MyoArete
Mission: Develop Utrophin-based therapies for treating all DMD patients
MyoArete: About Us

Founder: Tejvir S. Khurana, MD, PhD

Professor, Physiology & Pennsylvania Muscle Institute, Perelman School of Medicine, UPENN
• Discovered the Dystrophin-Related Protein (DRP) (now known as Utrophin)
• Discovered motifs/mechanisms for utrophin gene regulation
• Inventor of Patent/Patent filings related to utrophin upregulation for DMD therapy
• KOL for preclinical evaluation of therapeutic strategies for DMD: Author of TREAT-NMD
  SOPs for preclinical evaluation of muscle and respiratory system for DMD

Advisor: Donna M. Huryn, PhD

Professor, Pharmaceutical Sciences, School of Pharmacy, University of Pittsburgh & Adjunct Professor of Chemistry, UPENN
• Eminent Medicinal Chemist, Fellow, American Chemical Society
• Co-Inventor of Patents/Patent filings related to utrophin upregulation for DMD therapy
• Vast experience in Academia and Pharmaceutical Industry, including at Hoffman-La Roche and Wyeth Research

Investor Relations: Neal Lemon, PhD, MBA

• Associate Director, Technology Licensing, Penn Center for Innovation (PCI), Perelman School of Medicine, UPENN
MyoArete Overview

1. The Disease: DMD & Dystrophin

2. The Competition: Current DMD Therapeutic approaches

3. Competitive Advantage: MyoArete’s Utrophin-upregulation Approach for DMD Therapy

4. MyoArete Product: MyoAr small molecules for Utrophin-based DMD Therapy
DMD: Salient Features

• Due to *DMD* gene deletions causing loss of Dystrophin
• Incidence 1:3500 : ca. 50K patients in US and Europe
• Presents by 5 Yrs; loss of ambulation by the early teens
• Life span reduced (typically 30’s)
• Unmet clinical need

• No cure as yet
• Autosomal homologue (*surrogate*) of dystrophin
• Can functionally compensate for absence of dystrophin in muscle when upregulated / overexpressed
The Competition: DMD Therapeutic Approaches

Gene therapy

Sarepta, Pfizer, Solid (micro Dys AAV Trials)

Exon-skipping

Exon 51, 53, 45

Cell therapy

Utrophin upregulation

Post-Transcriptional:
  MyoAr Small Mol
  MyoAr SBO
  MyoAr Gene Edit

Pharmacological

e.g. Steroids

Dystrophin-dependent

Dystrophin-independent

The Competition: DMD Therapeutic Market

- DMD Market Size is estimated to be $4.1 Billion by 2023

Annual Net Sales at Sarepta (drugs targeting c. 20% DMD patients)

- $ Million
  - 2016: 0
  - 2017: 150
  - 2018: 250
  - 2019: 350
  - 2020 (Est): 450

- Annual Net Sales at Sarepta (drugs targeting c. 20% DMD patients)
Competitive Advantage: MyoArete’s Disruptive approach for DMD

Foundational Therapy for DMD
- Applicable to all patients, irrespective of mutation status
- No need for gene delivery
- Escapes immune surveillance, since Utrophin is expressed in DMD
- Additional benefits predicted when added on to current therapies
- Pharmacologically achievable via MyoArete small molecules

Mechanism of Action
- Open the Throttle (Promoter activation/ transcriptional)
- Release the Brakes (Repress the Repression / post-transcriptional)
MyoAr Small molecule Program: HTS to identify drugs for DMD

Activating drug

5’UTR Utrophin | luciferase gene | 3’UTR Utrophin

Luciferase

Luciferin

+ ATP
+ CO₂

Oxyluciferin

+ AMP
+ Ppi
+ CO₂

light

Innovation Grants to Nurture Initial Translational Efforts (IGNITE Program): NS-102838
MyoAr Small Molecules: Hits-to-Lead

