Adverum Biotechnologies Announces Clinical Progress Across Gene Therapy Pipeline

August 1, 2018

- *Dosed First Patient in Cohort 3 in the ADVANCE Phase 1/2 Trial of ADVM-043*
- *Submitted Investigational New Drug (IND) Application for ADVM-022*
- *Plans to submit an IND Application to the FDA for ADVM-053 in 4Q18*

MENLO PARK, Calif., Aug. 01, 2018 (GLOBE NEWSWIRE) -- Adverum Biotechnologies, Inc. (Nasdaq:ADVM), a clinical-stage gene therapy company targeting unmet medical needs in serious rare and ocular diseases, today announced updates for three of its next-generation adeno-associated virus (AAV)-based therapy programs: ADVM-043, targeting alpha-1 antitrypsin (A1AT) deficiency; ADVM-022 targeting wet age-related macular degeneration (wAMD); and ADVM-053 targeting hereditary angioedema (HAE).

“We are excited to be able to share positive progress in our three lead gene therapy programs today and to share our continued commitment to improving the quality of life for patients with unmet medical needs,” said Leone Patterson, interim president and chief executive officer of Adverum Biotechnologies. “We have dosed the first patient in Cohort 3 of the ADVANCE trial for ADVM-043 in A1AT deficiency and are encouraged by the safety and tolerability profile of ADVM-043 seen to date. As this trial continues to move forward, we expect to report preliminary data from patients in Cohorts 1 through 3 by the end of this year. In addition, we have completed the IND submission of ADVM-022 for wet AMD and are planning to submit our IND for ADVM-053 in HAE in the fourth quarter of this year which we believe demonstrates the robustness of our pipeline and the dedication of the Adverum team to developing ground-breaking therapies.”

ADVM-043 Updates

- **The first patient in Cohort 3 was dosed with ADVM-043 gene therapy in the ADVANCE Phase 1/2 clinical trial**
- **Adverum expects to report preliminary data from patients in Cohorts 1 through 3 in the ADVANCE trial by the end of this year**

Based on a review of the preliminary safety data from patients in Cohort 2, the independent data monitoring committee (DMC) recommended dose escalation to Cohort 3, and the first patient was dosed with a single administration of ADVM-043 at a dose of ~1.5E13 vg/kg (1.2E15 total vg) in late July 2018.

The ADVANCE Phase 1/2 clinical trial is a multi-center, open-label, dose-escalation study of ADVM-043 in patients with A1AT deficiency. Cohort 1 patients (n=2) received an intravenous (IV) dose of ADVM-043 of ~1E12 vg/kg (8E13 total vg), Cohort 2 patients (n=2) received a dose of ~5E12 vg/kg (4E14 total vg), and Cohort 3 patients will receive a dose of ~1.5E13 vg/kg (1.2E15 total vg). Per protocol, patients being treated with standard-of-care weekly IV infusions of A1AT protein are required to “wash-out” for at least two months prior to receiving ADVM-043. The primary endpoint in the ADVANCE trial is safety and tolerability, and secondary endpoints include changes in plasma concentrations of both total and M-specific A1AT levels. Adverum plans to use the preliminary data from the ADVANCE study to inform next steps, including potential further dose escalation. Additional information about this clinical trial can be found at ClinicalTrials.gov under trial identifier number NCT02168686.

ADVM-022 Updates

- **Submitted IND application for ADVM-022 to initiate a Phase 1**

ADVM-022 long-term preclinical data in nonhuman primate model of wAMD was recently presented at the American Society of Gene & Cell Therapy in May 2018. The data showed that after 13 months, a single intravitreal injection of ADVM-022 was found to be safe and statistically significant ($p<0.0001$) in preventing the development of Grade IV lesions compared to the vehicle control group. The efficacy at 13 months was consistent with earlier-reported data, demonstrating that ADVM-022 induced long-term efficacy that was comparable to aflibercept, an anti-Vascular Endothelial Growth Factor (VEGF) standard-of-care therapy. Additionally, mean CNV complex areas were significantly smaller ($p<0.0001$) in the ADVM-022 and aflibercept groups, compared with vehicle, when analyzed by spectral domain optical coherence tomography (SD-OCT).

In addition, the long-term preclinical data in nonhuman primate model of wAMD showed ADVM-022 induced sustained intraocular expression of aflibercept for up to 16 months following a single intravitreal injection. Robust levels of aflibercept protein were detected up to 16 months in aqueous and vitreous humor and, more importantly, in retina and choroid tissues, where neovascularization occurs in wAMD.

ADVM-053 for HAE

- **Plan to submit an IND application to the FDA for ADVM-053 in the fourth quarter of 2018**

About ADVM-043
ADVM-043 (AAVrh.10-A1AT) is designed as a single-administration treatment to potentially induce long-term A1AT protein expression. In a preclinical proof-of-concept study, ADVM-043 demonstrated robust protein expression above therapeutic levels in mice following either intravenous (IV) or intrapleural (IP) administration. In another study in non-human primates, evidence of stable long-term expression of hA1AT transgene was observed out to one year following IP administration of ADVM-043.

About Alpha-1 Antitrypsin (A1AT) Deficiency
A1AT deficiency is an orphan disease affecting approximately 100,000 individuals in the United States. The disease is caused by mutations in the SERPINA1 gene, resulting in very low levels of A1AT. A1AT deficiency is associated with the development of emphysema and premature death.

