Adverum Biotechnologies Reports New Interim Data from Cohorts 1 and 2 of OPTIC Phase 1 Trial of ADVM-022 Intravitreal Gene Therapy for Wet AMD at Angiogenesis, Exudation, and Degeneration 2020

February 8, 2020

-- Robust efficacy with evidence of a dose response --
-- 6/6 patients rescue-injection-free in cohort 1, with 3 patients at 52 weeks --
-- 4/6 patients rescue-injection-free in cohort 2 (lower dose) at 24 weeks --

-- Company to host and webcast a discussion with key opinion leaders Sunday, February 9, at 10:00 am EST --

REDWOOD CITY, Calif., Feb. 08, 2020 (GLOBE NEWSWIRE) -- Adverum Biotechnologies, Inc. (Nasdaq: ADVM), a clinical-stage gene therapy company targeting unmet medical needs in ocular and rare diseases, today announced new interim clinical data from the OPTIC Phase 1 dose-ranging clinical trial of ADVM-022 intravitreal injection gene therapy. OPTIC includes treatment-experienced patients with wet age-related macular degeneration (AMD). The data are being presented today by David S. Boyer, M.D., senior partner, Retina-Vitreous Associates Medical Group and adjunct clinical professor of ophthalmology with the University of Southern California/Keck School of Medicine in Los Angeles, at the Angiogenesis, Exudation, and Degeneration 2020 Annual Meeting in Miami.

A copy of the presentation is available on the Adverum corporate website under Events and Presentations in the Investors section.

For the first time, data are being presented from patients in cohort 2 (n=6) at 24 weeks following treatment with a single intravitreal injection of a three-fold lower dose of ADVM-022 (2 x 10^11 vg/eye) compared to the cohort 1 dose (6 x 10^11 vg/eye). New data as detailed in the table below include:

- ADVM-022 demonstrated a robust efficacy signal and evidence of a dose response:
  - Cohort 1: 6 of 6 patients remain rescue-injection-free at a median follow up of 50 weeks, with 3 patients at 52 weeks.
  - Cohort 2: 4 of 6 patients remain rescue-injection-free at 24 weeks at the lower dose.
- In both cohorts combined, 10 of 12 (83%) patients remain rescue-injection-free. For these patients:
  - Vision was generally maintained as demonstrated by stable mean best corrected visual acuity (BCVA) compared to baseline.
  - Retinal anatomy improvements were achieved and maintained as demonstrated by mean central subfield thickness (CST) compared to baseline.
- ADVM-022 continues to demonstrate a favorable safety profile and be well tolerated with no drug-related or procedure-related serious adverse events (SAEs), no drug-related systemic adverse events, and no adverse events meeting the criteria for dose-limiting toxicities (DLTs).
- ADVM-022-related adverse events (AEs) have been mild (71%) to moderate (29%).
- Low-grade ocular inflammation was commonly reported and was responsive to steroid eye drops.

OPTIC Phase 1 Clinical Trial Data:

Results Following a Single ADVM-022 Dose:	**Cohort 1**	**Cohort 2**
Patients	6	6
Dose ADVM-022	Higher Dose 6 x 10^11 vg/eye	Lower Dose 2 x 10^11 vg/eye
Follow-up (median)	50 weeks	24 weeks
Rescue Injections:		
Number of patients requiring anti-VEGF rescue injections	0/6 patients	2/6 patients
Total anti-VEGF rescue injections	0 injections	6 injections

Safety:			
Systemic adverse events	0	0	
Dose-limiting toxicities (DLTs)	0	0	
Serious adverse events (SAEs)[1]	1	0	
Drug/procedure related SAEs	0	0	
Follow-up	44 weeks (median)	24 weeks	
Change in BCVA[2]:		Full cohort	Rescue-free patients
Mean (ETDRS letters)[3]	-1.0	-4.8	-0.8
Range (ETDRS letters)	-7 / +7	-19 / +16	-14 / +16
Change in CRT[3]:			
Mean (mm)[4]	-25.5	-27.8	-30.8
Range (mm)[4]	-117 / +32	-61 / -8	-61 / -8

1 This event (retinal detachment) was deemed unrelated to ADVM-022 or any study procedure.

2 Best corrected visual acuity (BCVA) as measured by Early Treatment Diabetic Retinopathy Study (ETDRS) (i.e., sight charts). Data through December 1, 2019 (Cohort 1).

