Imbria Presents Positive Clinical Data for Ninerafaxstat from IMPROVE-DiCE at the European Society of Cardiology Congress 2022

Treatment with ninerafaxstat significantly improved cardiac energetics, steatosis and left ventricular (LV) diastolic function in patients with type-2 diabetes mellitus (T2DM) and obesity

BOSTON, Mass., August 26, 2022 – Imbria Pharmaceuticals, Inc., a clinical stage, cardiometabolic company developing novel therapies designed to enhance cellular energetics, today announced positive clinical results from the Phase 2, IMPROVE-DiCE trial demonstrating that ninerafaxstat in patients with T2DM and obesity normalized cardiac energetic, reduced cardiac steatosis and improved diastolic function. The results were presented at the European Society of Cardiology (ESC) congress in Barcelona, Spain during the moderated poster session titled "Cardiovascular Magnetic Resonance (CMR) in the evaluation of cardiomyopathies and heart failure."

"These findings from the IMPROVE-DiCE trial unlock the potential for clinical benefit in high unmet need indications associated with impaired cardiac energetics and function including non-obstructive hypertrophic cardiomyopathy and heart failure," said Oliver Rider, MRCP(UK), DPhil (Oxon), Associate Professor of Cardiovascular Medicine, University of Oxford. "We look forward to initiating and exploring the impact of ninerafaxstat in patients with heart failure with preserved ejection fraction (HFpEF) and T2DM in Part 2 of the IMPROVE-DiCE trial."

Key findings from the trial include:

- Short-term treatment with ninerafaxstat resulted in a statistically significant (P<0.01) increase in resting cardiac phosphocreatine (PCr)/adenosine triphosphate (ATP) by ~32% (median pre-treatment PCr/ATP = 1.6, post-treatment PCr/ATP = 2.1), consistent with an improvement in cardiac energy reserves and meeting the trial's primary objective
- Cardiac steatosis leads to organ dysfunction through lipotoxicity and has been linked to impaired LV diastolic function. Ninerafaxstat significantly reduced cardiac steatosis by ~34% (P<0.05), a prominent abnormality present in patients with T2DM and in HFpEF
- The energetic and metabolic effects of ninerafaxstat translated into improved cardiac diastolic function with a significant increase in normalized LV filling rate by cardiac MR imaging (P<0.05)

"With nearly 64 million people worldwide living with heart failure, a leading cause of disability and death globally, and no current treatments specifically aimed at symptoms and quality of life, there is a critical need for patient-centric innovative solutions," said Jai Patel, MRCP(UK), chief medical officer at Imbria. "Modulation of energy metabolism represents a promising and unique therapeutic strategy for patients with cardiometabolic disorders characterized by cardiac energy deficit. By enhancing cardiac reserve capacity, patient symptoms, functional capacity, and quality of life may be significantly improved. The findings provide validation of the mechanism of action of ninerafaxstat and support further investigation of its treatment potential in heart failure states associated with T2DM."

A copy of the poster will be available in the "Media Center" section of the Imbria website at www.imbria.com.

About cardiometabolic disorders

Cardiometabolic disorders are characterized by a cluster of interrelated metabolic abnormalities that are risk factors for both cardiovascular disease and T2DM. Hallmark features include obesity (particularly abdominal), insulin resistance, dyslipidemia, and hypertension. The prevalence of cardiometabolic

disorders has reached epidemic proportions: obesity affects ~40% of all American adults, 37 million adults have diabetes, and a further 96 million have prediabetes.

Patho-physiologically, the metabolic drivers of cardiometabolic disease are thought to derive from the intersection of abnormal adiposity (abnormal mass, function, and distribution) and dysglycemia (referring to T2DM or prediabetes). T2DM and obesity both lead to profound alterations in cardiac metabolism and are strongly associated with the development of heart failure. These changes include a loss of metabolic flexibility that characterizes the healthy heart, with an overreliance on fatty acids for fuel and a reduced ability of the heart to metabolize glucose, its most efficient energy substrate, depleting cardiac energetics. Impaired cardiac energy substrate metabolism and energetics are implicated in the development of symptomatic heart failure.

About ninerafaxstat (formerly IMB-1018972)
Our lead product candidate, ninerafaxstat, is a novel, investigational cardiac mitotrope in development for a range of cardiac diseases characterized by a fundamental imbalance between energy consumption and energy supply in the heart resulting in cardiac energy deficiency. As a partial fatty acid oxidation (pFOX) inhibitor, ninerafaxstat is designed to shift cardiac substrate selection towards glucose oxidation which generates more energy in the form of ATP per unit of oxygen consumed than any other carbon substrate, increasing cardiac metabolic efficiency to support better cardiac mechanical efficiency and function. Ninerafaxstat, is currently in Phase 2 clinical development in three indications: non-obstructive hypertrophic cardiomyopathy, stable angina, and HFpEF.

About IMPROVE-DiCE
IMPROVE-DiCE is a two-part, translational, open-label Phase 2 trial conducted at the University of Oxford evaluating the safety, tolerability and pharmacodynamic effects of ninerafaxstat on cardiac energetics, metabolism, and function in patients with T2DM and obesity (Part 1) and HFpEF (Part 2). The primary outcome of Part 1 of the trial is based on the change in the cardiac PCr/ATP ratio, a validated non-invasive measure of cardiac energy status, determined by ^{31}P-magnetic resonance (MR) spectroscopy before and after eight weeks of treatment with ninerafaxstat (200 mg orally twice daily). IMPROVE-DiCE is the first clinical trial utilizing multi-nuclear and state-of-the-art hyperpolarized MR spectroscopy to quantify the metabolic and energetic responses to an investigational metabolic modulator in cardiovascular disease.

About Imbria
Imbria is a privately held, clinical stage company developing novel therapies for patients with life-altering cardiometabolic disorders. Our clinical stage pipeline is focused on restoring or improving the cell's ability to produce energy in disorders where energetic impairment is a fundamental contributor, including cardiovascular disease and specific inborn errors of metabolism. The lead product candidate, ninerafaxstat, is currently in Phase 2 clinical development in three indications: non-obstructive hypertrophic cardiomyopathy, stable angina, and HFpEF. The pipeline also includes IMB-203, designed to address the energy deficiency in patients with rare inborn errors of mitochondrial metabolism. For additional information, please visit www.imbria.com.

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