



Adverum Biotechnologies Reports Positive 24-Week Data from First Cohort of OPTIC Phase 1 Trial of ADVM-022 Intravitreal Gene Therapy to Treat Wet AMD

September 12, 2019

-- Zero anti-VEGF rescue injections required after one-time intravitreal dose of ADVM-022 --

-- Sustained improvements in retinal anatomy --

-- Was safe and well tolerated --

-- Data being presented during podium presentation at
Retina Society 2019 Annual Meeting --

-- Adverum to host conference call and webcast on
Thursday, September 12 at 5:30 a.m. PT / 8:30 a.m. ET / 1:30 p.m. BST --

MENLO PARK, Calif., Sept. 11, 2019 (GLOBE NEWSWIRE) -- Adverum Biotechnologies, Inc. (Nasdaq: ADVM), a clinical-stage gene therapy company targeting unmet medical needs in ocular and rare diseases, today announced the presentation of positive 24-week clinical data from the first cohort of patients (n=6) treated with a one-time intravitreal (IVT) dose of ADVM-022 in the OPTIC phase 1 clinical trial in wet age-related macular degeneration (wet AMD). Patients treated in this cohort achieved vision maintenance and improvements in retinal anatomy, with zero anti-VEGF rescue injections required, after a one-time intravitreal dose of ADVM-022, through week 24. These patients previously required frequent anti-VEGF injections to control their wet AMD and to maintain functional vision. ADVM-022 was safe and well tolerated.

These data are being presented on Thursday, September 12, 2019 at 7:41 a.m. BST by Szilárd Kiss, M.D. during a podium presentation at the Retina Society 2019 Annual Meeting in London, UK. Adverum will host a conference call and webcast beginning at 1:30 p.m. BST (5:30 a.m. PT/8:30 a.m. ET) to review the data. Dr. Kiss's presentation slides will be available at the conclusion of the company's webcast presentation under the [Events and Presentations](#) in the Investors section of the company's website located at www.adverum.com.

OPTIC Phase 1 Clinical Trial 24-week Data from First Cohort (n=6)

Baseline Characteristics of Patients:	First Cohort
Dose of intravitreal injection ADVM-022	6 x 10 ¹¹ vg/eye
Mean age	79 years
Mean number of years since diagnosis	3.3 years
Mean number of prior anti-VEGF injections	35 injections (range 7-109)
Mean number of anti-VEGF injections in 8 months prior to screening	6.2 injections
Average annualized anti-VEGF injection frequency ¹	9.3 injections
Mean BCVA ² study eye	65.8 letters
Approximate Snellen equivalent	20/50
Mean CRT ³ study eye	369 μm

24-week Results Following One-time ADVM-022 Dose:	First Cohort
Rescue Injections:	
Number of patients requiring anti-VEGF rescue injections	0 patients
Mean number of anti-VEGF rescue injections	0 injections
Change in BCVA:	
Mean change in BCVA	-2 letters
Range change in BCVA	-9.1 letters, +5.1 letters (90% CI)
Change in CRT:	
Mean change in CRT	-52.7 μm

Range change in CRT	-86.5 μm , -18.8 μm (90% CI)
Safety:	
Serious adverse events (SAEs)	0
Dose-limiting toxicities (DLTs)	0
Systemic adverse events (AEs) potentially related to ADVM-022	0
Ocular AEs potentially related to ADVM-022	19 events in 6 patients: Mild (14) ⁴ Moderate (5) ⁴ <ul style="list-style-type: none"> • Intermediate uveitis x2 • Vitreous cells • Anterior chamber cells x2

- 1 Calculated based on number of anti-VEGF injections in past 8 months
- 2 Best corrected visual acuity (BCVA) as measured by Early Treatment Diabetic Retinopathy Study (ETDRS) (ie, sight charts)
- 3 Central retinal thickness (CRT), also referred to as central subfield thickness (CST), assessed using Optical Coherence Tomography (OCT) imaging and measured by independent Central Reading Center
- 4 Common Terminology Criteria for Adverse Events v5.0, general guidelines

"Typically, patients with wet AMD require frequent anti-VEGF injections to maintain vision, representing a substantial treatment burden that often results in vision loss due to undertreatment. The single largest unmet clinical need for these patients is for a long-lasting anti-VEGF treatment," said Szilárd Kiss, M.D., retinal specialist, who is presenting the data at the Retina Society meeting. "These data on ADVM-022 are compelling, as they demonstrate for the first time that a one-time gene therapy delivered by intravitreal injection has the potential to provide sustained efficacy and transform the treatment paradigm for patients with wet AMD."

