Vertex Presents Positive Long-Term Data On CASGEVY™ (exagamglogene autotemcel) at the American Society of Hematology (ASH) Annual Meeting and Exposition and Provides Program Update

December 8, 2024

- Data from long-term follow-up of patients in clinical trials further demonstrate durability of the transformative benefits of CASGEVY™ -

- Safety profile consistent with busulfan conditioning and autologous hematopoietic stem cell transplant -

- Vertex provides update on progress in bringing CASGEVY to patients -

BOSTON--(BUSINESS WIRE)--Dec. 8, 2024-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced longer-term data for CASGEVY™ (exagamglogene autotemcel) from global clinical trials in people with severe sickle cell disease (SCD) or transfusion-dependent beta thalassemia (TDT). CASGEVY is the first and only approved CRISPR/Cas9 gene-edited therapy.

The results, presented at the American Society of Hematology (ASH) Annual Meeting and Exposition, continue to demonstrate the transformative, durable clinical benefits of CASGEVY. The longest follow up for both SCD and TDT patients now extends more than 5 years, with a median of 33.2 months and 38.1 months, respectively.

“These comprehensive data provide additional evidence of the benefits of eradicating transfusion requirements for people with transfusion-dependent beta thalassemia and vaso-occlusive crises for those with sickle cell disease,” said Franco Locatelli, M.D., Ph.D., Professor of Pediatrics at the Catholic University of the Sacred Heart of Rome, Director of the Department of Pediatric Hematology and Oncology at Bambino Gesù Children’s Hospital, Chair of Vertex’s TDT Program Steering Committee, and Presenting Author of the CASGEVY clinical data at ASH. “With median follow-up around three years there is strong evidence for the durability of these beneficial effects following treatment with CASGEVY.”

“CASGEVY is changing the outlook for people living with sickle cell disease and beta thalassemia, with these data reinforcing the immense clinical value a durable one-time therapy can provide to patients,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. “We have a strong commitment to build on our progress in bringing CASGEVY to patients around the world.”

New long-term follow-up data presented from the CASGEVY trials

- In SCD, 39/42 (93%) evaluable patients (those with at least 16 months of follow-up) were free from vaso-occlusive crises (VOCs) for at least 12 consecutive months (VF12) in CLIMB-121 and CLIMB-131 combined. The mean duration of VOC-free was 30.9 months, with a maximum of 59.6 months.
    - The three evaluable patients who have not achieved VF12 have derived meaningful clinical benefit including by reducing their rate of hospitalization for VOCs by 91%, 71% and 100%.
- In TDT, 53/54 (98%) evaluable patients (those with at least 16 months of follow-up) achieved transfusion-independence for at least 12 consecutive months with a weighted average hemoglobin of at least 9 g/dL (TI12) in CLIMB-111 and CLIMB-131 combined. The mean duration of transfusion independence was 34.5 months, with a maximum of 64.1 months.
    - The one evaluable patient who has not yet achieved TI12 has been transfusion free for 8.2 months.
- Both SCD and TDT patients reported sustained and clinically meaningful improvements in their quality of life, including physical, emotional, social/family and functional well-being, and overall health status.
- The safety profile of CASGEVY continues to be generally consistent with myeloablative conditioning with busulfan and autologous hematopoietic stem cell transplant.
- Patients continue to demonstrate stable levels of fetal hemoglobin (HbF) and allelic editing across all ages and genotypes in the trials.

Vertex had seven abstracts accepted at the ASH annual meeting as outlined below:

- Oral presentation, Abstract #512, entitled “Durable Clinical Benefits with Exagamglogene Autotemcel for Transfusion-Dependent β-Thalassemia”
- Poster presentation, Abstract #4954, entitled “Durable Clinical Benefits with Exagamglogene Autotemcel for Severe Sickle Cell Disease”
- Poster presentation, Abstract #1098, entitled “Estimated Prevalence of β-Thalassemia in the United States in 2023”
- Publication only, Abstract #7454, entitled “Health-Related Quality-of-Life Improvements after Exagamglogene Autotemcel in Patients with Transfusion-Dependent Beta Thalassemia”
- Publication only, Abstract #7453, entitled “Health-Related Quality-of-Life Improvements after Exagamglogene Autotemcel in Patients with Severe Sickle Cell Disease”
- Publication only, Abstract #7660, entitled “Adherence, Clinical and Economic Outcomes in Patients with Sickle Cell Disease

with Recurrent Vaso-Occlusive Crises Treated with L-Glutamine, Voxelotor, or Crizanlizumab Covered By Medicaid and Commercial Insurance in the United States"

- Publication only, Abstract #7661, entitled "Clinical Complications and Healthcare Resource Utilization in Medicaid and Commercially Insured Patients with Sickle Cell Disease Receiving Frequent Red Blood Cell Transfusions"

Progress in bringing CASGEVY to patients around the world

CASGEVY is approved for both SCD and TDT in the U.S., the European Union, Great Britain, Canada, Switzerland, Bahrain and the Kingdom of Saudi Arabia, and Vertex plans to make submissions in the United Arab Emirates and Kuwait. More than 45 authorized treatment centers have been activated globally to support the delivery of CASGEVY, and more than 40 patients have had a first cell collection.

