At the beginning of 2017, we re-assessed our strategic priorities to focus in on three different areas: innovation, community engagement, and next generation scientists.

We are continually assessing our impact, taking a data-driven approach to how we invest our research dollars. See page 3, to learn more about how we have supported devices in the past decade.

As the year draws to a close, we are excited to share the many new research activities under way at the Foundation. For example, earlier this year we launched the Epilepsy Innovation Institute (E2I), designed to be an incubator for new ideas in the epilepsy space. E2I has initiated the My Seizure Gauge Challenge and is asking the community for input about a future seizure forecasting device (see page 6).

We continue to support research grants and are proud to announce 4 new SUDEP research prizes on page 5 and a new therapy commercialization grant awardee on page 6.

We have strengthened existing partnerships and formed new ones. We are grateful to the local Epilepsy Foundation organizations in Greater Chicago, Kentuckiana, Eastern PA, Heart of Wisconsin, Northeastern New York and Minnesota for their financial support of the Research & New Therapies program this year. We are thrilled to welcome a new partnership developed this past quarter with Citizens United for Research in Epilepsy (CURE) to co-fundraise for research in epilepsy. See page 4 or go to http://myshotatepilepsy.org/ to learn more about how to participate and help support research.

Please visit our website to learn more about the exciting initiatives that we have underway.

www.epilepsy.com/research

Sincerely,

Brandy Fureman, PhD
VP of Research & New Therapies
189 new participants enrolled in our Rare Epilepsy Network (REN) registry. The Epilepsy Foundation spearheads the REN in partnership with Columbia University, Research Triangle International (RTI) and a coalition of over 25 different patient organizations. The network conducts and facilitates research to improve outcomes for people with rare conditions associated with epilepsy and seizures. This past year, the REN completed two study requests from:

- Children’s Hospital of Pennsylvania Sleep Study
- University of Washington Caregiver Burden Study

If you are a researcher, feel free to request data at https://ren.rti.org/Researchers

24 companies registering to be part of the Research Roundtable in Epilepsy, an annual meeting convening industry, non-profits, regulators from the US and Europe, clinicians, researchers and people impacted by epilepsy to address major hurdles in new therapeutic development. Numbers have increased 30% from the previous year.

15 research grants were awarded totaling over 1 million dollars. These grants went to:

- 5 Next Generation Scientists
- 4 SUDEP Research Teams
- 3 Shark Tank Awardees for products that would benefit the epilepsy community
- 2 New Therapy Commercialization Grantees
- 1 Cannabinoid Researcher

7 Scientific Meetings hosted and/or financially supported by the Foundation. These meetings brought together hundreds of individuals from companies, people impacted by epilepsy, clinicians, researchers and other nonprofits.

Epilepsy Foundation by the Numbers
Looking back on the 2017 Calendar Year. This year, we have . . .

6 articles co-authored by the Epilepsy Foundation with 3 Editorials published in Epilepsy & Behavior, 1 Manuscript currently under review at Journal of Pediatrics, 1 Manuscript accepted at eNeuro, and 1 article published in Neurology this past October (see page 3 for published article information).

4 research quarterlies issued. This was the first year that we started our quarterly community updates and we are excited to continue this process for 2018.

1 newly launched Clinical Trials Portal to help our community find epilepsy studies and learn about clinical trials.

1 new research program launched – Epilepsy Innovation Institute (E²) – which takes on higher risk projects to funnel new ideas in the clinical pipeline. E²’s first initiative is known as My Seizure Gauge, and will examine the changes that occur in the body preceding a seizure. We are getting better and better at forecasting the weather. We want to do the same with seizures.

We are incredibly proud of the work that we have accomplished this past year – but this is just the beginning. We will continue to foster the development of new scientists and support research that leads to better treatments and care. We strive for excellence, innovation, and radical thinking to end epilepsy.

Join us.

Donate to support research today.
Assessing our Impact – Supporting Device Development

Since 2008, the Epilepsy Foundation has invested over 4.6 million in 39 different epilepsy device development projects through our Epilepsy Therapy Project research program. See the breakdown below of our investment portfolio.

