CMTA Funds Preclinical Work on Modulating Unfolded Protein Response in CMT1B Mice

GLENOLDEN, PA, USA, April 25, 2023 /EINPresswire.com/ -- The Charcot-Marie-Tooth (CMT) Association announced a $33,000 grant on April 25 that will enable Maurizio D'Antonio, PhD, to establish if molecules that selectively activate the ATF6 pathway of the Unfolded Protein Response (UPR) can engage targets in the peripheral nerves of CMT1B mouse models. If so, D'Antonio and his team at San Raffaele Scientific Institute in Milan, Italy will perform a time-course study to identify the best dosing strategy.

CMT1B neuropathy is caused by a mutation in the myelin protein zero (MPZ/P0) gene. It is one of the four most prevalent types of CMT, causing around 5 percent of cases. The mutated protein causes deficits within the myelin sheath, which insulates the nerve and is needed for efficient transmission of nerve impulses. Retention of the mutant protein within cells and activation of cellular stress pathways such as the UPR are a common disease-causing mechanism among MPZ mutations.

D'Antonio and his team have been studying the role of the UPR in demyelinating neuropathies for many years, and the CMTA has funded previous research in this area. This has enabled the team to collect strong evidence that the UPR pathways are a good target for therapies to treat CMT1B and CMT1A.

"Modulation of the UPR is emerging as an exciting therapeutic option for many conditions, including demyelinating types of CMT," D'Antonio said, adding: "Thanks to the CMTA funding we will establish if targeting the ATF6 pathway is a viable option for CMT1B. Positive results will allow us to quickly move to preclinical trials in different CMT1B models with selective activators of ATF6."

D'Antonio will also explore the possibility of combinatorial therapies targeting multiple UPR pathways simultaneously, which may result in a synergistic beneficial effect. Positive results would stimulate the development of these compounds for clinical trials.

CMT is a progressive hereditary disease of the peripheral nerves that causes people to lose the normal use of their hands, feet and legs. Symptoms include sensory loss, foot deformity (very high arched feet) and foot drop (inability to hold foot horizontal); a slapping gait (feet slap on the floor when walking); loss of muscle; numbness; difficulty with balance and walking. Hands and arms may also be affected. CMT affects approximately one in 2,500 people, or around 3 million people worldwide.

About the CMTA:
The CMTA is a patient-led nonprofit whose mission is to cure CMT. It does so with an aggressive, multipronged attack, bringing together a group of top-flight researchers and experts and directly funding their work. The CMTA launched its Strategy to Accelerate Research, or STAR, in 2008 to capitalize on breakthroughs in genetics and dramatically speed up the pace of CMT research. Since then, the CMTA has invested more than $23.5 million in STAR and has made great strides toward developing treatments for CMT.

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