# CF GET LOUD

## CADTH Reimbursement Review
## **Patient Input**

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Name of the Drug and Indication: Triple Combination Therapy/Trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor for the treatment of Cystic fibrosis)

Name of the Patient Group: CF Get Loud

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## Contents

## About CF Get Loud

We are Canadian CF patients and caregivers fighting for CF patients.

CF Get Loud is Canada's largest CF grassroots movement. We were founded and are led by three CF patients and one CF mom. We have grown to represent a community of over 4,000 patients, families and allies across Canada who have gotten LOUD, with the goal of bringing hope, in the form of new life-saving medicines, to our community. Our origin story is a direct response to the barriers to access Trikafta, and we have grown into a mighty advocacy group focused on empowering our community and allies to make change and help overcome the challenges the CF community faces in Canada. Understanding the constantly evolving political landscape and regulatory barriers that restrict and delay access to life-saving medications has been our driving force. Additionally, we strive to look beyond this one issue and aim to serve our community wherever the need arises. We engage with Canadian CF families, and help elevate the voices of those individuals and caregivers with a unified message.

We have felt the hearts of our community through a multitude of conversations, engagements and virtual events. We have learned about the journeys and lived experiences of many CF families; difficulties, triumphs, joys and sorrows that have taken us from laughter to tears and back.

## Information Gathering (process)

Our patient advocacy group reaches from coast to coast across Canada. Most of our members are CF patients and caregivers. Since our inception, we have run a number of campaigns for Canadians with CF to share their stories, including their experience with the disease, experience with currently available treatments and the improved outcomes they expect from the drug, as well as experiences with the drug under review.

