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Trevena Announces TRV027 Selected for Study in Global REMAP-CAP Trial in COVID-19 Patients

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REMAP-CAP is led by experts in pandemic response and builds upon a worldwide clinical trial network evaluating treatments for COVID-19

Interim review of Imperial College London TRV027 study data supports transition to larger study

REMAP-CAP trial to study TRV027 in up to 300 patients

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CHESTERBROOK, Pa., April 21, 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 inclusion in an international, multi-site, adaptive, Phase 2-Phase 3 trial in COVID-19 patients.

The trial is being conducted and funded as part of REMAP-CAP (Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia), a global network of clinicians, institutions, and research facilities with the objective of evaluating treatments with the potential to reduce mortality, ICU use, and morbidity in severely ill patients with COVID-19. REMAP-CAP is financially supported by an array of governments and research organizations worldwide.

"I am pleased with the addition of TRV027 to REMAP-CAP, a globally recognized research network that is leading the search for cutting-edge COVID-19 therapies," said Carrie Bourdow, President and Chief Executive Officer of Trevena, Inc. "TRV027 holds immense potential as a treatment for the severe multi-organ damage and blood clotting caused by COVID-19, and I look forward to supporting the investigation of our novel asset in this innovative and expansive trial."

The trial, known as the REMAP-CAP COVID-19 ACE2 RAS Modulation Domain, is designed specifically to evaluate treatments targeting the renin-angiotensin system (RAS) and determine whether modulation of the RAS is an effective strategy for preventing multiorgan failure and mortality in hospitalized COVID-19 patients. TRV027, which is based on Nobel Prize winning technology, combats disruption within the RAS 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.

“I am excited by the opportunity to study TRV027, a novel AT_1 receptor selective agonist, as part of REMAP-CAP’s investigation of innovative treatments for COVID-19,” said Anthony Gordon, M.D., Professor of Anaesthesia and Critical Care at Imperial College London and a National Institute for Health Research (NIHR) Research Professor. “REMAP-CAP’s adaptive trial design allows us to gather a plethora of data on a treatment’s efficacy – particularly in certain patient populations or when administered in conjunction with other types of therapies — and I look forward to seeing what information we can glean from TRV027 as we evaluate its performance in COVID-19 patients.”

As previously announced, TRV027 is being investigated in a proof-of-concept study by Imperial College London. A recent review of the interim data by the study’s Data Monitoring and Safety Committee (DMSC) found that there were no safety concerns with TRV027, and the DMSC supported advancing TRV027 to a larger, more extensive study with clinical efficacy outcomes. Imperial College London anticipates winding down its study in the near future and is supporting the transition of TRV027 into the REMAP-CAP COVID-19 RAS domain study. David Owen, M.D., Ph.D., the chief investigator of Imperial College London’s TRV027 study, has joined the investigator team committee for the REMAP-CAP RAS domain study.

About the REMAP-CAP COVID-19 ACE2 RAS Modulation Domain

This is an international, multi-site, randomised, Phase 2-Phase 3 adaptive clinical trial in hospitalized patients with acute illness due to suspected or proven COVID-19, including patients admitted to ICU. Four active treatments are included in the study protocol, including TRV027, with 200-300 patients expected to be enrolled in each arm. TRV027 will be administered in conjunction with an ACE inhibitor. The primary outcome is a composite of in-hospital mortality and provision of organ failure support while admitted to an ICU in the 21 days following randomization. The trial is also evaluating clinical outcomes including ICU and hospital length of stay, ventilator-free days, and organ failure-free days.

About REMAP-CAP

REMAP-CAP (Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia) is a platform trial designed by clinicians who cared for patients and conducted research during the 2009 H1N1 pandemic. Planning began in 2011. REMAP-CAP is supported by multiple government grants.

REMAP-CAP builds on the combined input of the world’s leading ICU trial networks and experts in infectious disease, immunology, critical care, emergency medicine, Bayesian statistics, and clinical trial execution. These existing networks have enrolled tens of thousands of patients into trials. They have extensive experience designing, conducting, and reporting clinical trials that enroll patients who are severely ill.

The goal of REMAP-CAP is to generate evidence that can be applied during the pandemic to reduce mortality, reduce ICU use, and reduce morbidity in severely ill patients with COVID-19 infection. For the past several years, REMAP-CAP has been recruiting patients with severe CAP in the inter-pandemic period. REMAP-CAP is currently recruiting in more than 300 sites across 21 countries. REMAP-CAP was designed to adapt to an acute

pandemic need: that time came slightly over a year ago. Changes necessary for the pandemic have been approved or submitted for approval and many patients with COVID-19 have been and are being enrolled. More information can be found at https://www.remapcap.org/.

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 AT1 receptor in nonclinical studies. In previous clinical trials, there was a low dropout rate associated with TRV027, and no significant safety issues were reported. 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.

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