Progress through Partnerships

ANNUAL REPORT 2017

STAR is shining brighter than ever before!

CMTA
Charcot-Marie-Tooth Association

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The Charcot-Marie-Tooth Association is a leading non-profit organization dedicated to finding a cure for CMT. The CMTA's Strategy to Accelerate Research (STAR) program brings top researchers together with pharmaceutical and biotechnology partners to accelerate scientific breakthroughs and develop therapies. The CMTA also offers inclusive community services to help patients and families live their best life with CMT. These include over 70 local branches, a robust Advisory Board of Experts, Camp Footprint exclusively for teens with CMT, annual Patient & Family Conferences and online support communities.

OUR MISSION

To support the development of drugs to treat CMT, to improve the quality of life for people with CMT and, ultimately, to find a cure.

OUR VISION

A World Without CMT.

Dear Friends,

In 2008, we took bold steps toward solidifying our vision of a world without CMT with the launch of our Strategy to Accelerate Research (STAR) program. While we have spent the last decade dedicated to making progress through partnerships – bringing together researchers with pharmaceutical and biotechnology companies and patients to find treatments for CMT – we believe we will look back on 2017 as one of the most pivotal years in our journey.

In 2017 alone, we spearheaded projects in CMT types 1A, 1B, 1X, 2A, 2E and 4C, bringing the number of projects the CMTA funded with the top labs worldwide to 18 active initiatives. 2017 was also an unprecedented year of growth in our pursuit of treatments for CMT as we increased our research alliance network with pharmaceutical and biotechnology companies from a handful to over 10 partners. We are thrilled to report this growth has continued into 2018, and we now have more than 20 research alliance and service partners – the CMTA is recognized as the premier organization because of its research tools, network of experts, testing infrastructure and patient partnerships.

Consequently, we are making significant headway in learning how we can both halt the progression of CMT and reverse the damage it causes. This was seen through our partnership and breakthrough announcement with Ionis Pharmaceuticals. Other announcements followed recently, and many more are to come.

In the meantime, we are continuing to help people with CMT in their daily life. The CMTA currently has 70 branches in the United States and Canada. The CMTA also sponsors 22 Centers of Excellence where people with CMT can receive world-class, multidisciplinary care from renowned CMT clinicians and experts. In communities across the country, we're hosting events including Walk 4 CMT, Cycle (and Walk!) 4 CMT, the Oxford "Fun"Athlon and the New York Gala and Auction, among others, to raise much-needed awareness and funds to fight CMT. Our branch partners have truly furthered the CMTA's mission in their own communities.

While 2017 has been a year of progress through partnerships, our work is far from done. We continue to need your support. Thank you for your contributions of time, talent and financial resources. We remain confident that with our thriving community, dedicated partners, scientific expertise and unrelenting drive, we will someday live in a world without CMT.

Sincerely,

Amy Gray
Chief Executive Officer

Gilles Bouchard
Chairman of the Board

Like most kids,

Claire dreams about what she's going to be when she grows up. She thinks of becoming a world-class gymnast, tumbling on the ground, vaulting through the air and balancing on the beam. Other days, Claire's head is among the stars, thinking of life as an astronaut. Yet, her love for science and animals makes life as a veterinarian sound like a perfect fit.

But, like 2.8 million people worldwide, Claire is living with Charcot-Marie-Tooth disease, and some days, those dreams of becoming a gymnast, an astronaut or a vet – or even just doing the most basic of tasks – seem to be out of reach.

PROGRESS Through Research Partnerships

At the CMTA, our goal is to put those dreams back within reach. That's why we are accelerating our efforts to create a world without CMT through STAR, our Strategy to Accelerate Research.

