Vertex Announces Positive Results From Pivotal Trials of Vanzacaftor/Tezacaftor/Deutivacaftor, Next-In-Class Triple Combination Treatment for Cystic Fibrosis

February 5, 2024

– Treatment with the once-daily vanza triple CFTR modulator regimen met all primary and key secondary endpoints in two randomized controlled trials in people with CF ages 12 years and older –

– Results were more pronounced in the single-arm study in children ages 6 to 11 years, demonstrating the potential that treating early in life may prevent disease development –

– Vanza triple was generally well tolerated across all three studies –

– Vertex plans to file for approval with global regulators for people with CF ages 6 years and older by mid-2024, and use priority review voucher in the U.S. –

BOSTON--(BUSINESS WIRE)--Feb. 5, 2024-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced positive results from its once-daily vanzacaftor/tezacaftor/deutivacaftor (the "vanza triple") program, the most comprehensive Phase 3 pivotal program ever conducted by Vertex for the treatment of cystic fibrosis (CF), a progressive, multi-organ disease caused by dysfunction of the CFTR protein. The Phase 3 program included two randomized, double-blind, active-controlled, 52-week trials, SKYLINE 102 and SKYLINE 103, evaluating the efficacy of vanzacaftor (20 mg)/tezacaftor (100 mg)/deutivacaftor (250 mg) once daily in people with CF ages 12 years and older who have at least one *F508del* mutation or a mutation responsive to triple combination CFTR modulators (CFTRm), compared to TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor). A third Phase 3 single-arm, 24-week, open-label study, RIDGELINE 105, evaluated the safety and efficacy of the vanza triple in children with CF ages 6 to 11 years with at least one mutation responsive to triple combination CFTRm.

In SKYLINE 102 and SKYLINE 103, following a 4-week run-in on TRIKAFTA, baseline measurements of percent predicted forced expiratory volume in 1 second ($ppFEV_1$), sweat chloride (SwCl) and other efficacy parameters were obtained, after which patients were randomized to either the vanza triple or TRIKAFTA. As in the SKYLINE trials, all children in the RIDGELINE 105 study received at least 4 weeks of TRIKAFTA to establish a baseline for $ppFEV_1$, SwCl and other efficacy parameters prior to receiving vanza triple.

In both SKYLINE 102 and SKYLINE 103, the primary endpoint of absolute change from baseline in $ppFEV_1$ through week 24 was met and showed that treatment with vanza triple was non-inferior to treatment with TRIKAFTA.

The key secondary endpoints in SKYLINE 102 and SKYLINE 103 were absolute change from baseline in SwCl through week 24 compared to TRIKAFTA; proportion of patients pooled across the two trials, with SwCl below 60 mmol/L through week 24 compared to TRIKAFTA; and proportion of patients pooled across the two trials, with SwCl below 30 mmol/L through week 24 compared to TRIKAFTA.

Head-to-head against TRIKAFTA, on the first key secondary endpoint, the vanza triple was superior in reducing SwCl levels in SKYLINE 102 and SKYLINE 103. In the second and third key secondary endpoints, which were pooled across SKYLINE 102 and SKYLINE 103, the vanza triple achieved superiority in the proportion of patients below 60 mmol/L (the diagnostic threshold for CF) and below 30 mmol/L (carrier level) compared to TRIKAFTA.

The results from other secondary endpoints were consistent with results of the primary and key secondary endpoints. Additionally, the results at 52 weeks were consistent with results at 24 weeks.

The primary endpoint in the RIDGELINE 105 study in children 6 to 11 years old was safety. On the secondary endpoint measuring the absolute change in mean SwCl levels through week 24, the vanza triple reduced SwCl by -8.6 mmol/L compared to a baseline on TRIKAFTA. 95% of children achieved SwCl levels below 60 mmol/L and the majority of children treated with the vanza triple achieved normal levels of CFTR function with SwCl levels below 30 mmol/L.

Treatment with the vanza triple was well tolerated in all three studies, and the safety was similar between the vanza triple and TRIKAFTA treatment groups in SKYLINE 102 and SKYLINE 103. The safety of the vanza triple in children 6 to 11 years old was similar to the safety in people 12 years of age and older.

