Duchenne Master Protocol Collaboration: PPMD/I-ACT

Parent Project Muscular Dystrophy

JOIN THE FIGHT. END DUCHENNE.

Pat Furlong
Pat@parentprojectmd.org

Review of FDA Meeting: August 7

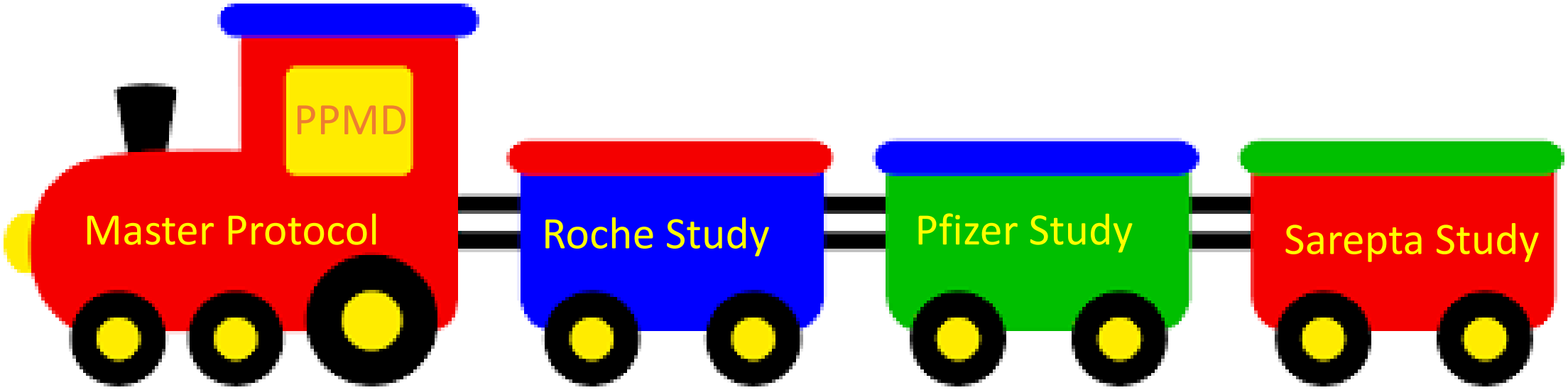
- Started with overview of where we are
- FDA Comments
  - We are going down right path.
  - Need infrastructure as well as industry support. The two sides must converge.
  - Need a unified group of investigators that agree to collective action; standard protocol, data collection, storage and management, etc
  - Envision a trial network to form, begin to standardize data collection, processes, systems etc. Could pilot infrastructure with one trial.
  - Also envision an arm for a robust natural history study. It is clear that FDA would like to see data from a well controlled natural hx study.
- Next Steps
- f/u with others, research what exists, environmental scan of trial landscape

Master Protocol

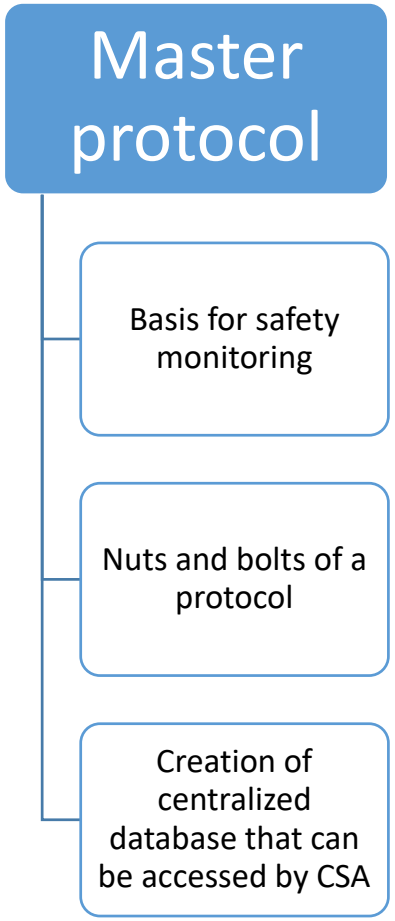
- Comparing investigational agents
  - Not ideal for DMD as it would require a larger study to be adequately powered vs comparison to placebo
  - Multiple programs vs placebo is feasible
- Create stratification based on criteria (age, disease state, genetics)
  - Will need to permit patients to have decision on study options
  - Sponsors will want access to all pts, not to be excluded to favor another study
- Duration is not always equal
  - Flexibility is needed for 24 vs 48 vs 96 week studies
  - Platform study would enable comparing with different durations

