

## Cystic Fibrosis Research

- The Cystic Fibrosis Foundation supports a wide range of research that focuses not only on improving the quality of life for people with cystic fibrosis today, but also on accelerating innovative research and drug development to add tomorrows.
- In 2018, we spent approximately \$189 million on laboratory research, preclinical drug development, clinical research, and high-quality, specialized care — more than at any other time in the history of the Foundation.
- The Foundation is aggressively pursuing and funding innovative research to ensure that everyone with cystic fibrosis will have an effective treatment to target the underlying cause of the disease.

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## Laboratory Research

- The CF Foundation funded \$44 million in cutting-edge, innovative laboratory research in 2018.
- This infusion of funds highlights the critical importance of fundamental research in advancing new therapies by increasing our understanding of the disease and identifying new opportunities for developing treatments.
- The CF Foundation Therapeutics Lab is a one-of-a kind CF research facility that bridges the gap between academic discovery and the pharmaceutical industry. Based in Lexington, Mass., the lab identifies and tests potential groundbreaking therapies for CF, readying them for further development.
- More than half of the work at the CF Foundation Therapeutics Lab is concentrated on nonsense and rare mutations, and the lab recently launched an initiative to create a cell culture bank with cells from people with CF who have rare mutations.

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## Clinical Research

- In 2018, the Foundation spent around \$52 million to fund academic-led clinical trials as well as real world research that takes into account the realities of daily life and human behavior.
- This funding helped to support the most robust pipeline of potential new therapies for CF in the history of the Foundation with more than 25 new drugs in development.
- The Foundation enabled 64 multi-center clinical trials in 2018, more than doubling the number of trials from just six years ago.
- The breadth of trials has also increased, focusing not only on CFTR modulators, but also on a variety of treatments for complications of the disease, such as infections, excessive mucus, inflammation, and digestive issues.

- These trials were made possible because of the largest CF clinical trials network in the world, the [Therapeutics Development Network](#) (TDN), which includes 92 care centers with specialized research teams able to perform clinical trials.
- Additionally, because CF is a rare disease, the CF Foundation provides financial support to encourage companies to focus on CF and help advance therapies that would be unlikely to move beyond the lab and into clinical trials, spending approximately \$45 million last year to fund preclinical discovery and drug development research.

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## CFTR Modulation

- In 2018, the Cystic Fibrosis Foundation spent more than \$11 million on research to develop new and more effective cystic fibrosis transmembrane conductance regulator (CFTR) modulators to restore the function of the defective CFTR protein.
- The FDA is reviewing a new drug application for the first triple-combination modulator, which combines the new drug VX-445 (elexacaftor) with tezacaftor/ivacaftor (Symdeko®).
- Next-generation modulators have the potential to be significantly more effective than current FDA-approved CFTR modulators and to benefit more people with CF than ever before, including individuals with only one copy of the F508del mutation.
- A technique called “theratyping” could also enable pharmaceutical companies to use lab tests to expand treatments to patients whose very rare mutations make clinical trials impractical.

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## CFTR Restoration – Nonsense and Rare Mutations Research

- The Cystic Fibrosis Foundation is funding groundbreaking new approaches to develop treatments for individuals who have nonsense or other rare mutations that do not respond to CFTR modulators.
- We have drastically increased the size of our investment in this area and last year spent more on research to develop treatments for people with nonsense and rare mutations than on research into CFTR modulators.
- Additionally, by the end of 2018, we had committed more than \$90 million to the Nonsense and Rare Mutations Research and Therapeutics Initiative.
- One potential treatment for all mutations — mRNA therapy — began clinical trials in mid-2018.
- The CF Foundation awarded up to \$11 million in 2018 to fund the largest high-throughput screening for readthrough agents the Foundation has conducted to date. As part of this contract, more than 2 million compounds will be screened to identify candidates that may be developed into drugs for people with nonsense mutations.
- To further expedite the development of new treatments for individuals with nonsense mutations, the [RARE cell-collection study](#) was launched in early 2018. Researchers are collecting cells from individuals with two stop mutations to allow testing of promising new therapies (readthrough agents as well as other compounds).

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## Treating and Preventing Complications

- Treatments for complications of CF — such as infections, inflammation, excessive mucus, and digestive issues — are so important that in 2018, the CF Foundation spent significantly more money in this area of research than in any other.
- Approximately \$62.5 million went to fund nearly 300 projects related to complications.

- There are also more than 15 drugs in the pipeline to treat complications of CF, including potential anti-infectives, anti-inflammatories, mucociliary clearance therapies, and nutritional agents.

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## Infections

- The CF Foundation is investing in innovative and novel techniques to tackle chronic, life-threatening infections.
- In 2018, the Foundation announced the new \$100 million Infection Research Initiative to improve outcomes associated with infections.
- We funded more than 100 different projects in 2018 to improve our understanding of these infections and to develop new and more effective anti-infectives for people with CF.
- This includes supporting more than 10 industry antimicrobial programs, many of which are in either preclinical or early-stage clinical trials.
- Research is underway on CF microorganisms. Studying the microbial ecology of the airways as well as bacteria in the environment will help researchers develop better strategies to prevent, manage, and treat infections.

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## Inflammation

- The CF Foundation is funding 35 projects to identify the causes of excessive inflammation and devise methods to reduce it.
- These projects include four ongoing clinical trials to test potential anti-inflammatory medications.
- In early 2018, the Foundation awarded up to \$25 million to a company for the development of a potential anti-inflammatory drug.

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## Mucus

- The Foundation is funding more than 35 projects to develop new and more effective treatments to improve the clearance of mucus from the lungs of people with CF.
- Some promising potential therapies include agents that thin the mucus, so it can be cleared away more easily.

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## Digestive System, CFRD, and Reproductive Health

- Although the lungs are typically the most commonly affected part of the body in CF, most people with this disease also experience complications linked to the digestive system. Therefore, the Foundation funded nearly 20 separate programs in 2018 to address gastrointestinal (GI) complications.
- The Foundation spearheaded the formation of a group of GI specialists to focus on the treatment and research of GI issues in CF. This group is working on the GALAXY study to gauge which GI symptoms affect people with CF the most so that researchers can prioritize them for further study.
- The endocrine system, which uses hormones to regulate many aspects of the body, is also affected by the disease. To better understand the impact of CF on the endocrine system, the Foundation provided \$1.6 million in 2018 for research into CF-related diabetes (CFRD), reproductive health, and bone health.

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## Lung Transplants

- With more than 250 people with CF undergoing lung transplantation every year, the Foundation is determined to improve the lung transplant journey.
- Since the Foundation launched the CF Lung Transplant Initiative in 2016, we have committed \$23.5 million to standardize and improve the delivery of lung transplant clinical care; increase understanding of post-transplant complications, including chronic rejection; and develop new therapies for lung transplantation through clinical studies.
- As part of the initiative, the Foundation set up a consortium of 10 lung transplant sites that are sharing best practices and establishing a shared biorepository that can be used to test potential therapies.

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## Cure

- Our long-term goal is to create a cure that would benefit all people with cystic fibrosis regardless of their mutations.
- The most promising options for a cure are either adding normal CFTR genes to cells using gene therapy or repairing the defective CFTR genes using gene editing.
- In 2018, the Foundation devoted more than \$6 million to fund more than 30 groundbreaking gene editing, gene delivery, and stem cell research projects.
- Although these technologies have progressed rapidly in the last few years, it will be many years before they reach people with CF.