2024 IMPACT REPORT

Accelerating Discovery, **Transforming Lives**

Children's Tumor Foundation

The Children's Tumor Foundation (CTF) is the drug discovery engine for NF. Everything we do is to bring treatments to patients as we work toward a cure. By connecting patients, doctors, scientists, and pharma, we drive treatments, advance care, and deliver results for millions affected by neurofibromatosis or schwannomatosis. Our patient-first collaborative approach accelerates drug development and brings life-changing therapies to patients faster – driven by our mission to end NF.

Mission and Vision

The CTF mission is to drive research, expand knowledge, and advance care for the NF community. Our vision is to end NF.

About NF

NF refers to a group of genetic conditions that cause tumors to grow on nerves. These include neurofibromatosis type 1 (NF1) and all types of schwannomatosis (SWN), including *NF2*-related schwannomatosis (*NF2*-SWN), formerly called neurofibromatosis type 2.

NF occurs in 1 of every 2,000 births, affecting more than 4 million people worldwide.

Anyone can be born with NF and it affects everyone differently. NF can lead to blindness, deafness, bone abnormalities, disfigurement, learning challenges, disabling pain, or cancer.

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"We will leave no stone unturned in our quest to end NF, and with your continued partnership, the future for those affected by NF has never been brighter."

— Annette Bakker, PhD
Chief Executive Officer,
Children's Tumor Foundation

Dear Friends and Supporters,

At the Children's Tumor Foundation (CTF), everything we do is to drive treatments for NF patients. The past year has been nothing short of transformative for the NF community. Your steadfast support has turned possibilities into realities, and I am thrilled to share these remarkable achievements with you.

The advances of 2024 culminated in early 2025 with the FDA approval of Gomekli (mirdametinib)—the second-ever approved treatment for NF1 and the first for adult patients. This breakthrough builds on the earlier success of Koselugo and powerfully validates our strategic approach. We don't simply partner with pharmaceutical companies; we passionately advocate for the repurposing of shelved drugs for rare diseases, which is precisely what we did to ensure this drug made its way to our community. We celebrate this monumental achievement that reshapes the future of NF treatment.

This breakthrough propels our broader mission. CTF is dedicated to tackling tumors on all fronts—eliminating them, preventing their occurrence, and accelerating treatments to mitigate their harmful effects. Our objective is to secure approval for at least one therapeutic option for every manifestation of NF1 and SWN, including *NF2*-SWN.

Our investment in NFlection Therapeutics yielded impressive results in their Phase 2b clinical trial of a topical gel for cutaneous neurofibromas, now preparing to advance to Phase 3. For patients with *NF2*-SWN, our INTUITT-NF2 platform trial published groundbreaking results in the *New England Journal of Medicine*, demonstrating brigatinib's promise in shrinking tumors.

Equally exciting is the progress toward a blood-based biomarker test for malignant peripheral nerve sheath tumors (MPNSTs), which has moved into its next critical phase in partnership with CureNFwithJack. This non-invasive approach could fundamentally transform how NF1 patients are monitored, with the goal of detecting cancer months before traditional imaging, and enabling life-saving early interventions.

We also launched a fundraising campaign to establish a new NF Therapeutics Accelerator Fund. In the coming years, CTF will play a direct role in the discovery and development of next-generation treatments for NF. The fund's work will enable pharmaceutical and biotech companies to get to the finish line faster for our patients. The fund stands as a bold testament to our unwavering promise: no potential treatment should languish in development when it could be transforming patients' lives.

Our strategic plan calls for us to double our investment in research to continue driving groundbreaking discoveries that can lead to treatments and cures. No matter what happens, CTF will ensure that NF science has the resources to flourish.

Our partnership with Dolphins Challenge Cancer at Sylvester Comprehensive Cancer Center represents our largest-ever investment in schwannomatosis research. This undertaking aims to understand the cellular mechanisms behind tumor growth and pain—one of the most debilitating aspects of this condition.

Throughout our 47-year history, CTF has been willing to take calculated risks and invest in possibilities ahead of the curve. Our recent announcement of the establishment of CureAge Therapeutics in partnership with Deep Science Ventures exemplifies this approach, creating a dedicated biotech focused on developing genetic therapies for NF1. This venture, alongside our continued support of Healx's AI-driven drug discovery platform, represents our commitment to exploring every possible avenue for treatment.

As I reflect on the extraordinary progress of the past year, I am filled with profound gratitude for you—our community of supporters, researchers, clinicians, and most importantly, patients and families. Together, we are transforming the NF landscape at an accelerating pace. We will leave no stone unturned in our quest to end NF, and with your continued partnership, the future for those affected by NF has never been brighter.

