Adverum Biotechnologies Announces Positive Interim Data from Cohorts 1-4 from OPTIC Phase 1 Trial of ADVM-022 Intravitreal Gene Therapy for Wet AMD

November 14, 2020

-- Maintained efficacy and greatly reduced anti-VEGF treatment burden after a single IVT injection of ADVM-022 --

-- Robust preliminary aqueous anti-VEGF protein expression observed at 18 months in Cohort 1 –

-- Well tolerated with ocular cell grades and steroid eye drop use decreasing over time --

-- First pivotal trial planned for mid-2021 following regulatory agency discussions --

-- Company to host webcast with Key Opinion Leaders to discuss new OPTIC data today, Saturday, November 14, 2020 at 7:30 am PT / 10:30 am ET --

REDWOOD CITY, Calif., Nov. 14, 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 positive new interim data from Cohorts 1-4 of the OPTIC Phase 1 clinical trial of ADVM-022 intravitreal (IVT) injection gene therapy in patients requiring frequent anti-VEGF injections for their wet age-related macular degeneration (AMD).

“With these impressive OPTIC data and the removal of the partial clinical hold on ADVM-022 by the FDA, our goal is to continue to advance into pivotal trials to demonstrate the transformative potential of our gene therapy,” said Laurent Fischer, M.D., chief executive officer of Adverum. “We are excited that ADVM-022 has the potential to be a “one and done” IVT injection that may dramatically reduce the treatment burden for the millions of patients with wet AMD and DME worldwide. Particularly during COVID-19, we are reminded of the benefits that ADVM-022, a novel gene therapy that has demonstrated long-term treatment benefit after one in-office IVT injection, could deliver to patients. Our Adverum team is laser-focused on accelerating the development and future commercial launch plans for ADVM-022. I am humbled by the dedication of the retina specialists and their staff, and our employees, to help progress our clinical trials which generate the data necessary to drive our mission of helping patients with severe ocular diseases.”

Adverum reported new interim data from the OPTIC trial (October 15, 2020 cutoff date) that further demonstrate the transformative potential of ADVM-022 to greatly reduce the anti-VEGF injection burden for patients with wet AMD:

- ADVM-022 continues to maintain efficacy at both high and low doses (n=30)
  - Mean BCVA[1] maintained
  - Mean CRT[2] maintained to improved
- Durability out to 92 weeks from a single IVT injection with zero supplemental injections in Cohort 1 (high dose)
- Robust preliminary aqueous anti-VEGF protein expression observed at 18 months in Cohort 1 (high dose)
  - Mean aqueous anti-VEGF protein level 1840 ng/mL
- Substantial reduction in annualized anti-VEGF injection frequency[3] following ADVM-022 in patients who previously required frequent injections:
  - High dose: 99% reduction
  - Low dose: 85% reduction
- Most patients are supplemental anti-VEGF injection free in OPTIC:
  - High dose: 14/15[4] patients injection free
  - Low dose: 10/15[5] patients injection free
- ADVM-022 continues to be well tolerated with a favorable safety profile at both high and low doses
  - All ADVM-022-related ocular adverse events (AE) were mild (78%) to moderate (22%)
  - Ocular inflammation, when observed, has been responsive to steroid eye drops and overall is decreasing over time
  - No clinical or fluorescein evidence of posterior inflammation
    - No vasculitis, retinitis, choroiditis, vascular occlusions, or endophthalmitis

OPTIC Phase 1 Clinical Trial Data:

Results Following a Single ADVM-022 Dose:	**Cohort 1**	**Cohort 2**	**Cohort 3**	**Cohort 4**
Patients	n=6	n=6	n=9	n=9
Median (Range) Follow-up Visit (Weeks)	**86** (64 to 92)	**64** (64 to 68)	**48** (32 to 48)	**16** (12 to 24)

