Vertex Presents New Data on CASGEVY®, Including First-Ever Data in Children Ages 5-11 Years, at the American Society of Hematology Annual Meeting and Announces Plan for Global Regulatory Submissions

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- Data from pivotal studies of CASGEVY in children ages 5-11 years with severe sickle cell disease or transfusion-dependent beta thalassemia demonstrates the transformative potential of the therapy in younger patients -

- Efficacy and safety data in children 5-11 years are consistent with the durable and positive benefit/risk profile established from clinical studies in patients 12 years of age and older -

- Vertex expects to initiate global regulatory submissions for CASGEVY in children 5-11 years in 1H 2026 -

BOSTON--(BUSINESS WIRE)--Dec. 6, 2025-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced data from multiple studies demonstrating the clinical benefits of CASGEVY® (exagamglogene autotemcel) in people ages 5 years and older living with severe sickle cell disease (SCD) or transfusion-dependent beta thalassemia (TDT). The results, including the first presentation of clinical data from pivotal studies in children ages 5-11 years, and longer-term data from the pivotal studies of people with severe SCD and TDT ages 12 years and older, will be presented at the American Society of Hematology (ASH) Annual Meeting. CASGEVY is currently approved for eligible people ages 12 years and older with SCD or TDT in the United States, Great Britain, the European Union, the Kingdom of Saudi Arabia, the Kingdom of Bahrain, Kuwait, Qatar, Canada, Switzerland and the United Arab Emirates.

“These results — the first clinical data ever presented on any genetic therapy for children ages 5-11 years with SCD — again demonstrate the transformative potential of CASGEVY,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. “With dosing completed in the 5-11 age group and the Commissioner’s National Priority Voucher for CASGEVY in this population in hand, we are excited to begin global regulatory filings in the first half of next year and bring this potentially transformative therapy to eligible children as soon as possible.”

“As an investigator in the clinical program for patients 12 years and older and after having real-world experience with CASGEVY as an early commercial treatment center, I have seen firsthand the transformative impact this therapy has had on older patients with SCD or TDT. I am excited to hopefully be able to offer this option to my younger patients soon, early in life, before some of the most devastating impacts of these diseases begin,” said Haydar Frangoul, M.D., M.S., Medical Director of Pediatric Hematology and Oncology at Sarah Cannon Research Institute and HCA Healthcare’s TriStar Centennial Children’s Hospital, Member of Vertex’s SCD Program Steering Committee, and presenting author of the 5-11 years old CASGEVY data at ASH.

First presentation of data in children ages 5-11 years treated with CASGEVY

- In children with SCD, 11 patients have been dosed with CASGEVY in the Phase 3 CLIMB-151 clinical study, and all (4/4) patients with sufficient follow-up achieved the primary endpoint of being free from vaso-occlusive crises (VOCs) for at least 12 consecutive months (VF12).
    - No patient experienced a VOC following infusion with CASGEVY, with the longest duration of VOC-free of approximately two years (range 3.2–24.1 months).
- In children with TDT, 13 patients have been dosed with CASGEVY in the Phase 3 CLIMB-141 clinical study, and all (6/6) patients with sufficient follow-up achieved the primary endpoint of transfusion independence for at least 12 consecutive months while maintaining a weighted average hemoglobin (Hb) of at least 9 g/dL (TI12).
    - Following CASGEVY infusion, 12/13 are transfusion free, with the longest duration of transfusion free just under two years (range 2.3–22.5 months).
    - One patient died from pneumonia in the setting of multi-organ failure due to severe veno-occlusive disease related to the busulfan conditioning.
- The safety profile of CASGEVY in younger patients is consistent with myeloablative conditioning and autologous transplant in both SCD and TDT, as established in clinical studies in older patients.
- Consistent with studies in older patients, children treated with CASGEVY have durable increases in fetal hemoglobin (HbF) and stable allelic editing.

Longer-term data for people with SCD and TDT ages 12 years and older treated with CASGEVY

New longer-term data from the pivotal clinical studies of CASGEVY in people 12 years and older will also be presented at ASH.

These data, as of April 2025, continue to demonstrate the transformative, durable clinical benefits that CASGEVY provides to people living with SCD or TDT. In SCD, 100% of patients (45/45) achieved VF12 in either CLIMB-121 or the long-term follow-up study CLIMB-131, with a mean duration of VOC-free for 35.3 months (range 12.9–67.7 months). In TDT, 98.2% (55/56) achieved TI12 in either CLIMB-111 or CLIMB-131 with a mean duration of transfusion independence of 41.4 months (range 13–72.3 months). The safety profile remained consistent with myeloablative conditioning and autologous transplant in both SCD and TDT.

About Sickle Cell Disease (SCD)
SCD is a debilitating, progressive and life-shortening disease. It 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 vaso-occlusive crises (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. 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.

About Transfusion-Dependent Beta Thalassemia (TDT)
TDT is a serious, life-threatening genetic disease. It 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. 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.

About CASGEVY® (exagamglogene autotemcel)
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.

The use of CASGEVY in children ages 5-11 years is investigational.

About the CLIMB Studies
The Phase 1/2/3 open-label studies, CLIMB-111 and CLIMB-121, are designed to assess the safety and efficacy of a single dose of CASGEVY in patients ages 12-35 years with TDT or with SCD and recurrent VOCs. Patients will be followed for approximately two years after CASGEVY infusion in these studies. CLIMB-141 and CLIMB-151 are ongoing Phase 3 open-label studies, designed to assess the safety and efficacy of a single dose of exagamglogene autotemcel in patients ages 2-11 years with TDT or with SCD and recurrent VOCs. Enrollment and dosing are complete for the 5-11-years-old cohort in both studies with the plan to extend to ages 2-4 years.

Each patient will be asked to participate in the ongoing long-term, open-label study, CLIMB-131. CLIMB-131 is designed to evaluate the long-term safety and efficacy of CASGEVY in patients with up to 15 years of follow up after CASGEVY infusion.

Next steps for CASGEVY in children ages 5-11 years
Enrollment and dosing are complete for the 5-11 years cohort in both studies. Vertex expects to initiate global regulatory filings for this age group, including a supplemental Biologics License Application (sBLA) in the U.S., in the first half of next year. Vertex recently received a Commissioner's National Priority Voucher for CASGEVY in the 5-11 years age group from the U.S. Food and Drug Administration to accelerate the review of the sBLA once submitted. Products under the program will be subject to a 1–2-month review clock from the start of FDA's review and will also benefit from enhanced communication opportunities with the agency.

U.S. INDICATIONS AND IMPORTANT SAFETY INFORMATION FOR CASGEVY

WHAT IS CASGEVY?

CASGEVY is a one-time therapy used to treat people ages 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 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 16 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.

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, statements made by Carmen Bozic, M.D., and Haydar Frangoul, M.D., M.S., and statements regarding expectations for the clinical benefits of CASGEVY, plans to initiate global regulatory submissions for children 5-11, including in the U.S., in the first half of 2026, expectations that the use of a Priority Voucher will accelerate the review of the sBLA, expectations for the design of the CLIMB studies, including plans to follow patients after infusion, expectations that each patient will be asked to participate in the CLIMB-131 study and expectations that the studies will be extended to children 2-4 years of age. 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 registration or further development of its potential medicines in a timely manner, or at all, due to safety, efficacy or other reasons, that the company may be unable to make the anticipated regulatory submissions on the expected timeline, or at all, 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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