The CMTA has spent more than $8 million in recent years to fund research projects in 1A, 1B, 1X, 2A, 2E and 4C. STAR's unique character stems from the willingness of the scientists to come together to advance CMT research collaboratively, sharing ideas, discoveries and research findings. Below are some updates of the work funded through STAR by disease type:

TYPE 1A

CMT1A is caused by the duplication of the Peripheral Myelin Protein 22 (PMP22) gene, which leads to the demyelination of the peripheral nerves. One recently announced breakthrough came from our partnership with Ionis, which has pioneered development of antisense oligonucleotide (ASO) technology. Rodent studies showed a dramatic improvement in two models of CMT1A, and Ionis is currently working on developing refined versions for testing in clinical trials. Our partnership with Genzyme, a Sanofi company, enabled us to screen their entire compound collection, and we are now testing a leading candidate in a variety of secondary assays and animal models. In addition, the alliance has now expanded to the evaluation of additional molecules that have emerged from other Sanofi programs, and a number of these drug prototypes are being tested as well. Laboratory and animal models of CMT1A have been made available to five additional CMTA alliance partners for testing of therapeutic compounds. Dr. Michael Shy, together with the members of our Clinical Expert Board (CEB), is leading the effort to develop the best outcome measures and biomarkers for clinical trials of CMT1A therapeutics.

TYPE 1B

This CMT subtype is caused by mutations in the Myelin Protein Zero (MPZ) gene. Scientific Advisory Board members Drs. Michael Shy, Lawrence Wrabetz and Maurizio D'Antonio are experts in this area. In partnership with InFlectis BioScience, we are engaged in further testing of a novel molecule called Sephin, which has shown dramatic improvement in the S63del mouse model of CMT1B. Also, we now have mouse models of all three major clinical presentations of CMT1B. In the late onset type, we are testing how inhibiting axon degeneration pathways can stabilize motor and sensory neurons, an approach which is the focus of pharmacological development by several CMTA partner companies. This will be the first test of such pathways in a CMT model, and it is possible that this approach may have broad applicability to other types of CMT.

TYPE 1X

Until now, there was only one mouse model of CMT1X, but it was not a direct replica of the human mutations in GJB1. Therefore, the CMTA has sponsored the development of four mouse models of CMT1X, one of which has been developed in partnership with Dr. Robert Burgess at Jackson Laboratories. These models will be used to test therapeutic approaches such as the inhibition of macrophages. Dr. Rudolf Martini at the University of Würzburg, Germany has found that reducing this type inflammation has a very positive effect in a mouse model of CMT1X. In addition, CMT1X also is characterized by degeneration of motor neurons and is therefore an ideal target for the axon degeneration therapies mentioned above for CMT1B. Finally, the work of Dr. Kleopas Kleopa at the Cyprus Institute of Neurology and Genetics has shown the first example of a successful gene therapy in a CMT1X mouse model, and he is continuing these studies toward clinical trials with this novel type of therapy for not only CMT1X but also CMT4. The CMTA convened a workshop with some of the world's top gene therapy experts to help identify the key steps in translating these findings into human clinical trials for CMT1X. Again this approach can be applied to other types of CMT.

Mario Saporta, M.D. and his team at the University of Miami CMTA Center of Excellence.

TYPE 2A

CMT2A is caused by dominant mutations in Mitofusin 2 (MFN2). The STAR team has developed two excellent rat models for CMT2A which are being made available to the research community and represent an important tool to test potential new modulators of mitofusin activity. Stem cell models of CMT2A have also been developed for CMTA-sponsored research in the laboratory of Dr. Robert Baloh at Cedars-Sinai Medical Center. As part of its Patients as Partners in Research initiative, the CMTA has sponsored a study with the University of Iowa CMT Clinic and CMTA Center of Excellence to look at pulmonary function for people who have CMT2A. To fund this important study, J.D. and Brenda Griffith made a donation to the CMTA in memory of their daughter Marah. In partnership with several companies, therapeutic approaches under study include inhibition of axon degeneration, as well as the development of gene therapy, which has recently been shown to be successful in another motor neuron disease known as Spinal Muscular Atrophy (SMA). Finally, other candidate molecules have emerged from academic research and animal studies, and planning is underway to test these as well.

TYPE 2E

CMT2E is caused by dominant mutations in the neurofilament light protein (NEFL) gene. Mutations in NEFL cause CMT2E. With support from the CMTA, one of the best mouse models of CMT2E, made by Dr. Ronald Liem at Columbia University, has been extensively characterized in collaboration with Dr. Steven Scherer at the University of Pennsylvania. Both human and mouse stem cells containing CMT2E mutations have been differentiated into motor neurons and are being used in drug screens to identify therapies that prevent aggregations of neurofilaments seen in CMT2E.