- MyoAr HTS Screen#1: SelleckChem 40K

- MyoAr HTS Screen#2: OCL 100 K

Loro et al. Sci Rep. 2020
Utrophin upregulation PoC studies in *mdx* mice

MyoAr HTS Screen#1:
- SelleckChem 40K

MyoAr HTS Screen#2:
- OCL 100 K

Loro et al. *Sci Rep.* 2020
MyoArete small molecule Discovery using OCL

MyoAr HTS Screen#1:
- SelleckChem 40K

MyoAr HTS Screen#2:
- OCL 100 K

<table>
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<th>PID</th>
<th>Product Name</th>
<th>Smiles</th>
<th>Structures</th>
<th>Luciferase Assay</th>
<th>Primary Assay</th>
<th>Counter Assay</th>
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IC50 > 40uM
EC50 > 40uM

y-axis: Z-scores  x-axis: Concentration (uM)
The Pipeline / Pathway

Y1: Screening development
- SelleckChem screen
- SelleckChem dose-resp
- SelleckChem validation
- 5 plates of OCL library screen and counter

Y2: OCL library screening & SAR
- Complete OCL screen (96000 compounds)
- Dose-response (~200)
- SAR analysis
- Isolate most promising (~50)

Y3: Hit2Lead & preclinical studies
- In vitro validation
- Select and re-synthesize ~5 hits
- Hit2Lead: ADME, luciferase, orthogonal assays

Yn: IND enabling and clinical studies
- IP / Licensing/infrastructure
- Lead optimization
- Preclinical mouse PoC studies
- Toxicity studies
- PK/PD studies

NINDS grant# NS102838-1
MyoArete
# MyoArete: Utrophin IP Status at PCI

<table>
<thead>
<tr>
<th>Penn Tech ID</th>
<th>Title</th>
<th>Patent Application</th>
<th>Filing Date</th>
<th>Publication Date</th>
<th>Issue date</th>
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<tbody>
<tr>
<td>15-7411</td>
<td>DMD Antisense therapeutic approach for up-regulation of utrophin</td>
<td>US utility application 16/319,355</td>
<td>7/19/2017</td>
<td>10/3/2019</td>
<td>N/A</td>
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<td>17-8073</td>
<td>FANA-let7 oligos mediated utrophin upregulation for DMD gene therapy</td>
<td>US utility application 16/982,467</td>
<td>3/19/2019</td>
<td>9/26/2019</td>
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<td>18-8707</td>
<td>Utrophin Genome editing for treating Duchenne Muscular Dystrophy (DMD)</td>
<td>US provisional application 63/056,397</td>
<td>07/24/2020</td>
<td>N/A</td>
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<td>21-9570</td>
<td>PMO based Utrophin: let7c miRNA site blocking oligos (SBOs) for treating Duchenne Muscular Dystrophy (DMD)</td>
<td>US provisional application 63/117,419</td>
<td>11/23/2020</td>
<td>N/A</td>
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<td>U4833</td>
<td>Utrophin upregulation via inhibition of microRNA's</td>
<td>US utility patent 8,916,532</td>
<td>1/20/2012</td>
<td>5/17/2012</td>
<td>12/23/2014</td>
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<td>20-9100</td>
<td>Utrophin upregulation compounds for muscular dystrophy therapy</td>
<td>US provisional application 62/961,191</td>
<td>1/14/2020</td>
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Use of Seed Round Funds ($5MM) 2021-2023
Goal: Complete pre-IND enabling studies for MyoAr Small Mol

**Develop MyoArete Business Infrastructure**
- Identify & Engage CEO
- Identify & Engage General & Patent Counsel(s)

**Round 1 Hits to Lead**
- SAR by Purchase (~20-25 molecules/hit) & In Vitro validation (ADME, Utrn luciferase, Utrn western blot)

**Round 2 Lead Optimization**
- Directed SAR (~100 analogs) & In Vitro validation (ADME, Utrn luciferase, Utrn western blot)

**In Vivo Studies**
- PK/PD, Safety Pharmacology and Tox Studies
- Efficacy studies in mdx mouse model of DMD

12 months
10 months