The market for A1AT deficiency therapeutics was approximately $575 million in the U.S., $700 million in North America and $1.2 billion worldwide in 2016. The current standard-of-care treatment for patients with this disease who have developed emphysema includes weekly IV infusions of a plasma derived A1AT, at an estimated cost of $100,000 annually per patient. This current treatment regimen is burdensome and can result in underdosing, which in turn can lead to worsening lung function.

About ADVM-022
Adverum's gene therapy candidate ADVM-022 utilizes a proprietary vector capsid (AAV.7m8) carrying an aflibercept coding sequence under the control of a proprietary expression cassette and is administered as a single intravitreal injection. Vascular endothelial growth factor (VEGF) activity is associated with wAMD progression and vision loss. Anti-VEGF standard-of-care therapies administered every 4-8 weeks have shown the potential to prevent disease progression and preserve or even improve patients' vision. Treatment with ADVM-022 is designed to minimize the burden of frequent anti-VEGF injections, the current standard-of-care treatment for wAMD.

About Wet Age-Related Macular Degeneration (wAMD)
Approximately 1.2 million Americans suffer from wet age-related macular degeneration (wAMD).The current average age of AMD patients is 80 years old. The number of people with the disease is expected to double to 4.4 million by 2050 as the population ages.

Wet AMD (wAMD) is an advanced form of AMD where blood vessels begin to invade the cellular space between layers of cells in the retina. These new blood vessels are often leaky, which results in fluid and blood in the retina and causes vision loss. While wAMD represents approximately 10% of the number of cases of AMD overall, it is responsible for 90% of AMD-related severe vision loss. The disease is more common in Caucasians than in people of other ethnicities; age-related macular degeneration accounts for more than 54% of all vision loss in this population. Each year, approximately 150,000 to 200,000 Americans develop wAMD, with the number expected to grow due to the aging US population.

Currently, wAMD is treated with frequent injections of anti-VEGF protein into the eye. Compliance with this regimen can be difficult for patients and their caregivers, leading to compliance deficiencies and loss of vision from underdosing.

About ADVM-053
ADVM-053 (AAVrh.10-C1EI) is designed as a potential single-administration treatment to provide sustained release of the C1 esterase inhibitor ("C1EI") protein to eliminate protein level variability and prevent breakthrough angioedema attacks. In preclinical studies, a single intravenous administration of ADVM-053 increased C1EI protein expression above therapeutic levels.

About Hereditary Angioedema (HAE)
HAE is an orphan disease affecting approximately 8,000 individuals in the U.S. This disease is caused by a genetic mutation that results in low levels of C1EI. Low C1EI levels can be associated with sudden swelling and edema of respiratory airways, gastrointestinal tract, and extremities.

The current standard-of-care prophylaxis treatment regimen generally requires IV infusions or subcutaneous injections of C1EI 2-3 times a week, at an estimated cost of $0.5 million – $0.6 million annually per patient in the U.S. This treatment regimen can be burdensome for patients and their caregivers, and patients may still experience breakthrough edema attacks despite treatment.

About Adverum Biotechnologies, Inc.
Adverum is a clinical-stage gene therapy company targeting unmet medical needs in serious rare and ocular diseases. Adverum has a robust pipeline that includes product candidates designed to treat rare diseases alpha-1 antitrypsin (A1AT) deficiency and hereditary angioedema (HAE) as well as wet age-related macular degeneration (wAMD). Leveraging a next-generation adeno-associated virus (AAV)-based directed evolution platform, Adverum generates product candidates designed to provide durable efficacy by inducing sustained expression of a therapeutic protein. Adverum has collaboration agreements with Regeneron Pharmaceuticals to research, develop, and commercialize gene therapy products for ophthalmic diseases and Editas Medicine to explore the delivery of genome editing medicines for the treatment of inherited retinal diseases. Adverum's core capabilities include clinical development and in-house manufacturing expertise, specifically in process development and assay development. For more information please visit www.adverum.com.

Forward-Looking Statements
Statements contained in this press release regarding matters events or results that may occur in the future are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements regarding Adverum's expectations to report preliminary data from patients in Cohorts 1 through 3 by the end of this year, Adverum's plans to use the preliminary data from the ADVANCE study to inform next steps, including potential further dose escalation, and Adverum's plans to submit an IND Application for ADVM-053 for HAE in the fourth quarter of 2018, all of which are based on certain assumptions made by Adverum on current conditions, expected future developments and other factors Adverum believes are appropriate in the circumstances. Adverum may not consummate any of these plans or these product, clinical development or regulatory goals in a timely manner, or at all, or otherwise carry out the intentions or meet the expectations or projections disclosed in its forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, the risk of a delay in the enrollment of patients in Adverum's clinical studies or in the manufacturing of products to be used in such clinical studies, as well as the risks and uncertainties facing Adverum described more fully in Adverum's periodic reports filed with the Securities and Exchange Commission (SEC), especially under the caption "Risk Factors" in its latest Quarterly Report on Form 10-Q filed with the SEC on May 9, 2018. All forward-looking statements contained in this press release speak only as of the date on which they were made. Adverum undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Contact for Adverum:
Katherine Bock
Vice President Investor Relations
& Corporate Communications
650-656-9347
kbock@adverum.com


Primary Logo

Source: Adverum Biotechnologies, Inc.