# Adverum Biotechnologies Reports Positive Interim Data from Cohorts 1-3 of OPTIC Phase 1 Trial of ADVM-022 Intravitreal Gene Therapy for Wet AMD

May 4, 2020

*-- Robust efficacy and evidence of a dose response from single intravitreal injection (IVT) of ADVM-022 --*

*-- Long-term durability beyond 1 year from single IVT injection of ADVM-022 with zero rescue injections in Cohort 1 --*

*-- Encouraging early data from Cohort 3 --*

*-- Company to host a conference call and webcast with key opinion leaders today at 2:15 pm PDT --*

REDWOOD CITY, Calif., May 04, 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 Cohorts 1-3 of the OPTIC Phase 1 dose-ranging 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) and provided a business update.

For the first time, interim data are being presented from patients in Cohort 3[1, 2] and updated data are being presented from Cohorts 1 and 2 following treatment with a single IVT injection of ADVM-022. April 1, 2020 is the cutoff date for all data being presented. New data as detailed in the table below further demonstrate the transformative potential of ADVM-022 to greatly reduce anti-VEGF injection burden in wet AMD:

- ADVM-022 continues to show robust efficacy
- Long-term durability beyond 1 year from a single IVT injection with zero rescue injections in Cohort 1
- Further evidence of a dose response:
  - -- $6x10^{11}$ vg/eye: 6/6 patients rescue injection free
  - -- $2x10^{11}$ vg/eye: 8/11[3] patients rescue injection free
- ADVM-022 continues to be well tolerated with a favorable safety profile in all 3 cohorts:
  - -- ADVM-022 related ocular AEs mild (69%) to moderate (31%)
  - -- No ADVM-022 related SAEs or non-ocular adverse events
  - -- No evidence of vasculitis, retinitis, or choroiditis
  - -- Ocular inflammation, when observed, has been responsive to steroid eye drops
- Early evidence from Cohort 3 suggests that a 6-week prophylactic regimen of steroid eye drops results in fewer adverse events and less inflammation, compared to a 13-day prophylactic regimen of oral steroids as used in Cohorts 1 and 2. In all 9 patients in Cohort 3:
  - -- No cellular inflammation graded at a score above 1+ in any patient
  - -- No patients have required more than steroid eye drops
  - -- Only 8 ADVM-022-related AEs in 4 patients have been observed, all mild or moderate
- Early anatomic and vision improvements observed in Cohort 3, with first 5 patients with 20 weeks follow-up showing:
  - -- Mean CRT[4] reduction (-137.8 mm)
  - -- Mean BCVA[5] gain (+6.8 letters)

**OPTIC Phase 1 Clinical Trial Data:**

| **Results Following a Single ADVM-022 Dose:** | **Cohort 1** | **Cohort 2** | **Cohort 3[1]** |
|---|---|---|---|
| Patients | n=6 | n=6 | n= 9 |
| Dose ADVM-022 | **Higher Dose**<br>6 x 10^11 vg/eye | **Lower Dose**<br>2 x 10^11 vg/eye | **Lower Dose**<br>2 x 10^11 vg/eye |
| Follow-up (median) | 60 weeks | 36 weeks | 20 weeks |
| Prophylactic steroid regimen | 13-day oral | 13-day oral | 6-week eye drops[2] |
| **Rescue Injections:** | | | |
| Number of patients requiring anti-VEGF rescue injections | 0/6 patients | 2/6 patients | 1/5 for first 5 patients with 20 weeks follow-up |
| Total anti-VEGF rescue injections | 0 injections | 8 injections | 2 injections |
| | | | |

| Follow-up BCVA[5] and CRT[4]: | 52-64 weeks (median 60) | 32-40 weeks (median 36) | | First 5 patients with 20 weeks follow-up | |
|---|---|---|---|---|---|
| | **All Patients** 100% (6/6) Rescue Free | **All Patients** | **Rescue Free Patients** 67% (4/6) | **All Patients** | **Rescue Free Patients** 80% (4/5) |
| BCVA mean change from baseline (letters) | -2.7 | -2.8 | +2.3 | +6.8 | +8.8 |
| CRT mean change from baseline (mm) | -26.2 | -40.8 | -30.0 | -137.8 | -149.8 |

[1] The first 5 patients had 20 weeks of follow-up as of April 1, 2020. The remaining 4 patients had 4-12 weeks of follow-up, insufficient for assessment of efficacy.