<table>
<thead>
<tr>
<th>DEVICE INVESTMENT PORTFOLIO (2008 - 2017)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-invasive Seizure Monitoring &amp; Alert Systems</td>
<td>30.88%</td>
</tr>
<tr>
<td>Neurostimulation Therapies</td>
<td>28.09%</td>
</tr>
<tr>
<td>Surgical Procedure Devices</td>
<td>14.26%</td>
</tr>
<tr>
<td>Device Software Updates</td>
<td>10.01%</td>
</tr>
<tr>
<td>Developing New Diagnostic Tools</td>
<td>8.20%</td>
</tr>
<tr>
<td>Subdural EEG Implant</td>
<td>4.32%</td>
</tr>
<tr>
<td>Intracranial Drug Delivery</td>
<td>3.88%</td>
</tr>
<tr>
<td>Brain Cooling Device</td>
<td>0.54%</td>
</tr>
</tbody>
</table>

Around a third of our investments have gone towards non-invasive seizure monitoring and alert systems. Another third of our investments has gone towards developing neurostimulation therapies and protocols. The remaining third of our investment has predominantly gone towards improving brain surgery procedures, enhancing algorithms for seizure detection, and developing new diagnostic tools. See below for examples of what we have supported over the past 10 years.

**Non-invasive Seizure Monitoring & Alert Systems.**

In 2009, we funded the development of SmartWatch by Smart Monitor. This was one of the first watches to fuse sensor, mobile, and cloud technologies with big-data analytics to create an ease of use monitoring and alert system device for people living with epilepsy. Following our investment, other companies began to develop their own watches for the epilepsy space from Apple’s EpiWatch to Empatica’s Embrace.

In 2011, we funded SAMiT™ by HiPass Design for developing a sleep activity monitor to detect abnormal movements in the night. This was one of the first video monitors developed that capitalized on infrared and mobile technologies for caregivers to know when unusual movements occurred during the night.

“Winning the first Epilepsy Foundation Shark Tank Competition in 2011 allowed me to transform SAMi from an expensive custom solution for us into a refined, much less costly tool for others.”

— Charles W. Anderson, President, HiPass Design

**Neurostimulation Therapies**

In 2008, we funded the development of the Monarch eTNS (Trigeminal Nerve Stimulation) device – a new noninvasive nerve stimulation device to stop seizures. Those studies paved the way for the Monarch eTNS device to obtain approval by the European Union. Currently, Monarch eTNS, by Neurosigma, is being reviewed by the FDA.

“This study led to two [follow-on] NIH grants for the development of Trigeminal Nerve Stimulation, and laid the groundwork for the further development of Trigeminal Nerve Stimulation as a potential treatment for Major Depression...[W]e are extremely grateful for the support of the Epilepsy Foundation, and wish to thank our colleagues at the Epilepsy Foundation for their support and encouragement for these pilot feasibility studies.”

— Christopher M. DeGiorgio, MD, FAAN, Professor and Vice Chair, UCLA Department of Neurology

**Improving Surgical Procedures**

In 2011, we supported the development of Visualase® by Medtronic. Visualase is an MRI-Guided Laser Ablation Technology for Minimally Invasive Neurosurgery to reduce the risk of open-brain surgery for people living with epilepsy.

“Aside from the funding, validation by ETP experts who vetted our project, and found it to be a worthwhile pursuit, has been a significant factor in our rapid progress and expansion into new centers.”

— Ashok Gowda, PhD, Founder of Visualase, Inc — acquired by Medtronic in 2014, President & CEO, BioTex, Inc.
In 2016, the Epilepsy Foundation launched the *Research Roundtable* initiative. Our goal was to bring together companies involved in epilepsy therapeutics and diagnostics with epilepsy specialists and clinical trialists, major epilepsy non-profit organizations, the Food and Drug administration and the European Medicine Agency to address major roadblocks to new epilepsy therapy advancement. The inaugural roundtable meeting was held on May 19-20, 2016, in Washington, DC. The topic was “Reducing placebo exposure in epilepsy clinical trials.”