ADVM-022 Dose	**High dose** 6 x 10^11 vg/eye	**Low dose** 2 x 10^11 vg/eye		**Low dose** 2 x 10^11 vg/eye		**High dose** 6 x 10^11 vg/eye
Prophylactic Steroid Regimen	**13-day oral**	**13-day oral**		**6-week eye drops**		**6-week eye drops**
Supplemental Anti-VEGF Injection Use:						
Number of patients supplemental injection free	6/6 patients	3/6 patients		7/9 patients		8/9 patients
Total supplemental anti-VEGF injections	0 injections	17 injections in 3 patients		8 injections in 2 patients		1 injection in 1 patient
Follow-up BCVA[1] and CRT[2]:						
	All Patients	All Patients	Supp. IVT-free Patients 50% (3/6)	All Patients	Supp. IVT-free Patients 78% (7/9)	N/A
BCVA mean change from baseline (letters)	-2.5	+0.2	+1.0	-0.9	+4.1	N/A
CRT mean change from baseline (µm)	-19.7 µm	-1.0 µm	-23.7 µm	-113.4 µm	-132.7 µm	N/A
Ocular Inflammation and Management:						
% patients with any cellular inflammation at most recent visit	33%	0%		11%		22%
Average # of daily steroid eye drops[6]	1.2	0.5		0.8		1.9

1 Best corrected visual acuity (BCVA)
2 Central retinal thickness (CRT)
3 Annualized rate (Before) = (number of IVTs in 12 months prior to ADVM-022) / (days from the first IVT in the past 12 months to ADVM-022 / 365.25)
Annualized rate (After) = (number of aflibercept IVTs since ADVM-022) / (days from ADVM-022 to the last study follow-up / 365.25)
4 All patients from Cohort 1 (n=6) and Cohort 4 (n=9)
5 All patients from Cohort 2 (n=6) and Cohort 3 (n=9)
6 Average calculated across entire cohort at their last follow up visit

Carl D. Regillo, M.D., F.A.C.S, director of the Wills Eye Hospital Retina Service said, “The sustained anatomical response observed in OPTIC in my experience is unprecedented, extending out beyond 18 months following a single intravitreal injection of ADVM-022. In addition, ADVM-022 has been well tolerated, and ocular inflammation, when observed, is responsive to steroid eye drops and decreases over time. ADVM-022 is a novel gene therapy that has demonstrated the potential to transform the treatment of patients living with wet AMD.”

Aaron Osborne, MBBS, chief medical officer of Adverum, added, “In OPTIC, we have enrolled the wet AMD patients requiring frequent injections to manage their condition, so we are very pleased with the significant reduction in anti-VEGF treatment burden demonstrated in both the high and low dose of ADVM-022. Additionally, the robust ocular anti-VEGF levels are a clear indication of ADVM-022’s stable, continuous therapeutic protein expression out to 18 months. We will continue to monitor our 30 patients and plan to present longer-term data, including additional anti-VEGF protein expression data from patients who consent to aqueous taps, in the first half of 2021. We are planning for our end-of-Phase 1 meeting with the U.S. FDA on our development program, including the initiation of our first pivotal clinical trial in wet AMD in mid-2021. With these continued impressive data, we believe that both doses warrant further investigation.”

Future Plans
ADVM-022 in wet AMD

- Present longer-term data from OPTIC Phase 1 trial, including additional anti-VEGF protein expression data, in the first half of 2021
- Initiate a pivotal trial mid-2021

ADVM-022 in DME

- Present clinical data from INFINITY Phase 2 trial in the second half of 2021

Adverum Webcast:
Date: November 14, 2020
Time: 7:30 – 9:00 am PT (10:30 am – 12:00 pm ET)
Presenters:

- Carl D. Regillo, M.D., F.A.C.S, director of the Wills Eye Hospital Retina Service and investigator in the OPTIC Phase 1 trial
- Steven Yeh, M.D., associate professor, director, section of uveitis and ocular immunology, Emory Eye Center
- David S. Boyer, M.D., senior partner, Retina-Vitreous Associates Medical Group and adjunct clinical professor of ophthalmology, University of Southern California/ Keck School of Medicine, Los Angeles, investigator in the OPTIC Phase 1 trial

The live video webcast will be accessible under Events and Presentations in the Investors section of the company's website. To participate in the conference call, dial 1-877-705-6003 (domestic) or 1-201-493-6725 (international) and refer to the “Adverum Biotechnologies’ OPTIC Clinical Data Discussion Conference Call.” It is recommended call participants dial in 15 minutes in advance. The archived audio webcast will be available on the Adverum website following the call and will be available for 30 days.

