Cartesian Therapeutics Announces Landmark Study in The Lancet Neurology of First Successful Clinical Trial of RNA Cell Therapy in Autoimmunity

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Modifying patients' T-cells with mRNA to express a chimeric antigen receptor (rCAR-T therapy), a novel approach to treat myasthenia gravis and other autoimmune diseases.

Gaithersburg, MD —June 22, 2023 – Cartesian Therapeutics, a clinical-stage biotechnology company pioneering cell therapies for autoimmune diseases, announced today the publication of a landmark paper in *The Lancet Neurology.* The study describes Descartes-08, a cutting-edge RNA CAR-T (rCAR-T) therapy administered to patients with generalized myasthenia gravis (MG), a debilitating autoimmune neurological disease. The data demonstrate marked and long-lasting clinical improvement in patients with MG. This is the first clinical trial using rCAR-T to treat autoimmunity, and the first successful Phase 2 trial using an engineered cell therapy to treat autoimmunity.

"Conventional, DNA-engineered CAR T-cells are highly effective in treating several blood cancers, but associated toxicities and the need for lymphodepletion chemotherapy limit their use beyond oncology," said Dr. Miloš Miljković, Chief Medical Officer at Cartesian. "To expand the capabilities of cell therapy to new areas and improve safety, we engineered CAR T-cells with RNA and used them to treat patients with MG."

The study enrolled 14 patients with generalized MG. Patients received 6 infusions of rCAR-T therapy, administered as an outpatient treatment, without lymphodepletion. Patients were followed for a median duration of 6 months (range: 3–9 months). rCAR-T was well tolerated, with no dose-limiting toxicities, cytokine release syndrome, or neurotoxicity. Clinical improvements were marked and long-lasting across four validated MG disease scoring systems. Strikingly, at 6 months, the average improvements were about 3-fold greater than thresholds considered clinically meaningful. Clinical benefit was sustained long-term for most patients, even months after completing the course of therapy. Three patients achieved complete or near-complete eradication of all disease symptoms; two other patients who relied on chronic IVIg therapy prior to enrollment ceased to need this therapy after Descartes-08 treatment.

"Currently, the mainstay of myasthenia therapy is chronic use of broad immunosuppression, which has many drawbacks," said Dr. James Howard, Professor of Neurology at University of North Carolina – Chapel Hill and a senior author on the paper. "The prospect of inducing potent, durable responses and reducing or eliminating use of immunosuppressive therapy is very appealing to the myasthenia community. Based on the compelling results of this paper, we are now enrolling patients with MG into a randomized placebo-controlled study, the first study of its kind for an engineered adoptive cell therapy."

"We are grateful to our community of MG patients and physicians for enabling clinical development of novel therapeutics such as rCAR-T," said Samantha Masterson, President & CEO of Myasthenia Gravis Foundation of America. "A safe, personalized therapy with durable clinical benefit would be a welcome addition to the growing toolkit of MG treatments."

The results described in *The Lancet Neurology* suggest that rCAR-T may be useful in treating a variety of other autoimmune diseases and may overcome many of the risks and toxicities associated with conventional DNA-based CAR-T cells.

The full paper, titled "Safety and Efficacy of Autologous RNA Chimeric Antigen Receptor T-cell (rCAR-T) Therapy in Myasthenia Gravis: a prospective, multicenter, open-label, non-randomized phase 1b/2a study", is available online, along with an accompanying commentary on the paper by Dr. Andreas Meisel, Professor of Neurology at the NeuroCure Clinical Research Center in Berlin. In addition to Dr. Howard, the paper is co-authored by Dr. Tahseen Mozaffar of University of California – Irvine (co-senior author), Drs. Volkan Granit and Michael Benatar of University of Miami (co-first authors), Dr. Nizar Chahin of Oregon Health and Science University, Dr. Gregory Sahagian of Neurology Center of Southern California, Dr. Marc Feinberg of SFM Research – Boca Raton, Dr. Adam Slansky of Neurology Associates – Orlando, Dr. Tuan Vu of University of South Florida, and other members of the MG-001 Study Team. The study was funded in part by the National Institutes of Health (NIH) with a grant from the National Institute of Neurological Disorders and Stroke (NINDS grant NS115426).

About MG

Myasthenia gravis (MG) is a chronic autoimmune disorder that causes disabling muscle weakness and fatigue. For most people with MG, the disease is characterized by the presence of antibodies against the acetylcholine receptor, a protein found on the surface of nerve cells that plays a key role in muscle contraction. There is currently no cure for MG, and treatment typically requires chronic immunosuppressive medicines, with their attendant risks and side effects.

About MGFA

The Myasthenia Gravis Foundation of America (MGFA) is the largest, leading patient advocacy organization solely dedicated to finding a cure and improved treatments for the rare neuromuscular disease myasthenia gravis (MG). We fund the most promising critical research discoveries and provide patient-centric programs and educational materials to connect members of the global MG Community and improve the lives of those living with MG. You can visit MGFA at myasthenia.org.

About Descartes-08

Descartes-08 is a first-in-class rCAR-T in clinical development for MG and other autoimmune diseases. Compared to conventional DNA-based CAR T-cell therapies, rCAR-T does not require lymphodepletion chemotherapy, has predictable and controllable pharmacokinetics, and avoids the risk of genomic integration. These attributes are expected to make Descartes-08 safer than DNA-based cell therapies. Descartes-08 is a personalized (autologous) therapy during which cells are collected, engineered with RNA, and returned to the same individual in an outpatient setting. A course of therapy consists of six weekly infusions. For more information about enrolling into the Phase 2b trial, visit cartformg.org.

About Cartesian Therapeutics

Cartesian is pioneering RNA cell therapies for autoimmune diseases and cancer. The company's lead asset, Descartes-08, is a first-in-class, RNA-engineered chimeric antigen receptor T-cell therapy (rCAR-T) in Phase 2b clinical development for patients with generalized myasthenia gravis. Cartesian operates a wholly owned, state-of-the-art cGMP manufacturing facility in Gaithersburg, MD. For more information visit cartesiantherapeutics.com.

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