Duchenne Research and Clinical Trials

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SVP, Research Strategy, PPMD

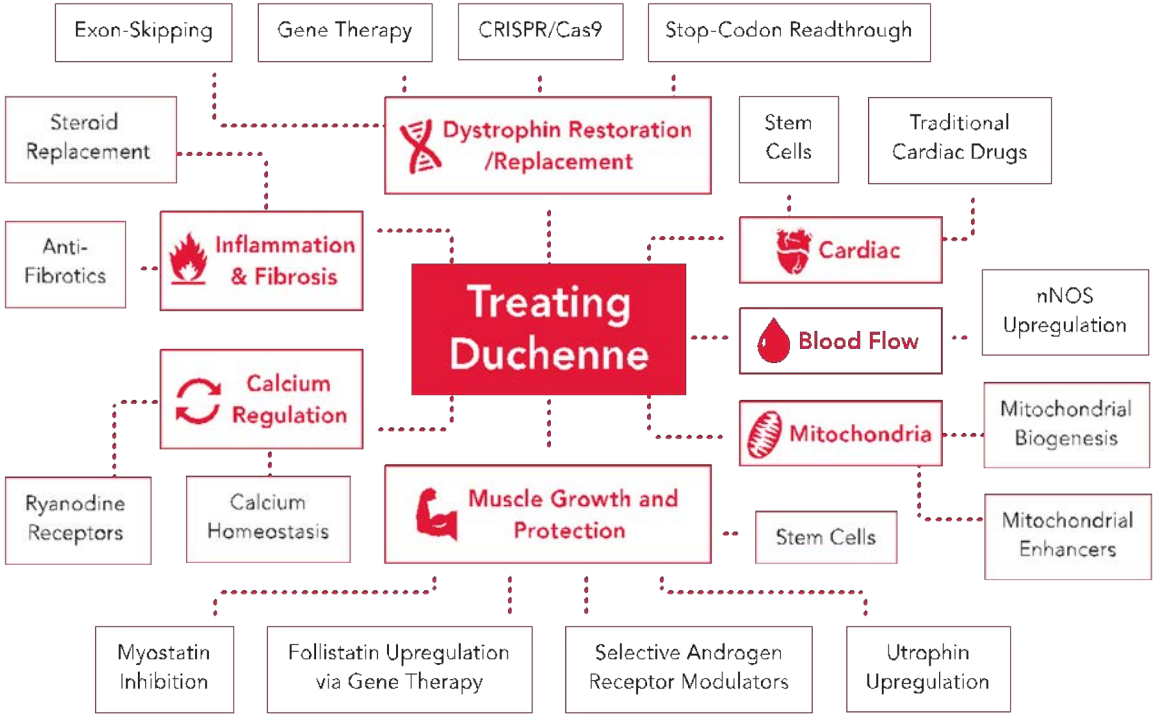
Parent Project Muscular Dystrophy

JOIN THE FIGHT. END DUCHENNE.

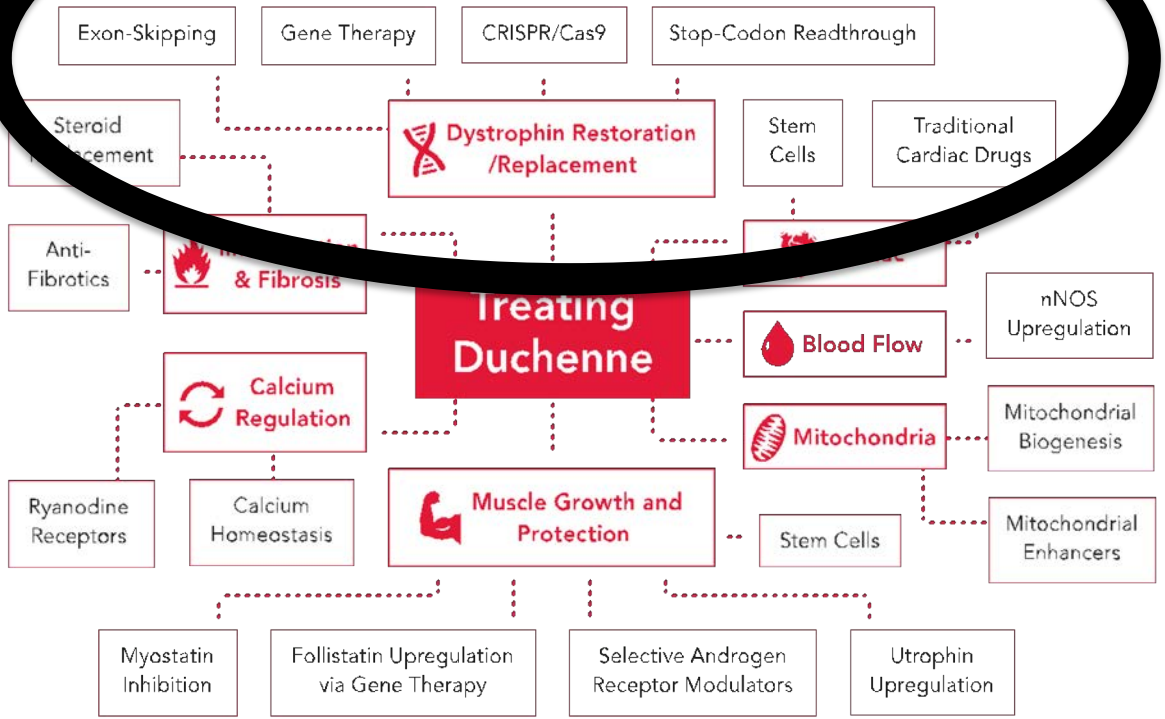
Agenda

- Overview:
  - Current Therapeutic Approaches and Clinical Trials
  - Strategies to Accelerate the Process