TYPE 4

CMT4C is caused when both versions of an important gene required for healthy myelin (SH3TC2) are deficient. To restore function of these genes, the gene therapy approach described above for CMT1X has also been tried for CMT4C by Dr. Kleopas Kleopa and has shown very positive results. We anticipate this approach will be applicable to other forms of CMT4.

Partnerships Lead to **PROGRESS**

The CMTA's funding strategy is focused on translational research that will lead to therapeutic treatments of CMT. We have formed powerful alliances and partnership agreements with the pharmaceutical, biotechnology and research service industries, major universities, along with non-profit research organizations and the National Institutes of Health (NIH).

Our list of partners has more than doubled in 2017 to 10 companies across three continents, including Genzyme (a Sanofi Company) and Ionis Pharmaceuticals, among others. These companies are leaders in the latest genetic and neurological technologies – such as CRISPR, gene therapy, gene silencing and axon and muscle regeneration. And the momentum continues into 2018. Our number of research alliance and service partners has once again doubled, now including more than 20.

genzyme
A SANOFI COMPANY

The CMTA formed an alliance to test **Genzyme's** large libraries of molecules to identify those that suppress PMP22 levels in CMT1A. Following testing of close to two million molecules at Sanofi, a number of chemical classes have been identified that suppress PMP22 levels in CMT1A. Candidates from these chemicals are now being tested in animal models of the disease in order to confirm functional improvements indicating recovery from disease symptoms. In addition, the alliance has now expanded to the evaluation of additional molecules that have emerged from other Sanofi programs. Several of these drug prototypes are now being tested in animal disease models of CMT1A. The overall aim of the joint CMTA-Genzyme team is to identify drug candidates that can advance to testing in patients.

