AAVantgarde Receives FDA Clearance to Progress Stargardt Disease Asset, AAVB-039, into CELESTE, a Phase 1/2 Clinical Trial

- *AAVB-039 delivers the full-length ABCA4 -protein, addressing the root cause of the disease and enabling treatment of all patients, independent of mutation*
- *CELESTE is informed by the STELLA prospective natural history study, which is currently enrolling patients in the United States and Europe*
- *AAVB-039 uses AAVantgarde's proprietary dual AAV intein platform. The platform has achieved unprecedented preclinical data demonstrating high transduction, protein expression, and safety in multiple large animal models*

MILAN, July 15, 2025 — AAVantgarde Bio (AAVantgarde), a clinical-stage biotechnology company developing next-generation gene therapies for inherited retinal diseases, today announced that the U.S. Food and Drug Administration (FDA) has cleared its Investigational New Drug (IND) application for AAVB-039, the company's gene therapy program for Stargardt disease.

AAVantgarde is now initiating 'CELESTE', a first-in-human Phase 1/2 clinical trial in the United States, to evaluate the safety, tolerability, and initial efficacy of AAVB-039 in patients with Stargardt disease. This is the most common inherited form of macular degeneration and a leading cause of vision loss in children and young adults.

AAVB-039 aims to address the underlying genetic cause of the disease by restoring the full-length ABCA4 protein and has the potential to benefit all patients with ABCA4 mutations. AAVB-039 utilizes AAVantgarde's proprietary dual AAV intein platform, which enables the delivery of large genes.

> "This FDA clearance marks a pivotal milestone for AAVantgarde and our Stargardt program," said Dr. Natalia Misciattelli, Chief Executive Officer of AAVantgarde. "With AAVB-039 now in clinical development, we are advancing our second therapeutic candidate toward addressing the urgent needs of patients with inherited retinal diseases. Moreover, the news reinforces our evolution from pioneering dual AAV-

based, retina-targeting therapies into a clinical-stage company with a growing pipeline of candidates. Looking ahead, we remain focused on generating meaningful clinical data and building a portfolio of transformative treatments that can redefine what's possible for patients living with severe genetic disorders."

"The IND clearance for AAVB-039 is a testament to the scientific foundation and translational potential of our proprietary dual AAV intein platform," said Professor Alberto Auricchio, Chief Scientific Officer and Scientific Founder of AAVantgarde. "Delivering large genes like ABCA4 has been a challenge in the field. Our approach, validated by rigorous preclinical studies showing quantified high transduction, expression, and long-term safety in multiple relevant models offers a potential therapeutic that addresses the genetic root cause for patients with Stargardt disease."

Alongside CELESTE, AAVantgarde is conducting STELLA, a prospective natural history study at selected centers of excellence across the U.S., Europe and the UK. The study has informed the clinical trial design and continues to better characterize Stargardt disease.

Additionally, the company's first clinical-stage program, AAVB-081, is in Phase 1/2 development for retinitis pigmentosa caused by Usher syndrome type 1B and represents the first-ever dual AAV gene therapy tested clinically in an ocular indication. Early clinical data demonstrates good preliminary safety and encouraging signs of efficacy. Together, these programs reflect AAVantgarde's commitment to advancing scientifically rigorous, best-in-class genetic medicines for currently untreatable diseases.

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About AAVantgarde Bio

AAVantgarde Bio is a clinical stage, biotechnology company advancing best-in-class therapies for patients with inherited retinal diseases. The company's lead programs target Stargardt disease and retinitis pigmentosa due to Usher syndrome type 1B, two severe, inherited retinal diseases with no approved treatments. AAVB-039 and AAVB-081 are investigational, dual AAV gene therapies designed to address the root genetic causes of these diseases. With a strong foundation in translational science and a commitment to clinical excellence, AAVantgarde is working to bring transformative therapies to patients. For more information, please visit: www.aavantgarde.com

About Stargardt Disease

Stargardt disease is the most common form of inherited macular degeneration. Inherited in most cases as autosomal recessive, Stargardt disease is caused by mutations in the ABCA4 gene, leading to the accumulation of toxic retinoid byproducts in the retina and progressive vision loss._The ABCA4 gene is 6.8 kilobases in length, too large to be packaged within a standard, single AAV vector. Stargardt disease affects an estimated 60,000 to 75,000 individuals across the U.S. and E.U and currently there are no approved treatments.

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.

Contact:

Magda Blanco – Head of Corporate Development

Email: info@aavantgarde.com