Vertex Provides Updates on Phase 1/2 Clinical Trial of VX-880 for the Treatment of Type 1 Diabetes

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- Clinical proof-of-concept achieved based on positive data from the first two patients dosed at half the target dose of cells in Part A of Phase 1/2 study -

- First patient achieved insulin independence at Day 270; positive data in second patient; third patient has received full target dose with initiation of Part B -

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

- Phase 1/2 study is on Clinical Hold in the U.S.-

BOSTON--(BUSINESS WIRE)--Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today provided updates on its Phase 1/2 clinical trial of VX-880, an investigational stem cell-derived, fully differentiated pancreatic islet cell replacement therapy for people with type 1 diabetes (T1D) with impaired hypoglycemic awareness and severe hypoglycemia. Two patients in Part A received VX-880 at half the target dose. The first patient dosed in Part A of the study achieved insulin independence at Day 270, with a HbA1c of 5.2%. The second patient dosed in Part A has shown robust increases in fasting and stimulated C-peptide, and reductions in exogenous insulin requirements through Day 150. Taken together, the data from the first two patients in Part A established proof-of-concept for VX-880. Per the study protocol, the Independent Data Monitoring Committee reviewed the totality of the safety and efficacy data from the first two patients dosed in Part A of the study and recommended advancement to Part B, where patients receive the full target dose of VX-880. The first patient to receive the full target dose has achieved the Day 29 follow-up milestone.

Across the program, VX-880 has been generally well tolerated to date. There have been no serious adverse events (SAEs) considered related to VX-880. The majority of adverse events (AEs) were mild or moderate in all patients treated to date. The safety profile was generally consistent with the immunosuppressive regimen used in the study and the perioperative period.

The company also announced the VX-880 Phase 1/2 study has been placed on clinical hold in the U.S. by the Food and Drug Administration (FDA) due to a determination that there is insufficient information to support dose escalation with the product.

“We are surprised by the clinical hold placed on the study. The results from the first two patients treated with half the target dose establish proof-of-concept by demonstrating that VX-880 can restore glucose-regulated insulin production and improve glycemic control. Indeed, achievement of insulin independence by the first patient is a landmark milestone. Further, the totality of the safety and efficacy data for all three patients dosed to date gives us high confidence in our benefit-risk assessment of VX-880 and its potentially transformative profile,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. “We are committed to working with the FDA to understand and address their questions, so that the trial can resume at U.S. sites as soon as possible.”

Safety and Efficacy Results

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.

Patient 1

Results from Day 90 and Day 150 were previously reported. The patient achieved insulin independence at Day 270 with a HbA1c level of 5.2%. The study protocol defines insulin independence as no exogenous insulin use for at least one week, HbA1c ≤ 7%, fasting serum glucose ≤126 mg/dL, post-prandial serum glucose of ≤180 mg/dL, and fasting or stimulated C-peptide ≥166 pmol/L.

Through Day 270, there were no SAEs considered related to VX-880. There were two SAEs, one of rash and one of dehydration, neither of which were considered related to VX-880. The majority of the AEs were considered mild to moderate. The most common AEs were severe hypoglycemic events, which were not related to VX-880, and occurred in the perioperative period.

Patient 2

Islet cell function was evaluated at baseline and at Day 90 after VX-880 infusion using a Mixed Meal Tolerance Test (MMTT) with quantification of C-peptide levels, a direct marker for endogenous insulin production. At baseline prior to VX-880 infusion, fasting

and stimulated C-peptide levels were undetectable, indicating no endogenous insulin production. At Day 90, stimulated C-peptide increased to a peak of 202 pmol/L, indicating that VX-880 restored glucose-responsive insulin production. At Day 150, HbA1c decreased to 7.1% compared to a baseline of 7.5%, and exogenous insulin use decreased by 30%.

Through Day 150, there were no SAEs, and all AEs were considered mild to moderate. The most common AEs were headache and hypomagnesemia, which were not considered related to VX-880.

Patient 3

The third patient received the full target dose of VX-880 and has reached the Day 29 follow-up visit.

Early data show increasing fasting C-peptide and improving glycemic control through Day 29. Comprehensive evaluation of islet cell function will be evaluated based on the MMTT during the Day 90 visit.

Through Day 29, there were no SAEs considered related to VX-880. The patient had one SAE of neutropenia, which was not considered related to VX-880. The majority of the AEs were considered mild to moderate. The most common AE was nausea, which was not considered related to VX-880.

Cells Plus Device Program

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 chronic 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.

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, statements by Carmen Bozic, M.D., in this press release, and statements regarding (i) the potential benefits and safety of VX-880, (ii) our plans and expectations regarding interactions with the FDA, including our ability to resume our Phase 1/2 program for VX-880 at U.S. sites; (iii) our plans to continue to progress the Phase 1/2 program for VX-880, and (iv) our plans and expectations regarding our additional programs in T1D, including the completion of IND-enabling studies for the encapsulated islet cell program and including anticipated regulatory filings in 2022. 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 small 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 and efficacy, that internal or external factors that could delay, divert, or change our plans and objectives with respect to our research and development programs, 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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