

ANNUAL REPORT 2021



FROM OUR PRESIDENT



CHARLENE SON RIGBY
PRESIDENT & MOM

We are excited to share our first annual report with you. Despite all the global challenges wrought by the pandemic, research on STXBP1 disorders has advanced. The STXBP1 Foundation has been at the forefront, pushing forward research and collaboration to accelerate meaningful therapies for our STXBP1 community. We start this report with our 2021 goals and then share key updates on our and our community's efforts. In 2021, we significantly increased our funding for research, launched a clinical trial readiness initiative, and worked to strengthen and support our community. With several pharmaceutical and academic drug development programs underway, this work is time critical. Further, I am delighted to welcome our new scientific director, James Goss, PhD who will help to further propel our efforts in 2022.

Thank you for your support this year. We are enthusiastic about our achievements and progress in 2021, but our patients and families have an urgent need for path altering treatments, so we know we must go faster. Onward to 2022!

With Hope and Urgency,

A handwritten signature in black ink that reads "Charlene Son Rigby". The signature is fluid and cursive.

Charlene Son Rigby
President & Co-Founder

- Create awareness in the disorders associated with STXBP1 mutations
- Fund and Drive Research to accelerate discovery of a cure
- Provide families with tools to help them understand the disease & how to get involved
- Advocate to improve early detection
- Foster activism to help change policies in favor of orphaned diseases
- Improve the lives of our STXBP1 Family

OUR MISSION



2021 GOALS



- Make significant progress on therapy development and clinical trial readiness
- Raise \$2M by 2022 to fund our research priorities
- Build Community
- Create Ongoing Awareness to Support Research Engagement and Community Development
- Maintain operational transparency

2021 HIGHLIGHTS

With your support, we are advancing research to accelerate therapies. We are also building community and supporting our families on this challenging journey.

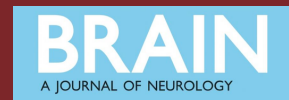
1 >\$500K in Grants and Sponsored Research funding



2 First clinical trial launched for STXBP1, for 4-phenylbutyrate



3 Landmark 534 patient study published in prestigious journal, Brain



4 Hired new Scientific Director, James Goss, PhD



5 250+ participants and fundraisers moving for the Annual STXBP1 Move to Cure



6 New clinic funded at Children's Colorado



7 Study with Rarebase funded to screen all FDA-approved drugs in human neurons



8 3 new studies for Clinical Trial Readiness initiated:
• Citizen Natural History for Electronic Medical Records
• Disease Concept Model for STXBP1
• ORCA study for Communication



9 55 Rare Bears gifted to STXBP1 kids through partnership with Rare Science



10 15 stem cell lines for STXBP1 patients being generated for research through partnership with Simons Searchlight



RESEARCH NEWS

Scientific research is core to accelerating therapies and one day a cure for STXBP1 disorders.



CLINICAL TRIAL FOR 4-PHENYLBUTYRATE

The first clinical trial with a therapy targeting the STXBP1 protein launched in February 2021!

We are thankful to Jacqueline Burre, PhD and Zach Grinspan, MD, MS and their teams at Weill Cornell, for their work that started in the lab to identify 4-phenylbutyrate through to this clinical trial.

4-phenylbutyrate is an FDA-approved drug for urea cycle disorders. It could also help STXBP1 patients. In this trial, 5 patients have completed the trial, with a total of 10 patients to be enrolled.

This clinical trial has been funded by grants from the ODC's Million Dollar Bike Ride - Lulu's Crew Team STXBP1, and Clara Inspired. In addition, the STXBP1 Foundation and Clara Inspired are providing a Patient Assistance Fund to cover unreimbursed medical and travel expenses.

