# Charcot-Marie-Tooth Disease Type 2C (CMT2C)

# Patient Focus Group Meeting

June 22, 2023

# EXECUTIVE REPORT

**Prepared by:**
*The Charcot-Marie-Tooth Association (CMTA)*
*PO Box 105*
*Glenolden, PA 19036*
***In partnership with:** Actio Biosciences*

# Contents

# Background

On June 22, 2023, the Charcot-Marie-Tooth Association (CMTA), in collaboration with Actio Biosciences (Actio Bio), hosted a virtual patient focus group for individuals diagnosed with Charcot-Marie-Tooth Disease Type 2C (CMT2C), also known as TRPV4 Neuropathy.

Engaging volunteer experts from the CMT2C patient community, the patient focus group meeting centered around capturing the CMT2C patient journey, identifying existing unmet needs, and gathering valuable insights on future treatment goals. Moderated by CMTA, patient participants were given a platform to directly share their experiences in a manner that will contribute towards new advancements in research and the development of new potential treatments for CMT2C.

Focus group participants were asked to complete a secure digital survey prior to the meeting. A combination of the survey responses submitted [14 participants] and verbal responses captured during the focus group meeting [9 participants] are presented in this report.

**CMTA and Actio Biosciences thank all CMT2C patient focus group participants.**

## Summary: Key Insights & Findings

- There is an urgent need for advancements in research and the development of new therapeutic options for the CMT2C community.
- Patients need diagnostic improvements that reduce the timeframe between the first appearance of symptoms and receiving the CMT2C diagnosis—reducing the diagnostic odyssey (average time to diagnosis). Participants reported a 14.6-year-long diagnostic odyssey.
- A high percentage of patients in the focus group have undergone genetic testing (13/14, 92.9%).
- Patients experience a profound decline in their ability to perform everyday tasks as their CMT2C symptoms progress, with challenges including vocal cord function, mobility and respiratory impairments and other areas impacting ability to perform tasks of daily living
- The CMT2C community is in urgent need of new therapies to help manage the entire spectrum of disease severity and to slow or stop its progression.
- There is an active and engaged CMT2C support group on Facebook for patients and caregivers to connect with each other and share information.
- CMT2C patients can help advance research and the development of new therapies by participating in the CMT2C Natural History Study at John Hopkins University.

## Participants Demographics (n=14)

- The age of participants ranged from 4.7 years (represented by a parent) to 76.8 years. The average age was 43.1 years.
- Participants included 9 females and 5 males.
- Nine (9) participants identified as Caucasian/White, 2 Asian, 1 Italian, 1 Kashmiri, and 1 Hispanic/White.
- Over 92% of participants (13/14) were based in the United States, and one participant was based in Hungary.

## CMT2C Patient Journey: From Diagnosis to Current Management

### A. Age of Onset

Participants reported CMT symptoms appearing as early as birth, and as late as age 62. The average age of symptom onset was 7.8 years.

Various initial symptoms were reported, including vocal cord weakness, difficulties walking/standing, club feet, breathlessness, hand weakness, hearing loss, clumsiness, numbness in toes, and deformities in the hands, legs, and feet.

### B. Diagnostic Odyssey: Timeframe Between Onset & Diagnosis

Every participant reported a different length of time between symptom onset and receiving their CMT2C diagnosis.

During this timeframe, many participants reported having to seek out multiple specialists for their diagnosis. In some cases, participants also reported they had been misdiagnosed with other, often more common diseases. Some of these misdiagnoses included Spinal Muscular Atrophy (SMA), Perennial Scapular Atrophy, Axonal Neuropathy, and Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP).

The average timeframe between symptom onset and receiving their CMT2C diagnosis was **14.6 years.**

### C. CMT2C Diagnosis

The age of the CMT2C diagnosis ranged from 9 months to 42 years. The average age was 22.3 years.

Of the 14 survey participants, 13 (92.9%) confirmed they had undergone genetic testing, with only 1 participant reporting they "did not know." Of the 13 participants who had, testing confirmed CMT type and subtype in 12 (*92.3%) of those tested.*
In addition to genetic testing, 50% of participants reported undergoing physical examinations and nerve conduction studies by their physician. Three (3) participants also reported having a family history of CMT2C.

## D. Daily Impacts of CMT2C

Participants experienced a profound decline in their ability to perform everyday tasks as their CMT2C symptoms progressed. Notable challenges included:

- Vocal cord impairments limiting ability to communicate.
- Lost ability to work – can no longer type or use a calculator.
- Reduced ability to manage household tasks, cleaning, cooking, etc.
- Stairs are particularly difficult.
- Can’t walk far, not able to walk without assistance/supervision.
- Needs help going to the toilet.
- Reliance on a wheelchair for anything over 100 yards.
- Travel is a huge ordeal - requires an oxygen tank and a lot of preparation and planning.
- Any activity outside of the house – I have become a recluse.
- Getting to a bathroom on time.
- Respiratory function weakness requiring use of a breathing machine/ventilator at night.
- Hearing loss and use of hearing aids, difficult to function without them.
- Full 24-7 care needed.
- Cannot eat and has to use a feeding tube.
- Any physical task requires regular breaks every 15-20 mins.
- Can’t keep up with others/my friends.
- Anything using my hands is difficult, can’t open things.
- Can’t get in and out of my own home.