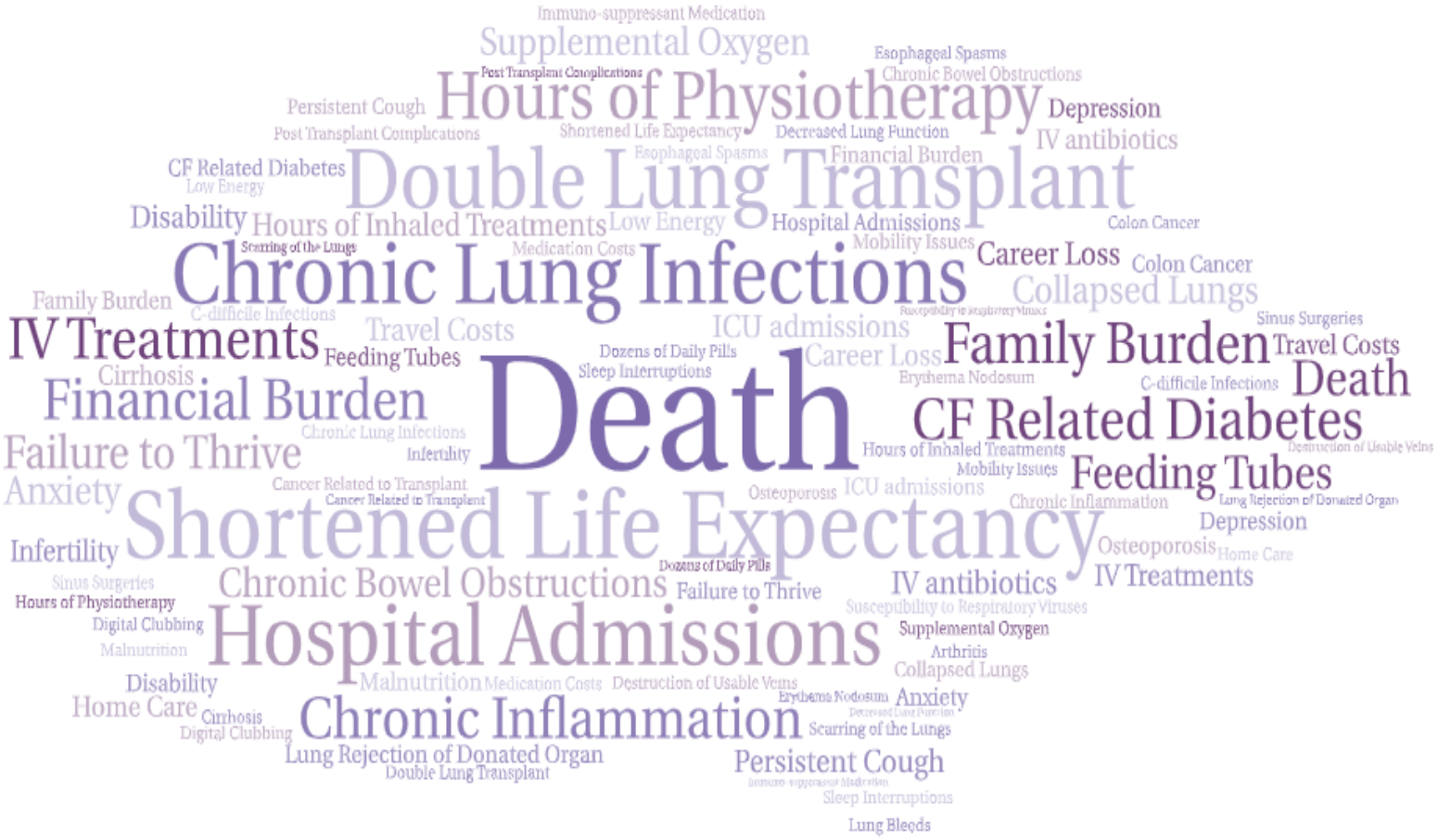
One of our education projects last year was our Letter for Lives initiative (July 2020), in which we received copies of 11,364 letters from Canadians speaking to the unique impact Trikafta has or will have on Canadian lives. We have also hosted a CF community town hall (May 2020), where we heard from experts and leaders in our own community about the ground-breaking nature of Trikafta and what it means for CF families across Canada. Furthermore, we heard from more than 20 Canadians who are currently receiving Trikafta as part of the Compassionate Care program from Vertex administered through the Special Access Program (SAP). Many of these individuals have endured the physically and mentally exhausting journey of undergoing tests and evaluation required to qualify for a double lung transplant, with the hopes of receiving a second chance at life. Due to this life-saving medication, these patients have a unique story to tell in Canada since they have experienced firsthand the dichotomy between staring death in the face and regaining their ability to thrive and be a productive member of society, without having to undergo transplant surgery. This metamorphosis from slowly dying to active living is evident in every single individual we have spoken to and is representative not just of the physical effects of Trikafta, but also the mental and emotional impact that access to this drug will have on Canadian families.

These initiatives and projects have provided CF Get Loud with a diverse and rich data set with a unique and comprehensive perspective of the Canadian CF community and that data has helped to inform this submission.

## Disease Experience

CF is a progressive disease that affects primarily the lungs and digestive system, but other organs and systems can be impacted as well. It is a complex and devastating disease. CF results in premature death 100% of the time. However, this no longer needs to be the reality for Canadians with CF, and this evaluation that CADTH conducts can be instrumental in changing that.

The following word cloud visualizes the dozens of feelings, interventions, concerns and issues that Canadians with CF experience. The descriptions have been selected after analyzing over 11,000 letters that were submitted last year, as noted above, and reflect real-world experience from the perspectives of patients and caregivers. These concerns, emotions and impacts on quality of life are further explored and evident in Appendices B & C, which include personal testimonials and photos of Canadians with CF before and after they received Trikafta.



In this context, the goal of a CF patient and their loved ones is to hold the line against irreversible damage to our bodies as steadfastly as possible, for as long as possible. As noted above, CF ends in a painful death, often at a very young age, despite every effort to maintain health for as long as possible.

People living with CF are unable to build enough body mass to fight off infections because our digestive system is compromised, often requiring a feeding tube for supplemental nutrition. Our livers can be damaged and often bear the burden of necessary and frequent antibiotic treatments to keep recurring lung infections at bay. A damaged liver leads some to require a liver transplant and this is unfortunately considered maintenance of the disease if our lungs are capable of carrying on. When these organs manage to remain functional, there are various additional complications that will arise.

