Bringing Brigatinib to Neurofibromatosis Type-2 Patients: From Promising Potential to Platform Clinical Trial

Children’s Tumor Foundation and Takeda Pharmaceuticals Launch INTUITT for NF2 in Partnership with 6 Leading Medical Centers

NEW YORK (PRWEB) May 29, 2020 -- The Children’s Tumor Foundation (CTF) announced today a significant advancement in care for neurofibromatosis type 2 patients with the launch of a new clinical trial called INTUITT-NF2, an innovative platform trial which will evaluate multiple treatments simultaneously. This initiative is a result of the landmark work of CTF’s visionary Synodos for NF2 research collaborative, its NF2 Accelerator Initiative, an investment from Takeda Pharmaceuticals, the participation of scientists at the National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health (NIH), and the vital Synodos NF2 leadership from Massachusetts General Hospital (MGH), Johns Hopkins University (JHU) and Indiana University (IU). The Principal Investigator of INTUITT NF2 is Dr Plotkin from MGH and the five additional participating centers are Johns Hopkins University (JHU), New York University (NYU), University of California at Los Angeles (UCLA), the Mayo Clinic in Minnesota (Mayo), and the University of Miami (UM). This alliance across the academic, pharma, and patient landscapes has shortened the time from initial research to active trial, thereby bringing promising treatment options to patients who need them.

The name INTUITT-NF2 stands for ‘Innovative Trial for Understanding the Impact of Targeted Therapies in NF2’, and its innovation is in responding to – and acting against – specific traits unique to NF2 patients. Neurofibromatosis causes tumors to grow on nerves throughout the body, with most NF2 patients affected by vestibular schwannomas on the eighth cranial nerve, which carries sound and balance information to the brain. NF2 affects 1 in 25,000 people of all populations equally, and in addition to schwannomas can develop meningiomas and ependymomas, with patients suffering hearing loss, severe balance problems, facial weakness/paralysis, and debilitating seizures, among other serious conditions. The INTUITT-NF2 trial will enroll patients with progressive tumors of any type – schwannoma, meningioma, or ependymoma – to allow for the simultaneous study of the various tumor types, rather than one tumor type alone. This approach will accelerate the information gathering and results analysis processes.

This milestone development in NF2 research and care is the result of insights that came out of the Foundation’s Synodos for NF2 effort, which launched in 2014 and in collaboration with NCATS identified brigatinib as a promising drug for NF2 patients. The Synodos project brought together a multidisciplinary team of scientists from 12 world-class labs at academic and medical centers of excellence to address the confounding problem patients and researchers alike faced in that research results appeared to contradict each other – with some work showing positive results and others negative results. This siloed approach to the disease was hampering progress, and all agreed that an “audacious new way” was needed. Patients heeded that call and provided funding to the Children’s Tumor Foundation to launch a new, and for its time, a somewhat radical approach to the disease. In this model, called Synodos, researchers would work together on a Manhattan-project style approach to the disease, and they would share data and results in real-time. The funders behind that approach (lead funders the Galloway family, Carol Harrison Kalagher, the Thoms family) also ensured that patients be included in the research and clinical meetings that would define these methodologies.

The multidisciplinary Synodos team launched its work (Synodos stands for “on the same path, together”), and established the first-ever NF2 preclinical drug pipeline with cell and animal models connected to a sequencing enterprise so as to better understand the biology behind drug response and non-response. This information was
shared among all members of the group for phase one of the project, and eventually made public available to any researcher through the establishment of dataportal.org.

“The launch of the Synodos project was driven by our belief that by bringing all stakeholders together we could solve the medical problems that seemingly had no answers,” said Annette Bakker, PhD, President of the Children’s Tumor Foundation. “The patients and the medical and research experts all shared the same passion and purpose – to solve the mysteries of NF2 – but traditional approaches were getting in the way of needed solutions. Thanks to the persistence of the patients and the courageousness of the researchers, the group revealed new insights into NF2 biology and established a platform from which could spring high-potential therapies not just for NF2 but other types of NF and even other types of disease.”