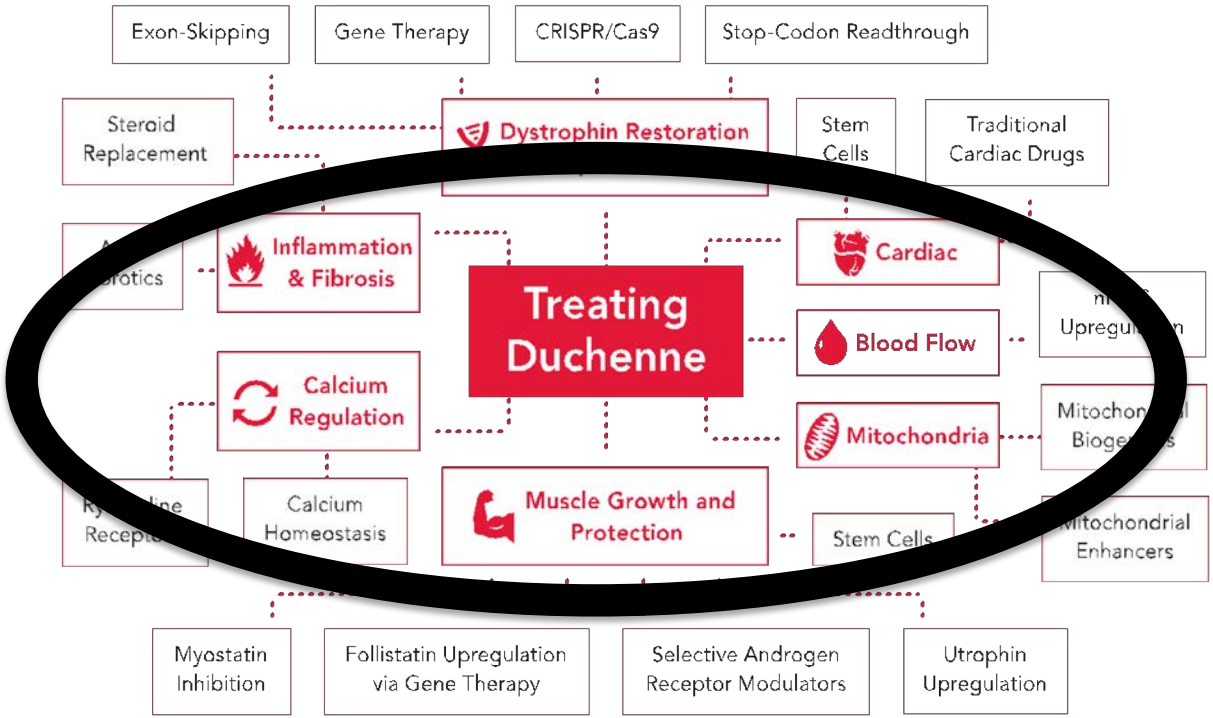
Therapeutic Approaches in Duchenne



Therapeutic Approaches in Duchenne

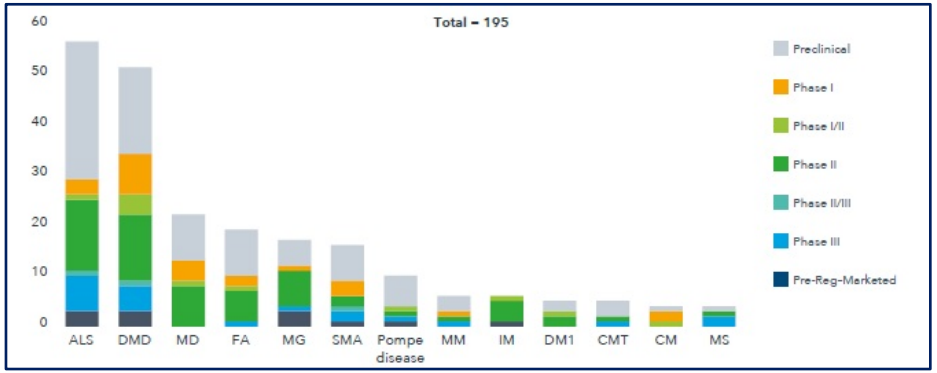


Therapeutic Approaches in Duchenne



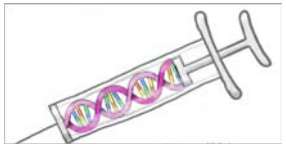
Duchenne is the Neuromuscular Disease with the 2nd largest drug development pipeline

(IQVIA Institute report, 2018)



PPMD Research Funding

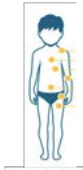
Total active committed multiyear projects



