Adverum Biotechnologies Provides Program Updates

November 1, 2018

- *Preliminary data from the ADVANCE Phase 1/2 Study in A1AT deficiency showed ADVM-043 in doses of up to* 1.5 x 10^{13} vg/kg *were safely administered and well tolerated; Protein expression did not meet a clinically meaningful level*
- *Company to provide update on rare disease programs in 1H19*
- *On-track to initiate OPTIC clinical trial in 4Q18; Long-term non-human primate efficacy data of ADVM-022 in wet AMD demonstrated durable expression of aflibercept sustained out to 22 months with single intravitreal injection*

MENLO PARK, Calif., Nov. 01, 2018 (GLOBE NEWSWIRE) -- Adverum Biotechnologies, Inc. (Nasdaq: ADVM), a clinical-stage gene therapy company targeting unmet medical needs in ophthalmology and rare diseases, today provided a program update for its gene therapy product candidates.

The Company announced its decision to discontinue the development of ADVM-043, an investigational AAVrh.10-based gene therapy for the treatment of A1AT deficiency. Based on the review of the ADVANCE Phase 1/2 study, the data did not demonstrate the potential to reach M-protein threshold levels of 11µM.

“Over the past year, our team has been focused on the clinical, regulatory, and manufacturing execution for our lead gene therapies,” said Leone Patterson, chief executive officer of Adverum Biotechnologies. “We have carefully evaluated the preliminary data from the ADVANCE study. While ADVM-043 was safely administered and was well tolerated, the preliminary protein expression unfortunately did not reach a level that justified moving the program forward with the current vector. We truly appreciate the participation by the investigators, the patients and their caregivers, the support of the Alpha-1 Foundation and the dedication of the Adverum team to advance a new treatment option for patients living with A1AT deficiency. The next steps will be to conduct additional preclinical studies, utilizing our gene therapy expertise and platform technology, to determine the best candidates to advance forward in development for the rare disease programs. An update on the plan for these programs will be provided in the first half of 2019.

Ms. Patterson continued, “For wet AMD, we presented long-term preclinical data this year, at both the ASGCT and ESGCT Annual Congresses, demonstrating ADVM-022’s durability of biological activity for 13 months and aflibercept expression up to 22 months in non-human primates. We remain on-track this quarter to initiate the OPTIC Phase 1 clinical trial for ADVM-022 in patients with wet AMD to assess this unique anti-VEGF gene therapy approach using a single intravitreal administration.”

ADVM-043 for Alpha-1 Antitrypsin (A1AT) Deficiency in the ADVANCE Phase 1/2 Study
Adverum is reporting preliminary topline data from the ADVANCE Phase 1/2 study for ADVM-043 in patients with A1AT deficiency which include data from the first three cohorts of patients. A total of six patients have been administered ADVM-043 gene therapy at three increasing doses (2 subjects per dose). All patients received a prophylactic tapering corticosteroid regimen. The primary endpoint in the study is safety and tolerability and secondary endpoints include changes in plasma concentrations of M-specific A1AT protein. In the study, patients received a single intravenous administration of ADVM-043, which utilizes the serotype AAVrh.10 vector expressing A1AT.

Primary Endpoint:
Preliminary data demonstrated that ADVM-043 can be safely administered and is well tolerated with a mean follow up period of 25 weeks post administration at doses of 1.0 x 10^{12} vg/kg (8.0 x 10^{13} vg), 5.0 x 10^{12} vg/kg (4.0 x 10^{14} vg) and 1.5 x 10^{13} vg/kg (1.2 x 10^{15} vg) respectively. Safety monitoring will be ongoing for up to 52 weeks post-dosing for all three cohorts.

As of October 24, 2018:

- A total of 15 adverse events (AEs) were reported
  -- Two AEs of elevated alanine aminotransferase (ALT; Grade 1, mild) were deemed possibly related to ADVM-043. The ALTs normalized within a few days after an increase in prednisone dose
- All AEs were mild (Grade 1) in severity, except for one unrelated serious adverse event (SAE), considered Grade 3 in severity attributable to the patient’s preexisting indwelling port

Secondary Endpoint:
Preliminary protein level data from the study showed, with a mean follow up of 25 weeks post administration:

- M-specific A1AT protein measurements did not reach clinically meaningful levels of expression. Although some level of activity was observed, the protein level only reached a maximum of 200nM in the study;
- No dose response was observed between the three cohorts

ADVM-022 in Wet Age-related Macular Degeneration (wAMD)
Adverum recently presented long-term preclinical efficacy data in wAMD, for ADVM-022 a novel gene therapy candidate utilizing a proprietary vector capsid (AAV.7m8), at the European Society of Gene & Cell Therapy’s (ESGCT) 26 th Annual Congress. The ADVM-022 data was selected as one of the top-scoring abstracts and was presented in a lightning talk followed by a poster session on October 17, 2018. Key highlights included:

- A single intravitreal administration of ADVM-022 in NHPs at dose ranges of 2 x 10^{11} vg/eye to 2 x 10^{12} vg/eye provided stable intraocular expression of aflibercept at levels comparable with the levels measured in aflibercept recombinant protein-injected eyes approximately 3 to 4 weeks post-dose in all of the following: vitreous humor, aqueous humor, retina and choroid
- A single intravitreal administration of ADVM-022 provided robust expression of aflibercept, sustained for approximately two years post-dose in non-human primates (NHPs)

In May 2018, long-term preclinical efficacy data in NHP models on ADVM-022 in wAMD were presented at the American Society of Gene & Cell Therapy (ASGCT) 21st Annual Meeting. Key highlights included:

- The efficacy of ADVM-022 at 13 months post-administration was consistent with earlier reported data, demonstrating that 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 untreated vehicle control group

- ADVM-022 induced long-term efficacy that was comparable to aflibercept, an anti- VEGF standard-of-care therapy. ADVM-022 was well-tolerated, with no serious adverse events

In September 2018, Adverum received Fast Track designation for ADVM-022 in wAMD from the U.S. Food and Drug Administration (FDA). Adverum plans to initiate the OPTIC Phase 1 clinical trial for ADVM-022 in patients with wAMD in the fourth quarter of 2018.

Rare Disease Programs
Based on the most recent data from the ADVANCE clinical trial, the Company is reviewing the learnings from the study, notably on the AAVrh.10 capsid in order to inform further development of gene therapy candidates for the treatment of rare diseases. The Company plans to conduct additional preclinical studies to determine the best gene therapy candidate to advance. The Company plans to provide an update on the rare disease programs in the first half of 2019 and will not submit an IND application for ADVM-053 for the treatment of hereditary angioedema (HAE) in the fourth quarter of 2018.

About Adverum Biotechnologies, Inc.
Adverum is a clinical-stage gene therapy company targeting unmet medical needs in ophthalmology and rare diseases. 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 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 projected timing to advance ADVM-022 into the clinic in the fourth quarter, Adverum's expectation of providing an update on its rare disease programs in the first half of 2019, and Adverum's plans to conduct additional preclinical studies, 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 plans or product or clinical development goals in a timely manner, or at all, or otherwise be able to 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 August 8, 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.

Investor and Media Inquiries:
Katherine Bock
Vice President Investor Relations & Corporate Communications
Adverum Biotechnologies, Inc.
650-656-9347
kbock@adverum.com

ADVERUM_ID_RGB 200x49.jpg

Source: Adverum Biotechnologies, Inc.