Hub design

- Similar to a Platform study, but creates company specific protocols based off of a master protocol
- A company specific amendment to the Master would allow each company to add their specific testing or biomarkers and retain confidential information
- A study consists of the Master Protocol with company specific amendment.
- There will be multiple different deviations of the same master protocol

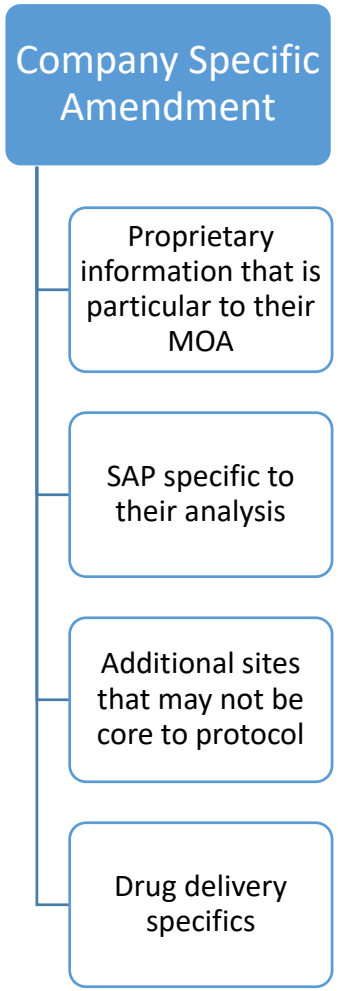


PPMD creates the Core Hub protocol



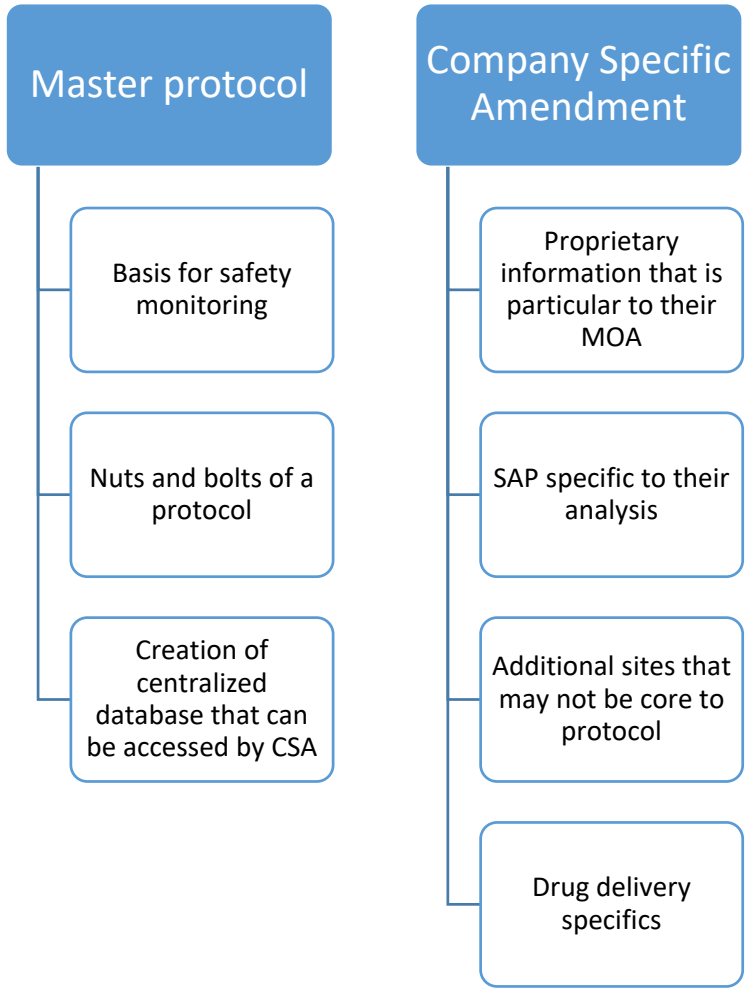
- Master protocol in about 80% of a complete protocol
- IRB – EC approved protocol indicates that a majority of the sites and countries are willing to accept and resource a core activities of a protocol
- Sites require less resources because all studies using the MP have similar requirements

