Tricida Announces Publication of Positive TRC101 Pivotal Trial Results in The Lancet

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SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Mar. 11, 2019-- Tricida, Inc., (Nasdaq: TCDA) a pharmaceutical company focused on the development and commercialization of its drug candidate, TRC101 (veverimer), a non-absorbed, orally-administered polymer designed to treat metabolic acidosis in patients with chronic kidney disease (CKD), announced that *The Lancet* published online detailed results from its Phase 3, multicenter, parallel, randomized, double-blind, placebo-controlled trial, TRCA-301, in 217 patients with CKD and metabolic acidosis. Full results of the trial are available in *The Lancet*:

Veverimer versus Placebo in Patients with Metabolic Acidosis Associated with Chronic Kidney Disease: A Multicentre, Randomised, Double-blind, Controlled, Phase 3 Trial

“TRC101 substantially increased blood bicarbonate levels in the TRCA-301 trial,” said Donald E. Wesson, M.D., M.B.A., Professor of Medicine at Texas A&M Health Sciences Center College of Medicine in Dallas, TX, lead investigator of the study and primary author of *The Lancet* paper. “This alone was an important finding, given the strong evidence of a link between metabolic acidosis and CKD progression, but the results also showed promise of improvement in physical functioning after 12 weeks of treatment with TRC101, which may be related to amelioration of the deleterious effects of acidosis on muscle and bone.”

“The publication of our Phase 3 TRC101 clinical trial results in *The Lancet*, a leading independent general medical journal, is an important milestone for Tricida and shows that interest in metabolic acidosis extends beyond the nephrology community,” said Gerrit Klaerner, Ph.D., CEO and President of Tricida, and a coauthor of *The Lancet* paper. “I would especially like to thank the nephrology thought leaders, including Drs. Donald Wesson, David Bushinsky, Navdeep Tangri, and Vandana Mathur, who assisted with the study and participated in writing the manuscript for *The Lancet* publication.”

Results from the TRCA-301 clinical trial were previously presented at the American Society of Nephrology Kidney Week 2018 meeting. The Company provided a summary of the topline trial data in a June 5, 2018 press release.

Primary and Secondary Endpoints Met with High Statistical Significance

The TRCA-301 clinical trial achieved both its prespecified primary and secondary endpoints. After 12 weeks of treatment, the primary endpoint, the proportion of patients achieving a ≥4 mEq/L increase from baseline in blood bicarbonate at Week 12 or a blood bicarbonate in the normal range, was met by 59.2% of patients in the TRC101-treated group compared to 22.5% of patients in the placebo group ($p<0.0001$). The secondary endpoint, the least squares (LS) mean blood bicarbonate increase from baseline to Week 12 was 4.4 mEq/L (TRC101) vs. 1.8 mEq/L (placebo) ($p<0.0001$).

Promising Data from Prespecified Exploratory Physical Functioning Endpoints

Because of the potential for adverse effects of acidosis on muscle, two measures of physical functioning were evaluated as prespecified exploratory endpoints in the trial. The first exploratory endpoint examined the effect of treatment with TRC101 on self-reported responses to the 10-question SF-36 Physical Function subscale of the Kidney Disease and Quality of Life survey, which quantifies patients' reported degree of limitation in performing daily activities such as climbing stairs and walking. The second exploratory endpoint objectively measured physical functioning, assessed using a repeated chair stand test involving a timed measurement of five repetitions of moving from a seated to standing position.

At Week 12, self-reported physical functioning increased significantly in TRC101-treated patients compared to placebo-treated patients ($p = 0.0122$). At the end of 12 weeks of treatment, physical functioning, as measured objectively by the repeated chair stand test, numerically improved in the TRC101 group ($p = 0.0249$) and numerically worsened in the placebo group ($p = 0.5727$), but the between-group difference was not statistically significant ($p = 0.0630$). As the physical functioning results were not normally distributed, post-hoc rank-based statistical analyses were conducted and showed consistent results for patient-reported physical function ($p=0.0117$) and a stronger association for the between-group difference in the time to complete the repeated chair stand test ($p=0.0027$), both favoring TRC101.

Safety Profile Assessed

Dosing compliance, defined as ≥80% of doses administered, was >98%. The overall safety profile of TRC101 observed in the trial was consistent with that expected for the general population of patients with Stage 3 to 5 CKD and with similar non-absorbed polymer drugs with a site of action in the gastrointestinal tract. There were two deaths in the study and both occurred in the placebo group. The incidence of serious adverse events was low and balanced between the two arms and none were considered related to study drug by the site investigators or occurred in more than one patient. The most common body system in which adverse events in the TRC101 group occurred was gastrointestinal; of these, non-treatment limiting diarrhea was the most common event: 11 (9%) versus 3 (3%) in the TRC101 and placebo groups, respectively. The most common treatment-related adverse events were also in the gastrointestinal system, occurring in 5 (5%) patients in the placebo group and 16 (13%) in the TRC101-treated group, and most of these were mild or moderate. Treatment-related gastrointestinal adverse events that occurred in more than one subject were diarrhea, flatulence, nausea and constipation. Over 95% of the patients in each group completed the trial.

