Scarlett smiles for the camera with her mom

AXONAL CMT: TYPE 2 STAR RESEARCH

One of the most exciting areas of progress in Type 2 research has been the development of gene therapy for spinal muscular atrophy (SMA), which affects the same motor neurons that are affected in CMT2.

GENE THERAPY

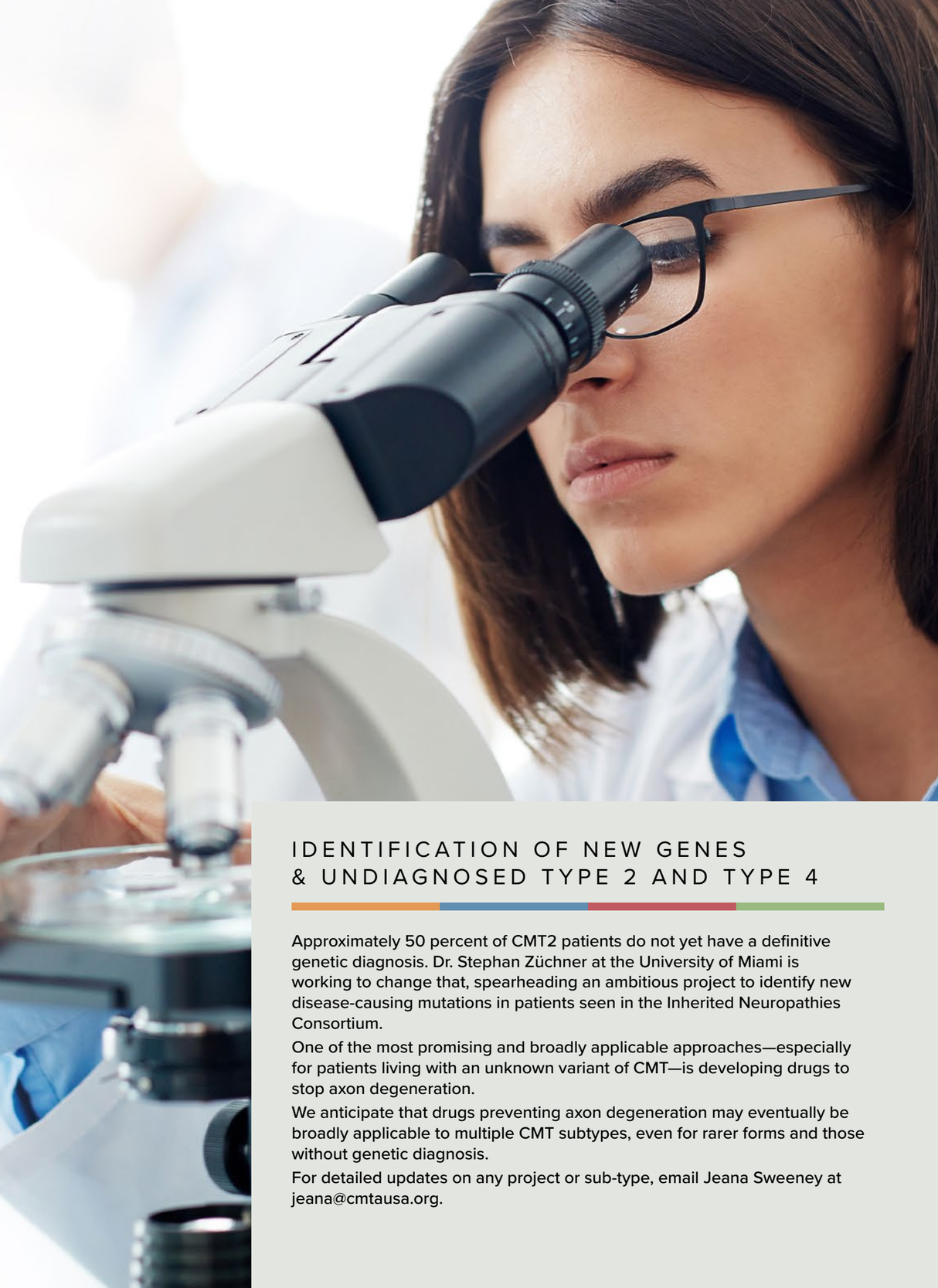
The CMTA is:

- Supporting pilot studies of gene therapy in CMT mouse models after convening a meeting of gene therapy experts to outline the next steps in bringing this therapeutic strategy to CMT2.
- Recruiting leaders in the gene therapy field to our Scientific Advisory Board to guide our efforts in this area.
- Following a gene therapy trial for one peripheral neuropathy (GAN) at the National Institutes of Health. Parallel initiatives are also underway for CMT4J and CMT2S, and projects for several additional types of axonal CMT are in the planning stage.
- Partnering with Dr. James Wilson at the University of Pennsylvania and Passage Bio to use gene therapy to treat CMT2A.
- Funding work with two eminent experts, Drs. Bruce Conklin and Luke Judge of the Gladstone Institutes and UCSF Departments of Medicine and Pediatrics, to explore applying the new technology of genome editing (CRISPR) to CMT2A, CMT2E and CMT2F.

SMALL MOLECULE THERAPIES

As noted above, the progression of all types of CMT occurs as the longest axons are lost in a process called axon degeneration.

- CMTA partners are working on developing chemical inhibitors of recently identified biochemical triggers of axon degeneration. The CMTA plans to explore the applicability of this recent technology to multiple forms of CMT2 using the many models of CMT that have been generated within our network.
- The most common cause of CMT2A is mutation of the Mitofusin 2 gene. Researchers have recently identified custom-designed molecules that can stimulate the activity of mitofusin proteins and we are discussing with them the possibility of testing this therapy in our recently developed rat models of CMT2A.
- We are funding Dr. Mario Saporta's work at the University of Miami using human stem cells to develop assays and test additional libraries of drugs for treatment in CMT2E.
- We are supporting work in Dr. Ron Liem's lab at Columbia University to screen already FDA-approved compounds to treat CMT2E.



IDENTIFICATION OF NEW GENES & UNDIAGNOSED TYPE 2 AND TYPE 4

Approximately 50 percent of CMT2 patients do not yet have a definitive genetic diagnosis. Dr. Stephan Züchner at the University of Miami is working to change that, spearheading an ambitious project to identify new disease-causing mutations in patients seen in the Inherited Neuropathies Consortium.

One of the most promising and broadly applicable approaches—especially for patients living with an unknown variant of CMT—is developing drugs to stop axon degeneration.

We anticipate that drugs preventing axon degeneration may eventually be broadly applicable to multiple CMT subtypes, even for rarer forms and those without genetic diagnosis.

For detailed updates on any project or sub-type, email Jeana Sweeney at jeana@cmtausa.org.