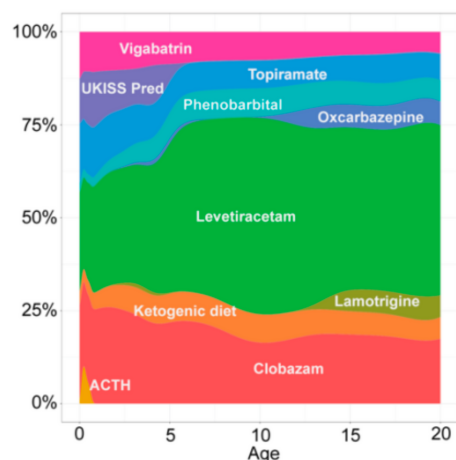


PUBLICATIONS

Undeterred by the pandemic, dedicated scientists continued to advance STXBP1 research. Two key publications in 2021:

- 534 STXBP1 patient study that included patients from across the world including Italy, China, Germany, Netherlands, Belgium, Denmark, UK, Brazil and the US. *Xian et al 2021*
- Identification of GABAergic neurons as responsible for much broader and severe STXBP1 disorder symptoms in mice, though glutamatergic neurons also contribute to symptoms. *Joo et al 2021 (preprint)*

B Distribution of ASM prescriptions



Xian et al 2021

OVER \$500K IN FUNDING FOR RESEARCH IN 2021

The STXBP1 Foundation works with multiple collaborators and stakeholders to support research to accelerate development of therapies for our patient community. We are thrilled to list these recipients of the grants and research funding awards that deliver on our mission to fund and drive research that will accelerate the discovery of a cure for STXBP1 disorders. Over \$500K in funding has been awarded in 2021!

RECIPIENT	FUNDING	PROJECT DESCRIPTION
Ciitizen	\$52,500	Electronic Medical Record Study
Rarebase	\$150,000	Screen full FDA approved library in iPSCs
Columbia University <i>Drs. Frankel & Makinson</i>	\$89,400	Mouse & organoid assays
Colorado Children's <i>Dr. Scott Demarest</i>	\$20,000	Neurogenetics Multidisciplinary Clinic
Children's Hospital of Philadelphia	\$50,000	STXBP1 Disease Concept Model
U. Pennsylvania <i>Dr. Elizabeth Heller</i>	\$154,753	Regulation of Gene Expression of STXBP1

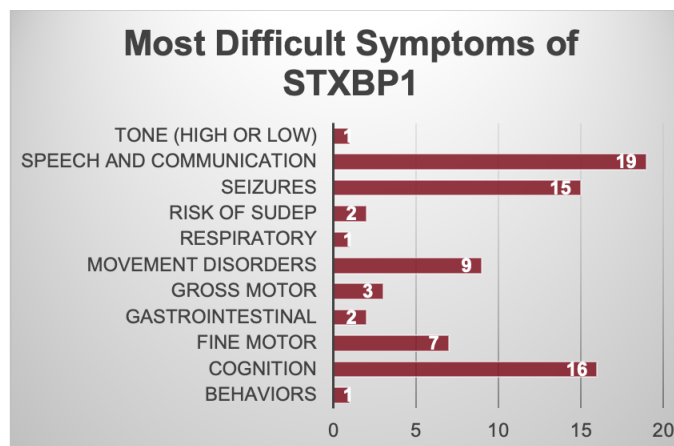
In addition, the following researchers have been awarded grants through the Orphan Disease Center Million Dollar Bike Ride Program from Lulu's Crew Team STXBP1.

RECIPIENT	FUNDING	PROJECT DESCRIPTION
Baylor <i>Dr. Jimmy Holder</i>	\$71,658	Genetic Modifiers of STXBP1
Columbia University <i>Dr. Chris Makinson</i>	\$71,658	Organoid Model Development

Learn more about all of these projects [at our website](#).

CLINICAL TRIAL READINESS

At the start of 2021, we kicked off a Clinical Trial Readiness initiative. We are excited that STXBP1 research is expanding from basic and translational research to clinical research. Multiple pharmaceutical and biotech companies are developing precision therapies for STXBP1 disorders. We urgently need to develop clinical trial readiness to maximize the likelihood of successful clinical trials. Here we highlight several of the foundation's Clinical Trial Readiness initiatives.



STXBP1 Summit+ Post-Event Survey Sept 2021

SCALES & ENDPOINTS MEETING

The STXBP1 Foundation convened a research meeting in January 2021 to initiate a discussion and collaboration on developing endpoints in addition to seizures, so we can capture other outcomes that are also important to our families (see chart above). These endpoints would be used in natural history studies and clinical trials.



