Vertex Presents New Data from VX-880 Phase 1/2 Clinical Trial at the American Diabetes Association 82nd Scientific Sessions

June 6, 2022

– Patient 1 showed blood glucose time-in-range change from 40.1% on 34.0 units per day of exogenous insulin at baseline to 99.9% and insulin independence at Day 270 –

– Patient 2 showed blood glucose time-in-range change from 35.9% on 25.9 units per day of exogenous insulin at baseline to 51.9% with a 30% reduction in exogenous insulin use at Day 150 –

– As previously reported, proof-of-concept achieved with first two patients treated at half the target dose of VX-880 demonstrating glucose responsive insulin secretion, improvements in HbA1c and reductions in exogenous insulin –

– VX-880 generally well tolerated in all patients dosed to date; majority of adverse events were mild or moderate –

– Two additional abstracts also accepted for presentation –

BOSTON--(BUSINESS WIRE)--Jun. 6, 2022-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today provided additional data on patients dosed in Part A of its Phase 1/2 clinical trial of VX-880, an investigational stem cell-derived, fully differentiated pancreatic islet cell replacement therapy for people with T1D with impaired hypoglycemic awareness and severe hypoglycemia. As reported last month, both patients treated with half the target dose of VX-880 achieved glucose-responsive insulin production, improvements in glycemic control and reductions in exogenous insulin requirements. The data presented today show significant increases in the blood glucose time-in-range compared to baseline, following treatment with VX-880. Time spent in target range is a clinically important metric in diabetes management that reflects the amount of time a patient's blood glucose level is measured in the desired, target blood sugar range. The accepted American Diabetes Association (ADA)/European Association for the Study of Diabetes (EASD) target for time-in-range (blood glucose between 70 and 180 mg/dL) is 70%.

These data were presented during the American Diabetes Association 82nd Scientific Sessions Conference on June 6, 2022 in New Orleans, Louisiana from 9:00 to 9:15 a.m. CDT as an oral abstract presentation, "Stem Cell-Derived, Fully Differentiated Islet Cells for Type 1 Diabetes" (abstract/publication #259-OR). A link to the presentation is included here.

The presentation included data from both patients dosed in Part A of the study, designed to assess the safety profile of VX-880 at half the target dose. Patient 1 showed a blood glucose time-in-range increase from 40.1% at baseline to 99.9% at Day 270 and was insulin independent. Patient 2 showed a time-in-range increase from 35.9% at baseline to 51.9% at Day 150 with a 30% reduction in exogenous insulin use.

VX-880 has been generally well tolerated in all patients dosed to date, with the majority of adverse events being mild or moderate.

"The glucose time-in-range data presented today at ADA demonstrate the remarkable glycemic control that can be achieved after treatment with VX-880," said Bastiano Sanna, Ph.D., Executive Vice President and Chief of Cell and Genetic Therapies at Vertex. "Elevations in blood sugar are important to control, as are fluctuations over time, as both increase the risk of complications in patients with T1D. The first two patients treated with VX-880 have not only achieved improved HbA1c and decreased insulin requirements, but also higher time-in-range. Taken altogether, these data provide further evidence of the potential for VX-880 as a functional cure for people living with T1D."

"As a treating physician, I have seen the profound burden of this disease on patients, especially those who experience severe hypoglycemia. The ability to restore a patient's islet function and improve glycemic control, and subsequently reduce exogenous insulin dependence, has significant potential to improve patients' lives," said Camillo Ricordi, M.D., Professor of Surgery, Director of the Diabetes Research Institute and the Cell Transplant Center at the University of Miami Miller School of Medicine, and Steering Committee Chair for the VX-880 clinical trial. "These results from the first two patients treated with half of the target dose are remarkable and encouraging as we continue investigating treating patients with type 1 diabetes with this stem cell-derived therapy."

"The potential impact of this treatment on patients cannot be overstated," said James Markmann, M.D., Ph.D., Professor of Surgery and Chief of the Division of Transplant Surgery at Massachusetts General Hospital, who treated Patient 1. "This study shows a significant leap forward in the potential treatment of patients with type 1 diabetes."

Additional Vertex presentations at ADA this year included an oral presentation, "Persistence of Impaired Awareness of

Hypoglycemia, Severe Hypoglycemic Events and Suboptimal Glycemic Control Despite Advanced Diabetes Technologies" (abstract/publication #92-OR), and poster, "Gaps Remain in Achieving Target T1D Glycemic Goals Despite Advanced Technologies" (poster #652-P).

To date, three patients have been dosed in the Phase 1/2 study with VX-880. Two patients received half the target dose of cells in Part A of the study. A third patient has received the full target dose in Part B of the study.