The use of placebos in clinical trials is a staple of trial design, in that it serves as a control for comparison and meaningful interpretation of the data. Most clinical trials of investigational agents in epilepsy are conducted as “add-on” trials in participants with treatment-resistant seizures. This means that the investigational agent or placebo is added on to the participant’s current therapies, which are held at stable levels for the duration of the clinical trial. During that period, participants may be continuing to have seizures, and this is particularly likely in the placebo group. We are increasingly concerned about prolonged placebo exposure because of data showing a higher rate of sudden unexpected death in epilepsy (SUDEP) in trial participants with uncontrolled seizures.

We strive to protect participants in clinical trials while at the same time ensuring that the trial provides interpretable results so that we learn how to improve treatment for future patients. But what happens when administration of placebo compromises the well-being of the participant? How can placebo exposure be limited while still maintaining the integrity and interpretability of the trial results?

The 2016 research roundtable agenda centered around emerging clinical designs from other fields and the merit and limitations for each approach for future epilepsy clinical trials.

This meeting resulted in a high-profile publication which discusses how different trial designs could be implemented ranging from active-control add-on trials, placebo add-on to background therapy with adjustment, time to event designs, adaptive designs, platform trials with pooled placebo control, a pharmacokinetic / pharmacodynamic approach to reducing placebo exposure, and shorter trials when drug tolerance has been ruled out.

The article came out this past October 2017, in the journal of *Neurology*. One can read the article here.

Each research roundtable meeting happens annually and addresses a different roadblock to developing new therapeutics. Our 2017 meeting focused on pediatric drug development. Our 2018 meeting will focus on assessing clinical populations and clinical endpoints. We will be updating you on these meetings and their resulting publications moving forward.

"That’s It! This is our shot to take. Let’s not throw it away.”
– Miguel Cervantes

The Epilepsy Foundation is joining forces with CURE (Citizens United for Research in Epilepsy) for the #MyShotAtEpilepsy Challenge to promote awareness and raise funds for epilepsy research that will lead to a cure. All proceeds from the campaign will be split between both organizations and used to advance breakthroughs in epilepsy treatments and research.

The initial proceeds will be used to support the genetic sequencing of hundreds of individuals from the Rare Epilepsy Network and their subsequent enrollment into the Epilepsy Genetics Initiative for recurrent analysis. These individuals suffer from severe epilepsies with an unknown genetic cause.

http://myshotatepilepsy.org/
Sudden unexpected death in epilepsy (SUDEP) is the leading cause of death in young adults with uncontrolled seizures. Each year, more than 1 out of 1,000 people with epilepsy die from SUDEP. If seizures are uncontrolled, the risk of SUDEP increases to more than 1 out of 150.

One theory for SUDEP is the presence of compromised cardiac or respiratory function occurring before, during, or after the seizure. However, it is difficult to predict what a specific person’s risk level might be for SUDEP. In the last issue of the Research Quarterly, we wrote about the SUDEP Biomarker Challenge which challenged researchers to find predictive biomarkers to identify people at risk for SUDEP or life-threatening seizures that compromise cardiac or respiratory function. A biomarker is a measurable biological substance in the body. For example, blood sugar can be a biomarker for diabetes risk or cholesterol for heart disease.

*If we can identify who is at high risk, then we can try different interventions to prevent SUDEP from happening.*

Eleven teams from around the world submitted to our Production of Proof of Concept Data challenge. Here, applicants had to demonstrate that their proposed biomarker that indicates risk of SUDEP has the potential for real-world application. These could be pilot studies that are done in preclinical models or in human populations. The four awarded teams are now continuing to develop their predictive tool for SUDEP. They were:

**Team:** Barbara L. Kroner, PhD, John M. Schreiber, MD, Lowell H. Frank, MD  
**Project:** Early Detection of Myocardial Injury as a Biomarker for SUDEP in Living Epilepsy Patients  
This team tested a relatively easy to perform and non-invasive tool to image the heart and look for ventricular myocardial deformation as an indicator for SUDEP risk.