Aaron Osborne, MBBS, MRCOphth, chief medical officer of Adverum, added, "We are excited that there were zero rescue injections through 24 weeks in this cohort of patients, all of whom previously required frequent injections to avoid losing vision. In addition to being safe and well tolerated, a single injection of ADVM-022 resulted in sustained anatomical improvements and vision maintenance. Given these positive results from OPTIC, we are working with key stakeholders to continue development and seek regulatory approval of ADVM-022 to meet our goal of delivering this novel gene therapy candidate as soon as possible to patients with wet AMD and diabetic retinopathy, our second indication for ADVM-022. I'd like to thank the investigators, patients, and caregivers for their ongoing participation in the OPTIC trial."

Future Outlook – Planned Milestones

- On Friday, October 11, 2019 at 4:26 p.m. PT, Dr. Szilárd Kiss will present 24-week data from the first cohort of the OPTIC trial during a podium presentation at a late-breaking development session during the Retina Subspecialty Day Program of the American Academy of Ophthalmology 2019 Annual Meeting in San Francisco, CA.
- An update on further development plans for the OPTIC trial will be provided in the fourth quarter of 2019.
- 52-week data from the first cohort of patients as well as 24-week data from the second cohort of patients in the OPTIC trial will be presented in the first half of 2020.
- Submission of an investigational new drug application for ADVM-022 in diabetic retinopathy is planned in the first half of 2020.
- Adverum expects to be able to occupy its new corporate headquarters in Redwood City, CA by the end of this year, allowing for the expansion of in-house process development capabilities to the 1000-liter production scale.

Conference Call Information

Adverum will host a conference call and webcast to review the data presented on September 12, 2019 at 1:30 p.m. BST (5:30 a.m. PT/8:30 a.m. ET). Individuals can participate in the conference call by dialing 1-866-420-8347 (domestic) or 1-409-217-8241 (international), and referring to the "Adverum Biotechnologies Conference Call." The webcast will be accessible under [Events and Presentations](#) in the Investors section of the company's website located at www.adverum.com. The archived audio webcast will be available on Adverum's website following the call for 30 days.

About the OPTIC Phase 1 Trial of ADVM-022 in Wet AMD

The multi-center, open-label, phase 1, dose-escalation 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 the first cohort, patients (n=6) received ADVM-022 at a dose of 6×10^{11} vg/eye, and in the second cohort, patients (n=6) received a dose of 2×10^{11} vg/eye due to the robust preliminary anatomical response observed from patients in the first cohort. Patients will be administered a tapering prophylactic corticosteroid regimen. The primary endpoint of the trial is the safety and tolerability of ADVM-022 at 24 weeks 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 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

Adverum's gene therapy candidate for wet AMD and diabetic retinopathy, 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. ADVM-022 is designed to deliver long-term efficacy by significantly reducing the treatment burden of frequent anti-VEGF injections and improving real-world vision outcomes for patients with wet AMD and diabetic retinopathy.

In September 2018, Adverum received Fast Track designation for ADVM-022 for the treatment of wet AMD from the FDA.

About Wet Age-related Macular Degeneration (Wet 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. Disease progression results in the death of retinal cells and loss of vision. Wet AMD, also known as neovascular AMD, is an aggressive form of AMD, affecting around 10-15% of patients living with AMD, but accounting for approximately 90% of severe vision loss due to the disease. In patients with wet 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 long-term eye injections every 4-8 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, Inc.

Adverum is a clinical-stage gene therapy company targeting unmet medical needs in ocular and rare diseases. Adverum develops gene therapy product candidates designed to provide durable efficacy by inducing sustained expression of a therapeutic protein. Adverum's core capabilities include clinical development, novel vector discovery and in-house manufacturing expertise, specifically in scalable process development, assay development, and current Good Manufacturing Practices quality control. 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 for advancing ADVM-022; the potential benefits of ADVM-022; the expected timing of reporting clinical data; the expected timing of submitting an IND for diabetic retinopathy; the expected timing of occupying Adverum's new facility; and the expected growth in the incidence of wet AMD, 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; obtaining regulatory approval for gene therapy product candidates; 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 August 8, 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.

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