Vertex Presents Positive VX-880 Results From Ongoing Phase 1/2 Study in Type 1 Diabetes at the American Diabetes Association 83rd Scientific Sessions

June 23, 2023

– All six patients treated with VX-880 engrafted islet cells, produced endogenous insulin (C-peptide) and had improved glycemic control while reducing or eliminating insulin use –

– The two patients with at least one year of follow-up met the criteria for the primary endpoint of elimination of severe hypoglycemic events (SHEs) and HbA1c <7.0 –

– Both of these patients also achieved insulin independence with HbA1c values of 5.3% and 6.0% –

– VX-880 generally well tolerated in all patients dosed to-date –

– Based on these results, trial advanced to Part C with concurrent dosing –

BOSTON--(BUSINESS WIRE)--Jun. 23, 2023-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today presented data on all patients dosed in Parts A and B of its Phase 1/2 clinical trial of VX-880, an investigational stem cell-derived, fully differentiated islet cell therapy, in people with type 1 diabetes (T1D) with impaired hypoglycemic awareness and severe hypoglycemic events (SHEs). All six patients treated with VX-880 had undetectable fasting C-peptide (endogenous insulin secretion) at baseline, a history of recurrent SHEs in the year prior to treatment and required an average of 34.0 units of insulin per day. Following treatment, all six patients demonstrated endogenous insulin secretion, improved glycemic control as measured by HbA1c, improved time-in-range on continuous glucose monitoring, and reduction or elimination of exogenous insulin use. Patients with greater than 90 days of follow-up had elimination of SHEs in the evaluation period.

One patient in Part A received a half-target dose of VX-880 and was followed for approximately nine months, at which time this patient received a second half dose. This patient subsequently withdrew consent (not related to adverse events [AEs]) and was therefore not evaluable for the primary endpoint.

Two patients treated with VX-880 had at least 12 months of follow-up after the last infusion and were therefore evaluable for the study's primary efficacy endpoint of elimination of SHEs between Day 90 and Month 12 with a reduction of HbA1c (<7.0% or a decrease of at least 1% compared to baseline). Both of these patients met the criteria for the primary endpoint of the study. In addition, these two patients are insulin independent. Patient A1 had HbA1c of 5.3% at Month 21, compared to 8.6% at baseline, and Patient B1 had HbA1c of 6.0% at Month 12, compared to 7.6% at baseline. Both patients showed over 95% time-in-range based on continuous glucose monitoring. The ADA recommended target is ≥70%.

The three additional patients in Part B, each administered the full target dose of VX-880 given as a single infusion, have follow-up between 29 and 90 days and have shown endogenous insulin secretion, reduction in HbA1c, improvements in glucose time-in-range, and reductions in daily exogenous insulin use. Their trajectory is consistent with that observed in the two patients with more than one year of follow-up at equivalent periods of follow-up after VX-880 infusion.

VX-880 has been generally well tolerated in all patients dosed to date. The majority of AEs were mild or moderate, and there were no serious AEs related to VX-880 treatment. The most common AEs were dehydration, diarrhea, hypomagnesemia and rash. As previously reported, one subject had SHEs in the perioperative period.

As a result of these safety and efficacy data in Parts A and B, the independent data review committee has recommended moving to Part C of the trial, which allows for concurrent dosing of patients at the full target dose of VX-880.

"These data represent a foundational advance in the potential treatment of T1D, bringing us one step closer to a potentially curative therapy for patients who are waiting," said Felicia Pagliuca, Ph.D., Disease Area Executive, Type 1 Diabetes at Vertex. "These data are particularly meaningful in the context of our overall investigational T1D program, as these same VX-880 cells are the building blocks for our Phase 1/2 VX-264 cells-plus-device program, as well as our research-stage hypoimmune islet cell program."

"The reproducible efficacy across multiple patients and endpoints, including the level of glucose control and the elimination of SHEs, observed in this trial is highly unusual in T1D patients treated with exogenous insulin, wherein only ~25% of people with T1D meet the recommended HbA1c target of 7.0%, and is truly remarkable," said Trevor Reichman, M.D., Department of Surgery, University of Toronto. "The normalization of HbA1c without the need for exogenous insulin one year after therapy with VX-880 is

historic and offers hope that the transformative therapies the T1D community has been waiting for may finally become reality."

These data were presented during the American Diabetes Association 83rd Scientific Sessions Conference on June 23, 2023 in San Diego, California at 3:50 p.m. PT as an oral presentation, "Glucose-Dependent Insulin Production and Insulin-Independence in Type 1 Diabetes from Stem Cell-Derived, Fully Differentiated Islet Cells: Updated Data from the VX-880 Clinical Trial" (abstract/publication #836-P), as part of the "Designer Beta Cells" symposium from 3:45 p.m. to 5:15 p.m. PT. These data will be shared as a poster on Sunday, June 25 from 11:30 a.m. to 12:30 p.m. PT.

About Vertex T1D Programs in Clinical Development

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 chronic immunosuppressive therapy to protect the islet cells from immune rejection.

The VX-880 trial has expanded to additional sites that are active and enrolling in Norway, Switzerland and the Netherlands.

VX-880 was recently granted PRIME designation by the European Medicines Agency in March 2023, in addition to Fast Track Designation by the U.S. FDA in March 2021. PRIME designation is granted to innovative new therapies that have demonstrated the potential to significantly address an unmet medical need.

About the VX-880 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. Approximately 17 patients will be enrolled in the clinical trial. Enrollment is ongoing in this study.

About VX-264
VX-264 is an investigational cell therapy in which allogeneic human stem cell-derived islets are encapsulated in a channel array device designed to shield the cells from the body's immune system. VX-264 is designed to be surgically implanted and is currently being evaluated for patients with T1D.

About the VX-264 Phase 1/2 Clinical Trial
The clinical trial is a Phase 1/2, single-arm, open-label study in patients who have T1D. This will be a sequential, multi-part clinical trial to evaluate the safety, tolerability and efficacy of VX-264. Approximately 17 patients will be enrolled in the global clinical trial. Enrollment is ongoing in this study.

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. 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; there is currently no cure for diabetes.

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 clinical pipeline of investigational small molecule, mRNA, cell and genetic therapies (including gene editing) in other serious diseases where it has deep insight into causal human biology, including sickle cell disease, beta thalassemia, APOL1-mediated kidney disease, acute and neuropathic pain, type 1 diabetes and alpha-1 antitrypsin deficiency.

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 13 consecutive years on Science magazine's Top Employers list and one of Fortune's 100 Best Companies to Work For. 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 Felicia Pagliuca, Ph.D., and Trevor Reichman, M.D., in this press release, (ii) our plans, expectations for, and the potential benefits of VX-880 and VX-264, and (iii) 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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