

Cure Rare Disease FAQ

Basic statistics about rare disease & Duchenne muscular dystrophy (Source: NORD)

- o 7,000+ rare diseases
 - 50% of patients with rare disease are children
 - 1/3 of those children impacted by rare disease will not live to their 5th birthday
 - Only 5% have effective treatments or a cure
- o 10% of the population (or 30 million Americans) suffer from a rare disease
- o The economic burden of rare disease was \$966 billion in 2019 (Source: EveryLife Foundation)
 - \$437 billion of that burden came from the indirect cost of productivity loss for caregivers and patients
- o Some of the mutations and conditions CRD is working to develop therapeutics for have patient populations in the single digits in the United States

What's unique about Cure Rare Disease?

- o Cure Rare Disease currently focuses on developing therapeutics that will halt or reverse the progression of rare and ultra-rare genetic neuromuscular and neurodegenerative diseases. We anticipate that the learnings from these efforts may help to guide therapeutic development for diseases outside of CRD's focus.
- o CRD has 19 active drug development programs, including Duchenne muscular dystrophy (DMD), several subtypes of Limb-girdle muscular dystrophy, SCA3, and ADSSL1. Potential therapeutics for these conditions are in varying stages of development and progress independently of the therapeutics being developed for mutations of DMD (an August 2022 pipeline can be viewed on [our website](#) for more information on the development of each therapeutic). The process is designed to be generalizable to other rare, monogenic diseases.
- o We have formed an unprecedented collaboration with leaders in the therapeutic development space, brought them together and focused them around the mission of developing therapeutics.
- o Beyond drug development, we have a strong interest in ensuring and improving equitable access to life-saving therapeutics. While the current reimbursement structure will likely not work for ultra-rare diseases, we are pursuing efforts to establish reimbursement.

How is Cure Rare Disease's approach different from other non-profits?

- o Rather than have a call for proposals, CRD explores and then chooses to engage in a therapeutic development effort for a particular disease or mutation. Once selected, CRD then forms a world-class research team around the effort. Once the team is formed, the operations are funded with the goal of getting to a clinical trial.
- o While basic research is critical, it is not something that CRD funds.

Why is Cure Rare Disease a non-profit?

- o Commercial entities are incentivized to develop therapeutics for as large a population as possible. CRD is a non-profit for several reasons. Firstly, as a non-profit, we are able to treat small patient populations to get insights before partnering with industry to treat the rest of the population, if amenable. Secondly, we can pursue the treatment of ultra-rare conditions, which may not have commercial potential due to small patient numbers. Thirdly, as a non-profit we can access talented advisors and contributors who are outside of CRD since we are non-competitive. Bringing together multiple perspectives regardless of competition helps to get the best ideas elucidated. Lastly, by engaging the FDA early and often, we are able to reduce regulatory risk which can significantly slow a program.

How do you scale this therapeutic effort?

- o With the approval to begin a clinical study of our first therapeutic, CRD-TMH-001, we have validated the ultra-rare drug development framework which is actively being applied to other diseases and mutations. Once we've shown that this process can safely and effectively treat several diseases, we will have a firm understanding of the best methods to employ and will become more cost and time-efficient as we scale to help hundreds, if not thousands, of rare and ultra-rare disease patients.

How does the organization continue to support this effort once scaled?

- o We estimate that once we've had several early successes with therapeutics for rare and ultra-rare neuromuscular diseases, the cost will fall for subsequent patients to \$2.8-3.5M per patient. The long-term goal is to work with payers (insurance companies) to get insurance to cover this approach.

How is this different from what drug companies are doing?

- o Our process for drug development focuses on interdisciplinary collaboration. Moreover, we can engage advisors and contributors from across a wider spectrum of talent than commercial entities. These factors combine to accelerate, without compromising safety, our drug development efforts. Moreover, we can pursue treatment for ultra-rare diseases which may not have commercial potential.

How does Cure Rare Disease make money?

- o We rely on our donors, partner corporations and grants to fund our work. While we are not concerned with making a profit, we need to be certain that we have the financial wherewithal to fund the development and clinical application of the therapeutic. We diversify our income from multiple sources to ensure that we are financially salient. For successful drug development efforts, we will seek to partner off the therapeutic to industry to allow the rest of the population amenable to that therapeutic to be treated.

What is CRISPR?

- CRISPR is a technology that allows for researchers to pinpoint a very precise location of genetic code (DNA) and modify it – either by cutting an erroneous piece to alter DNA or by using transcriptional activators (a protein, in this case the Cas9 protein, whose function is to produce more of what it binds to) to increase expression of a target gene (as we are doing in our first clinical study).

Why are you using genetic medicines? Why not small molecules?

- Cure Rare Disease focuses on genetic medicines because of the precision that they can have to treat monogenic diseases and because the success of one therapeutic development effort can inform other development efforts.

Why so many collaborators?

- Each collaborator we are working with has world-class level mastery over a specific area of focus. While all researchers are trained in broad areas, each researcher has a specialty they are renowned for, which is exactly what we need when working with such rare and ultra-rare diseases. Moreover, each researcher benefits from the insights and knowledge that others bring to the table and are able to cross-pollinate ideas to help move faster.

Where is the research done?

- CRD conducts the majority of our research through our collaborators. Each collaborator does specific research for us, such as UMass being the one to establish cell lines while Yale and Sick Kids are responsible for the development of the CRISPR therapeutics. Our partnerships include 8 academic centers and numerous industry partners across the Northern Hemisphere.

How does CRD ensure that the research is done timely?

- For each collaborator, we have a research agreement in place which dictates what they will do, how much it will cost and when it will be completed. Of course, science is an uncertain endeavor, but we do our best to keep on track.

How does CRD ensure that the best scientific decisions are being made?

- We have brought together the world's experts in this development. Moreover, we have integrated the researchers in a way that allows for candid feedback and discussion on proposed next steps. **There is no one researcher calling the shots but rather a collective which incorporates the deep knowledge of the group into every decision we make to optimize our chances of success.**

Who pays for the treatment once the clinical trial is completed?

- Once a clinical trial is complete for a specific indication and shows an acceptable efficacy/safety outcome, CRD will partner the technology to a pharmaceutical company to treat the rest of the population who is amenable to that drug, ensuring access for all.