DEAR FRIENDS,

I am continuously inspired by the resilience of the cystic fibrosis community. In the face of another year of challenges, your determination has been vital to the tremendous progress we are making to support the development of transformative therapies for tomorrow and to help people with CF live their best lives today.

In 2021, we reached new heights as we worked together to drive advances in three critical areas – Cure, Care, and Community.

The Cystic Fibrosis Foundation continued to invest boldly, funding the most promising science to accelerate treatments for the underlying cause of CF and to find a CURE for every person with the disease, no matter their mutations.

Our multidisciplinary CARE model continues to evolve to meet the changing needs of people with CF, while also putting the expertise of the individual living with CF at the center of their care team. Innovations in CF care will continue to improve on one of last year’s most remarkable achievements – attaining a median predicted survival of 50 years for people with CF. We expect to see life expectancy continue to climb as CFTR modulators become available to younger people with CF, including this year’s FDA approval of Trikafta® for children ages 6-11 moving us even closer to that goal.

As we make greater progress in improving health outcomes, we have sharpened our focus on addressing health inequities in the CF COMMUNITY, and strengthened our commitment to embedding racial justice principles in all we do. Over the past year, we listened closely to Black, Hispanic, and other people of color about their experiences with cystic fibrosis. The perspectives that these community members generously shared will guide the Foundation as we aim to help improve care, health outcomes, representation, and inclusion among all people with CF.

Recognizing the critical benefits of connection for the CF community, the Foundation created more opportunities to bring people together to learn and find support, facilitating more than 600 virtual and chapter events. From the hundreds who ROSE UP for a cure and walked in Great Strides, to the generous donors who supported our launch of our Milestones III: Driven by a Dream campaign, we are energized by your enthusiasm and commitment.

The force behind all these successes is the cystic fibrosis community, and your passion is what fuels our shared mission. I have no doubt that together we will move forward to achieve our highest goal of finding a cure and ensuring that no one person is defined by their disease.

With gratitude,

Michael P. Boyle, MD
President and CEO
Cystic Fibrosis Foundation
IGNITING THE DEVELOPMENT OF GENETIC THERAPIES
Genetic therapies are the key to developing a cure for CF. We are committed to turning today’s genetic therapy research into tomorrow’s cures. The road ahead has many challenges, but we face them with the same resolve that we applied in the early days of modulator research, which has come to transform care for many people with CF.

We are particularly excited about several genetic therapy collaborations that have great potential to drive progress.

ONE OF OUR BOLDEST INVESTMENTS EVER
In a first-of-its-kind deal, the Foundation committed up to $110 million to a collaboration with Pioneering Medicines, an initiative of Flagship Pioneering, to fund a new company specifically focused on CF. This company will bring together emerging technologies from several Flagship-founded companies – each focused on a different piece of the genetic therapy puzzle. In the near term, the company will advance at least two innovative genetic therapy approaches for CF.

TAKING ON THE MOST PRESSING BARRIERS TO GENETIC THERAPIES
Developing genetic therapies for cystic fibrosis can be more challenging than for other genetic diseases because of the lungs’ natural defense mechanisms. We are working with Deep Science Ventures to tackle these challenges by assessing the most pressing barriers to genetic therapies, exploring the feasibility of potential solutions, and designing proof-of-concept studies. Our goal is to uncover and design new technologies that will move us closer to a cure for cystic fibrosis.

To further our mission, we are identifying and attracting the world’s best scientists across both industry and academia – especially experts in genetic therapies – to focus their research on CF.
AGGRESSIVELY PURSUING TREATMENTS FOR NONSENSE AND RARE MUTATIONS

Despite extraordinary progress in helping people with cystic fibrosis live longer and healthier lives, there are many people with CF, including those with rare or nonsense mutations, who are still waiting for a breakthrough treatment for the underlying cause of their disease. We are excited to fund multiple innovative genetic therapy research strategies that have the potential to help these members of our community.

HOMING IN ON SPlicing MUTATIONS

Splicing mutations disrupt the production of functional cystic fibrosis transmembrane conductance regulator (CFTR) messenger ribonucleic acid (mRNA), which is required for cells to produce the CFTR protein. We awarded up to $8.4 million to SpliSense to develop a therapy for people with CF who have splicing mutations. If successful, it could potentially inform the development of additional therapies for other rare mutations.