## E. Psychological Impacts of CMT2C

*Diagnosis*

Participants reported a wide spectrum of emotions in the months following the CMT2C diagnosis. Many shared that it was a relief to finally find out what was wrong and have a name for it, but that it was quickly replaced by feelings of hopelessness, knowing that there were no available treatments to help them.

Participants with children also reported treading a fine line, wanting to be open and honest but not wanting to share their struggles or talk about them too much through fear of worrying their children.

Beyond diagnosis, participants also reported feelings of depression, dependency, and social isolation due to the progressive loss of fine motor skills and advancing disability.

## F. Symptom Management & Treatments

There are currently no approved therapies for the treatment of CMT2C. Participants also reported a lack of available medications to address the symptoms of their disease, further highlighting a clear unmet need and a requirement for the development of new therapies.

While not all participants reported experiencing pain, 2 participants reported using Tylenol, and 1 participant a Fentanyl patch, for pain management.

Despite the lack of available therapies, participants reported using non-invasive ventilators (for nighttime use), orthotic braces, and various adaptive devices to help with symptom management. One participant reported using vibration therapy below their knees prior to going to bed to help improve their sleep.

## G. New Treatment Goals

Outside of a complete cure, participants were asked to list the top three (3) things they hope a new potential therapy would address. Categorizing the responses in order of those most frequently reported (from top to bottom), participants said they would like any new treatment to:

1) Slow and/or stop disease progression.
2) Improve respiratory function; prevent and/or eliminate the need for a ventilator at night.
3) Improve mobility/balance.
4) Prevent, stop, and/or restore vocal cord deterioration.
5) Prevent/restore hearing loss.
6) Improve hand function/prevent numbness and pain in hands.
7) Improve muscle strength in upper and lower extremities.

Capturing the conflict that some patients feel about their disease, one participant said, "I don't need to get anything back; I'm ok with just stopping it from *getting worse. My identity is woven up in CMT2C; I feel strange about there being a cure. I'm ok with minimizing further decline."*

Another participation shared,
"I have to continuously ask someone else for help, and by the end of the day, I'm mentally at a low point - It feels infantilizing to need help with literally everything."

## H. Where do you go to find new information about CMT2C?

Participants reported the following sources of information and community support:

- CMTA's Patients as Partners in Research program sends CMT2C news and information by email when there are opportunities to participate in natural history studies, etc. I created a profile and shared my subtype so they can let me know about 2C developments.
- The CMT2C Facebook group.
- The CMTA Facebook page and discussion group are great for community support.
- NIH NCBI PubMed – can set up alerts with CMT2C and TRPV4 keywords so I receive an email when new scientific papers are published.
- ClinicalTrials.gov website maintained by the NIH – link to TRPV4 Natural History Study listing.
- From the research team at Johns Hopkins University (home of CMT2C Natural History Study).

## I. Would you be interested in participating in a clinical trial for CMT2C at some time in the future? Why, or why not?

Participants were asked to think about what factors might prevent them from taking part.

All participants responded positively that they would be interested in participating in a clinical trial. Here is a summary of their additional feedback and barriers to participation:

- Yes, 100 time yes, I would want to take part. I know there would be some risk, but I think it would be as mitigated as it can be. Willing to do it not just as a benefit to me but to be a benefit to others.
- I can't lie down on my back; there needs to be testing/assessments for those of us who can't lie flat due to CMT-related breathing impairment. If we can find a way to get around this before the study starts, that would be good.

- I would be concerned about privacy and about information being shared with people beyond our group, but I would be willing to participate.
- Yes, I would be interested. One concern would be if I could die from it (the treatment).
- Cost of travel may prevent participation.
- We are not based in the US, so would depend on how many times we would have to travel.
- Travel is difficult. I can't fly. Travel is exhausting. Would improve access if some testing could be done locally, using the CMTA Center of Excellence network.

**J. <u>If you could pick one thing to say to a company working on CMT2C, what would you tell them? Or in other words, what do you believe is most important for the company to know?</u>**

- Thank you for picking a disease to study that not a lot of people are afflicted with. If there is something that comes from this work, our lives would be changed, unbelievably so, so thank you.
- Thank you, it's a small patient group, but people's lives are severely affected. I hope you continue with your research, and I will help with that in any way.
- Thank you. You are our hope.
- Thank you for your interest and determination. You could completely change people's lives. There could still be a lot of people undiagnosed, so it could be a big patient group.
- Thank you to Johns Hopkins and CMTA for their work on 2C. If there is anything I can do to support please let me know.

