2021 RESEARCH UPDATE

CYSTIC FIBROSIS FOUNDATION

Prepared for: Ms. Martha Keller
Information as of July 2021

Every person with cystic fibrosis should have the chance to live a long, healthy life. Recognized globally, the Cystic Fibrosis Foundation continues to lead the way in the fight against cystic fibrosis, fueling extraordinary medical and scientific progress. Working alongside the CF community, the CF Foundation has fostered the development of more than a dozen CF treatments — an unprecedented number in a short span of time — and helped add decades of life for people with CF. Despite this progress, many people with CF do not benefit from existing therapies for the underlying cause of the disease. Many children and adults with CF still face the sobering prospect of a shortened lifespan. Our vision is a cure for every person with cystic fibrosis and a life free from the burden of this disease.

Today, we invite you to learn about some of the research and scientific efforts underway, which donor support helps make possible.

PROGRESSING OUR PATH TO A CURE

The CF Foundation launched its groundbreaking *Path to a Cure* initiative in October 2019 to accelerate treatments and drug development for the underlying cause of the disease for all people with CF and ultimately deliver a cure. This initiative centers around three core strategies to address the underlying cause of CF: repairing broken cystic fibrosis transmembrane conductance regulator (CFTR) protein, restoring CFTR protein when none exists, and fixing or replacing the underlying genetic mutation to address the root cause of CF. Each approach requires a different set of scientific tools and knowledge, leading the Foundation to bring together researchers and industry leaders from a range of disciplines to advance multiple areas of research in parallel.

We are making significant progress on the Path.

Advancing Research in Genetic-based Therapies
The CF Foundation funded more than 20 industry programs to advance genetic-based therapies in 2020 — our best hope for curing cystic fibrosis. This includes programs in CFTR restoration, gene-editing programs, and gene delivery programs. The delivery of genetic-based therapies to the lungs is a key hurdle to developing effective treatments for all people with CF. This research is more complex than anything we have ever done and requires a substantial investment.

Maximizing the Impact of CFTR Modulators
CFTR modulators continue to transform daily life for many people with CF. To help those eligible for modulators live even healthier lives, we are supporting continued research into additional therapeutic options and broader access to currently approved therapies. To help ensure people with CF and their care providers have a better understanding about the triple-combination therapy

Trikafta®, we are currently supporting several large clinical studies that will assess the longer-term impact of this important new therapy.

- PROMISE: Explore effects on lung function, GI symptoms, pancreatic function, diabetes, and other manifestations of CF
- SIMPLIFY: Determine if it is possible to safely reduce the daily treatment burden of CF
- BEGIN: Evaluate the ongoing impact of modulators on children and young infants

Continuing to Innovate through Venture Philanthropy

The CF Foundation's pioneering venture philanthropy model spurred the discovery of multiple breakthrough therapies that target the underlying cause of CF. We anticipate that many of these modulators will add decades of life to those with CF. The Foundation is taking important steps to adapt and evolve our approach to bring new science and technologies into CF.

Together with the Longwood Fund, a biotech-focused venture capital firm, we are establishing a CF-focused incubator to build companies from the ground up that prioritize the needs of people with CF. This approach will enable the Foundation to play a more active role in shepherding promising early technologies from academia to industry and attracting new companies into CF.

ADDRESSING THE MANIFESTATIONS OF CF

As people with CF continue to live longer, their needs are becoming more complex. The Foundation continues to expand its research to address the manifestations — or serious health conditions — that arise as a result of CF's damaging effects to the body, such as GI, liver disease, diabetes, infections, and advanced lung disease.

Areas of Focus

- *Infection Research Initiative:* Chronic, hard-to-treat infections remain a daily challenge for most people with CF. Since launching the Infection Research Initiative in 2018, the Foundation has awarded more than $80 million for infection-related research, including more than 160 awards in 2020 that address many facets of CF infections. Research topic areas include pathogen-specific studies, research that could potentially benefit people who culture for multiple types of organisms, and new approaches to addressing infection.
- *Lung Transplant Initiative:* Lung transplantation remains a vital option for people with CF who have advanced lung disease. The Foundation continues to improve the lung transplant journey through our Lung Transplant Initiative. In 2020, we designated Cleveland Clinic as a Biorepository Coordinating Center and have built a Patient Registry of lung transplant recipients to store clinical data. This data will be used to combat Chronic Lung Allograft Dysfunction, the most common, life-limiting post-transplant complication. Additionally, more than 40 CF care centers have been working with lung transplant centers to drive better outcomes.