In addition to the decline of our bodies, many suffer from the unseen effects of CF. These include, but are not limited to, depression, anxiety and hopelessness. The mental anguish caused by the ever-present awareness of one's mortality cannot be expressed in words and are often not quantified in these analyses.

## Experience with Currently Available Treatments

As illustrated above, CF affects many organs and different systems in the body. Treatment for one symptom can create additional negative side effects, exacerbate organ damage and/or other unpleasant symptoms. Available treatments are reactionary in nature and are designed to address the symptoms of the disease. While these treatments can slow the progression of the disease, they ultimately fail. Until the development of CFTR modulators, all available treatments were maintenance medications; therapeutics to manage and react to new symptoms and lung infections as they occur.

The development of CF related diabetes often exacerbates an already complicated balance between specialized nutritional needs and an overwhelming regiment of daily medications. A CF patient will take an average of 70 pills per day and complete approximately three hours of daily inhaled treatments and respiratory physiotherapy. CF patients end up building our lives around treatments and medications rather than have medications and treatments that allow us to live improved lives.

Ruptured veins from repeated intravenous antibiotics often result in PICC (peripherally inserted central catheter) lines and central IV ports which carry their own inherent risks. In addition, drug allergies and the development of bacterial drug resistance often begin eliminating antibiotic treatment options one by one. Despite these numerous medical interventions, the battle against CF is lost, little by little. Lung function gradually (sometimes rapidly) declines to the point that we arrive at the final "currently available treatment" intervention: a double lung transplant.

In short, the currently available treatments involve a rigorous and time-consuming schedule that fills much of our day. Over time, they are hard on all systems of the body and can further the decline of already compromised organs.

## Improved Outcomes

Let's be clear: Trikafta is a life-changing and life-saving medication. It will dramatically change much of the current trajectory and burden of this disease provided it is accessible before permanent lung and other organ damage has occurred.

Families who have newborns diagnosed with CF and individuals whose disease progression has been mild or who have not experienced a period of rapid decline will benefit not only from improved health in the short term but also slowed disease progression in the long term. The expected outcome is that CF evolves from being a swift and efficient killer to a disease that is more predictable and can be managed with close monitoring. It is an exciting time to be a CF patient! We now live in a time when a disease caused by a genetic defect can be potentially neutralized and corrected through precision medicine in the form of gene modulators. Months of hospital admissions, many invasive medical procedures and countless minor treatments and appointments will not be required in the same way. The daily burden of disease management will be lifted as some of those treatments either become redundant or more effective and less time-consuming.

For the young adult who is fighting with all their strength to stay alive and slow the deterioration of their health, Trikafta means:


These are not hypothetical outcomes. They represent a consistent account of what life after just a few weeks or months on this life-saving medication looks like. We have experienced this firsthand and have received anecdotal accounts from community members (see Appendix B) who receive Trikafta via the SAP (Special Access Program).

## Experience with Drug Under Review

As shown in the section above, there are many positive impacts experienced by those who take the drug under review. However, there are two clinical outcomes that may be the most important and have the most impact on CF patients.

- Deferred lung transplant
- Negative CF diagnostic sweat test (sweat chloride levels below 60 millimoles per liter)

As stated earlier, two of our executive team members at CF Get Loud have firsthand experience with the outcomes presented. Due to their extremely poor health, they were granted access to Trikafta through the SAP (Special Access Program). They have both been able to postpone a double lung transplant that was fast approaching, are revitalized and have gained back their lives in ways that words cannot truly capture.

The primary diagnostic test to confirm a CF diagnosis is a sweat chloride test. Months after starting Trikafta, they both completed a sweat chloride test and the results came back in the normal range, that is, negative for CF. From a diagnostic perspective, their defective genes have been corrected to the point that they no longer test positive for CF which indicates their bodies are working as they should. However, the drug under review cannot reverse years of pre-existing damage, and that is the reason it should be made available not only as a last resort, but also to those who have not declined and sustained permanent damage to their organs that would result in a lower quality of life.

