Madrigal Pharmaceuticals

Madrigal Q1 2022 Update

May 9, 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 Statements

This communication contains "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: our clinical trials, including the anticipated timing of disclosure, presentations of data from, or outcomes from our trials; research and development activities; market size and patient treatment estimates for NASH and NAFLD patients; the timing and results associated with the future development of our lead product candidate, MGL-3196 (resmetirom); our primary and secondary study endpoints for resmetirom and the potential for achieving such endpoints and projections; plans, objectives and timing for making a Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) submission to FDA; optimal dosing levels for resmetirom; projections regarding potential future NASH resolution, safety, fibrosis treatment, cardiovascular effects, lipid treatment and/or biomarker effects with resmetirom; the potential efficacy and safety of resmetirom for non-cirrhotic NASH patients and cirrhotic NASH patients; ex-U.S. launch/partnering plans; the predictive power of liver fat reduction, as measured by non-invasive tests, on NASH resolution with fibrosis reduction or improvement; the predictive power of liver fat, liver volume changes or MAST scores for NASH and/or NAFLD patients; the effects of resmetirom' s mechanism of action; the achievement of enrollment objectives concerning patient number, safety database and/or timing for our studies; the predictive power of NASH resolution and/or liver fibrosis reduction or improvement with resmetirom using non-invasive tests, including the use of ELF, FibroScan, MRE and/or MRI-PDFF; the ability to develop clinical evidence demonstrating the utility of non-invasive tools and techniques to screen and diagnose NASH and/or NAFLD patients; the predictive power of non-invasive tests generally, including for purposes of diagnosing NASH, monitoring patient response to resmetirom, or recruiting a NASH clinical trial; potential NASH or NAFLD patient risk profile benefits with resmetirom; the potential for resmetirom to become the best-in-class and/or first-to-market treatment option for patients with NASH and liver fibrosis; and our possible or assumed future results of operations and expenses, business strategies and plans, capital needs and financing plans, trends, market sizing, competitive position, industry environment and potential growth opportunities, among other things. 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," "be," "believes," "can," "continue," "could," "demonstrate," "design," "estimates," "expectation," "expects," "forecasts," "future," "goal," "hopeful," "inform," "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. Although management presently believes that the expectations reflected in such forward-looking statements are reasonable, it can give no assurance that such expectations will prove to be correct and you should be aware that actual results could differ materially from those contained in the forward- looking statements.

Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to: our clinical development of resmetirom; enrollment uncertainties, generally and in relation to COVID-19-related measures that may be continued for an uncertain period of time or implemented; outcomes or trends from competitive studies; future topline data timing or results; the risks of achieving potential benefits in studies that include 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 entitled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2021, our Quarterly Report on form 10-Q for the Quarter ended March 31, 2022, and in our other filings with the SEC.

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Agenda

Introduction	Paul Friedman, M.D., Chief Executive Officer
MAESTRO Program Updates	Becky Taub, M.D., Chief Medical Officer and President of R&D Stephen Harrison, M.D., Medical Director for Pinnacle Clinical Research, San Antonio, Texas, Visiting Professor of Hepatology, Oxford University, and Principal Investigator of the MAESTRO studies
Commercial Update	Remy Sukhija, Chief Commercial Officer
Financial Update	Alex Howarth, Chief Financial Officer
Q&A	

Opening Remarks

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Madrigal is Building on its Leadership Position in NASH

The expansion of our clinical development program reflects our conviction in resmetirom as a potential transformational therapy for patients with NASH

- MAESTRO-NAFLD-1 data continue to reinforce the safety and efficacy profiles of resmetirom

- We believe the new MAESTRO-NASH Outcomes Study:
  - Addresses a high unmet need for patients with with early NASH cirrhosis (well-compensated)
  - Has the potential to accelerate the path to full approval of resmetirom
  - Expands the NASH market opportunity, optimizing the therapeutic and commercial value of resmetirom for Madrigal and potential business development partners

- The MAESTRO-NASH Biopsy study will now have dual primary endpoints
  - One point fibrosis reduction will move up the hierarchy to a primary endpoint along with NASH resolution
  - Dual primaries allow for a successful outcome of the study that can be filed for subpart H approval if either the NASH resolution or one point fibrosis reduction liver biopsy endpoint is met

