Drug Development and Clinical Trials

Pat Furlong
Parent Project Muscular Dystrophy
Where Are We?

-LATE 1990’s
- Total NIH funding for MD is $17M
- No new drugs in development
- Average lifespan for DMD is late teens
- No guidelines for care
- No patient registries
Where Are We Now?

- LATE 1990’s
- Total NIH funding for MD is $17M
- No new drugs in development
- Average lifespan for DMD is late teens
- No guidelines for care
- No patient registries

• TOTAL NIH funding all MDs ($78M)
• >17 new drugs in DMD trials
• >Many others in preclinical development
• Care guidelines for DMD disseminated globally & update underway
• DMD Lifespan increased by 10+ years
• Natural History Studies, Registries and other drug development tools
Schematic Natural History of DMD

Prior to Treatment, 1960s
- Loss of Standing
- Loss of Ambulation
- Loss of Self-Feeding
- Death

- Loss of Standing
- Loss of Ambulation
- Loss of Self-Feeding
- Ventilation
- Death

Contemporary: With Steroids and Improved Cardiac Management
- Loss of Standing
- Loss of Ambulation
- Loss of Self-Feeding
- Ventilation
- Death

Steroids affect disease progression in DMD over the entire course of the disease, prolonging clinically meaningful functions (time to loss of milestones)
Study Types

• Multi-Phase Clinical Trials
  – Phase I: First in humans (mechanistic, usually in healthy volunteers, dosing, small n)
  – Phase Ila: Safety and Efficacy
  – Phase IIb: “Pivotal”
  – Phase III: Classical RCT
  – Phase IV: Post-Marketing

• Epidemiology and Natural History Studies
Duchenne Therapeutic Approaches

- Exon-Skipping
- Gene Therapy
- CRISPR/Cas9
- Stop-Codon Readthrough
- Steroid Replacement
- Inflammation & Fibrosis
- Calcium Regulation
- Ryanodine Receptors
- Calcium Homeostasis
- Myostatin Inhibition
- Follistatin Upregulation via Gene Therapy
- Selective Androgen Receptor Modulators
- Utrophin Upregulation

Dystrophin Restoration/Replacement

Cardiac

Blood Flow

Mitochondria

nNOS Upregulation

Mitochondrial Biogenesis

Mitochondrial Enhancers

Treating Duchenne

Muscle Growth and Protection
# Clinical trials pipeline 2017

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<th>DRUG</th>
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*Pipeline graphic represents the clinical trial FAQ sheets included in this booklet and it not intended to be a comprehensive list.*
Clinical trials pipeline

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- Target/MOA
- Study Design
- Some inclusion/exclusion criteria
- Endpoints
- Sites
Study Design

Phase?
- randomized
- Different doses?
- Placebo Controlled 2:1

Extension Study/EAP

LENGTH OF STUDY?  STUDY SITE?
- Frequency of visits

INFORMED CONSENT/ASSENT

OUTCOME MEASURES – Primary, Secondary, Exploratory
In development

Just by joining

A main goal of PPMD's DuchenneConnect registry is to connect registrants with actively recruiting clinical trials and research studies.

Duchenne Therapeutic Approaches

- Exon-Skipping
- Gene Therapy
- CRISPR/Cas9
- Stop-Codon Readthrough
- Steroid Replacement
- Anti-Fibrotics
- Inflammation & Fibrosis
- Calcium Regulation
- Ryanodine Receptors
- Calcium Homeostasis
- Myostatin Inhibition
- Follistatin Upregulation via Gene Therapy
- Selective Androgen Receptor Modulators
- Utrophin Upregulation

Dystrophin Restoration /Replacement

- Stem Cells
- Traditional Cardiac Drugs
- Cardiac
- Blood Flow
- Mitochondria
- nNOS Upregulation
- Mitochondrial Biogenesis
- Mitochondrial Enhancers

Treating Duchenne

- Muscle Growth and Protection
  - Stem Cells

Parent Project Muscular Dystrophy
LEADING THE FIGHT TO END DUCHENNE
Duchenne Therapeutic Approaches

- Exon-Skipping
- Gene Therapy
- CRISPR/Cas9
- Stop-Codon Readthrough
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- Anti-Fibrotics
- Inflammation & Fibrosis
- Calcium Regulation
- Ryanodine Receptors
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- Follicatin Upregulation via Gene Therapy
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- Cardiac
- Blood Flow
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- Mitochondrial Biogenesis
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Treating Duchenne

Muscle Growth and Protection
Duchenne Therapeutic Approaches

- Exon-Skipping
- Gene Therapy
- CRISPR/Cas9
- Stop-Codon Readthrough
- Steroid Replacement
- Anti-Fibrotics
- Inflammation & Fibrosis
- Calcium Regulation
- Ryanodine Receptors
- Calcium Homeostasis
- Dystrophin Restoration /Replacement
- Stem Cells
- Traditional Cardiac Drugs
- Cardiac
- Blood Flow
- Mitochondria
- nNOS Upregulation
- Mitochondrial Biogenesis
- Mitochondrial Enhancers
- Myostatin Inhibition
- Member of the TGF-ß Family
- Myostatin Inhibition via Gene Therapy
- Selective Androgen Receptor Modulators
- Utrophin Upregulation
- Stem Cells
- Muscle Growth and Protection
- Treating Duchenne

Parent Project Muscular Dystrophy
LEADING THE FIGHT TO END DUCHENNE
Find a Clinical Trial

The following clinical trial and research study FAQ sheets are family-friendly summaries of clinical trials and research studies for people with Duchenne and Becker, as well as female carriers. There are also FAQ sheets for current pre-clinical research that is soon to be in clinical trial. These FAQ sheets are written for the program book of the PPMD Annual Connect Conference (held every June) in consultation directly with the Researchers. Although we try to include the majority of studies in the United States, this is not intended to be a comprehensive list.

Please note that while the Antidote Clinical Trial finder tool will also give you similar information there are some differences which are reviewed in the table below.

Click here to list all FAQs by Title

<table>
<thead>
<tr>
<th>Feature</th>
<th>Antidote Clinical Trial Finder Tool</th>
<th>DuchenneConnect FAQ's</th>
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THANK YOU TO ALL THE BOYS AND FAMILIES PARTICIPATING IN TRIALS

Pat@parentprojectmd.org