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## **Vertex and Parion Sciences Establish Collaboration to Develop Epithelial Sodium Channel (ENaC) Inhibitors in Cystic Fibrosis and Other Pulmonary Diseases**

*-ENaC inhibition aims to restore or improve hydration of cell surfaces in the lungs to improve lung function-*

*-Parion to receive \$80 million up-front payment with potential for additional development and regulatory milestones and royalty payments-*

BOSTON & DURHAM, N.C.--(BUSINESS WIRE)-- [Vertex Pharmaceuticals Incorporated](#) (Nasdaq: VRTX) and Parion Sciences today announced that the companies will collaborate to develop investigational epithelial sodium channel (ENaC) inhibitors for the potential treatment of cystic fibrosis (CF) and other pulmonary diseases. Under the agreement, Vertex gains worldwide development and commercial rights to Parion's investigational ENaC inhibitors, including P-1037 and P-1055, for CF and other pulmonary diseases. P-1037 is currently being evaluated in an exploratory Phase 2a study in people with CF, regardless of genotype. Vertex and Parion plan to begin an additional Phase 2a study that adds P-1037 to treatment with the investigational combination of lumacaftor and ivacaftor for people with CF who have two copies of the F508del mutation. Parion will receive an \$80 million up-front payment from Vertex with the potential to receive additional development and regulatory milestone payments and tiered royalties related to P-1037 and P-1055 in CF and other pulmonary diseases.

"This collaboration with Parion complements our ongoing work in CF and supports our two key goals in this disease - to increase the number of people eligible for new CF medicines and to enhance the benefit of treatment," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "The goal of these planned studies of P-1037 is to determine whether ENaC inhibition can improve lung function in people with CF, including those with mutations unlikely to respond to treatment with the investigational combination of lumacaftor and ivacaftor. Beyond CF, this agreement helps to diversify our pipeline by providing opportunities to evaluate P-1037 as part of Phase 2a studies in multiple other diseases that impact the lungs."

"ENaC inhibition represents a promising opportunity to potentially enhance the benefit of existing treatments for people with CF, and we have worked diligently to bring P-1037 from our research labs and into Phase 2 development," said Paul Boucher, President and Chief Executive Officer of Parion. "Vertex is the leader in developing new medicines that treat the underlying cause of CF. We are pleased to enter into this collaboration to unify the scientific expertise of both companies to advance P-1037 in CF and other pulmonary diseases."

Cystic fibrosis is a rare genetic disease that is caused by defective or missing cystic fibrosis transmembrane conductance regulatory (CFTR) proteins resulting from mutations in the *CFTR* gene. The defective or missing CFTR proteins result in poor flow of salt and water into and out of the cell in a number of organs, including the lungs. The defective CFTR protein that causes CF is also believed to increase the function of ENaC, which may contribute to dehydration of the cell surface of lungs in people with CF. In CF, the poor flow of salt and water in cells prevents cilia on the surface of the cell from beating properly, which leads to a buildup of abnormally thick, sticky mucus that can cause chronic lung infections and progressive lung damage, eventually leading to death.

### **About the Collaboration**

Under the terms of the collaboration, Vertex obtained worldwide development and commercial rights to Parion's lead investigational ENaC inhibitors, including P-1037 and P-1055, for the potential treatment of CF and all other pulmonary diseases. Parion received an \$80 million up-front payment and has the potential to receive up to an additional \$490 million in development and regulatory milestone payments for development of ENaC inhibitors in CF, including \$360 million related to global filing and approval milestones. Parion has the potential to receive up to \$370 million in additional development and regulatory milestones for P-1037 and P-1055 in non-CF pulmonary indications. Parion may also receive an additional \$230 million in development and regulatory milestones should Vertex elect to develop an additional ENaC inhibitor from Parion's research program. Parion will receive tiered royalties on potential sales of P-1037 and P-1055 in CF and other pulmonary diseases that range from the low double digits to mid-teens as a percentage of sales. Vertex will lead future development activities for P-1037 and P-1055 in CF and other pulmonary diseases.

Parion recently initiated an exploratory Phase 2a study of inhaled P-1037 in approximately 120 people with CF. The study is enrolling people with a confirmed diagnosis of CF and any *CFTR* mutation, including those who have mutations not expected to

respond to ivacaftor alone. The study is evaluating the use of P-1037, with and without hypertonic saline, compared to placebo. Patients in the study will continue to receive standard CF medicines.

