Public Comment on ICER Draft Scoping Document for Brensocatib for Non-Cystic Fibrosis Bronchiectasis (NCFB): Effectiveness and Value

I appreciate the opportunity to share with ICER the personal lived experiences of my stepmother, Fern Leitman, who was a bronchiectasis patient for most of her life, and of myself and my family as her caregivers.

Because my correspondence and records date back at least two decades, I have been able to reconstruct a snapshot of the factors contributing to the economic burden this disease placed upon Fern and my father, Philip, beyond only the immediate healthcare costs. While it is far from a full account, the information I compiled is illustrative of the economic fallout that occurs because of a serious, chronic disease like bronchiectasis.

This is a handful of exacerbations based on my documentation:

- Ten-day stay in a local hospital in January 2009. I stayed overnight two nights in a row because she was experiencing periods of delirium, and we felt her having a familiar face nearby would be helpful.
- 22-day stay in Denver at National Jewish, in October-November 2010.
- Five-day stay in a local hospital in 2013.
- In 2014, an aggregate of 39 days in hospital between January and October due to exacerbations and declining health.

Hurricane Katrina made landfall in Miami on the evening of August 25, 2005. Fern and my father were in San Francisco at the time and had to remain there for four extra days because there was no electricity in their neighborhood – this meant she could not keep her medications refrigerated, could not use her airway clearance equipment that needed to be plugged in, and could not sterilize the equipment as needed.

In October 2005, Hurricane Wilma made landfall on the 24th, taking down approximately 98% of Miami's power grid for an extended period. Fern and my father were in Denver at the time for a visit at National Jewish Health and had to extend their trip by more than a week as there was, once again, no power in their neighborhood. Furthermore, they were awaiting test results from a lab at a local medical arts complex, which they were unable to obtain because at the time, the entire medical arts complex was operating on generators, causing delays in non-urgent lab work.

In all, Fern and Philip had to fund trip extensions for at least 12 days, which include hotel, car rental, and food. In addition, $17,000 worth of Fern's medication was lost that year due to the inability to properly refrigerate it after the storms. Because of this, Fern and Philip decided to install a full generator at the house which could power the main functions for up to a week. (See Appendix A.) The cost for this installation was $20,000, but weighed against the expenses of having to evacuate Fern out of Florida ahead of a hurricane, or having her stay away from home after a storm until their house was habitable again, it was deemed the most cost-effective way to manage these situations.

The snapshot above captures one small part of the economic fallout from just one lifelong sufferer of bronchiectasis.

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I offer you Fern's own words from a 2012 FDA workshop[1] on the development of new drugs for bronchiectasis: "The insurance process has given my husband Philip some sleepless nights. So far, his advocacy has prevailed, but my costs are now close to $150,000 per year."

Those were ***the patient's*** direct costs of medications and outpatient and inpatient treatment. I know this because I often helped my father sort through the explanations of benefits and bills. This amount does not account for the costs borne by payers and healthcare systems involved in taking care of her.

ICER correctly takes into consideration the social and emotional burden of disease in addition to the economic burden and looks at the burdens placed upon both patient and caregiver. As Fern observed in 2012, "The disease and the treatments, both medical and physical, affect my quality of life and impact my family."

It remains unclear, however, how one quantifies the non-economic burdens. I am uncertain how to effectively communicate a quantitative cost to this, so I begin with the simple statement that while it remains unquantifiable, the fallout that caregivers and family members experience is enormous and much farther-reaching than most people realize.

Often the reach of the impact is invisible to those outside, looking in. How does one assign a numeric or dollar value to this? It is my opinion that no such formula exists, though this does not negate the importance of trying to account for the cost of such losses.

My parents missed nearly my entire first semester of law school while Fern recovered from a lobectomy. Once they returned home and I was able to, I began managing my class schedule to allow time to help with Fern's airway clearance at least once a week.

Lack of predictability in a patient's life spills over to the family. I can think of many examples and offer just a few. A friend was able to secure for me four sought-after tickets to a show. Two of the tickets ended up going unused because Fern woke up that morning feeling so poorly, she was unable to leave the house.

The variability of her condition sometimes profoundly impacted the way Fern felt physically. One rainy afternoon, I was in a car accident but because the inclement weather had so adversely affected Fern's health that day, she was unable to get to me. My father and brother were both out of town. I cannot imagine the frustration and fear any parent must feel when one of their children is hurt and they cannot get to them.