INNOVATING TO MAKE GENE DELIVERY A REALITY

We are supporting many studies that are researching gene delivery, a process needed to deliver a gene therapy to the body without triggering an immune response. We funded Carmine Therapeutics to test a new technology to deliver the CFTR gene into the cell and in GenexGen Inc. to develop a drug to dampen the body’s immune response.

TARGETING NONSENSE MUTATIONS WITH GENE EDITING

We are funding multiple early, proof-of-concept research studies, including Life Edit Therapeutics to explore a unique gene editing technology in CF. Our funding will enable the company to explore options that could correct the six most common nonsense mutations in cystic fibrosis. We are also investing in Specific Biologies to study a gene editing approach aimed at correcting the three most common nonsense mutations in CF.

We funded 89 studies to pursue treatments for all people with CF, regardless of mutations.

EXPANDING ACCESS TO MODULATORS

2021 heralded a new era in CF care, in part because of the dramatic beneficial effects of Trikafta® (elexacaftor/tezacaftor/ivacaftor) for many people with cystic fibrosis with certain mutations. With the FDA approval of Trikafta in June for children ages 6-11, younger people now have access to this treatment, which may help stave off the most common CF complications before they start. Today, a clinical trial is underway to evaluate Trikafta in children ages 2-5 and we are hopeful that it will bring a transformative treatment option to some of the youngest members of the cystic fibrosis community.

Together, We Are Building Momentum

In 2021, we continued to seek out the most promising research opportunities to potentially benefit all people with CF as part of our $500 million Path to a Cure initiative.

Gene Delivery

For genetic therapies to work in CF, specifically engineered DNA or RNA molecules must enter cells of the lung or other affected organs. Gene delivery is the process of delivering these molecules into cells.

Gene Editing

Gene editing uses the cell’s own DNA repair machinery to correct a mutation in the DNA. To correct a CFTR mutation in the DNA, the tools needed for gene editing must insert themselves into the cell.

mRNA Therapy

mRNA therapy involves repairing or replacing messenger RNA, which carries the instructions for making the CFTR protein from the DNA to the protein-making machinery of the cell.
To advance drug development and a search for a cure, the Cystic Fibrosis Foundation has contracts with several companies to help fund the development of potential treatments and/or cures for cystic fibrosis. Pursuant to these contracts, the Foundation may receive milestone-based payments, equity interests, royalties on the net sales of therapies, and/or other forms of consideration. Resulting revenue received is used in support of its mission. See “How Drugs Get on the Pipeline” at www.cff.org/howdrugsgetonthepipeline for more.

Together, We Are Pursuing Tomorrow’s Treatments

The Foundation’s Drug Development Pipeline comprises potential treatments for the root cause of CF and its many complications, including mucociliary clearance, inflammation, infection, and nutrition/GI.

2021 PIPELINE PROGRESS

To advance drug development and a search for a cure, the Cystic Fibrosis Foundation has contracts with several companies to help fund the development of potential treatments and/or cures for cystic fibrosis. Pursuant to these contracts, the Foundation may receive milestone-based payments, equity interests, royalties on the net sales of therapies, and/or other forms of consideration. Resulting revenue received is used in support of its mission. See “How Drugs Get on the Pipeline” at www.cff.org/howdrugsgetonthepipeline for more.
ACHIEVING A LANDMARK LONGEVITY MILESTONE

A key benchmark of our progress has always been the median predicted age of survival among people with cystic fibrosis. For children born between 2016 and 2020, the median predicted survival age reached 50 years for the first time ever. This achievement is a powerful tribute to the decades of perseverance by the entire CF community and a milestone we are committed to surpassing.

MAKING REMARKABLE IMPROVEMENTS IN IMPORTANT HEALTH OUTCOMES

- 23.2% fewer pulmonary exacerbations among adults compared to previous year
- 109 fewer lung transplants compared to previous years
- 60% of 10-year-olds have normal lung function, up from 30% a decade earlier

Source: 2020 Patient Registry Annual Data Report

OPTIMIZING CARE FOR INDIVIDUALS TAKING TRIKAF TA

With many people living with cystic fibrosis now taking Trikafta and experiencing changes in their health, we’re investing in research to better understand how to optimize care and further empower people with CF to steer their own care.