- The new loan facility will help fund the expansion of the resmetirom clinical development program and further strengthens Madrigal's balance sheet

MAESTRO Program Updates

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Summary of MAESTRO-NAFLD-1 from January 31st Webcast

- Resmetirom was safe and well-tolerated at the top dose of 100 mg as well as 80 mg in MAESTRO-NAFLD-1
- Key secondary endpoints were achieved in MAESTRO-NAFLD-1 at both 80 and 100 mg dose groups including MRI-PDFF, LDL-C, apolipoprotein B, and triglyceride reductions consistent with parallel randomized 100 mg open label arm
- 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
- 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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Multiple Presentations at EASL's International Liver Congress

Late-breaking presentation: *"Primary data analyses of MAESTRO-NAFLD-1, a 52 week double-blind placebo-controlled phase 3 clinical trial of resmetirom in patients with NAFLD"* [Saturday, June 25 at 3:00 PM. Presenter: Stephen Harrison]

Oral presentations:

- *"Impact of resmetirom-mediated reductions in liver volume and steatosis compared with placebo on the quantification of fibrosis using second harmonic generation in a serial liver biopsy study"* [Thursday, June 23 at 4:00 PM. Presenter: Dean Tai]
- *"Utility of FIB-4 thresholds to identify patients with at-risk F2-F3 NASH based on screening data from a 2000 patient biopsy confirmed cohort of resmetirom Phase 3 clinical trial, MAESTRO-NASH"* [Saturday, June 25 at 9:15 AM. Presenter: Jörn Schattenberg]
- *"Biomarkers, imaging and safety in a well-compensated NASH cirrhotic cohort treated with resmetirom, a thyroid hormone receptor beta agonist, for 52 weeks"* [Saturday, June 25 at 5:45 PM. Presenter: Stephen Harrison]

Posters:

- *"A higher Fibrosis-4 (FIB-4) score is associated with higher healthcare costs and hospitalizations in patients with nonalcoholic steatohepatitis"* [Presenter: Elliot Tapper]
- *"Retrospective AI-based measurement of NASH histology (AIM-NASH) analysis of biopsies from Phase 2 study of Resmetirom confirms significant treatment-induced changes in histologic features of non-alcoholic steatohepatitis"* [Presenter: Janani Iyer]

Madrigal Satellite Symposium: *"Identifying, Managing and Treating Patients with NASH and Significant Fibrosis – Current Practice and Future Perspectives"* [Thursday, June 23, 6:30 PM]

All times London

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Additional Data from MAESTRO-NAFLD-1

- Detailed results of MAESTRO-NAFLD-1 are under embargo until the late-breaking presentation at EASL
- Similar to what has been reported for the 100 mg open-label arm, patients in the resmetirom 80 mg and 100 mg double-blind arms achieved reductions from baseline in ALT ($p=0.002$; <0.0001) relative to placebo
- Transient 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
- Treatment-emergent adverse events ≥ grade 3 in severity occurred in 7.6% of patients in the resmetirom 80 mg group, 9.0% in the 100 mg group and 9.1% in the placebo group
  - Withdrawals due to adverse events were 2.4% in the 80 mg group, 2.8% in the 100 mg group and 1.3% in the placebo group
  - GI-related adverse events (diarrhea, nausea) were increased relative to placebo at the initiation of therapy but not after the first few weeks

FibroScan and MRE

- FibroScan CAP (controlled attenuation parameter) scores reflective of hepatic fat were statistically significantly ($p<0.0001$) reduced in resmetirom arms as compared with placebo
- FibroScan liver stiffness reductions were similar in the 100 mg open-label and double-blind arms
  - Responder analyses of FibroScan vibration-controlled transient elastography (VCTE) >=2 kPa reduction from baseline comparing resmetirom 100 mg open-label and double-blind arms with placebo showed a statistically significant increase in responders in resmetirom treatment arms (~44% averaged across the resmetirom arms) compared with placebo (25%)
    - Reductions in FibroScan VCTE appeared to be dose related
  - Mean reduction in FibroScan VCTE in resmetirom double-blind patients were greater than placebo but not statistically significant
- Magnetic resonance elastography (MRE) responders as measured by kPa reduction were significantly greater in resmetirom-treated groups compared with placebo, and showed a similar effect in all resmetirom dose arms
- The intrinsic variability of the FibroScan (35-40%) limits its use as a sole measure to diagnose or follow NASH patients. FibroScan is an excellent office-based enrichment test: rules out patients without significant fibrosis and identifies potential NASH fibrosis patients. However:
  - The screening FibroScan >=8.5 kPA predicts significant fibrosis on biopsy in MAESTRO-NASH in approximately 50%
  - MRE >=2.9 predicts significant fibrosis on screening biopsy in 80% in MAESTRO-NASH (MRE intrinsic variability = 19%)
  - Additional biomarker (composites) or more specific imaging tests like MRE/MRI-PDFF +/- FibroScan may increase accuracy in diagnosing and monitoring patients with NASH