Vertex is continuing to work with reimbursement authorities to secure sustainable access for patients. Through this work, Vertex has agreements to provide CASGEVY in multiple countries, including the U.S., England (TDT), Austria, Bahrain and the Kingdom of Saudi Arabia, and continues to make strong progress in others, including positive Health Technology Assessments (HTAs) in Canada for both diseases and advancing access negotiations for SCD patients in England. In the U.S., Vertex recently secured an industry-first, voluntary agreement with the Centers for Medicare & Medicaid Services (CMS) on a single outcomes-based arrangement available to all state Medicaid programs to ensure broad and equitable access to CASGEVY. To support this progress on patient access and growing patient demand, Vertex has received approval for a third manufacturing facility for CASGEVY with our partner Lonza.

About Sickle Cell Disease (SCD)

SCD is a debilitating, progressive and life-shortening disease. SCD patients report health-related quality of life scores well below the general population, and the lifetime health care costs in the U.S. of managing SCD for patients with recurrent VOCs is estimated between $4 and $6 million. SCD is an inherited blood disorder that affects the red blood cells, which are essential for carrying oxygen to all organs and tissues of the body. SCD causes severe pain, organ damage and shortened life span due to misshapen or "sickled" red blood cells. The clinical hallmark of SCD is VOCs, which are caused by blockages of blood vessels by sickled red blood cells and result in severe and debilitating pain that can happen anywhere in the body at any time. SCD requires a lifetime of treatment and results in a reduced life expectancy. In the U.S., the median age of death for patients living with SCD is approximately 45 years. A cure for SCD today is a stem cell transplant from a matched donor, but this option is only available to a small fraction of patients living with SCD because of the lack of available donors.

About Transfusion-Dependent Beta Thalassemia (TDT)

TDT is a serious, life-threatening genetic disease. TDT patients report health-related quality of life scores below the general population and the lifetime health care costs in the U.S. of managing TDT are estimated between $5 and $5.7 million. TDT requires frequent blood transfusions and iron chelation therapy throughout a person's life. Due to anemia, patients living with TDT may experience fatigue and shortness of breath, and infants may develop failure to thrive, jaundice and feeding problems. Complications of TDT can also include an enlarged spleen, liver and/or heart, misshapen bones and delayed puberty. TDT requires lifelong treatment and significant use of health care resources, and ultimately results in reduced life expectancy, decreased quality of life and reduced lifetime earnings and productivity. In the U.S., the median age of death for patients living with TDT is 37 years. Stem cell transplant from a matched donor is a curative option but is only available to a small fraction of people living with TDT because of the lack of available donors.

About CASGEVY™ (exagamglogene autotemcel [exa-cel])

CASGEVY™ is a non-viral *ex vivo* CRISPR/Cas9 gene-edited cell therapy for eligible patients with SCD or TDT, in which a patient's own hematopoietic stem and progenitor cells are edited at the erythroid specific enhancer region of the *BCL11A* gene through a precise double-strand break. This edit results in the production of high levels of fetal hemoglobin (HbF; hemoglobin F) in red blood cells. HbF is the form of the oxygen-carrying hemoglobin that is naturally present during fetal development, which then switches to the adult form of hemoglobin after birth. CASGEVY has been shown to reduce or eliminate VOCs for patients with SCD and transfusion requirements for patients with TDT.

CASGEVY is approved for eligible SCD and TDT patients 12 years and older by multiple regulatory bodies around the world.

About the CLIMB Trials

The ongoing Phase 1/2/3 open-label trials, CLIMB-111 and CLIMB-121, are designed to assess the safety and efficacy of a single dose of CASGEVY in patients ages 12 to 35 years with TDT or with SCD and recurrent VOCs. The trials are closed for enrollment. Patients will be followed for approximately two years after CASGEVY infusion in these trials. Each patient will be asked to participate in the ongoing long-term, open-label trial, CLIMB-131. CLIMB-131 is designed to evaluate the long-term safety and efficacy of CASGEVY in patients who received CASGEVY, including those in other CLIMB trials. The trial is designed to follow patients for up to 15 years after CASGEVY infusion.

U.S. INDICATIONS AND IMPORTANT SAFETY INFORMATION FOR CASGEVY (exagamglogene autotemcel)

WHAT IS CASGEVY?