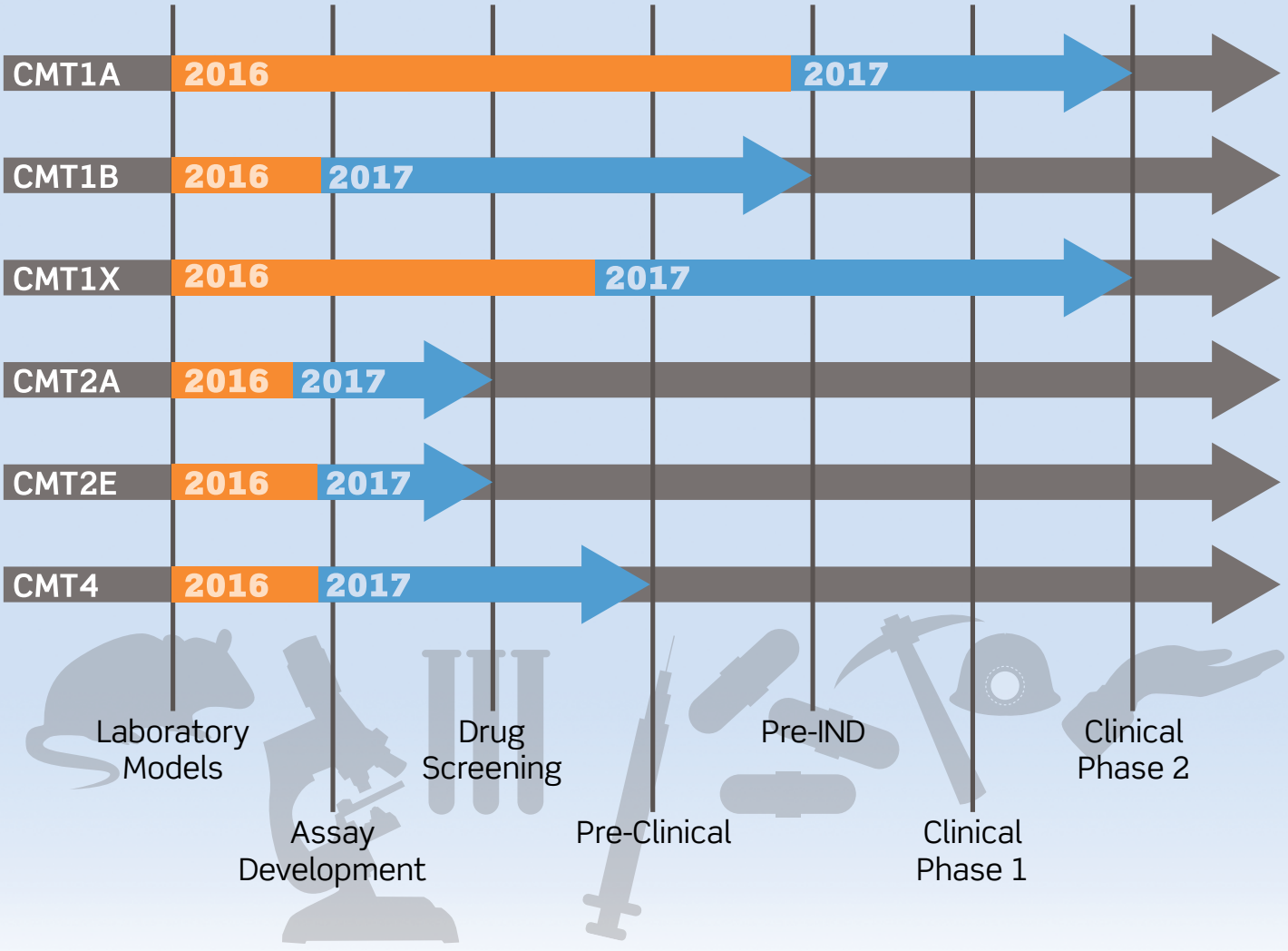
Thanks to CMTA-funded research, **Ionis Pharmaceuticals** has identified promising therapeutic approaches for CMT1A. A paper published December 4, 2017, in the *Journal of Clinical Investigation* (JCI) identified a promising early-stage therapeutic approach with antisense technology for CMT1A, the most common form of the disease. Ionis researchers used their expertise as a world leader in developing antisense oligonucleotides, which precisely target the products of genes that cause CMT. They developed antisense drugs designed to reduce the amount of the PMP22 messenger RNA (mRNA), which in turn reduces production of the PMP22 protein. The researchers then tested the strongest antisense compounds in two different animal models of CMT1A. Studies in two rodent models of CMT1A not only stopped progression of the disease, but also showed improvement of some symptoms.

The CMTA has entered into an alliance partnership with **InFlectis BioScience**, a clinical stage company committed to the development of innovative therapeutics harnessing the Integrated Stress Response (ISR) for the treatment of a broad range of diseases. The company plans to demonstrate the clinical effectiveness of its drug candidate IFB-088 for the treatment of Charcot-Marie-Tooth disease types 1A and 1B and plans to begin a Phase 1 study of IFB-088. The CMTA and InFlectis BioScience alliance team is collaborating on pre-clinical studies, clinical planning and understanding the impact of CMT on patients.

The CMTA also formed a partnership with **Acceleron Pharma**, a Cambridge, MA based biopharmaceutical company dedicated to developing medicines to treat serious and rare diseases, including CMT. Acceleron has developed ACE-083, which is a locally-acting therapeutic candidate designed to target muscles to maximize growth and strength. Acceleron is developing ACE-083 for disorders such as CMT, in which improved muscle strength in target muscles may provide a clinical benefit and enhance quality of life. The partnership with Acceleron includes preclinical research and close collaboration with the broader CMT community through the CMTA's Patients as Partners in Research initiative aimed at raising awareness for the thousands of patients living with CMT.

The CMTA and **Regenacy Pharmaceuticals**, a clinical-stage biopharmaceutical company developing breakthrough treatments for diabetic and other peripheral neuropathies, are engaged in a collaboration to validate the role of the enzyme HDAC6 in multiple forms of CMT. Based on the terms of the collaboration, Regenacy has an opportunity to expand on the groundbreaking work of Dr. Ludo van den Bosch at University of Leuven (recently published) and Dr. Andrew Grierson at University of Sheffield to show the role of HDAC6 in several forms of CMT Type 2. The collaboration will focus on evaluating the efficacy of ricolinostat in animal models of CMT to support initiation of clinical trials. This relationship is taking advantage of the extensive suite of expert preclinical testing capabilities the CMTA has assembled and makes available to groups such as Regenacy that want to evaluate therapeutic potential in a CMT disorder.

