# Tricida Provides Update on FDA Interactions

February 25, 2021

**Tricida Has Received an Appeal Denied Letter from the Office of New Drugs of the FDA in Response to its Formal Dispute Resolution Request**

SOUTH SAN FRANCISCO, Calif., Feb. 25, 2021 (GLOBE NEWSWIRE) -- Tricida, Inc. (Nasdaq: TCDA), a pharmaceutical company focused on the development and commercialization of its investigational drug candidate, veverimer, a non-absorbed, orally-administered polymer designed to treat metabolic acidosis in patients with chronic kidney disease (CKD), today provided an update on its U.S. Food and Drug Administration (FDA) interactions.

Tricida has received an Appeal Denied Letter (ADL), from the Office of New Drugs (OND) of the FDA in response to its Formal Dispute Resolution Request (FDRR) submitted in December 2020. While the FDRR was focused on whether the magnitude and durability of serum bicarbonate change seen in the TRCA-301/TRCA-301E trial is reasonably likely to predict clinical benefit in the treatment of metabolic acidosis in patients with CKD, the OND's decision additionally addressed other deficiencies identified in the Complete Response Letter (CRL), which Tricida received in August 2020. The additional issues addressed included the reliability of the data from the TRCA-301/TRCA-301E trial due to the disproportionate impact of data from a single high-enrolling clinical site on the trial's results and the applicability of the trial results to the U.S. patient population given that the majority of the subjects in the study were enrolled in sites outside of the United States or were in regions that the FDA does not consider "U.S.-like," such as Eastern Europe.

In the ADL, the OND acknowledged that the TRCA-301/TRCA-301E trial met its serum bicarbonate endpoints with statistical significance but concluded that the extent of serum bicarbonate increase observed in the TRCA-301/TRCA-301E trial is not reasonably likely to provide a discernible reduction in CKD progression. The OND also concluded that the confirmatory trial, VALOR-CKD, is underpowered to detect the effect size (13%) predicted by the original Tangri model (also known as the Predictive MA Model) based upon the placebo-subtracted mean treatment effect observed in the TRCA-301/TRCA-301E trial.

The OND also provided feedback on other concerns that are particularly relevant in an NDA supported by a single registrational trial. The OND noted concerns around the trial results being strongly influenced by a single site, and the majority of sites for the TRCA-301/TRCA-301E trial being in Eastern Europe, where differences in patient management, including concomitant medications and diet, might affect the treatment response to veverimer and raise a concern of the applicability to a U.S. patient population. The FDA did not raise any concerns related to its completed inspection of the highest-enrolling clinical trial site and there was no FDA Form 483 issued. Also, while the OND did not suggest that there was a specific unblinding issue in the TRCA-301/TRCA-301E trial, the OND noted concerns around adequate blinding and that, while the measures in place to protect the study blind in the TRCA-301/TRCA-301E trial were reasonable, they may not have optimally protected the blind.

Although the ADL provides greater clarity on the potential path for approval of veverimer through the Accelerated Approval Program, Tricida believes the timeline to meet the requirements for accelerated approval as suggested in the ADL may not result in the most rapid development path for veverimer. For example, the OND suggested that Tricida meet with the Division of Cardiology and Nephrology (the Division) to discuss submission of 52-week serum bicarbonate results from the fully randomized VALOR-CKD trial and that such submission should include a substantial proportion of U.S. and "U.S.-like" patients. The OND also indicated that, if the results of this trial were to demonstrate a meaningfully larger treatment effect on serum bicarbonate than seen in the TRCA-301/TRCA-301E trial, results from VALOR-CKD, along with the results from the TRCA-301/TRCA-301E trial, could address the deficiencies identified in the CRL. However, the OND noted that whether these data would support accelerated approval would remain a review issue and therefore would be subject to the Division's assessment of the adequacy of the magnitude of increase in serum bicarbonate. Moreover, based on the concerns expressed, we believe that the FDA could require an additional trial or trials to confirm the magnitude, durability of effect or applicability to the U.S. population for resubmission of the veverimer NDA through the Accelerated Approval Program.

