpoints; reduces LDL, and has favorable safety/tolerability profile with QD oral dosing in Phase 3. Information shown represents market research; not clinical data. 2. US HCP Compensated Cirrhosis Opportunity Primary Market Research (Hep/GI n=112); 2Q2022

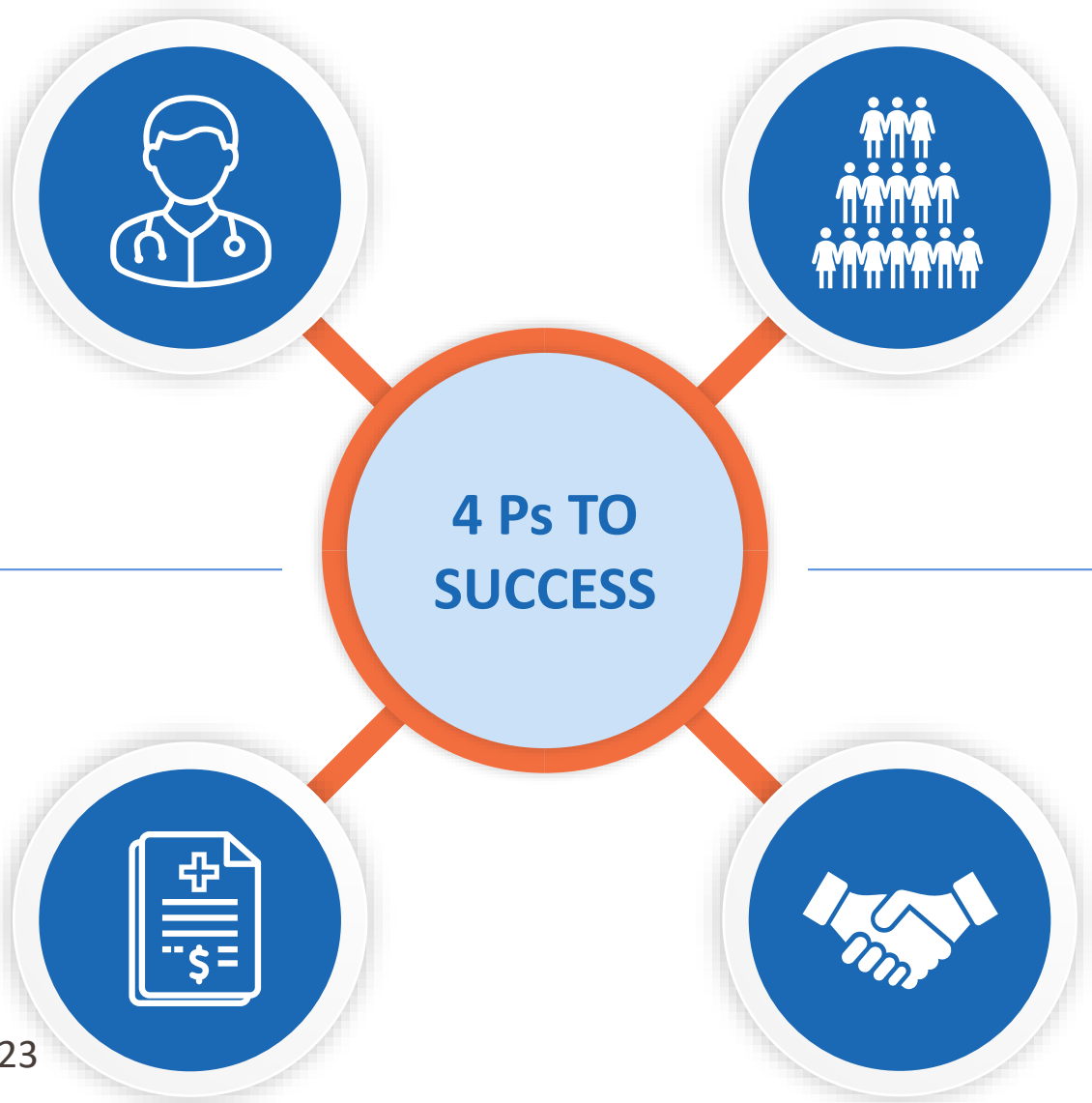
NASH Market Development is Underway

Prescribers

- Field Medical is identifying and engaging NASH thought leaders in the U.S. and Europe
- "NASH Explored" disease education program launched in Q2
- Expanded presence at key medical congresses focused on gastroenterology, hepatology, endocrinology

