vTv Therapeutics Announces Positive Results from Mechanistic Study Indicating No Increased Risk of Ketoacidosis with TTP399 during Acute Insulin Withdrawal in Patients with Type 1 Diabetes

October 12, 2021

Study achieved primary endpoint of non-inferiority on measurement of key blood ketone levels

Patients taking TTP399 reported no events of hypoglycemia, while four events of hypoglycemia were reported in the placebo arm

Start-up activities for Phase 3 program ongoing with trials expected to begin in early 2022

HIGH POINT, N.C., Oct. 12, 2021 (GLOBE NEWSWIRE) -- vTv Therapeutics Inc. (Nasdaq: VTVT) a clinical-stage biopharmaceutical company focused on the development of orally administered treatments for type 1 diabetes and psoriasis, today announced positive results of a mechanistic study of TTP399 in patients with type 1 diabetes (T1D). The study demonstrated that patients with T1D taking TTP399 experienced no increase in ketone levels relative to placebo during a period of acute insulin withdrawal, indicating no increased risk of ketoacidosis. Consistent with previous clinical studies, improved fasting plasma glucose levels and fewer hypoglycemic events were observed in the TTP399 treated group during the week of treatment prior to the insulin withdrawal test.

The U.S. Food and Drug Administration (FDA) has declined to approve SGLT2 inhibitors as an adjunctive therapy in T1D, with concerns over the potential risks of diabetic ketoacidosis (DKA) in focus. DKA can lead to hospitalization and, if untreated, death. In order to address these concerns, vTv, following the FDA's recommendation, conducted this mechanistic study to demonstrate that treatment with TTP399, a liver-selective glucokinase activator, will not result in increased production of ketones, a precursor to ketoacidosis.

"This mechanistic study confirms the hypothesis that treatment with TTP399 lowers glucose, results in less hypoglycemia, and does not increase the formation of ketones" said Jeremy Pettus, MD, Assistant Professor of Medicine, University of California, San Diego and an investigator for the study. "These results overcome a major hurdle faced by other potential adjunct therapies, particularly those from the SGLT2 class."

"The results from this trial suggest that TTP399 can lower blood glucose without increasing the risk of DKA," said Jonathan Rosen, PhD, Associate Director of Research at JDRF. "This is so important because DKA remains a challenge in people with type 1 diabetes and insulin by itself is not enough for most people with T1D to achieve optimal health outcomes—we need safe, effective adjunctive therapies to complement insulin."

The study enrolled 23 people with type 1 diabetes using insulin pumps, randomized to receive TTP399 (n=12) or placebo (n=11) orally once daily for approximately seven days. On the last day of dosing, an acute insulin withdrawal test was performed by stopping the patients' insulin pumps and measuring levels of beta-hydroxybutyrate (BOHB) and other key metabolic markers over a period of up to 10 hours or until certain safety stopping criteria were met. The design of this study was based on similar studies, which showed significant increases in BOHB in patients taking SGLT2 inhibitors relative to those taking placebo.[1,2]

The demographics between the two arms of the study were well balanced, with approximately 80% of patients in the study utilizing closed-loop or hybrid-closed loop systems during the treatment period. The average HbA1c levels at baseline were 6.8% and 7.1% in the placebo and TTP399 arms, respectively.

The study achieved its primary endpoint by demonstrating non-inferiority relative to placebo in the proportion of subjects reaching pre-specified concentration limits of BOHB, a biomarker for ketoacidosis, over the period of acute insulin withdrawal. BOHB is the primary ketone body found in blood. During the insulin withdrawal phase of the study, no significant differences were observed between the active and placebo arms in the patients' BOHB profiles or the mean duration of the test. All patients completed at least three hours of the insulin withdrawal test. During this initial period of time, the area under the curve for the levels of BOHB was numerically lower for the TTP399 treated group than that for placebo. In addition, the concentration of bicarbonate, an important buffer that regulates acidity levels in blood, was higher in the TTP399 treated group than in the placebo group, indicating a lower risk of ketoacidosis in the group taking TTP399.