**Team:** Kristen H. Gilchrist, PhD, Meghan Hegarty-Craver, PhD, William Gaillard, MD  
**Project:** Cardio-Respiratory Biomarkers of SUDEP from an Unobtrusive Wearable Monitor  
This team developed a seizure detection algorithm from a commercial Electrocardiogram (ECG) wearable sensor that can analyze both heart rate variability and respiratory changes to identify those at risk of SUDEP.

**Team:** Peter Carlen, MD, Berj Bardakjian, PhD, Stiliyan Kalitzin, PhD, Martin del Campo, MD  
**Project:** Multivariate computer based classification of biomarkers for SUDEP  
This team will use a machine learning algorithm to identify a panel of markers linking EEG, heart rate, and respiration data to identify those at high risk of SUDEP.

**Team:** Carolina Ciumas, PhD, Philippe Ryvlin, MD, PhD, Samden Lhatoo, MD  
**Project:** PRESUDE - Brainstem MRI biomarker to Predict the risk of Sudden Unexpected Death in Epilepsy  
This team is developing an imaging diagnostic tool that checks brainstem response to respiratory stress as a potential indicator for SUDEP risk.

*THE SUDEP INSTITUTE IS LOOKING FOR APPLICANTS TO SOLVE THE REMAINING MILESTONE!*

Solvers must now demonstrate that their selected biomarker(s) actually have predictive efficacy and value in the broader human population. You did not need to apply to the other parts of the challenge to participate.

**Submission Deadline:** Race to the Finish, with solutions accepted on a rolling basis up to October 20, 2020. Submissions will be reviewed as they are received and at the discretion of the SUDEP Institute. The first submission that meets all the challenge criteria will be awarded the prize.  
**Award:** $800,000 for successful completion
Spring 2017 New Therapy Commercialization Grant Award

Wolfgang Löscher, DVM
Head, Department of Pharmacology, Toxicology, and Pharmacy, Head, Center for Systems Neuroscience Hannover University of Veterinary Medicine Hannover, Germany

Research Topic: Anti-Seizure and Anti-Epileptogenic Effects of New, Selective mTOR Inhibitors

Tuberous Sclerosis is a rare epilepsy subtype caused by a genetic mutation that results in a hyper activation of the mTOR pathway. Everolimus, a drug which inhibits mTOR activity, was recently approved by the European Union to treat seizures in Tuberous Sclerosis patients. However, there are some concerns with the off-target side effects of everolimus. For example, everolimus disrupts the immune system. Originally, the drug was developed to be an immunosuppressant and is FDA approved for that indication. Moreover, everolimus does not get into the brain very easily, which has implications on the dosing required for treating seizures.

Dr. Löscher has recently partnered with PIQUR Therapeutics, a company which developed a new class of mTOR inhibitor compounds. These next generation mTOR inhibitor drugs have a better safety profile than everolimus. With this grant, Dr. Löscher will test their lead compounds on a battery of animal models to assess the compounds effectiveness at reducing seizures. If the data are promising, these studies will be the preliminary evidence needed to start a small clinical trial in Tuberous Sclerosis patients within 24 months.

Several studies indicate that the mTOR signaling pathway is also overactive in other epilepsy conditions. Interestingly, some of these studies also suggested mTOR inhibitor treatment following an acquired brain injury (such as a stroke or head trauma) could prevent epilepsy. Therefore, Dr. Löscher will also test whether these compounds could prevent the development of post-traumatic epilepsy in animal models with induced epilepsy. The work from this grant will be used to demonstrate proof of concept of these compounds as a treatment for epilepsy beyond Tuberous Sclerosis.

Take the Survey: Shape the Future

The Epilepsy Innovation Institute (E²) wants to better identify and understand the changes in the body that precede a seizure on a timescale of minutes, hours, and days before. Ultimately, we want to create a seizure gauge that assesses seizure likelihood on a continual basis. This initiative is known as the My Seizure Gauge Challenge.

Your opinion counts!

