AAVantgarde announces first patient dosed in First-In-Human Phase 1/2 LUCE-1 study, evaluating AAVB-081 (Dual-AAV) in retinitis pigmentosa related to Usher Syndrome type 1B

September 16, 2024 — AAVantgarde Bio (AAVantgarde), an Italy-based global biotechnology company, announced that the first subject has been dosed in the LUCE-1 trial, a Phase 1/2 open label clinical trial to assess safety and tolerability of AAVB-081, using the company's proprietary dual hybrid gene therapy platform to deliver MYO7A protein in subjects with retinitis pigmentosa related to Usher Syndrome Type 1B (USH1B).

This dual-AAV technology for large gene delivery comes from the research of Prof. Alberto Auricchio at TIGEM, an international research institute based in Naples that is owned and managed by the Telethon Foundation. AAVantgarde is a spin-off of TIGEM, and has an exclusive license for the AAV-dual technology for inherited retinal diseases.

The first subretinal gene therapy procedure in the LUCE-1 study was supervised by Prof. Francesca Simonelli, Head of the Ophthalmology Unit at the University Hospital of Campania "Luigi Vanvitelli" (Naples). This hospital is one of 3 clinical sites for the Phase 1/2 trial. Dr. Simonelli is global Chief Investigator at the University Hospital of Campania "Luigi Vanvitelli" that is the lead dosing site for the LUCE-1 study.

"I am delighted to be involved as Principal Investigator in this first-in-human Phase 1/2 clinical study of AAV-081 for patients with retinitis pigmentosa related to USH1B," said **Prof. Simonelli**. "Through this innovative program, we aim to revolutionize our approach to understanding and treating these underserved patients. We are poised to generate robust evidence that will not only advance scientific knowledge, but also directly impact patient care."

Dr. Jayashree Sahni, CMO of AAVantgarde said "It is an honour to work closely with Prof. Simonelli in this first-in-human clinical trial and leverage her great expertise in developing gene therapies for ophthalmology indications, with a goal of bringing this potentially novel therapy to the USH1B patient community as expeditiously as possible."

Prof. Alberto Auricchio, Founder and CSO of AAVantgarde added "It is very exciting to have our dual hybrid technology finally tested clinically in an ophthalmology indication. I am very hopeful

that all these years of research prove their value in helping these patients that have such a high unmet need."

Dr. Natalia Misciattelli, CEO of AAVantgarde added "We are honoured to have Prof. Simonelli as Principal Investigator for this clinical study aimed at providing hope for USH1B patients that have no therapeutic options to prevent them from losing their sight. Prof. Simonelli is a pioneer in gene therapy in ophthalmology and her extensive experience in this space will be invaluable to the successful development of this novel therapy."

About the AAVB-081 program

AAVB-081 is an intra-retinal AAV8-based dual hybrid product targeting MYO7A-associated Usher syndrome (USH1B). AAVantgarde's dual hybrid platform uses two AAV8 vectors, each containing one half of an expression cassette encoding for the Myo7A gene and works at the cell nucleus level, recombining the two halves of the transgene back into a single one within the cell. This technology translates into an efficient recombination that generates therapeutically meaningful protein levels in animal models.

About the LUCE-1 Trial

LUCE-1 is a Phase 1/2 multicenter, open-label, dose escalation study investigating safety, tolerability and preliminary efficacy of 3 dose levels of dual AAV8.MYO7A (AAVB-081) administered subretinally in subjects with retinitis pigmentosa associated with Usher Syndrome Type 1B.

About Usher syndrome type 1B

Usher syndrome type 1B (Usher1B) is an inherited disease that affects the retina and the inner ear. Usher1B is caused by mutations in the *MYO7A* gene. The therapeutic gene to treat Usher1B is 6.7 kb long and is therefore too large to fit inside a standard AAV vector. Approximately 20,000 patients in the U.S. and E.U. have Usher1B. These children are born deaf, have vestibular dysfunction, and begin to progressively lose vision in their first decade of life. Although there are surgical treatments available to treat deafness in these patients, there are no treatments available to treat progressive vision loss and blindness in these patients.

About AAVantgarde Bio

AAVantgarde Bio is a clinical stage, Italian headquartered, international biotechnology company that has developed two proprietary Adeno-Associated Viral (AAV) vector platforms to address the gene therapy cargo capacity limitations of AAV vectors. The AAVantgarde platforms could be used to deliver large genes to ocular and non-ocular tissues. Co-founded by Professor Alberto Auricchio at TIGEM (Telethon Institute of Genetics and Medicine) in Naples, Italy, and Telethon Foundation, AAVantgarde will initially validate the platform in the clinic in two inherited retinal diseases with clear unmet need. For more information, please visit: www.aavantgarde.com

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