With shared determination,

Annette Bakker, PhD
Chief Executive Officer

Treatment Landscape

Approved Treatments for NF

For decades, patients with any form of NF faced a stark reality: despite the condition's prevalence and impact, there were no treatments approved by the U.S. Food and Drug Administration (FDA). Today, that landscape has changed. Through relentless advocacy, strategic partnerships, and breakthrough research catalyzed and funded by CTF, two treatments now carry FDA approval, marking historic progress for the entire NF community.

Gomekli (Mirdametinib): First Treatment for Adult NF1 Patients

In early 2025, the FDA approved Gomekli (mirdametinib), the second-ever approved treatment for NF1 and the first specifically for adult patients. This approval represents a transformative moment for individuals living with NF1 plexiform neurofibromas (PNs), who previously had limited treatment options.

This exemplifies CTF's unique approach to accelerating therapies. The Foundation's NF Preclinical Initiatives first identified that the MEK inhibitor drug mirdametinib had the potential to significantly shrink NF tumors, paving the way for a revolutionary shift in NF treatment.

CTF played a pivotal role in advancing mirametinib's development when it was at risk of being shelved, by helping to create SpringWorks Therapeutics to ensure it reached patients. Over the past decade, we have partnered closely with SpringWorks, supporting clinical trial recruitment, enhancing their understanding of NF1, and persistently driving the treatment's progress. That work has culminated in a new, approved option for NF patients of all ages.

"CTF advocated for drugs like mirdametinib that had been stopped in development at other pharmaceutical companies, because they saw the promise that it held for patients with NF1-PN based on the available phase 2 data."

— Saqib Islam, CEO
SpringWorks Therapeutics

Koselugo (Selumetinib): Breaking Ground

In 2020, CTF celebrated the first-ever FDA-approved treatment for NF when the MEK inhibitor Koselugo (selumetinib) received approval for pediatric patients with inoperable plexiform neurofibromas.

A direct result of CTF's early stage research discovery, this milestone followed comprehensive clinical testing at the National Cancer Institute (NCI), where over 70% of NF1 patients with inoperable plexiform neurofibromas experienced tumor reductions ranging from 20% to 60%.

These FDA approvals have sparked significant interest from pharmaceutical companies who now recognize a viable pathway for developing effective NF treatments. This growing industry engagement will accelerate progress toward our goal of FDA approvals for all manifestations across all types of NF, including *NF2*-SWN and other SWN.

“We’re grateful for the connectivity CTF brings with this partnership to NF patients, clinics, and experts. It is known from other disease foundations that investments from medical research foundations like CTF may convince other investors that supporting NFlection is the right path forward.”

— Bill Hodder, CEO
NFlection Therapeutics

Treatments on the Horizon

While approved treatments represent tremendous progress, CTF's commitment to developing a robust treatment pipeline for all forms of NF continues with promising advances in 2024.

NFX-179 Topical Therapy: A Strategic Impact Investment

For NF1 patients with cutaneous neurofibromas (cNFs)—small tumors that develop on or just under the skin—a promising new treatment option is advancing. NFlection Therapeutics announced positive results from its Phase 2b clinical trial evaluating NFX-179 gel, a topical treatment, that significantly shrank cNFs while showing a strong safety record with minimal side effects.

Based on these encouraging results, NFlection plans to advance the program to Phase 3 development in 2025 following meetings with U.S. and European regulators. This progress was supported by CTF's strategic impact investment in NFlection—part of CTF's commitment to developing treatments for all NF manifestations.

If successful, this topical treatment will address a significant unmet need, as cNFs affect nearly all adults with NF1 and can cause both physical discomfort and psychological distress.

Brigatinib in INTUITT-NF2 Platform Trial: Publication Milestone

A landmark publication in the *New England Journal of Medicine* has highlighted the potential of brigatinib for *NF2*-SWN, marking a significant advance for patients with this form of NF.

Brigatinib's journey exemplifies the power of novel research approaches and how repositioning existing drugs can create new opportunities for rare disease treatment. The drug—initially developed for lung cancer—was identified as a potential *NF2*-SWN treatment through Synodos for NF2, a CTF-driven team science project uniting scientists, clinicians, and industry partners to accelerate treatment development.

The drug was evaluated through the INTUITT-NF2 platform trial. Platform trials represent a trailblazing approach for NF because they enable multiple therapies to be tested simultaneously. This unique approach significantly reduces the time and costs traditionally associated with clinical research, enabling faster access to potential treatments.

The published results showed promising outcomes: brigatinib shrank 10% of growing tumors and 23% of all tumors in *NF2*-SWN patients, promising a vital new option for patients with limited treatment options.

"The platform-basket trial design allows rapid evaluation of investigational agents for genetic conditions with multiple manifestations. In this study, brigatinib seemed to help with different types of tumors in people with *NF2*-SWN."

— Scott R. Plotkin, MD, PhD
Massachusetts General Hospital
and Harvard Medical School

Pioneering MPNST Biomarker Development

One of the most serious complications of NF1 is the development of cancerous tumors known as malignant peripheral nerve sheath tumors (MPNSTs), which affect approximately 10% of NF1 patients over their lifetime. Early detection is critical, but it has been challenging until now.