3 Central retinal thickness (CRT), also referred to as central subfield thickness (CST) assessed using Optical Coherence Tomography (OCT) imaging and measured by an independent Central Reading Center Data through December 1, 2019 (Cohort 1).

4 BCVA and CST values for patient with retinal detachment (unrelated to study treatment) used last observations prior to detachment.

"I am very encouraged that this difficult-to-treat patient population enrolled in OPTIC is maintaining vision and anatomical improvements for an extended period of time," said David S. Boyer, M.D., senior partner, Retina-Vitreous Associates Medical Group and adjunct clinical professor of ophthalmology with the University of Southern California/Keck School of Medicine in Los Angeles, California. "Additionally, ADVM-022 continues to be safe and well tolerated, with ocular inflammation that is manageable with steroid eye drops. Patients with wet AMD and their caregivers carry a significant treatment burden from the current standard-of-care anti-VEGF injections, and real-world vision outcomes are suboptimal due to undertreatment. ADVM-022 as a one-time intravitreal injection therapy could transform the treatment paradigm for patients and their caregivers."

Aaron Osborne, MBBS, chief medical officer of Adverum, added, "ADVM-022 has demonstrated a robust efficacy signal and evidence of a dose response in the OPTIC Phase 1 trial with data from 12 patients and two doses now available. Patients in cohort 2 received a three-fold lower dose of ADVM-022 than in cohort 1, and 4 of 6 of these patients are rescue injection-free through 24 weeks, whilst all 6 patients in cohort 1 remain rescue free with a median follow up of 50 weeks. OPTIC is progressing well, with the key objectives for cohorts 3 and 4 being to further evaluate dose response and to assess a 6-week prophylactic course of steroid eye drops instead of the 13-day oral steroid prophylaxis used in cohorts 1 and 2. We look forward to presenting clinical data from all four cohorts of OPTIC during this important year in the clinic for our novel gene therapy, ADVM-022."

KOL Discussion Tomorrow:
In addition, Adverum will host an event with expert retinal specialists to discuss the OPTIC data presented at Angiogenesis and the potential opportunity for ADVM-022. The discussion will be held on Sunday, February 9, 2020 beginning at 10:00 am EST. The event will be webcast live from Adverum's website at www.adverum.com in the Investors section under the Events and Presentations page. A replay of the webcast will be archived and available for replay following the event. A copy of the slide presentation will also available on the Adverum corporate website under Events and Presentations in the Investors section.

About the OPTIC Phase 1 Trial of ADVM-022 in Wet AMD
The multi-center, open-label, Phase 1, dose-ranging trial is designed to assess the safety and tolerability of a single intravitreal (IVT) administration of ADVM-022 in patients with wet AMD who are responsive to anti-vascular endothelial growth factor (VEGF) treatment. In cohort 1, patients (n=6) received ADVM-022 at a higher dose of 6 x 10^11 vg/eye and in cohort 2, patients (n=6) received ADVM-022 at a lower dose of 2 x 10^11 vg/eye. In cohort 3, patients (n=9) also are receiving a dose of 2 x 10^11 vg/eye and in cohort 4, patients (n=9) will receive a dose of 6 x 10^11 vg/eye. Patients in cohorts 3 and 4 will receive prophylactic steroid eye drops instead of oral steroids which were used in cohorts 1 and 2. The primary endpoint of the trial is the safety and tolerability of ADVM-022 after a single IVT administration. Secondary endpoints include changes in best-corrected visual acuity (BCVA), measurement of central retinal thickness (CRT), as well as mean number of anti-VEGF rescue injections and percentage of patients needing anti-VEGF rescue injections. Each patient enrolled will be followed for a total of two years.

