Adverum Biotechnologies Announces New INFINITY Phase 2 Trial for ADVM-022 in Diabetic Macular Edema, Reports Recent Business Progress and First Quarter 2020 Financial Results

May 28, 2020

-- INFINITY is a randomized, active comparator-controlled trial --

-- INFINITY trial initiated for patients with diabetic macular edema, the most common cause of vision loss in people with diabetic retinopathy --

-- Positive interim clinical data recently presented for ADVM-022 in OPTIC Phase 1 trial for wet AMD; data from all four cohorts expected to be presented by year-end --

-- Company to host conference call today at 1:30 pm PDT / 4:30 pm EDT --

REDWOOD CITY, Calif., May 28, 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 the initiation of INFINITY, a Phase 2, multi-center, randomized, double-masked, active comparator-controlled trial to assess a single intravitreal (IVT) injection of ADVM-022 in patients with diabetic macular edema (DME). The company also reported financial results for the first quarter ended March 31, 2020 and provided a corporate update.

The INFINITY trial will enroll approximately 33 patients and 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. Additional objectives include assessments of treatment burden, visual acuity, retinal anatomy and safety outcomes.

Participants in this double-masked trial will be randomized to one of three arms for their study eye treatment:

- Arm 1 will receive the higher dose of ADVM-022 at $6x10^{11}$ vg.
- Arm 2 will receive the lower dose of ADVM-022 at $2x10^{11}$ vg.
- Arm 3 will receive aflibercept at a dose of 2 mg.

“I’m thankful for the strong commitment and resilience our employees have exhibited towards advancing our pipeline despite the challenges of COVID 19,” said Leone Patterson, president and chief executive officer, Adverum Biotechnologies. “We continue to execute on our goal to develop and commercialize our novel gene therapy candidate ADVM-022 as a potential one-time treatment for patients with wet age-related macular degeneration (AMD) and DME, the two largest indications for anti-VEGF treatment. With the recent approval of our Investigational New Drug application for ADVM-022, we have initiated INFINITY in DME, a high-need subgroup of patients within the larger DR population. Additionally, we look forward to presenting data from all four cohorts of the OPTIC Phase 1 trial for ADVM-022 in wet AMD by the end of this year.”

Aaron Osborne, MBBS, chief medical officer of Adverum Biotechnologies stated, “Over 30 million people are impacted by diabetes in the United States. DME affects approximately 5% of people with diabetes and is the most common cause of vision loss in people with diabetic retinopathy (DR). We believe that the exciting data seen to date for ADVM-022 in the ongoing OPTIC trial in wet AMD highlight this therapy’s transformative potential to deliver long-term control of serious retinal vascular diseases, including DME. INFINITY has been designed to provide robust, controlled data on ADVM-022 in DME and will be conducted at trial sites across the United States.”

Recent Progress

- The U.S. Food and Drug Administration (FDA) approved Adverum’s IND application for ADVM-022 (AAV.7m8-aflibercept) for the treatment of DR. The company has initiated INFINITY, a Phase 2, multi-center, randomized, double-masked, active comparator-controlled trial, to assess a single IVT injection of ADVM-022 in patients with DME, the most common cause of vision loss in patients with DR. INFINITY will enroll approximately 33 patients and 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. Additional objectives include assessments of treatment burden, visual acuity, retinal anatomy and safety outcomes.

- In early May, positive interim clinical data were presented from Cohorts 1-3 of the OPTIC Phase 1 dose-ranging clinical trial of ADVM-022 in patients requiring frequent anti-VEGF injections for wet age-related macular degeneration (wet AMD). Following a single IVT injection, ADVM-022 showed long-term durability beyond 1 year with zero rescue injections in Cohort 1. Additionally, early evidence from Cohort 3 suggested 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.
  - Began dosing patients in April in Cohort 4 (n=9, dose 6×10^{11} vg and a 6-week prophylactic regimen of steroid eye drops).

- Data from all four cohorts expected to be presented by year-end.

- Scott Whitcup, M.D. was appointed to Adverum's Board of Directors. Dr. Whitcup has over 20 years of biopharmaceutical industry experience, with extensive expertise in drug development and regulatory approvals, including products for the treatment of patients with ocular disease.

- The company raised approximately $140.9 million in net proceeds from an underwritten public offering in February 2020.

COVID-19
In March 2020, the San Francisco Bay Area of California, where Adverum has its corporate headquarters, mandated a Shelter-in-Place Executive Order in response to the World Health Organization declaring a pandemic related to coronavirus (COVID-19). The company's primary focus is on the health and safety of its employees, patients, and healthcare providers. In mid-March, the company implemented a number of actions, including a work-from-home policy for employees whose jobs have not required them to be on-site. The company has maintained certain essential in-person laboratory functions in order to advance key research and development initiatives supported by the implementation of updated onsite procedures. The company believes these measures and others have allowed it to mitigate, but not eliminate, the effects on and risks of on-site operations posed by the COVID-19 pandemic.

In the OPTIC Phase 1 trial, patients with wet AMD are in high-risk categories for COVID-19 complications based on age, comorbidities, or both. The company is working closely with clinical trial sites to monitor and attempt to minimize the potential negative impacts of the evolving COVID-19 outbreak on patient safety, patient enrollment, continued participation of patients already enrolled in the company's clinical studies, protocol compliance, data quality, and overall study integrity. Despite these efforts, the company continues to assess whether the COVID-19 pandemic will significantly impact trial enrollment or completion of the current or planned clinical studies. Additionally, although the company has sufficient drug supply for its current clinical trials, it is working with its product supply partners to implement measures where possible to attempt to mitigate the COVID-19 pandemic's effects on and risks to its future clinical supply needs and long-term timelines, which may result in additional expenses.