ELECTRONIC MEDICAL RECORD STUDY

STXBP1 Foundation is sponsoring a [natural history study with Ciitizen](#). In the study, medical record data is being collected for 150 STXBP1 patients across hospitals and medical providers. This will help build a more comprehensive understanding of STXBP1 symptoms and progression, or changes over time.



ORCA COMMUNICATION MEASURE

Communication challenges have been consistently identified by our families as a top concern. Traditional measures of communication often focus on verbal communication, which often don't allow us to accurately measure communication skills of our children. STXBP1 Foundation is working with Duke and COMBINEDBrain to adapt the Observer-Reported Communication Ability (ORCA) measure for potential use in clinical trials. Duke has been awarded an FDA grant to [expand the ORCA scale to STXBP1](#) and 13 other disorders.



COLORADO CHILDREN'S NEUROGENETICS CLINIC

STXBP1 Foundation is launching a [Neurogenetics Multidisciplinary Clinic](#) at the Children's Hospital Colorado in partnership with three other rare disease organizations. Dr. Scott Demarest is the Principal Investigator. Through this clinic, we aim to expand clinical expertise for STXBP1 to support better clinical care for STXBP1 patients, and to prepare for clinical trials.

COMMUNITY

As we close out 2021, we are even more dedicated (or committed) to strengthening and supporting our community (to stick with your intro note). Together, we will continue to move mountains and lead the charge to a cure.



STXBP1 SUMMIT+ FAMILY MEETING

The STXBP1 Summit+ Family Meeting was held 17 - 19 September. With over 400 registrants, this virtual meeting brought researchers, clinicians, and industry partners together with our family community. Topics included research and therapy development updates, transition to adulthood, and advocacy. The agenda included our first research update in German given by Dr. Steffen Syrbe from University of Heidelberg.

To make the most of the virtual setting, we kicked off the event with a pajama zoom party with headline performer STXBP1 dad Casey Baum, and we introduced regional and affinity group lounges to facilitate connections virtually.

MOVE TO CURE

The 5th Annual Move To Cure STXBP1 Disorders event took place 25 - 26 September. We challenged the community to move 9 miles - whether it was 9 miles among 9 friends, or one person running 3 miles 3 times or someone hiking a 9 mile trail! The purpose of this challenge is to raise awareness of STXBP1 Disorders, fundraise for STXBP1 research, and bring the community “together” for an important cause and some fun!

This year, we raised over \$80,000 for research, and 250+ people around the world participated.



COMMUNITY



REGIONAL, AFFINITY & GLOBAL GROUPS

Our regional groups have been growing despite the pandemic! These groups support each other on a local basis. We now have 8 regions in the US.

This year, the Grands Society for Grandparents in our STXBP1 community was launched.

We also want to highlight our amazing sibling STXBP1 advocacy organizations: Asociación Síndrome STXBP1 in Spain, STXBP1 Italia in Italy, Rare Smile in Israel, and now STXBP1 Syndrom in Germany.

SEPTEMBER AWARENESS MONTH

September is STXBP1 Awareness Month! Why September? The STXBP1 gene is on the 9th chromosome and September is the 9th month of the year. In addition to the STXBP1 Summit+ Family Meeting and the 5th Annual Move to Cure, we promoted awareness all month with community spotlights, Did You Know cards, and a social media campaign.

STXBP1 Disorders
Leading the Charge For a Cure

Did you know...

Among patients with epilepsy who had genetic testing, STXBP1 is the 5th most common genetic diagnosis.

Symonds, J.D., Mctague, A. Epilepsy and developmental disorders: Next generation sequencing in the clinic. European Journal of Paediatric Neurology. (2019)