"We are very pleased with today's results, which demonstrate the vanza triple is non-inferior to TRIKAFTA in improving lung function and superior to TRIKAFTA in lowering levels of sweat chloride in people living with CF, setting a new standard for the level of CFTR protein function achievable, and raising the very high bar set by TRIKAFTA," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. "We look forward to submitting our application to regulators with the aim of bringing this potential medicine to patients as quickly as possible."

"I have been working as a pediatric pulmonologist for more than four decades and have seen first-hand the dramatic impact of CFTR modulators on people with CF, transforming CF from a life-shortening disease to today, where we see the potential for halting the disease before it starts. These results were particularly striking in the pediatric study where 95% of children achieved a SwCl level below 60 mmol/L, the diagnostic cut-off for a positive test for CF, and more than 50% of children achieved a SwCl level below carrier levels where they may see no symptoms of disease at all," said Bonnie Ramsey, M.D., Professor Emerita of Pediatrics, University of Washington School of Medicine, Senior Consultant to the CF Foundation Therapeutics Development Network and Co-Chair of Vertex's CFTR Modulator Steering Committee. "The efficacy seen with the vanza triple gives me great hope for CF patients in the future."

Efficacy Results:

In both active-controlled trials SKYLINE 102 and SKYLINE 103 in people with CF ages 12 years and older, the primary endpoint of absolute change from baseline in $ppFEV_1$ through week 24 was met. All patients received TRIKAFTA during a 4-week run-in prior to randomization, and baseline values were measured at the end of the TRIKAFTA run-in. The vanza triple was shown to be non-inferior to TRIKAFTA (SKYLINE 102: LS mean difference of 0.2; 95% CI: -0.7, 1.1; 1-sided *P*<0.0001 and SKYLINE 103: LS mean difference of 0.2; 95% CI: -0.5, 0.9; 1-sided *P*<0.0001).

For the first key secondary endpoint, in the trial of people with CF heterozygous for *F508del* and a minimal function mutation (F/MF) (SKYLINE 102), the absolute mean change from baseline in SwCl through week 24 was -7.5 mmol/L for those taking the vanza triple, compared to +0.9 mmol/L for those taking TRIKAFTA, demonstrating a statistically significant and clinically meaningful improvement in CFTR function (LS mean difference of -8.4; 95% CI: -10.5, -6.3; *P*<0.0001). In the trial of people with CF with other mutations responsive to triple combination CFTRm (SKYLINE 103), the absolute mean change from baseline in SwCl through week 24 was -5.1 mmol/L for those taking the vanza triple, compared to -2.3 mmol/L for those taking TRIKAFTA, again demonstrating statistically significant and clinically meaningful improvement in CFTR function (LS mean difference of -2.8; 95% CI: -4.7, -0.9; *P*=0.0034).

For the second and third key secondary endpoints based on the pooled analysis across SKYLINE 102 and SKYLINE 103, following treatment with the vanza triple, 86% of people with CF across both trials had a SwCl level below the diagnostic threshold of 60 mmol/L through 24 weeks, compared to 77% of people treated with TRIKAFTA (odds ratio 2.21; 95% CI: 1.55, 3.15; *P*<0.0001). Following treatment with the vanza triple, 31% of people across both trials had a SwCl level below carrier level of 30 mmol/L through 24 weeks, compared to 23% of people treated with TRIKAFTA (odds ratio 2.87; 95% CI: 2.00, 4.12; *P*<0.0001). Consequently, in these combined trials, there was about a two-times greater likelihood in the odds of achieving a SwCl level below 60 mmol/L for those treated with the vanza triple compared to TRIKAFTA and about a three-times greater likelihood in the odds of achieving a SwCl level below 30 mmol/L for those treated with the vanza triple compared to TRIKAFTA.