Payers

- NASH disease state education accelerating with payers
- Health economics and outcomes research underway
- Scientific exchange using MAESTRO-NASH data in 2023
- Cost Effectiveness and Budget Impact modelling discussions in 2023



Patients

- Expanded relationships with Patient Advocacy Groups in 2021
- Sponsored International NASH Day and other education programs led by patient advocacy groups
- Disease education marketing campaign for NASH patients targeted to begin in 2023

Partners

- Establish commercialization partner(s) for ex-US territories
- Partnering discussions underway with large multinational pharmaceutical companies
- Plan to establish partnership following Phase 3 MAESTRO-NASH data release

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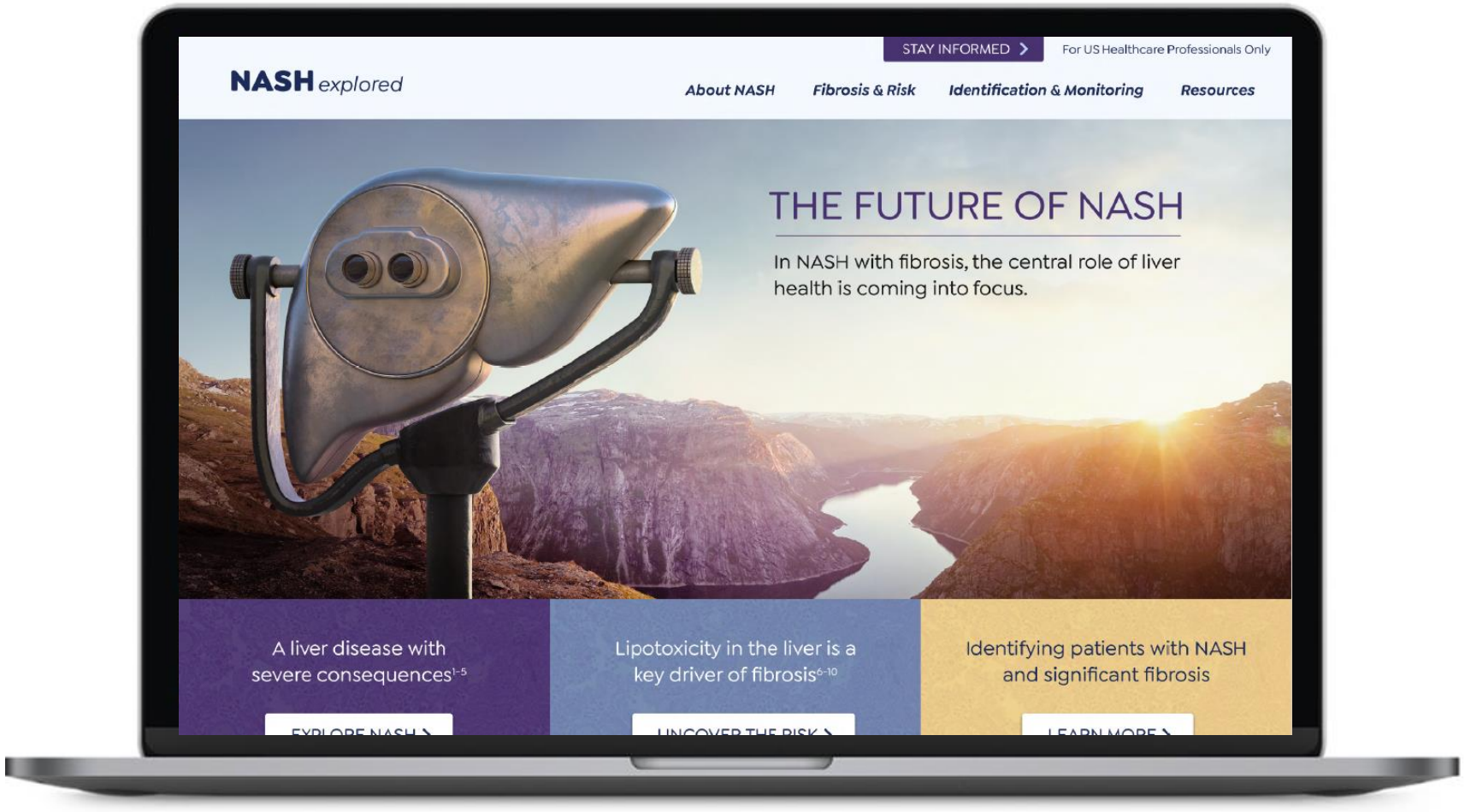
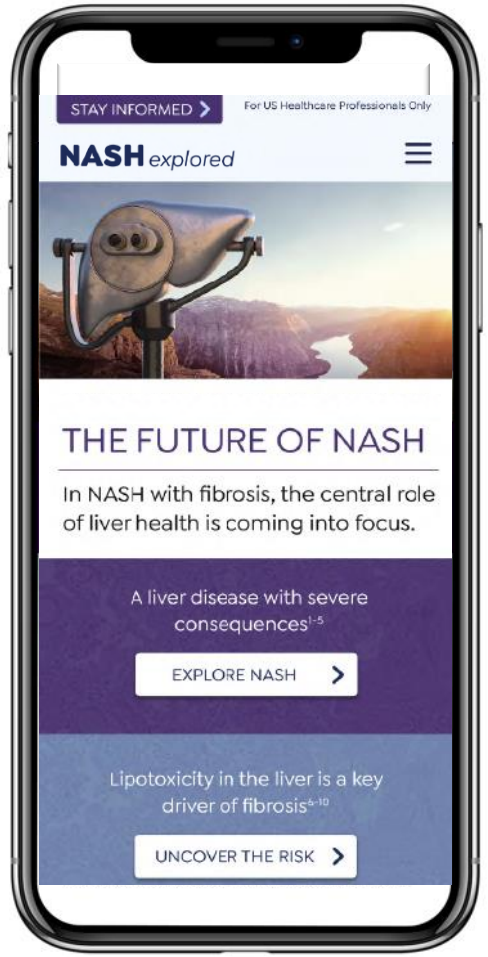
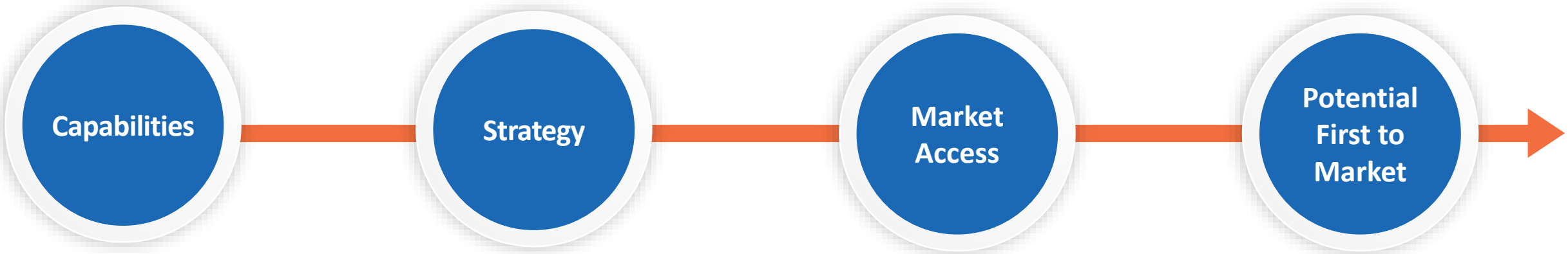
NASH Explored: Disease Education Campaign for Healthcare Providers