- The HERO-2 study aims to characterize real-world outcomes for people taking Trikafta by enabling them to use an online tool to actively track their health and report symptoms and treatment use over 12 months — all from the comfort of their own home. This research will inform the evolution of CF care, help prioritize future research, and support programs to meet the needs of people taking modulators.
- The SIMPLIFY study is exploring whether teens and adults taking Trikafta can safely stop two relatively burdensome therapies — inhaled hypertonic saline and dornase alfa — to potentially make day-to-day life easier.
- The PROMISE study, which is looking at the effects of Trikafta on the entire body, is the largest clinical study fully funded by the Foundation. It is starting to report data on the impact of Trikafta on multiple areas beyond lung function in both children and adults.

57% of people in the CF Foundation Patient Registry are adults, growing by about 1% each year.
IMPROVING OUTCOMES FOR PEOPLE WITH ADVANCED LUNG DISEASE

Not everyone living with cystic fibrosis has benefited equally from advances in treatments and care. As part of our commitment to caring for all people with CF wherever they are on their journey, we continue to make great strides in our Advanced CF Lung Disease Initiative to support people with advanced disease and lung transplantation.

In collaboration with the Cleveland Clinic, we launched the Lung Transplant Biorepository and Patient Registry to further understand the factors that affect lung transplant outcomes and identify ways to prevent complications.

In addition, the Foundation invested $3.5 million in Pulmocide Limited to develop an inhaled treatment to prevent Aspergillus fungal infections, one of the most common infections in lung transplant recipients. People with CF are at greater risk of this infection because they are more likely to have fungus in their airways, even before transplant, which can lead to an invasive infection after transplant.

Evolving and strengthening our care model

With advances in cystic fibrosis treatments transforming care for many people, and more adults than children with CF than ever before, no two CF journeys are the same. That’s why we are continuing to evolve our care model to meet the needs of all people living with CF in a rapidly changing community. We’re focusing on building upon innovations from the pandemic (such as telemedicine) and creating options for more individualized care. While it’s early days, we are considering how the care model can:

- Reflect the needs of a diverse community
- Incorporate more specialized care
- Coordinate care across providers and institutions
- Put patient data in the hands of people with CF so they are better equipped to help drive their care with their care team
Together, We Are Exploring New Ways to Fight Infections

As we seek new opportunities to invest in the development of transformative therapies for tomorrow, we are also working to address the complications of living with CF today, including infections that can lead to increased risk of worsening lung disease.

Supporting Policies That Stimulate the Development of Novel Antibiotics

In addition to directly funding research, the Foundation is supporting public policies to encourage others to invest in developing novel antibiotics. In June, the Foundation affirmed support for the bipartisan PASTEUR Act, proposed legislation that aims to spur vital investment in new antibiotics. If passed, the legislation has the potential to revitalize the global marketplace for antibiotics, bringing urgently needed medicines for drug-resistant infections to patients – benefiting people with cystic fibrosis, and all Americans.

Driving Innovative Research

Pseudomonas is one of the most common bacteria found in people with CF, and once it’s established in the airways, it’s very difficult to eliminate. The Foundation is investing up to $3 million in Kinnear Pharmaceuticals to conduct preclinical testing of its investigational broad-spectrum anti-infective, which has the potential to treat multi-drug-resistant Pseudomonas and other infections in people living with CF.

Nontuberculous mycobacteria infections are difficult to treat and are becoming increasingly prevalent among people with CF. The current standard of care involves lengthy courses of antibiotics that are associated with serious side effects. The Foundation is investing up to $2.17 million in Beyond Air® to support the development of a portable inhaled nitric oxide treatment. Researchers believe that increasing levels of nitric oxide in the body could help eliminate bacteria and increase lung function in people with CF.

In 2021, we reached our goal of funding $100 million for our Infection Research Initiative nearly two years ahead of schedule.
Together, We Are More Than This Disease

2021 was another challenging year for many people in the CF community. We found hope, however, during difficult times by forging deeper connections that taught us more about what it means to live with cystic fibrosis and what’s possible when we come together.

