Adverum Biotechnologies Announces Positive Interim Data from Cohorts 1-4 from OPTIC Phase 1 Trial of ADVM-022 Intravitreal Gene Therapy for wet AMD, Reports Recent Business Progress and Second Quarter 2020 Financial Results

August 10, 2020

-- Continued robust treatment response from both high and low doses --

-- Long-term durability beyond 15 months from single IVT injection with zero rescue injections in Cohort 1 --

-- Well tolerated across all Cohorts; encouraging early safety data from Cohort 4 --

-- OPTIC enrollment complete; planning to start pivotal trial in wet AMD mid-2021 --

-- Company to host conference call and webcast with Key Opinion Leader Dr. Arshad Khanani today at 1:30 pm PT / 4:30 pm ET --

REDWOOD CITY, Calif., Aug. 10, 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). The company also reported recent business progress and financial results for the second quarter ended June 30, 2020.

For the first time, interim data from all four cohorts of the OPTIC trial (July 23, 2020 cutoff date), including preliminary safety data from Cohort 4, are presented. These data further demonstrate the transformative potential of ADVM-022 to greatly reduce the treatment burden for patients with wet AMD:

- ADVM-022 continues to show robust treatment response
  - Mean BCVA[1] maintained
  - Mean CRT[2] maintained to improved
- Long-term durability beyond 15 months from single IVT injection with zero anti-VEGF rescue injections in Cohort 1 (high dose)
- Further evidence of a dose response:
  - High dose: 6/6[3] patients rescue injection free
  - Low dose: 10/15[4] patients rescue injection free
- Substantial reduction in annualized anti-VEGF injection rate following administration of ADVM-022[5]:
  - High dose: 100%
  - Low dose: 87%
- ADVM-022 continues to be well tolerated with a favorable safety profile in all 4 cohorts (n=30)
  - All ADVM-022-related ocular adverse events (AE) were mild (78%) to moderate (22%)
    - One AE of special interest of moderate recurrent uveitis deemed to be related to ADVM-022 was responsive to steroid eye drops (Cohort 1)
  - Ocular inflammation, when observed, has been responsive to steroid eye drops
  - No clinical or fluorescein[6] evidence of posterior inflammation
    - No vasculitis, retinitis, choroiditis, vascular occlusions, or endophthalmitis
- Early evidence from Cohort 4, consistent with Cohort 3, suggests that a prophylactic regimen of steroid eye drops results in fewer adverse events and less inflammation, when compared to a prophylactic regimen of oral steroids as used in Cohorts 1 and 2. In Cohorts 3 and 4, no patients have required more than steroid eye drops.

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 follow-up visit (weeks)	**72**	**52**		**36**		**4**
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**
Rescue Injections:						
Number of patients requiring anti-VEGF rescue injections	0/6 patients	3/6 patients		2/9 patients		0/9 patients
Total anti-VEGF rescue injections	0 injections	13 injections		5 injections		0 injections
Mean annualized anti-VEGF injection frequency before and after ADVM-022[5]	Before: 9.6 After: 0	Before: 10.0 After: 1.3				N/A
Reduction in mean annualized anti-VEGF injection frequency after ADVM-022[5]	100%	87%				N/A
Follow-up BCVA[1] and CRT[2]:						
	All Patients	All Patients	Rescue Free Patients 50% (3/6)	All Patients	Rescue Free Patients 78% (7/9)	N/A
BCVA mean change from baseline (letters)	-3.2	-2.0	0	+4.0	+6.4	N/A
CRT mean change from baseline (mm)	-21.0 mm	-24.8 mm	-8.3 mm	-118.6 mm	-152.7 mm	N/A

1 Best corrected visual acuity (BCVA)
2 Central retinal thickness (CRT)
3 All patients from Cohort 1 (n=6)
4 All patients from Cohort 2 (n=6) and Cohort 3 (n=9)
5 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)
6 Fluorescein angiography of posterior pole

Arshad M. Khanani, M.D., M.A., managing partner and director of clinical research, Sierra Eye Associates, clinical associate professor of ophthalmology, University of Nevada, and top enrolling investigator in the OPTIC trial said, “In my experience the sustained anatomical treatment response following a single intravitreal injection of ADVM-022 is unprecedented, which is remarkable considering that the patients enrolled in OPTIC were difficult-to-treat and had previously required frequent injections to maintain their vision. The safety profile to date shows that ADVM-022 is well tolerated, and that the prophylactic steroid eye drop regimen has been effective at limiting early ocular inflammation. I believe that ADVM-022 has the potential to be a transformational gene therapy improving real-world outcomes for patients living with wet AMD.”