In the single-arm, open-label study in children 6 to 11 years old with CF and at least one mutation responsive to triple combination CFTRm (RIDGELINE 105), the vanza triple demonstrated safety, the primary endpoint. Secondary endpoints included evaluation of absolute change in SwCl from baseline through week 24, absolute change in $ppFEV_1$ from baseline through week 24, the proportion of children with SwCl levels of <60 mmol/L through week 24, and the proportion of children with SwCl <30 mmol/L through week 24, among other endpoints. Prior to receiving the vanza triple, all children were on TRIKAFTA for at least 4 weeks, and the baseline values were measured at the end of the 4-week run-in. Children with CF in the study maintained their baseline level of lung function ($ppFEV_1$ of 99.7) with an absolute LS mean change from baseline through week 24 of 0.0 (95% CI: -2.0, 1.9) and had an absolute mean change in sweat chloride of -8.6 mmol/L (95% CI: -11.0, -6.3) from baseline levels of 40.4 mmol/L while on TRIKAFTA.

Following treatment with the vanza triple, 95% of children in the study had a SwCl level below 60 mmol/L through 24 weeks (95% CI: 87%, 99%) and 53% of children had a SwCl level below 30 mmol/L (95% CI: 41%, 64%).

Primary and Key Secondary Outcomes in Active-Controlled Phase 3 Trials in People with CF Ages 12 Years and Older (SKYLINE 102 and SKYLINE 103)

Primary Endpoint: Absolute Change from Baseline* in $ppFEV_1$ through Week 24†

	Baseline mean (SD)	LS mean change (SE)	LS mean difference vs. TRIKAFTA (95% CI)	*P* for non-inferiority, one-sided
SKYLINE 102				
TRIKAFTA N=202	67.2 (14.6)	0.3 (0.3)	--	--
Vanza Triple N=196	67.0 (15.3)	0.5 (0.3)	0.2 (-0.7, 1.1)	<0.0001
SKYLINE 103				
TRIKAFTA N=289	66.4 (14.9)	0.0 (0.2)	--	--
Vanza Triple N=284	67.2 (14.6)	0.2 (0.3)	0.2 (-0.5, 0.9)	<0.0001

First Key Secondary Endpoint: Absolute Change from Baseline* in Sweat Chloride through Week 24†

	Baseline mean (SD)	LS mean change (SE)	LS mean difference vs. TRIKAFTA (95% CI)	*P* for superiority, two-sided
SKYLINE 102				
TRIKAFTA N=202	54.3 (18.2)	0.9 (0.8)	--	--
Vanza Triple N=196	53.6 (17.0)	-7.5 (0.8)	-8.4 (-10.5, -6.3)	<0.0001
SKYLINE 103				
TRIKAFTA N=289	42.1 (17.9)	-2.3 (0.7)	--	--
Vanza Triple N=284	43.4 (18.5)	-5.1 (0.7)	-2.8 (-4.7, -0.9)	0.0034

Second Key Secondary Endpoint: Proportion of Patients with Sweat Chloride <60 mmol/L through Week 24† (Pooled Across SKYLINE 102 and SKYLINE 103)

	Baseline* % patients	Through Week 24 % patients	Odds ratio** vs. TRIKAFTA (95% CI)	*P* for superiority, two-sided
Pooled TRIKAFTA N=491	74%	77%	--	--
Pooled Vanza Triple N=480	76%	86%	2.21 (1.55, 3.15)	<0.0001

Third Key Secondary Endpoint: Proportion of Patients with Sweat Chloride <30 mmol/L through Week 24† (Pooled Across SKYLINE 102 and SKYLINE 103)

	Baseline* % patients	Through Week 24 % patients	Odds ratio** vs. TRIKAFTA (95% CI)	*P* for superiority, two-sided
Pooled TRIKAFTA N=491	21%	23%	--	--
Pooled Vanza Triple N=480	19%	31%	2.87 (2.00, 4.12)	<0.0001

* Baseline values were measured after a 4-week run-in on TRIKAFTA.
† Through Week 24 was defined as average of measurements at Weeks 16 and 24.
** Estimated by generalized estimating equation model; odds ratio >1 favors the vanza triple.
CI = confidence interval; LS = least squares; SD = standard deviation; SE = standard error.

