LEXEO Therapeutics Announces Data Presentations at the 25th American Society of Gene & Cell Therapy (ASGCT) Annual Meeting

– *Preclinical studies support clinical development of pipeline programs, including novel gene therapies for the treatment of genetically defined cardiovascular and central nervous system diseases*

NEW YORK – May 3, 2022 (GLOBE NEWSWIRE) – LEXEO Therapeutics (LEXEO), a clinical-stage gene therapy company advancing a pipeline of adeno-associated virus (AAV)-based gene therapy candidates for genetically defined cardiovascular and central nervous system (CNS) diseases, today announced that new preclinical data supporting its plakophilin-2 (*PKP2*) arrhythmogenic right ventricular cardiomyopathy (ARVC) program, Friedreich's ataxia (FA) cardiomyopathy program, and second-generation *APOE4* Alzheimer's disease program will be presented at the 25th Annual Meeting of the American Society of Gene & Cell Therapy (ASGCT), which is being held live in Washington, D.C. and virtually from May 16-19, 2022.

"This year we are presenting important preclinical data supporting our most advanced cardiovascular gene therapy programs in FA and ARVC," said Nolan Townsend, Chief Executive Officer of LEXEO. "The advances in these programs and others will help bolster our leadership position in the cardiovascular gene therapy category."

Four abstracts, including two oral presentations, were selected for ASGCT. Details of each presentation are as follows:

Title: Plakophilin-2 Gene Therapy Prevents and Rescues Arrhythmogenic Right Ventricular Cardiomyopathy in a Novel Mouse Model Harboring Patient Genetics
Presenter: Farah Sheikh, Ph.D., University of California San Diego, School of Medicine
Date/Time: Tuesday, May 17, 2022 at 5:30 PM ET
Session Title: AAV Vectors – Preclinical and Proof-of-concept Studies II
Abstract Number: 543

- **Abstract highlights:** A preclinical study of a novel mutated *PKP2* knock-in mouse model that recapitulates all classic ARVC disease features found that early and late administration of PKP2 via AAV represents an effective and clinically relevant approach to prevent and rescue ARVC disease development. Study researchers hypothesized that PKP2 protein dose is a critical driver of ARVC, and that *PKP2* gene therapy via AAV strategies can prevent and rescue ARVC development. The data suggest that a one-time early-stage administration of AAV-PKP2 was sufficient to restore PKP2 protein to wild type levels and completely prevent (i) cardiac desmosomal and gap junction dissolution, (ii) cardiac right and left mechanical dysfunction, (iii) cardiac electrical dysfunction, and (iv) pathological cardiac tissue remodeling (fibrosis) in adult *PKP2* mutant mice at 4 weeks of age. Survival analyses further highlighted 100% survival of adult *PKP2* mutant mice up to 6 months of age with early stage AAV-PKP2 administration, and that a one-time late stage (4-week-old mice) administration of AAV-PKP2 had immediate benefit with 100% survival 4 months post-injection.

Title: Identification of the Minimum Therapeutic Intravenous Dose of AAVrh.10hFXN to Treat the Cardiac Manifestations of Friedreich's Ataxia
Presenter: Carlos Munoz Zuluaga, M.D., Weill Cornell Medicine
Date/Time: Wednesday, May 18, 2022 at 5:30 PM ET

Session Title: AAV Vectors – Preclinical and Proof-of-concept Studies III
Abstract Number: 936

- **Abstract highlights:** This preclinical study identified a therapeutically effective dose of AAVrh10 expressing human FXN (AAVrh.10hFXN) that has the potential to be clinically relevant for the treatment of the cardiac manifestations of FA. Assessment by echocardiography demonstrated that a dose of $1.8x10^{12}$ gc/kg (qPCR determined) led to a beneficial outcome with significant improvement in ejection fraction and fractional shortening compared to untreated mice. This dose mediated a 21.5 % improvement in mortality. In nonhuman primates, the levels in the heart were comparable to levels in the range estimated necessary to convert the FA homozygote to an FA heterozygote, which based on prior research, present no clinical manifestations of FA.

Additional presentations highlighting LEXEO's pipeline and platform technology include the following:

Title: Second Generation AAV-mediated Gene Therapy to Mitigate Risk for Alzheimer's Disease in APOE4 Homozygotes
Presenter: Rachel A. Montel, Ph.D., Weill Cornell Medicine
Date/Time: Wednesday, May 18, 2022 at 5:00 PM ET
Session Title: Novel Therapeutic Targets to treat CNS Disorders
Abstract Number: 665

Title: Positron Emission Tomography I-124-labeled AAV Assessment of CSF to Blood Diffusion and Consequent Systemic Distribution of AAV Capsids Following CSF Administration of AAV Vectors
Presenter: J.B. Rosenberg, Ph.D., Weill Cornell Medicine
Date/Time: Tuesday, May 17, 2022 at 5:00 PM ET
Session Title: Enhanced AAV Targeting
Abstract Number: 890

All abstracts for the ASGCT Annual Meeting are available on ASGCT's website.

About LEXEO Therapeutics
LEXEO Therapeutics is a New York City-based, clinical-stage gene therapy company focused on addressing some of the most devastating genetically defined cardiovascular and central nervous system diseases affecting both larger-rare and prevalent patient populations. LEXEO's foundational science stems from partnerships and exclusive licenses with leading academic laboratories at Weill Cornell Medical College and the University of California, San Diego, two preeminent institutions on the cutting edge of gene therapy research. LEXEO is advancing a deep and diverse pipeline of AAV-based gene therapy candidates in rare cardiovascular diseases, *APOE4*-associated Alzheimer's disease, and CLN2 Batten disease, and is led by pioneers and experts with decades of collective experience in genetic medicines, rare disease drug development, manufacturing, and commercialization. For more information, please visit www.lexeotx.com or LinkedIn.

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