As a caregiver, it was important to avoid exposure to respiratory/communicable ailments as much as possible. I did not go to see popular movies in theaters in the first few weeks of release, as I wanted to avoid crowded theaters. This pattern of avoidance also meant canceling plans with friends if they had even a sniffle, or if one of their children did -- the risk was too great. On a regular basis, I rescheduled at least 25% of my planned activities with my friends.

Because Fern was the patient and Philip the primary caregiver, I sometimes deprioritized my own health. Over time, this led to a mental shift towards nondisclosure, where I would not reveal any medical issue until or unless it was necessary. This pattern of thinking became habit and persists to this day.

For example, when I found a lump in my breast, I did not tell them at the time. I waited until my mammogram was scheduled and then mentioned that I had the appointment; only when I was asked why, did I reveal the reason. At the time, my reasoning was that they were in Denver dealing with Fern's health issues, and mine were less important. On another occasion, my mother flew over from England to take care of me after a minor surgical procedure, because I did not believe Fern and Philip had the bandwidth to deal with my medical needs.

The final 10 months of Fern's life were perhaps the most challenging. The strain of her declining health and increasing caregiving needs took an increasing toll on my father, who in turn relied more heavily on me for assistance. I spent hours at a time, and sometimes the entire day, out of the office running errands and assisting wherever I could. Based on my own documentation, I spent an aggregate of at least nine workdays away from my duties.

During the summer, my father's physical health showed the adverse effects of the strain he was under when he collapsed while at a doctor's appointment for Fern. Fortuitous timing and location aside, he ended up hospitalized for two days while I moved into their house to take over his caregiver duties.

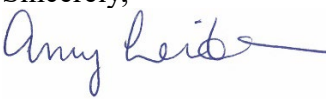
I leave you with one final memory, illustrating the emotional impact created by the physical fallout of bronchiectasis and the often-resulting infections which multiply that fallout exponentially.

I can recall one occasion where we were discussing a new potential therapy for NTM lung disease which was being tested against a particular species of NTM. It was not the same species that Fern had, but she wondered if it might work for her. She was told that it wasn't tested for and didn't appear to work for the strain she has.

I will never forget the look on Fern's face at this comment. The expression "her face fell" is the best way to describe it, and still it is inadequate to convey how she looked. To me, it was like watching hope drain away. I remember the restaurant we were at. I remember the table we sat at. It is a moment that haunts me today, and it will for the rest of my life. I wish the technology existed to erase it from my memory.

Some scars never fully heal. Even though my caregiver duties ended on October 13, 2014, some of the effects still linger.

Sincerely,



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Appendix A

This generator was installed after the 2005 hurricane season to mitigate costs associated with the power outages resulting from storms, which caused extended stays out of town and loss of costly medications. The generator is powered by a buried fuel tank which holds up to 1,000 gallons of propane gas and required additional work on the electrical panel inside the house to facilitate the power coming in from the generator. If overuse of appliances and lights are kept to a minimum, the generator can power the house for up to one week.

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COPD Foundation DBA Bronchiectasis and NTM Association

Comments on ICER Draft Scoping Document for the Assessment of

Brensocatib for Non-Cystic Fibrosis Bronchiectasis

Our comments are not in order of significance, but rather chronologically structured to follow the format of ICER's draft scoping document. Those comments in ***BOLD*** *we consider to be high priority.*