Aaron Osborne, MBBS, chief medical officer of Adverum, added, “We have completed dosing patients in OPTIC, with 30 patients being followed up across four cohorts, and we look forward to presenting additional data from these cohorts by the end of this year. With the exciting data presented to date from OPTIC highlighting the potential of ADVM-022 to dramatically reduce treatment burden for patients with wet AMD, we plan to seek U.S. and international regulatory authorities’ input as we progress towards initiating a pivotal clinical trial in mid-2021.”

Laurent Fischer, M.D., chief executive officer of Adverum stated, “With these impressive OPTIC data, we are now poised to move our potentially transformative therapy into pivotal trials. ADVM-022, a novel gene therapy providing continuous delivery of aflibercept, has the potential to be a “one and done” IVT injection that would dramatically reduce the treatment burden for the millions of patients with wet AMD and DME worldwide. As we continue to see positive data from ongoing trials, we are preparing to accelerate our development and future commercial launch plans for ADVM-022. We continue to add industry-leading talent to our team and are beginning to expand our business operations and capabilities, including clinical, regulatory, manufacturing, and pre-commercial functions. It’s an exciting time at Adverum, and I’m humbled by the dedication of the retina specialists, their patients and our employees for their tireless efforts to help patients with severe ocular diseases during a pandemic.”

Recent Progress
Clinical Development
INFINITY Phase 2 Clinical Trial of ADVM-022 in Diabetic Macular Edema

- Began randomizing patients in the INFINITY trial. INFINITY is a Phase 2, multi-center, randomized, double-masked, active

comparator-controlled trial in approximately 33 patients with diabetic macular edema (DME). Diabetes impacts over 30 million people in the United States and over 400 million people globally and is increasing in prevalence. Approximately 5% of adults with diabetes are impacted by DME, a vision-threatening complication of diabetic retinopathy.

- INFINITY is designed to demonstrate superior control of disease activity following a single IVT injection of ADVM-022 compared to a single aflibercept injection, as measured by time to worsening of DME disease activity in the study eye
- Additional objectives include assessments of treatment burden, visual acuity, retinal anatomy and safety outcomes

Future Plans
ADVM-022 in wet AMD

- Present clinical data from Cohorts 1-4 of OPTIC Phase 1 trial by year-end 2020
- Initiate a pivotal trial mid-2021

ADVM-022 in DME

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

Manufacturing

- Initiating process scale-up from 200L to 1000L scale to support the future commercial product launch of ADVM-022
- Beginning to plan for in-house GMP capabilities with initiation of site selection

COVID-19
To date, Adverum has experienced limited impact from COVID-19 on its operations and ongoing clinical programs, including the OPTIC and INFINITY clinical trials. The company is continuing to monitor and attempt to address or limit the potential impacts of COVID-19 on its employees and operations, patient safety, patient enrollment, continued participation of patients already enrolled in the company's clinical studies, protocol compliance, data quality, and overall study integrity.

Financial Results for the Three Months Ended June 30, 2020

- **Cash, cash equivalents and short-term investments** were $280.1 million as of June 30, 2020, compared to $166.0 million as of December 31, 2019. Adverum expects this quarter-end cash position to fund operations into 2022.
- **Research and development expenses** were $19.2 million for the three months ended June 30, 2020, compared to $9.0 million for the same period in 2019. Research and development expenses increased primarily due to higher material production costs and personnel-associated costs. Stock-based compensation expense included in research and development expenses was $1.7 million for the second quarter of 2020.
- **General and administrative expenses** were $10.6 million for the three months ended June 30, 2020, compared to $7.1 million for the same period in 2019. General and administrative expenses increased primarily due to higher personnel-associated costs as well as depreciation expense for Adverum's new headquarters. Stock-based compensation expense included in general and administrative expenses was $3.1 million for the second quarter of 2020.
- **Net loss** was $29.2 million, or $0.36 per basic and diluted share, for the three months ended June 30, 2020, compared to $15.0 million, or $0.23 per basic and diluted share, for the same period in 2019.