Encapsulated Islet Cell Program & Development of Hypoimmune Cells

Vertex is also pursuing additional programs in T1D, including one in which these same stem cell-derived islets are encapsulated in an immunoprotective device to be surgically implanted without the use of concomitant immunosuppression, and another program where cells are modified to produce hypoimmune stem cell-derived islets. IND-enabling studies for the encapsulated cells program are underway, and the company remains on track to submit an IND in 2022.

About VX-880

VX-880 is an investigational allogeneic stem cell-derived, fully differentiated, insulin-producing islet cell therapy manufactured using proprietary technology. VX-880 is being evaluated for patients who have T1D with impaired hypoglycemic awareness and severe hypoglycemia. VX-880 has the potential to restore the body's ability to regulate glucose levels by restoring pancreatic islet cell function, including glucose-responsive insulin production. VX-880 is delivered by an infusion into the hepatic portal vein and requires maintenance immunosuppressive therapy to protect the islet cells from immune rejection.

About the Phase 1/2 Clinical Trial

The clinical trial is a Phase 1/2, multi-center, single-arm, open-label study in patients who have T1D with impaired hypoglycemic awareness and severe hypoglycemia. This study is designed as a sequential, multi-part clinical trial to evaluate the safety and efficacy of VX-880. In Part A, the first two patients received half the target dose. In Part B, five patients will receive the full target dose, after which concurrent dosing at the full target dose will occur in Part C. Approximately 17 patients will be enrolled in the clinical trial. The Phase 1/2 study is on clinical hold in the U.S. and is ongoing in Canada.

About Type 1 Diabetes

T1D results from the autoimmune destruction of insulin-producing islet cells in the pancreas, leading to loss of insulin production and impairment of blood glucose control. The absence of insulin leads to abnormalities in how the body processes nutrients, leading to high blood glucose levels. High blood glucose can lead to diabetic ketoacidosis and over time, to complications such as kidney disease/failure, eye disease (including vision loss), heart disease, stroke, nerve damage and even death.

Due to the limitations and complexities of insulin delivery systems, it can be difficult to achieve and maintain balance in glucose control in people with T1D. Hypoglycemia often results because of the difficulty in balancing the different factors that impact glucose levels, including insulin, diet and exercise. Hypoglycemia remains a critical limiting factor in glycemic management, and severe hypoglycemia can cause loss of consciousness, coma, seizures, injury and can be fatal. Over time, patients with T1D can develop impaired awareness of hypoglycemia, meaning they are no longer able to perceive the early signs of a hypoglycemic event, which can be dangerous and result in life-threatening events.

Current standards of care do not address the underlying causes of the disease, and there are limited treatment options beyond insulin for the management of T1D.

About Vertex

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases. The company has multiple approved medicines that treat the underlying cause of cystic fibrosis (CF) — a rare, life-threatening genetic disease — and has several ongoing clinical and research programs in CF. Beyond CF,Vertex has a robust pipeline of investigational small molecule, cell and genetic therapies in other serious diseases where it has deep insight into causal human biology, including sickle cell disease, beta thalassemia, APOL1-mediated kidney disease, pain, type 1 diabetes, alpha-1 antitrypsin deficiency and Duchenne muscular dystrophy.

Founded in 1989 in Cambridge, Mass., Vertex's global headquarters is now located in Boston's Innovation District and its international headquarters is in London. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia and Latin America. Vertex is consistently recognized as one of the industry's top places to work, including 12 consecutive years on Science magazine's Top Employers list and one of the 2021 Seramount (formerly Working Mother Media) 100 Best Companies. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on Facebook, Twitter, LinkedIn, YouTube and Instagram.

Special Note Regarding Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, (i) statements by Bastiano Sanna, Ph.D., Dr. Camillo Ricordi and Dr. Jim Markmann in this press release, (ii) our plans, expectations for, and the potential benefits of VX-880, (iii) our plans to continue to progress the Phase 1/2 program for VX-880 and IND-enabling studies for the encapsulated islet cell program, including anticipated regulatory

filings in 2022, and (iv) our plans for dosing and enrollment of patients. While Vertex believes the forward-looking statements contained in this press release are accurate, these forward-looking statements represent the company's beliefs only as of the date of this press release and there are a number of risks and uncertainties that could cause actual events or results to differ materially from those expressed or implied by such forward-looking statements. Those risks and uncertainties include, among other things, that data from a limited number of patients may not be indicative of final clinical trial results, that data from the company's research and development programs may not support registration or further development of its compounds due to safety, efficacy, and other risks listed under the heading “Risk Factors” in Vertex's most recent annual report and subsequent quarterly reports filed with the Securities and Exchange Commission at www.sec.gov and available through the company's website at www.vrtx.com. You should not place undue reliance on these statements, or the scientific data presented. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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