In collaboration with CureNFwithJack, CTF is advancing an innovative biomarker project that could revolutionize MPNST detection and monitoring. Building on earlier CTF-funded research, scientists have demonstrated that analyzing cell-free DNA (cfDNA)—tiny fragments of tumor DNA circulating in the bloodstream—can effectively distinguish cancerous MPNSTs from benign or premalignant tumors.

This noninvasive approach offers the potential for earlier, faster, and more precise cancer detection. It could reduce reliance on invasive biopsies and frequent imaging scans to monitor tumor changes. The technique has even demonstrated the ability to predict tumor relapse months before traditional imaging would detect it.

The next phase of this project focuses on expanding testing for high-risk NF1 patients, implementing serial testing for improved predictability, expanding the biobank of plasma samples, and preparing the cfDNA blood test for integration into routine clinical care.

"We are incredibly proud to support this critical phase of research. This work has the potential to save lives, and we are honored to be part of making that future a reality."

— Elizabeth O'Brien, Co-Founder and Chief Executive Officer of CureNFwithJack

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These developments—from FDA-approved treatments to promising therapies in the pipeline and revolutionary diagnostic approaches—demonstrate the remarkable transformation occurring in the NF treatment landscape. **Each breakthrough builds upon the last, accelerating toward CTF's goal of effective treatments for all forms of NF and all NF manifestations.**

Accelerating Discovery

"Our shared experiences brought a new strength, reminding me that while *NF2*-SWN may be rare, our resilience is not. I advocate for NF research not only for myself but for the next generation who deserves more treatment options, more awareness, and a clearer path forward. Every breakthrough in research, every connection in our community, is another step toward a better future."

— McKinnon Galloway, *NF2*-SWN patient and 2019 CTF National Ambassador

While FDA-approved treatments represent significant milestones, behind each approved therapy stands decades of scientific discovery. In 2024, CTF expanded its research portfolio across multiple fronts—part of our strategy to double research funding and create more "shots on goal." With federal funding in jeopardy, our commitment and investment in research are more critical than ever.

Research Investments

In addition to our pioneering **MPNST Biomarker Development** partnership, highlighted on page 9, these key research investments are driving rapid advancements toward treatment development.

NF2-SWN Gene Therapy Research

State-of-the-art research funded by CTF is driving innovation in gene therapy for *NF2*-SWN. Conducted at the Leibniz Institute on Aging in Germany and the Children's Medical Research Institute in Australia, this pioneering project explores a new approach to treating peripheral nerve sheath tumors, including schwannomas and related tumors. These tumors arise from pathogenic variants in the *NF2* gene, which disrupt the production of Merlin, a tumor-suppressing protein. By leveraging advanced genome editing technology, researchers are working to correct this underlying defect and develop a potential therapeutic strategy.

This research was leveraged by CTF's NF2 Accelerator Initiative, and builds upon discovery from earlier CTF-funded gene therapy studies. The collaboration brings together leading experts—Prof. Helen Morrison, a specialist in *NF2*-SWN tumor biology, and Dr. Samantha Ginn, a leader in genome editing—to push the boundaries of what is possible in *NF2*-SWN research. This project represents a vital investment of more than $1 million in cutting-edge science, expanding our understanding of *NF2*-SWN and paving the way for future therapies.

Optic Pathway Glioma Study

The Jeffrey Owen Hanson Optic Pathway Glioma study, a collaborative effort between CTF and the Children's Hospital of Philadelphia (CHOP), grew significantly in 2024. This multi-center study has set out to understand the natural history of NF1-associated optic pathway gliomas (OPGs) and develop evidence-based management guidelines for clinicians.

OPGs develop in 15-20% of children with NF1 and can cause significant vision impairment. However, predicting which tumors will threaten vision and require intervention remains challenging. By the end of 2024, the study had enrolled 271 participants across 25 NF clinics, approaching its expanded enrollment goal of 300 patients. Supported by the Gilbert Family Foundation, moving forward, enrollment will expand to 500, allowing for more robust statistical analysis that may further inform future therapeutic interventional studies.

In June 2024, researchers presented preliminary findings on the clinical and imaging characteristics of the first 250 participants at the CTF Global NF Conference. Chaired by leading investigators Dr. Michael Fisher and Dr. Robert Avery of CHOP, this lengthy observational study will help clinicians determine when interventions like chemotherapy are necessary and when they can be safely avoided.

"Our commitment is to driving the best research through collaborative and innovative endeavors. We believe strongly in the value of leveraging funding from partners to bring the best players together as a team to accelerate research, delivering effective and safe treatments to patients faster."