Through our lived experience with the drug under review, and through several comprehensive interviews with other Canadians that have also gained access to it through the SAP, it is important to note that the improved outcomes listed in the previous section are the reality that individuals with CF are experiencing now and have communicated to CF Get Loud.

Visible physical improvements and the decrease of clinical symptoms are one way to view and quantify the positive impacts the drug under review has. In addition to that, and as important, are the unseen symptoms described earlier, the mental and emotional impacts of a medication that changes the trajectory of our disease. These positive impacts, though difficult to quantify, must not be discounted or forgotten.

Hope has been injected into our nightmare. The solution for our losing battle has given us the ability to plan for the future and allowed light to shine into the darkness. The ripple effect permeates all areas of life as personal growth prospects rise, and the doom and gloom start to dissipate. The prospect of family planning and a life beyond the immediate disease management routine starts to become reality. The ability to pursue professional aspirations is rekindled and the prospect of again being a contributing member of society is invigorating and exciting. The societal benefits of the drug under review extend

beyond the scope of our immediate circles and grow exponentially as it gives patients and their caregivers renewed health, purpose, independence and vitality.

## Companion Diagnostic Test

There is no companion diagnostic test for this therapy.

Gene modulating therapy works for individuals with specific genetic mutations that respond to the medicine.

Eligibility criteria for the drug under review should be based on genetic mutation only (F508 plus 1) as the US FDA has indicated. If further study determines individuals without a F508 genetic mutation could benefit, they should be eligible as well. Canadians born with CF should have access to every therapy that their genetic mutations respond to if it is approved as safe for their age group.

There must not be restrictions or performance measures attached to the recommendation for this therapy and all those that can benefit from it should be able to access it based on consultation with their CF physician.

The drug under review will have profound impacts on CF patients and their caregivers in Canada provided it is used as intended, as a standard preventative therapy that will prevent and limit damage to our bodies and correct defective cell functions. It should not be a limited therapy to prescribe after currently available medications have failed.

Each individual with CF experiences and are physically/mentally impacted by the disease in unique ways. CF is a complex disease and manifests in various ways depending on the individual so use of performance metrics outside of genetic mutation is an inappropriate and flawed measure. CF Get Loud endeavours to ensure that no CF patient who could benefit is left behind, as miracles of modern medicine become available after a lifetime of research.

## Anything Else

Three other CFTR modulators have received Notices of Compliance from Health Canada over the past eight years. Unfortunately, they remain widely inaccessible for most Canadians with CF, with the exception of one drug that most, but not all, who benefit from it are able to access in several provinces. Canada has fallen behind in access for CFTR modulators, including the drug under review. The United States, the EU and the UK have approved use of this drug and their CF patients are benefiting from it as the Canadian CF community waits and deteriorates as our disease progresses. CF can't wait any longer and should not have to as a truly life-saving therapy is suspended out of reach.

**On average, we will lose one Canadian with CF per week, with a median age of 30.**

Canadians with CF have watched with excitement (as well as some envy) as patients in the US, Europe and the UK share their transformations on social media, accomplishing goals that prior to accessing Trikafta would not have been possible. Some received their second chance over one year ago, before a respiratory pandemic made our lives even more complicated and vulnerable. Please treat this therapy with the **urgency** it deserves so that the health of CF patients in Canada is preserved and more resilient in the face of the COVID-19 pandemic.

## Appendix A: Patient Group Conflict of Interest Declaration

Our group has compiled data from advocacy initiatives held since January 2020 that the Canadian CF community participated in. No additional help outside our patient group was received to complete this submission. Our group did not receive any help to collect or analyze the data used in this submission. Our group has not had any financial payment from any company or organization since our inception. We are a patient and family volunteer group.

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Jacob Jaramillo

Position: Director

Patient Group: CF Get Loud

Date: February 12, 2021

# Appendix B: Testimonials

**Stephanie Stavros**
*Greenwood, Ontario*

My name is Stephanie Stavros and I am a 37-year-old patient living with Cystic Fibrosis.
Without Trikafta, 2020 would have looked very different. I would either have been recovering from a double lung transplant (if lucky) or my 5-year-old son and my husband would have been grieving my death.

