ROSAMUND STONE ZANDER and HANSJOERG WYSS TRANSLATIONAL NEUROSCIENCE CENTER

Boston Children's Hospital

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Rosamund Stone Zander and Hansjoerg Wyss Translational Neuroscience Center (TNC) *Annual Progress Report (2025)*

Five years, infinite impact

In the last five years, the Rosamund Stone Zander and Hansjoerg Wyss (Zander Wyss) TNC's pioneering scientists and expert clinicians have advanced translational research, mentored rising stars in neuroscience, collaborated with patient advocacy groups and industry partners, secured millions of dollars in additional funding and, importantly, given families answers and hope.

Now we stand at the cusp of the future—a time when all children with brain disorders can experience a brighter youth and a healthier adulthood. Reflecting on how we arrived at this momentous juncture, this year's annual report highlights some of what the Zander Wyss TNC achieved between 2021 and 2025.

Catalyzing a wave of support

Spotlight: Aligning Research to Impact Autism (ARIA)

In late 2025, Boston Children's received a $7.5 million grant for Dr. Sahin and the Zander Wyss TNC to help lead and coordinate the Innovative Medicine and Precision Approaches to Clinical Trials (IMPACT) Network—a multisite clinical trial infrastructure focusing on rapid therapeutic development for neurodevelopmental disorders (NDDs). As a co-leader of the network's Clinical Coordinating Core, the Zander Wyss TNC will provide scientific supervision and clinical research support to sites around the world conducting clinical trials for novel treatments for NDDs.

Boston Children's selection as a lead hub for this major clinical research initiative is a testament to the hospital's decades-long commitment to, investment in, and leadership of NDD research and clinical care across the nation and globally.

Expanding clinical research studies

In 2021, the Zander Wyss TNC supported 30 active clinical research studies—which grew to 80 ongoing trials in 2025. Roz's generosity facilitated the launch of an astounding **109 total studies** conducted over five years.

This research includes drug trials for rare conditions like CDKL5 deficiency disorder and Rett syndrome—which can significantly impact a child's development—as well as natural history studies that provide vital information about poorly understood conditions. More than 30 rare and ultra-rare neurodevelopmental disorders are now being studied by clinical researchers at the Zander Wyss TNC.

Spotlight: Clinical Research Unit

In 2023 Boston Children's gave the Zander Wyss TNC space to open a dedicated Clinical Research Unit (CRU) at 2 Brookline Place—the site of the hospital's Brain, Mind, & Behavior Center (BMBC). This space allows for collaboration across many BMBC divisions and programs, including genetics and genomics, developmental medicine, behavioral neurology, the Autism Spectrum Center, and the Department of Psychiatry. The CRU streamlines research operations focused on neurodevelopmental disorders—from pharmaceutical trials and device studies to behavioral intervention trials and natural history studies—at no cost to those who partner with the Zander Wyss TNC.

The 2 Brookline Place building was designed with input from expert clinicians and researchers who specialize in neurodevelopmental disorders to optimize accessibility and comfort for patients and families, with features like separate, quiet waiting rooms and autism-friendly lighting. The CRU includes clinical research space with four outpatient study visit rooms, dedicated research nursing and investigational drug pharmacy services, child life specialists to provide behavioral support, and a research laboratory for sample processing and storage. To date, 28 principal investigators have used the CRU for their clinical research study visits.

Recruiting stellar faculty

The TNC has hired six faculty members to date, all leaders within the TNC's scientific core facilities and early-career investigators making breakthrough discoveries in neurodevelopment and neurodegeneration.

We're thrilled to share that the center, in partnership with the Department of Psychiatry, recently recruited **Audrey Thurm, PhD**, a clinical scientist and a child clinical psychologist focused on analyzing phenotypes for neurogenetic conditions and harmonizing data across natural history and clinical trial studies. Dr. Thurm leverages her expertise in understanding developmental trajectories of neurodevelopmental disorders, particularly in those individuals who are lower functioning or nonverbal, to study outcome measures for use in clinical trials. Of course, drug and therapy trials cannot be conducted without validated outcome measures that prove the medication's effectiveness, so Dr. Thurm's work is crucial to our ability to accelerate the pace of translation and promote inclusion of the broad spectrum of affected individuals in clinical trials.