The CMTA is working vigorously to find treatments, and ultimately a cure for all types of CMT. We are investing in projects that will benefit virtually all people with CMT. The chart below shows the progress made along the path to clinical trials.



CMTA
Charcot-Marie-Tooth Association

2017
by the numbers

$1,900,000
spent on STAR

18
research projects

$250,000
raised by Walks 4 CMT

30
Walks 4 CMT held

88% of every dollar donated spent on mission

10
research partners

>90%
of CMT patients covered by an active research project

70
branches

290
branch meetings held

4
CMTA Patient & Family Conferences

471
Patient & Family Conference attendees

21
physical and occupational therapists attended the PT/OT conference

64
campers

35
camp counselors

856,647
page views on www.cmtausa.org

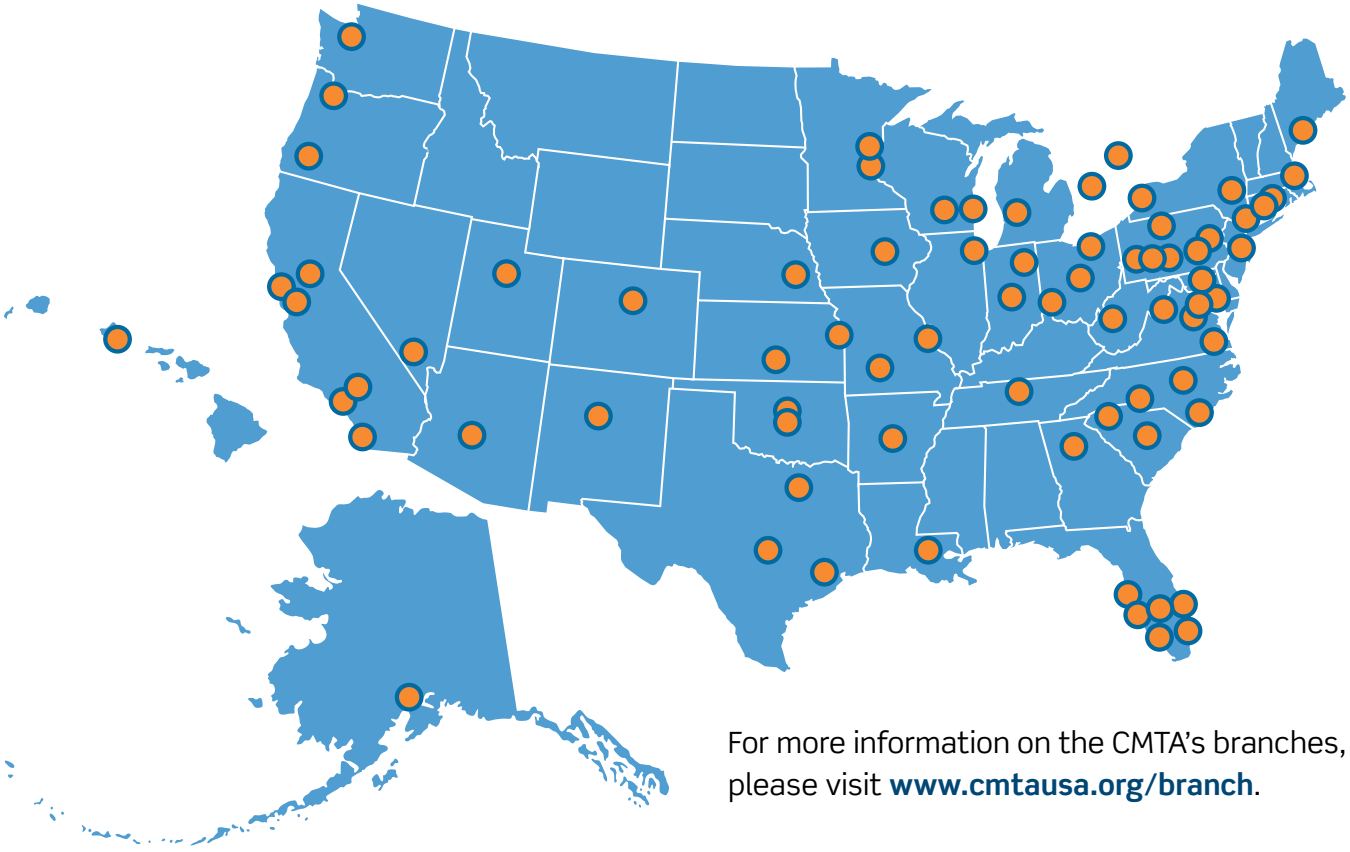
40,270
social media followers by end of 2017