[2] In Cohort 3, patients received 6-week prophylactic topical steroid regimen in place of the 13-day prophylactic oral steroid regimen used in Cohorts 1 and 2.

[3] 4/6 patients from Cohort 2 and 4/5 patients from Cohort 3 with 20 weeks follow up

[4] Central retinal thickness (CRT)

[5] Best corrected visual acuity (BCVA)

Arshad M. Khanani, M.D., M.A., director of clinical research, Sierra Eye Associates and principal investigator in the OPTIC trial said, “It’s impressive to see the long-term durability demonstrated at the higher dose of ADVM-022 in a patient population that previously required frequent injections to maintain their vision and are now beyond one year of follow-up with no rescue injections. Additionally, preliminary evidence in Cohort 3 shows vision and anatomical improvements and that the 6-week prophylactic steroid eye drop regimen is effective at minimizing early ocular inflammation. These are very positive data, and it is exciting to see that this intravitreal gene therapy has the potential to completely change the treatment paradigm for patients with wet AMD.”

Aaron Osborne, MBBS, chief medical officer of Adverum, added, “We are encouraged by the robust efficacy signal and evidence of a dose response in the OPTIC trial with interim data from 3 cohorts. Also, momentum in OPTIC is strong as we are currently enrolling patients in Cohort 4 at the higher dose of 6 x 10^11 vg/eye using the same steroid regimen as Cohort 3. We look forward to reporting additional data in the second half of this year from OPTIC. Beyond wet AMD, we are on track with our plans to advance ADVM-022 in diabetic retinopathy, our second indication, and we continue to expect to begin enrolling patients in our planned clinical trial in the second half of this year.”

**Business Update**

- Adverum reports $297 million in cash, cash equivalents and short-term investments as of March 31, 2020, compared to $166 million as of December 31, 2019. In February 2020, Adverum raised approximately $140.8 million in net proceeds from an underwritten public offering. The Company expects this quarter-end cash position to fund operations into 2022.
- Due to COVID-19, and the shelter-in-place mandated in the State of California, Adverum implemented a mandatory work-from-home policy for all non-essential activities.
  -- To minimize the chance of community infection, the company has limited on-site activities to only the most time-critical or necessary operational activities.
  -- Pursuant to the SEC’s recent order under section 36 of the Securities Exchange Act of 1934, Adverum now expects to file its Form 10-Q for the first quarter of 2020 with the SEC on May 28, 2020.

**2020 Milestones**
**First half**

- Submit an investigational new drug application for ADVM-022 in diabetic retinopathy, a key VEGF-driven cause of vision loss among working-age adults

**Second half**

- Present data from all four cohorts of the OPTIC trial
- Begin enrolling patients in a planned Phase 1/2 clinical trial for ADVM-022 in diabetic retinopathy to expand Adverum’s clinical development pipeline

**Conference Call and Webcast Today:**
In addition, Adverum will host a conference call and webcast with expert retinal specialists to discuss the new OPTIC data and the potential opportunity for ADVM-022. The discussion will be held on Monday, May 4, 2020 beginning at 2:15 pm PDT (5:15 pm EDT). Individuals can participate in the conference call by dialing 1-866-420-8347 (domestic) or 1-409-217-8241 (international) and refer to “Adverum Biotechnologies’ KOL Discussion Call.” It is recommended call participants dial in 15 minutes in advance. The webcast and slides for the call will be accessible under Events and Presentations in the Investors section of the company's website. 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**
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 received a dose of 2 x 10^11 vg/eye and in Cohort 4, patients (n=9) are receiving a dose of 6 x 10^11 vg/eye. Patients in Cohorts 3 and 4 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 the need for anti-VEGF rescue injections. Each patient enrolled will be followed for a total of two years.

Ten 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 initiate a planned Phase 1/2 clinical trial of ADVM-022 for the treatment of diabetic retinopathy in the second 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: the potential for ADVM-022 in treating patients with wet AMD expressed in Dr. Khanani's and Dr. Osborne's quotes; Adverum's expectations as to the timing of reporting additional data in the second half of 2020, and as to its plans to advance ADVM-022 in diabetic retinopathy by filing an investigational drug application in the first half of 2020 and begin enrolling patients in a planned Phase 1/2 clinical trial in the second half of 2020; 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; the effects of the COVID-19 pandemic on the company's operations; 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-K filed with the SEC on March 12, 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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