Thanks to the tremendous efforts of the CF community – the heartbeat of our Foundation – we are stronger together after a year of showing up for one another in more ways than ever before:

- **More opportunities for learning and connecting** through virtual conferences and events.
- **More input** from people with CF to guide research, care, and program and resource development to best meet the unique needs of our diverse community.
- **More active listening** to communities that have been historically underserved so that we can effectively help all people with CF live their healthiest lives possible.
- **More possibilities for innovation** as we again exceeded our fundraising goals, enabling us to keep advancing critical research for people living with CF.

MORE THAN $86 MILLION RAISED TO FUND OUR MISSION

From Great Strides to epic climbs, hikes, and rides, the CF community came together in support of a cure of CF:

- **Milestones III: Driven by a Dream**, an extraordinary effort to help advance the development of genetic therapies and treat manifestations of CF, surpassed $57 million. We thank the Milestones III Committee Chair, Joseph O’Donnell, and the many donors that have made gifts to support the campaign.
- **ROSE UP**, a virtual event developed and led by adults with CF, brought together hundreds of people to raise $450,000 in its second year. We thank ROSE UP sponsors, AbbVie, Vertex Pharmaceuticals Inc., Walgreens, and Nestle Health Sciences.
- **Matching Your Support**: Thank you to the Stremick Family and the Delaney Binker Family Cure Cystic Fibrosis Miami Foundation for generously matching the community’s donations toward Giving Tuesday and our legacy society.

MORE VIRTUAL COMMUNITY CONFERENCES BRING THE COMMUNITY TOGETHER

RESEARCHCON

Researchers, clinicians, and community members discussed the latest on cystic fibrosis research and topics of interest — including the session “See Us: Faces of Disparities in CF Care and Experience.”

“It was eye-opening, honest, vulnerable, a little heartbreaking, but ultimately hopeful.”

CF MINICON: TRANSPLANT

Attendees learned about and shared their experiences with transplant and living with advanced CF lung disease, which created opportunities for open conversations and community connections.

“Panels brought waves of emotion. This is a tough disease. But the overwhelming takeaway was hope, respect, and support. Very well done.”

BREATHECON

This event brought together adults with CF to discuss the challenges of living with the disease.

“Loved the closed captioning, general increased focus on accessibility, and seeing a more diverse pool of speakers.”

$86M+
RAISED TO FUND OUR MISSION

Together, Neema, we’re working toward a future without cystic fibrosis.
MORE VOLUNTEERS MAKING A DIFFERENCE

2021 was a big year for both Tomorrow’s Leaders, a group for young professionals who believe in the Foundation’s mission, and Grampions, a group of grandpersons passionate about helping people with CF live their best lives. Tomorrow’s Leaders engaged their 1,500 active members through 17 professional and personal development sessions. And this year, around 400 Grampions joined the program to participate in events like National Grandparents Day, where activities ranged from music trivia to a comedy show.

MORE THAN 8,000 REQUESTS FOR HELP FIELDDED BY COMPASS

CF Foundation Compass is where people with cystic fibrosis and their families can turn for help navigating the challenges of living with CF. Last year, case managers fielded more than 8,000 requests, saving more than $1.5 million for the people they served.

In 2021, Compass was recognized with official accreditation from the Alliance of Information and Referral Systems, the sole source of standards, accreditations, and certification for community information and referral services.

MORE INPUT FROM THE COMMUNITY TO INFORM EVERYTHING WE DO

We are listening closely to what matters most to the CF community. One way we gain this important input is through Community Voice, which grew in 2021 to gather community perspectives on 85 projects, with topics ranging from COVID-19, to experience of care, to health equity. These conversations led to many constructive changes, including our first Spanish-language event in 2021. Read more in the Community Voice 2021 Year in Review.

We are committed to serving all people with CF by improving care, outcomes, representation, and creating an inclusive environment for those who are under-resourced. Through our diversity, racial justice, and inclusion initiative, we are advancing this vital work. One of our many efforts included responding to the NIH’s Call for Information on Diversity and Inclusion to improve racial equity, diversity, and inclusion in the biomedical research workforce.

