Adverum Announces Shortened Timelines and Clear Development Path for ADVM-022 Intravitreal Gene Therapy in Wet AMD, Reports Recent Business Progress and Fourth Quarter 2020 Financial Results

March 1, 2021

-- BLA submission targeted in 2024 --

-- Alignment on clinical development and CMC requirements from recent interactions with FDA --

-- Two global Phase 3 trials expected to enroll 900 patients in total; Targeted to initiate in 4Q 2021 --

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

REDWOOD CITY, Calif., March 01, 2021 (GLOBE NEWSWIRE) -- Adverum Biotechnologies, Inc. (Nasdaq: ADVM), a clinical-stage gene therapy company targeting unmet medical needs in ocular and rare diseases, today announced that it has gained alignment with the U.S. Food and Drug Administration (FDA) on the clinical development path for ADVM-022, an investigational single, in-office intravitreal (IVT) injection gene therapy for the treatment of wet age-related macular degeneration (AMD). The Company also reported financial results for the fourth quarter ended December 31, 2020, and provided a business update.

“Having clarity from U.S. regulators on our pivotal plans for ADVM-022 is a significant step forward in accelerating our mission to transform the lives of millions of patients around the world living with wet AMD and at risk of losing their vision,” said Laurent Fischer, M.D., chief executive officer at Adverum Biotechnologies. “Based on the results in our OPTIC trial to date and our discussion with the FDA, we can now initiate two global Phase 3 trials and have alignment on both clinical development and CMC requirements to support a BLA submission anticipated in 2024. Our team is well prepared to execute this new fast-to-market approach. In preparation of our potential commercialization of ADVM-022 targeting the treatment of millions of patients worldwide, we are expanding our CMC capabilities and investing in an in-house GMP manufacturing facility. Our goal is to deliver a one-time, in-office treatment that preserves patient sight for life.”

About the Global Phase 3 Program for ADVM-022 for the Treatment of Wet AMD
Based on the favorable safety and efficacy profiles observed to date from ADVM-022 in the OPTIC trial as well as interactions with the FDA, Adverum is planning to accelerate its clinical development program by conducting two global Phase 3 trials targeted to initiate in parallel in the fourth quarter of 2021. Pending successful outcomes of these trials, Adverum anticipates being able to submit its Biologics License Application for ADVM-022 for wet AMD in 2024.

The most recent OPTIC data presented at Angiogenesis 2021 demonstrated that patients who received 2 x 10^11 vg/eye of ADVM-022 experienced an 85% reduction in annualized anti-VEGF injections and two-thirds remained supplemental anti-VEGF injection free with median follow up of 48 weeks. Patients completing two years in OPTIC are being enrolled into an extension trial to be followed for up to five years.

The two Phase 3 trials will study the efficacy and safety of two doses of ADVM-022 straddling the 2 x 10^11 vg/eye dose used in the OPTIC trial. In the Phase 3 trials of approximately 450 patients each, patients newly diagnosed with wet AMD will be randomized to one of three arms, receiving a single IVT injection of either 3 x 10^11 vg/eye or 1 x 10^11 vg/eye of ADVM-022 compared to aflibercept IVT every 8 weeks. The primary endpoint will be non-inferiority to aflibercept based on change from baseline in Best Corrected Visual Acuity (BCVA) at one year.

“The remarkable durability and anatomical improvements seen with a single IVT injection of ADVM-022 in the OPTIC trial suggest that our therapy could provide clinically important benefits over currently marketed therapies and other late-stage programs in development for wet AMD,” said Aaron Osborne, MBBS, chief medical officer at Adverum Biotechnologies. “In our OPTIC trial, we enrolled difficult-to-treat wet AMD patients who required frequent anti-VEGF injections to maintain their vision. Our Phase 3 clinical trials will enroll newly diagnosed wet AMD patients and will be comparable to the designs of previous intravitreal anti-VEGF agents’ Phase 3 trials. With our intravitreal approach, we look forward to working with clinical trial sites to rapidly enroll these studies for potential BLA submission in 2024.”

Recent Progress

- Reed V. Tuckson, M.D. joined Adverum’s board as an independent director. Dr. Tuckson brings extensive healthcare policy knowledge from his experience in multiple facets of the healthcare industry, including a 13-year tenure in senior leadership positions at UnitedHealth Group.
- Dawn Svoronos joined Adverum’s board as an independent director. Ms. Svoronos has three decades of global biopharmaceutical industry experience, spanning the United States, Canada, Europe, and Asia, gained during her 25-year career at Merck & Co.
- Christopher J. DeRespino joined Adverum as chief business officer, a newly created position. Mr. DeRespino will lead the company’s corporate strategy and global business development efforts. He brings significant biopharmaceutical experience

gained at Amgen, Pfizer, and Onyx.

- Long-term preclinical data were published on ADVM-022 in *Translational Vision Science & Technology (TVST)*, an official journal of the Association for Research in Vision and Ophthalmology (ARVO). This preclinical study in non-human primates is the longest safety and expression study to date, with measurements out to 30 months following a single IVT injection. The full online publication can be accessed from the TVST website.
- Patient enrollment was completed in the INFINITY Phase 2 trial to evaluate a single intravitreal injection of ADVM-022 for the treatment of diabetic macular edema (DME). Data from this randomized trial are expected in the second half of 2021. INFINITY is designed to demonstrate superior disease control compared to a single aflibercept injection, measured by time to worsening of DME disease activity. Additional objectives assess frequency of supplemental aflibercept to the study eye, visual acuity (BCVA), retinal anatomy (OCT), Diabetic Retinopathy Severity Scale (DRSS), and safety outcomes.
- Investing in a new state-of-the-art Good Manufacturing Practices (GMP) commercial facility in Durham, North Carolina, which is expected to be production-ready by the end of 2023. This facility capitalizes on Adverum's internal AAV manufacturing expertise while providing security and flexibility to support the potential commercialization of ADVM-022.
- Licensed to LEXEO Therapeutics exclusive worldwide rights to its novel gene therapy candidate for cardiomyopathy due to Friedreich's Ataxia.

