Affinia Therapeutics Presents Preclinical Data for Genetic Cardiomyopathy and Sporadic ALS Programs with Novel Cardiotropic and BBB-Penetrant AAV Capsids at the American Society of Gene & Cell Therapy 2024 Annual Meeting

Novel cardiotropic capsids transduce more than 90% of cardiomyocytes in non-human primates (NHPs) and detarget the liver and dorsal root ganglia (DRG); show safety and efficacy in a mouse model of cardiac dysfunction

Novel BBB-penetrant capsid transduces more than 50% of neurons in NHPs across spinal cord, cortex, and deep-brain regions and detarget the liver and DRG; shows greater than 50% reduction of Ataxin-2, a gene believed to be involved in ALS

WALTHAM, Mass. – May 10, 2024 – Affinia Therapeutics ("Affinia"), an innovative gene therapy company with a proprietary platform for rationally designed adeno-associated virus (AAV) vectors and gene therapies for rare and prevalent devastating diseases, today announced the presentation of new preclinical data on its novel AAV capsids for genetic cardiomyopathies and diseases of the central nervous system (CNS) such as amyotrophic lateral sclerosis (ALS), as well as the Company's high-yield manufacturing process. This research will be presented in oral sessions today at the American Society of Gene and Cell Therapy (ASGCT) 2024 Annual Meeting, being held May 7-11, 2024 in Baltimore, MD and virtually.

Affinia has leveraged its proprietary platform to rationally design capsids with increased tropism to cardiac muscle, skeletal muscle, or CNS with more uniform tissue distribution than AAV9. This improved biodistribution is attained while detargeting the liver and dorsal root ganglia (DRG), both potential sites of toxicity. Affinia's novel capsids have favorable manufacturing yields and levels of preexisting population immunity. Preclinical efficacy and safety results with a cardiotropic vector encoding for the BAG3 protein provide proof-of-concept data to support the expansion to multiple cardiomyopathies. In addition, preclinical efficacy and safety results with a blood-brain barrier (BBB)-penetrant vector encoding for the knockdown of Ataxin-2 (Atxn2), a gene believed to be involved in sporadic ALS, provide proof of concept data to support the expansion to multiple CNS diseases.

"Compared with AAV9, our next-generation bespoke capsids demonstrate superior cardiac transduction while detargeting the liver and DRG in single-clone NHP studies. Similarly, our BBB-penetrant capsid exhibits widespread distribution across the brain with more than 50% neurons transduced, while also detargeting the liver and DRG," said Charles Albright, Ph.D., Affinia's Chief Scientific Officer. "The Affinia capsids are highly differentiated from conventional AAVs being used in cardiac and CNS programs currently in clinical trials, and we look forward to advancing programs with our capsids toward the clinic."

In an oral presentation today, Affinia will present clonal data in non-human primates (NHPs) for its novel, BBB-penetrant AAV capsid that has potential as a treatment for sporadic ALS. The capsid transduces more the 50% of neurons across spinal cord, cortical, and deep-brain regions. Dose-dependent increases in percent of neurons transduced, vector genome

biodistribution, and transgene-mRNA expression were observed. Biochemical and in-situ hybridization measurements of Atxn2 showed a reduction of greater than 50% in multiple CNS regions, the threshold required for potential therapeutic benefit. In spinal cord, the measurements were in cells relevant to ALS, the lower motor neurons. No adverse safety events were observed.

The oral presentation entitled, "Reduction of Atxn2, a therapeutic target for sporadic ALS, in non-human primates using a novel, intravenously delivered AAV capsid," will be presented by Giridhar Murlidharan, Ph.D., Senior Director, Head of Vector Translational Biology at Affinia, today, Friday, May 10, 2024 at 4:00-4:15 pm ET (Room 307-308; abstract 304).

A second oral presentation will feature Affinia's proprietary manufacturing process in HEK-293 suspension cells, yielding greater than 50% full capsids and greater than 1e15vg/L yield at harvest, with broad applicability across conventional and novel AAV capsids. These upstream performance measures translate to significant potential quality and cost advantages in the final product relative to current gene therapy manufacturing processes. The oral presentation entitled, "A proprietary HEK293 AAV production system can achieve greater than 50% full capsids with greater than 1e15vg/L at harvest enabling scalable chromatography-based polishing with high yield and purity," will be delivered by Matt Edwards, MBA, Senior Director, Head of Process Science at Affinia, today, Friday, May 10, 2024 at 4:00-4:15 pm ET (Ballroom 3; abstract 290).

Affinia has also been invited to present on the rational design of cardiotropic capsids that detarget the liver and DRG. Sherry Cao, Ph.D., Senior Vice President, Computational Science will deliver the presentation entitled, "Machine-learning guided rational design of cardiotropic capsids that detarget liver and DRG," on Saturday, May 11, 2024 at 8:00 am ET in Room 339-342.

"Targeted delivery has long been a challenge, limiting the potential for gene therapy to unlock diseases and help patients," said Laura Richman, MBA, D.V.M., Ph.D., D.A.C.V.P., Chief Development Officer of Affinia. "Affinia capsids achieve high transduction efficiency in NHP cardiac and CNS regions while detargeting the liver and DRG potentially improving benefit-risk and differentiating our programs in the clinic. The data in a mouse model of cardiac dysfunction showing safety and improvement in cardiac function supports development of our cardiotropic capsids in cardiomyopathies. Likewise, the data in NHPs showing sufficient reduction of Atxn2 supports development of our BBB-penetrant capsid in sporadic ALS and has applicability to multiple other CNS diseases."

In addition, members from Affinia's leadership team have been invited to chair the following sessions:

Scientific Symposium: "Innovations in Cardiac Gene and Cell Therapy"
Chair: Laura Richman, MBA, D.V.M., Ph.D., DACVP, Chief Development Officer
Date/Time: Saturday, May 11, 2024, 8:00-9:45 am ET
Location: Room 339-342

Scientific Symposium: "Challenges to Immunological Responses to Therapeutic Interventions"
Co-chair: Roberto Calcedo, Ph.D., Vice President, Preclinical and Immunology
Date/Time: Saturday, May 11, 2024, 10:15 am-12:00 pm ET

Location: Room 339-342

Category of Abstracts: B5 – Neurologic Diseases Section 4
Chair: Lisa Stanek, Ph.D., Vice President, Translational Science
Date/Time: Friday, May 10, 2024, 3:45-5:00 pm ET
Location: Room 307-308

Affinia also held two poster presentations. The first poster showcased data that confirm the safety and therapeutic efficacy of a novel cardiotropic AAV capsid in an animal model of cardiac dysfunction with a potential therapeutic application in genetic cardiomyopathies (abstract 605). The company also presented a poster on a screening platform for the discovery of novel, next-generation CNS tropic capsids, based on binding to cell receptors that facilitate BBB transcytosis and with potential applicability to non-AAV targeted delivery modalities (abstract 982). Abstracts can be found at https://annualmeeting.asgct.org/.

About Affinia Therapeutics
Affinia Therapeutics is pioneering a shift to a new class of rationally designed gene therapies that treat rare and prevalent diseases. Affinia Therapeutics' proprietary Affinia Rationally designed Therapeutics (ART) platform is intended to synergistically improve the efficacy, safety, and manufacturability of adeno-associated virus (AAV)-based gene therapies through the development of next-generation capsids, promoters, and manufacturing approaches. For more information, visit https://www.affiniatx.com.

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