



FDA Listening Session on Neurofibromatosis (NF) Summary Report Session Date: June 13, 2019



Executive Summary

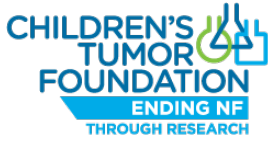
On June 13, 2019, six young people with neurofibromatosis (NF), and caregivers traveled to Silver Spring, MD along with the Children's Tumor Foundation (CTF) staff to offer vivid, unforgettable personal accounts of living with a rare disease NF, to officials from the US Food and Drug Administration (FDA).

The focus of the meeting was on people living with NF and caregivers who shared about:

- The symptoms, burden and impact of living daily with neurofibromatosis type 1 and type 2
- The current management and treatment options for NF
 - What types of clinical treatment benefits could make the most impact on people's lives?
- Their patient and caregiver perspective on how well "available" therapies are working

The event was initiated in collaboration with the National Organization for Rare Diseases (NORD) and organized by [CTF Patient Engagement](#) Director, Traceann Rose, who worked directly with Patient Affairs Staff at the FDA to create the day's agenda and prepare the young representatives for their roles.

The [Children's Tumor Foundation](#) is a 501(c)(3) not-for-profit organization dedicated to funding and driving innovative research that will result in effective treatments for the millions of people worldwide living with neurofibromatosis (NF), a term for three distinct disorders: [NF1](#), [NF2](#), and [schwannomatosis](#). NF causes tumors to grow on nerves throughout the body and may lead to blindness, deafness, bone abnormalities, disfigurement, learning disabilities, disabling pain, and cancer. NF affects 1 in every 3,000 births across all populations equally. There is no cure yet – but the Children's Tumor Foundation mission of driving research, expanding knowledge, and advancing care for the NF community fosters our vision of one day ending NF.



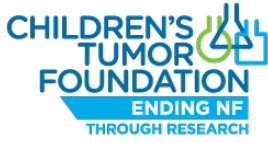
Meeting Participants

Neurofibromatosis community participants at the FDA Listening Session included:

- Annette Bakker, President, Children's Tumor Foundation
- Traceann Rose, Director Patient Engagement
- Maureen Hussey - Patient Advocate/Caregiver
- Jack Burke - Patient Advocate
- Jesse Sorman - Patient Advocate
- Brianna Worden - Patient Advocate
- McKinnon Galloway - Patient Advocate
- Aidan Fraser - Patient Advocate
- Pam Knight, Clinical Program Director, Children's Tumor Foundation
- Connie Sorman, Senior Manager, Stewardship and Volunteer Development
- Janna Walter - Patient Advocate/Caregiver
- Jayce Daniel Walter - NF Sibling
- Elizabeth O'Brien Burke - Patient Advocate/Caregiver
- Debbie Drell - Director of Membership, National Organization for Rare Disorders
- Beth Goldstein - Associate Squire Patton Boggs

The format, Patient Listening Session, is an informal one-hour discussion designed to help those involved in the drug approval process understand the obstacles and unmet needs of patients who might benefit from emerging new drug treatments. There are distinct differences in the clinical manifestations and variability in the development of disease manifestations within each of the forms of NF. Consequently, for the purposes of the format of the Listening Session and the limited time allotted, pediatric patients were chosen to represent the condition. The patients stories and dialogues below were supplemented by statements from Annette Bakker, President of the Children's Tumor Foundation about the overall disease state and the importance of the [NF Registry](#). The NF Registry is a patient-centered database that allows those living with any form of NF to contribute to research and stay up-to-date on studies of potential treatment. Still, the meeting punctuated the familiar burdens and struggles of living with all types of neurofibromatosis as well as some of the differences in disease progression among them.

Following an emotional session in which representatives and their parents described their medical journeys and hopes for the future, Andrea-Furia Helms, Director of the Patient Affairs Staff, expressed gratitude on behalf of the agency, saying, "You are the experts in NF. We need to hear from you. Your stories are critical for us to understand."