Financial Results for the Three Months Ended March 31, 2020

- **Cash, cash equivalents and short-term investments** were $297.1 million as of March 31, 2020, compared to $166.0 million as of December 31, 2019. In February 2020, Adverum raised approximately $140.9 million in net proceeds from an underwritten public offering. Adverum expects this quarter-end cash position to fund operations into 2022.
- **Research and development expenses** were $14.8 million for the three months ended March 31, 2020, compared to $10.1 million for the same period in 2019. Research and development expenses increased primarily due to higher material production costs, personnel-associated costs, and increased facilities costs related to the company's new facility.
- **General and administrative expenses** were $9.0 million for the three months ended March 31, 2020, compared to $5.6 million for the same period in 2019. General and administrative expenses increased primarily due to higher personnel-associated costs, including stock-based compensation expenses, and professional service and consultant expenses.
- **Net loss** was $22.9 million, or $0.31 per basic and diluted share, for the three months ended March 31, 2020, compared to $14.5 million, or $0.23 per basic and diluted share, for the same period in 2019.

Conference Call Information
Adverum will host a conference call and audio webcast today at 1:30 pm PT / 4:30 pm ET to report its first quarter 2020 financial results, discuss the INFINITY Phase 2 trial, and provide an update on recent business progress. The live audio webcast and accompanying slide presentation will be accessible under Events and Presentations in the Investors section of the company's website. To participate in the conference call dial 1-866-420-8347 (domestic) or 1-409-217-8241 (international) and refer to the "Adverum Biotechnologies' First Quarter 2020 Earnings Call." It is recommended call participants dial in15 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 INFINITY Phase 2 Trial of ADVM-022 in DME
INFINITY is a Phase 2, multi-center, randomized, double-masked, active comparator-controlled trial designed to assess a single intravitreal (IVT) injection of ADVM-022 in patients with diabetic macular edema (DME), the most common cause of vision loss in patients with DR.

The INFINITY trial will enroll approximately 33 patients and 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. Additional objectives include assessments of treatment burden, visual acuity, retinal anatomy and safety outcomes.

Across the United States, leading retinal clinical trial sites will participate in the INFINITY trial. For additional information, please visit www.INFINITYclinicaltrial.com.

About Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME)
Over 30 million people are impacted by diabetes in the United States. Diabetic retinopathy (DR) affects approximately one in three adults with diabetes and can put patients at risk of vision loss. DR can be diagnosed at different severity levels, and is the most common cause of blindness in working-age adults in the U.S.

Diabetic macular edema (DME) is a vision-threatening complication of DR that can occur at any severity stage of DR. DME is characterized by retinal thickening in the area of the macula, and the risk of DME increases with the worsening of the DR severity score (DRSS). DME affects approximately 5% of people with diabetes and is the leading cause of vision loss in patients with DR.

The current standard-of-care therapy for DME is anti-VEGF intravitreal injections. These are effective but typically require frequent and long-term injections for patients to maintain good vision. Compliance with these regimens can be difficult for patients, leading to undertreatment and vision loss. Real-world outcomes in DME with anti-VEGF therapy are meaningfully worse than in clinical trials.[1]

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 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 as to its plans to advance ADVM-022 in DME by beginning to enroll patients in the INFINITY trial and the expected enrollment numbers; Adverum’s expectations that its current cash position will fund its operations into 2022; and Adverum’s expectations that it will present data from all four cohorts of the OPTIC Phase 1 trial for ADVM-022 in wet AMD by the end of this year. 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 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 May 28, 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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[1] TA Ciulla, et al. Diabetes Care 2003 Sep; 26(9): 2653-2664.

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

	March 31, 2020	December 31, 2019
	(Unaudited)	(1)
Assets		
Current assets:		
Cash and cash equivalents	$ 130,162	$ 65,897
Short-term investments	166,904	100,138
Prepaid expenses and other current assets	3,382	9,835

Total current assets	300,448	175,870
Operating lease right-of-use asset	20,406	20,963
Property and equipment, net	26,727	24,884
Restricted cash	999	999
Deposit and other long-term assets	19	11
Total assets	$ 348,599	$ 222,727
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 4,663	$ 4,103
Accrued expenses and other current liabilities	8,079	11,271
Lease liability, current portion	4,025	4,034
Total current liabilities	16,767	19,408
Lease liability, net of current portion	27,753	28,214
Other noncurrent liabilities	126	148
Total liabilities	44,646	47,770
Stockholders' equity:		
Common stock	8	7
Additional paid-in capital	712,713	560,704
Accumulated other comprehensive loss	(833)	(725)
Accumulated deficit	(407,935)	(385,029)
Total stockholders' equity	303,953	174,957
Total liabilities and stockholders' equity	$ 348,599	$ 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 March 31,	
	2020	**2019**
Operating expenses:		
Research and development	14,751	10,131
General and administrative	9,040	5,576
Total operating expenses	23,791	15,707
Operating loss	(23,791)	(15,707)
Other income, net	885	1,218
Net loss	(22,906)	(14,489)
Net loss per share — basic and diluted	$ (0.31)	$ (0.23)
Weighted-average common shares outstanding - basic and diluted	73,797	63,125

Source: Adverum Biotechnologies, Inc.