1. In order to most appropriately describe the condition, we propose that page 1, paragraph 1 be considered for revision as follows: "Bronchiectasis is a chronic, progressive lung disease characterized by chronic, usually daily cough, sputum production and loss of lung function. There are numerous underlying etiologies that are associated with bronchiectasis. Although people have varying symptoms, many have chronic productive cough, and exacerbations that may involve worsening of these chronic symptoms along with shortness of breath, fatigue, increased sputum, and sputum purulence (color and viscosity). Bronchi, the tubes through which air flows into the lung tissue, become enlarged and chronically infected with bacteria. Bronchiectasis is characterized by a 'vicious vortex' of recurrent infection, structural lung changes, inflammation, and deterioration in mucociliary clearance (i.e., the way that the body clears the lung of mucus). Bronchiectasis is identified by the finding of dilatation of the bronchi on computed tomography (CT) scans of the lungs. The diagnosis of bronchiectasis as a clinical syndrome also requires the appearance of typical symptoms related to breathing and coughing[1]. Bronchiectasis results in significant negative effects on quality of life due to impaired social and physical functioning related to the chronic cough and impaired lung function. Most people will have periodic exacerbations causing worsened symptoms. Adding to the impaired quality of life is the significant burden related to the various treatments that are recommended for many people[2,3]. Bronchiectasis can be associated with many underlying conditions that can affect the airways, including cystic fibrosis. Although cystic fibrosis can cause bronchiectasis, the clinical syndrome discussed in this document refers to the much larger population of people with bronchiectasis unrelated to cystic fibrosis which is sometimes referred to as non-cystic fibrosis bronchiectasis (NCFB)."
2. The phrase "vicious vortex" should replace "vicious cycle" throughout the document.
3. The incidence and prevalence of bronchiectasis increases significantly with advancing age after the 5th decade of life.
4. It is unconfirmed that two out of three people with bronchiectasis experience at least one exacerbation per year. This statistic comes from one unique series.
5. Page 2, paragraph 1, sentence 3 refers to risk factors for bronchiectasis severity, not for the condition itself.

6. Some of the most common risk factors for the development of bronchiectasis include post-infectious, primary ciliary dyskinesia (PCD), immunoglobulin deficiencies, autoimmune disorders, alpha-1 antitrypsin deficiency, and chronic aspiration; in approximately 30-40% of people with bronchiectasis an underlying cause is not found despite appropriate investigation.
7. Page 2, paragraph 2, sentence 2 proposed rewrite as follows: “For stable outpatients, regular airway clearance therapy at home can include use of devices (hand-held oscillatory appliances and vests) that mechanically provide chest-physical therapy, nebulized saline solution to loosen the mucus, chest percussion therapy, and breathing maneuvers. This therapy is usually recommended to be performed at least twice daily and can be quite time-consuming, contributing to the impairment of quality of life suffered by people with bronchiectasis.”
8. The lung surgery and transplant rates are small, not rare. Suitability for surgery is based on the age and strength of the person with the disease being focal.
9. **Impacts to quality of life from bronchiectasis are significant due to clinical and socioeconomic burdens[4,5,6].**
10. **Bronchiectasis affects peoples’ entire days and symptoms affect daily activities of living.**
11. Outpatient visits for people with bronchiectasis can occur every three to six months, with monthly outpatient interventions required for those whose bronchiectasis is not well controlled.
12. **Early diagnosis of bronchiectasis is possible with chest CT for people who are often misdiagnosed with asthma, chronic bronchitis, or chronic obstructive pulmonary disease (COPD).**
13. The following statement on page 3, paragraph 2 is clearer as follows: “The apparent increase in prevalence is likely related (in part) to increased awareness and increased use of CT imaging.”

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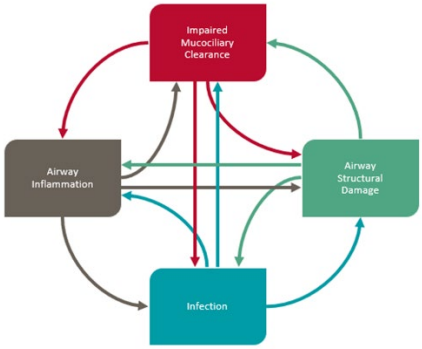
Subject: Feedback on ICER Assessment of Brensocatib

3/26/2025

Dear ICER Team,

I would like to commend the Institute for Clinical and Economic Review (ICER) for its thorough assessment of Brensocatib for the treatment of non-cystic fibrosis bronchiectasis (NCFB). Your efforts to evaluate the clinical effectiveness and value of this treatment are greatly appreciated and vital for advancing patient care. However, I would like to raise a couple of important points we believe warrant further consideration for this review:

The Vicious Vortex: The interconnectedness of impaired mucociliary clearance, inflammation, infection, and structural lung damage, often referred to as the "vicious vortex"[1] is a fundamental concept in understanding bronchiectasis and its treatment. The evidence from this ICER review shows a direct impact on inflammation but does not fully address infection, structural damage, or airway clearance. Each patient suffering from bronchiectasis is unique, and treatment management through a single trait approach will have minimal effect in addressing all the challenges of the vicious vortex[2].