— Annette Bakker, PhD
CEO, Children's Tumor Foundation

Schwannomatosis Research at Sylvester Comprehensive Cancer Center

In a seminal partnership, CTF and Dolphins Challenge Cancer (DCC) launched a $1.7 million research initiative at the Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine. This collaboration targets schwannomatosis, one of the most challenging and understudied forms of NF.

Led by Dr. Antonio Iavarone, a distinguished pediatric neuro-oncologist and Deputy Director of Sylvester Comprehensive Cancer Center, this pioneering study employs cutting-edge technologies to investigate the intricate interplay between tumor cells and their microenvironment. By utilizing advanced single-cell analyses, the research team aims to elucidate how different cell types contribute to schwannomatosis progression and the debilitating pain that often accompanies it.

This venture builds upon insights generated by CTF's previous $1 million Synodos for Schwannomatosis collaborative, which revealed that individual cells play distinct roles in schwannomatosis pathology. Dr. Iavarone's extensive experience studying the cellular composition of tumors, including NF low-grade gliomas, positions him uniquely to advance understanding of this complex condition.

Beyond its immediate implications for schwannomatosis patients, this research has potential to improve pain management strategies across all forms of NF and may offer insights into other related conditions.

We extend our heartfelt gratitude to CTF Board Chair Emeritus Richard Horvitz and Erica Hartman-Horvitz for their generous financial support of both the previous Synodos study and this new partnership. Their steadfast commitment to advancing NF research in all its forms is invaluable and deeply appreciated.

"We have kicked off a partnership that dreams are made of. The Children's Tumor Foundation along with Dolphins Challenge Cancer teaming up with Sylvester Comprehensive Cancer Center to fund groundbreaking NF research is just a perfect match—a match that the millions living with NF will benefit from."

— Gabriel Groisman,
CTF Board Chair

2024 Research Awards

The Discovery Fund for NF Research represents CTF's commitment to investing in the brightest scientific minds and tackling all forms of NF. In 2024, CTF awarded research grants across multiple award programs designed to accelerate discovery and drive innovation. The investigations below not only fund great science but also expand the field by attracting and retaining talented researchers dedicated to ending NF.

Young Investigator Awards

The Foundation's Young Investigator Award (YIA) program, our longest-running research award mechanism, continues to attract emerging scientific talent to the NF field. In 2024, CTF committed over $900,000 to the Young Investigator Awards, funding eight promising researchers:

NF1 Research:

- **Ramya Ravindran** (Cincinnati Children's Hospital) is studying how inflammation drives neurofibroma development
- **Alex Dyson** (Massachusetts General Hospital) is investigating *NF1*'s role in neurological complications
- **Pernelle Pulh** (INSERM, France) is identifying targets for cutaneous neurofibroma prevention and treatment
- **Alexis Stillwell** (Pennington Biomedical Research Center) is analyzing skeletal manifestations in NF1
- **Sarah Morrow** (Indiana University) is investigating ZNF423's role in malignant tumor development

NF2-SWN Research:

- **Anna Nagel** (University of Central Florida) is deciphering cell death pathways for improved *NF2*-SWN therapies
- **Isam Naber** (UCLA) is analyzing inner ear proteins to address hearing loss in *NF2*

LZTR1-SWN Research:

- **Georgia Daraki** (Leibniz Institute of Aging) is exploring *LZTR1*'s role in pain development

Many past YIA recipients have established lifelong careers in NF research, demonstrating the program's effectiveness in building scientific expertise in the field.

Clinical Research Awards

The Foundation's Clinical Research Awards (CRA) support early-stage pilot clinical trials and interventions for all forms of NF. In 2024, CTF committed approximately $600,000 to these patient-centered research studies:

- **Konstantina Stankovic** (Stanford University) is studying plasma biomarkers to predict hearing loss and tumor progression in vestibular schwannoma *NF2*-SWN patients
- **Laura Lehman** (Boston Children's Hospital) is investigating moyamoya in children with NF1, developing non-sedation screening techniques to enable earlier intervention
- **Stephen Gilene** (Cincinnati Children's Hospital) is identifying biomarkers in NF1 patients with plexiform neurofibromas treated with binimetinib
- **Pamela Wolters and Julia Finkel** (National Cancer Institute and Children's National Medical Center), are evaluating a pain measurement device for NF patients who may struggle with traditional pain assessment methods

Drug Discovery Initiative Awards

The Drug Discovery Initiative (DDI) program stimulates therapeutic development by funding researchers exploring novel or repurposed treatments. In 2024, CTF awarded more than $995,000 to DDI awards:

- **Keila Torres** (MD Anderson) is combining BET blockade, PARP inhibition, and radiation to treat aggressive MPNSTs
- **Ljubica Caldovic** (Children's Research Institute) is targeting vulnerabilities in NF1 high-grade gliomas
- **Daochun Sun** (Medical College of Wisconsin) is repurposing an asthma drug to enhance plexiform neurofibroma treatment
- **Lei Xu** (Massachusetts General Hospital) is testing an FDA-approved HIF-2 inhibitor for vestibular schwannomas
- **Kimberly Ostrow** (Johns Hopkins) is exploring novel inhibitors to address schwannomatosis-related pain

Other Awards

CTF provides other specialized awards to support projects with specific objectives that might not fit traditional funding mechanisms. These four awards represent an investment of $450,000, one supporting a clinical trial, and three as part of a strategic collaboration with the American Society of Gene & Cell Therapy (ASGCT), designed to bring leading non-NF researchers into the field to accelerate progress in gene therapy approaches for all forms of NF.