Spotlight: Caring for kids with Chopra-Amiel-Gordon syndrome (CAGS)

At Boston Children's, we see every day how research breakthroughs directly improve care for children and families—and how what we learn from them drives the next discoveries. Take, for instance, Ronan, who first started experiencing seizures when he was 2 years old. His pediatrician initially thought the seizures were caused by fever—hardly an uncommon occurrence in toddlers—and that he would eventually outgrow them. However, when Ronan's seizures continued into kindergarten, a local neurologist suggested genetic testing to find the cause of his epilepsy.

The tests revealed that Ronan has CAGS, which was first described by the Zander Wyss TNC's **Maya Chopra, MBBS**, and her colleagues only two years prior. "It was such fortuitous timing," says Ronan's mother, Caitlin. "If we had done the testing in 2020, when his seizures started, we would have never known he had CAGS."

Still, with CAGS being so newly described and extremely rare, most clinicians have never heard of the complex disorder. Even Ronan's beloved neurologist had never cared for anyone with the condition. After he recommended Boston Children's as the best place to seek specialized CAGS care, Caitlin emailed Dr. Chopra. She responded within hours to talk to the family about what is known about CAGS and about the natural history study she leads at the Zander Wyss TNC.

In January 2025, the family traveled from Washington, D.C., to the Zander Wyss TNC so Ronan could participate in the study. Caitlin tears up while describing their experience. "As soon as we walked in, I felt so safe. Ronan wasn't just some patient with an ultra-rare genetic condition. We were surrounded by people who know what CAGS is, getting expert care at a place where Ronan is treated like a kid."

Publishing breakthroughs in leading journals

Disseminating knowledge through peer-reviewed publications ensures that discoveries made by Zander Wyss TNC investigators advance the field of neuroscience, inform the work of other researchers, and accelerate answers for patients. These publications also help our faculty secure funding from federal sources and private foundations. Since 2021, Zander Wyss TNC researchers have published **170 articles**, many of which appear in prestigious journals such as *Science, Annals of Neurology*, *Cell Reports*, and the specialized journals within the *Nature* portfolio.

Spotlight: Advancements in CRISPR gene editing

Zander Wyss TNC faculty member **Mandana Arbab, PhD**, focuses on using CRISPR gene editing to interrupt trinucleotide repeats (TNR), that is, sequences of three nucleotides repeated consecutively in DNA or RNA segments. Limited repeats are common and safe, but having too many repeats causes genetic disorders like Huntington's disease and Friedreich's ataxia in adults, and, in children, fragile X syndrome.

Earlier this year, a paper co-written by Dr. Arbab and published in the highly regarded journal *Nature Genetics* demonstrates that using CRISPR base editing technology to introduce small, random interruptions in TNR sequences can stabilize them and prevent further expansion. This stabilization was shown in both patient cell lines and mouse models.

What makes this approach particularly promising is that multiple conditions are caused by the same TNR sequences in different parts of the genome. In the years ahead, if the therapy proves effective in just one of these conditions, it could lead to a universal treatment for related disorders.

As a destination for experts studying complex diseases, Boston Children's is home to numerous scientists like Dr. Arbab who can focus on a particular disorder while

also zooming out to see a spectrum of connected conditions. This is how we drive breakthroughs.

Nurturing young investigators

Supporting the next generation of leaders through fellowships and pilot grants is critical to the success of the TNC. Today, three of the Rosamund Stone Zander fellows continue to investigate novel therapeutics for neurodevelopmental disorders at Boston Children's while inaugural fellow Kristina Johnson, PhD, is an assistant professor at Northeastern University and principal investigator in Northeastern's Neurodevelopmental Dynamics Lab.

At the same time, recipients of the Zander Wyss TNC's pilot grants are making important strides toward new treatments for neurodevelopmental conditions—progress that is capturing the interest of other funders and philanthropists. For example, 2021 pilot grant awardee **Jeffrey R. Holt, PhD**, received pivotal support from the 2024 Boston Investment Conference (an annual fundraiser for research at Boston Children's) to further his work on a gene therapy for hearing loss, and in 2025 he was elected as a member of the National Academy of Sciences. And 2024 awardee **Don Kong, PhD**, is now leading a pediatric brain development research initiative at Boston Children's that was made possible by philanthropy.