In 2019, I was in end-stage lung disease and my digestive system was failing me. I had lost everything. I lost my career, my independence and my ability to be an active parent. I was tethered to an oxygen tank and an IV pole. My body was worn down from the steroids and ICU-grade antibiotics running through my small body 10 hours a day. My intestines developed a c-difficle infection, my bone density decreased, and my energy was depleted. Walking became unsteady and at times impossible. Simple tasks like bathing and speaking became difficult.

I was being evaluated for a double lung transplant and pain management became a critical part of my health regime. My lungs were scarred, my ribs cracked easily, and lung bleeds increased. One evening a large bleed landed me in the ICU. My family feared the worst.

When Trikafta was approved in the US, I was shocked that it wasn't on its way to Canada. I didn't have time to wait. Thankfully, because I was dangerously close to losing my battle with CF, the manufacturer granted me Compassionate Care for Trikafta.

On Jan 23rd, 2020, my life was saved and dramatically changed when I took my first dose of Trikafta.

I was asked by my care team to make goals for my Trikafta journey. My goals were to independently bathe myself, laugh without a coughing fit and dance with my son.

Within hours of taking it, my body began to transform.

Within 10 days, I reached each goal with ease. Within 7 days I gained back years of lost lung function. Within 6 months I gained back a decade of lost lung function. My lung function when from 28% to 41%. For 36 years, my body was malnourished. I didn't have fat on my body to protect and nourish me. Within 3 months on Trikafta, I gained 30 pounds. For the first time as an adult I have normal liver levels. My sense of smell and taste returned,

and brightness came back to my skin tone. The most unbelievable part is that I now test NEGATIVE for CF as long as I am taking Trikafta.

I find myself for the first time in my adult life taking deep, full breaths. My body has relaxed. It is no longer in a war with itself and I can finally get a full night's sleep. At home, I used to go to bed with tears streaming down my face, worried that I wouldn't wake up in the morning. I would position my lungs in a way that I could find a stream of air amongst the thick fluid while I slept. I would pray that my shallow source of air wouldn't fail me while I slept. Many times, my limited lung capacity would fill with large volumes of blood and we would have to rush to the hospital in the middle of the night.

While in the hospital, falling asleep would cause alarm bells to sound as my oxygen dropped and my heart rate spiked. I had my best friend sleep next to me to hold me through panic attacks while I searched for air. My husband would take shifts being by my side and when I drifted off to sleep, he would have to wake me up and yell "BREATHE Stephanie!" as alarm bells rang on all the screens connected to me. My then 4-year-old son would visit me in the hospital and even talking to him would take more energy than I had.

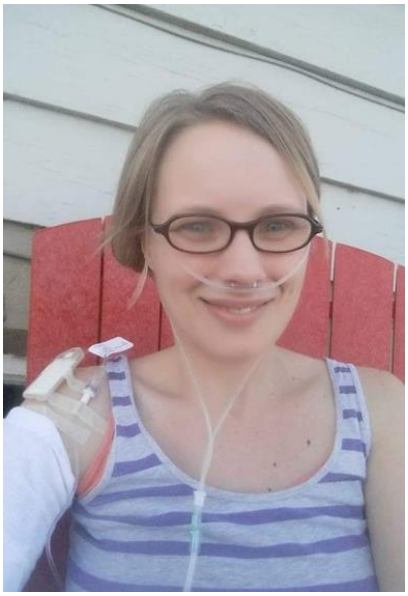
Taking Trikafta has allowed my husband to complete a full day of work. It's allowed my parents to relax after 37 years of being CF caregivers. These 3 simple pills taken every day brought me back to my son. I am now the present and active mother that I dreamed of being. My chronic pain has disappeared, and I am stronger than I have been in more than a decade. I've transformed from a 36-year-old that needed to be supported to use the washroom to a 37-year-old that for the first time in life, has gone running.