Gene Therapy $3,384,005

Preclinical Research $1,054,704

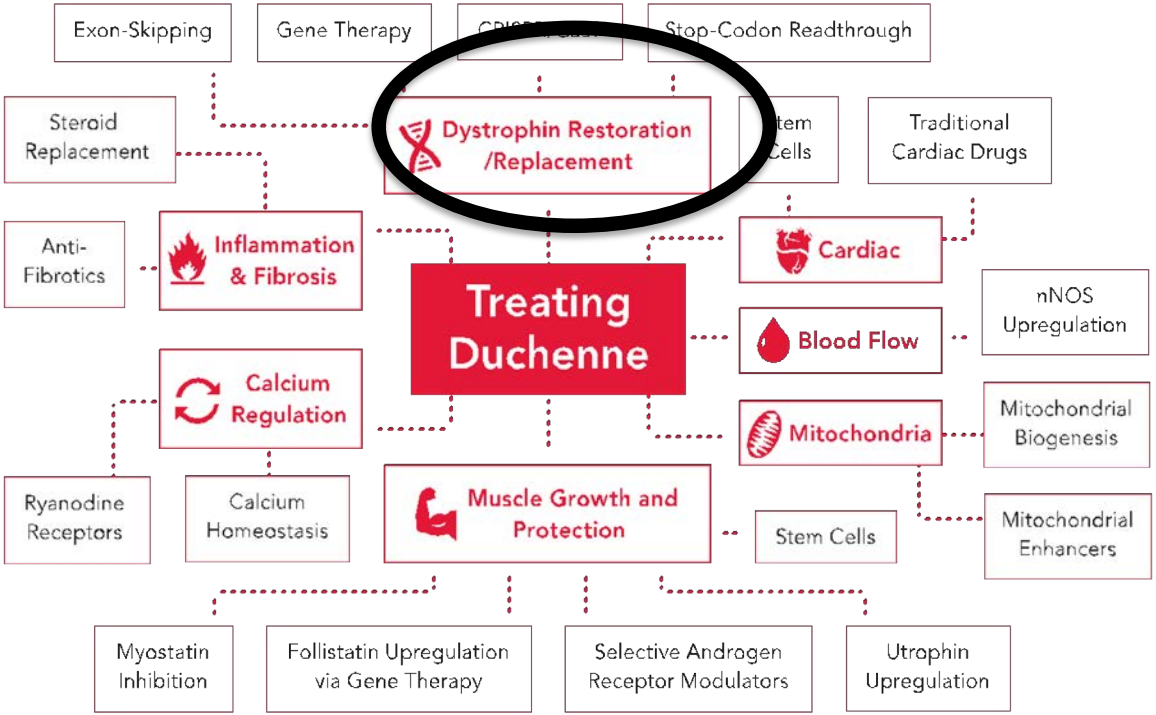
Drug Development Tools $1,525,000



Understanding Natural History $1,208, 500

Robotics $241,040

Clinical Trials in Duchenne



