Amlogenyx

Amlogenyx Presents Preclinical Data on AM805, a Potentially Transformative Investigational Gene Therapy for Alzheimer's Disease

A novel approach using a lysosomal enzyme to prevent and reverse amyloid accumulation inside as well as outside neurons, with greater potency, delivered in a one-time gene therapy

The therapeutic strategy has the potential to clear amyloid storage inside dysfunctional neurons and restore function, superior to monoclonal antibody drugs that just slow cognitive decline

The program has a regulatory path set in the U.S. and UK, heading to a clinical trial in 2027

Data highlighted in an oral presentation at the 2026 American Society of Gene & Cell Therapy (ASGCT) Annual Meeting

NOVATO, Calif. — May 13, 2026 — Amlogenyx, Inc., a biotechnology company focused on developing gene therapies for Alzheimer's disease and other neurodegenerative diseases, today announced preclinical data demonstrating that its investigational AAV9-mediated gene therapy, AM805 (AAV9-PPCA), substantially reduces both intracellular and extracellular amyloid-β (Aβ42) across multiple Alzheimer's disease (AD) models. The findings will be discussed in an oral presentation at the 2026 American Society of Gene & Cell Therapy (ASGCT) Annual Meeting.

"Targeting amyloid within the lysosome using a catalytic enzyme offers a fundamentally different and potentially more effective approach to treating Alzheimer's disease than current antibody-based approaches," said Emil Kakkis, MD, PhD, Chairman of the Board at Amlogenyx. "Notably, in the studies presented at ASGCT, reduction of intracellular amyloid correlated more strongly with functional improvement than extracellular plaque reduction alone, including in preclinical models of later-stage disease, reinforcing the role of intracellular Aβ42 as a key driver of neurotoxicity. We believe these findings support AM805 as a potentially transformational therapy capable of halting, or even reversing, the course of this devastating disease, and look forward to advancing into the clinic in the coming year."

Accumulation of amyloid is an established driver of Alzheimer's disease, disrupting cellular homeostasis by impairing synaptic function, activating microglia, and triggering chronic

neuroinflammation. Lysosomal dysfunction is increasingly recognized as playing a central role in intracellular amyloid accumulation. Protective protein/cathepsin A (PPCA) is a lysosomal enzyme that cleaves the C-terminus of Aβ42, preventing oligomer formation and can degrade monomeric, oligomeric, and even high-molecular-weight amyloid species while also restoring proper lysosomal acidification and function.

In 5xFAD and Tg2576 mouse models, AM805 significantly reduced both intraneuronal Aβ42 accumulation, including amyloid localized to neuronal cell bodies and axons, as well as the size and number of amyloid plaques outside the cells. Higher levels of PPCA expression were associated with up to 60–80% reductions in amyloid burden, which is comparable to– and in many cases, exceeds– levels reported for approved Alzheimer's disease monoclonal antibodies. Results were consistent across multiple routes of administration and in animals with established pathology at the time of dosing.

Intrathecal administration of AM805 was well tolerated at therapeutically relevant doses, with no significant adverse findings. The safety and efficacy findings also highlight the importance of a unique cross-correcting mechanism of AM805, where PPCA secreted from a small fraction of transduced cells is taken up by neighboring cells to enable widespread amyloid clearance, even in regions with lower direct transduction, enabling therapeutic benefit at relatively low gene therapy dosing.

The data will be discussed at 11 a.m. ET on May 13 in an oral presentation titled "Transforming treatment of Alzheimer's with AAV-mediated delivery of the lysosomal amyloid cleaving protease, protective protein/cathepsin A (PPCA) by successfully reducing both intracellular and extracellular amyloid."

The Company plans to pursue an Investigational New Drug (IND) application submission to the U.S. Food and Drug Administration for AM805 later this year and initiate a Phase 1/2 study in 2027.

About Alzheimer's Disease

Alzheimer's disease is a progressive, degenerative brain disorder and the most common cause of dementia, gradually affecting memory, thinking, behavior, and the ability to carry out daily activities. It is characterized by changes in the brain that begin years before symptoms appear and worsen over time. A hallmark of the disease is the abnormal accumulation of amyloid in the brain, which is believed to play an important role in the development and progression of Alzheimer's. Alzheimer's affects millions of individuals and families worldwide, underscoring the urgent need for continued research, earlier detection, improved treatments, and comprehensive support for patients and caregivers.

About AM805

AM805 is a novel protease delivered via AAV9 gene therapy for the treatment of Alzheimer's disease that functions to reduce amyloid, a biomarker that helps predict the progression of Alzheimer's disease. AM805 utilizes an AAV9 gene therapy vector to deliver protective protein cathepsin A (PPCA), a lysosomal carboxypeptidase that degrades amyloid, directly to the brain. AM805 has been shown to substantially reduce amyloid (Aβ42) in preclinical models of Alzheimer's disease – beyond the capabilities of traditional monoclonal antibody treatments. This investigational one-time gene therapy for Alzheimer's disease has the potential to significantly alter the course of the disease by preventing and reversing amyloid plaque build-up and promoting neuronal health.

About Amlogenyx

Amlogenyx is dedicated to the development of a novel gene therapy strategy to reduce amyloid accumulation in the brain in order to prevent and treat diseases such as Alzheimer's disease. Treatment with monoclonal antibodies to reduce amyloid has been shown to potentially slow the disease but not stop or reverse it, underscoring the need for improved treatment options. The Company is developing AM805, a novel protease therapy shown to reduce amyloid (Aβ42) accumulation in preclinical models of Alzheimer's disease. Amlogenyx is a subsidiary of Ultragenyx. For more information on Amlogenyx, please visit the company's website at: https://www.amlogenyx.com/.

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