HEREDITARY NEUROPATHY FOUNDATION

cmtupdate

Impact That Matters

Driving CMT Research with the Patient's Voice

This update is dedicated in loving memory to HNF member, Alex Sofianakos

CMT UPDATE
WINTER 2023

Allison T. Moore
Founder and CEO
Hereditary Neuropathy Foundation

Dear CMT Community,

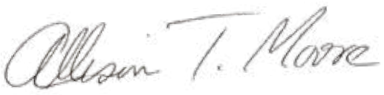
As we start the new year energized and ready to continue our mission of bringing treatments and cures for CMT, we have rebranded our *CMT Update* newsletter to feature our lead research programs including the GRIN patient registry, the HNF-funded research milestones that have been met, and how patients can continue to participate in the process. The *CMT Update* will continue to be published quarterly.

Originally launched in 2013, GRIN has evolved. What started as a single, natural history survey is now a series of surveys including: mental outlook, gastrointestinal, medical cannabis, a specific survey for an ultra-rare type of CMT called CNTNAP1, and a comprehensive head-to-toe series of NIH-funded, ClinGen surveys which we hope will help us to identify previously unrecognized comorbidities to CMT. Since launch, over 3000 registrants have shared their important diagnostic journey, signs and symptoms, how CMT impacts daily life, willingness to participate in research, and much more! Many thanks to Brian and Katie McCormack for their generous donation supporting GRIN.

To date, the data collected has helped HNF and its partners in industry, academia, and government characterize various types of CMT - describe clinical presentation, make symptom correlations and uncover important medical conditions resulting from CMT, such as pain and respiratory issues. All of this helps target our research spending based on actual patient need and the likelihood of success. GRIN has proven to be a premier resource to industry for enrolling patients in clinical research and trials. Several manuscripts, abstracts and poster presentations for professional conferences have come from analysis of GRIN data. When patients join GRIN, they are participating in research and impacting the future of treatments and cures.

Be sure to check back periodically as we share our progress and important insights that drive research and industry decision-making on therapy development.

Best,



Allison T. Moore

HNF developed the **Therapeutic Research in Accelerated Discovery (TRIAD)** as a collaborative effort with academia, government and industry, to develop treatments for CMT. Currently, TRIAD involves many groups that span the drug discovery, drug development, and diagnostics continuum.

TRIAD
THERAPEUTIC RESEARCH IN ACCELERATED DISCOVERY

HNF IS RESHAPING DRUG REPURPOSING FOR CMT

In this first 2023 issue, we ask that you help us prepare to advance one of our important Therapeutic Research in Accelerated Discovery (TRIAD) research initiatives, "Repurposed Drugs for CMT."

HNF has completed the Discovery stage with the identification of dozens of potential drug candidates for several types of CMT. Now we are initiating the Preclinical stage of the collaboration, during which the candidate drugs will be further tested for in vitro activity in cellular models of CMT.

HNF has partnered with Rarebase, a public benefit precision medicine company that has screened a large library of FDA-approved small molecules to identify candidates for various types of CMT. Their tech-enabled drug discovery platform is called Function™. There are many published discoveries on the genetic cause of many types of CMT, including an understanding of the basic mechanism of disease and potential targets for FDA-approved drug repurposing. It is this understanding that allows HNF and Rarebase to target the genetic root cause of CMT.

Unlike developing a brand-new drug, which costs tens to hundreds of millions of dollars and on average 10-17 years to bring a new drug to market, reports indicate that repurposed drugs may be approved within 3-12 years, on average. The HNF team is excited about this promising strategy of accelerating potential treatments much faster.

HNF thanks all those patients that provided blood samples to develop the cellular models that are needed for this next phase.

As a CMT patient and/or caregiver of a loved one with CMT, we need you to participate in research by joining GRIN.

grin.acrossmatrix.com

Can Existing Drugs Treat CMT?

HNF, in partnership with Rarebase, is leading the charge in the first-ever research initiative to tackle multiple types of CMT in one project using its tech-enabled drug discovery platform called "Function™." Rarebase is screening a compound library of thousands of FDA-approved and experimental drugs, targeting ten subtypes of CMT. Join Rarebase Co-Founder & COO, Omid Karkouti, as we dive deeper into this exciting new technology and what it means for treating CMT.

Click above image to watch webinar

Rarebase

3,884 FDA-Approved and experimental drugs were screened for...