The Foundation also conducted a survey and recruited focus groups, resulting in the Communities of Color Report. These findings allowed us to better understand the unique needs of people of color in the CF community and inform ongoing conversations about what it truly means to live with cystic fibrosis.

MORE CALLS FOR ACTION: MAKING AN IMPACT ACROSS THE COUNTRY

In 2021, our volunteer advocates took collective action, connecting with lawmakers to drive our legislative and regulatory agenda forward.

ADVOCACY ENGAGEMENT BY STATE

Engagement is inclusive of letters, statements, testimonies, and public comments to state-level policy and decision-makers.

MAP KEY

- 2 engagements
- 3 engagements
- 4 engagements
- 5 engagements
- 6+ engagements
**National Corporate Champions**

Curing cystic fibrosis and caring for people with CF is a community effort and takes many resources. We are grateful for the generosity of our National Corporate Champions, who provide direct support of $100,000 or more to support our search for the cure and efforts to improve the lives of people with CF.

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<td>Merrill, a Bank of America Company</td>
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  Chair
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  President and CEO
- **Irena Barisic**  
  Executive Vice President and Chief Financial and Administrative Officer
### Statements of Financial Position

Condensed Financial Information*  
As of December 31, 2021 and 2020

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<tr>
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<th>2021</th>
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<td><strong>Total assets</strong></td>
<td><strong>$5,691,109,975</strong></td>
<td><strong>$5,369,999,661</strong></td>
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| **LIABILITIES AND NET ASSETS** |               |               |
| Accounts payable and other liabilities | $42,584,432 | $34,541,037   |
| Awards payable                | 231,895,234  | 236,465,610   |
| **Total liabilities**          | **274,479,666** | **271,006,647** |

| **NET ASSETS**                |               |               |
| Without donor restrictions    | 5,398,556,832 | 5,089,568,156 |
| With donor restrictions       | 18,073,477    | 9,424,858     |
| **Total net assets**          | **5,416,630,309** | **5,098,993,014** |
| **Total liabilities and net assets** | **$5,691,109,975** | **$5,369,999,661** |

### ORGANIZATION

The accompanying financial statements include the operations of the Cystic Fibrosis Foundation, including all of its field offices (the "Foundation").

### CASH AND CASH EQUIVALENCES

Cash and cash equivalents represent demand deposits, money market funds and money market mutual funds. Cash equivalents consist of highly liquid investments with original maturities of three months or less and present an insignificant risk of change in value. Cash and cash equivalents that are held as part of the Foundation’s investment portfolio are reported within investments.

### INVESTMENTS

Investments as of December 31, 2021 included primarily fixed income securities, global public equity securities and interests in alternative investment funds. Authoritative guidance requires an entity to maximize the use of observable inputs when measuring fair value. The guidance describes three levels of inputs that may be used to measure fair value: Level 1 - Quoted prices in active markets for identical assets or liabilities; Level 2 - Observable inputs other than Level 1 prices, such as quoted prices for similar assets; Level 3 - Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets. The Foundation carries its cash and cash equivalents, all investment balances and certain other assets at fair value. Financial instruments measured at fair value on a recurring basis as of December 31, 2021 were $2,317,689,475 in Level 1 assets, $1,574,697,498, which are measured at fair value using quoted market prices or net asset value (NAV) as a practical expedient, and $1,374,936,498 in Level 2 assets, and $22,405,262 in Level 3 assets. Level 2 assets include $8,422,325 which are part of cash equivalents in the statement of financial position. Investments totalling $1,574,697,498, which are measured at fair value using net asset value as a practical expedient, have not been categorized in the fair value hierarchy.

### PROGRAM-RELATED INVESTMENTS

The Foundation makes program-related investments in companies with cystic fibrosis-related projects. These include direct equity investments, investments in equity funds, and a convertible promissory note. Equity investments are stated at fair value using quoted market prices or net asset value (NAV) as a practical expedient. The promissory note is recorded at net realizable value and included in receivables, net on the statement of financial position.