- **Bum-Joon Park** (PRG S& TECH INC) is conducting a Phase 1/2 clinical trial of PRG-N-01 and collecting MRI data in *NF2*-SWN patients
- **Lukas Landegger** (Stanford University) is developing AAV-mediated gene therapy to target vestibular schwannoma in *NF2*-SWN patients (in collaboration with ASGCT)
- **Chance Meers** (Columbia University) is harnessing specialized RNA-guided nucleases for targeted site-specific genetic modification in NF (in collaboration with ASGCT)
- **Ngoc Tam Tran** (University of Massachusetts) is analyzing how AAV vectors with special terminal repeats integrate into the genomes of cells for potential gene therapy applications (in collaboration with ASGCT)

Accelerating Treatments

A Strategic Vision:
No Great Idea Dies on the Vine

At the Children's Tumor Foundation, we are driven by a powerful principle: no promising treatment for NF should be held back by structural barriers or lack of resources. The traditional drug development pathway moves too slowly for patients who need treatments. Our strategic approach to accelerating treatments targets the bottlenecks that typically delay bringing promising therapies to patients living with any manifestation of NF1 or SWN, including *NF2*-SWN.

At CTF, we take a proactive approach to drug discovery. We actively scour the pipeline to uncover promising candidates rather than waiting for breakthroughs to emerge naturally.

CTF has created a uniquely efficient pathway from discovery to approved treatment through transformative funding mechanisms, strategic partnerships, and a commitment to removing obstacles in the development pipeline. This integrated ecosystem ensures that when a promising treatment emerges—whether from academic research, pharmaceutical pipelines, or AI-driven discovery—it receives the support needed to advance through critical development stages.

NF Therapeutics Accelerator Fund

In 2024, CTF established the NF Therapeutics Accelerator Fund, a venture philanthropy campaign tailored to deliver breakthroughs in NF treatments. The NF Accelerator Fund addresses the central challenge in NF treatment development: the traditional system isn't built for speed or risk-taking in rare disease spaces. Leveraging CTF's in-house pharmaceutical expertise, this effort creates a pathway that ensures promising treatments reach patients.

This model offers pharmaceutical partners a compelling value proposition—a fast, low-risk testing environment for NF treatments—and provides early-stage biotechs with crucial funding to cross the "valley of death," maximizing the chances of success across multiple therapeutic approaches.

When CTF invests time, expertise, or capital in a drug that eventually becomes available, the Foundation receives a return on that investment, which is then reinvested back into CTF. This creates a sustainable funding cycle that powers future research and drug discovery efforts.

This comprehensive fund includes several integrated components, including CTF's **Preclinical Hub** (testing drugs before they reach patients), **Platform Basket Trials** (studying whether drugs work in patients), and **Strategic Commercial Investments**. Together, these components create a seamless pipeline from discovery to approved therapies.

CTF Preclinical Hub: Investment in *NF2*-SWN Meningioma Model

The CTF Preclinical Hub—a key part of our strategy to speed up treatment development—made significant progress in 2024. Building on the earlier success of CTF's Preclinical Consortium and Synodos initiatives, the Hub creates a network where potential NF treatments can be quickly tested before reaching patients. CTF serves as the central coordinator and will connect partners with emerging drug testing models to ensure that promising therapies are evaluated swiftly before progressing to clinical trials.

This year, the CTF Preclinical Hub made an investment in a team of multi-disciplinary researchers working on *NF2*-SWN at the University of Plymouth's Brain Tumour Research Centre of Excellence. This project addresses a critical gap in *NF2*-SWN research by developing a humanized meningioma mouse model.

"We believe this project could play a vital role in the process, creating a model on which therapies can be tested to ensure they are safe and effective. In the long run, that could ultimately shorten the time it takes for drugs to be validated and used for patient treatment."

— Liyam Laraba, PhD
Research Fellow,
University of Plymouth

This breakthrough enables scientists to study complex interactions between human immune cells and meningioma tumor cells in living systems—accelerating the development pathway for potential immunotherapies and other treatment modalities.

The investment represents a critical step forward in meningioma therapy development, leveraging the University of Plymouth's leadership in brain tumor research and the Children's Tumor Foundation's commitment to accelerating the development of revolutionary treatment options. By addressing the complexities of *NF2*-SWN, the collaboration will improve the odds of success in clinical trials and deliver better treatment options for patients living with these challenging tumors.