PROGRESS Through Communities

Over the course of a decade, the CMTA's research program has focused on answering the question that looms large to all of us: "What is the cure for CMT?" But, for patients like Claire – and families like hers – our community outreach efforts focus on answering the everyday questions like, "What kind of doctor should I see?," "Where can I meet other people living with CMT?" and "How can I live the best life possible with CMT?" Our goal is to help 2.8 million people worldwide better navigate life with CMT, and we depend on volunteers and supporters in communities across the country to help make this a reality.

With more than 70 branches throughout the United States and Canada, we provide our members with education and support through branch meetings and educational sessions with physicians, researchers, therapists and other people living with CMT. In 2017 alone, our members attended 290 branch meetings in various communities throughout the country to connect, share experiences and create their own circle of support. These meetings and events are carefully planned and hosted by our amazing and selfless branch leaders, many of whom are living with CMT themselves.

CMTA BRANCHES



For more information on the CMTA's branches, please visit **www.cmtausa.org/branch**.

PROGRESS Through Awareness and Events

As our branches have expanded, so too have the number of events hosted by branch volunteers, especially during September, which is CMT Awareness Month. In 2017, CMTA branches supported 30 Walks 4 CMT. Hundreds of people across the country participated to raise funds to support the CMTA's efforts to find treatments and a cure for CMT. CMTA members and CMTA branch leaders also hosted grassroots fundraisers including Cycle 4 CMT, special dinners, fishing tournaments, bingo nights, awareness nights and wine tastings, among others, all with a common goal – to raise much-needed funds – and awareness – for CMT.

Thousands of community members host and attend CMTA events throughout the year.

Michael Shy, M.D., visits with his patient Tessa at the University of Iowa, which is a CMTA Center of Excellence.

PROGRESS Through Partnership with CMTA Centers of Excellence

One of the ways the CMTA improves the quality of life for those with CMT is by sponsoring patient-centric, multi-disciplinary CMT clinics, led and staffed by world class CMT clinicians and researchers. Through the CMTA's Centers of Excellence, children, adults and families affected by CMT receive comprehensive care by CMT experts. The Centers roughly correspond to the sites that make up the NIH Inherited Neuropathies Consortium (INC) – a group of academic medical centers, patient support organizations and clinical research resources sponsored in part by the CMTA.

As the CMTA works on clinical trials for candidate therapies, CMTA Centers of Excellence will become even more important. The success of these trials will largely depend on how much we know about how different types of CMT progress over time and whether novel medications are slowing the course of the disease. Through our 22 Centers of Excellence, we are building patient registries, natural histories and outcome measures with our research partners, enabling them to perform faster and more effective clinical trials.

For more information on the CMTA Centers of Excellence, please visit **www.cmtausa.org/coe**.

PROGRESS Through Education

The CMTA organizes Patient & Family Conferences every year, often in collaboration with a CMTA Center of Excellence or multi-disciplinary CMT clinic. These all-day conferences allow people with CMT to get up-to-date information on the CMTA's STAR program from scientists leading efforts to find treatments for CMT. There, they met people who understand what life with CMT is like. CMTA Patient & Family Conferences also include feature presentations from local clinicians and health care providers on topics such as the causes and diagnosis of CMT, physical and occupational therapy, orthotics and bracing, orthopedic surgery, genetic counseling and more. In 2017, more than 471 patients and their family members attended CMTA Patient & Family Conferences in Miami, Philadelphia, Pittsburgh and Phoenix.