### AWARDS PAYABLE AND COMMITMENTS

The Foundation generally awards medical/scientific grants and contracts for periods of three years or less. Grants are awarded contingent upon renewal criteria at the beginning of each award period. Awards are expensed at the time the Foundation unconditionally commits to fund the grant or, for those contracts with measurable performance milestones, when the milestone has been met. As of December 31, 2021, in addition to awards payable, the Foundation has medical scientific grant commitments of approximately $89,709,000 which extend through 2027. These subsequent year awards are contingent upon renewal criteria, and therefore the costs and liabilities are not reflected in the financial statements. Certain agreements provide for future contracted drug discovery and development research payments amounting to approximately $110,397,000. These costs will be expensed when the services are provided.

### LIQUIDITY AND AVAILABILITY OF RESOURCES

The Foundation’s financial assets available for general expenditures, such as program expenses, grants and other operating expenses, within one year of December 31, 2021 are $3,331,200,123. The Foundation’s Board of Trustees approves an annual operating budget and the Investment Committee of the Board of Trustees approves redemptions from the investment portfolio sufficient to meet projected cash needs. The Foundation maintains cash and highly liquid securities sufficient to meet anticipated cash needs for operations, capital commitments, and new investments over an eighteen-month rolling period.

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*The independently audited financial statements of the Cystic Fibrosis Foundation are available online at the Foundation’s website, cff.org.*
Statements of Activities

Condensed Financial Information*  
For the years ended December 31, 2021 and 2020

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<td>Licensing, royalties, and other revenue</td>
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<th>SUPPORTING SERVICES</th>
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<td>Total expenses</td>
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<td>(Decrease) increase in net assets from operations</td>
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<th>OTHER CHANGES IN NET ASSETS</th>
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<td>Net nonoperating investment income</td>
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<td>Increase in net assets</td>
</tr>
</tbody>
</table>

*The independently audited financial statements of the Cystic Fibrosis Foundation are available online at the Foundation’s website, cff.org.

MEASURE OF OPERATIONS  
The Foundation includes in its measure of operations all support received from the public, income on investments designated for operations, royalty revenue, other revenue and all costs of program and supporting services. The measure of operations excludes interest and dividends and realized and unrealized gains or losses on nonoperating and program-related investments. Nonoperating investments are amounts identified for investment over the intermediate to long term.

REVENUE RECOGNITION  
Contributions are recorded as revenue when received or when the donor has made an unconditional promise to give. Contributions received for future events are recorded as refundable advances and are recognized as revenue in the year in which the event takes place. Conditional promises to give are not recognized until the conditions on which they depend are substantially met. Contributions of assets other than cash, including gifts-in-kind, are recorded at their estimated fair value at the date of the gift. Contributions received are recorded as revenues with or without donor restriction. All donor-restricted support, including related investment income and realized and unrealized gains and losses, is recorded at their estimated fair value at the date of the gift. Contributions received are recorded as revenues with or without donor restriction. All donor-restricted support, including related investment income and realized and unrealized gains and losses, is recorded as revenues with or without donor restriction. All donor-restricted support, including related investment income and realized and unrealized gains and losses, is recorded as revenues with or without donor restriction. All donor-restricted support, including related investment income and realized and unrealized gains and losses, is recorded as revenues with or without donor restriction.

LEASE COMMITMENTS  
The Foundation is obligated under various operating leases for office space as of December 31, 2021. The approximate future minimum rental commitments, subject to escalation, are $31,920,000. The Foundation has entered into sublease agreements with tenants to occupy its former headquarters and certain chapter office spaces. As of December 31, 2021, the approximate future minimum sublease rental payments due from sublease tenants are $2,247,000.

Revenues from contracts with customers are recognized when or as performance obligations have been satisfied. Licensing revenue is recognized at a point in time for licenses issued to use intellectual property or over time for licenses granted to access intellectual property. Sales-based royalty revenue is recognized at the later of when (1) the sales occur and (2) the associated performance obligation has been satisfied. Licensing and royalty revenue are included in other revenue in the statement of activities. Amounts received in advance of the performance period are recorded as deferred revenue.
The mission of the Cystic Fibrosis Foundation is to cure cystic fibrosis and to provide all people with CF the opportunity to lead long, fulfilling lives by funding research and drug development, partnering with the CF community, and advancing high-quality, specialized care.