Media Release
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Phase 2 data of aprocitentan, Idorsia's dual endothelin receptor antagonist, presented at ESC 2019

- Phase 2 dose-finding study demonstrated the blood pressure lowering effect of aprocitentan
- A global Phase 3 study "PRECISION" in patients whose blood pressure remains uncontrolled despite receiving at least three antihypertensive medications is ongoing
- As part of the Phase 3 program, the company is initiating an additional study "INSPIRE-CKD" for the treatment of patients with uncontrolled blood pressure and chronic kidney disease stage 3 or 4

Allschwil, Switzerland – August 31, 2019
Idorsia Ltd (SIX: IDIA) today announced that the results of the Phase 2 study with aprocitentan were presented at the European Society of Cardiology (ESC) 2019 Congress in Paris, France.

Hypertension (high blood pressure) is one of the most common cardiovascular risks, and its prevalence continues to rise. According to a recent study, there are more than 1 billion people living with hypertension worldwide. Left uncontrolled, hypertension can lead to life-threatening conditions such as stroke, ischemic heart disease, or kidney disease.

Aprocitentan is an orally active dual endothelin receptor antagonist (ERA). Aprocitentan at doses of 12.5 and 25 mg is currently being investigated for the treatment of patients whose blood pressure is uncontrolled despite receiving triple antihypertensive medications (categorized as resistant hypertension) in a global Phase 3 registration study, "PRECISION". The doses were selected based on a Phase 2 dose-finding study which evaluated the efficacy, safety and tolerability of a once-a-day oral regimen of four dose levels of aprocitentan in patients with essential hypertension. Results of this Phase 2 study were presented at ESC Congress 2019.

Phase 2 study in adults with essential hypertension presented at ESC

Parisa Danaietash, PhD from Idorsia gave an oral presentation entitled *"Efficacy and safety of various doses of the new dual endothelin receptor antagonist aprocitentan in the treatment of hypertension"*.

Eligible patients with hypertension (mean sitting systolic/diastolic blood pressure 149.7/97.6 mmHg) received aprocitentan 5, 10, 25 or 50 mg, matching placebo or lisinopril 20 mg as a positive control, once daily for 8 weeks using a randomized, double-blind, parallel-group study design. Blood pressure was measured at baseline and weeks 2, 4, 8, and 10 (withdrawal) with an automated office blood pressure (AOBP) device, which recorded and averaged multiple blood pressure readings while the patient was unattended and resting quietly.

A total of 490 eligible patients were randomized, with 430 patients successfully completing the double-blind treatment period. Decreases in sitting systolic/diastolic AOBP, from baseline to week 8 were 10.3/6.3, 15.0/9.9, 18.5/12.0 and 15.1/10.0 mmHg for aprocitentan 5, 10, 25, and 50 mg, respectively vs. 7.7/4.9 mmHg for placebo and 12.8/8.4 mmHg for lisinopril. No changes in heart rate or body weight were observed for any dose of aprocitentan.

Estimated increases in plasma volume were 3.0%, 5.1%, 6.9%, and 9.5% for aprocitentan 5, 10, 25, and 50 mg, respectively, vs. 1.6% for lisinopril and a decrease of 0.3% for placebo. All these values are within the physiological variation range, i.e. below 10%. There was an expected dose-related decrease from baseline in the hemoglobin concentration in the aprocitentan groups (ranging from 1.3 to 6.7 g/L), versus increases of 2.2 and 0.1 g/L in the placebo and lisinopril groups, respectively.

The overall incidence of adverse events observed in the aprocitentan groups (ranging from 22.0% to 40.2%) was similar to that seen in the placebo group (36.6%). Overall, the most common events were hypertension, headache, and nasopharyngitis.

This study formed the basis for the ongoing Phase 3 investigation of aprocitentan as a potential treatment for patients whose blood pressure is uncontrolled despite receiving triple antihypertensive medications, conducted in collaboration with Janssen Biotech, Inc.