My season of life was coming to an end. My doctor said to me during an appointment, "Stephanie, women with CF in their mid-30s don't do well with CF. And by don't do well, I mean die." I started preparing paperwork. For the first time in life I saw each person close to me cry out of fear. We were losing hope… until Trikafta changed it all. I am now VIBRANT. I am a new person. Even my skin colour changed from pale-grey to a pink, oxygen rich tone.


Since starting this medication, I have witnessed my family's fearful tears transform into tears of joy and reprieve. They are witnessing my second chance at life and I am thriving. I'm writing this with 98% oxygenated blood while breathing room air. For a CF patient that was facing transplant, this still feels unreal. This is truly been a miracle for my health. I can only hope that all Canadians with CF can realize the power of this medicine.

**Amanda Bartels**
*Calgary, Alberta*

Thank you for the opportunity to provide a testimony from a patient's perspective on the benefits of Trikafta.



I am a 38-year-old wife and mom. Due to the excellent group benefits plan my husband has, I was fortunate to have access to the first and second-generation CFTR modulators. First, Orkambi in 2016 and then I switched to Symdeko in 2018. I accessed both drugs within only a couple months of Health Canada approval. After a steep decline in 2015, these drugs provided a stabilizing effect on my declining lung function and corrected my BMI with needed weight gain. Sadly, by 2019 even these drugs, which were partially correcting my defective genes, could not hold back the ravages of cystic fibrosis on my lungs. The result was increased exacerbations, bacterial lung infections and complications that required repeated hospital admissions, particularly in 2019.

2019 was the hardest year of my life. I had already been on continuous oxygen for a few years and spent nearly six months on intravenous medications and in the hospital for treatment of my CF exacerbations and lung collapse. I continued to decline, and after spending nearly 4 months in the hospital, my physician submitted an application for Special Access for Trikafta in the last quarter of 2019. Three months later in the beginning of 2020 that application was denied, and I was devastated. I was not sick enough yet, which was very difficult to comprehend after the year I had endured. My mental health is typically quite good, which is not true for many with a fatal disease like CF, but this crushed me. Knowing a drug existed that could save my life but was just out of my reach was incredibly difficult to deal with. At that time, I was undergoing tests to qualify for a double lung transplant and Trikafta was my last chance to avoid or postpone that process.

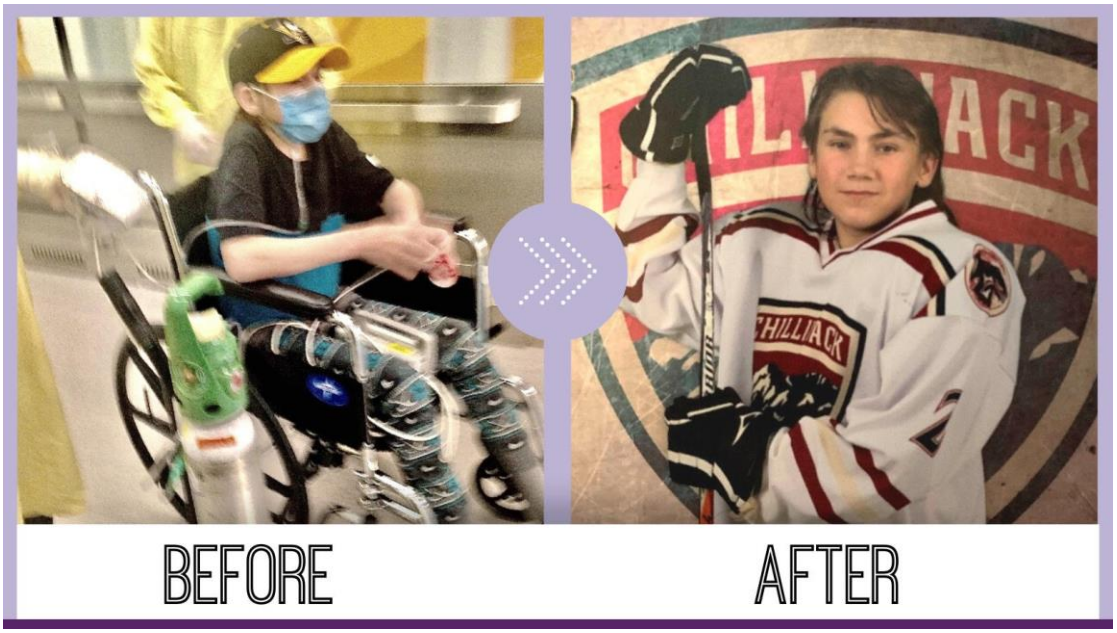
In spring 2020, after another hospitalization as COVID19 infections exploded across the country, a second application was made, and I was deemed sick enough to receive Trikafta through the special access program. Both I and my family were elated at this second chance! I did not want to raise my expectations too high and took things a day at a time as we waited for the first shipment of pills to arrive. Since then, life on Trikafta has exceeded every expectation and I could feel it working within hours of taking my first dose. The thick, sticky mucous that has lined my lungs for my entire life was mostly purged over the first few weeks. I have had zero CF exacerbations. I have had a nearly 10% increase in lung function and no need for IV antibiotics or hospital admissions. My daily airway clearing treatments and therapy no longer exhaust me and are more effective than they have been for many years. Plans to possibly move forward with listing for new lungs has been put on hold indefinitely. I put away my oxygen tanks within a couple of months, can take deep breaths and can exercise and am living life like a 38-year-old mother should be.