5 Types of CMT;

14 Genes

CMT1:

CMT1A
(PMP22 dup)

HNPP
(PMP22 del)

CMT2:

CMT2A
(MFN2 & MFN2 w/ optic atrophy)

CMT2K
(GDAP1 recessive)

SORD Deficiency

CMT4:

CMT4A
(GDAP1 dominant),

CMT4B
(MTMR2),

CMT4F
(PRX)

CMT4J
(FIG 4)

CMT6:

Mitochondrial Disease
(MTRFR, C12orf65), often clinically diagnosed as Leigh Syndrome, Spastic Parapheligia-55, Behr Syndrome, COXPD, and Ataxia.

OTHER INHERITED NEUROPATHIES:
CNTNAP, ADOA (OPA1)

MILESTONES

Drug Repurposing for CMT

2022
Stage I:

Discovery (identified drug repurposing candidates)

◆ **Completed**

2022-23
Stage II:

Testing top candidates in CRISPR-engineered cellular models of disease for potency and activity.

◆ **In Progress**

2023- 2024
Stage III:

(If applicable) Conduct clinical trials on top candidate(s)

TRIAD
THERAPEUTIC RESEARCH IN ACCELERATED DISCOVERY

BREAKING NEWS

PHAR NEXT

Pharnext unveils the latest progress of the PREMIER Phase III clinical trial for CMT1A

The PREMIER trial, initiated in March 2021, is an international, randomized, double-blind, two-arm placebo-controlled, pivotal Phase III study, where the primary objective is to evaluate the efficacy and safety of PXT3003 versus placebo in mild-to-moderate CMT1A patients, over a 15-month period. The dose of PXT3003 tested in the PREMIER trial corresponds to the high dose (HD) tested in the prior Phase III clinical study, the PLEO-CMT trial, and its ongoing open-label extension Phase III study, the PLEOCMT-FU trial. As agreed with regulatory agencies, the primary efficacy endpoint will be the Overall Neuropathy Limitations Scale ('ONLS') which measures functional motor disability. A total of 387 patients with mild-to-moderate CMT1A, was enrolled in the PREMIER trial (exceeding the initial enrolment target of 350 subjects as defined in the study protocol): 153 in the United States, 183 in Europe, 39 in Canada and 12 in Israel.

The 15-month double-blind phase of the PREMIER trial is followed by an open-label extension phase named PREMIER-OLE (Open Label Extension). All patients who completed the double-blind phase of the PREMIER trial are eligible to join the open-label extension phase, PREMIER-OLE, and have the opportunity to receive PXT3003 HD until the treatment is commercially available, should PXT3003 be approved in the US and Europe, respectively by the FDA and the EMA. The first patient entered the PREMIER-OLE phase in September 2022.

Furthermore, Pharnext successfully completed the manufacturing transfer and scale-up of PXT3003 from Unither's facility in Colomiers, France, to Unither's U.S.A. facility in Rochester, New York to prepare for potential marketing authorization of PXT3003. PXT3003 is now able to be manufactured in batches of up to 3,500 liters of oral solution, a volume potentially compatible with a commercial supply chain of PXT3003 enabling a more convenient and flexible form for CMT1A patients to use, allowing for better compliance.

The topline results announcement of this study is planned in Q4 2023

GLOBAL REGISTRY FOR INHERITED NEUROPATHIES

"IS THIS SYMPTOM RELATED TO CMT?"

This is a frequent question asked by many individuals living with CMT and their loved ones. Most of us are familiar with the most common symptoms of CMT, such as foot drop and hand weakness. However, many less-recognized symptoms can be just as disruptive to our lives but have not yet been studied or linked to CMT. The rarer the symptom, the more uncertain and isolated we may feel.

How do we know if our symptoms are CMT-related, and how can we drive research to better answer this question?

On Wednesday, March 1 @ 7-8:30pm EST, HNF will host a LIVE CMT-Connect Webinar:

"Making Sense & Science of CMT Symptoms"

THIS 90-MIN LIVE WEBINAR WILL INCLUDE:

Is my symptom CMT-related?

- CMT symptoms checklist
- Most common CMT signs & symptoms
- Less common symptoms
- Finding support from Patient Resources

The importance of converting CMT-related social media discussions into structured queryable data

- CMT Advocate Kenneth Raymond shares his experience & expertise

How does HNF turn symptoms into science?

