Idorsia announces collaboration with Janssen Biotech on aprocitentan (ACT-132577)

- Idorsia to receive milestone payment of USD 230 million
- Idorsia and Janssen Biotech to share costs of Phase 3 development equally
- Idorsia entitled to royalty payments on potential future net sales

Allschwil, Switzerland – 4 December 2017 – Idorsia Ltd (SIX:IDIA) announced today that Janssen Biotech, Inc. (Janssen), one of the Janssen Pharmaceutical Companies of Johnson & Johnson, has exercised its option to enter into a collaboration agreement with Idorsia to jointly develop and commercialize aprocitentan and any of its derivative compounds or products. Headline results from the phase 2 study were released on 22 May 2017.

Jean-Paul Clozel, CEO of Idorsia, commented: “I am delighted by Janssen’s decision to collaborate on the development of aprocitentan, which is a strong endorsement for our product. Together we can accelerate the next steps of development and bring this compound to patients in need of new treatment options as quickly as possible.”

Milestone: Following Janssen’s opt-in decision, Idorsia will receive a one-time milestone payment of USD 230 million that will be reflected in its fourth quarter 2017 financial results.

André Muller, Chief Financial Officer of Idorsia, explained: “The one-time milestone payment will be recognized in two parts: about 160 million US dollars are expected to be recognized immediately as contract revenue in the fourth quarter 2017, while the remainder of the milestone payment is expected to be recognized as contract revenue over the next three and a half years. Hence, combining this revenue with our unchanged financial guidance on non-GAAP operating expenses between 160 and 170 million Swiss francs, Idorsia expects to report a net loss close to breakeven, barring unforeseen events.”

Development: Both parties have joint development rights over aprocitentan. Idorsia will oversee the Phase 3 development and regulatory submission for the treatment of patients with hypertension that is not controlled by at least three therapies (called resistant hypertension in the medical community). The costs will be shared equally between both partners. Janssen will oversee the Phase 3 development and submission for any additional indications.

Commercialization: Janssen will have the sole worldwide commercialization rights. Idorsia is entitled to royalty payments on any future net sales generated. Royalty payments will amount to 20% of annual net sales up to USD 500 million, 30% of annual net sales between USD 500 million and USD 2 billion, 35% of annual net sales above USD 2 billion.

Martine Clozel, Chief Scientific Officer of Idorsia, said: “With this decision, Janssen has recognized the potential of aprocitentan, the latest product from a research effort that was initiated nearly 30 years ago and resulted in a broad understanding of the endothelin system...”
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and two endothelin receptor antagonists on the market. Aprocitentan can be envisioned to have many other potential applications, in addition to hypertension. This makes the collaboration with Janssen even more meaningful for us."

**About aprocitentan in development for resistant hypertension management (RHM)**

Aprocitentan is an orally active dual endothelin receptor antagonist that is being investigated for patients whose hypertension is uncontrolled despite the use of at least three antihypertensive drugs (called resistant hypertension in the medical community). Resistant hypertension is defined as persisting high systemic blood pressure (i.e., failure to lower blood pressure to a pre-defined threshold) despite concurrent administration of at least three antihypertensive therapies of different pharmacological classes at maximal or optimal doses, including a diuretic. Resistant hypertension is associated with a higher risk of cardiovascular disease. Patients with resistant hypertension are also more likely to have a medical history of chronic kidney disease and diabetes mellitus, amplifying their vulnerability and the complexity of treatment.

A Phase 2 study that evaluated the efficacy, safety and tolerability of aprocitentan in patients with essential hypertension to identify the optimal dose for further studies was completed in May 2017. Based on the positive dose-finding results and the feedback from health authorities, Idorsia is currently finalizing the design of a Phase 3 study. It will consist of a specifically designed study evaluating the initial and long-term effect of aprocitentan on systolic and diastolic blood pressure in patients requiring resistant hypertension management (RHM). The study is expected to start in 2018. If successful, the study will provide the basis for registration of the product.

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**Notes to the editor**

**About the dose-finding study with aprocitentan**

In May 2017, the clinical development team completed a multi-center, double-blind, double-dummy, randomized, placebo-controlled with an active-reference arm, parallel group, dose-finding study with aprocitentan, an orally active dual endothelin receptor antagonist, in patients with essential hypertension. The study evaluated the efficacy, safety and tolerability of a once-a-day oral regimen of 4 dose levels of aprocitentan (5, 10, 25, and 50mg) to identify the optimal doses for further studies.

In this study 490 patients were randomized to receive either aprocitentan 5, 10, 25, 50 mg, placebo, or lisinopril 20 mg once daily. After 8 weeks of treatment the mean reduction from baseline in diastolic blood pressure - as measured at trough with a novel automated office blood pressure device - ranged between 6.3 and 12.0 mmHg in a statistically significant dose-dependent manner for the aprocitentan groups versus a decrease of 4.9 mmHg in the placebo group and a decrease of 8.4 mmHg in the lisinopril group (in the per-protocol population comprised of 410 patients).

Systolic blood pressure reductions ranged from 10.3 to 18.5 mmHg in a statistically significant dose-dependent manner in the aprocitentan groups and were 7.7 and 12.8 mmHg in the placebo and lisinopril groups, respectively.

These findings were confirmed in all randomized patients (Intent-to-Treat principle) and by 24 hours Ambulatory Blood Pressure Monitoring.

The safety population included 327 patients in the aprocitentan groups, 82 patients in the placebo group and 81 in the lisinopril group. Aprocitentan was well tolerated across all four doses in this patient population. Discontinuation from study treatment due to an adverse event ranged between 1.2% and 3.7% for the aprocitentan groups versus 6.1% in the placebo group and 3.7% in the lisinopril group. The overall frequency of
adverse events was similar to those observed in the placebo group. In this study, there were two cases of increased liver enzymes above three times the upper limit of the normal range, one in the placebo and one in the aprocitentan 5 mg group. Four cases of peripheral edema were observed, two in the aprocitentan 25 mg group and two in the aprocitentan 50 mg group. Mean body weight remained unchanged from baseline in the aprocitentan 5, 10 mg groups, increased by 0.4 kg in the aprocitentan 25 and 50 mg groups, and by 0.3 kg in the placebo group and decreased by 0.3 kg on lisinopril. 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.

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 intend to develop Idorsia into Europe's leading biopharmaceutical company, with a strong scientific core.

Headquartered in Switzerland - a European biotech hub - 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 SIX Swiss Exchange (ticker symbol: IDIA) in June 2017 and has over 600 highly qualified specialists dedicated to realizing our ambitious targets.

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