Vertex Announces Program Updates for Type 1 Diabetes Portfolio

March 28, 2025

- VX-264 Phase 1/2 enrollment and dosing complete in Parts A and B: VX-264 was generally safe and well tolerated; efficacy data are not supportive of further clinical advancement -

- Zimislecel (VX-880) pivotal trial on track to complete enrollment and dosing in H1 2025; Vertex expects to submit marketing applications to global regulators in 2026 -

- Continue to progress multiple novel, research-stage immunoprotective approaches -

BOSTON--(BUSINESS WIRE)--Mar. 28, 2025-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced several updates on the Company's type 1 diabetes (T1D) portfolio.

VX-264 Update
Vertex has completed enrollment and dosing in Parts A and B of the Phase 1/2 VX-264 (cells + device) study and the planned analysis at Day 90 for Part B. In Part B of the study, participants received the full dose of the investigational fully differentiated pancreatic islet cell therapy encapsulated in a proprietary immunoprotective device. There were two primary endpoints in Part B, safety and change in peak C-peptide during a mixed-meal tolerance test (MMTT) from baseline at Day 90. VX-264 was generally safe and well tolerated; however, the study did not meet the efficacy endpoint. Increases in C-peptide, a marker of insulin production, were not observed at levels necessary to deliver benefit. Therefore, VX-264 will not be advancing further in clinical trials. Vertex plans to conduct further analyses, including of explanted devices, to better understand these findings.

Zimislecel Update
Zimislecel (formerly VX-880), Vertex's investigational fully differentiated islet cell therapy with standard immunosuppression, is in the Phase 3 portion of the Phase 1/2/3 study in patients with T1D with severe hypoglycemic events (SHEs) and impaired awareness of hypoglycemia. This pivotal trial is well underway and on track to complete enrollment and dosing in the first half of 2025, setting up global regulatory submissions in 2026. Zimislecel has previously been granted Regenerative Medicine Advanced Therapy (RMAT) and Fast Track designations from the U.S. Food and Drug Administration, Priority Medicines (PRIME) designation from the European Medicines Agency (EMA), and has secured an Innovation Passport under the Innovative Licensing and Access Pathway (ILAP) from the UK Medicines and Healthcare products Regulatory Agency (MHRA). Consistent with this progress, Vertex is investing in expanding its manufacturing and commercial capabilities to ensure launch readiness. If approved, eligible patients across the U.S. and Europe with recurrent SHEs despite best available care could benefit from zimislecel, and Vertex anticipates that initial approval could serve approximately 60,000 people with severe T1D.

T1D Research Update
Vertex is also pursuing research-stage T1D programs to evaluate additional approaches that could provide transformative benefit to people with T1D and reduce or eliminate the need for standard immunosuppressive regimens. These approaches include alternative immunosuppressive regimens, gene-edited hypoimmune stem-cell derived islet cell therapies, and novel devices to encapsulate islet cells.

"We'd like to thank the patients, physicians and T1D community who participated in the VX-264 study. Today's data show that more work needs to be done to advance the 'cells plus device' program, and we are committed to doing so," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer, Vertex Pharmaceuticals. "Equally, we are very pleased with the rapid progress of our zimislecel program, which is on track to complete enrollment and dosing in the Phase 3 study this summer, positioning us for global regulatory submissions in 2026. We're excited for the opportunity to bring the promise of zimislecel to patients as quickly as possible."

About Type 1 Diabetes

T1D results from the autoimmune destruction of insulin-producing beta cells in pancreatic islets. Insulin deficiency results in hyperglycemia and can lead to acute life-threatening complications such as diabetic ketoacidosis.

People with T1D are reliant on lifelong treatment with exogenous insulin that requires careful monitoring of blood glucose levels. Even with the availability of advanced exogenous insulin delivery and glucose monitoring systems, people with T1D can have periods of very low and very high blood sugar levels. Exogenous insulin has a narrow therapeutic range and carries an inherent risk of causing low blood sugar levels or hypoglycemic events, which can potentially result in arrhythmias, seizures, coma and even death. Due to the limitations and complexities of exogenous insulin treatment, it can be difficult for people with T1D to achieve and maintain good glucose control. Exposure to prolonged periods of high blood glucose levels, or hyperglycemia, can lead to long-term complications such as nerve damage, kidney disease/failure, eye disease (including vision loss), cardiovascular disease, stroke and even death.

HbA1c is a measure of average blood glucose over the most recent ~2-3 months, and the consensus guidance is to maintain an HbA1c of <7% to reduce the risk of long-term complications; only ~1 in 4 people with T1D globally meet this clinical target. Current standards of care do not address the underlying cause of the disease and leave people with T1D susceptible to both hypo- and hyperglycemia and their associated morbidity and mortality. There is no cure for T1D.

About Vertex

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases and conditions. The company has approved therapies for cystic fibrosis, sickle cell disease, transfusion-dependent beta thalassemia and acute pain, and it continues to advance clinical and research programs in these areas. Vertex also has a robust clinical pipeline of investigational therapies across a

range of modalities in other serious diseases where it has deep insight into causal human biology, including neuropathic pain, APOL1-mediated kidney disease, IgA nephropathy, primary membranous nephropathy, autosomal dominant polycystic kidney disease, type 1 diabetes and myotonic dystrophy type 1.

Vertex was founded in 1989 and has its global headquarters in Boston, with international headquarters in London. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia, Latin America and the Middle East. Vertex is consistently recognized as one of the industry's top places to work, including 15 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 LinkedIn, Facebook, Instagram, YouTube and X.

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., and statements regarding Vertex's plans and expectations for the clinical trial evaluating VX-264, including plans to conduct further analyses, expectations for the clinical trial evaluating zimislecel, including expectations for the trial to complete enrollment and dosing in the first half of 2025 and expectations for global regulatory submissions in 2026, plans to invest in manufacturing and commercial capabilities to ensure zimislecel launch readiness, expectations for the patient population that could benefit from zimislecel, and plans to progress multiple novel, research-stage immunoprotective approaches. 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 the company's research and development programs may not support development or registration of its compounds due to safety, efficacy or other reasons, that clinical trial data might not be available on the expected timeline, and other risks listed under Risk Factors in Vertex's most recent annual report 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. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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