My daughter just turned 10 and my hope when she was born had been to be here for her through puberty because no girl should be without her mom in that time of her life. That hope slipped away as my health declined drastically and I revised my 'goal' to age 10. Because of Trikafta I was here for her 10th birthday with my own, original lungs. In addition to that, I am currently more active and feel healthier than I have been since she was 6 months old when I developed pneumonia that robbed me of nearly 25% of my lung function. This is not supposed to happen for CF patients, particularly without having a lung transplant, as CF is a progressive disease. You just don't get better and improve, until now with Trikafta. The joy and relief this brought to my family is tangible and now I am blessed to plan a future with my husband and daughter that I will be a part of, hopefully for many years to come.

I did not know it in spring 2020, but I had forgotten what if felt like to truly breathe. Within a couple weeks of starting Trikafta my lungs cleared, and I could take a deep breath and walk across my front yard without oxygen and without having to stop to catch my breath. By the end of summer, I biked nearly 50 kilometers in an afternoon and the last time I could maybe do that was over 15 years ago. After nearly a year since my last hospitalization, I am now starting to forget the pain and impact of countless medical interventions, IVs, appointments, breathlessness and exhaustion and it is liberating.

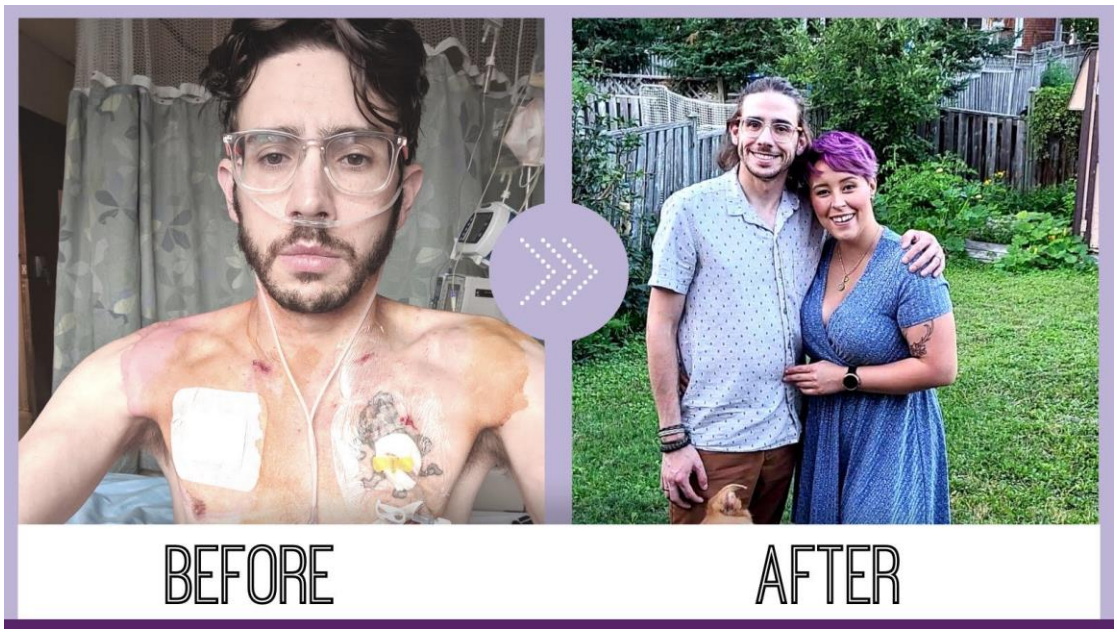
The only thing I am left wondering is how my life would have been different if Trikafta had been available to me as a 12-year-old, when I had nearly full lung function. Would cystic fibrosis, a deadly, unpredictable and devastating disease have been tamed and would my lungs have been spared the irreversible damage and extreme scarring I now have? I can only imagine how much my care has cost the health care system in Canada for the past 38 years, particularly the last decade, which would have continued to grow with the costs of additional hospitalizations and a potential lung transplant if Trikafta was not available for me. I am so hopeful for the future for all Canadians with cystic fibrosis who will benefit from this medication. It cannot come soon enough and needs to be provided for everyone, before irreversible damage occurs, so that children with CF may not have to go through what I have.

