cTAP: Pioneering collaborative analytics to accelerate therapy approval and access in rare disease

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Objectives: Break the cycle of iterative clinical trial design failures that delay patients' access to new therapies:

- bring the benefits of speed and flexibility to the consortium model
- accelerate learning from patient data
- explain/account for heterogeneity of disease progression
- build consensus and share learnings

Methods: Establish proof of principle by conducting a pilot in DMD

- Secure comprehensive access to de-identified patient clinical data
- Describe natural history
- Develop prognostic models to predict outcomes in clinical trials
- Apply to trial designs
- Share insights and tools with the entire community

Results:

Data Access: cTAP has established collaborations with clinical networks (Telethon Italy, NSUK, iDMD, iMDEX, CINRG), major clinical centers (UZ Leuven, CCHMC, CHOP), and sponsored clinical studies (Lilly, PTC therapeutics, Biomarin, Marathon Pharmaceuticals, and Summit plc) to secure access to a diverse set of anonymized individual patient clinical data.

cTAP's patient database accesses natural history, real world data, and clinical trial data from more than 3000 patients with DMD in the US and EU

Describing natural history: cTAP has previously demonstrated that heterogeneity in DMD is structured (Mercuri et al 2016), and that minimal clinical effect size for ambulatory outcome measures can be quantified (Goemans et al., 2018)

Develop prognostic models: cTAP has developed prognostic models for 6MWD, NSAA, 4SC, and loss of ambulation, each of which more than double prognostic power over previously published models (Goemans et al., 2016, 2018)

Application: cTAP has built an analytical portal to patient data that enables real time pressure-testing of trial designs against real world outcomes before starting a study, and creates matched natural history cohorts that can serve as external controls or augment placebo controls

Share insights: since its founding in 2015, cTAP has presented more than 6 new findings at major scientific forums every year, has 2 peer-reviewed manuscripts published and 2 in press, has reviewed findings with regulators, and provides updates to patient foundations at least annually.

Conclusions:

- Bring the benefits of speed and flexibility to the consortium model:

cTAP has preserved the principles of shared costs and open communication inherent in a pre-competitive consortium model. Additionally, cTAP i) successfully recognized and addressed the control of data-use that data-stewards have previously experienced as a significant barrier to sharing data, ii) developed a structured modular funding process to operationalize the principles of equal cost/equal benefit for companies across the spectrum from pre-clinical to commercialized products.

As a consequence, cTAP is the first initiative of its kind in DMD, is the first to access patient data across continents, and is the largest, and still growing, multi-national inventory of patient clinical data in the field.

- Accelerate learning from patient data:

Learning from patient data was accelerated by a combination of unprecedented access to patient data, application of advanced data science at scale, and a governance of goal-setting and funding focused on meeting the most pressing needs in therapy development in Duchenne.

- Explain and account for hetereogeneity of disease progression:

cTAP has applied validated analytic methods not previously deployed in Duchenne to characterize heterogeneity in this rare disease, to predict outcomes during the course of a clinical trial, and quantify any individual patient's risk of succumbing to their next clinical milestone.

- Build consensus and share learnings;

cTAP findings have been shared broadly through scientific communications. Discussions with regulators have 'primed the pump' on translation of findings to trial design and interpretation.

The cTAP pilot in Duchenne demonstrates an effective means of promoting collaboration to advance drug development for rare disease