Madrigal Pharmaceuticals

Liver Forum Sept 2024

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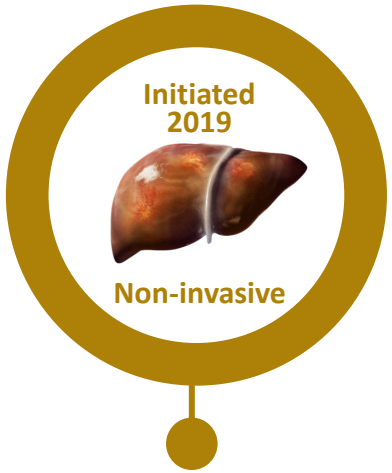
NASDAQ: MDGL

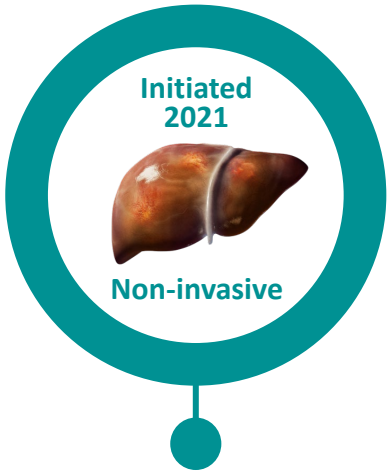
Phase 3 Resmetirom Clinical Development Program Spanning Disease Spectrum



MAESTRO NAFLD-1

N>1200 NAFLD patients
Safety & tolerability
over 52 weeks

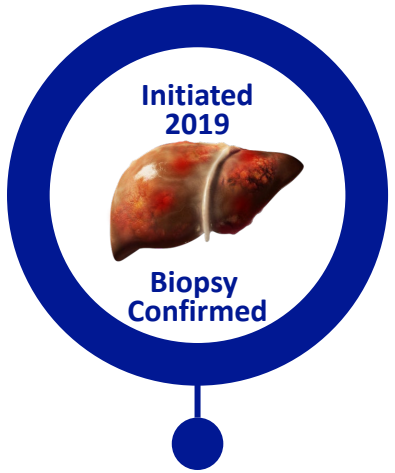
N=180 well-compensated NASH cirrhosis patients
Long-term Safety



MAESTRO NAFLD-OLE

(open label extension of MAESTRO NAFLD-1)

N>700 NAFLD patients
Safety & tolerability
>52 weeks

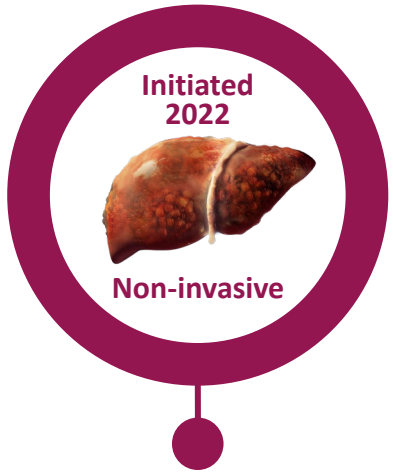


MAESTRO NASH

NASH F1B-F2-F3
Pivotal

N=966 NASH patients
NASH resolution
or fibrosis improvement
at Week 52

54-month ongoing clinical outcomes study



MAESTRO NASH OUTCOMES

N~800 well compensated NASH cirrhosis patients
Progression to decompensated cirrhosis

Supportive

Confirmatory

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Considerations for Patients Participating in Clinical Trials

- Resmetirom clinical program (2016 to 2024) was designed in collaboration with Dr. Stephen Harrison, study PI, and many other NASH expert Steering committee members
- Patient advocate and patients viewpoints were considered as the trials were designed and conducted
  - Many processes were not codified but made sense when considering patients' needs
- Consider what study outcomes are important to patients
  - Examples, PRO, Lack of progression to more serious disease
- Try to make the study as real world as possible in allowing inclusion and exclusion for patients to enroll, with safety and regulatory considerations given the highest priority in study design and conduct
  - Consider open label active treatment arms to monitor safety in subsets of patients that might otherwise be excluded
- Support extra testing, ie an ultrasound or consult, if a patient needs extra testing during the trial
- Use invasive testing only when necessary—example MAESTRO-NAFLD-1; MAESTRO-NASH-OUTCOMES
- Appreciate that patients participating in clinical research don't want to be on placebo
  - Power the study to allow significant fraction of enrolled patients to randomize to active treatment
  - Utilize open label arms, and extension arms to offer treatment to patients once the double blind portion of the study is completed
    - Examples, Madrigal Phase 2 NASH study, MAESTRO-NAFLD-1, MAESTRO-NASH (OLE) After 54 months completion, patients will be offered continuation on resmetirom; screen fails from MAESTRO-NASH were allowed to enroll in MAESTRO-NAFLD-1
  - Consider expanding enrollment to allow more patients to participate in the trial
    - Examples, enrollment expanded from 25 to 180 for open label well compensated cirrhotics because of patients desire to participate
    - Expansion of MAESTRO-NAFLD-1 from 700 to >1200

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