Individual companies create an amendment

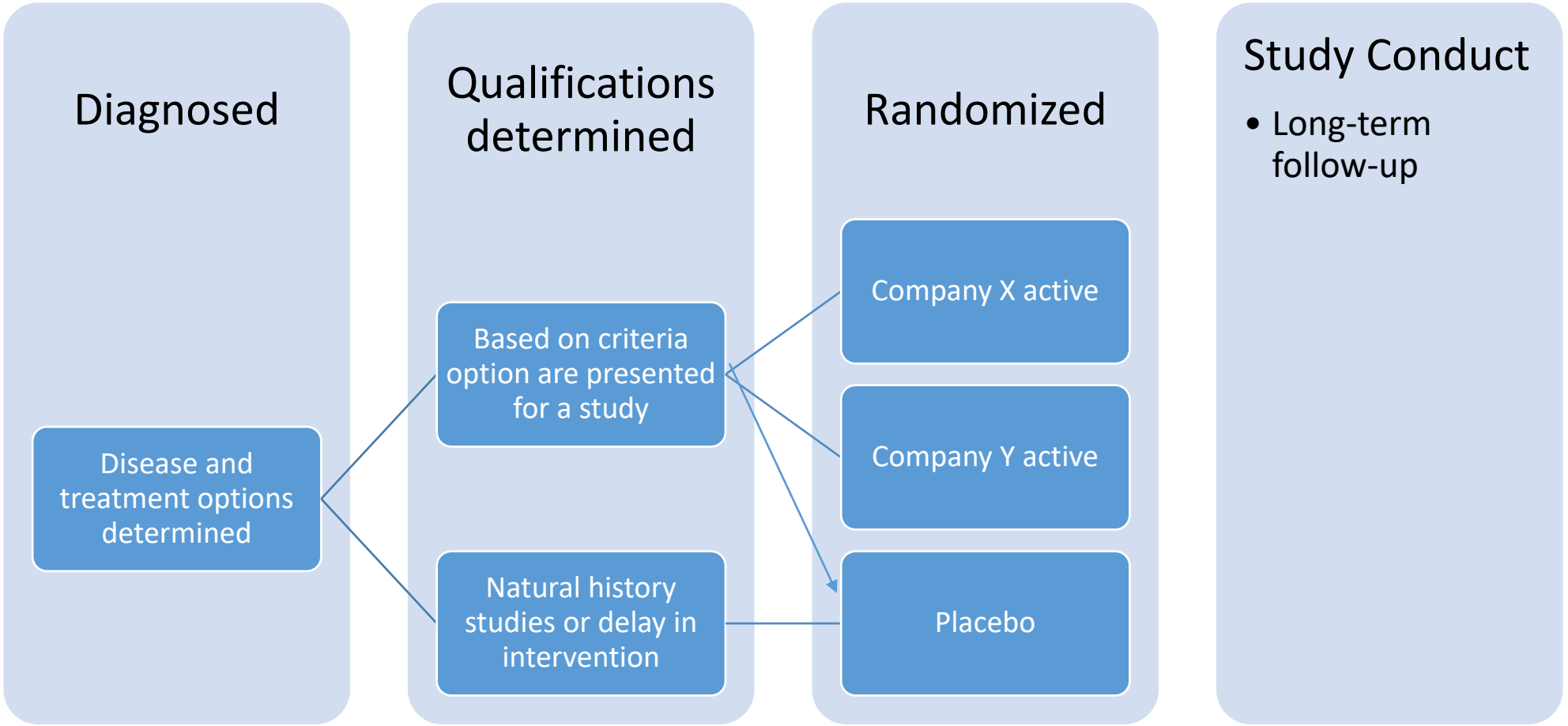


- Each sponsor creates a study specific amendment with their requirements
- IRB – EC only needs to review / approve this amendment (20%) with 80% of the protocol already approved
- Sites only need to contract and learn the 20% in the amendment