With a guarantee of shared data and a certainty of collaboration in hand, the Synodos team found that initial results did not meet efficacy criteria, but that new and vast insights into NF2 biology had been generated. Scientists from NCATS, led by Marc Ferrer, PhD, offered high throughput capabilities to the Synodos team to potentially uncover new drug opportunities. In that process, Takeda’s Brigatinib (an approved drug for use in non-small cell lung cancer unrelated to NF) was discovered to show robust efficacy in both vestibular schwannomas and in meningiomas. This breakthrough meant that while more understanding was still needed to identify the exact mechanisms behind this finding, it appeared that Brigatinib shrinks NF2 tumors.

“This finding was proof positive that merging innovations from the private sector together with sophisticated tools within the public sector can increase our understanding of disease,” said Dr. Marc Ferrer of NCATS.

Leading the INTUITT-NF2 trial are Scott Plotkin, MD, PhD of Massachusetts General Hospital and Jaishri Blakely, MD, of Johns Hopkins University. The goal of this new trial is to rapidly and efficiently screen multiple therapies simultaneously so as to enable faster approval studies that have the highest indication for success. The U.S. Food and Drug Administration (FDA) recently approved the initiation of this trial, and details on patient recruitment will be announced soon.

The INTUITT-NF2 trial will expand the possibilities for NF2 care in multiple ways. In a traditional clinical trial, patients are enrolled to test one drug treatment that will measure response for one specific tumor type (even if patients have more than one type in their bodies, as is often the case for NF2 patients). If that tumor type does not respond to the treatment, then the trial potentially fails, and patients wait as the development process has to restart again, perhaps with a different drug, or with a new process that looks at a different tumor type. The “one tumor type, one drug at a time” approach slows down the development of treatments for NF2.

By contrast, the INTUITT-NF2 trial will enroll patients with schwannomas, meningiomas, and ependymomas. For a given drug, the study will determine whether any one (or more) tumor types respond better than the others. This novel approach provides the opportunity to find active drugs for tumor types that have never been eligible for clinical trials previously. INTUITT-NF2 will also study multiple drugs over time as they become available (the study is beginning with brigatinib only). In this model, a patient whose tumors grows on brigatinib could be eligible to receive treatment with another drug within a short period of time.

Dr. Scott Plotkin of MGH, one of the initial Synodos leaders, has spearheaded the upcoming INTUITT basket trial, which should start seeing its first patients enrolled later this month.

“This new trial for NF2 patients will realize two principal objectives on our way to the development of approved treatments for NF2,” said Dr. Plotkin. “First, by focusing on all tumor types within patients, we are
able to expand patient eligibility for the trial, meaning we will increase our knowledge pool on how these treatments perform in patients. And secondly, the trial design allows for the addition of drugs to be tested rather quickly, again increasing what we know about their real-life impact on NF2 patients.”

The Principal Investigators of the trial are Scott Plotkin of MGH and Jaishri Blakeley of JHU. Participating clinicians include Jeffrey Allen, MD (NYU); Leia Ngiemphu, MD (UCLA); Dusica Babovic-Vuksanovic (Mayo), and Christine Dinh, MD (UMiami).

Both the Children’s Tumor Foundation (CTF) and Takeda Pharmaceuticals are supporting the financing of the INTUITT-NF2 trial. CTF’s investment is through its NF2 Accelerator Initiative, with lead funding from the Thoms Fund and KBF Canada.

To learn about NF2 research and the progress being made against neurofibromatosis, please visit ctf.org.

To learn more about the INTUITT-NF2 trial, please visit https://clinicaltrials.gov/ct2/show/NCT04374305.

About Children’s Tumor Foundation
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. For more information, please visit www.ctf.org.

About Takeda Pharmaceutical Company Limited
Takeda Pharmaceutical Company Limited is a global, values-based, R&D-driven biopharmaceutical leader headquartered in Japan, committed to bringing Better Health and a Brighter Future to patients by translating science into highly-innovative medicines. Takeda focuses its R&D efforts on four therapeutic areas: Oncology, Rare Diseases, Neuroscience, and Gastroenterology (GI). We also make targeted R&D investments in Plasma-Derived Therapies and Vaccines. We are focusing on developing highly innovative medicines that contribute to making a difference in people's lives by advancing the frontier of new treatment options and leveraging our enhanced collaborative R&D engine and capabilities to create a robust, modality-diverse pipeline. Our employees are committed to improving quality of life for patients and to working with our partners in health care in approximately 80 countries. For more information, visit takeda.com.
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