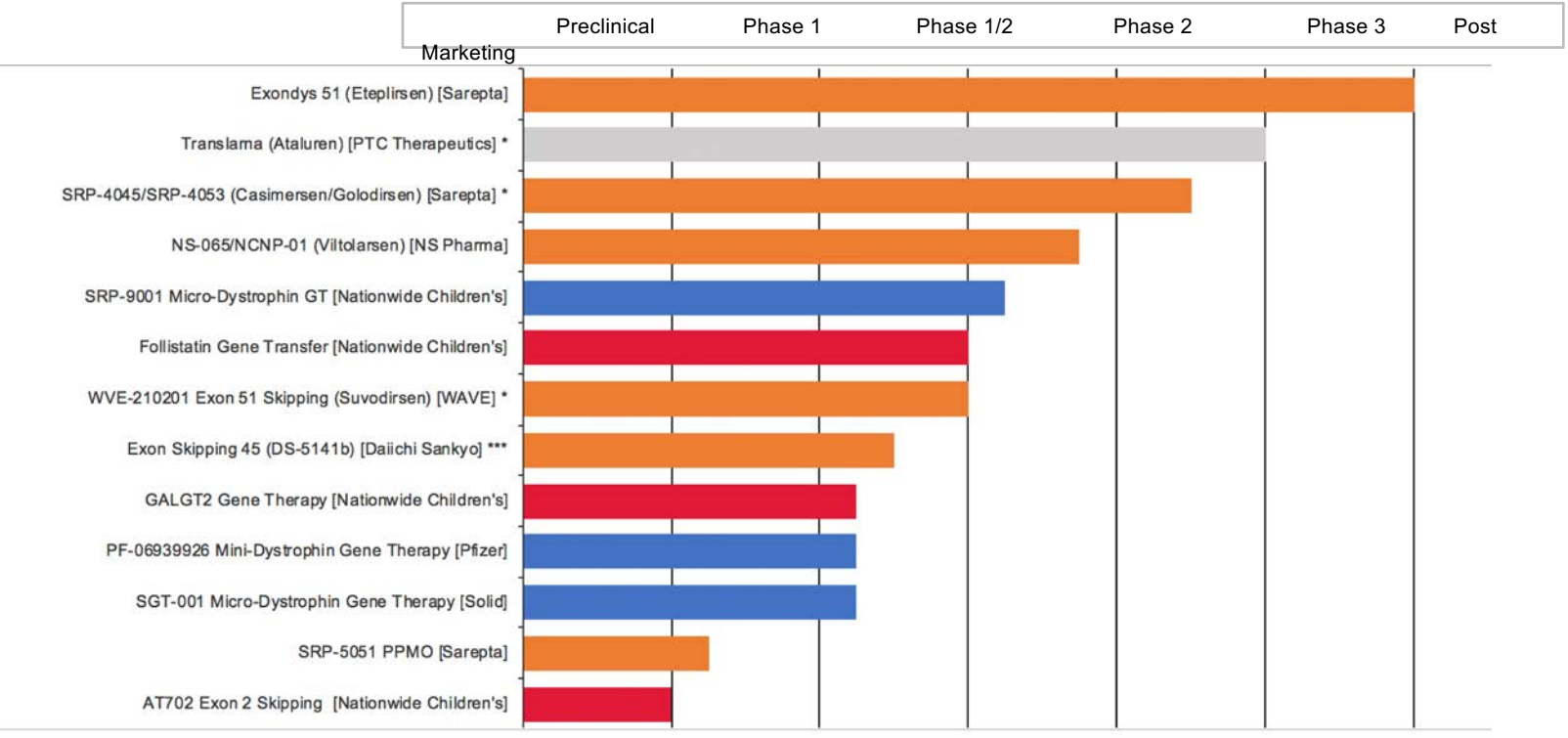
Stop Codor Readthrough

Exon skipping

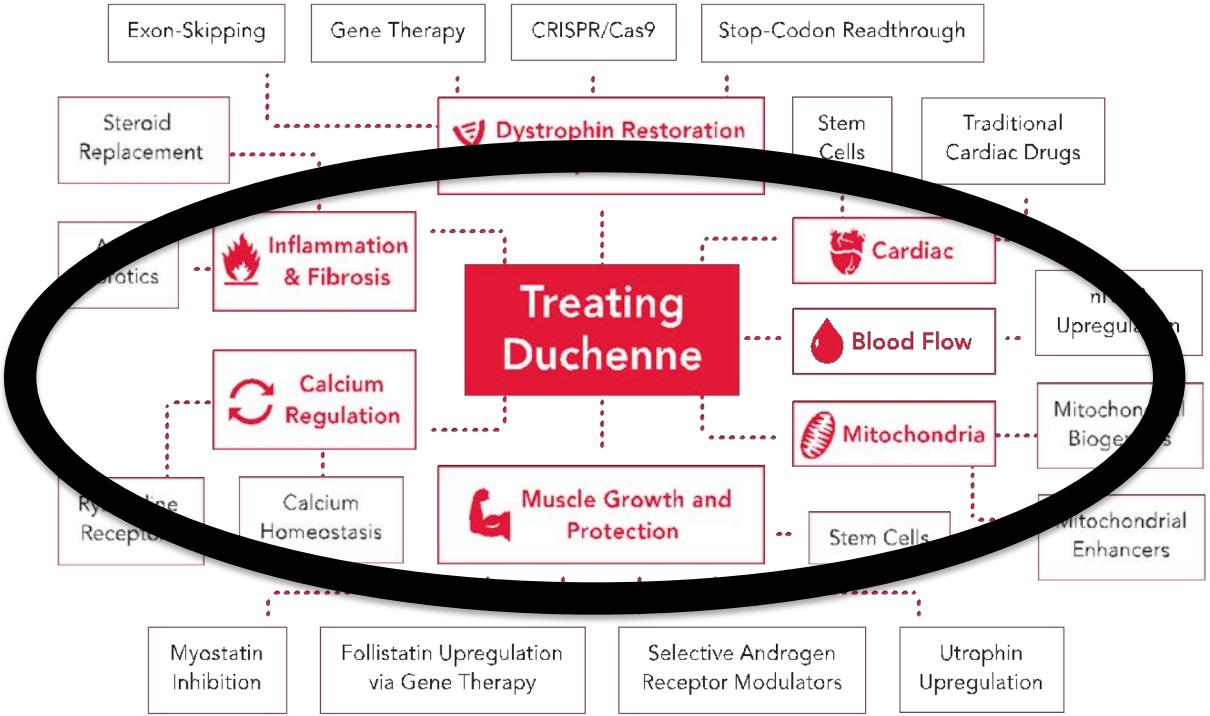
Gene Tx microdystrophin

Gene Tx Other

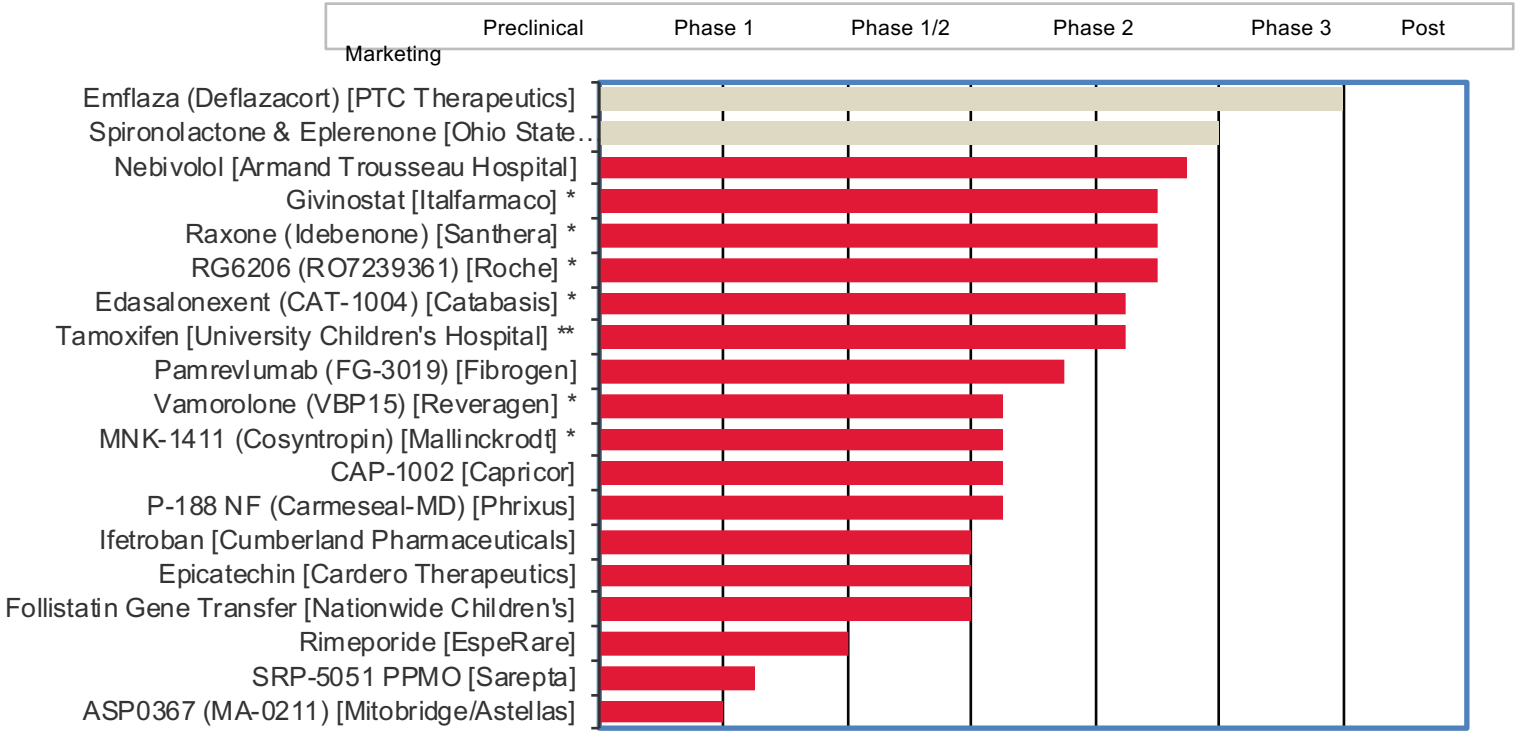
Dystrophin Restoration and Replacement