As we look to the future of seizure forecasting devices, we want your opinion on what device would work for you. Specifically, we want your input on experiences with seizures, seizure forecasting, and your opinion on whether such a device would be meaningful to you.

Findings from this survey will influence work in the My Seizure Gauge Challenge and the future development of a seizure forecasting device.

We welcome participation from people at least 18 years of age who are living with epilepsy or their primary caregivers and family members. The survey should take around 30 minutes to an hour to complete. All information obtained from this survey will be presented in summary form, grouped with other responses so that no one individual can be identified. Your data will be kept in the strictest confidence and will be accessible only to people working on this study.

We recognize that this is a long survey. Please answer all the questions to the best of your abilities.

Your input helps shape the directions that we take.

Take the Survey


Congratulations to the Epilepsy Foundation's Chief Scientific Officer Dr. Jacqueline French on being awarded the William G. Lennox Award at the 2017 American Epilepsy Society Meeting. This award recognizes those who have a record of lifetime contributions and accomplishments to epilepsy. Dr. French was also named a 2017 Highly Cited Researcher by Clarivate Analytics. This honor means Dr. French had enough citations to be ranked in the top 1% of articles published in the same year and field.
Clinical Trials Portal

This past April, the Epilepsy Foundation launched the Clinical Trials Portal, where you’ll find information about ongoing clinical trials and observational studies in epilepsy. This tool will help connect you to studies that match the type of epilepsy you or your loved one has.

Studies currently recruiting:

Fenfluramine Assessment in Rare Epilepsy (FAiRE): ZX008-1501/1504

FAiRE is exploring whether the investigational drug (ZX008) improves seizure control in children and young adults with Dravet syndrome. The goal of the ZX008-1501/1504 trials is to show that ZX008 is a safe and effective treatment for children and adolescents with Dravet syndrome when added on to their other seizure medications.

Preventing Epilepsy Using Vigabatrin In Infants with Tuberous Sclerosis Complex

This trial tests whether earlier treatment versus standard treatment with vigabatrin in infants with tuberous sclerosis complex (TSC) will have a positive impact on developmental outcomes at 24 months of age. It also tests whether early treatment prevents or lowers the risk of developing infantile spasms and uncontrolled seizures.

Focused Ultrasound for Treatment of Epilepsy

The study will evaluate the effectiveness and safety of an investigational device that uses sound waves (ultrasound) from outside the head to treat seizures that are not well controlled by medication and are due to a small growth of abnormal cells in the middle of the brain, most commonly hypothalamic hamartomas.

Go to our portal to learn more!

www.epilepsy.com/clinical_trials
Tracking Progress in the Clinical Pipeline

We keep track of the latest developments in the clinical pipeline from early stages to market through our online New Therapies Pipeline webpage. This page tracks development of epilepsy assets in 9 categories — Drugs, Enhanced Drug Delivery, Dietary Supplements, Therapeutic Devices, Seizure Detection and Prevention, Epilepsy Diagnosis, Safety Devices, Newly Marketed and Available to Patients, Dormant Projects.

Our latest updates for quarter 4 of 2017 include:

- 8 drugs recently added to the pipeline
- 5 drugs advancing through clinical trial phases
- 3 drugs no longer tracked due to failed clinical trial or no longer in the epilepsy space

Please go to epilepsy.com/pipeline to see the latest in drug and device development for epilepsy.

Did you find any information out of date?
Let us know by emailing ahansell@efa.org with PIPELINE UPDATE in the subject line.

Interested in grant opportunities?
The Epilepsy Research Connection is a collaborative effort to assist epilepsy researchers in looking for funding opportunities across different organizations. http://epilepsyresearchconnection.org/

We would like to thank the following organizations and individuals for supporting the Epilepsy Innovation Institute:

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Dr. Matthew & Brooklyn Thom
Mark & Margo Pinto
Michael Provo
Neu Family
Tony Coehlo
Tsymmetry
Warren Lammert
William Parrish

Interested in supporting Ei²?
Contact: Geoff Hoyt, Senior Director of Major and Planned Giving, National Office Epilepsy Foundation
ghoyt@efa.org