Vertex Announces Positive Day 90 Data for the First Patient in the Phase 1/2 Clinical Trial Dosed With VX-880, a Novel Investigational Stem Cell-Derived Therapy for the Treatment of Type 1 Diabetes

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- First patient dosed with VX-880 demonstrated restoration of insulin production and achieved C-peptide of 560 pmol/L in response to Mixed Meal Tolerance Test (MMTT) at Day 90 Visit -

- 91% decrease in daily insulin requirement and simultaneous robust improvements in glucose control as measured by HbA1c -

- Treatment was generally well tolerated -

BOSTON--(BUSINESS WIRE)--Oct. 18, 2021-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced positive Day 90 data for the first patient from the 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). This is the first demonstration of a patient with T1D achieving robust restoration of islet cell function from such a cell therapy.

The patient was treated with a single infusion of VX-880 at half the target dose in conjunction with immunosuppressive therapy. The patient achieved successful engraftment and demonstrated rapid and robust improvements in multiple measures, including increases in fasting and stimulated C-peptide, improvements in glycemic control, including HbA1c, and decreases in exogenous insulin requirement. VX-880 was generally well tolerated.

“These results from the first patient treated with VX-880 are unprecedented. What makes these results truly remarkable is that they were achieved with treatment at half the target dose,” said Bastiano Sanna, Ph.D., Executive Vice President and Chief of Cell and Genetic Therapies at Vertex. “While still early, these results support the continued progression of our VX-880 clinical studies, as well as future studies using our encapsulated islet cells, which hold the potential to be used without the need for immunosuppression.”

“As a surgeon who has worked in the field of islet cell transplantation for decades, this approach, which obviates the need for an organ donor, could be a game changer,” said James Markmann, M.D., Ph.D., Professor of Surgery and Chief of the Division of Transplant Surgery at Massachusetts General Hospital. “We are excited to progress this unique and potentially transformative medicine through clinical trials and to patients.”

“More than a decade ago our lab had a vision for developing an islet cell replacement therapy to provide a functional cure to people suffering from T1D,” said Doug Melton, Ph.D., Xander University Professor at Harvard and an Investigator of the Howard Hughes Medical Institute. “These promising results bring great hope that stem cell-derived, fully differentiated islet cells could deliver a life-changing therapy for people who suffer from the relentless life-long burden of T1D.”

Efficacy Results

The patient was diagnosed with T1D approximately 40 years ago and has been dependent on exogenous insulin. In the one year prior to treatment, the patient experienced 5 severe, potentially life-threatening hypoglycemic episodes. Prior to treatment with VX-880, the patient’s insulin dose was 34 units per day and fasting and stimulated C-peptide levels were undetectable, indicating that the patient was not making their own insulin. Per the study protocol, the patient received half the target dose of VX-880 through a hepatic portal vein infusion in combination with a standard regimen of immunosuppressive agents.

Fasting C-peptide, HbA1c and 7-day average daily insulin dose were measured at various intervals after VX-880 treatment through Day 90. Fasting C-peptide was detected early after treatment with VX-880 and increased rapidly to Day 90. In parallel, HbA1c and daily insulin dose decreased over time.

Islet cell function was evaluated at baseline and at Day 90 using a Mixed Meal Tolerance Test (MMTT) with quantification of C-peptide levels, a direct marker for insulin production. At baseline prior to VX-880 treatment, fasting and stimulated C-peptide levels were undetectable, indicating no endogenous insulin production. At Day 90 after VX-880 treatment, fasting C-peptide was 280 pmol/L, reflecting restored basal insulin production and increased after MMTT stimulation to a peak of 560 pmol/L, indicating that VX-880 restored glucose-responsive insulin production. Also at Day 90, HbA1c improved from 8.6% at baseline to 7.2%, and daily insulin dose decreased from 34 units per day prior to treatment with VX-880 to an average dose of 2.9 units per day over a 7-day period at the Day 90 visit, reflecting a 91% decrease in daily exogenous insulin use.

Baseline and Day 90 Measures of Islet Cell Function for Patient 1

	Baseline before VX-880 infusion	Day 90 after VX-880 infusion
Fasting C-peptide (pmol/L)	Undetectable*	280
Peak Stimulated C-peptide with MMTT (pmol/L)	Undetectable*	560

HbA1c (%)	8.6	7.2
Daily insulin dose (units/day)**	34	2.9

*The lower limit of quantitation of the C-peptide assay is 13 pmol/L.
**Daily insulin dose for baseline was measured on Day -3 prior to VX-880 infusion. For Day 90 post-infusion, average daily insulin dose was calculated over a 7-day period.

Safety Results

In this first patient, the safety of VX-880 was generally consistent with the immunosuppressive regimen used in this study. There were no serious adverse events (SAE) considered related to VX-880, and the majority of the adverse events were considered mild to moderate. The most common adverse events were severe hypoglycemic events, which were non-serious, not related to VX-880, and occurred in the perioperative period. Through Day 90, the patient had one SAE; this was a rash that was mild in severity, not related to VX-880, and resolved.

Next Steps

Based upon these data, Vertex plans to continue to progress the Phase 1/2 program for VX-880. There are multiple active sites in the U.S., and the Clinical Trial Application has been approved in Canada. Vertex is also progressing IND-enabling studies for its encapsulated islet cell program, which would potentially eliminate the requirement for immunosuppression, and plans to file an IND for this program 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. The first two patients will be treated with half the target dose, followed by dose escalation to the target dose in the subsequent patients. Approximately 17 patients will be enrolled in the 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 patients 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 medicines in other serious diseases where it has deep insight into causal human biology, including pain, alpha-1 antitrypsin deficiency and APOL1-mediated kidney diseases. In addition, Vertex has a rapidly expanding pipeline of cell and genetic therapies for diseases such as sickle cell disease, beta thalassemia, Duchenne muscular dystrophy and type 1 diabetes mellitus.

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 11 consecutive years on Science magazine's Top Employers list and a best place to work for LGBTQ equality by the Human Rights Campaign. 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. James Markmann, and Doug Melton, Ph.D. 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 one patient 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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