Clinical Trials in Duchenne

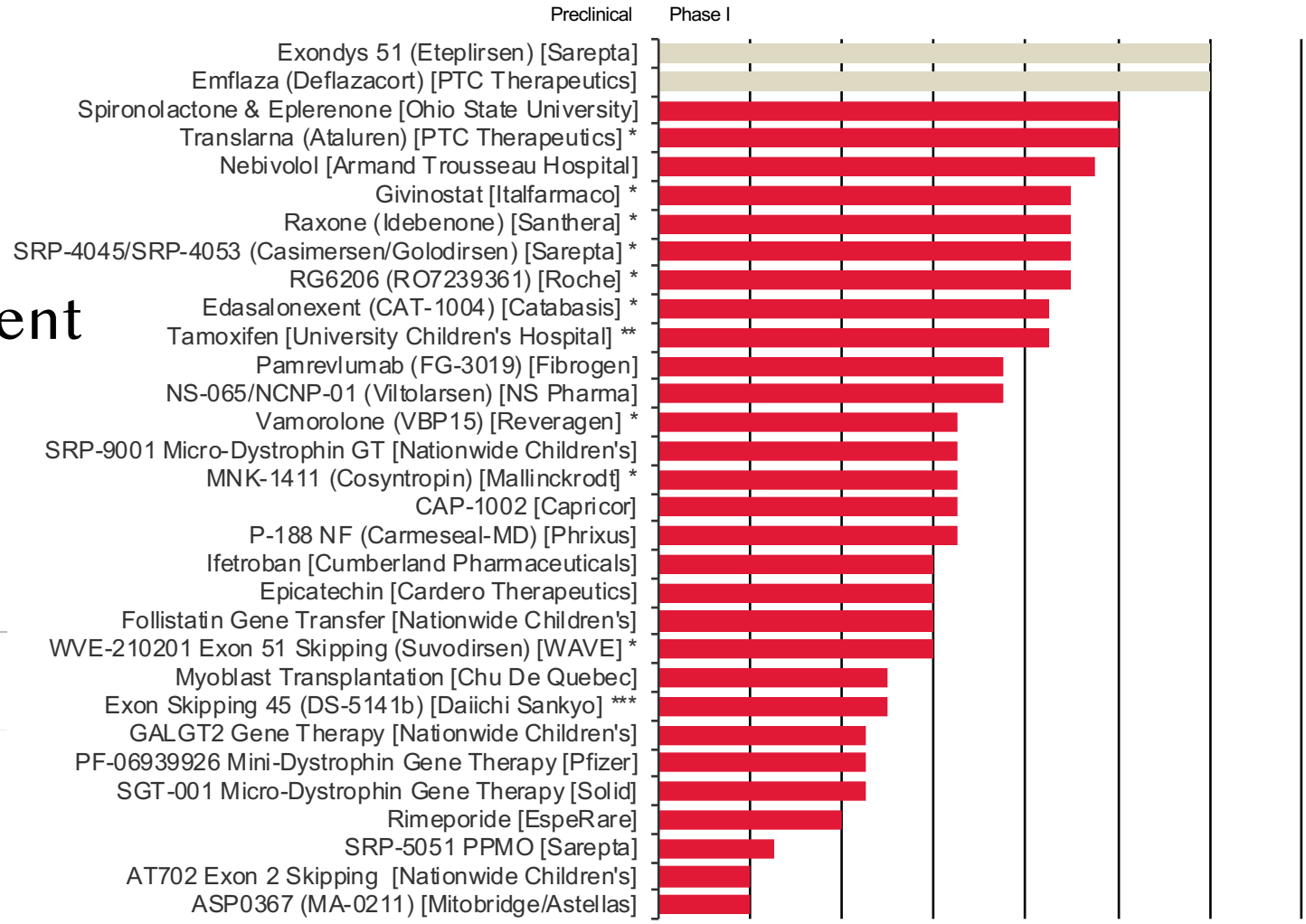


Treating the Downstream Effects of Dystrophin Absence



Parent Project Muscular Dystrophy

Duchenne Drug Development Pipeline 2019



* = will recruit/recruiting globally