Platform and Basket Trials: Revolutionizing Patient Drug Trials

CTF's commitment to accelerating treatments extends into platform clinical trials, uniquely transforming the evaluation of new therapies in patients.

The strategic alliance with **Global Coalition for Adaptive Research (GCAR)** and CTF follows a 3-year, 26-million-euro investment from the Innovative Health Initiative (IHI), resulting in the **EU-PEARL NF1** platform trial. Co-led by CTF and the Erasmus Medical Center in Rotterdam, this trial has reached a pivotal milestone. This year, GCAR, CTF and NF clinical specialists working in collaboration submitted a revised protocol and comprehensive briefing book to the European Medicines Agency (EMA) for formal scientific advice. The EMA has most recently responded favorably to the trial and plans for implementation. The team is now encouraged to move to the next phase of industry engagement and study start-up.

For patients with *NF2*-SWN, the **INTUITT-NF2** trial continues to expand its impact. Following the publication of promising results for brigatinib and other potential treatments in the *New England Journal of Medicine*, highlighted on page 7, the basket trial will continue to explore potential therapies across multiple tumor types to improve results even further in patients with *NF2*-SWN.

"We are excited to work with the Children's Tumor Foundation to build a patient-centric clinical trial that will rapidly and efficiently evaluate multiple investigational therapies for the treatment of NF."

—Meredith Buxton, PhD
CEO & President of the Global Coalition for Adaptive Research

Strategic Commercial Investments: Catalyzing the Next Generation of Therapies

Our investments in commercial enterprises represent a crucial element in our accelerated treatment development strategy. By providing targeted funding and expertise to companies with promising NF technologies, CTF both speeds the development of specific therapies and demonstrates the commercial viability of the NF treatment market—encouraging additional commitments in the field.

In addition to CTF funding toward **NFlection Therapeutics**, highlighted on page 7, the strategic commercial investments below are designed to accelerate the development of treatments for all forms of NF.

CureAge Therapeutics: An NF-Dedicated Biotech

In a historic development, early 2025 saw the official launch of CureAge Therapeutics, a first-of-its-kind biotech company focused on developing curative genetic therapies for NF1. The UK-based company was formed through a strategic collaboration between the Children's Tumor Foundation and **Deep Science Ventures (DSV)**, uniting scientific expertise and venture creation to address one of the most pressing unmet needs in rare disease treatment.

Recognizing the urgent need for next-generation therapies, CTF and DSV identified gene therapy as the most promising path forward and brought together a world-class team to develop a treatment that directly targets the underlying genetic cause of NF1.

CureAge's approach leverages lipid nanoparticles (LNPs) to precisely deliver therapeutic genetic material to Schwann cells, the key cells involved in NF1 tumor growth. With a dual-action strategy, CureAge aims to restore NF1 function and eliminate non-targeted tumor cells, providing a long-term cure for NF1 while developing a scalable platform for related diseases.

The name "CureAge," chosen by NF1 patients and families, represents both courage and the hope for a cure—reflecting the community's determination to push for truly life-changing treatments.

Healx Collaboration: AI-Driven Drug Discovery

The Foundation's strategic support of Healx's NF1 programs continues to yield remarkable results. A significant regulatory milestone was reached when Healx's lead compound, HLX-1502, received Fast Track designation from the FDA for NF1 treatment—a pathway designed to expedite the development and review of drugs addressing serious conditions with unmet medical needs.

HLX-1502 is being evaluated as a potential treatment for NF1 plexiform neurofibromas, with the goal of providing an alternative to existing MEK inhibitors, which have known side effects.

Since partnering with CTF in 2020, Healx has harnessed its cutting-edge AI platform alongside the Foundation's preclinical and clinical expertise to identify new treatments for NF1, demonstrating how targeted investments can speed up the development of next-generation therapies.

Recently, Healx administered the first dose in its Phase 2 trial for HLX-1502—a breakthrough achievement that underscores its trailblazing approach in advancing rare disease treatments and bringing renewed hope to NF patients. CTF is proud to be an integral partner in this journey, contributing our expertise, deep patient insights, and unwavering commitment to accelerating breakthroughs.

"CTF is a long-standing partner of Healx, and this investment underscores their confidence in the potential of Healx's neurofibromatosis program to bring novel treatments to patients with unmet need."

— Tim Guilliams, PhD
Co-founder and CEO of Healx

These strategic investments exemplify CTF's commitment to ensuring that promising treatments reach patients as quickly as possible. By engaging directly in the drug development process—from discovery through clinical testing to commercial development—the Foundation is creating multiple pathways to transformative therapies for the NF community. **Our message to patients and families remains clear: the treatments are out there, and we're uncovering and accelerating them on our timetable, not anyone else's.**

Foundations of Progress

The rapid advancement of NF treatments depends on something far more fundamental than technology or funding alone: the power of human connection. CTF has strategically cultivated a rich, interconnected community of patients, researchers, clinicians, and industry partners who together form the essential foundation upon which all progress rests. By creating cornerstone platforms for collaboration and forums for knowledge exchange, we've established the vital networks that make breakthroughs possible.