Preclinical evaluation in human bronchial epithelial cells from people with CF who have two copies of the F508del mutation showed that the addition of investigational P-1037 to the investigational combination of lumacaftor and ivacaftor resulted in an additional increase in both airway surface liquid and cilia beat frequency compared to baseline and to the use of P-1037 or lumacaftor/ivacaftor alone. Improvements in airway surface liquid height and cilia beat frequency are direct measures of increased hydration of the cell surface. This *in vitro* observation suggests that the addition of P-1037 to the investigational combination of lumacaftor and ivacaftor could enable enhanced function of the cell's cilia to clear mucus from the cell surface, potentially resulting in improved lung function. Based on these preclinical results, Vertex is preparing to conduct a Phase 2a study to evaluate whether the addition of P-1037 to the combination of lumacaftor and ivacaftor in people with CF who have two copies of the F508del mutation provides additional benefit as compared to the combination of lumacaftor and ivacaftor alone. This Phase 2a study is expected to begin in early 2016.

Beyond CF, Vertex and Parion plan to conduct additional Phase 2a studies of P-1037 across multiple other pulmonary diseases where the disease results in defective hydration of the cell surfaces in the lung. These diseases include Chronic Obstructive Pulmonary Disease (COPD), Non-CF Bronchiectasis (NCFB) and Primary Ciliary Dyskinesia (PCD). Parion will conduct Phase 2a development in these diseases and retains an option to participate in co-development and co-commercialization activities related to one of these non-CF pulmonary diseases.

Vertex continues to expect 2015 non-GAAP Research and Development and Sales, General and Administrative expenses to be in the range of \$1.05 to \$1.10 billion.

### **About Cystic Fibrosis**

CF is a rare, life-threatening genetic disease affecting approximately 75,000 people in North America, Europe and Australia. Children must inherit two defective *CFTR* genes — one from each parent — to have CF. There are more than 1,900 known mutations in the *CFTR* gene. Some of these mutations, which can be determined by a genetic, or genotyping, test, lead to CF by creating non-working or too few CFTR proteins at the cell surface. The defective or missing CFTR protein results in poor flow of salt and water into and out of the cell in a number of organs, including the lungs. This leads to the buildup of abnormally thick, sticky mucus that can cause chronic lung infections and progressive lung damage. The defective CFTR protein that causes CF is also believed to increase the function of ENaC, which may contribute to dehydration of the cell surface of lungs in people with CF. Today, the median predicted age of survival for a person with CF is between 34 and 47 years, but the median age of death remains in the mid-20s.

### **About Parion Sciences**

Parion Sciences is a development stage biopharmaceutical company dedicated to research, development and commercialization of treatments to improve and extend the lives of patients with innate mucosal surface defense deficiencies of the lung or eye. Parion has a diverse pipeline of pre-clinical and clinical candidates for the treatment of these diseases via distinctive mechanisms of action and approaches. Parion is at the forefront of ENaC development and leverages its scientific expertise in epithelial biology to expand the company's platforms and novel chemical compounds into new potential indications to treat mucosal defects. Parion has received grant funding from the National Institutes of Health and continues to have a long-standing and valued relationship with Cystic Fibrosis Foundation Therapeutics, Inc. For more information, please see our website at [www.Parion.com](http://www.Parion.com).

### **About Vertex**

Vertex is a global biotechnology company that aims to discover, develop and commercialize innovative medicines so people with serious diseases can lead better lives. In addition to our clinical development programs focused on cystic fibrosis, Vertex has more than a dozen ongoing research programs aimed at other serious and life-threatening diseases.

Founded in 1989 in Cambridge, Mass., Vertex today has research and development sites and commercial offices in the United States, Europe, Canada and Australia. For five years in a row, *Science* magazine has named Vertex one of its Top Employers in the life sciences. For additional information and the latest updates from the company, please visit [www.vrtx.com](http://www.vrtx.com).

### **Special Note Regarding Forward-looking Statements**

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, Dr. Chodakewitz's statements in the second paragraph of the press release, Mr. Boucher's statements in the third paragraph of the press release, information regarding Vertex's 2015 non-GAAP operating expenses and the information provided regarding the development timeframe of P-1037. 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 factors that could cause actual events or results to differ materially from those indicated by such forward-looking statements. Those risks and uncertainties include, among other things, that the company's expectations regarding its 2015 non-GAAP operating expenses may be incorrect (including because one or more of the company's assumptions underlying its expense expectations may not be realized) or that data may not support further development of the compounds subject to the collaboration due to safety, efficacy or other reasons, and other risks listed under Risk Factors in Vertex's annual report and quarterly reports filed with the Securities and Exchange Commission and available through the company's website at [www.vrtx.com](http://www.vrtx.com). Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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