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Trevena Announces TRV027 Selected by NIH-Funded ACTIV Initiative For COVID-19 Trial

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Vanderbilt University Medical Center (VUMC) is coordinating multiple-arm, multi-site ACTIV-4d study targeting RAAS

TRV027 to be dosed in ~300 COVID-19 patients

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CHESTERBROOK, Pa., May 06, 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 TRV027, the Company's novel AT_1 receptor selective agonist, has been selected for an NIH ACTIV (Accelerating COVID-19 Therapeutic Interventions and Vaccines) trial in COVID-19 patients.

"The NIH's ongoing ACTIV public-private partnership has facilitated the unprecedented development of cutting-edge vaccines and therapeutics to fight the COVID-19 pandemic. I am honored to be joining their mission as they continue to search for new treatments to combat the severe complications caused by the novel coronavirus," said Carrie Bourdow, President and Chief Executive Officer of Trevena, Inc. "Vanderbilt University Medical Center has emerged as a leader in COVID-19 research in the U.S., and I look forward to supporting their investigation of TRV027 as a potentially meaningful therapy for COVID-19 patients."

TRV027 combats disruption within the renin-angiotensin-aldosterone system (RAAS) by specifically binding to and rebalancing AT_1 receptor activation, 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, known as ACTIV-4d RAAS, is a component of the National Heart, Lung, and Blood Institute (NHLBI) of the NIH's CONNECTS (Collaborating Network of Networks for Evaluating COVID-19 and Therapeutic Strategies) initiative. The objective of ACTIV-4d RAAS is to evaluate treatments targeting the RAAS and to determine whether modulation of the RAAS is an effective strategy for preventing progression to critical illness, multiorgan failure, or mortality in hospitalized COVID-19 patients.

"The development of symptomatic treatments is critical in the fight against the COVID-19 pandemic. TRV027 represents a new approach to targeting the AT_1 receptor and reversing organ damage caused by RAAS imbalance, while harnessing the protective therapeutic

benefits of this receptor target," said Sean Collins, M.D., M.Sci., Principal Investigator of the ACTIV-4d trial, Co-Director of the Vanderbilt Coordinating Center and Professor of Emergency Medicine, Vanderbilt University Medical Center. "I am very pleased with this opportunity to study TRV027 and to have Trevena's support as we continue our search for new treatments for COVID-19 patients."

About ACTIV-4d

This is a multi-site, randomized, placebo-controlled, clinical trial with multiple treatment arms, each enrolling approximately 300 COVID-19 patients ≥ 18 years old. Multiple trial arms will test investigational agents, including TRV027, that target the RAAS through distinct mechanisms of action. The trial is evaluating the impact of TRV027 on recovery, supplemental oxygen use, need for mechanical ventilation and mortality.

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.

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 epilepsy and chronic neuropathic pain, 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.

For more information, please contact:

Investor Contact:
Dan Ferry
Managing Director
LifeSci Advisors, LLC
daniel@lifesciadvisors.com
(617) 430-7576

PR & Media Contact:
Sasha Bennett
Director
Clyde Group
Sasha.Bennett@clydegroup.com
(239) 248-3409

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