** = will recruit/recruiting EU only
*** – will recruit/recruiting Japan only

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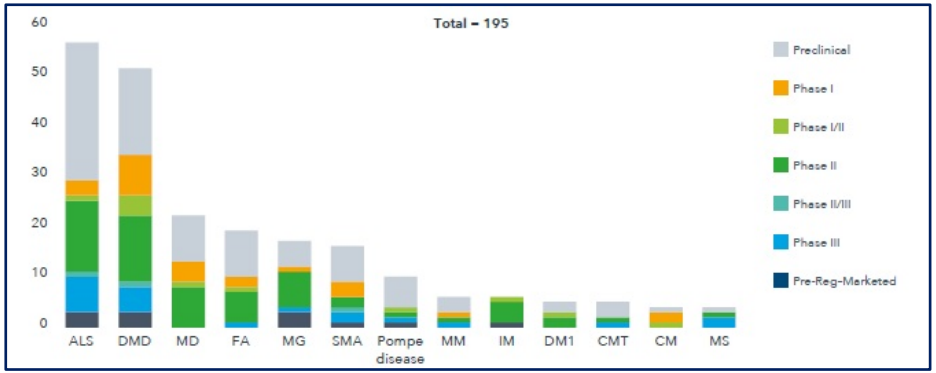
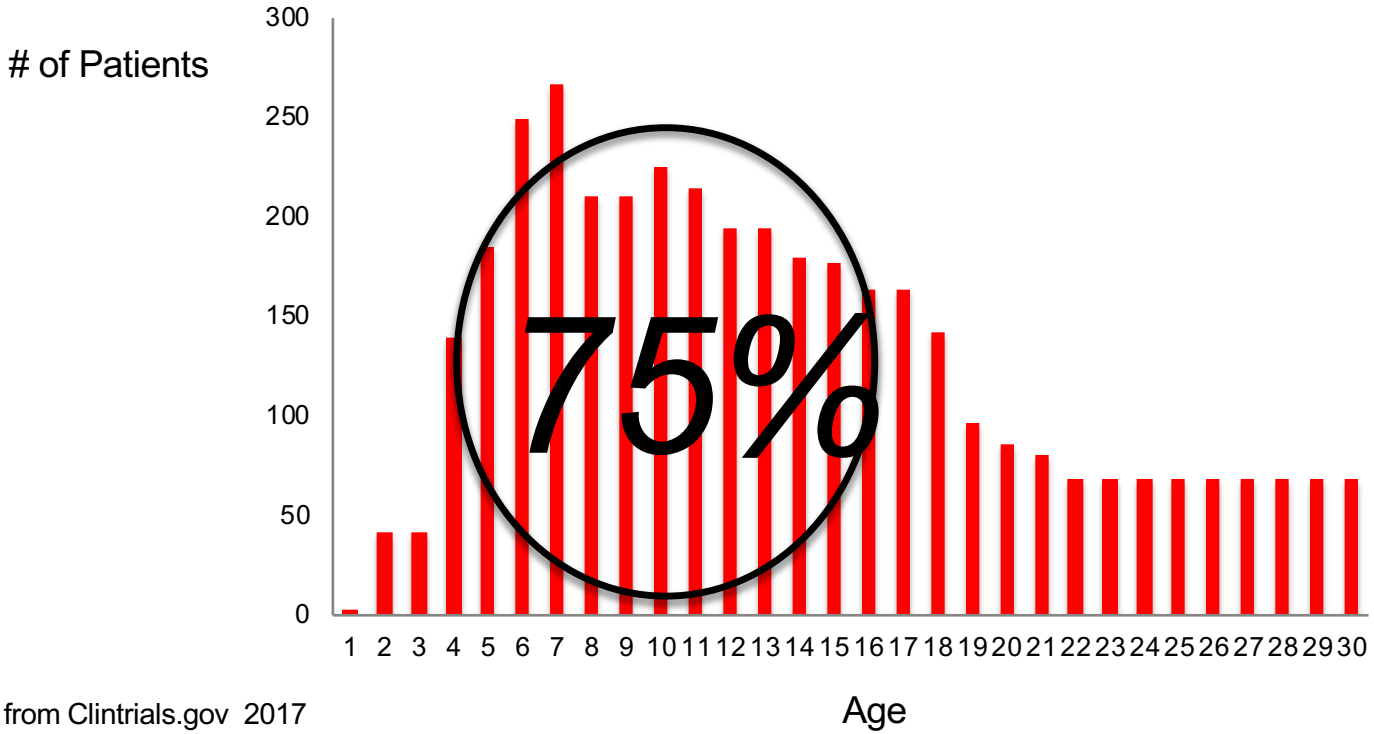