Eight leading retinal centers across the United States (U.S.) are participating in the OPTIC Phase 1 trial for ADVM-022. For more information on the OPTIC Phase 1 clinical trial of ADVM-022 in wet AMD, please visit https://clinicaltrials.gov/ct2/show/NCT03748784.

About ADVM-022 Gene Therapy
ADVM-022 utilizes a proprietary vector capsid, AAV.7m8, carrying an aflibercept coding sequence under the control of a proprietary expression cassette. ADVM-022 is administered as a one-time intravitreal injection, designed to deliver long-term efficacy and reduce the burden of frequent anti-VEGF injections, optimize patient compliance and improve vision outcomes for wet AMD and diabetic retinopathy patients.

In recognition of the need for new treatment options for wet AMD, the U.S. Food and Drug Administration granted Fast Track designation for ADVM-022 for the treatment of this disease.

Adverum is currently evaluating ADVM-022 in the OPTIC study, a Phase 1 clinical trial in patients 50 years and older with wet AMD. Additionally, Adverum plans to submit an Investigational New Drug Application for ADVM-022 for the treatment of diabetic retinopathy to the U.S. Food and Drug Administration in the first half of 2020.

About Wet Age-related Macular Degeneration (AMD)
Age-related macular degeneration (AMD) is a progressive disease affecting the macula, the region of the retina at the back of the eye responsible for central vision. In patients with wet AMD, an aggressive form of AMD, abnormal blood vessels grow underneath and into the retina. These abnormal blood vessels leak fluid and blood into and beneath the retina, causing vision loss.

Wet AMD is a leading cause of vision loss in patients over 60 years of age, with a prevalence of approximately 1.2 million individuals in the U.S. and 3 million worldwide. The incidence of new cases of wet AMD in the U.S. is approximately 150,000 to 200,000 annually, and this number is expected to grow significantly as the country's population ages.

The current standard-of-care therapy for wet AMD is anti-VEGF intravitreal injections. These are effective but typically require eye injections every 4-12 weeks in order to maintain vision. Compliance with this regimen can be difficult for patients, caregivers, and healthcare systems, leading to undertreatment and resulting in loss of vision.

About Adverum Biotechnologies
Adverum Biotechnologies (Nasdaq: ADVM) is a clinical-stage gene therapy company targeting unmet medical needs in serious ocular and rare diseases. Adverum is evaluating its novel gene therapy candidate, ADVM-022, as a one-time, intravitreal injection for the treatment of its lead indication, wet age-related macular degeneration. 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 plans to report additional clinical data for ADVM-022 from the OPTIC trial and to advance ADVM-022, including Adverum's plans to submit an Investigational New Drug Application for ADVM-022 for the treatment of diabetic retinopathy to the U.S. Food and Drug Administration in the first half of 2020, and the potential benefits of ADVM-022, 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 achieve any of these in a timely manner, or at all, or otherwise carry out the intentions or meet the expectations 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 risks inherent to, without limitation: Adverum's novel technology, which makes it difficult to predict the time and cost of product candidate development and obtaining regulatory approval; the results of early clinical trials not always being predictive of future results; the potential for future complications or side effects in connection with use of ADVM-022; the uncertainty of obtaining regulatory approval for gene therapy product candidates; potential delays in enrolling patients in clinical trials; reliance on third parties for conducting the OPTIC trial and vector production; and ability to fund operations through completion of the OPTIC trial and thereafter. Risks and uncertainties facing Adverum are described more fully in Adverum's Form 10-Q filed with the SEC on November 7, 2019 under the heading "Risk Factors." 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, except as required by law.

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