The CMTA also brings together specialists practicing in the CMT field. In November 2017, the CMTA hosted a meeting of physical and occupational therapists from CMTA Centers of Excellence. Therapists from 12 states and four countries came together in Phoenix, Arizona to discuss the assessment and management of individuals with CMT. Experts in the field, including several from the CMTA's Advisory Board, led the meeting of 17 physical therapists and four occupational therapists who are all dedicated and interested in working together to bring the best available care to individuals with CMT. An important outcome of the meeting was the creation of a CMT-specific guide for patients, physical therapists and occupational therapists.

Therapists from different states and countries gathered in Phoenix, Arizona last fall to examine the assessment and management of people living with CMT.

PROGRESS Through Our Youngest Patients

Life as a child with CMT can be challenging, but it also can be a whole lot of fun. Just ask the 64 campers and 35 counselors who attended the CMTA's Camp Footprint in 2017. As the only camp in the United States created just for kids with CMT, Camp Footprint is an annual, free, five-day sleepaway camp held at Camp Kon-o-Kwee in Fombell, Pennsylvania, for children ages 10 to 18. Camp Footprint empowers children with CMT with the courage, hope, skills and community for a lifelong journey of realizing their potential and developing their strengths. At camp, they learned to zipline, fish, kayak, ride horses and so much more – things they never thought they'd be able to do.

Through participation at Camp Footprint, campers make friendships based on shared experiences and understanding. An activity-driven week dedicated to exploration and creativity expertly engineered by our devoted staff, Camp Footprint is about building confidence and community. Central to the success of Camp Footprint are our counselors who volunteer their time to make each camper feel seen, heard and celebrated.

> "For one of the first times in my life, my concerns and physical struggles were the norm. I was not alone. Together, we were able to begin tackling these challenges. Everyone was really supportive of each other both physically and emotionally."
>
> *—Payton Rule, 18 years old, Belleville, Illinois*

Campers at the CMTA's Camp Footprint build lasting friendships.

BOARD OF DIRECTORS

The CMTA's Board of Directors is comprised of business owners, executives, doctors and lawyers who oversee the organization's operations and strategy. Because they are all affected by CMT, they are deeply committed to the organization, give generously of their time and collectively contributed more than $600,000 in 2017 to support the CMTA's mission.

Gilles Bouchard, Chairman

Gary Gasper, Treasurer

Herb Beron, Secretary

Thomas W. Dubensky, Jr., Ph.D.

Laura Fava

Alan Korowitz

Steve O'Donnell

Chris Ouellette

Elizabeth Ouellette

Phyllis Sanders, Esq.

Steven Scherer, M.D., Ph.D.

Michael Shy, M.D.

John Svaren, Ph.D.

Lawrence Wrabetz, M.D.

Special Advisor to the Board
Bruce Chizen

STAR ADVISORY BOARD

The CMTA's STAR Advisory Board includes 27 of the top CMT scientists from around the world. It comprises a Scientific Advisory Board, a Therapy Expert Board and a Clinical Expert Board.

John Svaren, Ph.D., Chair, Scientific Advisory Board

Mark Scheideler, Ph.D., Chair, Therapy Expert Board

Michael E. Shy, M.D., Co-Chair, Clinical Expert Board

Mary Reilly, M.D., Co-Chair, Clinical Expert Board

Frank Baas, M.D., Ph.D.

Robert H. Baloh, M.D., Ph.D.

Maurizio D'Antonio, Ph.D.

M. Laura Feltri, M.D.

Gabsang Lee, Ph.D.

Jun Li, M.D., Ph.D.

Rudolph Martini, Ph.D.

Albee Messing, VM.D., Ph.D.

Klaus-Armin Nave, Ph.D.

Brian Popko, M.D.

Mario Saporta, M.D., Ph.D.

Steven S. Scherer, M.D., Ph.D.

Lawrence Wrabetz, M.D.

Stephan Züchner, M.D., Ph.D.

David Herrmann, M.D.

Tage Honore, Ph.D.

Christopher Klein, M.D.

Lars J. S. Knutsen, Ph.D.

Claes Wahlestedt, M.D., Ph.D.

Richard Finkel, M.D.

Davide Pareyson, M.D.