Given the feedback provided by the FDA in the ADL, Tricida intends to continue the VALOR-CKD trial without further modifications at the present time with consideration of both the accelerated and traditional approval pathways. Tricida's planned interim analyses in the VALOR-CKD trial could result in early stopping for efficacy and resubmission of the NDA through a traditional approval pathway with a potential indication of treatment of metabolic acidosis to slow CKD progression. Tricida is also evaluating several options with respect to the VALOR-CKD trial that are focused on obtaining additional data prior to the end of 2022 on the effect of veverimer on (1) CKD progression; (2) physical functioning; and (3) serum bicarbonate. These options include the possibility of stopping the trial early for administrative reasons, which would allow analysis of the data using all alpha remaining at that time. In any event, Tricida believes data from VALOR-CKD will be very important in furthering the understanding of the regulatory path for approval of veverimer.

"The feedback that we received from OND makes clear that the results from the TRCA-301/TRCA-301E trial alone will not support accelerated approval of veverimer," said Gerrit Klaerner, Ph.D., Tricida's Chief Executive Officer and President. "We certainly hear and understand the need for additional data and believe that the VALOR-CKD trial is the best near-term source to provide that information."

**Tricida Conference Call Information**

Tricida will host its Fourth Quarter Financial Results and Business Update Conference Call and webcast today at 4:30 pm Eastern Time. The webcast or conference call may be accessed as follows:

**Tricida Conference Call**
**Thursday, February 25, 2021**
**4:30 pm Eastern Time**
**Webcast:** IR.Tricida.com

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| **Dial-in:** | **(800) 773-2954** |
| International: | (847) 413-3731 |
| **Conference ID:** | **50111253** |

A replay of the webcast will be available on Tricida's website approximately two hours following the completion of the call and will be available for up to 90 days following the presentation.

**About the VALOR-CKD Clinical Trial**

The ongoing VALOR-CKD trial is a renal outcomes clinical trial designed to determine if veverimer slows CKD progression in patients with metabolic acidosis associated with CKD. The VALOR-CKD trial is a randomized, double-blind, placebo-controlled, time-to-event trial. The primary endpoint in VALOR-CKD is defined as a composite of renal death, end-stage renal disease (ESRD) or a confirmed ≥ 40% reduction in estimated glomerular filtration rate (eGFR) (DD40). We anticipate randomizing approximately 1,600 subjects in VALOR-CKD and the trial is currently designed to terminate when the independent blinded Clinical Endpoint Adjudication Committee has positively adjudicated 511 subjects with primary efficacy endpoint events, which is anticipated to occur in the first half of 2024. The VALOR-CKD trial also includes two interim analyses for early stopping for efficacy after the accrual of 150 primary endpoint events, which is anticipated in the second half of 2021, and 250 primary endpoint events, which is anticipated in mid-2022. The VALOR-CKD trial also includes, as its first two secondary efficacy endpoints, evaluation of the effect of veverimer versus placebo after one year of treatment on patient-reported and objective measures of physical functioning, using the Kidney Disease and Quality of Life Physical Functioning Survey, or KDQOL Physical Functioning Survey, and the Repeated Chair Stand test, respectively. Although not part of any efficacy endpoints, the VALOR-CKD trial will also provide information regarding the change from baseline in serum bicarbonate in veverimer and placebo-treated subjects.

In November 2020, following the receipt of the CRL, Tricida revised the protocol for the VALOR-CKD trial based on feedback from the FDA in a July 2020 advice letter as well as additional work to understand both the hazard ratio and the anticipated serum bicarbonate effect of veverimer. In collaboration with Dr. Navdeep Tangri, M.D., Ph.D., of the University of Manitoba, Canada, Tricida developed a Time-Dependent Predictive Model in a cohort of more than 24,000 U.S. patients with metabolic acidosis and CKD. The results from this model show an 8.4% lower risk of CKD progression for each 1 mEq/L increase in serum bicarbonate. In addition, we believe the magnitude of the veverimer treatment effect in the TRCA-301/TRCA-301E trial is best described by the between-group difference in the medians, rather than the difference in the LS means, as the data are not normally distributed. The Week 52 median placebo-subtracted treatment effect in the TRCA-301/TRCA-301E trial was an increase in serum bicarbonate of 3.15 mEq/L. Using the Time-dependent Predictive Model, we predict that a median treatment effect of 3.15 mEq/L is associated with a hazard ratio of 0.76 for the VALOR-CKD renal outcome trial. Thus, with a sample size of 1,600 subjects, the trial has 87% power to show a 24% difference in primary endpoint events. These current assumptions for the powering of the VALOR-CKD trial were not considered by the OND in their response to the FDRR, and we have not yet received FDA comments on this revised draft protocol.