Airway Clearance: One gap in this assessment is the limited discussion on the important role of airway clearance in the management of bronchiectasis. Airway clearance therapy is a mainstay in bronchiectasis treatment[3]. It is known to be safe, effective, and critical for patients with bronchiectasis, as it helps to mobilize secretions, improve lung function, and reduce exacerbations[4,5]. Incorporating airway clearance into the assessment could provide a more comprehensive view of the treatment landscape. High-frequency chest wall oscillation (HFCWO) is the airway clearance treatment of choice for individuals who have a chronic productive cough, have tried another form of airway clearance therapy but continue to struggle with secretion burden. Advancing an individual's airway clearance regimen to HFCWO is not dependent on exacerbation history.

Quality of Life: Bronchiectasis is a chronic irreversible condition. Whether a device or a drug is prescribed to treat the condition, the outcome is to improve the patient's quality of life. The Quality of Life-Bronchiectasis (QOL-B) questionnaire is a valuable tool to assess patient reported outcomes of symptoms and functioning through eight scales[6]. However, bronchiectasis is a complex disease of multiple etiologies and co-morbidities, with variability in severity and symptoms[3,6]. Use of other health related quality of life (HRQL) questionnaires, such as the Chronic Airway Assessment Test (CAAT), or individualized patient reported outcomes are valuable assessment tools for physicians to monitor a patient's condition and quality of life[7]. Our own internal data has shown that 97% of patients feel better and 98% have improved sputum production after utilization of HFCWO therapy[8].

Treatment Cost: We encourage ICER to consider the total long-term cost of treating bronchiectasis in this framework. Since there is no single treatment modality to eliminate bronchiectasis, providers will continue to utilize all available tools to manage the costly vicious vortex. Therefore, understanding the cost of oral, inhaled, and intravenous antibiotics, the cost of airway clearance (HFCWO), and the cost of this new drug should be clearly spelled out so that patients, providers, and payors can shape their medical and treatment policies effectively. For example, patients utilizing HFCWO have shown a reduction in hospitalizations by 59% and emergency department visits by 75%[4,9]. Moreover, as a once in a lifetime cost device, average annual savings per patient due to reduced hospitalizations is $4,423[10].

Thank you for considering these points. I believe that including these aspects in the assessment will enhance the understanding of Brensocatib's role in treating bronchiectasis and ultimately benefit patient outcomes.

Sincerely,

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Electromed, Inc.

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March 31, 2025

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On behalf of NTM Info & Research (NTMir), we thank you for the opportunity to provide input to the Institute for Clinical and Economic Review (ICER) Draft Scoping Document for Brensocatib for Non-Cystic Fibrosis Bronchiectasis (NCFB): Effectiveness and Value.

NTMir is a 501(c)(3) non-profit organization dedicated to advocating for better education, early detection, and the development of new treatments to help patients living with nontuberculous mycobacteria (NTM) disease and other related comorbid illnesses such as bronchiectasis. As a national patient advocacy organization led by people with bronchiectasis and NTM who face daily challenges dealing with this serious chronic condition, we appreciate the ability to engage with ICER throughout the review process to share the patient and caregiver perspective as a tool to address some of the challenges that exist when evaluating novel therapies for people living with NCFB.

NCFB is a serious and complex chronic lung condition, increasing in prevalence each year, with no disease-modifying treatments available which directly address the underlying mechanisms which drive the development and progression of NCFB. To date, treatment has focused on management of symptoms and mitigation of exposure to pathogens which can cause additional pulmonary damage and require significant antimicrobial therapy, which has its own set of significant, sometimes dangerous side effects.[1] (See Appendix A, *Re: antimicrobial therapy*.)

NCFB imposes significant social, physical, and economic burdens on patients, who often require extensive hospital stays, more frequent outpatient care, and complicated medical therapy. Annual number of exacerbations, presence of comorbidities, and extent of lung damage have been found to be associated with an increase in the length of hospitalization.[2] The estimated annual aggregated health care costs for bronchiectasis in the United States alone exceed $14 billion.[3]

The ongoing threat of opportunistic infections, particularly NTM and *Pseudomonas aeruginosa*, concomitant to NCFB and its primary array of symptoms, adds greatly to the burden of treatment with additional medications and ongoing monitoring with CT scans and sputum testing. The use of additional antimicrobials can also increase patients' risks of developing antimicrobial resistance and other complications related to extensive antibiotic use.