Site and IRB facing, Country CTA facing



Patient Flow

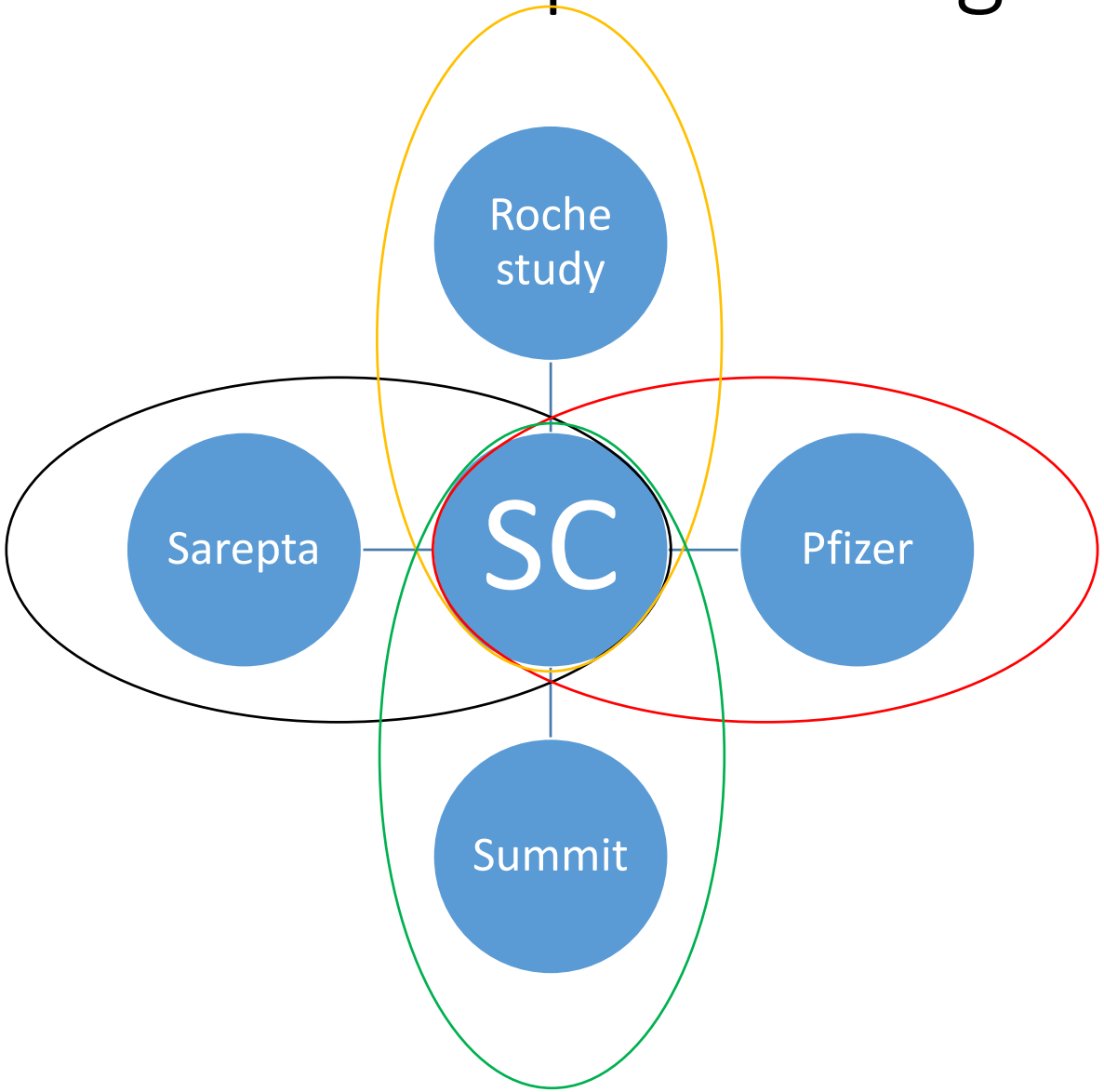


Example:

In this example – there is one “BELIEVE” protocol and each company has their own amendment that has their company specific (dosing, duration, biomarkers, specific TFT). They all still use the same CRO, database etc