Global NF Conference: Where Collaboration Catalyzes Discovery

The 2024 Global NF Conference in Brussels, Belgium brought together 849 researchers and clinicians from 43 countries, cementing its status as the premier scientific gathering in the NF field. This year's attendance included a significant 37% first-time participants, indicating the expanding reach of NF research.

The conference structured its agenda around five focused theme days covering critical areas:

- Gene Therapy Innovations
- Comprehensive Care Approaches
- Schwannomatosis-specific Research
- Novel Therapeutics Development
- AI and Biomarker Applications

With more than 100 speakers, the conference served as the central hub for knowledge exchange and collaboration. The inaugural Young Investigator Day provided critical mentorship to early-career researchers, supporting CTF's strategic goal of expanding and retaining scientific talent in the NF field.

"The community that looks after rare diseases, whether it's scientists, patient communities, or industries, are really the pioneers and heroes of modern medicine."

— Nathalie Moll, Director General of the European Federation of Pharmaceutical Industries (EFPIA)

The conference directly accelerates scientific progress through:

- **Consensus-building** on research priorities and clinical practice standards
- **Cross-disciplinary collaboration** that breeds forward-thinking approaches to complex challenges
- **Rapid dissemination** of unpublished findings that might otherwise take years to reach the wider community
- **Strategic partnerships** formed during specialized satellite meetings and networking events
- **Global harmonization** of research methodologies and clinical trial designs

The endorsement by the European Federation of Pharmaceutical Industries and Associations (EFPIA) Director General provided additional visibility for NF research within the pharmaceutical industry, potentially accelerating industry engagement.

NF Registry: Accelerating Clinical Trials

With over 11,000 participants, the NF Registry stands as the largest patient-entered database of people with NF globally and the only one designed to be available to all interested investigators. In 2024, CTF negotiated a contract to migrate the Registry to the NORD IAMRARE platform, scheduled for launch in June 2025. This strategic move will significantly enhance both patient participation and researcher utility while reducing operational costs.

The NF Registry powers research advancement through:

- **Clinical trial recruitment acceleration**, reducing a major bottleneck in treatment development
- **Demographic insights** that help ensure research benefits all patient populations
- **Pharmaceutical industry engagement**, attracting companies to develop NF therapeutics

Available in multiple languages, the NF Registry continues to expand its global reach and diversity of participants. A striking example of the Registry's impact came through a CTF-funded study on chronic pain in NF1. By recruiting directly through the NF Registry, researchers developed and validated the Neurofibromatosis Pain Module (NFPM), a tool that characterizes the multidimensional nature of NF1 pain, enabling more reliable measurement and smarter treatment decisions.

In partnership with Accenture, CTF developed a pioneering solution within its data warehouse to isolate de-identified registry, clinic, and outreach data, enabling researchers to conduct sophisticated multi-layered analyses that were previously impossible.

Excellence in NF Clinical Care: The NF Clinic Network Designation System

In 2024, the Foundation completed and implemented its groundbreaking NF Clinic Network (NFCN) Clinic Designation System, creating two distinct categories: Comprehensive NF Center and NF Specialty Program. These designations will transform the NF care landscape by establishing clear standards and driving continuous improvement across the network's 70+ NF clinics, which collectively serve approximately 20,000 patients annually.

Network Development Metrics:

- 69 clinics evaluated
- Comprehensive Centers identified: 29 for NF1, 22 for SWN (including *NF2*-SWN)
- Specialty Programs established: 34 for NF1, 16 for SWN (including *NF2*-SWN)

Clinics undergo evaluation through a comprehensive process that examines their NF expertise and patient volume, assessing whether they have the necessary specialized knowledge and sufficient cases to maintain proficiency. The evaluation also looks for a multidisciplinary team approach, commitment to NF education and training, active research participation, clinical trial access, and effective transition planning between pediatric and adult care.

The Designation System accelerates research by:

- **Creating standardized centers of excellence** ideal for multi-site clinical trials and studies
- **Establishing metrics** for clinical care quality that inform trial site selection
- **Building integrated research-clinical teams** that rapidly translate findings into practice
- **Identifying high-volume centers** capable of recruiting patients with specific NF manifestations
- **Encouraging comprehensive data collection** that supports retrospective and prospective studies

The system's separate designations for NF1 and SWN expertise ensure that patients with different forms of NF can find appropriate specialized care, while also facilitating targeted research recruitment.

The University of Florida Health Neurofibromatosis Clinic in Jacksonville joined the network in 2024, further expanding the Foundation's research and clinical care capabilities.

