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Objectives

- Who is Reata Pharmaceuticals?
- What is RTA 408?
- How is the MOXIe study progressing?
Reata Pharmaceuticals, Inc. is a privately held company located in Irving, Texas founded in 2002.

Reata is the leader in developing a novel class of drugs with potent transcriptional activity called antioxidant inflammation modulators (AIMs), which are potent activators of the biological transcription factor Nrf2.

Currently conducting multiple Phase 2 programs focused on Rare Bioenergetic Diseases:

- *Friedreich’s Ataxia (FA)*
- Mitochondrial Myopathies (MM)
- Pulmonary Arterial Hypertension (PAH)
Pharmacology of RTA 408 Antioxidant Inflammation Modulators (AIMs)

- AIMs mimic endogenous molecules that bind to Keap1, activating Nrf2 and inhibiting NF-κB
  - Increases mitochondrial function and cellular energy production
  - Increases antioxidant enzymes and reduces reactive oxygen (ROS)
  - Suppresses inflammation and pro-proliferative drive

- Mitochondrial dysfunction, oxidative stress, and inflammation are features of many diseases

- AIMs subject of more than 200 papers

- Pro-Inflammatory mediators:
  - Cytokines: IL1b, IL-6, TNF
  - Chemokines: MCP-1, MIP-2
  - ROS, RNS, iNOS

- Proliferative/Anti-Apoptotics:
  - Bcl-2, VEGF, Cyclin D1

- Antioxidative Enzymes:
  - ROS/RNS Detox: NQO1, SOD1, catalase, HO-1
  - GSH Homeostasis
  - Iron Detoxification: FTH1, FPN

- Bioenergetics (ATP Synthesis):
  - Glucose Uptake
  - Fatty Acid Oxidation
  - FADH2 and NADH
  - Biogenesis: PGC1α
What does this mean to patients?

- RTA 408 and Nrf2 induction directly improve mitochondrial activity
  - Increased number of mitochondria (biogenesis)
  - Increased fatty acid consumption by mitochondria (fuel consumption)
  - Increased efficiency of mitochondria (managing reducing equivalents)
  - Increased ATP production
### Overview of Design and Timing of Phase 2 Friedreich’s Ataxia Trial

<table>
<thead>
<tr>
<th>Design</th>
<th>Randomized, placebo-controlled, double-blind, dose-ranging study</th>
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<tbody>
<tr>
<td>Size</td>
<td>Up to 100 patients</td>
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<tr>
<td>Patients</td>
<td>Genetically confirmed Friedreich’s ataxia</td>
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<tr>
<td>Treatment</td>
<td>2-Part study with 12 week treatment duration for all patients</td>
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<tr>
<td>Part 1</td>
<td>• Cohorts 1-8: Randomized, placebo-controlled, double-blind, dose-ranging study to evaluate the safety, efficacy, and pharmacodynamic activity of RTA 408 at 2.5 mg, 5 mg, 10 mg, 20 mg, and higher dose levels (not to exceed 160 mg)</td>
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<td>Part 2</td>
<td>• Patients will be randomized 1:1:1 to receive RTA 408 (low dose or high dose) or placebo.</td>
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<td>Endpoints</td>
<td>Primary: Change in peak work during maximal exercise testing</td>
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<td></td>
<td>Secondary: Modified Friedreich’s Ataxia Rating Scale Score (FARS)</td>
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<tr>
<td>Status</td>
<td>Actively Enrolling</td>
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**Trial Sites and DSMB**

- **Sites in the United States**
  - CHOP/Penn – Dr. Lynch
  - University of Florida – Dr. Subramony
  - Emory University – Dr. Wilmot
  - Ohio State – Dr. Hoyle
  - University of South Florida – Dr. Zesiewicz
  - UCLA - Dr. Perlman

- **Independent, multidisciplinary Data Safety Monitoring Board (DSMB)** monitoring this study along with a similarly designed study in mitochondrial myopathy patients (MOTOR)
  - DSMB includes a cardiologist, neurologist, statistician, and patient advocate
  - DSMB coordinated by an independent statistical group
  - Monthly meetings for safety oversight
Current Status

- Part 1, Cohorts 1-4 (n=32) enrollment completed
- Part 1, Cohort 5 (n=8) enrollment targeted in January 2016
- Monthly DSMB reviews underway with no identified safety issues