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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 non-invasive monitoring of progression to liver decompensation events
  - FDA has publicly stated 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
  - MAESTRO-NASH Outcomes is 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 include development of ascites, bleeding varices, hepatic encephalopathy, and increase in MELD >=15 and are expected to occur at al 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

- Ongoing resmetirom open-label studies of more than 180 patients with well-compensated NASH cirrhosis (MAESTRO-NAFLD-1 open-label arm) support the potential of resmetirom in this patient population
  - Reported data from the patients with NASH cirrhosis in the open-label arm of MAESTRO-NAFLD-1 demonstrated that resmetirom reduced hepatic fat, liver enzymes, liver volume, fibrosis markers and atherogenic lipids
  - Madrigal will be presenting additional results from the MAESTRO-NAFLD-1 cirrhosis population in an oral presentation at EASL

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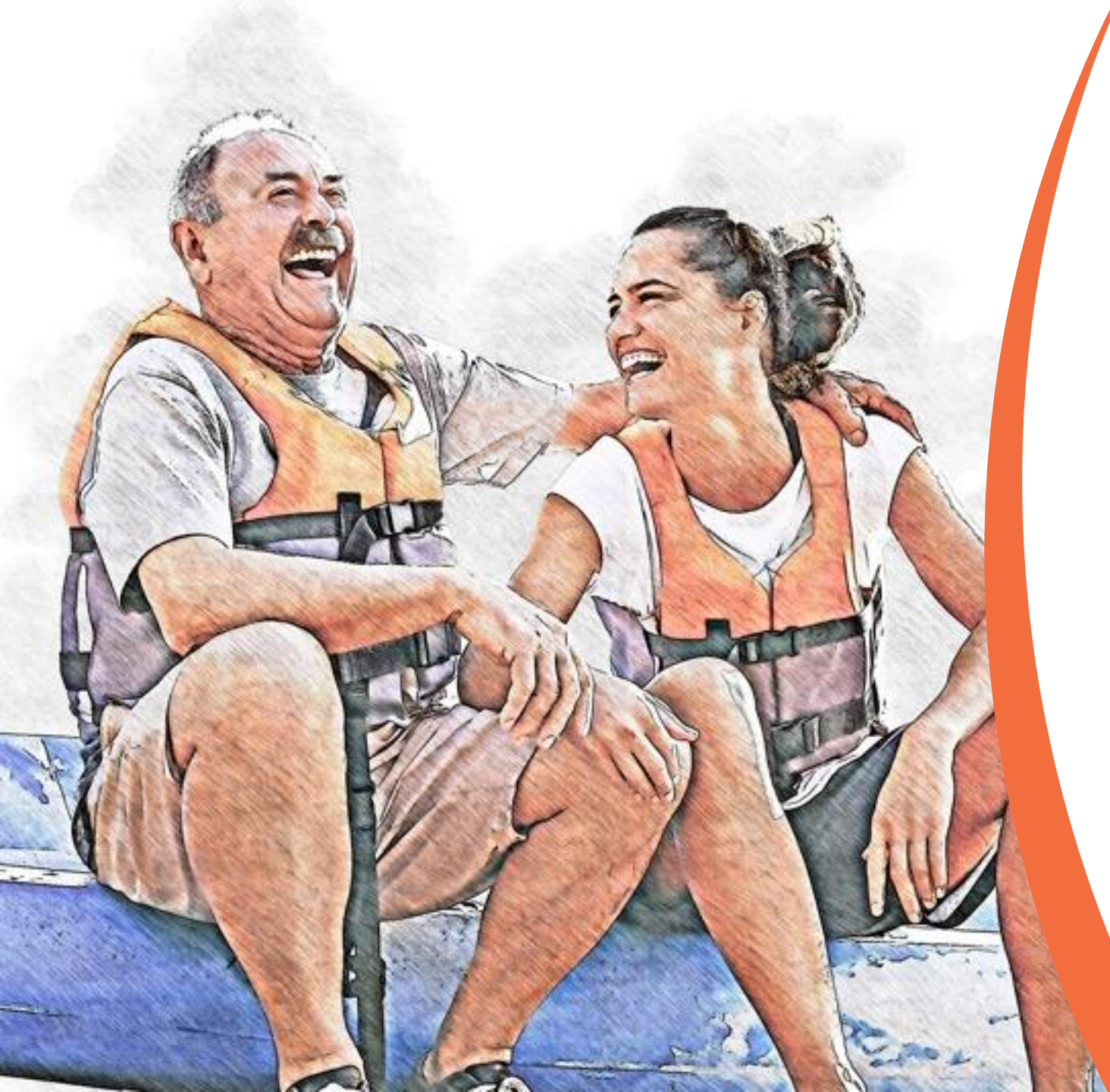