CASGEVY is a one-time therapy used to treat people aged 12 years and older with:

• sickle cell disease (SCD) who have frequent vaso-occlusive crises or VOCs

• beta thalassemia (β-thalassemia) who need regular blood transfusions

CASGEVY is made specifically for each patient, using the patient's own edited blood stem cells, and increases the production of a special type of hemoglobin called hemoglobin F (fetal hemoglobin or HbF). Having more HbF increases overall hemoglobin levels and has been shown to improve the production and function of red blood cells. This can eliminate VOCs in people with sickle cell disease and eliminate the need for regular blood transfusions in people with beta thalassemia.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about CASGEVY?

After treatment with CASGEVY, you will have fewer blood cells for a while until CASGEVY takes hold (engrafts) into your bone marrow. This includes low levels of platelets (cells that usually help the blood to clot) and white blood cells (cells that usually fight infections). Your doctor will monitor this and give you treatment as required. The doctor will tell you when blood cell levels return to safe levels.

- **Tell your healthcare provider right away** if you experience any of the following, which could be signs of low levels of platelet cells:
    - severe headache
    - abnormal bruising
    - prolonged bleeding
    - bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood

- **Tell your healthcare provider right away** if you experience any of the following, which could be signs of low levels of white blood cells:
    - fever
    - chills
    - infections

You may experience side effects associated with other medicines administered as part of the treatment regimen for CASGEVY. Talk to your physician regarding those possible side effects. Your healthcare provider may give you other medicines to treat your side effects.

How will I receive CASGEVY?

Your healthcare provider will give you other medicines, including a conditioning medicine, as part of your treatment with CASGEVY. It's important to talk to your healthcare provider about the risks and benefits of all medicines involved in your treatment.

After receiving the conditioning medicine, it may not be possible for you to become pregnant or father a child. You should discuss options for fertility preservation with your healthcare provider before treatment.

STEP 1: Before CASGEVY treatment, a doctor will give you mobilization medicine(s). This medicine moves blood stem cells from your bone marrow into the blood stream. The blood stem cells are then collected in a machine that separates the different blood cells (this is called apheresis). This entire process may happen more than once. Each time, it can take up to one week.

During this step rescue cells are also collected and stored at the hospital. These are your existing blood stem cells and are kept untreated just in case there is a problem in the treatment process. If CASGEVY cannot be given after the conditioning medicine, or if the modified blood stem cells do not take hold (engraft) in the body, these rescue cells will be given back to you. If you are given rescue cells, you will not have any treatment benefit from CASGEVY.

STEP 2: After they are collected, your blood stem cells will be sent to the manufacturing site where they are used to make CASGEVY. It may take up to 6 months from the time your cells are collected to manufacture and test CASGEVY before it is sent back to your healthcare provider.

STEP 3: Shortly before your stem cell transplant, your healthcare provider will give you a conditioning medicine for a few days in hospital. This will prepare you for treatment by clearing cells from the bone marrow, so they can be replaced with the modified cells in CASGEVY. After you are given this medicine, your blood cell levels will fall to very low levels. You will stay in the hospital for this step and remain in the hospital until after the infusion with CASGEVY.

STEP 4: One or more vials of CASGEVY will be given into a vein (intravenous infusion) over a short period of time.

After the CASGEVY infusion, you will stay in hospital so that your healthcare provider can closely monitor your recovery. This can take 4-6 weeks, but times can vary. Your healthcare provider will decide when you can go home.

What should I avoid after receiving CASGEVY?

- Do not donate blood, organs, tissues, or cells at any time in the future

What are the possible or reasonably likely side effects of CASGEVY?

The most common side effects of CASGEVY include:

- Low levels of platelet cells, which may reduce the ability of blood to clot and may cause bleeding
- Low levels of white blood cells, which may make you more susceptible to infection

Your healthcare provider will test your blood to check for low levels of blood cells (including platelets and white blood cells). Tell your healthcare provider right away if you get any of the following symptoms:

- fever
- chills
- infections
- severe headache

- abnormal bruising
- prolonged bleeding
- bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood

These are not all the possible side effects of CASGEVY. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of CASGEVY

Talk to your healthcare provider about any health concerns.

Please see full Prescribing Information including Patient Information for CASGEVY.

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 approved medicines that treat the underlying causes of multiple chronic, life-shortening genetic diseases — cystic fibrosis, sickle cell disease and transfusion-dependent beta thalassemia — and continues to advance clinical and research programs in these diseases. 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 acute and 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.

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Vertex 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, the statements by Franco Locatelli, M.D., Ph.D. and Carmen Bozic, M.D., in this press release, and statements regarding expectations for the anticipated transformative, durable clinical benefits of CASGEVY, plans to continue working with reimbursement authorities to secure sustainable access for patients, including our expectations for progress in Canada and England, and our plans for and design of the CLIMB studies. While we believe 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 eligible patient access to CASGEVY may not be achieved on the anticipated timeline, or at all, that data from the company's development programs may not support registration or further development of its compounds due to safety, efficacy, and other reasons, 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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