TRCA-301 Clinical Trial Design

Phase 3, multicenter, parallel, randomized, double-blind, placebo-controlled trial, TRCA-301, was conducted at 37 sites in the United States and Europe and enrolled 217 Stage 3b or 4 CKD patients with baseline blood bicarbonate levels between 12 mEq/L and 20 mEq/L. Subjects were randomized in a 4:3 ratio to receive TRC101 or placebo. The study drug dosing (TRC101 or placebo) continued for 12 weeks once daily. The primary outcome measure was change from baseline in blood bicarbonate (Time Frame: Week 12) and included comparison of TRC101 and placebo with regard to the proportion of patients with a change from baseline in blood bicarbonate ≥4 mEq/L or with blood bicarbonate in the normal range (22 to 29 mEq/L).

Eligible patients who completed the TRCA-301 trial were invited to participate in a 40-week safety extension trial, TRCA-301E. Of the 208 patients who completed the TRCA-301 trial, 196 were enrolled in the TRCA-301E safety extension trial.

In addition to Dr. Wesson, study authors included: Vandana Mathur, M.D. (MathurConsulting); Navdeep Tangri, M.D., Ph.D.(University of Manitoba), Yuri Stasiv, Ph.D.(Tricida), Dawn Parsell, Ph.D.(Tricida); Elizabeth Li, M.S.(PharmaStat LLC); Gerrit Klaerner, Ph.D.(Tricida) and David A. Bushinsky, M.D.(University of Rochester School of Medicine).

Metabolic acidosis is estimated to pose a health risk to approximately three million patients with CKD in the United States. It is a serious condition in which the body has accumulated too much acid and occurs when a patient's kidneys can no longer excrete sufficient acid or produce enough bicarbonate to balance acid production. The prevalence and severity of metabolic acidosis in people with CKD progressively rises as kidney function declines. As a chronic condition, metabolic acidosis is associated with an increased risk of CKD progression and death. It is also associated with an increased risk of muscle wasting and loss of bone density.

Metabolic acidosis in patients with CKD has traditionally been treated with sodium-based alkali supplements that enter the systemic circulation and neutralize accumulated acid. Alternative treatments for metabolic acidosis include vegetarian diets, but these limit patient choice and have low long-term adherence issues. An alternative potential treatment would remove, rather than neutralize, acid, without administering a sodium load. Removal of acid by binding it to a non-absorbed polymer, such as TRC101, then excreting it, is a potential first-in-class treatment of metabolic acidosis in patients with CKD.

About Tricida

Tricida, Inc. is a pharmaceutical company focused on the development and commercialization of it drug candidate, TRC101 (veverimer), a non-absorbed, orally-administered polymer designed as a potential treatment for metabolic acidosis in patients with chronic kidney disease (CKD). Metabolic acidosis is a condition commonly caused by CKD that is believed to accelerate the progression of kidney deterioration. It is estimated to pose a health risk to approximately three million patients with CKD in the United States. Tricida has successfully completed a Phase 3, double-blind, placebo-controlled trial of TRC101 in patients with CKD and metabolic acidosis. Tricida plans to submit a New Drug Application (NDA), in the second half of 2019, seeking approval of TRC101 through the U.S. Food and Drug Administration's (FDA's) Accelerated Approval Program.

For more information about Tricida, please visit www.Tricida.com.

Cautionary Note on Forward-Looking Statements

This press release includes forward-looking statements, including for example, statements about our ability to submit an NDA for TRC101 under the FDA's Accelerated Approval Program. Forward -looking statements involve known and unknown risks, uncertainties, assumptions and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. These risks and uncertainties include, among others, include the timing of Tricida's NDA submission; that many drug candidates that have completed Phase 3 trials do not become approved drugs on a timely or cost effective basis or at all; there can be no assurance that the FDA would approve an NDA under the Accelerated Approval Program, or at all, and even if approval for a drug is obtained, there can be no assurance that it will be adopted in the market or accepted as a benefit to patients and healthcare providers; possible safety and efficacy concerns and that we completely rely on third-party suppliers to manufacture TRC101. The forward-looking statements contained in this press release reflect Tricida's current views with respect to future events, and Tricida does not undertake and specifically disclaims any obligation to update any forward-looking statements.

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