Media Release
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Ad hoc announcement pursuant to Art. 53 LR

Idorsia announces the results of MODIFY, a Phase 3 study of lucerastat in Fabry disease

Allschwil, Switzerland – October 11, 2021
Idorsia Ltd (SIX: IDIA) today announced that MODIFY, the Phase 3 study to investigate the effect of lucerastat, as an oral substrate reduction therapy for the treatment of adult patients with Fabry disease, did not meet the primary endpoint.

Guy Braunstein, MD and Head of Global Clinical Development at Idorsia, commented:
"I'm very proud of everyone involved with MODIFY for delivering a very high-quality study, one of the largest in Fabry disease. Lucerastat was well tolerated and biochemically it did exactly what we were expecting; as previously seen, in this study we saw a substantial and consistent reduction of plasma Gb3, confirming the pharmacological activity of lucerastat. Despite this biological effect, no reduction in neuropathic pain was observed after six months of treatment, using the patient reported outcome tool."

Guy Braunstein, added:
"In MODIFY, many parameters have been collected and data are still being analyzed. In addition, most patients chose to continue in the open-label extension study and in a few weeks, we will see more results that will inform our decision on the future of lucerastat."

Jean-Paul Clozel, MD and Chief Executive Officer of Idorsia, commented:
"Taking into account the quality of the study, the volume of data we have collected, and some observations made in the six-month double-blind placebo-controlled treatment period, we need to wait for the results of the interim analysis of the open-label phase before making a decision. I expect to be in a position to share our future direction before the end of year."

Notes to the editor

About the MODIFY study (NCT03425539)
MODIFY was a multicenter, double-blind, randomized, placebo-controlled, parallel-group study to determine the efficacy and safety of lucerastat as an oral monotherapy in adult patients with Fabry disease. MODIFY determined the effect of study treatment on neuropathic pain during 6 months of treatment, measured with Idorsia's validated Fabry disease pain instrument. 118 patients were randomized in a 2:1 ratio to either lucerastat or placebo. At the end of the double-blind period, 107 patients entered into an ongoing open label extension study (NCT03737214), which is investigating the long-term safety and tolerability of lucerastat oral therapy and to further evaluate its clinical efficacy on renal and cardiac function, in adult patients with Fabry disease over a period of up to a further 48 months.

About Fabry disease

Fabry disease is a rare, genetic, lysosomal storage disorder that results in reduced or absent α-galactosidase A (alpha-GalA) an enzyme that normally breaks down a fatty product known as globotriaosylceramide (Gb3) in the cells of the body. Over time, this results in an accumulation of Gb3 deposits throughout the body, leading to progressive pathophysiology in the nervous system, such as neuropathic pain (pain primarily in the hands and feet), the gastrointestinal system, and the cardiovascular system, as well as in organs, including the kidneys, skin, ears, eyes, and lung. Symptoms of Fabry disease affect a patient's life expectancy and their quality of life. There is an unmet need for a well-tolerated, disease-modifying, oral treatment that addresses refractory symptoms and can be used regardless of *GLA* mutation or previous treatment.

Lucerastat in Fabry disease

Lucerastat, a small molecule glucosylceramide synthase inhibitor, is in development as a novel, substrate reduction therapy for Fabry disease. Preclinical studies showed that lucerastat is a soluble, bioavailable inhibitor of glucosylceramide synthase that reduces the accumulation of α-galactosidase A substrates in tissues affected by Fabry disease, including kidneys, liver, and dorsal root ganglia. In clinical pharmacology studies, lucerastat had reproducible pharmacokinetics, characterized by rapid absorption, quick elimination, and no evidence for saturation of absorption or elimination mechanisms. Across Phase 1 studies, lucerastat doses up to 4000 mg were well tolerated and the safety profile was not affected by concomitant treatments.

The safety, tolerability, pharmacodynamics, and pharmacokinetics of oral lucerastat were evaluated in an exploratory study in adult patients with Fabry disease. In this single-center, open-label, randomized study, 10 patients with Fabry disease were randomized to lucerastat for 12 weeks on top of ERT and 4 to ERT only. A rapid decrease in plasma Gb3, a marker of Fabry disease, and its precursors was observed, demonstrating that lucerastat 1000 mg b.i.d. inhibits glucosylceramide synthase and provides alpha-GalA substrate reduction with a fast onset in adult patients with Fabry disease receiving ERT.

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 a leading biopharmaceutical company, with a strong scientific core.

Headquartered near Basel, Switzerland – a European biotech-hub – Idorsia is specialized in the discovery, development, and commercialization of small molecules to transform the horizon of therapeutic options. Idorsia has a broad portfolio of innovative drugs in the pipeline, an experienced team of professionals covering all disciplines from bench to bedside, state-of-the-art facilities, and a strong balance sheet – the ideal constellation to translate R&D efforts into business success.

Idorsia was listed on the SIX Swiss Exchange (ticker symbol: IDIA) in June 2017 and has over 1000 highly qualified specialists dedicated to realizing our ambitious targets.

For further information, please contact

Andrew C. Weiss
Senior Vice President, Head of Investor Relations & Corporate Communications
Idorsia Pharmaceuticals Ltd, Hegenheimermattweg 91, CH-4123 Allschwil
+41 58 844 10 10
investor.relations@idorsia.com
media.relations@idorsia.com
www.idorsia.com

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