Guy Braunstein, MD and Head of Global Clinical Development, commented:
"The results of the Phase 2 study show a dose-dependent blood pressure lowering effect of aprocitentan and led to the selection of two doses, 12.5 and 25 mg, for further development. In our ongoing Phase 3 study, we investigate the effect of aprocitentan in patients with uncontrolled hypertension despite standardized triple background therapy. If successful, aprocitentan may become a new treatment for patients whose blood pressure is difficult to control with a combination of current medications, which represents an important medical need. This is very exciting since no antihypertensive medication working via a new pathway, and no ERA has reached this market within the last 30 years."

About INSPIRE-CKD

Idorsia is initiating an additional blinded, randomized, placebo-controlled, Phase 3 study with aprocitentan in patients with chronic kidney disease (CKD) stage 3 or 4 whose blood pressure remains uncontrolled despite the use of at least two antihypertensive medications. The primary objective of this study is to demonstrate the safety and blood pressure lowering effect of 4-weeks' treatment with aprocitentan when added to background antihypertensive therapy. The study is expected to commence enrolment in the first quarter of 2020, will enroll about 200 patients in approximately 100 sites from around 15 countries, and will last for about two years.

Notes to the editor

About PRECISION

In June 2018, Idorsia initiated PRECISION, a multi-center, double-blinded, placebo-controlled, randomized, parallel-group, Phase 3 study to demonstrate the antihypertensive effect of aprocitentan when added to standard of care in patients with resistant hypertension. Idorsia, in consultation with regulatory agencies, has designed a single study which will efficiently address both the short-term efficacy of aprocitentan and the durability of its effects in long-term treatment.

Patients with a history of resistant hypertension will undergo a thorough screening and run-in period. This will confirm the diagnosis of resistant hypertension by excluding pseudo or apparent resistant hypertension. During the screening period, the patient's background antihypertensive therapies will be transitioned to a standardized triple combination of a calcium channel blocker (amlodipine), an angiotensin receptor blocker (valsartan), and a diuretic (hydrochlorothiazide).

Patients with true resistant hypertension will then be randomized to receive aprocitentan 12.5 mg, 25 mg, or placebo once-daily. The study consists of 3 sequential treatment periods. The first is a double-bind treatment period designed to demonstrate the effect of aprocitentan on blood pressure after 4 weeks, compared to placebo. Patients then enter a treatment period where they receive aprocitentan 25 mg for 32 weeks. This is followed by a randomized double-blind withdrawal treatment period where patients will remain either on aprocitentan 25 mg or switch to placebo for 12 weeks. The latter treatment period is designed to demonstrate the durability of the blood pressure lowering effect of aprocitentan. Patients will then enter a 30-day safety follow-up period.

From the initial screened patient population, at least 600 patients will be randomized and at least 300 patients are expected to complete the study. The study will be conducted in approximately 100 sites in around 20 countries.

About the collaboration Agreement with Janssen Biotech, Inc.
In December 2017, Janssen Biotech, Inc. entered into a collaboration agreement with Idorsia to jointly develop and commercialize aprocitentan and any of its derivative compounds or products. Both parties have joint development rights over aprocitentan. Idorsia will oversee the Phase 3 development and regulatory submission. The costs will be shared equally between both partners. Janssen Biotech, Inc. will oversee the Phase 3 development and submission for any additional indications.

About Idorsia
Idorsia Ltd is reaching out for more - We have more ideas, we see more opportunities and we want to help more patients. In order to achieve this, we will develop Idorsia into one of Europe's leading biopharmaceutical companies, with a strong scientific core.

Headquartered in Switzerland - a biotech-hub of Europe - Idorsia is specialized in the discovery and development of small molecules, to transform the horizon of therapeutic options. Idorsia has a broad portfolio of innovative drugs in the pipeline, an experienced team, a fully-functional research center, and a strong balance sheet – the ideal constellation to bringing R&D efforts to business success.

Idorsia was listed on the SIX Swiss Exchange (ticker symbol: IDIA) in June 2017 and has over 750 highly qualified specialists dedicated to realizing our ambitious targets.

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