Company Overview

Yale Innovation Summit May 18, 2021

MITOTHERAPEUTIX

Using siMCJ to treat MCJ based metabolic disorders

Background

Mitotherapeutix established in 2014

- Focus: Development of drugs to treat metabolic disorders
- Drug Target: MCJ-mitochondrial regulator of metabolism- eliminate and increase energy > MCJ/DNAJC15 is resident in Liver, Kidney and Heart and is elevated in disease states: Fatty Liver/NASH; cirrhosis; acute and chronic kidney disease, heart failure.)

Therapeutic Impact: Modulation of this protein increases metabolism and has an impact in treating disease

Six murine models of liver disease- KO of MCJ has beneficial therapeutic effects

- Approach: Using siRNA based MCJ suppression to treat disease
 - Utilizing siRNA drug discovery and delivery program
 - Patented GalNAc liver delivery technology discovered and developed internally

Status: Completed initial in vivo testing of lead candidate in:

Non-human primates and demonstrated significant MCJ suppression

Pipeline: Multiple potential indications- "Platform in a drug"



* DC – Development Candidate

Mito- SiMCJ drug discovery process



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5

Summary:

✓ Unique MCJ target identified and patented

- ✓ Ability to enhance mitochondrial respiration and ATP generation without ROS production
- Drug discovery platform to treat multiple metabolic diseases
- ✓ GalNAc liver delivery technology discovered, developed and patented

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6

Summary:

✓NASH drug leads identified; excellent in vivo activity in mice and non-human primates

 Seeking \$5-10 million funding/partnership to advance the NASH program to IND filing and Phase 1 clinical trial

 Expecting approval of \$2.2MM NIH SBIR grant for NASH program that will accelerate IND enabling process

Looking for potential commercial partners and institutional investors

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7

MCJ (DnaJC15) is a "mitochondrial brake"



Barber et al. Nat. Communications 2017; Barber et al. Nat Communications 2020 🔁 💾 Mitotherapeutix

Non-Alcoholic Fatty Liver Disease (NAFLD)



Fatty liver diseases have been estimated to affect 25-30% of world population

MCJ is preferentially expressed in metabolically active tissues (liver, kidney, heart)





3- Mitotherapeutix

Hatle et al. Mol. Cell. Biol. 2013