EARLY PHASE

PIPELINE PRESSURE

Patients Needed by Age (n=3885)

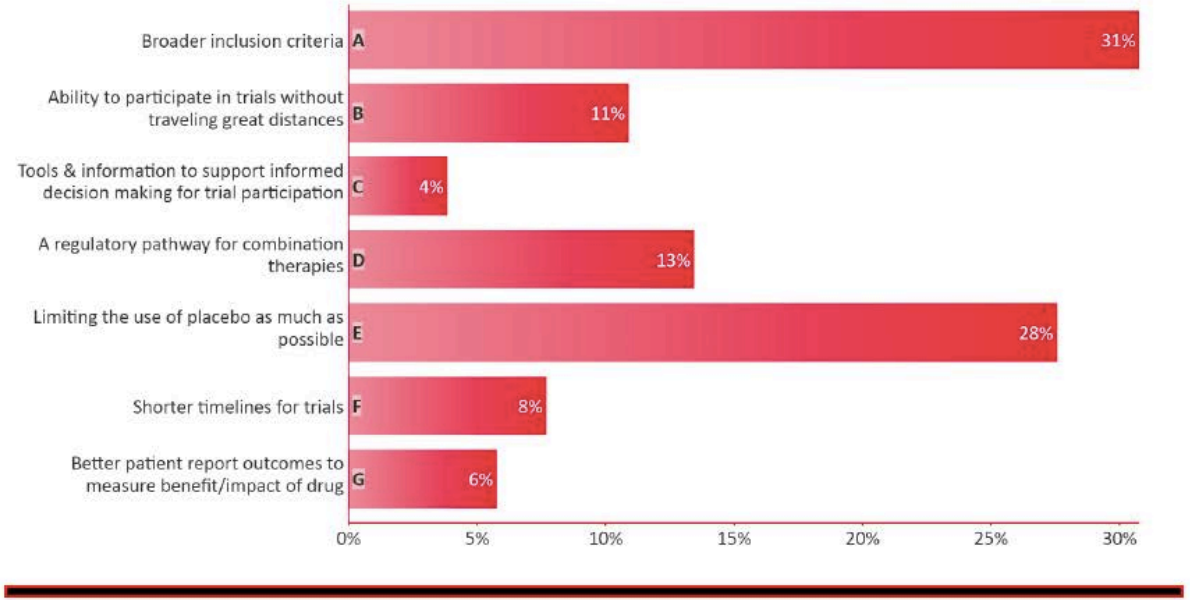
41 studies, Ph 2+,



Data from Clintrials.gov 2017

Patients want trials open to all and with limited use of placebo

Families only- From the perspective of your family, what are two of the greatest needs in the current clinical trial landscape? (Choose 2) (156 responses)

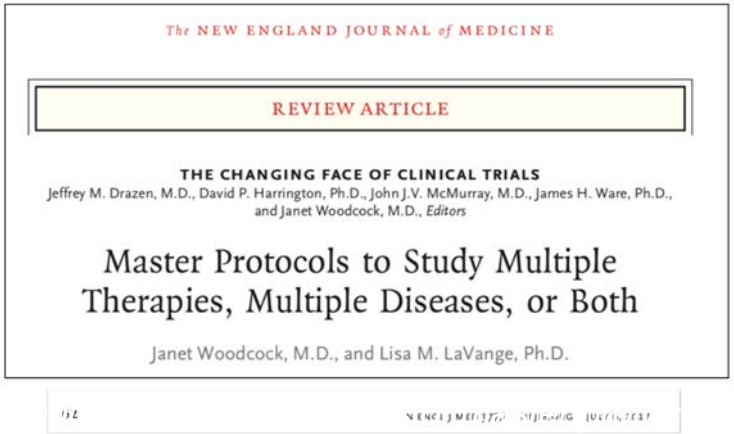


Source: PPMD Annual Conference 2018

The Problem(s)… It Just Takes Too Long

- I/E too narrow
- Trial sites too far away
- Boys can “age out” after only one study
- Significant number of boys randomized to placebo
- Individual trial start-up procedures are repeated = inefficiencies

One Important Solution… A Platform Trial



The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

THE CHANGING FACE OF CLINICAL TRIALS

Jeffrey M. Drazen, M.D., David P. Harrington, Ph.D., John J.V. McMurray, M.D., James H. Ware, Ph.D., and Janet Woodcock, M.D., *Editors*

Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both

Janet Woodcock, M.D., and Lisa M. LaVange, Ph.D.

*Two types of innovation are hallmarks of master protocols: the use of **a trial network with infrastructure** in place to streamline trial logistics, improve data quality, and facilitate data collection and sharing; and the use of a **common protocol** that incorporates innovative statistics“*

Platform Trials Bring Efficiency

- Create one **optimized** trial infrastructure and use it **perpetually** to study **multiple therapies**

Master Protocol

Operational Efficiencies

- ✓ **Faster start-up**
  - ✓ Trial-ready sites
  - ✓ Master Contracts
  - ✓ Central IRB
  - ✓ Ready EDC
- ✓ **High-quality execution**
  - ✓ Network of selected investigators and sites
  - ✓ Uniform data and samples
  - ✓ Recruitment and retention strategies
  - ✓ Robust monitoring

Scientific Efficiencies

- ✓ **Shared placebo**
  - ✓ Important to patients
  - ✓ Sample size savings
- ✓ **Adaptive design**
  - ✓ Real time decision making

Where Are We?

