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Company Name: AnGes Inc.
Presentative: Ei Yamada, President & CEO

COVID-19 Treatment AV-001: Preliminary Positive Phase 1 Clinical Trial Results for Vascular Normalization Therapy

AV-001 was Safe and Well Tolerated in Healthy Volunteers

Vasomune plans to initiate a Phase 2a proof-of-concept study following review with FDA to assess safety and efficacy in patients with severe COVID-19 disease

March 25, 2021 - AnGes and Vasomune Therapeutics, a clinical-stage biopharmaceutical company focused on the development of novel therapeutics for the treatment of diseases associated with vascular dysfunction, announced today positive top-line Phase 1 clinical trial results for AV-001, a first-in-class injectable Tie2 receptor agonist. Results from this study support the advancement of AV-001 to phase 2 clinical studies in patients with severe COVID-19 disease. Vasomune is codeveloping AV-001 with AnGes, Inc., and plans to file Clinical Trial Application (CTA) for AV-001 with Health Canada.

“Administration of single and multiple doses of AV-001 was safe and well tolerated, said Dr. Leela Vrishabhendra, Principal Investigator for the study. “These findings are encouraging and support the continued development of AV-001 in patients with COVID-19 disease.”

The Phase 1 randomized, double-blind, placebo-controlled study of 48 healthy volunteers, 20 to 63 years of age, was designed to assess the safety, tolerability and pharmacokinetics of AV-001 following administration of single-ascending and multiple-ascending doses up to 56 µg/kg/day for 7 consecutive days. In this study, AV-001 was safe and well tolerated and there were no discontinuations due to study medication, serious adverse events (SAEs), severe adverse events (AEs), adverse events of special interest (AESI), clinically significant abnormal laboratory values or abnormal ECGs. The pharmacokinetics of AV-001 was consistent across dose groups and after single and multiple injections providing a wide margin of safety over established threshold levels. Vasomune Therapeutics plans review these data with the US Food and Drug Administration (FDA) prior to initiation of a Phase 2a exploratory proof-of-concept study to assess the safety and efficacy in patients with severe COVID-19 disease.

About AV-001
Originally discovered and designed at Sunnybrook Hospital in Toronto, AV-001 is being developed by Vasomune Therapeutics, Inc. under a co-development agreement with AnGes, Inc. [TYO: 4563]. AV-001 is a novel investigational medicine that targets the Tie2 receptor, a transmembrane protein target most highly expressed on the surface of endothelial cells in the vasculature. AV-001 activates the nonredundant Tie2-angiopoietin signaling axis and through stimulation of multiple downstream pathways restores normal vascular function and endothelial stability. Vascular dysfunction contributes to the

underlying disease pathophysiology in patients with COVID-19 including respiratory distress, hyper-coagulopathy, viral sepsis, myocardial inflammation and acute kidney injury, especially in those patients with pre-existing vascular comorbidities, such as hypertension, diabetes and obesity. Emerging evidence suggests SARS-CoV-2 infects pulmonary endothelial cells and causes microvascular leaks, contributing to the initiation and propagation of respiratory distress in COVID-19 patients by altering blood vessel barrier integrity, promoting a coagulated state and inducing vascular inflammation (endotheliitis). In preclinical studies involving a lethal RNA virus infection animal model of influenza,
AV-001 has been shown to stabilize the vasculature by enhancing endothelial cell stability, restoring normal barrier defense and blocking vascular leak. Importantly, AV-001 monotherapy significantly improved survival and lung function compared to untreated controls and showed the benefit of enhanced recovery in combination with antiviral therapy.

About Vasomune Therapeutics, Inc.
Vasomune Therapeutics, Inc. is a private clinical-stage biopharmaceutical company developing the next generation of medicines to harness the body's ability to defend against illness. Originally founded in 2014, Vasomune discovers and develops drugs using a novel therapeutic approach focused on vascular normalization strategies. Vascular dysfunction is associated with the pathology of several disease states, including COVID-19, viral and bacterial-associated pneumonia, acute kidney injury, glaucoma, hemorrhagic shock, sepsis, stroke and complications associated with diabetes. Vasomune's corporate headquarters and laboratory is located in Toronto, Canada with US offices in San Mateo, CA. For more information about the company and its product candidates, please visit www.vasomune.com.

About AnGes, Inc.
AnGes, Inc., a biopharmaceutical company founded in December 1999, focuses on the development of gene-based medicines. In March 2019, AnGes obtained conditional and time-limited approval for its lead product, Collategene® (Hepatocyte Growth Factor, HGF, plasmid gene therapy), for the treatment of lower limb ischemic ulcers. In September 2019, AnGes commenced the commercialization in Japan of Collategene®. Collategene® is the world's first marketed drug using plasmid DNA. AnGes is currently focusing on the development of DNA vaccines for COVID-19 and hypertension, a Tie2 tyrosine kinase receptor agonist for COVID-19 treatment and an NF-κB decoy oligonucleotide for chronic discogenic lumbar back pain. Furthermore, AnGes acquired EmendoBio in December 2020 to expand its capabilities in genome-editing technologies. For more information, visit https://www.anges.co.jp/en/.

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