Patient Statements

Aidan Fraser: I am 19 years old and I have NF1. I have a large tumor on my neck, which goes up into my brain and down to my lungs and my left arm. I also have a number of smaller tumors throughout my body. I was diagnosed at 8 months old, became paralyzed at 15 months old, and again at 6 years old, when my tumor was pressing on my spinal cord. I had to relearn to walk both times. When I was 6 years old, I had a world first surgery to rebuild my spine. I had two surgeries a week apart, was in traction, and put in a halo for six months. We lived in the hospital for three months straight. I have had over twenty surgeries, four this year alone, and have been on some form of chemotherapy for 17 years. It has always been a struggle. When I was diagnosed there was no treatment at all, so I was on a cancer chemotherapy that made me very sick and did not help. I had chemo delivered into my heart once a week for 18 months. Every time I got a fever over 101 degrees I had to go to the hospital, but I almost always had a fever so I was in and out of the hospital for a year and a half. The treatment I am now on has helped a lot. It helped my tumor shrink 40% and now seems to keep it stable. However, on this medicine I have to fast for six hours a day, I am often nauseous and I do get sick regularly. I have always suffered from terrible nerve pain but the treatment has alleviated all of my nerve pain. It used to feel like someone was stabbing me every few minutes, so I am incredibly grateful for the medicine I am receiving. The problem is that I am actually one of the lucky people with NF, I am fortunate to have access to great doctors and the best care I could hope for. At the same time, I have been bullied, ignored and disregarded because of the way I look. When I walk down the street people stare at me. I understand because no one has seen someone who looks like me, but it is very, very hard. I just put my headphones on and try to do my own thing, but it's not easy. My mom sold our home at the end of Long Island and moved us to New York City because I was being bullied at school. I have more freedom in New York because everyone looks differently and I don't get noticed as much. I am lucky to have such a wonderful support system and medical resources but I am fully aware that for most people with NF, this is not the case. I am standing here today to tell you that NF is not uncommon, I am a result of a common genetic mutation. Neither my mum or my dad has the gene, so it was just bad luck. Really bad luck if you ask me. It is incredibly hard to be so sick, but also for it to be so visible disfiguring and therefore shunned. I'm asking for help, for myself and also for the entire NF community. I appreciate your time. Thank you.

Brianna Worden: I was diagnosed with NF type one at two months old. My plexiform encompasses my entire left side besides my left leg. From NF I have renal artery stenosis and hypertension which I am on medication for. I also deal with learning disabilities, chronic pain and fatigue. I've endured over 10 surgeries at Boston Children's Hospital including three spinal fusions where I had a 25% chance of ever walking again. A wrist stabilization, three tumor debulking to my left arm where each



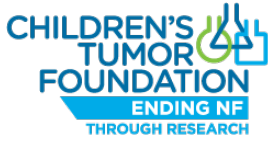
time they've removed about 3 pounds of the tumor. I was diagnosed the first time with Malignant neurosarcoma when I was a Freshman in high school. The cancer came back two more times after that. When I had one of the cancerous tumors removed from my throat my vocal cord was paralyzed for six months. This was the most difficult obstacle I have ever faced. Singing has been the only normalcy in my life and because of paralysis, I wasn't allowed to do the one thing I loved. I was on a liquid-based diet and I had to learn how to talk and swallow again. While I have my voice now, my vocal cord has partial paralysis. I have been on one Clinical Trial for NF, it was promising and shrinking some of my tumors but my kidneys begin to fail. Unfortunately, my blood pressure was too high to continue the trial, I was at risk of a stroke, and was told I would not survive if I continue the trial. Throughout my life, NF has had both positive and negative impacts on my life. Yes, I've been able to accomplish great things and be a spokesperson and advocate for those who suffer from this disorder. But I've missed out on a lot of things that I wish I could've done. Most of my high school years were spent in the hospital or at home with a tutor. I had to finish my last year of college online. I have been denied disability, I tried to work and unfortunately, I hurt my left arm at my job. As you can imagine this has caused a great deal of depression for me. During my junior year of college, I was told I may have a malignant tumor on my thyroid. I will be having a biopsy in a few months. An update of my medical issues is that I might need my left arm amputated because the tumors have grown so much in my left arm that it's actually eating my bones and I have lost a lot of function my arm dislocated frequently. NF doesn't just affect the patient. It affects the family of the patient both mentally and physically. While I do think finding a cure is necessary. I am very nervous about the various types of medications...being that I do have high blood pressure. I am excited to announce that I just graduated from Boston University, the top 10% of my class even while coping with NF. I am now 22 years old; I was told I would not survive over the age of seven and here I am speaking with you today. NF has made us strong, but it is important to look at all the aspects of this disorder and how medications will affect us mentally and physically. THANK YOU.