These infections also add to the economic burden of NCFB. Bronchiectasis patients are 50-75 times more likely to have NTM infections than those without the disease.[4] NCFB patients with *Pseudomonas*

aeruginosa infections have higher incidences of hospitalization which are also longer in duration and more costly overall.[5]

In bronchiectasis patients with new onset of NTM infections, the change in status is often associated with worsening radiographic lesions[6], signaling the potential start of irreversible lung damage that can lead to an increase in exacerbations and a decline in function over time. The prevalence of NTM in adults with NCFB is also on the rise.[7]

Qualitative data gathered directly from patients living with NCFB demonstrate their clear understanding of the relationship between their NCFB and their infection risks. As early as 2012, patient advocate Fern Leitman, who founded NTMir, spoke extensively of her lifelong experience as a bronchiectasis patient during a U.S. Food and Drug Administration (FDA) public workshop.[8] Though Fern passed away two years after that workshop, her words and thoughts are preserved in the documents she created and transcript of the meeting, and are excerpted to present her patient perspective. (See Appendix A.)

In 2015, the FDA hosted a Patient-Focused Drug Development meeting (PFDD) for NTM disease. At this meeting, patients described the symptoms and life impacts of living with NCFB, the inadequacy of current treatments and the incredible unmet medical need in this community. Bronchiectasis was referenced 69 times during that meeting, and respiratory symptoms of cough and dyspnea were referenced 95 times and 47 times, respectively. Fatigue and tiredness were referenced a total of 52 times as a symptom. [9] This cluster of symptoms is consistently identified by patients. They described this debilitating fatigue with examples of it interfering with basic daily functions including driving locally, cleaning their house, and cooking a meal. (See Appendix B.) We ask that ICER revise the Draft Scope to include fatigue as a primary symptom of concern for NCFB patients.

A 2018 article in CHEST presented the results of a needs assessment survey and stakeholder meetings held to develop a list of US patient-centered research priorities for NCFB. Notably, respondents and stakeholders identified considering "time and ease of administration in the development of new drugs" and identifying potential biomarker candidates as high priorities.

Treatment of exacerbations was ranked (44%) among the highest ranked research priorities of respondents, with 33% of survey respondents selecting "treatment of exacerbations or associated infections" as the top priority.[10] With regulatory emphasis on therapeutic development that meets the needs of patients according to their preferences, we suggest that ICER's review include this article as a point of reference and consider patient preferences when evaluating the therapy.

At an FDA workshop in 2019 on the development of treatments for pulmonary NTM disease, the results of a patient survey were presented. 465 patients with NTM lung disease responded to a 57-question survey on their experiences with NTM and their comorbidities, co-infections, treatments, clinical trials, and preferences for treatments and clinical trial design.[11] Both the quantitative and qualitative data indicate that patients deeply understand the interplay between their bronchiectasis and concomitant infections. 83% of respondents indicated that they have bronchiectasis, and of that subset, 45% identified a co-infection in addition to NTM.

Notably, when asked about "Top Symptoms Experienced" and "Most Bothersome Symptoms," respiratory symptoms – coughing (with or without expectorating mucus) and dyspnea – were three of the top four, with the fourth identified symptom being fatigue. When asked about preferences for treatment outcomes, patients identified improving respiratory symptoms and reducing the progression

of lung damage and disease. Within the qualitative data, patients made clear associations between cough and fatigue.[11] (See Appendix C.)

No review or assessment of the value of a potential therapy can be complete without a robust understanding of the impact of the disease on the patient and those within their orbit, as well as the severity of the unmet medical need. We thank ICER for the opportunity to present the voice of the patient as this review moves forward and request that they take into consideration the perspectives shared in this document to provide important context during the review of Brensocatib.

Respectfully,

Amy Leitman

Amy Leitman, JD
President, NTM Info & Research

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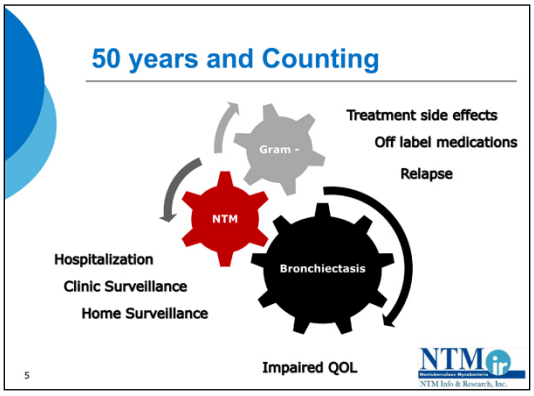
Appendix A: Excerpted Remarks from Fern Leitman's Comments at an FDA Workshop on Non-Cystic Fibrosis Bronchiectasis (Sept. 2012)



"I was diagnosed with bronchiectasis at the age of 14 after a major hemoptysis. I recall my father carrying me into Mercy Hospital in Miami. Then, he fainted!"