In addition to data collected during the insulin withdrawal test, data collected during the week-long treatment period preceding the insulin withdrawal test demonstrated that patients taking TTP399 experienced reductions in fasting plasma glucose (-27mg/dL in the TTP399 group vs -4mg/dL in the placebo group p=0.03). Furthermore, no increases in BOHB or free fatty acid, a precursor to BOHB, were observed. Consistent with previous clinical studies of TTP399, the drug was well tolerated with fewer subjects reporting treatment-emergent adverse events in the group taking TTP399 than in the placebo group. Importantly, patients taking TTP399 reported no events of hypoglycemia, while four events of hypoglycemia were reported in the placebo group.

“It is outstanding to have data supporting TTP399’s favorable profile with respect to ketoacidosis, as regulatory agencies have been highly attuned to DKA in their review of potential treatments for type 1 diabetes,” said Steve Holcombe, chief executive officer, vTv Therapeutics. “We are making progress towards finalizing the study designs of our Phase 3 pivotal program with the FDA’s continued feedback under Breakthrough Therapy designation and we expect to initiate these clinical studies in early 2022.”

A full analysis of the results from the mechanistic study will be submitted for publication in a peer-reviewed journal.

The mechanistic study was conducted with support from JDRF International, the leading global organization funding type 1 diabetes research.

---

[1] Herring et al, Diabetes Care 2020 https://doi.org/10.2337/dc19-2579

[2] Patel et al, Diabetes Technology & Therapeutics 2017 https://www.liebertpub.com/doi/10.1089/dia.2017.0267

About Type 1 Diabetes

Type 1 diabetes is an autoimmune disease in which a person’s pancreas stops producing insulin, a hormone that enables people to get energy from food. It occurs when the body’s immune system attacks and destroys the insulin-producing cells in the pancreas, called beta cells. While its causes are not yet entirely understood, scientists believe that both genetic factors and environmental triggers are involved. Its onset has nothing to do with diet or lifestyle. There is nothing you can do to prevent type 1 diabetes, and—at present—nothing you can do to cure it

About vTv Therapeutics

vTv Therapeutics Inc. is a clinical-stage biopharmaceutical company focused on developing oral, small molecule drug candidates. vTv has a pipeline of clinical drug candidates led by programs for the treatment of type 1 diabetes and psoriasis. vTv’s development partners are pursuing additional indications in type 2 diabetes, chronic obstructive pulmonary disease, renal disease, primary mitochondrial myopathy, and pancreatic cancer. For more information, please visit www.vtvtherapeutics.com or follow us on Twitter: @vTvTherapeutics.

Forward-Looking Statements

This release contains forward-looking statements, which involve risks and uncertainties. These forward-looking statements can be identified by the use of forward-looking terminology, including the terms “anticipate,” “believe,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and, in each case, their negative or other various or comparable terminology. All statements other than statements of historical facts contained in this release, including statements regarding the timing of our clinical trials, our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important 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. Important factors that could cause our results to vary from expectations include those described under the heading “Risk Factors” in our Annual Report on Form 10-K and our other filings with the SEC. These forward-looking statements reflect our views with respect to future events as of the date of this release and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. These forward-looking statements represent our estimates and assumptions only as of the date of this release and, except as required by law, we undertake no obligation to update or review publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this release. We anticipate that subsequent events and developments will cause our views to change. Our forward-looking statements do not reflect the potential impact of any future acquisitions, merger, dispositions, joint ventures or investments we may undertake. We qualify all of our forward-looking statements by these cautionary statements.

Contacts

Investors:

Corey Davis
LifeSci Advisors
CDavis@LifeSciAdvisors.com

or

Media:

PR@vtvtherapeutics.com

Source: vTv Therapeutics Inc.

Source: vTv Therapeutics Inc.