McKinnon Galloway: I am excited to be here and share my story and some of the emotional and physical hardships of living with my NF. When I was 16 years old, I got hit in the head with a volleyball and got a concussion. I went in for a routine MRI and found two brain tumors and six spinal tumors. The doctors sat me down and told me I had NF and said I would be deaf by the time that I graduated high school. To say that was shocking would be an understatement. We were devastated. I was so scared and didn't know what to do. But at that time, some new drugs started to come on the market. I am now 26 and since then I have been on 10 years of chemotherapy, one metabolic concoction, a phase one medical trial and two brain surgeries; one that took my hearing in my right ear. Because of the drugs that the FDA has approved I was able to keep my hearing in my left ear. And while I am so grateful for the medication in the past, this medication has started to affect my kidneys so bad that I will have to be pulled off of it soon. Which most likely means a brain surgery where they will cut my hearing



nerve and I will be deaf. My life can be difficult with this illness. I have balance problems, hearing problems, cataracts in my eyes, leg problems, and this doesn't include the emotional depression waves that I have been through because of NF. It is also difficult in my daily life despite the physical symptoms, such as appointment after appointment. This illness has affected my jobs, friends, relationships, and school. While this is terrifying, these new medicines that are coming down the pipeline, gives me hope. I have hope that we are so close to one of these new drugs being a cure. These medicines that are coming into the picture were not options ten years ago, and I am standing before you in the condition that I am in because of them. I am so excited about the new medicines coming down the pipeline because that can mean I could keep my hearing. I would not be afraid of new tumors growing in my brain and on my spine. I would not be worried about facial paralysis, growing tumors on my visual nerves and going blind. And I would not be worried about the millions of symptoms that come along with this horrible disease. Thank you.

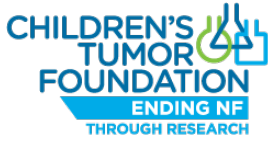
Jesse Sorman: - I was diagnosed with Neurofibromatosis type 1 or NF 1 for short, at 6 months of age. Thank you for allowing me to share my experience of living with NF. It is important for others to know the challenges that people with NF face so that patients can get the proper treatments they need to live without pain, fear, and medical complications. Living with NF has been difficult and growing up, I haven't had the same opportunities and abilities as others. As a child, I couldn't be a part of sport teams or keep up with the others during physical activities. I have a plexiform tumor in my right leg that has caused it to grow at a faster rate than my other leg, which has prevented me from being able to walk normally, to run like other kids, to climb, ride a bike and just do normal kid things. When I was 12, I started to have multiple surgeries to correct this discrepancy. I also have had numerous MRIs to make sure that my plexiform tumor is stable, and not malignant, as well as keeping track of my other tumors throughout my body. I have a lot of anxiety involved with this due to the fact that my tumors can grow, become malignant or about finding new tumors. I have many tumors all along the nerve roots of my spine, an optic glioma, and one behind my left knee on the peroneal nerve that causes pain to shoot down my leg sporadically or when the tumor is bumped. I also have dermal tumors all over my body and the number of them increases, as I get older. This affects me in a way where I can be externally judged by others, which can affect my ability to get jobs that I need to survive and causes anxiety about meeting new people and making friends. It worries me that there aren't any treatments available that are specifically meant for NF patients. This means that NF patients are getting treatment that is ineffective to them and can also cause adverse effects to their health. NF hasn't only affected me physically but academically and emotionally as well. Throughout my schooling career I have had learning disabilities that cause me to learn things at a slower rate than my peers. Because of this I have had to work much harder than my peers to be able to perform well in school. Even with the accommodations provided, school can be a challenge to me. I am currently studying to be a Veterinary Technician. The program is very involved and a lot of work. Even the students in my program who don't have learning difficulties find the content of the program very



challenging. You can probably imagine how hard it is for me. Standing in front of you today is really outside of my comfort zone and I almost didn't even do it. I am here because it's important for you to know how difficult this is for me, so that when you're making a decision about approving a drug that could help people with NF, you will remember that I shared my struggles with you. I hope by sharing my story I can help you understand the challenges of living with Neurofibromatosis. I have a lot of hope for my future and for the future of others that there will be advancements in research and FDA approved treatments for NF. Thank you for your time today.

