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Trevena Announces First Patient Enrolled in NIH-Funded ACTIV-4 Host Tissue Trial of TRV027 for COVID-19

TRV027 will be dosed in ~300 patients in nationwide trial led by Vanderbilt University Medical Center (VUMC)

CHESTERBROOK, Pa., July 26, 2021 (GLOBE NEWSWIRE) -- **Trevena, Inc. (Nasdaq: TRVN)**, a biopharmaceutical company focused on the development and commercialization of novel medicines for patients with central nervous system (CNS) disorders, today announced that the first COVID-19 patient has been enrolled in the NIH-funded ACTIV-4 Host Tissue (Accelerating COVID-19 Therapeutic Interventions and Vaccines) trial.

“There is no one solution to end COVID-19, and we are honored to play a role in the global effort to overcome this pandemic and mitigate its long-term impact on our communities,” said Carrie Bourdow, President and CEO of Trevena. “I am excited that patients are now being enrolled in this study and that TRV027 is the one of the first active treatment arms available for patient randomization.”

The trial, known as ACTIV-4 Host Tissue, is testing four investigational agents that combat dysregulation of the renin-angiotensin-aldosterone system (RAAS) and the immune system caused by a COVID-19 infection. TRV027 is a novel AT_1 receptor selective agonist that specifically binds to and rebalances AT_1 receptor activation within the RAAS, blocking the damaging pathway that leads to acute lung damage and abnormal blood clotting, while activating the cellular pathway that selectively targets reparative actions that improve lung function and promote anti-inflammatory effects.

The trial is enrolling approximately 1,600 patients at over 50 sites in the U.S. TRV027 is part of the initial trial launch, and additional study arms will be added to the trial over time. The study is evaluating the impact of each intervention on recovery, supplemental oxygen use, need for mechanical ventilation, organ failure, and mortality.

“As the COVID-19 pandemic continues to evolve, the development of interventions that can combat the vascular, fibrotic, and inflammatory damage done by the coronavirus remains a top priority,” said Sean Collins, M.D., M.Sci., Principal Investigator of the ACTIV-4 Host Tissue trial, Co-Director of the Vanderbilt Coordinating Center and Professor of Emergency Medicine, Vanderbilt University Medical Center. “I am very pleased that we have enrolled our first patient in the ACTIV-4 Host Tissue trial, and I look forward to investigating the potential of TRV027 to modulate the RAAS and improve outcomes for patients hospitalized with COVID-19.”

About ACTIV-4 Host Tissue

This is a multi-site, randomized, placebo-controlled, clinical trial with multiple treatment arms, each enrolling approximately 300-400 COVID-19 patients ≥ 18 years old. Four trial arms are testing investigational agents, including TRV027, that target the RAAS or the immune system through distinct mechanisms of action. The objective of the trial is to determine whether modulation of these systems is an effective strategy for preventing progression to critical illness, multiorgan failure, or mortality in hospitalized COVID-19 patients.

The trial is funded by the National Heart, Lung, and Blood Institute (NHLBI), part of the NIH.

About the NIH ACTIV Initiative

On April 17, 2020, the National Institutes of Health (NIH) announced the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership to develop a coordinated research strategy for prioritizing and speeding development of the most promising treatments and vaccines.

Coordinated by the Foundation for the National Institutes of Health (FNIH), ACTIV brings NIH together with its sibling agencies in the Department of Health and Human Services, including the Biomedical Advanced Research and Development Authority (BARDA), Centers for Disease Control and Prevention (CDC), and the U.S. Food and Drug Administration (FDA); other government agencies including the Department of Defense (DOD) and Department of Veterans Affairs (VA); The Operation; the European Medicines Agency (EMA); and representatives from academia, philanthropic organizations, and numerous biopharmaceutical companies.

For more information about the ACTIV therapeutic trials, including ACTIV-4 Host Tissue, visit the ACTIV website: https://www.nih.gov/research-training/medical-research-initiatives/activ.

About TRV027

TRV027 is a novel AT_1 receptor selective agonist that is currently being investigated by multiple institutions as a potential treatment for acute lung injury contributing to ARDS and abnormal blood clotting in COVID-19 patients. It has previously been studied in 691 individuals, has a well-characterized pharmacokinetic profile, and has demonstrated efficacy, potency, and selectivity at the AT_1 receptor in nonclinical studies. In previous clinical trials, there was a low dropout rate associated with TRV027, and no significant safety issues were reported. TRV027 is currently being evaluated in the REMAP-CAP COVID-19 ACE2 RAS Modulation Domain, an international, multi-site, randomized, Phase 2 / 3 adaptive clinical trial in hospitalized COVID-19 patients. In April 2021, the Company filed a non-provisional patent application and PCT application with the United States Patent and Trademark Office covering the use of TRV027 to treat ARDS and the prevention or treatment of abnormal clotting in COVID-19 patients.

About Trevena

Trevena, Inc. is a biopharmaceutical company focused on the development and commercialization of innovative medicines for patients with CNS disorders. The Company has one approved product in the United States, OLINVYK® (oliceridine) injection, indicated in adults for the management of acute pain severe enough to require an intravenous opioid

analgesic and for whom alternative treatments are inadequate. The Company's novel pipeline is based on Nobel Prize winning research and includes four differentiated investigational drug candidates: TRV250 for the acute treatment of migraine, TRV734 for maintenance treatment of opioid use disorder, TRV045 for diabetic neuropathic pain and epilepsy, and TRV027 for acute respiratory distress syndrome and abnormal blood clotting in COVID-19 patients.

Forward-Looking Statements

Any statements in this press release about future expectations, plans and prospects for the Company, including statements about the Company's strategy, future operations, clinical development and trials of its therapeutic candidates, plans for potential future product candidates and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "suggest," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the status, timing, costs, results and interpretation of the Company's clinical trials or any future trials of any of the Company's investigational drug candidates; the uncertainties inherent in conducting clinical trials; expectations for regulatory interactions, submissions and approvals, including the Company's assessment of the discussions with FDA, the timing of FDA's decision on the oliceridine NDA; available funding ; uncertainties related to the Company's intellectual property; uncertainties related to the ongoing COVID-19 pandemic, other matters that could affect the availability or commercial potential of the Company's therapeutic candidates; and other factors discussed in the Risk Factors set forth in the Company's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q filed with the Securities and Exchange Commission (SEC) and in other filings the Company makes with the SEC from time to time. In addition, the forward-looking statements included in this press release represent the Company's views only as of the date hereof. The Company anticipates that subsequent events and developments may cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so, except as may be required by law.

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