- The latest CMT symptom stats
- How GRIN improves CMT clinical trials
  - NEW Platform demo - Creating an account
  - Sneak peek at CMT surveys
- How data is shared & used by researchers & industry

LIVE Q&A

TO REGISTER FOR WEBINAR CLICK HERE:

https://us02web.zoom.us/webinar/register/WN_U5BeUJbeRLKOo3niUYl2nA

GRIN Coordinator Corner:

Joy Aldrich, the GRIN Coordinator, lives in Seattle, Washington, with CMT1A.

Joy is passionate about gourmet cooking, spending quality time with friends and her husband, Toby, and getting out and about with her service dog, Finn. Joy joined HNF eight years ago as a volunteer and officially joined as a staff member in Spring, 2016. "There isn't a corner of my life that CMT hasn't entered. It's intertwined with every aspect of my day, from small details to the most important choices of my life. No one understands CMT like those living with it every day. It's essential that we join GRIN to share our expertise to let researchers know how CMT impacts our daily lives."

JOIN GRIN

Turn CMT Symptoms into Science

39
Countries Represented

3422
Participants

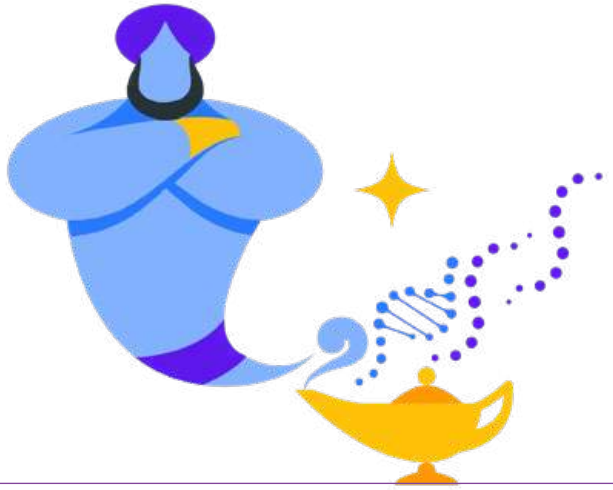
34
Types of CMT Represented

17.5%
Report Respiratory Issues

30%
of Patients Report Gastrointestinal Issues

Click!

JOIN GRIN



CMT GENIE

Despite the best efforts of our CMT community providing resources to obtain genetic testing, there are still barriers that remain challenging in obtaining a definitive diagnosis. HNF has changed that by developing the CMT Genie program. We are here to support and facilitate genetic counseling and provide immediate access to information and support for in-home testing and the translation of genetic reports to patients. Whether you need to learn more about variants identified in your DNA or seek further explanation of inheritance patterns, the CMT Genie is available to all patients and families affected by CMT, and for those that suspect CMT is the cause of their symptoms.

"The process was very easy. I met with Genome Medical and received the genetic test kit within a few days. The kit was well packaged in a small box and had everything I needed. Shortly after I shipped the kit back, I received an email to register online. Less than two weeks later, I received my test results – CMT1A, just as I suspected. Genome Medical notified me via text and email about scheduling a follow-up appointment to go over the results."

— Carrie H.

"I got the results which were negative. I am glad I did the testing, so I now know more than I did before about genetic variants I do not have. Kind of like Thomas Edison and his search for a filament for a light bulb."

— Jeff M.

Book a CMT Genie Call

Click here!

HNF
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- HNF Centers of Excellence
- The CMT Genie
- Join Team CMT
- Patient Resources

Global Registry for Inherited Neuropathies (GRIN):

A Patient-Powered Registry Boosts the Study of Charcot-Marie-Tooth (CMT) Disease

CMT is a genetic, degenerative neuromuscular disease that affects 1:2500 in the US and 2.5 million worldwide—many are still undiagnosed—and currently, there is no cure. CMT is progressive, and over time, muscles in the feet, legs, and hands lose strength. Muscles waste away and cause atrophy leading to mobility issues. It can have a serious impact on vision, hearing, breathing, speech, and swallowing in extreme cases. Some patients experience hip dysplasia, scoliosis, and/or blindness.

MISSION:
Global Registry for Inherited Neuropathies (GRIN) was developed to conduct patient-focused research and for the development of treatments and cures for Charcot-Marie-Tooth (CMT). GRIN is the only comprehensive patient registry collecting patient-reported information about living with CMT in combination with genetic reports, electronic health records, and other critical data for research. The patient voice is at the forefront of all we do.

The Hereditary Neuropathy Foundation mission is to increase awareness and accurate diagnosis of Charcot-Marie-Tooth (CMT) and related inherited neuropathies, support people living with CMT and their families with critical information to improve quality of life, and fund research that will lead to treatments and cures.

www.hnf-cure.org

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