Launch Preparation Is Underway



- Building infrastructure and organization in the U.S. with focus on Medical Affairs, Market Access, Data/Analytics, Marketing
- Field team to expand following readout of MAESTRO-NASH

- 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
2023

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

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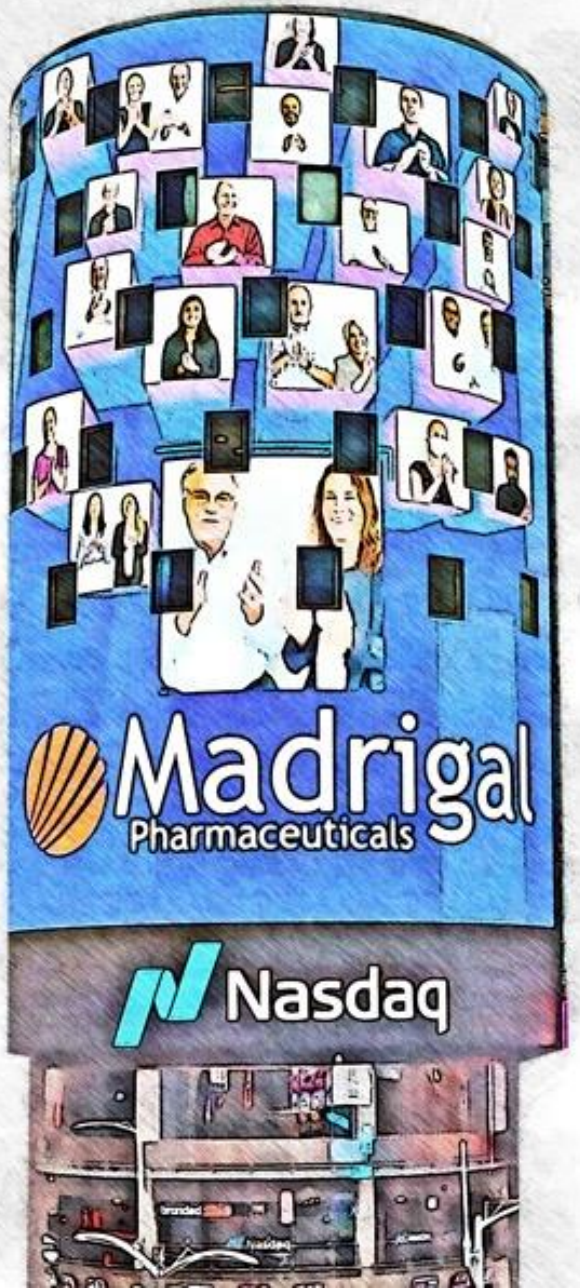


POSITIONED TO SUCCEED

Experienced Team Backed by Leading Healthcare Investors

Madrigal Pharmaceuticals

Experienced, Proven Leadership Team Focused on Successful Development and Commercialization of Resmetirom

Paul A. Friedman, MD
Chairman and Chief Executive Officer

Rebecca Taub, MD
Director, Founder, CMO and President of R&D

Alex Howarth
Chief Financial Officer

Brian J. Lynch
Chief Legal Officer

Remy Sukhija
Chief Commercial Officer

Robert Waltermire, PhD
Chief Pharmaceutical Development Officer

Dominic F. Labriola
Chief Data and Analytics Officer

Ed Chiang
SVP, Clinical and Technical Operations

Stephen Dodge, Pharm D, MBA
SVP, Global Medical Affairs

Thomas Hare, MS
SVP, Clinical Management

Sunil Kadam, PhD
SVP, Global Regulatory Affairs

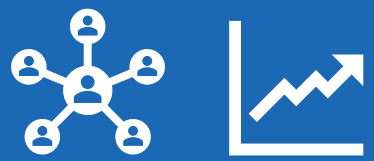
Kia Motesharei, PhD
SVP, Business & Corporate Development

Madrigal is Working to Deliver a Transformative Treatment for Patients with NASH with Significant Fibrosis

Clinical Development

- Initiating MAESTRO-NASH Outcomes
- Readout of Phase 3 MAESTRO-NASH biopsy study
- Filing for accelerated approval

Commercial Strategy



- Educating healthcare providers and patients
- Advancing our commercial strategy in the U.S.
- Establishing a commercial partner ex-U.S.