Conference Call and Webcast Information
Adverum will host a conference call and webcast today with Key Opinion Leader Dr. Arshad Khanani at 1:30 pm PT / 4:30 pm ET to present new data from the OPTIC Phase 1 clinical trial of ADVM-022 in wet AMD and provide an update on recent business progress. The live webcast will be accessible under Events and Presentations in the Investors section of the company's website. To participate in the conference call dial 1-855-327-6837 (domestic) or 1-631-891-4304 (international) and refer to the "Adverum Biotechnologies' Conference Call." It is recommended call participants dial in 15 minutes in advance. The archived webcast and slide presentation 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 a high dose (6 x 10^11 vg/eye) of ADVM-022 in Cohort 1 (n=6) and Cohort 4 (n=9) and patients received a 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 anti-VEGF rescue 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 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; Adverum’s expectations that it will present additional data from all four cohorts of the OPTIC Phase 1 trial for ADVM-022 in wet AMD by the end of this year; Adverum’s expectations as to its plans to advance ADVM-022 in wet AMD by initiating a pivotal trial mid-2021 and in DME by continuing to enroll patients in the INFINITY trial, including without limitation its expected enrollment numbers for the INFINITY trial; Adverum’s expectations that it will present data from the INFINITY trial in the second half of 2021; Adverum’s expectations that it will accelerate its development, manufacturing, and commercial launch plans for ADVM-022; and Adverum’s expectations that its current cash position will fund its operations into 2022. 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 August 10, 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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Adverum Biotechnologies, Inc.
Consolidated Balance Sheets
(In thousands)

	June 20 2020	December 31, 2019
	(Unaudited)	(1)
Assets		
Current assets:		
Cash and cash equivalents	$ 27,359	$ 65,897
Short-term investments	252,780	100,138
Prepaid expenses and other current assets	2,542	9,835
Total current assets	282,681	175,870
Operating lease right-of-use assets	20,011	20,963
Property and equipment, net	27,466	24,884
Restricted cash	999	999
Deposit and other long-term assets	19	11
Total assets	$ 331,176	$ 222,727
Liabilities and stockholders' equity		
Current liabilities:		

Accounts payable	$ 10,367	$ 4,103
Accrued expenses and other current liabilities	6,666	11,271
Lease liability, current portion	4,221	4,034
Total current liabilities	21,254	19,408
Lease liability, net of current portion	27,258	28,214
Other noncurrent liabilities	101	148
Total liabilities	48,613	47,770
Stockholders' equity:		
Common stock	8	7
Additional paid-in capital	720,288	560,704
Accumulated other comprehensive loss	(598)	(725)
Accumulated deficit	(437,135)	(385,029)
Total stockholders' equity	282,563	174,957
Total liabilities and stockholders' equity	$ 331,176	$ 222,727

(1) Derived from Adverum’s annual audited consolidated financial statements.

Adverum Biotechnologies, Inc.
Consolidated Statements of Operations
(In thousands except per share data)
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	**2019**	**2020**	**2019**
Operating expenses:				
Research and development	$ 19,177	$ 8,970	$ 33,928	$ 19,101
General and administrative	10,598	7,132	19,638	12,708
Total operating expenses	29,775	16,102	53,566	31,809
Operating loss	(29,775)	(16,102)	(53,566)	(31,809)
Other income, net	575	1,148	1,460	2,366
Net loss	$ (29,200)	$ (14,954)	$ (52,106)	$ (29,443)
Net loss per share — basic and diluted	$ 0.36	$ (0.23)	$ (0.68)	$ (0.46)
Weighted-average common shares outstanding - basic and diluted	80,229	63,740	77,010	63,429

Source: Adverum Biotechnologies, Inc.