## References

(1) McCray BA, Schindler A, Hoover-Fong JE, et al. Autosomal Dominant TRPV4 Disorders. 2014 May 15 [Updated 2020 Sep 17]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK201366/

## About CMTA

The CMTA is a community-focused, community-driven 501(c)(3) nonprofit organization with a mission to support the development of new treatments for CMT, to improve the quality of life for people with CMT, and, ultimately, to find a cure. As the leading global philanthropic funder of CMT research, the CMTA unites the community with clinicians and industry experts to accelerate the advancement of treatments, with investments of more than $24 million since 2008. For more information, visit https://www.cmtausa.org

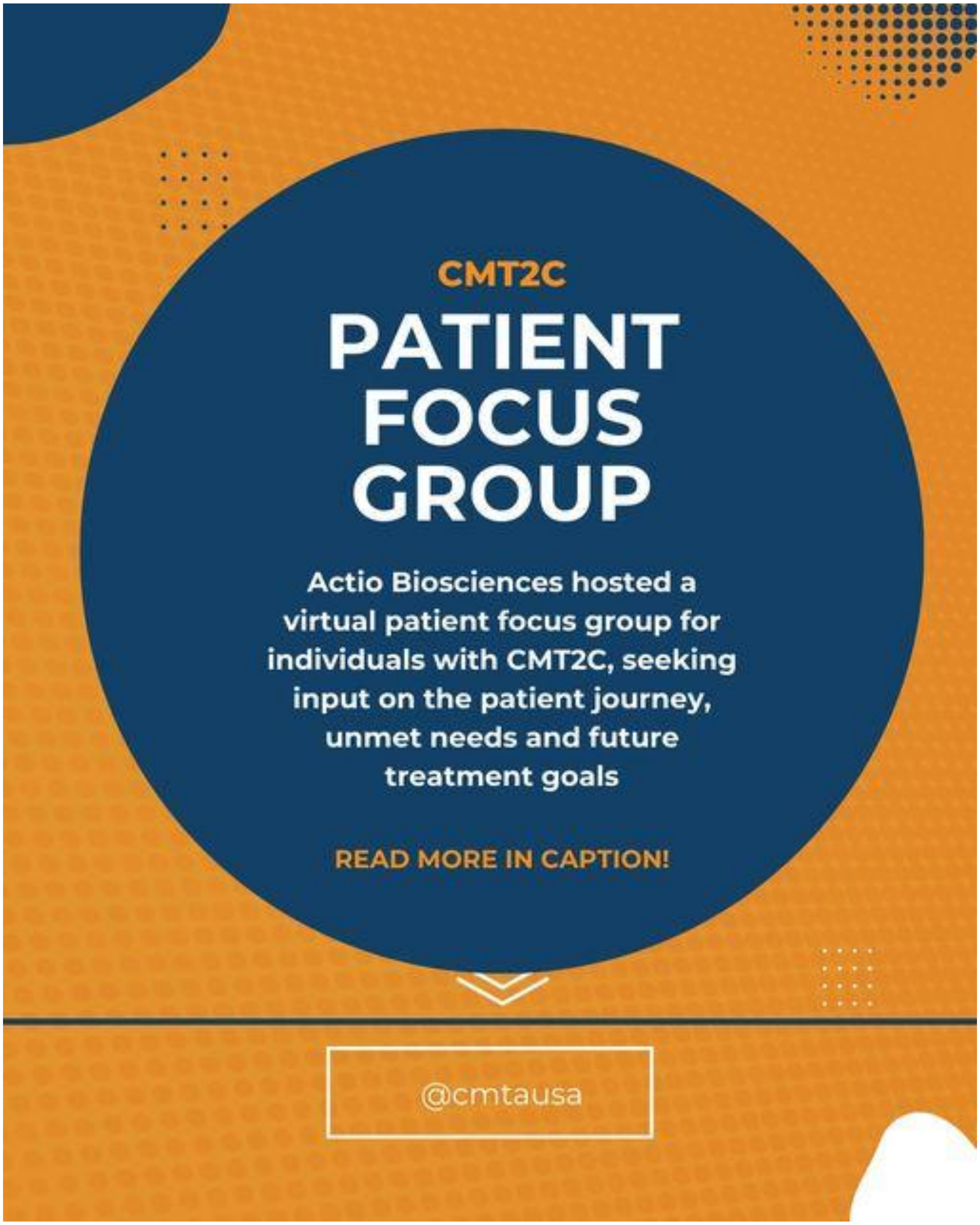
## About Actio Biosciences

Founded in October 2021, and headquartered in San Diego, CA, Actio Biosciences is leveraging advances in precision medicine to develop new therapeutics that target shared genetics in rare and common diseases—bringing meaningful medicines from one to many. Actio Biosciences in preclinical development of an oral, small molecule inhibitor of TRPV4 for the treatment of CMT2C.
For more information, please visit ActioBiosciences.com.

## APPENDIX

A copy of the Survey that was completed by all participants ahead of the focus group meeting is here

https://forms.office.com/r/8zFedDHYzV?origin=lprLink



Actio Biosciences hosted a virtual patient focus group for individuals with CMT2C, seeking input on the patient journey, unmet needs and future treatment goals