Commercial and Financial Updates

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U.S. Launch Prep Update

- NASH market development activities have accelerated in 2022

- We are preparing for a specialty product launch focused on “NASH specialists”
  - NASH specialists are a subset of hepatologists, gastroenterologists and endocrinologists who already manage a substantial number of patients with NASH with fibrosis

- We are engaging with all key stakeholders. In 2022, we have:
  - Gained a deep understanding of market dynamics with the HCP, payer and patient lenses based on extensive market research and advice from thought leaders
  - Advanced health economics and outcomes research that will inform future value assessments of resmetirom
  - Held disease education sessions with payers that together cover ~80% of all branded prescriptions in the U.S.

U.S. Launch Prep: NASH Market Development is Underway

Prescribers

- Field Medical is identifying and engaging NASH thought leaders in the U.S. and Europe
- “NASH Reimagined” disease education program launching 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
- Sponsoring 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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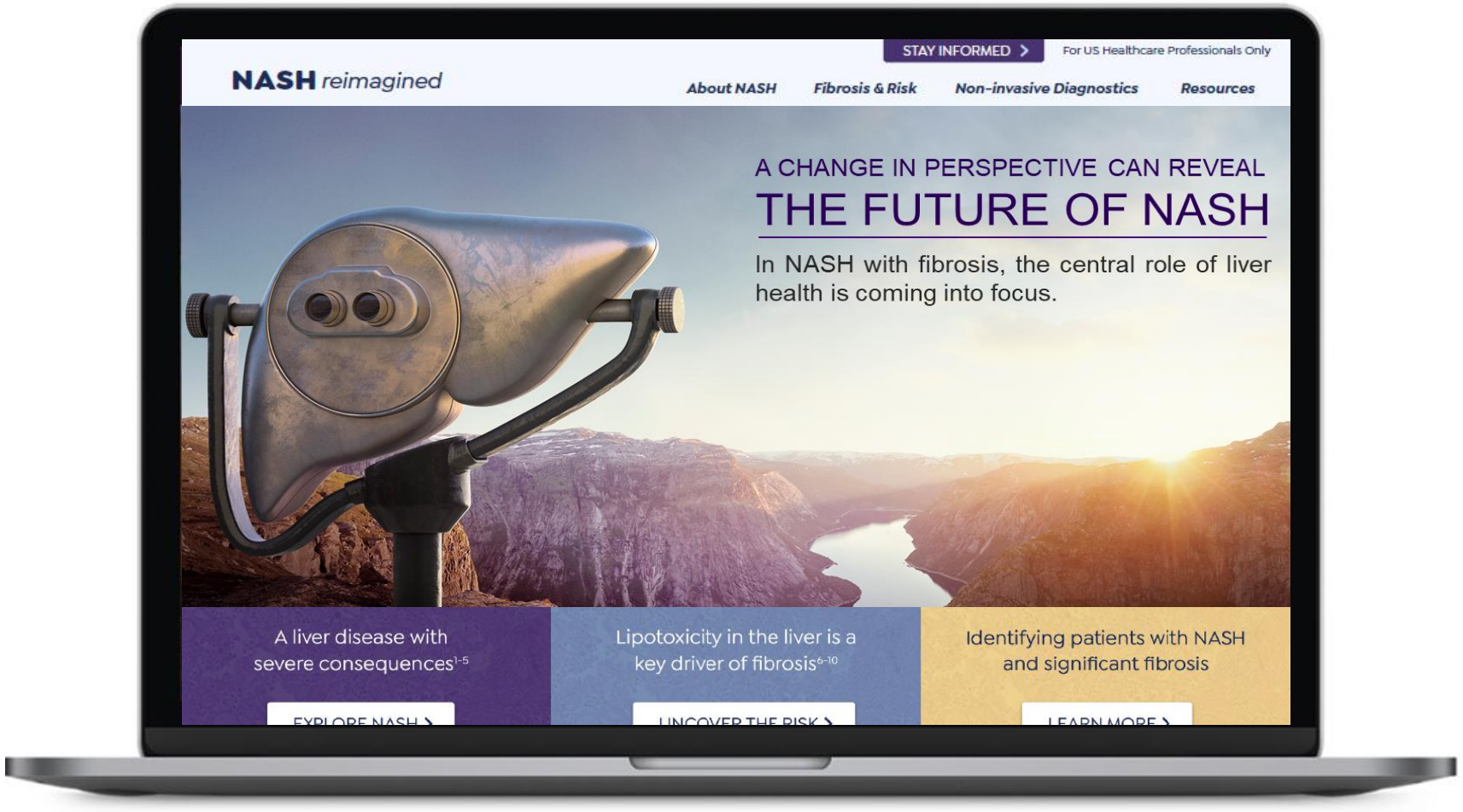
