Adverum Biotechnologies Reports Additional Clinical Data from First Cohort of OPTIC Phase 1 Trial of ADVM-022 Intravitreal Gene Therapy for Wet AMD at the American Academy of Ophthalmology 2019 Annual Meeting

October 11, 2019

-- Zero anti-VEGF rescue injections required in the first cohort and durable efficacy with median follow up of 34 weeks --
-- Sequential enrollment planned for OPTIC third and fourth cohorts --
-- Company to host and webcast a discussion with key opinion leaders on Saturday, October 12 at 10:30 am PT --

MENLO PARK, Calif., Oct. 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 additional clinical data for the first cohort of patients (n=6) in the ongoing OPTIC phase 1 clinical trial of ADVM-022, the company's intravitreal injection gene therapy, in treatment-experienced patients with wet age-related macular degeneration (wet AMD). The data are being presented today during a podium presentation at the Retina Subspecialty Day Program of the American Academy of Ophthalmology (AAO) 2019 Annual Meeting in San Francisco, CA. In addition, Adverum will host a discussion with key opinion leaders on Saturday, October 12, 2019 at 10:30 am PT, which will be webcast live and archived on the Events and Presentations section of the company's website.

Adverum also announced enrollment plans for the third and fourth cohorts in the ongoing OPTIC trial. The third cohort (n=9) has been initiated and patients will be treated with ADVM-022 at a dose of 2 x 10^11 vg/eye, the same dose used in the second cohort. Subsequently, patients in the fourth cohort (n=9) will be treated with ADVM-022 at a dose of 6x10^11 vg/eye, the same dose used in the first cohort. Since inflammation has generally been mild and responsive to steroid eye drops, patients in the third and fourth cohorts will receive prophylactic steroid eye drops instead of prophylactic oral steroids.

Previously, on September 12, 2019, Adverum presented data from the first cohort in the ongoing OPTIC trial at a pre-specified 24-week time point. Today, additional data for this cohort are being presented, including key outcomes with a median follow-up of 34 weeks. In treatment-experienced patients previously requiring frequent anti-VEGF injections to maintain vision, the data continue to demonstrate that the single ADVM-022 injection in this cohort was sufficient to maintain vision, with zero rescue injections required for any of the six patients. These additional data with a median follow-up of 34 weeks at a range of 28-44 weeks included:

- Zero rescue injection required for any patient based upon protocol-defined criteria:
  - Loss of >10 letters in best corrected visual acuity (BCVA) (using the ETDRS protocol) from baseline AND intraretinal or subretinal fluid observed by spectral-domain optical coherence tomography (SD-OCT) – with an increase in fluid judged by the investigator to be the cause of the visual loss; or
  - Increase in central subfield thickness >75 µm from baseline as assessed by SD-OCT; or
  - Presence of vision-threatening hemorrhage due to macular degeneration.
- Retinal anatomy improvements as observed on OCT scans were sustained.
- Vision was maintained, demonstrated by stable mean BCVA compared to baseline.
- ADVM-022 was safe and well-tolerated, with no serious adverse events (SAEs), no dose limiting toxicities (DLTs), and no Grade 3 adverse events (AEs).

An additional analysis of 24-week safety data presented today showed that inflammation, which is anticipated with ocular gene therapy, was manageable with steroids.

OPTIC Phase 1 Clinical Trial Data from Cohort 1 (n=6)

Baseline Characteristics:	**Value**
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	35.3 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 Approximate Snellen equivalent	65.8 letters 20/50
Mean CRT[3] study eye	369.2 µm

Results following a single ADVM-022 dose:	
Median follow-up (weeks)	34
Minimum/Maximum follow-up (weeks)	28-44
Follow-up cutoff date	October 1, 2019
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 (ETDRS letters)	-1.5
Minimum/Maximum (ETDRS letters)	-9 / +5
Safety:	
Grade 3 adverse events (AEs) [4]	0
Serious adverse events (SAEs)	0
Dose-limiting toxicities (DLTs)	0

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) (i.e., 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 Grade 3 or severe adverse event using CTCAE general guidelines criteria

"The data for ADVM-022 are promising, as this is the first time that an intravitreal injection gene therapy has provided sustained efficacy for patients with wet AMD who currently require frequent ocular anti-VEGF injections to maintain their vision," said Szilárd Kiss, M.D., retinal specialist, who presented the data at AAO. "Now, with a 34-week median follow up, a one-time treatment that achieves the goal of improving retinal anatomy and preserving vision would clearly be transformative for these patients and fulfill an important unmet need in wet AMD."

