DRAVET SYNDROME FOUNDATION
Raising hope & changing lives through research

AUGUST 2021

STRATEGIC PLAN PROGRESS REPORT

In 2018, Dravet Syndrome Foundation (DSF) developed a 5-year strategic plan to articulate the long-range direction and priorities for our organization. The content for our strategic plan was derived by examining the Dravet syndrome landscape. We listened to a broad range of input from key stakeholders within our community regarding current community priorities, emerging needs, and organizational strengths and vulnerabilities.

We are pleased to offer our 3rd annual update on our progress from July 2020 - July 2021.

SPECIAL NOTE RE: COVID-19

Restrictions resulting from the pandemic continue to impact our awareness, educational, and fundraising events. We made the difficult decision to delay any in person events through July 2021. Thanks to our rigorous financial development and management over the years, DSF has remained stable in times of uncertainty, and we have not had any cutbacks on our programs or services.

We continue to monitor the constantly changing COVID landscape to see when and where we can safely meet and resume in person events. We have been relying heavily on technology to keep us connected and to continue our fundraising activities during the pandemic. These efforts are vital to assure continued support through our Research Grant Program to assure that research is not stalled in the field of Dravet syndrome. While the pandemic has slowed our fundraising efforts, we are determined to not interrupt progress towards our mission.

GOAL 1: RESEARCH AND PROFESSIONAL EDUCATION

Through collaboration and communication with our research community, we can improve the timeline for better treatments and a cure. By supporting opportunities that allow for greater education on Dravet syndrome throughout the healthcare system, we can increase diagnosis and assure the best quality of life.

Accomplishments from July 2020 - July 2021

- Hosted the 11th annual *DSF Research Roundtable* and began planning the 12th annual event. We are hopeful that the American Epilepsy Society meeting will proceed as planned in Chicago this December and we will be able to host this meeting in person. If not, we will pivot to a virtual event.
- Developed DSF's *Listen + Learn* CME-accredited webinar series featuring experts from our Medical Advisory Board. The sessions provide guidance and share current treatment approaches for professionals who care for patients with Dravet syndrome.
- Participation by our Scientific Director and other staff in several virtual professional conferences to ensure the voice and perspective of the Dravet syndrome community was a part of the conversation.



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GOAL 2: INCREASE REVENUE TO SUPPORT OUR PROGRAMS

Funding growth is challenging particularly for a rare disease nonprofit. By increasing and diversifying our revenue streams we can ensure we have a sustainable operating model that meets the demands of our continuously growing community, and guarantee our success and longevity.

Accomplishments from July 2020 - July 2021

Due to the ongoing impact from the COVID19 pandemic, all of our fundraising events were either cancelled, postponed, or modified into virtual events.

- Hosted our second *Party in Your PJs for Dravet* in place of our annual signature gala. This year we honored our Scientific Advisory Board Members.
- Began promotion of our *Steps Toward a Cure* series of walks and 5Ks as a week-long virtual event that will take place from September 18-25, 2021.
- Began rescheduling postponed 2021 gala events for new dates in 2022.

GOAL 3: EXPAND FAMILY EDUCATION & ADVOCACY

We will continue to support patients and families with disease education and advocacy needs through maintenance and expansion of patient resources, as well as family-to-family support.

Accomplishments from July 2020 - July 2021

- Hosted a virtual conference in June 2021 that offered two days of sessions, highlighting important updates in Dravet syndrome research and clinical care.
- Led the development of the *Seizure Action Plan Coalition,* along with the Lennox-Gastaut Foundation and the TSC Alliance. This effort is designed to raise awareness of what a seizure action plan (SAP) is; the importance of a SAP in the health management of those with epilepsy; and resources to develop an individualized SAP.
- Developed our *Newly Diagnosed Patient Kit*, which includes a printed guide for newly diagnosed families, as well as a medication bag and other materials to assure families have the tools and resources they need to manage their loved one's care.
- Organized virtual *Day of Dravet* workshops for October 2021, which will replace our annual in-person events, with a focus on daily living and caregiver concerns.
- Distributed $22,398 through our *Patient Assistance Grant Program*.
- Increased membership in our private parents support group by approximately 6%.
- Hired a communications company to expand and oversee our social media communication and help increase awareness of Dravet syndrome.



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GOAL 4: ENHANCE COMMUNITY DEVELOPMENT & COMMUNICATIONS

By increasing the leadership roles of our staff, board, volunteers, and donors we can build on current strengths through internal capabilities and resources, while strengthening our community connections. We recognize the importance of an ongoing assessment of our role within the community and the most effective use of our resources, as well as the need to continually communicate our priorities, goals, strategies, and accomplishments to inform and engage our stakeholders.

Accomplishments from July 2020 - July 2021

- Establishment of 2021 initiatives, based on the goals and objectives set by the Board of Directors
- Development of a *Board Recruitment Committee* to attract and interview potential new board members.
- Addition of a *Family Network Support Group Liaison* staff member.

RESEARCH STRATEGY

Our 5-year strategic plan addresses the three highest priorities for research in our community. 1) Cure; 2) Treat; and 3) Learn. By distributing resources among these arms, DSF will continue to balance the need for progress toward a cure and the immediate need for better treatments and new pathways toward that cure.

Since drafting our 5-year strategic plan in 2018, DSF has awarded an additional $1.3M in research grants, $540K of which has been invested into research on genetic approaches to treating Dravet syndrome.

Cure: DSF has continued to focus research on ways to cure Dravet at the genetic level. We awarded grants totaling $540K to basic science researchers attempting to correct the sodium channel insufficiency through microRNA-mediated expression, CRISPR/dCas-9 modulated expression, alternative splicing techniques, and development of new gene therapy delivery vectors.

