Vertex Provides Pipeline and Business Updates in Advance of Upcoming Investor Meetings

January 7, 2024

BOSTON--(BUSINESS WIRE)--Jan. 7, 2024-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced multiple program updates ahead of upcoming investor meetings in January, including the company's scheduled webcast from the 42 nd Annual J.P. Morgan Healthcare Conference on Monday, January 8, 2024 at 11:15 a.m. ET/8:15 a.m. PT.

"2023 was marked by continued strong performance in the cystic fibrosis business and acceleration of our development stage pipeline, propelling the company into 2024 with tremendous momentum," said Reshma Kewalramani, M.D., Chief Executive Officer and President of Vertex. "We continue to reach more patients than ever before with our CF medicines; we've launched CASGEVY™ in theU.S., UK and Bahrain following the historic approvals of this gene editing therapy late last year, and we are well positioned to advance our mission of bringing additional transformative medicines to people with serious diseases."

Disease Areas with Approved Medicines

Cystic Fibrosis

- **Next-in-class triple combination**: Completed three pivotal studies evaluating the next-in-class, triple combination CFTR modulator therapy vanzacaftor/tezacaftor/deutivacaftor compared to TRIKAFTA® in patients with CF ages 6 years of age and older (ages 12+ in SKYLINE 102 and 103 studies; ages 6-11 in the RIDGELINE study). Vertex expects to share the results of all three studies in early 2024.
- **VX-522:** Completed dosing in the single ascending dose (SAD) portion of the Phase 1/2 study of VX-522 in patients with CF and initiated the multiple ascending dose (MAD) portion of the study. VX-522 is a CFTR mRNA therapeutic that Vertex is developing in collaboration with Moderna for the >5,000 patients with CF who do not make any CFTR protein and cannot benefit from CFTR modulators.
- **Epidemiology update:** Vertex revised its estimates for the number of patients living with cystic fibrosis from ~88,000 to ~92,000 in the U.S., Europe, Australia, and Canada.

Sickle Cell Disease (SCD) and Transfusion-Dependent Beta Thalassemia (TDT) – CASGEVY

- Received regulatory approvals for CASGEVY in the fourth quarter of 2023 in the U.S. for sickle cell disease, and in Great Britain and Bahrain for the treatment of both SCD and TDT; also received positive CHMP opinion for CASGEVY for both SCD and TDT from the European Medicines Agency (EMA).
- The FDA has assigned a Prescription Drug User Fee Act (PDUFA) action date of March 30, 2024, for CASGEVY in TDT. Additional regulatory submissions for CASGEVY are currently under review in Switzerland and the Kingdom of Saudi Arabia, with submission in Canada planned for the first half of 2024.
- Completed enrollment in two global Phase 3 studies of CASGEVY in patients 5 to 11 years of age with SCD or TDT.
- Signed an agreement with Synergie Medication Collective, a medication contracting organization founded by a group of Blue Cross and Blue Shield affiliated companies covering approximately 100 million people, to provide access to CASGEVY.
- Activated 9 authorized treatment centers (ATCs) in the U.S. and 3 in Europe, with an ultimate goal of activating approximately 50 ATCs in the U.S. and 25 in Europe.
- **Epidemiology update:** Vertex revised its estimates for the number of patients living with severe sickle cell disease, from ~25,000 patients to ~30,000 patients in the U.S. and Europe, with additional patients in Bahrain and the Kingdom of Saudi Arabia. Vertex's updated estimate for patients with transfusion-dependent beta thalassemia is revised from ~7,000 to ~5,000 patients in the U.S. and Europe, with additional patients in Bahrain and the Kingdom of Saudi Arabia.

Pipeline Disease Areas

Acute Pain

- **VX-548:** Completed three Phase 3 studies of VX-548 for the treatment of moderate to severe acute pain, including two randomized placebo-controlled studies: one following abdominoplasty and one following bunionectomy surgery, as well as a third single-arm safety and effectiveness study, which enrolled both surgical and non-surgical patients with moderate to severe acute pain. Vertex expects to share the results of all three studies in early 2024.
- **VX-993:**
    - Completed a Phase 1 study of an oral formulation of VX-993, a next-generation NaV1.8 inhibitor, and anticipates initiating a Phase 2 study for the treatment of moderate to severe acute pain in 2024.

- Vertex also anticipates initiating a Phase 1 study of an intravenous formulation of VX-993 for the treatment of moderate to severe acute pain in 2024.

Peripheral Neuropathic Pain (PNP)

- **VX-548:**
  - Following the December 2023 release of positive Phase 2 results with VX-548 in diabetic peripheral neuropathy, which represents ~20% of peripheral neuropathic pain patients, Vertex plans to meet with regulators in the first quarter of 2024 and anticipates advancing VX-548 into pivotal development.
  - Initiated a Phase 2 study of VX-548 in lumbosacral radiculopathy, another type of peripheral neuropathic pain and the largest patient segment (over 40%) within the PNP category.
- **VX-993:** Vertex also anticipates initiating a Phase 2 study with an oral formulation of VX-993 for the treatment of PNP in 2024.