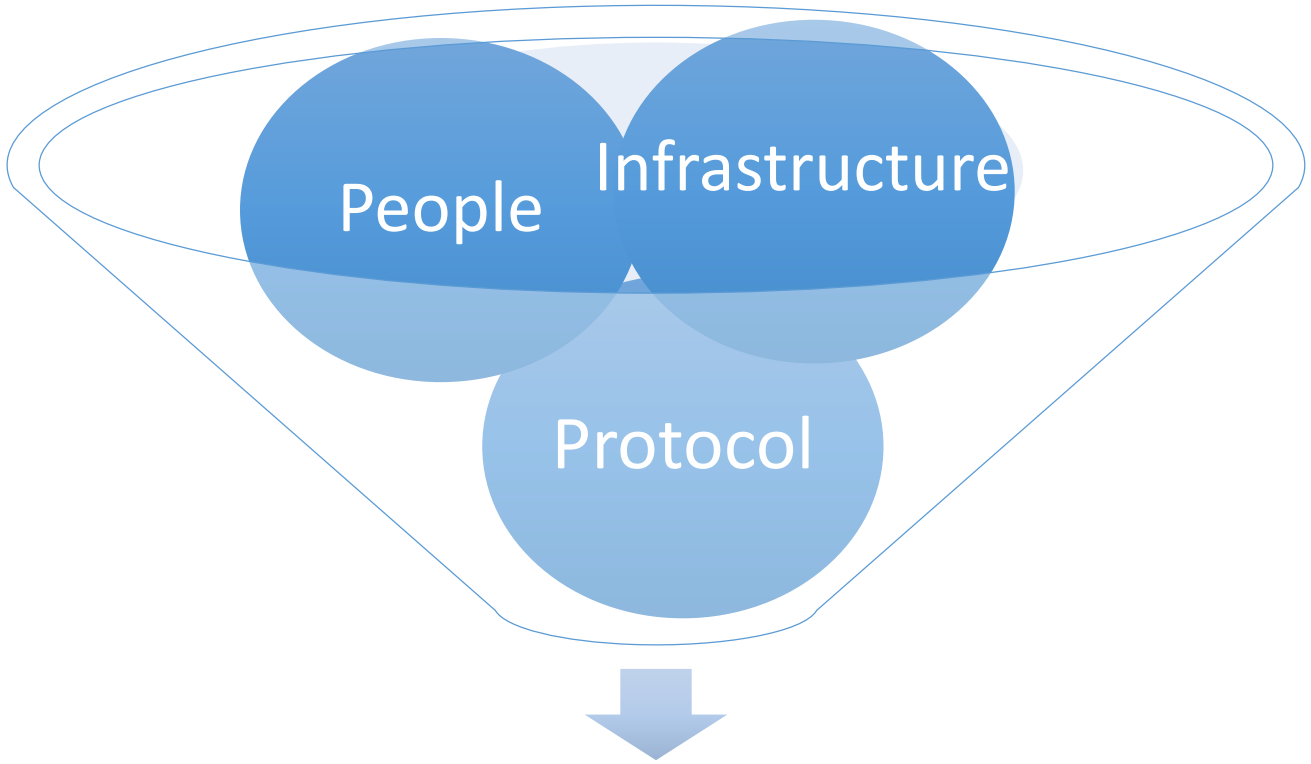
- BELIEVE PROTOCOL: This is the core protocol
- BELIEVE NFkB- this would include catabasis specific endpoints on top of the basic
- BELIEVE 52 – this study would probably be a 96 week study for Sarepta and involve biopsies
- BELIEVE Myo – this would be a myostatin study using the master protocol, plus more myometry. No biopsies and only 48 weeks
- BELIEVE Raxone – this would focus more on pulmonary endpoints and other company specific biomarkers .

Hub and spoke design



- This shows 4 different studies that all have the base design in common.
- They will use a common CRO, database, etc
- They get all the benefit of the Master Platform design, while being able to tailor their study specific and confidential information

Developing a Master Protocol for Duchenne
three key ingredients



People

- Industry -
  - Inform design of master protocol;
  - First mover partners willing to participate;
  - Assist with influencing other key stakeholders

- PIs
  - Willingness to work collectively and differently – shared resources and processes
  - Assist with design of master protocol

- Regulators
  - Support and flexibility

Protocol

Trial Design Skeleton

- allows for any possible patient subgroups,
- handling of multiple arms and combinations,
- defines randomization scheme,
- modeling of patient outcomes and different endpoints
- the addition or removal of different arms seamlessly,
- design adaptations, decision rules, and trial outcomes

Infrastructure

- What capacity is needed?
  - # of sites, staffing, assessments, etc.
- What networks already exist? Can parts be reused?
  - DMD Imaging, NeuroNext, CINRG, others? Sites?
- IRB? Consent?
- Governance?
- CRO?
- Database and Data Management?

Information Gathering Phase

- Assess clinical trial landscape to characterize what trials/compounds/combinations potentially could participate in the master protocol effort.
- Assess what infrastructure/ staffing /skills would be needed by sites in order to be a site for a master protocol trial
- Identify resources needed and key questions to be answered for centralization necessary for implementation of a master protocol.
  - CRO?, Data Management? DataBase? IRB? Consent?
- Work with stakeholders to assess clinical trial networks already built; CINRG, Imaging-DMD, CDCC's, NeuroNext, I-ACT; evaluate their strengths and weaknesses. Come up with the best solution using parts of what is already built – or perhaps starting from scratch?
  - Create a list of criteria to evaluate existing networks

General Plan

People	This WG to continue to provide input, start socializing idea with CDCC Directors/KOLs
Protocol	Berry Consultants to help, iterative process, use resources from this group, Pis and others
Infrastructure	Work with C-PATH/D-RSC or others to help short term with information gathering phase, will require input from this group, will define “asks” up front

In 4-6 months Public Workshop
Goal: Create Implementation Plan
Two Parts: Protocol presentation and Infrastructure findings
All stakeholders present
Consensus on Implementation Plan and Buy In to Skeleton Trial Design