Aaron Osborne, MBBS, chief medical officer of Adverum, added, "The clinical profile of ADVM-022 demonstrates this gene therapy's potential to be a significant advance for patients with wet AMD. It is very encouraging that there continues to be zero rescue injections in this cohort of treatment-experienced patients with more than 6 months follow-up on all patients. We are expanding the development of ADVM-022 and are excited to share that enrollment is now open for the third cohort in OPTIC. We look forward to being able to deliver this novel intravitreal gene therapy candidate as soon as possible to patients with wet AMD and diabetic retinopathy, our second indication for ADVM-022. We are grateful for all of the investigators, patients, and caregivers who continue to participate in the OPTIC trial."

Future Outlook – Planned Milestones

- Adverum plans to begin dosing patients in the third cohort of the OPTIC trial in the fourth quarter of 2019 and plans to begin enrollment in the fourth cohort in the first quarter of 2020.
- Adverum plans to present 52-week data from the first cohort of patients in the OPTIC trial as well as 24-week data from the second cohort of patients in the first half of 2020.
- Adverum plans to submit an investigational new drug application for the treatment of ADVM-022 in diabetic retinopathy 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.

Podium Presentation Details:

Event: 2019 American Academy of Ophthalmology

Title: 24-week Results of Phase 1 Study of Intravitreal Gene Therapy with ADVM-022 for Neovascular AMD (OPTIC Trial)

Abstract: 30062032

Section: Section VIII: Late Breaking Developments, Part I

Date: October 11, 2019

Time:	4:26 p.m. – 4:31 p.m. PT
Location:	WEST 3002; Moscone Center, San Francisco, CA
Speaker:	Szilárd Kiss, M.D., Director of Clinical Research in the Department of Ophthalmology at Weill Cornell Medical College

Key Opinion Leader Event and Webcast:
The Company will host an event with expert retinal specialists to discuss the OPTIC data presented at AAO. The discussion will be held on Saturday, October 12, 2019, at 10:30 am PT, and will be webcast live and archived on the Events and Presentations section of Adverum's website. The presentation slides will be available at the conclusion of the company's webcast under the Events and Presentations in the Investors section of the company's website located at www.adverum.com.

About the OPTIC Phase 1 Trial of ADVM-022 in Wet AMD
The multi-center, open-label, phase 1 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 x 10^11 vg/eye and in the second cohort (n=6) 2 x 10^11 vg/eye. In the third cohort (n=9), patients will receive a dose of 2 x 10^11 vg/eye and in the fourth cohort (n=9), patients will receive a dose of 6x10^11 vg/eye. Patients in the first and second cohorts received prophylactic oral steroids, while patients in the third and fourth cohorts will receive prophylactic steroid eye drops. The primary endpoint of the trial is the safety and tolerability of ADVM-022 after a single IVT administration. Secondary endpoints include change in best-corrected visual acuity (BCVA), change in central retinal thickness (CRT) and macular volume, as well as mean number of anti-VEGF rescue injections and percentage of patients needing anti-VEGF rescue injections. Each patient enrolled in the study 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
ADVM-022 utilizes a propriety 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, reduce the burden of frequent anti-VEGF injections, optimize patient compliance, and to 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 a 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 (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. 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 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
Adverum Biotechnologies (Nasdaq: ADVM) is a clinical-stage gene therapy company targeting unmet medical needs for 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 for advancing ADVM-022, 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; 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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