September 30, 2021

Trevena Announces Results of TRV027 Proof-of-Concept Study in COVID-19 Patients

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92% probability that TRV027 has a potential beneficial impact on primary endpoint of D-dimer levels, a biomarker associated with critical illness and mortality

~12 days lower average hospital length of stay in patients treated with TRV027 compared to placebo

TRV027 is currently being evaluated in a randomized controlled study (NIH ACTIV-4) and a global adaptive platform study (REMAP-CAP)

TRV027 is a novel AT_1 receptor selective agonist with the potential to treat acute lung damage / abnormal blood clotting associated with COVID-19

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Company to host conference call today, September 30th, 2021, at 8:00 a.m. ET

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CHESTERBROOK, Pa., Sept. 30, 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 data from 30 patients enrolled in the proof-of-concept study of TRV027, the Company's novel AT_1 receptor selective agonist, in hospitalized COVID-19 patients. The results showed that TRV027 was well-tolerated and provided initial evidence of its potential to improve biomarker and clinical endpoints associated with COVID-19 disease severity and progression. The study was led and funded by Imperial College London, with additional support through the British Heart Foundation Imperial Centre for Research Excellence Award.

"I am pleased to announce the results from this analysis, which provide initial evidence of the therapeutic potential of TRV027 to improve COVID-19 patient outcomes. With the ACTIV and REMAP-CAP COVID-19 platform trials currently evaluating TRV027, and data expected as early as mid-2022, we look forward to building upon these promising results," said Carrie Bourdow, President and CEO of Trevena. "I would like to thank the patients and their families who participated, as well as Imperial College London for their partnership and interest in investigating our novel molecule."

The primary endpoint was mean change from baseline D-dimer levels at three days. D-dimer is a biomarker used to monitor the risk of abnormal clotting throughout the vascular system. In patients with COVID-19, elevations in circulating D-dimer are also known to be an accurate predictor of critical disease progression and death. Among TRV027 treated patients, 70% (7 of 10) experienced a reduction in circulating D-dimer, compared to 27% (3 of 11) of patients on placebo. TRV027 was associated with a 92% probability of a potential beneficial treatment effect, based on a Bayesian model analysis recommended by the study's Data Monitoring and Safety Committee (DMSC).

Notably, a post-hoc analysis indicated that patients receiving TRV027 experienced a 12 day reduction in average length of hospital stay compared to placebo (11.4 vs. 23.3 days), with a median reduction of 4 days (8 vs. 12).

"The overall outcomes from this analysis showing a reduction of D-dimer and a reduced length of hospital stay suggest that TRV027 may effectively combat dysregulation of the renin angiotensin system caused by a COVID-19 infection and thereby improve clinical outcomes," said David Owen, M.D., Ph.D., Faculty of Medicine, Imperial College London and Head of Clinical Studies, NIHR Imperial Clinical Research Facility. "I am pleased that our efforts yielded these exciting findings, and I look forward to continue investigating this novel compound in two global multi-site platform trials."

In March 2021, the study's DMSC reviewed this data and unanimously found no safety or efficacy concerns, and it supported advancing TRV027 to a larger, more extensive study with clinical efficacy outcomes. As a result, the DMSC recommended closing enrollment at the interim analysis (~30 patients) prior to reaching the full study population number necessary to detect statistically significant treatment differences. The DMSC also recommended use of a Bayesian analysis on the primary endpoint to take full advantage of the accumulated data.

TRV027 is now being evaluated in two larger efficacy studies: ACTIV-4 Host Tissue led by Vanderbilt University Medical Center / NIH in the U.S. (ClinicalTrials.gov Identifier: NCT04924660), with data expected as early as mid-2022, and REMAP-CAP in the U.K. These two global, multi-site, multi-arm COVID-19 platform trials are expected to generate extensive scientific data in up to 600 patients on the potential clinical impact of TRV027 to prevent critical illness progression, multiorgan failure, and mortality in hospitalized patients with COVID-19 infection.

Conference Call and Webcast Information

The Company will host a conference call and webcast with the investment community on September 30, 2021, at 8:00 a.m. Eastern Time featuring remarks by Carrie Bourdow, President and Chief Executive Officer and Mark Demitrack, M.D., Senior Vice President and Chief Medical Officer.

Title:	TRV027 Proof-of-Concept Data Presentation
Date:	Thursday, September 30, 2021
Time:	8:00 a.m. ET
Conference Call Details:	Toll-Free: (855) 465-0180

International: (484) 756-4313
Conference ID: 6687853

Webcast: https://edge.media-server.com/mmc/p/piusmnaa

About the TRV027 Proof-of-Concept COVID-19 Trial (COVRAS)

This was a randomized, double-blind, placebo-controlled proof-of-concept study that enrolled 30 hospitalized, non-ventilated patients aged 18 or older with a confirmed COVID-19 infection. 21 patients (n=10 for TRV027, n=11 for placebo) received at least 3 days of their assigned infusion and were evaluable for primary analysis. The primary objective of the study was to determine whether the coagulopathy associated with COVID-19 infection was driven by overactivation of the renin angiotensin system (RAS). The secondary objective was to determine whether dysregulation of other organ systems associated with COVID-19 infection is driven by overactivation of the RAS.

Among 28 patients who received treatment, 10 experienced at least one adverse event (AE) (n=5 for TRV027, n=5 for placebo), and 7 experienced at least one serious AE (SAE) (n=4 for TRV027, n=3 for placebo). All SAEs, including 3 deaths (n=2 for TRV027, n=1 for placebo), were assessed by the study clinician to be unrelated to study drug assignment or study procedures. At the 30 day follow-up, 24 patients survived (n = 12 for TRV027, n=12 for placebo).

Imperial College London sponsored and funded the study, with additional support through the British Heart Foundation Imperial Centre for Research Excellence Award and the NIHR Imperial Clinical Research Facility. The Company provided TRV027 in support of the study.

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. 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.

For more information, please visit www.Trevena.com.

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, commercialization of approved drug products and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "objective," "predict," "project," "suggest," "target," "potential," "will," "would," "could," "should," "continue," "ongoing," or the negative of these terms or 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 commercialization of any approved drug product, 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 the FDA or other regulatory agencies about any and all of its programs; uncertainties related to the commercialization of OLINVYK; 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
Associate Vice President
Clyde Group
Sasha.Bennett@clydegroup.com
(239) 248-3409

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