Efficacy Outcomes in a Single Arm, Open-Label Study in Children with CF Ages 6 to 11 Years (RIDGELINE 105)

Absolute Change from Baseline* in ppFEV$_1$ through Week 24†

	Baseline mean (SD)	LS mean change (SE)	95% CI
Vanza Triple N=78	99.7 (15.1)	0.0 (1.0)	-2.0, 1.9

Absolute Change from Baseline* in Sweat Chloride through Week 24†

	Baseline mean (SD)	LS mean change (SE)	95% CI
Vanza Triple N=78	40.4 (20.9)	-8.6 (1.2)	-11.0, -6.3

Proportion of Children with Sweat Chloride < 60 mmol/L through Week 24†

	Baseline* % children	Through Week 24 % children	95% CI
Vanza Triple N=78	84%	95%	87%, 99%

Proportion of Children with Sweat Chloride < 30 mmol/L through Week 24†

	Baseline* % children	Through Week 24 % children	95% CI
Vanza Triple N=78	39%	53%	41%, 64%

***** Baseline values were measured after at least 4 weeks on TRIKAFTA.

†Through Week 24 was defined as average of measurements at Weeks 16 and 24.

CI = confidence interval; LS = least squares; SE = standard error; SD = standard deviation.

Safety Results:

In SKYLINE 102 and SKYLINE 103, the majority of adverse events (AEs) were mild to moderate and generally consistent with the manifestations of CF. The incidence of serious adverse events (SAEs) and the incidence of AEs leading to treatment discontinuation was low and balanced between the vanza triple and TRIKAFTA groups. Overall, the safety data were generally consistent between the vanza triple and TRIKAFTA.

Common TEAEs* (≥10% in any Treatment Group, Pooled SKYLINE 102 and SKYLINE 103)

Preferred Term	TRIKAFTA N=491 n (%)	Vanza Triple N=480 n (%)
Subjects with any TEAEs	469 (95.5)	459 (95.6)
Infective pulmonary exacerbation of cystic fibrosis	158 (32.2)	133 (27.7)

Cough	101 (20.6)	108 (22.5)
COVID-19	127 (25.9)	107 (22.3)
Nasopharyngitis	95 (19.3)	102 (21.3)
Headache	63 (12.8)	76 (15.8)
Upper respiratory tract infection	67 (13.6)	72 (15.0)
Oropharyngeal pain	60 (12.2)	69 (14.4)
Diarrhea	59 (12.0)	58 (12.1)
Influenza	26 (5.3)	52 (10.8)
Pyrexia	50 (10.2)	52 (10.8)
Fatigue	46 (9.4)	51 (10.6)
Nasal congestion	47 (9.6)	48 (10.0)
Sputum increased	50 (10.2)	45 (9.4)

*TEAE: treatment-emergent adverse events.

In RIDGELINE 105, the majority of AEs were also mild to moderate and generally consistent with the manifestations of CF. The incidence of SAEs was low, and the overall safety of the vanza triple was similar in children 6 to 11 years old as in people ages 12 years and older. The incidence and nature of AEs was also similar to those seen in previous CFTRm studies of children 6 to 11 years old.

Next Steps

Vertex is on track to make global regulatory submissions by mid-2024 including a New Drug Application (NDA) to the Food and Drug Administration and a Marketing Authorization Application with the European Medicines Agency for people with CF ages 6 years and older. The company will use a priority review voucher in the U.S. The priority review voucher entitles the holder to designate an NDA for priority review, which provides an expedited 6-month review instead of the standard 10-month review.

The full data set from these studies will be presented at future medical meetings later this year.

About the Vanza Triple Phase 3 Program
The Phase 3 program in people with cystic fibrosis ages 12 years and older consisted of two randomized, double-blind, active-controlled 52-week trials, SKYLINE 102 and SKYLINE 103, which evaluated the safety and efficacy of the vanza triple in comparison to TRIKAFTA. SKYLINE 102 randomized and dosed 398 people with CF ages 12 years and older with one *F508del* mutation and one minimal function mutation (F/MF). SKYLINE 103 randomized and dosed 573 people with CF ages 12 years and older who were homozygous for *F508del* mutations (F/F), heterozygous for *F508del* and a gating (F/G) or a residual function mutation (F/RF) or have at least one other mutation responsive to triple combination CFTR modulators and no *F508del* mutation. All patients received TRIKAFTA during a 4-week run-in prior to randomization, and the baseline values for all endpoints were measured at the end of the TRIKAFTA run-in.