## Appendix C: Before and After

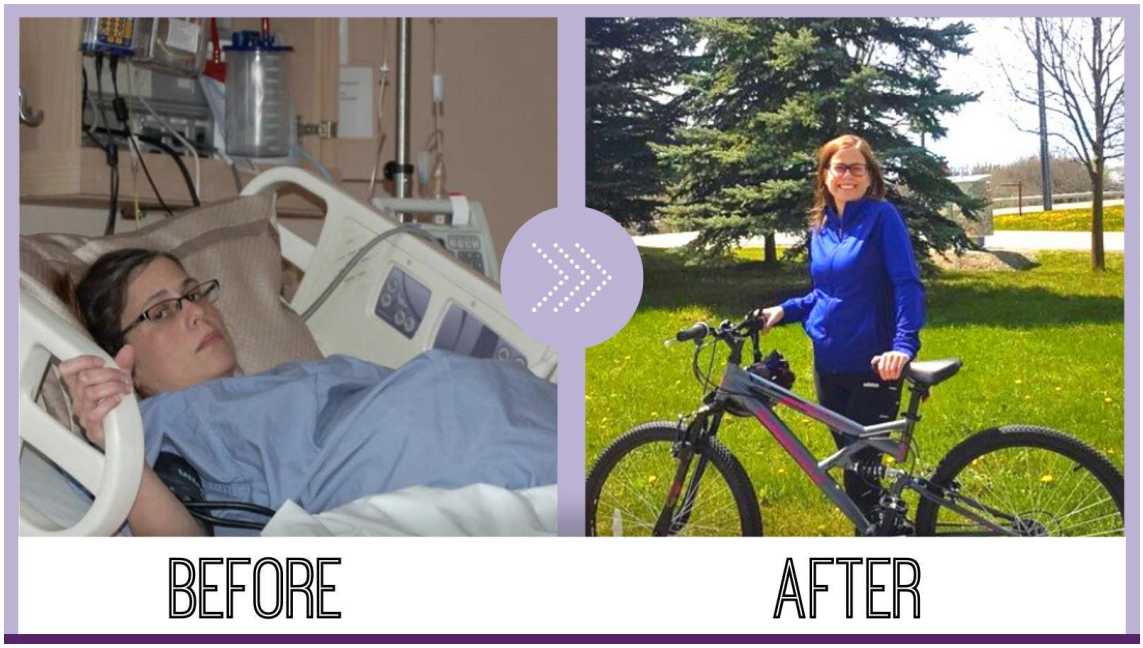



**Steven James, 17**


**Ashley Roy, 27**




**Kyle Laplante, 38**




**Sue Alonzi, 49**