STXBP1disorders.org
#STXBP1



GIVING TUESDAY

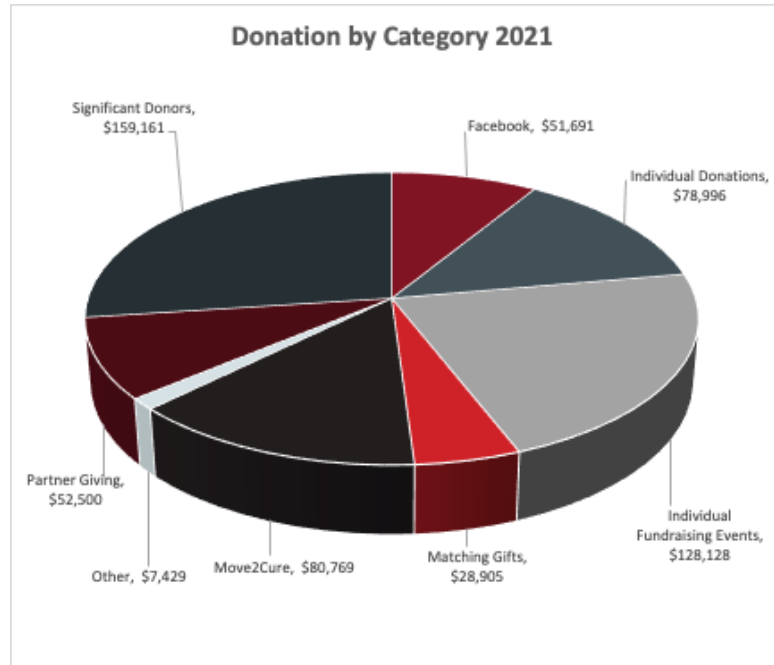
On Giving Tuesday our global community came together. Donors gave generously in honor of over 130 STXBP1 kids; supporting MORE research, MORE clinical trials, MORE days without seizures, MORE smiles, and MORE hope! STXBP1 grandparents and the Grands Society stepped up to the challenge and helped us to smash our \$25K goal, with a grand total of \$43.6K raised!

FINANCIALS & TRANSPARENCY

In 2021, we had an incredible year and nearly DOUBLED our revenues from 2020. We also surpassed total revenues of \$1 million since the Foundation was established in mid-2017! None of this would have been possible without the generous support of donors like you. Further, we were able to put \$568K, or 90% of total expenditures, towards grants and research to continue our mission of accelerating discovery of a cure! We have great momentum going into 2022 and are looking forward to another record breaking year!

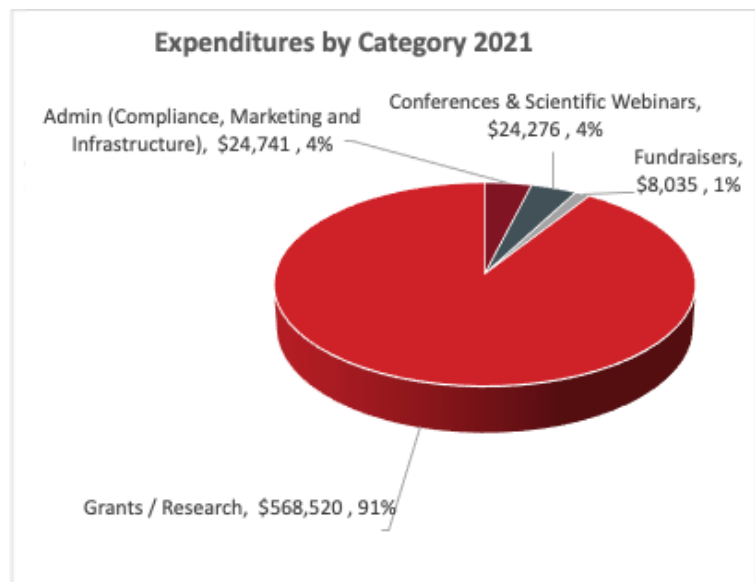
2021 FUNDS RAISED

During 2021 we were able to execute on diversifying our revenue streams as well as continuing to build on our well established revenue streams. We took the record breaking revenue from 2020 of \$300k and increased it by 96% to finish 2021 with \$588k in revenue! We are so very grateful for all of our generous supporters who helped us to hit these goals.



2021 EXPENSES

In 2021, we spent over 95% of total expenditures on programming costs. This far surpasses the typical spend of charities that allocate about 75% to programming and the remaining 25% to administrative dollars. We spent \$568K (or 90%) on grants and research, \$24k (or 4%) on conferences and scientific webinars, and the remaining 5% of costs were spent on administrative and fundraising costs. We continue to strive to maximize EVERY SINGLE DOLLAR we receive and put the most money possible towards research and ultimately a cure.



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STXBP1disorders.org/ways-to-give

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