"I have had multiple episodes of hemoptysis, some severe but not requiring interventional radiology. I've learned to stay calm and often antibiotics are needed. For most of my life each cold became a major bacterial infection often resulting in hospitalization."

"This slide summarizes some of my challenges with bronchiectasis for over 50 years and NTM for more than 40 years."

Re: antimicrobial therapy: "Effects of drugs range from GI distress to more serious reactions from rash, hearing loss and eyesight damage as well as impact on kidneys. I have had all five but the worst is a friend that lost much of her hearing during a losing battle with bronchiectasis and NTM, and she had been an audiologist."

"My typical day includes up to 5 hours a day for medicines, airway clearance and exercise. My current regimen includes oral, inhaled and IV medicines. Every day, my morning starts with a nasal wash and coughing up secretions. Then I inhale a medicine and run my first IV of the day. I exercise and proceed on to airway clearance with an acapella before lunch. I repeat the process before dinner and take additional antibiotics before bedtime. I tell other patients that airway clearance reduces the work antibiotics need to do. When I have an additional infection, my treatments have, at times, increased to 7 IVs a day along with additional oral and inhaled medicines."

"My own experience includes rather resistant *Pseudomonas* but despite the limitations of sensitivity testing and constant positive cultures the bugs have undergone "crowd control" by judicious selections of antibiotics that have been inhaled, IV and oral along with diligent airway clearance."

"Most importantly, there are no vacations from bronchiectasis and for me none from NTM."

Appendix B: Excerpted Patient Comments from Patient-Focused Drug Development Meeting for Pulmonary Nontuberculous Mycobacterial Disease (Oct. 14, 2015)

"You just cough up because the **bronchiectasis** has gotten worse."

"As long as there's **bronchiectasis** – and we don't even have a clue about, it seems to me, about bronchiectasis and how to deal with it, that's the underlying disease I have, and that's there."

"I have never had a negative abscessus culture and have never been off an average of 6 to 7 drugs a day targeting NTM, the bacterial and fungal infections."

"Drugs have slowed, but they've not stopped the deterioration. Of course, **bronchiectasis** progresses."

"I don't hear anybody, really, as far as the medical and the pharmaceuticals, trying to deal with this cascade in the lungs, inflammatory in the lungs. I think it's perhaps the number one thing that we need to do for **bronchiectasis** patients."

Appendix C: Qualitative Feedback Collected from Patients in a Survey of Symptoms, Treatment Preferences, and Clinical Trial Experiences

Patients on Their Most Bothersome Symptoms:
"I cough every morning upon waking, so I don't feel rested."

"Coughing all the time with excessive mucous is a bother, interfering with everyday life."

"Relentless cough leads to vomiting."

"The shortness of breath was noticeable and affected my ability to do the things I was previously able to do."

"Coughing is exhausting. Coughing around others also makes them feel like you have a communicable disease so it can isolate you."

"It's embarrassing to have to cough up mucous and blood in front of clients, friends and even family."

"I have to plan activities based on whether it is a "good" day or not. I have to excuse myself from social gatherings to expectorate. I have to interrupt activities to take care of the mucus I generate."

Preferences in Treatment Outcomes:
"Get rid of the bleeding, get rid of the mucous, get rid of the NTM."

"Prevent further lung damage."

"I am most concerned with TOTAL lung health… **getting this infection under control means I am less likely to have exacerbations** that in turn require additional antibiotics in future."

What Bothers Patients Most About Their Disease:
"The cough and the mucus and the fatigue."

"What bothers me most is the **irreversible damage done to my lungs**."

"It is with me daily. It is chronic. It is incurable. It has **damaged my lungs permanently**."

If Treatment Could Change One Thing:
"Maybe a medication that would reduce **Bronchiectasis** or reduce cavities?"

"I wish there was a **treatment to minimize the permanent damage done to my lungs**."