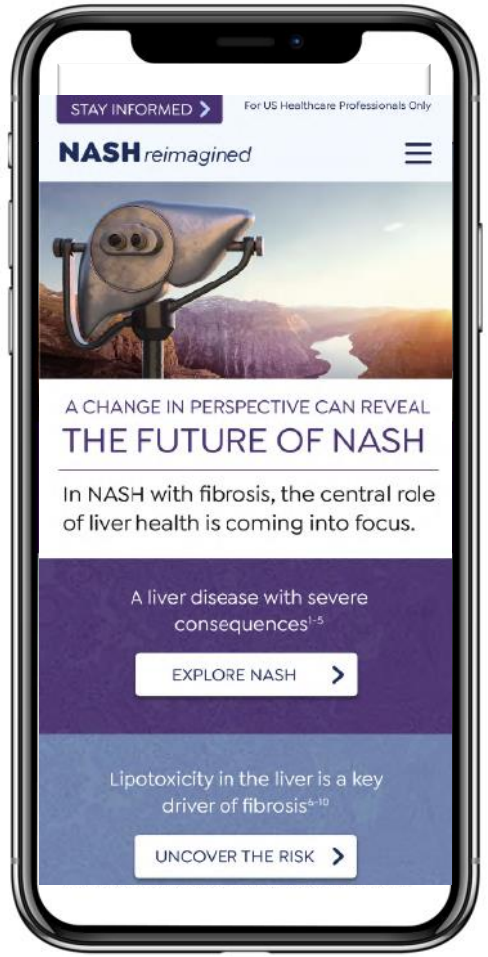
NASH Reimagined: Disease Education Campaign for Healthcare Providers





Q1 2022 Financial Summary

Cash, cash equivalents and marketable securities at March 31st, 2022	$220.0M
Operating expenses Q1 2022	$57.6M
R&D expenses Q1 2022	$47.9M
Cash burn[1] Q1 2022	$49.9M

	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)

Term Loan Facility

- Madrigal has secured a $250 million term loan facility with Hercules Capital, Inc.
  - Under the terms of the loan agreement, $50 million was drawn at closing
  - Madrigal may also draw an additional $125 million in two separate tranches upon achievement of resmetirom clinical and regulatory milestones
  - An additional $75 million may be drawn by Madrigal to support operational activities, subject to the approval of Hercules Capital

- The committed capital strengthens Madrigal's balance sheet, providing an additional source of funding both to support the expanded clinical program and ramp-up for a potential launch of resmetirom in the U.S.

- Additional details of the loan agreement can be found in our 8-K filed with the Securities and Exchange Commission

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Q&A

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Thank You