December 30, 2020

Dear Friends and Family,

Last year at this time we were contemplating the promise that a new year brings and to say 2020 presented obstacles we couldn't anticipate is redundant, yet we found the silver lining in opportunities lost to regroup and refocus on our mission. This year we find ourselves contemplating our future in a much different light, asking propelling questions and making tough decisions. Given the constraints that most rare disease communities face, how can we best use limited resources? How can we partner with others to realize timely progress? How can newfound opportunities in telemedicine and video-based applications afford new potential directions for rare disease communities to connect or share data with scientists?

Reflecting on past years, it is remarkable how fast science is moving. Genetic therapies are under early development for CDKL5 Deficiency Disorder. We must prepare for any future we are afforded to trial disease-modifying treatments. To be ready for clinical trials for any medicines that target CDKL5 Deficiency Disorder at the genetic or symptom level, IFCR has made a substantial investment in clinical trial readiness and outcome measure development. This early funding prevented delays in progress for our International CDKL5 Clinical Research Network (ICCRN) and enabled the resubmission of the Network's recently-funded NIH U01 award (work to start in 2021).

2020 Highlights

- Awarded $500,000 in research support.
- A notable number of CDD-related research papers were published.
- Added four professionals to our Medical and Scientific Advisory Board.
- Hosted our first virtual Family Education and Awareness Conference, "Destination: CURE," in a series of pre-recorded and live, interactive educational CDKL5 webinars.
- Released the "Voice of the Patient" Report summarizing the 2019 Patient-focused Drug Development meeting.
- Received ICD-10 designation for CDKL5 Deficiency Disorder.
- Connect CDKL5 captured over **350 patients** from **30 countries**, including **70 males**
- Partnered to launch the CDKL5 Registry Alliance, including these three efforts:
    - **Connect CDKL5:** an International Patient Platform built by IFCR to develop a comprehensive collection of CDKL5 Deficiency patients worldwide. Notably, Connect CDKL5 gives patients reluctant or unable to participate in other research

registries a voice in the research community that makes no demand to participate in research.

- **International CDKL5 Disorder Database (ICDD)**: is an IFCR-sponsored natural history database collecting parent-reported and genetic data founded in 2012 by Drs. Helen Leonard and Jenny Downs at the Telethon Kids Institute. The ICDD and US-based Centers of Excellence integrated efforts as the ICCRN in 2020. More than **330 patients** from more than **40 countries** are registered to the ICDD database.
- **CDKL5 Registry**: The CDKL5 registry collects data for research and pharmaceutical development. The CDKL5 Registry is a joint effort funded and supported by the LouLou Foundation and the Orphan Disease Center at the University of Pennsylvania's Perelman School of Medicine.

FAMILY SUPPORT & RESOURCES

This year, we've created several supportive and educational resources for CDKL5 families. Whether they are newly diagnosed or have been living with CDKL5 Deficiency Disorder for years, there are resources to support daily living. Do you have an idea for new resources to include in our library in 2021? Send us an email at ifcr@cdkl5.com! We have sneak peeks of what is coming and would love to hear what interests you most.

"Destination: CURE" Family Education Conference Recap (thank you to our sponsors):

- Quality of Life & Living Well at Home
- A Deeper Dive into CDKL5 Genetics
- Hot topics: Research update, treatments, and covid19
- How come there are so many databases?
- Exploring variation in the clinical presentation of CDD
- What's the deal with all the consent forms? Learn about ICCRN & the current clinical research landscape
- Optimizing Existing Epilepsy Treatments
- Gastrointestinal Concerns in CDKL5 Deficiency Disorder
- Sleep and CDKL5 Deficiency Disorder
- Therapeutic Night-time Positioning

IFCR continued support of our CDKL5 Centers of Excellence: we take pride in funding eight COEs across the US that (1) deliver multidisciplinary care to CDD patients, (2) collaboratively participate in uniform data collection via the ICCRN, and (3) openly share data with other data repositories and stakeholders (after a reasonable data embargo for publication).

UPCOMING RESOURCES IN 2021

Patient Advocacy Tools for Accessible Science:

- **CDKL5 Roundtable** is a web-based resource written by scientists for the nonscientist to understand the research goals, general approach, and results. There is no RIGHT direction to take the commentary, but we encourage critical analysis of the science that hopefully provokes new ideas *while maintaining* the patient community's expectations. Researchers will explain CDKL5 science in plain language and address topics such as (1) strengths and weaknesses of a manuscript, (2) what questions remain unanswered to establish proof-of-principle, (3) what additional work remains along the bench-to-bedside pipeline, or (4) what future avenues deserve investigation given such results. Launching in 2021, a

sneak peek of posts includes a review of this paper, CDKL5 mRNA present within single neurons across the entire cortex of the mouse brain and, this paper, The Role of NMDA Receptors in ASD-like Traits of CDD.

- **CDKL5 Town Halls** will continue the tradition of the virtual, interactive program held during the "Destination: CURE" virtual conference to provide families an opportunity to engage scientists and clinicians about their work. Experts will review current science and recent progress in the field, and questions will be welcome. Early topics may include a review of video-based motor assessments and how to participate in studies and using animal models of CDD to study the pathogenesis of CDD (how does it cause disease), phenotypes (how does disease present), and types of gene therapy development.

- **Family Support Representative (FSR) Program Relaunch**
  1. **1:1 peer support:** FSR volunteers introduce new community member to IFCR, offer support, provide useful resources to other CDKL5 families, and help them register for Connect CDKL5 (without any pressure to fundraise for IFCR)
  2. **Outreach Goals:** Every month, FSR volunteers contact community members in their geographic area. Periodically, FSR volunteers reach out to medical practices to inform them about IFCR.
  3. **Family Surveys:** Check in with the families periodically to get feedback on the FSR program and other resources IFCR could provide families.

IFCR recognizes every one of our fierce, supportive, and committed families who lead the way in the world of rare disease. As a family-led organization, we rely on this small but mighty growing community of international families to drive our mission forward. Another year has come and gone. Despite the changes and challenges that this year brought for many, the IFCR community continued to experience exponential growth thanks to people like YOU!

It takes a TEAM to move the needle and ours is filled with wonderful scientists, clinicians, advocacy partners, industry partners, and impacted families, and we are so grateful for all that you do for the IFCR community! Take some time to reflect on the remarkable progress we've made together in 2020 despite Covid-19. Thanks to you, we're more motivated than ever and approach 2021 with excitement in pursuit of treatments and, ultimately, a cure for CDKL5.

On behalf of the IFCR Board of Directors,

Heidi Grabenstatter, PhD, Director of Science