Tricida initiated enrollment in the VALOR-CKD trial in the fourth quarter of 2018 and has established sites throughout North America, Europe, Latin America and Asia-Pacific. As of February 22, 2021, the VALOR-CKD trial has randomized 1,433 of 1,600 subjects with an average treatment duration of approximately one year and has accrued 69 subjects with positively adjudicated primary endpoint events. In November 2020, based on feedback from the FDA, recruitment for VALOR-CKD was closed in all regions except for the United States, Canada and Western Europe. At the end of recruitment, Tricida anticipates approximately 67% of subjects to be enrolled at Eastern European sites, 19% at US, Western European and Canadian sites, 7% at Latin American sites, and 7% at sites in the Asia-Pacific region. Tricida's goal is to complete enrollment in the trial by the end of 2021; to meet this goal it may need to reopen recruitment at sites outside of the United States, but it will not reopen recruitment at sites in Eastern Europe. Tricida intends to ensure that no single site in the VALOR-CKD trial provides ≥ 5% of the total number of trial subjects. FDA's acceptance of the VALOR-CKD data in support of an NDA resubmission, including the acceptability of the data from non-US countries or regions which will comprise a substantial proportion of the data from the trial, will ultimately be a review issue.

**About Tricida**

Tricida, Inc. is a pharmaceutical company focused on the development and commercialization of its investigational drug candidate, veverimer (TRC101), a non-absorbed, orally-administered polymer designed to treat metabolic acidosis in patients with CKD. Tricida is currently conducting a renal outcomes clinical trial, VALOR-CKD, to determine if veverimer slows CKD progression in patients with metabolic acidosis associated with CKD. There are no FDA-approved treatments for chronic metabolic acidosis, 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.

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

**Cautionary Note on Forward-Looking Statements**

This press release includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Forward-looking statements relate to expectations concerning matters that are not historical facts. Words such as "projects," "believes," "anticipates," "plans," "expects," "intends," "may," "will," "could," "should," "would," and similar words and expressions are intended to identify forward-looking statements. Any statements contained herein which do not describe historical facts, including the Company's expectations with regard to its interactions and communications with the FDA, its plans and expectations as to the pathway to approval of veverimer by the FDA and the design of its ongoing clinical trial, VALOR-CKD, and its expectations regarding financial runway are forward-looking statements which involve risks and uncertainties that could cause actual results to differ materially from those discussed in such forward-looking statements. Such risks and uncertainties include, without limitation, whether the FDA will accept the Company's resubmission of an NDA for veverimer; the timing of the FDA's approval of veverimer, if at all; the potential availability of the Accelerated Approval Program and the approvability of veverimer under that program; the Company's plans and expectations with regard to its interactions with the FDA; the Company's plans and expectations for VALOR-CKD and future clinical and product development milestones; the Company's financial projections and cost estimates; and risks associated with the Company's business prospects, financial results and business operations. These and other factors that may affect the Company's future business prospects, results and operations are identified and described in more detail in the Company's filings with the Securities and Exchange Commission (SEC), including the Company's most recent Annual Report filed on Form 10-K and the subsequently filed Quarterly Report(s) on Form 10- Q. You should not place undue reliance on these forward-looking statements, which speak only as of the date of this press release. Except as required by applicable law, the Company does not intend to update any of the forward-looking statements to conform these statements to actual results, later events or circumstances or to reflect the occurrence of unanticipated events.

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