Jack Burke: I'm 14 years old. I have NF but NF does not have me! I was diagnosed with NF at age 2 and started MRIs at that time. I have a left eye plexiform neurofibroma and had a left eye debulking surgery at age 6. I have since discovered that I have plexiforms on both my left and right eye orbit areas. I have others as well. At age 7, I was diagnosed with a brainstem glioma and had to undergo a year of chemotherapy. As a result of the pressure along my brainstem, I developed a syrinx on my spine and had to have brain surgery at age 10. I am also currently recovering from surgeries on both of my feet this past year. NF affects my life in many ways. Walking in my shoes means that I have over 10 doctors. I have had over 40 MRIs. I have had speech, occupational or physical therapies since I was 3. I have to work harder at school sometimes. I am at the doctor a lot, which causes me to miss school frequently, and I have had more needle pokes than I can count. I have had much pain after each and every surgery. I worry. I worry about my tumors growing, and about getting new ones. It is really horrible to have NF – especially when there is no cure or effective treatment. That is why I decided to do my part and raise money for NF research – and have raised millions of dollars so far. I would like drugs to be developed that particularly target NF. After all, NF is like a cancer in some ways, but different in some ways too. For instance, the chemo I took for my glioma has been around for about 30 years, and the doctors were not even certain if it would affect my NF glioma or not. Many times, for those of us with NF, we don't need tumors to completely disappear – we just need them to shrink or not grow (but of course we prefer they disappear forever!!). Our tumors also act differently, so I would like to see drugs that directly target NF. Finally, I want to thank you for having me here today. It is SO important for our voices to be heard. We at Children's Tumor Foundation and also my foundation, CureNFwithJack, work really hard, every day, to advocate for a cure. Thank you.

Maureen Hussey: I am here today to represent my 13-year-old daughter Maggie. Maggie was diagnosed with NF shortly after turning 5 years old. Soon after Maggie's birth we began to notice she was behind in achieving her developmental milestones. Maggie is the second of our three children and they are very close in age. While her older brother and baby sister were moving quite easily through baby and toddler hood, Maggie was clearly behind. Several trips to specialists in child development yielded offers for early interventions and special education services which

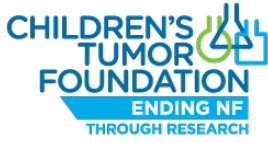


we gratefully accepted but no clear diagnosis or explanation other than pervasive developmental delay. On Maggie's 5th birthday she experienced the first of what we later learned were complex partial seizures having a dozen or so episodes in 24 hours. Our local hospital sent us to a major hospital with pediatric neurologists and after an MRI and a full history Maggie was diagnosed with NF1 by the NF Clinic at Children's National Medical Center. We were stunned at the realization that our daughter had a genetic disease and that her life would not be what we had prayed for which was a healthy and normal one.

I am here today as a caregiver speaking on Maggie's behalf because the neurological manifestations of NF have left Maggie intellectually disabled. I would LOVE to see my 13-year-old daughter speak to you today herself and share her daily struggles with reading, writing, relationships, sleep, attention, physical activities and epilepsy, but she is not here because she still doesn't understand what NF is and that it is the cause of her differences. Maggie is 13 but has the intellectual capability of a 5 or 6-year-old. The neurocognitive effects of NF have left Maggie unable to function each day safely and without oversight in the world as most 13-year old would. She has remained at the same grade level for the past 3 years despite the hard work she puts in every day. We are now beginning to understand that it's unlikely Maggie will achieve what should have been her full potential.

We have been told that Maggie's learning disabilities are on the more severe side of NF but it remains the case that upwards of 80% of individuals living with NF experience some form of a learning-related disability and many more experience ADHD and trouble with the executive functioning skills that are critical to everyday life. Learning and cognitive impairments in NF1 have some of the greatest lifetime morbidity. They often lead to social problems, difficulties finding and keeping employment, anxiety and sometimes depression. As Maggie grows, we see first-hand the daily struggles of those born with cognitive disabilities — they are often isolated, sometimes sad and unfortunately kept from experiencing normal social events and milestones with their peers.