- Protocol Synopsis
- Regulatory Support
- Steering Committee in process
- Infrastructure needs being developed
- Community Meeting September 9th, 2019

Other Ways to Help Solve the Problem: Disease Progression Modelling

D-RSC Initial Objectives

- ✓ Development of a data sharing platform for Duchenne clinical data
  - Fourteen datasets in house, mostly mapped, those that can be shared with the consortium shared with the consortium.
- ✓ Development and publication of a CDISC therapeutic area standard for Duchenne muscular dystrophy
  - Therapeutic area user guide published
- Develop a disease progression model for Duchenne muscular dystrophy via application of the consortium shared data
  - MAP drafted, LOI accepted by FDA.

D-RSC
DUCHENNE REGULATORY SCIENCE CONSORTIUM
CRITICAL PATH INSTITUTE

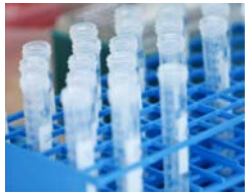
cTAP to Present Late-breaking Results Supporting Advancements in Clinical Trial Design for Duchenne Muscular Dystrophy at the World Muscle Society Congress

October 01, 2018 08:00 AM Eastern Daylight Time

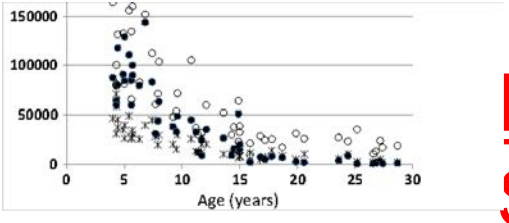
CAMBRIDGE, Mass.--(BUSINESS WIRE)--The collaborative Trajectory Analysis Project (cTAP), a multi-stakeholder, pre-competitive global coalition in Duchenne muscular dystrophy, today announced the acceptance of a late-breaking abstract for presentation at the 23rd International Congress of the World Muscle Society. This is in addition to the two previously accepted submissions that cTAP collaborators will present at the Congress, which is being held October 2-6, 2018 at the Intercontinental Hotel in Mendoza, Argentina.

COLLABORATIVE TRAJECTORY ANALYSIS PROJECT

Other Ways to Solve the Problem: Enabling Discovery and Research

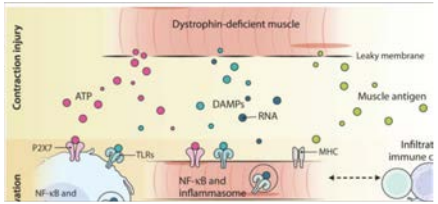


BioBanking



BioMarkers
Serum Proteins,
Fat Fraction,
Urine fragments

Other Ways to Solve the Problem: Refining our Understanding



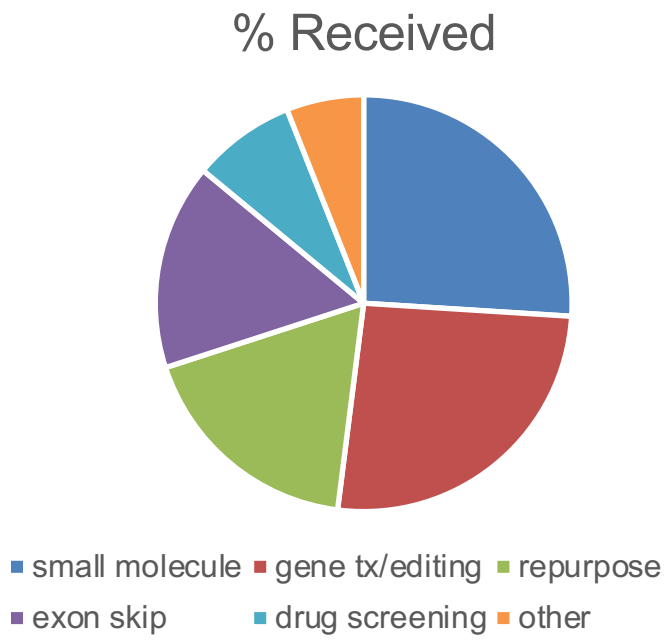
Inflammation & Immunity

testing (MMT)				
MMT	Average of 26 muscles	−0.72	<0.0001	Time to sta
MMT	Upper extremity muscles only	−0.63	<0.0001	Time to sta from cha
MMT	Lower extremity muscles only	−0.72	<0.0001	Purdue Pe
Quantitative muscle testing (QMT)	% of Predicted normal	−0.56	<0.0001	Jebsen-Ta hand fun
QMT	Upper extremity	−0.55	<0.0001	Pinch grip
QMT	Lower extremity	−0.57	<0.0001	Pinch grip
Grip strength (QMT)	Right hand	−0.63	<0.0001	Forced vita (FVC) Sit
Grip strength (maximum voluntary isometric contraction of grip	Peak force	−0.64	<0.0001	FVC supine

PRO Development

Cardiac RFA 2019 :

Innovative therapeutics and technologies for improvement of Duchenne cardiac care and treatment



- 39 applications received
- Culled down to 9 for full review
- Awards to be made this fall

Questions remain once we have more treatment options…

We must…

- Ensure treatments are covered by payers
- Continue to improve care and management and ensure it is standardized
- Ensure the patient voice informs all the work being done

Thank you!