Upcoming Milestones
ADVM-022 in Wet AMD:

- Initiate two global Phase 3 pivotal trials for ADVM-022 in wet AMD in the fourth quarter of 2021
- Present long-term OPTIC data, including one-year data from Cohort 3 (2 x 10^11), in the second quarter of 2021

ADVM-022 in DME:

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

GMP Commercial Manufacturing:

- Begin build-out of new GMP commercial manufacturing facility in North Carolina with multiple production suites, expected to be production-ready by the end of 2023 in preparation for commercialization of ADVM-022

Conference Call Information
Adverum will host a conference call today with Key Opinion Leader Dr. Arshad Khanani at 1:30 pm PT / 4:30 pm ET on the ADVM-022 pivotal program for the treatment of wet AMD and provide an update on recent business progress. 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." Due to high call volume, it is recommended call participants dial in 15 minutes in advance.

Financial Results for the Three Months Ended December 31, 2020

- **Cash, cash equivalents and short-term investments** were $429.7 million as of December 31, 2020, compared to $454.5 million as of September 30, 2020 and $166.0 million as of December 31, 2019. Adverum expects this year-end cash position to fund operations into mid-2022.
- **Research and development expenses** were $22.7 million for the three months ended December 31, 2020, compared to $11.4 million for the same period in 2019. Research and development expenses increased primarily due to higher personnel-associated costs, material production costs, and clinical trial expenses. Stock-based compensation expense included in research and development expenses was $2.2 million for the fourth quarter of 2020.
- **General and administrative expenses** were $13.7 million for the three months ended December 31, 2020, compared to $8.3 million for the same period in 2019. General and administrative expenses increased primarily due to higher personnel-associated costs, professional services costs, and depreciation expense for Adverum's new headquarters. Stock-based compensation expense included in general and administrative expenses was $4.0 million for the fourth quarter of 2020.
- **Net loss** was $37.6 million, or $0.39 per basic and diluted share, for the three months ended December 31, 2020, compared to $18.9 million, or $0.29 per basic and diluted share, for the same period in 2019.

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.

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 the 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 intentions to conduct two Phase 3 trials that will both initiate in the fourth quarter of 2021, including the anticipated trial designs and that Adverum looks forward to working with clinical trial sites to rapidly enroll these studies; Adverum’s anticipated Biologics License Application submission in 2024; the timing of receiving and presenting data from ongoing and planned trials; Adverum’s expectations regarding when its Durham, North Carolina facility will be production-ready and the amount that Adverum will invest in this facility; the statements under the caption “Upcoming Milestones”; Adverum’s expectations that its year-end cash position will fund operations into mid-2022; and the potential efficacy and safety of ADVM-022 in wet AMD and DME. Actual results 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; and the potential for future complications or side effects in connection with use of ADVM-022. Risks and uncertainties facing Adverum are described more fully in Adverum’s Quarterly Report on Form 10-Q for the quarter ended September 30, 2020 and any subsequent filings with the SEC 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.

Adverum Biotechnologies, Inc.
Consolidated Balance Sheets
(In thousands)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 62,424	$ 65,897
Short-term investments	367,305	100,138
Prepaid expenses and other current assets	4,709	9,835
Total current assets	434,438	175,870
Property and equipment, net	27,725	24,884
Operating lease right-of-use asset	19,376	20,963
Restricted cash	999	999
Deposit and other non-current assets	29	11
Total assets	$ 482,567	$ 222,727
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	2,810	4,103
Lease liability, current portion	4,473	4,034
Accrued expenses and other current liabilities	13,588	11,271
Total current liabilities	20,871	19,408
Lease liability, net of current portion	26,235	28,214
Other non-current liabilities	1,114	148
Total liabilities	48,220	47,770
Stockholders' equity:		
Common stock	10	7
Additional paid-in capital	937,134	560,704
Accumulated other comprehensive loss	(261)	(725)
Accumulated deficit	(502,536)	(385,029)
Total stockholders' equity	434,347	174,957
Total liabilities and stockholders' equity	$ 482,567	$ 222,727

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

	Three months ended December 31,		Years ended December 31,	
	2020	2019	2020	2019
	(Unaudited)			
Collaboration and license revenue	$ -	$ -	$ -	$ 250

Operating expenses:				
Research and development	22,728	11,374	73,309	40,419
General and administrative	13,652	8,279	44,641	28,376
Total operating expenses	36,380	19,653	117,950	68,795
Operating loss	(36,380)	(19,653)	(117,950)	(68,545)
Other income, net	(138)	728	1,557	4,059
Net loss before income taxes	(36,518)	(18,925)	(116,393)	(64,486)
Income tax provision	(1,114)	-	(1,114)	-
Net loss	(37,632)	(18,925)	(117,507)	(64,486)
Net loss per share — basic and diluted	$ (0.39)	$ (0.29)	$ (1.38)	$ (1.01)
Weighted-average common shares outstanding - basic and diluted	97,506	65,104	85,146	64,102

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