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Appendix

- Financial Summary
- Global Market Opportunity

NASDAQ: MDGL

Q2 2022 Financial Summary

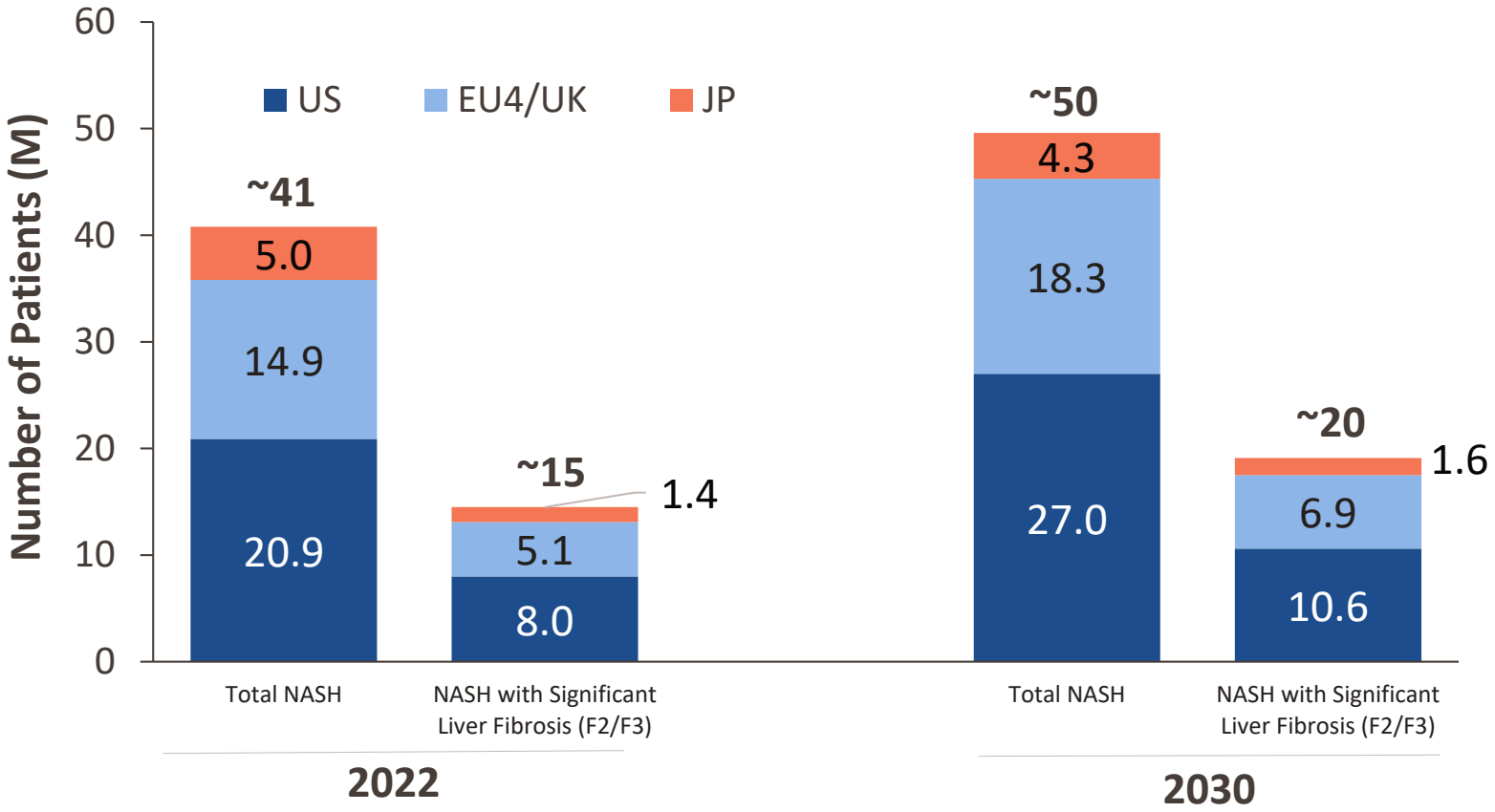
Cash, cash equivalents and marketable securities at June 30, 2022		$211.8M
Operating expenses as of June 30, 2022		$127.9M
R&D expenses as of June 30, 2022		$106.4M
Cash burn[1] as of June 30, 2022		$107.3M

	Total Facility	Available
ATM	$200M	$159.2M
Long Term Debt	$250M[2]	$200.0M

1. Cash burn represents net cash used in operating activities 2. Available in four defined tranches (with ability to draw two of the tranches subject to meeting certain milestone criteria)

NASH with Significant Fibrosis Represents a Sizeable Market Opportunity

The Prevalence of NASH with Significant Fibrosis (F2/F3) is About ~15 M Across the Major Markets and Expected to Grow Meaningfully Over the Next Decade[1]



- Expected epidemiology growth is based on historical and projected changes in adult prevalence of obesity and type 2 diabetes
- Growth is driven by increasing prevalence of risk factors, growing and aging populations, and disease progression

1. Estes C, et al. Hepatology. 2018:67(1):123-33.