Joshua Burns, Ph.D.

Michael McDermott, Ph.D., Consultant

ADVISORY BOARD

These CMT experts provide invaluable information on a wide range of topics including bracing, genetic counseling, physical and occupational therapy, emotional well-being, resources for parents and kids, disability benefits and surgery.

Jonah Berger, M.Ed.

Gregory Carter, M.D., M.S.

Bob DeRosa

Katy Eichinger, Ph.D., PT, DPT, NCS

Tim Estilow, OTR/L

Shawna Feely, M.S., CGC

Valery Hanks, OTR/L, C/NDT

Sarah Kesty, M.A.

Kate Lair, M.A, ALHC

Sean McKale, C.O., L.O.

Bethany Noelle Meloche

Tom Meloche

David Misener, B.Sc. (HK), CPO, MBA

Elizabeth Misener, Ph.D., LMSW

James Nussbaum, PT, Ph.D., SCS, EMT

Sabrina Paganoni, M.D., Ph.D.

Glenn Pfeffer, M.D.

Clark Semmes

Carly Siskind, M.S., CGC

Greg Stilwell, DPM

David Tannenbaum, LCSW

Amy Warfield, PT, DPT

STAFF

The CMTA's staff is filled with top talent and possesses a strong commitment to the vision of the organization – to create a world without CMT. Most members either have CMT, or they are personally connected to it through family and friends. They won't rest until there is a cure.

Amy Gray, Chief Executive Officer

Andi Cosby, National Events Manager

Frank Gaidjunas, Director of Marketing and Communications

Leslie Nagel, Marketing Coordinator

Kim Magee, Director of Finance and Administration

Laurel Richardson, Director of Community Outreach

Jeana Sweeney, Director of Development

Elizabeth Ouellette, Board Member, Full-Time Volunteer

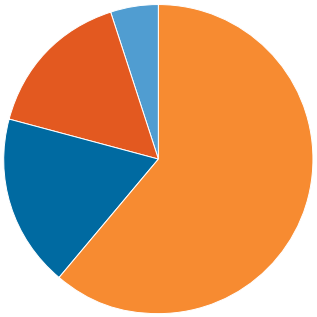
Consolidated Statement of Financial Position

December 31, 2017

More than 85% of expenditures are invested in our mission.

REVENUE

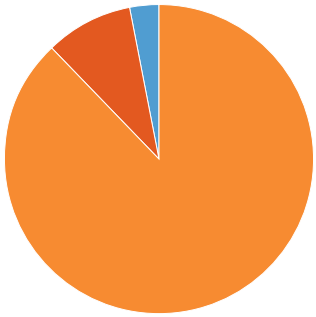
$3,138,829



- Contributions (62%)
- Special Events (18%)
- Branch Revenue (16%)
- Grants Received (4%)

TOTAL EXPENSES

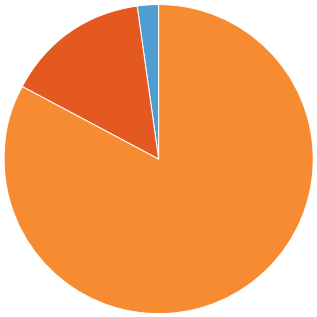
$2,539,687



- Mission Services (88%)
- Fundraising (9%)
- Management/General (3%)

MISSION EXPENSES

$2,239,791



- Research (83%)
- Education & Awareness (15%)
- Branches (2%)

REVENUE	**DECEMBER 31, 2017**
Contributions	$1,937,566
Special Events (net of expenses)	$555,460
Branch Revenue	$494,088
Grants Received	$151,314
Investment Income	$835
Sale of Promotional Products (net of expenses)	($434)
TOTAL REVENUE	**$3,138,829**
TOTAL EXPENSES	
Mission Services	$2,239,791
Fundraising	$216,448
Management/General	$83,448
TOTAL EXPENSES	**$2,539,687**
MISSION EXPENSES	
Research	$1,858,108
Education & Awareness	$338,744
Branches	$42,939
TOTAL PROGRAM EXPENSES	**$2,239,791**

Through your partnership,
we are progressing toward a cure.

P.O. Box 105
Glenolden, PA 19036

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