About the OPTIC Phase 1 Trial of ADVM-022 in Wet AMD
This 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. Patients received high dose (6 x 10^11 vg/eye) of ADVM-022 in Cohort 1 (n=6) and Cohort 4 (n=9) and patients received low dose (2 x 10^11 vg/eye) of ADVM-022 in Cohort 2 (n=6) and Cohort 3 (n=9). Patients in Cohorts 3 and 4 received six weeks of prophylactic steroid eye drops rather than 13 days of prophylactic 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 the need for supplemental anti-VEGF injections. Each patient enrolled will be followed for a total of two years.

Eleven leading retinal centers across the United States are participating in the OPTIC Phase 1 trial for ADVM-022. For more information, 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 (IVT), designed to deliver long-term efficacy and reduce the burden of frequent anti-VEGF injections, optimize patient compliance and improve vision outcomes for patients with wet age-related macular degeneration (wet AMD) and diabetic macular edema (DME).

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 wet AMD.

Adverum is currently evaluating ADVM-022 in the OPTIC Phase 1 clinical trial in patients with wet AMD and the INFINITY Phase 2 trial in patients with DME.

About 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[1]. 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 [2,3].

The current standard-of-care therapies for wet AMD are anti-VEGF proteins. These therapies can be burdensome, as patients generally require chronic intravitreal (IVT) injection of anti-VEGF protein every 4-12 weeks. Compliance with this regimen can be difficult for patients and their caregivers, leading to compliance deficiencies and loss of vision from underdosing. It is estimated that these standard-of-care branded anti-VEGF therapies used for the treatment of wet AMD, DR, retinal vein occlusion, and other ocular diseases generated in excess of $11 billion in sales worldwide in 2019[4].

[1] Arch Ophthalmol. 2004;122(4):564-572. doi:10.1001/archopht.122.4.564.

[2] Brown GC, Brown MM, Sharma S, et al. The Burden of Age-Related Macular Degeneration: A Value-Based Medicine Analysis. Transactions of the American Ophthalmological Society. 2005.

[3] California Retina Consultants. Advances in Wet AMD. Available at: https://www.californiaretina.com/advances-in-wet-amd/

[4] Year-end 2019 financial statements from Regeneron, Roche, and Novartis.

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 advancing the clinical development of its novel gene therapy candidate, ADVM-022, as a one-time, intravitreal injection for the treatment of patients with wet age-related macular degeneration and diabetic macular edema. 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: the potential for ADVM-022 in treating patients with wet AMD and DME; the expected growth of the incidence of new cases of wet AMD in the U.S. as its population ages; Adverum's expectations that it will present longer-term data from the OPTIC Phase 1 trial for ADVM-022 in wet AMD in the first half of 2021 and data from the INFINITY Phase 2 trial for ADVM-022 in DME in the second half of 2021; Adverum's plans to accelerate the development and future commercial launch plans for ADVM-022; and Adverum's expectations as to its plans to advance ADVM-022 in wet AMD by initiating a pivotal trial mid-2021. All of these statements 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 preliminary or interim results of clinical trials to change as the clinical trial continues or in connection with the preparation and analysis of final 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 and INFINITY trials and vector production; the effects of the COVID-19 pandemic on the company's operations and on the company's ongoing clinical trials; and ability to fund operations through completion of the OPTIC and INFINITY trials and thereafter. Risks and uncertainties facing Adverum are described more fully in Adverum's Form 10-Q filed with the SEC on November 5, 2020 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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