The primary endpoint of both SKYLINE 102 and SKYLINE 103 was the absolute change from baseline in ppFEV$_1$ through week 24, and the primary analysis was non-inferiority of the vanza triple compared to TRIKAFTA. The first key secondary endpoint in SKYLINE 102 and SKYLINE 103 was absolute change from baseline in sweat chloride through week 24 compared to TRIKAFTA; the second key secondary endpoint was the proportion of patients pooled across the two studies, with SwCl below 60 mmol/L through week 24 compared to TRIKAFTA; and the third key secondary endpoint was the proportion of patients pooled across two studies, with SwCl below 30 mmol/L through week 24 compared to TRIKAFTA. All three key secondary endpoints were evaluated in a hierarchical manner and multiplicity controlled for superiority to TRIKAFTA.

A third Phase 3 single-arm, open-label study, RIDGELINE 105, dosed 78 children with CF ages 6 through 11 years and evaluated the pharmacokinetics, safety and tolerability, and efficacy of the vanza triple for 24 weeks, after a baseline established on TRIKAFTA. Children received TRIKAFTA for at least 4 weeks prior to receiving vanza triple, and the baseline values for all endpoints were measured at the end of the TRIKAFTA run-in. The primary endpoint was safety and tolerability. The secondary endpoints were efficacy endpoints and included absolute change in SwCl from baseline through week 24, absolute change in ppFEV$_1$ from baseline through week 24, the proportion of children with SwCl <60 mmol/L through week 24, and the proportion of children with SwCl <30 mmol/L through week 24, among other endpoints.

About vanzacaftor/tezacaftor/deutivacaftor (the “vanza triple”)

In people with CF, mutations in the *CFTR* gene lead to decreased quantity and/or function of the CFTR protein channel at the cell surface. Vanzacaftor and tezacaftor are correctors designed to increase the amount of CFTR protein at the cell surface by facilitating the processing and trafficking of the CFTR protein. Deutivacaftor is a potentiator designed to increase the channel open probability of the CFTR protein delivered to the cell surface to improve the flow of salt and water across the cell membrane.

Investigational vanzacaftor/tezacaftor/deutivacaftor was granted Fast Track and Orphan Drug Designations from the U.S. Food and Drug Administration for the treatment of cystic fibrosis.

The vanza triple will be subject to a meaningfully lower single-digit royalty obligation, compared to the rate payable on Vertex's current CF portfolio.

About Cystic Fibrosis
Cystic fibrosis (CF) is a rare, life-shortening genetic disease affecting more than 92,000 people globally. CF is a progressive, multi-organ disease that affects the lungs, liver, pancreas, GI tract, sinuses, sweat glands and reproductive tract. CF is caused by a defective and/or missing CFTR protein resulting from certain mutations in the *CFTR* gene. People with CF must inherit two defective *CFTR* genes — one from each parent — to have CF, and these mutations can be identified by a genetic test. While there are many different types of *CFTR* mutations that can cause the disease, the vast majority of people with CF have at least one *F508del* mutation. *CFTR* mutations lead to CF by causing CFTR protein to be defective or by leading to a shortage or absence of CFTR protein at the cell surface. The defective function and/or absence of CFTR protein results in poor flow of salt and water into and out of the cells in a number of organs. In the lungs, this leads to the buildup of abnormally thick, sticky mucus, chronic lung infections and progressive lung damage that eventually leads to death for many patients. The median age of death is in the 30s, but with treatment, projected survival is improving.

Diagnosis of CF is often made by genetic testing and is confirmed by testing sweat chloride (SwCl), which measures CFTR protein dysfunction. The diagnostic threshold for CF is SwCl ≥60 mmol/L, while levels between 30-59 indicate CF is possible and more testing may be needed to make the diagnosis of CF. A SwCl level of <30 mmol/L is seen in people who carry one copy of the CF gene but do not have any manifestation of disease (carriers). Higher levels of SwCl are associated with more severe disease. Restoring CFTR function leads to lower levels of SwCl. SwCl levels below 60 mmol/L are associated with improved outcomes such as better and more stable lung function, fewer pulmonary exacerbations, better quality of life and improved survival. Restoring SwCl levels below 30 mmol/L has long been the ultimate treatment goal for Vertex, as levels below 30 mmol/L are considered normal and are typical of CF carriers who do not have disease.

About TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) U.S. INDICATIONS AND USAGE

TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 2 years and older who have at least one copy of the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or another mutation that is responsive to treatment with TRIKAFTA. Patients should talk to their doctor to learn if they have an indicated CF gene mutation. It is not known if TRIKAFTA is safe and effective in children under 2 years of age.

IMPORTANT SAFETY INFORMATION

Before taking TRIKAFTA, patients should tell their doctor about all of their medical conditions, including if they: are allergic to TRIKAFTA or any ingredients in TRIKAFTA, have kidney problems, have or have had liver problems, are pregnant or plan to become pregnant because it is not known if TRIKAFTA will harm an unborn baby, or are breastfeeding or planning to breastfeed because it is not known if TRIKAFTA passes into breast milk.

Patients should tell their doctor about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. TRIKAFTA may affect the way other medicines work, and other medicines may affect how TRIKAFTA works. The dose of TRIKAFTA may need to be adjusted when taken with certain medicines. Patients should ask their doctor or pharmacist for a list of these medicines if they are not sure. Patients should especially tell their doctor if they take: antibiotics such as rifampin or rifabutin; seizure medicines such as phenobarbital, carbamazepine, or phenytoin; St. John's wort; antifungal medicines including ketoconazole, itraconazole, posaconazole, voriconazole, or fluconazole; antibiotics including telithromycin, clarithromycin, or erythromycin.

Patients should avoid food or drink that contains grapefruit while taking TRIKAFTA.

TRIKAFTA can cause serious side effects, including:

Liver damage and worsening of liver function in patients with severe liver disease that can be serious and may require transplantation. Liver damage has also happened in patients without liver disease.

High liver enzymes in the blood, which is a common side effect in patients treated with TRIKAFTA**.** These can be serious and may be a sign of liver injury. The patient's doctor will do blood tests to check their liver before they start TRIKAFTA, every 3 months during the first year of taking TRIKAFTA, and every year while taking TRIKAFTA. Patients should call their doctor right away if they have any of the following symptoms of liver problems: pain or discomfort in the upper right stomach (abdominal) area; yellowing of the skin or the white part of the eyes; loss of appetite; nausea or vomiting; dark, amber-colored urine.

Serious allergic reactions have happened to patients who are treated with TRIKAFTA. Call your healthcare provider or go to the emergency room right away if you have any symptoms of an allergic reaction. Symptoms of an allergic reaction may include: rash or hives; tightness of the chest or throat or difficulty breathing; swelling of the face, lips and/or tongue; difficulty swallowing; and light-headedness or dizziness.

Abnormality of the eye lens (cataract) has been noted in some children and adolescents treated with TRIKAFTA. If the patient is a child or adolescent, their doctor should perform eye examinations before and during treatment with TRIKAFTA to look for cataracts.

The most common side effects of TRIKAFTA include headache, upper respiratory tract infection (common cold) including stuffy and runny nose, stomach (abdominal) pain, diarrhea, rash, increase in liver enzymes, increase in a certain blood enzyme called creatine phosphokinase, flu (influenza), inflamed sinuses, and increase in blood bilirubin.

Patients should tell their doctor if they have any side effect that bothers them or that does not go away. These are not all the possible side effects of TRIKAFTA. For more information, patients should ask their doctor or pharmacist.

Please click here to see the full Prescribing Information for TRIKAFTA.

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 APOL1-mediated kidney disease, acute and neuropathic pain, type 1 diabetes, myotonic dystrophy type 1 and alpha-1 antitrypsin deficiency.

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 14 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 Twitter/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 Bonnie Ramsey, M.D., in this press release, and statements regarding our beliefs about the potential benefits of vanzacaftor/tezacaftor/deutivacaftor, our plans to make global regulatory submissions by mid-2024, including a New Drug Application to the U.S. Food and Drug Administration and a Marketing Authorization Application with the European Medicines Agency, our plans to use a priority review voucher in the U.S. and our expectations for an expedited review, and our plans to present the full data set from these studies. 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 regulatory submissions may not be completed on the anticipated timeline, or at all, 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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