APOL1-Mediated Kidney Disease (AMKD) – Inaxaplin (VX-147)

- Completed enrollment in the Phase 2B dose-ranging portion of the study of inaxaplin for the treatment of patients with AMKD.
- Vertex expects to select the inaxaplin dose for the Phase 3 portion of the Phase 2/3 pivotal trial and begin Phase 3 in the first quarter of 2024.

Type 1 Diabetes (T1D)

- **VX-880:** Completed enrollment in Parts A, B, and C of the Phase 1/2 study of VX-880, an allogeneic, stem cell-derived, fully differentiated, insulin-producing islet cell therapy, used in conjunction with standard immunosuppression, in patients with T1D and impaired awareness of hypoglycemia and recurrent hypoglycemic events.
  - Efficacy:
    - As of the last data cut, all 14 patients dosed with VX-880 demonstrated islet cell engraftment and production of endogenous insulin.
    - All Part A and B patients, except for one patient who withdrew consent from the study, demonstrated glycemic control to target ADA recommended levels with HbA1C <7% and no longer required exogenous insulin. Part C patients have trajectories similar to Part A and B patients.
  - Safety:
    - The safety profile of VX-880 to date is consistent with immunosuppressives, the perioperative period and past medical history.
    - Two patient deaths, both unrelated to VX-880, have occurred. Vertex has placed the study on a protocol-specified pause, pending review of the totality of the data by the independent data monitoring committee and global regulators.

- **VX-264:** The clinical trial for VX-264, which encapsulates the same VX-880 cells in a device that is designed to eliminate the need for immunosuppressants, is a multi-part, Phase 1/2 study.
  - Part A has initiated, enrolled and dosed multiple patients.
  - The study remains ongoing in multiple centers and countries as Vertex prepares for Part B initiation.

Myotonic Dystrophy Type 1 (DM1) – VX-670

- Received clearances from Health Canada and Medicines and Healthcare Products Regulatory Agency (MHRA – UK) for Clinical Trial Applications (CTA) for VX-670 for patients with DM1. Vertex initiated the Phase 1/2 clinical trial in patients with DM1 in Canada and will initiate the study in the UK near-term.
- Vertex also submitted an Investigational New Drug (IND) application to the FDA for VX-670. The FDA requested additional information, which resulted in a clinical hold. Vertex is working to address FDA comments and initiate the study in the U.S.
- VX-670 is an oligonucleotide that targets the underlying cause of DM1, linked to a cyclic peptide that promotes effective delivery into cells. DM1 is the most prevalent muscular dystrophy in adults with ~110,000 people living with the disease in the U.S. and Europe.

Autosomal Dominant Polycystic Kidney Disease (ADPKD) – VX-407

- Completed IND-enabling studies of VX-407 for the treatment of ADPKD and anticipates beginning a Phase 1 clinical trial in healthy volunteers this year.
- VX-407 is a first-in-class small molecule corrector that targets the underlying cause of ADPKD in a subset of patients with responsive PKD1 mutations, estimated at ~25,000 (or ~10%) of the overall ~250,000 ADPKD patient population. ADPKD is the most commonly inherited kidney disease.

J.P. Morgan Healthcare Conference Presentation and Webcast

Dr. Kewalramani will present at the 42nd Annual J.P. Morgan Healthcare Conference on Monday, January 8, 2024 at 11:15 a.m. ET/8:15 a.m. PT.

A live webcast of management's remarks will be available through the Vertex website, www.vrtx.com, in the "Investors" section under the "News and Events" page. A replay of the conference webcast will be archived on the company's website.

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 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 and Latin America. 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 Reshma Kewalramani, M.D., in this press release, and statements about our expectations for our CF program, including plans to share results of our vanzacaftor/tezacaftor/deutivacaftor studies in early 2024, our expectations for CASGEVY™, including plans for additional regulatory submissions, and plans to activate approximately 50 ATCs in the U.S. and 25 in Europe, our expectations for our acute pain program, including plans to share results from the three Phase 3 studies in early 2024, and plans to initiate Phase 1 and Phase 2 studies evaluating VX-993 in 2024, our expectations for our PNP pain program, including plans for meetings with regulators, plans to advance VX-548 into pivotal development, and plans to initiate a Phase 2 study of VX-993 in 2024, our plans to select the inaxaplin dose and begin Phase 3 in the first quarter of 2024, expectations for our T1D program, including anticipated review of VX-880 data by the independent data monitoring committee and global regulators, and our plans to initiate Part B of the VX-264 study, expectations for our DM1 program, including plans to initiate a clinical trial for VX-670 in the UK and plans to work with the FDA on the VX-670 study in the U.S. and initiate the study in the U.S., and expectations for our ADPKD program, including plans to begin a Phase 1 clinical trial for VX-407 in 2024. 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 a limited number of patients may not be indicative of final clinical trial results, that clinical trial data might not be available on the expected timeline, 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, that our discussions with regulators may be delayed or cause delays in our pipeline programs, 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. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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