Patient Engagement:
Bringing Patient Voices to Regulators

In May 2024, CTF orchestrated a critical FDA Listening Session focused on cutaneous neurofibromas (cNF). This strategic engagement brought together:

- **6 patient representatives** sharing firsthand experiences
- **40+ FDA staff** participating
- **14 different FDA divisions** represented
- **4 FDA Centers** engaged

This session educated regulators about the significant impact of cNFs on quality of life, challenging the historical view of these tumors as merely "cosmetic" issues. By connecting patients directly with decision-makers, CTF is paving the way for more informed regulatory processes around emerging cNF treatments—a top priority for the NF community.

"Cutaneous neurofibromas can significantly impact an individual's physical and emotional well-being, and it's offensive to dismiss them as merely cosmetic concerns. Dismissing these concerns fails to recognize the profound impact it has on individuals."

— NF Patient Representative
as spoken at the FDA Listening Session

Through these cornerstone programs, CTF creates crucial meeting points where ideas, insights, and innovations flow freely. When researchers share their latest findings at the conference, when patients contribute their experiences to the Registry, when clinicians apply cutting-edge approaches in their practice, they each add to a powerful shared resource that speeds progress. By bringing all these voices to the same table, **CTF ensures that no promising idea is overlooked and no patient need goes unaddressed on our journey to end NF.**

Everything we do is about one goal: getting treatments to patients faster. And none of it happens without you. Thank you for being part of this movement, today, and every day.

This kind of progress doesn't happen on its own. Medical research foundations like CTF aren't just funders, we're catalysts. We de-risk scientific discoveries, bridge gaps, and create a clear path to the clinic. We bring biotech, pharma, academia, and patient communities together, ensuring that the best scientific ideas don't get stalled–they make it to the people who need them.

The Children's Tumor Foundation has evolved; we are laser focused on drug discovery and development on our path to a cure for NF. Every dollar invested moves a drug forward, speeds up trials, and brings treatments to patients faster.

This is the CTF model. And it's working.

CTF Impact by the Numbers

Bold Leadership

- **47 years** of funding groundbreaking NF research
- **2 FDA-approved drugs for NF1**, including the first-ever for adults
- **First-ever platform trials** for NF (INTUITT for *NF2*-SWN and EU-PEARL for NF1)
- **68 clinical trials in progress**, triple the number from a decade ago
- **20+ pharmaceutical and biotech companies** now engaged in NF research
- **Strategic commercial investments** in targeted gene therapy and AI-driven drug discovery
- **800+ research projects** funded throughout CTF's history

2024 Research Investment

- **21 new research investigations** funded across all forms of NF:
  - 8 Young Investigator Awards spanning NF1, *NF2*-SWN, and *LZTR1*-SWN
  - 5 Drug Discovery Initiative Awards targeting critical manifestations
  - 4 Clinical Research Awards advancing patient-centered studies
  - 4 Other Awards to advance clinical trial and gene therapy studies
- **Preclinical Hub initiative** awarded to develop a *NF2*-SWN meningioma model
- ***NF2*-SWN gene therapy investment** is paving the way for future therapies
- **Schwannomatosis research funding** at Sylvester Comprehensive Cancer Center

Research Engagement

Global NF Conference:

- 849 participants from 43 countries
- 37% first-time attendees
- 288 abstract submissions
- 220 poster presentations
- 100+ speakers across 5 specialized thematic days

NF Registry:

- 11,000+ registered participants
- Migration to enhanced NORD IAMRARE platform underway
- Critical resource for trial recruitment and natural history studies

Clinical Impact

NF Clinic Network Designation System implemented:

- 69 clinics evaluated
- 29 Comprehensive Centers for NF1
- 22 Comprehensive Centers for SWN
- 34 NF Specialty Programs for NF1
- 16 NF Specialty Programs for SWN

- **20,000 patients** served annually
- **25 clinics** participating in the Jeffrey Owen Hanson OPG study
- **271 patients** enrolled in multi-institutional OPG study

Strategic Partnerships & Collaborations

- **American Airlines** data analytics collaboration
- **Deep Science Ventures** partnership launching CureAge Therapeutics
- **Dolphins Challenge Cancer** co-funding schwannomatosis research
- **Global Coalition for Adaptive Research** platform trial implementation
- **SpringWorks Therapeutics** bringing mirdametinib to approval
- **NFlection Therapeutics** advancing Phase 3 development of NFX-179 Gel
- **Healx obtaining FDA Fast Track designation** for AI-discovered NF1 drug
- **FDA listening session** on cutaneous neurofibromas engaging 40+ staff across 14 divisions
- **CureNFwithJack** collaboration on MPNST Biomarker Development

Thank you for partnering with us to end NF.

CHILDREN'S TUMOR FOUNDATION
ENDING NF THROUGH RESEARCH

Board of Directors

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