NF affects Maggie in some way in almost every part of her daily life. She is in a modified academic program with self-contained instruction and some inclusion for electives always with 1-1 learning support. She receives occupational and speech therapy several times a week and is under the care of a developmental pediatrician to manage ADHD, anxiety and sleep problems with both medication and behavioral modifications. She asks us all the time "when can I stop taking my medicine?" This is a heartbreaking question each time she asks since the answer is, we just don't know. While finding a cure for NF is the ultimate goal, we must address the current needs of children and adults living with NF and those include the many painful, life changing and life-threatening physical problems AND also the developmental side of NF which greatly affects the quality of life of NF patients. While we worry about the growth of Maggie's brain tumors and the presentation of new tumors over time; it is the uncertainty of how



Maggie sees the world and digests everyday interactions that concern us every day. And, determining how we as her parents ensure her care once we aren't here for her impacts our entire family now and well into the future.

The treatments currently being investigated give us hope for a better future for Maggie and the progress since her diagnosis eight years ago is reassuring and for that we are grateful. Our family is proud to share Maggie's story with you all today and we thank you for the work you do for those with rare diseases like NF.

Discussion and Question and Answers

Also present at the session were FDA officials from the Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER), Oncology Center of Excellence (OCE), Office of Orphan Products Development (OODP), and Office of Clinical Policy and Programs (OCPP), and Patient Affairs Staff (PAS).

The FDA asked the youngsters for more details about the burden of NF, access to clinical trials, and ways to change the process to serve patients better, for example, with de-centralized clinical trials that would reduce the amount of time away from work, school, and family.

Answering questions from the clearly engaged and concerned FDA audience members about how FDA could improve the clinical trial experience, the patient reps highlighted:

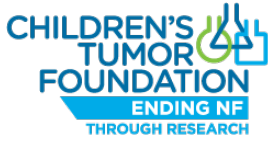
- difficulties in finding opportunities and deciding about clinical trial participation
- getting different specialists to communicate with one another
- and the lost potential of talented young people who spend too much of their time with doctors and in hospitals.

Unspoken, but strongly implied by the patient reps, was the idea that efficient FDA approval by FDA of safe, effective drugs now in development could revolutionize lives and free up much of this potential.

FDA was also interested in hearing about CTF-sponsored efforts to standardize clinical trial endpoints by supporting [Response Evaluation in Neurofibromatosis and Schwannomatosis \(REiNS\)](#), which REiNS and CTF Patient Representative Maureen Hussey was about to explain in detail.

CTF Clinical Programs Director Statement

Pam Knight, Director of Clinical Programs at CTF augmented patients' stories by sharing the broader NF community perspective on preferences, treatment options and hopes of for the future.



NF1 causes countless symptoms, and there is no way to know if or when they will show up or how severe they will be. It's a lifetime of "watch and wait." Plexiform neurofibromas are only one of the things to be watched, for their threat of disfigurement and dysfunction as well as their malignant potential. They and other NF1 manifestations such as optic nerve glioma and bone dysplasia's are common sources of relentless pain. Many studies report pain as top of the list of concerns for patients and their parents, followed by, and intertwined with, concerns and anxiety regarding appearance, and being stigmatized. NF1 pain is often accompanied by problems with sleep, GI complications, and overall quality of life. Currently there is no specific treatment for NF1 pain. Opioids, anticonvulsants, and OTC analgesics are prescribed, but largely ineffective. Surgical removal of tumors is often impossible due to tumor involvement with nerves and blood vessels. Even when surgery is feasible, it may fail to resolve or even worsen pain. What is needed is a drug. One class of drugs currently in development, MEK inhibitors, show promise in shrinking NF tumors and have shown some evidence of also being able to reduce pain, even without significant tumor shrinkage. The availability of a drug treatment that could deliver true pain relief, and at the same time also shrink tumors and relieve other related aspects of the NF1 disease burden, would free many thousands of children and young adults to explore their full potential and enjoy active, productive lives.

While the combination of long-distance travel and re-living physical and emotional challenges took a toll, all agreed the day was a great success. As CTF President Annette Bakker noted, the interaction between FDA and patients' representatives demonstrated an amazing evolution toward empowered patients. Andrea-Furia Helms, Director of the Patient Affairs Staff of the FDA expressed similar feelings by noting that the day's meeting can help inform FDA's work and it would not be the last opportunity for patient reps to engage with FDA.

Disclaimer

Discussions in FDA Rare Disease Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report reflects the account of the perspectives of patients and caregivers who participated in the Rare Disease Listening Session with the FDA. To the extent possible, the terms used in this summary to describe specific manifestations of Neurofibromatosis, health effects and impacts, and treatment experiences, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire Neurofibromatosis patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.