- DSF funded a multi-institutional grant focused on optimizing a novel gene therapy delivery approach for the SCN1A gene.

- DSF continues to support Stoke Therapeutics, a biotechnology company developing an antisense oligonucleotide (ASO) treatment aimed at increasing healthy SCN1A expression, to be delivered several times each year.

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RESEARCH STRATEGY (continued)

- DSF also supports Encoded Therapeutics, a biotechnology company developing a one-time gene therapy that would permanently enhance expression of the remaining healthy copy of SCN1A. Encoded plans to begin enrolling for clinical trials for their therapeutic, ETX101, in late 2021.

- DSF seeks and maintains relationships with biotechnology companies that are in early stages of pre-clinical development of disease-modifying therapies for Dravet syndrome.

- DSF expanded our Clinician-Researcher grant category ($75K/1 year) to include clinicians-in-training as eligible applicants in order to encourage the career development of clinician-researchers knowledgeable about Dravet syndrome.

2. **Treat:** DSF has continued to support the development of clinical treatments aimed at reducing seizures in Dravet syndrome by working with pharmaceutical and biotechnology companies to bring their treatments to the market. In 2020, Zogenix received FDA approval of fenfluramine (Fintepla) and since the Strategic Plan's inception, clinical trials have begun for the following treatments:

    - Tak-935 (Soticlestat, inhibits 24-hydroxycholesterol synthesis to restore glutamate levels) Ovid completed the Phase 2 ELEKTRA study showing safety and tolerability of Tak-935, as well as efficacy to decrease seizure frequency in Dravet syndrome. In March 2021, Ovid handed global rights for Tak-935 back to Takeda. Phase 3 Studies are planned to initiate in late 2021.

    - EPX-100 (clemizole, repurposed antihistamine, 5-HT modulation) Epygenix is currently enrolling for phase 2 ARGUS trial in the US; first patient dosed in November 2020. Received initial approval to proceed with trials in Canada in August 2020.

    - EPX-200 (lorcaserin, repurposed weight-loss drug, 5-HT modulation). Epygenix has been granted orphan drug designation for Dravet syndrome from the FDA and EMA.

    - E2023 (lorcaserin, repurposed weight loss drug- previously Belviq, 5-HT modulation). Eisai Inc. began a Phase 3 trial for lorcaserin in October 2020 and continues enrollment in 2021 across sites in the US and Canada.

    - STK-001 (TANGO, antisense oligonucleotide) A second paper was published detailing the preclinical efficacy of TANGO in a mouse model of Dravet syndrome (Han et al 2020 Science Translational Medicine). The first patient in the MONARCH trial was dosed with Stoke Therapeutics' STK-001 in

RESEARCH STRATEGY (continued)

late August 2020, and as of August 2021 they have completed dosing patients in the single ascending dose portion of the trial. They continue enrollment for the multiple ascending dose portion of MONARCH in the US and are beginning a similar trial, termed ADMIRAL, in the UK in late 2021 that has been approved to test higher doses of STK-001. Patients completing dosing in MONARCH are eligible for enrollment in an ongoing open-label extension study, SWALLOWTAIL. Initial data from the single ascending dose portion of MONARCH is expected in September 2021.

3. **Learn:** While tremendous progress toward better treatments and curing the underlying cause have been made since 2018, there is undoubtedly much to learn about Dravet syndrome and its manifestations in humans. DSF has awarded grants aimed at understanding how SCN1A mutations affect the heart, metabolic pathways, synaptic pathways, and brain development in animal models and humans.

    - DSF funded a research project investigating the adult presentation of Dravet syndrome, including the examination of comorbidities like movement and gait.

    - DSF funded a grant investigating how the brain controls breathing in a mouse model of Dravet syndrome that could help better our understanding of SUDEP risk.

    - DSF funded a fellowship aiming to use machine learning to better predict and detect seizures using a mouse model of Dravet syndrome.

    - DSF supported efforts for two Natural History studies of Dravet syndrome, the BUTTERFLY Study (Stoke Therapeutics) and the ENVISION study (Encoded Therapeutics).



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SHORT-TERM GOALS (1-2 years)		
Cure	**Treat**	**Learn**
Discover the effects of therapeutically increasing SCN1A expression on symptoms and disease course	Establish a Clinical Research Award	Support organoid and other models of DS
Determine whether targeting specific interneurons is necessary	Work towards establishing an ICD-10 code specific to DS	Explore mechanisms related to SUDEP, including breathing
If necessary, investigate mechanisms for specifically targeting interneurons for increasing SCN1A expression	Prepare the patient community for involvement in research	Identify and describe the natural history of DS
Investigate viruses with interneuron-specific promoter	Identify and describe the natural history of DS against which new treatments can be measured	Continue research on the mechanisms of DS and identification of potential pathways for treatment

LONG-TERM GOALS (3-5 years)		
Cure	**Treat**	**Learn**
Target SCN1A upregulation to interneurons	Identify the best interventions for seizures and comorbidities	Support researchers as they explore new models
Explore other mechanisms of increasing expression	Support clinical studies through research grants and patient engagement	Examine new imaging techniques to assess network dysfunction at the cellular level
Investigate gene therapy techniques that may prove useful in future DS studies		

Not Started
In Progress
Done/ Significant Progress

Accomplishments:

- DSF expanded the eligible applicants for the Clinician-Research Grant category ($75K/ 1 year) to include clinician-trainees, encouraging early-career research and knowledge of Dravet syndrome.
- DSF supported movement to clinical trial phase for Encoded Therapeutics.
- DSF continued support of clinical trial efforts for Stoke Therapeutics.
- DSF awarded grants supporting:
    - the development of a new gene therapy delivery approach
    - investigation into the mechanisms of SUDEP
    - advancement of machine learning to better predict and detect seizures