



Media Release

June 18, 2018

Idorsia is initiating REACT – Phase 3 registration study with clazosentan

- REACT assesses clazosentan for the prevention of clinical deterioration due to vasospasm-related delayed cerebral ischemia following subarachnoid hemorrhage
- Japanese registration program with clazosentan is on-track to deliver results by year-end
- Idorsia establishes Idorsia Pharmaceuticals Japan
- Idorsia to host an investor webcast to discuss the Phase 3 program today at 14:00hrs CEST

Allschwil, Switzerland – June 18, 2018

Idorsia Ltd (SIX: IDIA) today announced that it is initiating a Phase 3 study, REACT, to investigate the efficacy and safety of clazosentan for the prevention of clinical deterioration due to vasospasm-related delayed cerebral ischemia in patients following an aneurysmal subarachnoid hemorrhage.

About aneurysmal subarachnoid hemorrhage and cerebral vasospasm

Aneurysmal subarachnoid hemorrhage (aSAH) is a sudden life-threatening bleeding occurring in the subarachnoid space. It is caused by the rupture of an aneurysm – a weak, bulging spot on the wall of a cerebral artery. Emergency surgical repair (endovascular coiling or microsurgical clipping) is required to stop the hemorrhage.

The bleeding and the release of a vasoconstrictor, endothelin, by the neighboring vascular endothelium, causes many patients to experience vasospasm (constriction of arteries in the brain). This diminishes blood flow to the brain and as a consequence, about one third of patients experience worsening of their neurological condition. Patients with thick and diffuse blot clots are at a significantly higher risk of experiencing cerebral vasospasm. Today, patients with vasospasm are typically treated with hemodynamic therapy, or more invasive neurovascular intervention such as balloon angioplasty or intra-arterial administration of vasodilators.

E. Francois Aldrich, M.B., Ch.B., M. Med., F.C.S. Professor of Neurosurgery, Chief of Cerebrovascular Surgery Neurosurgery, University of Maryland commented:

"It is very frustrating to see our patients survive the initial trauma of the brain hemorrhage and seemingly make a recovery, only for the vasospasm to take hold and cause significant long-term damage. Current 'rescue' therapy for cerebral vasospasm involves invasive neurovascular intervention that often needs to be repeated multiple times over the course of several days, needs to be performed by highly-trained specialists in an intensive care setting, and is itself associated with medical risks. Clazosentan may avoid or reduce this considerable ordeal for the patient, and the healthcare team."

About clazosentan

Several studies have built our understanding of clazosentan, an intravenous endothelin receptor antagonist, regarding its impact on preventing or reversing cerebral vasospasm. These studies suggest that clazosentan has the potential to prevent vasospasm-related delayed cerebral ischemia and to decrease the need for invasive neurovascular intervention.

Martine Clozel, MD and Chief Scientific Officer, commented:

“We know that endothelin plays a major role in cerebral vasospasm after aSAH. Clazosentan is an endothelin receptor antagonist which was optimized for its potential to be active in the brain and adapted to intensive care administration. Clinical studies with clazosentan have built a deep understanding of its role in preventing or reversing cerebral vasospasm. I am confident that we can now show that clazosentan can prevent vasospasm-related clinical deterioration in high risk patients.”

About the REACT study

REACT is a prospective, multi-center, double-blind, randomized, placebo-controlled, parallel-group, Phase 3 study to assess the efficacy and safety of clazosentan in preventing clinical deterioration due to vasospasm-related delayed cerebral ischemia, in adult patients with aSAH. Approximately 400 patients, regardless of whether their hemorrhage has been treated with surgical clipping or endovascular coiling are expected to be enrolled. Patients will be enrolled from 100 trial sites across 15 countries who will be randomized to either 15 mg/hr clazosentan or placebo for a treatment period of up to 14 days. The study is expected to run for around 27 months.

REACT will enroll aSAH patients identified as being at high-risk of developing delayed ischemic neurological deficit because of high volume of their hemorrhage, as assessed by CT scan on hospital admission. Patients experiencing asymptomatic moderate to severe cerebral vasospasm within 14 days of securing the aneurysm may also be included.

Guy Braunstein, MD and Head of Global Clinical Development, commented:

“REACT builds on the learnings from previous clinical studies with clazosentan, which have served to identify the optimal treatment dose and the characteristics of the patient that are most likely to benefit from treatment. Those studies have also established an extensive safety profile with over 1’800 patients treated. Compared to current acute intra-arterial intervention that only targets vasospasm in major blood vessels, clazosentan reaches the smaller blood vessels. It therefore has a potential to an effect across the whole brain circulation.”

About the registration program in Japan

A Phase 2 study in Japanese and Korean patients showed that 10 mg/hr clazosentan significantly reduced vasospasm, and vasospasm-related morbidity and mortality events. On that basis, a registration program was initiated with clazosentan in Japan in May 2016. Aneurysmal subarachnoid hemorrhage is a significant problem in Japan with a prevalence around twice as high as in the rest of the world.

The program consists of two prospective, multicenter, double-blind, randomized, placebo-controlled studies to assess the efficacy and safety of clazosentan in reducing vasospasm, and vasospasm-related morbidity and mortality events in adult patients with aneurysmal subarachnoid hemorrhage. Patients are randomized to either 10 mg/hr clazosentan or placebo for up to a cumulative maximum of 15 days following the onset of aSAH. The two studies follow the same study design, with one enrolling patients whose aSAH was treated by surgical clipping and the other enrolling patients who were treated for aSAH by endovascular coiling. Both studies are close to full recruitment with 160 patients in each study and results are expected by the end of 2018.

About Idorsia Pharmaceuticals Japan

Idorsia Pharmaceuticals Japan was established under leadership of Dr Satoshi Tanaka in 2018 in preparation for the potential launch of Idorsia’s first product, clazosentan for the prevention of cerebral vasospasm following aneurysmal subarachnoid hemorrhage. The organization, led by Satoshi and his professional team, also conducts clinical development of Idorsia’s innovative and promising

compounds for the specific needs of the Japanese Health Authority and has a central role for East Asian cross-border clinical development activities, such as in South Korea.

Jean-Paul Clozel, MD and CEO, commented:

“I am very pleased to announce the establishment of Idorsia Japan relatively early in the life of Idorsia. From our previous experience we recognize that Japan can be a very important contributor to both global clinical development and commercial success. Led by Dr. Satoshi Tanaka, the organization is preparing for success of the ongoing Japanese registration program with clazosentan, which has the potential to become Idorsia’s first marketed product. We will then also leverage our presence in Japan to advance the global development programs with our portfolio of drugs in other indications.”

Notes to the editor

About Dr. E. Francois Aldrich

Dr. Aldrich joined the Department of Neurosurgery at the University of Maryland in 1993 after six years on the faculty at the University of Texas Medical Branch in Galveston. He has over 30 years neurosurgical experience where he has dedicated his career to the microsurgical treatment of a wide variety of complex neurosurgical cases in adults. He has consistently received many ‘U.S. News, Top Doc’ awards and is regularly included in the ‘America’s Best Physicians’ list. Dr. Aldrich is a Professor of Neurosurgery, Vice Chair of the Department of Neurosurgery, Residency Program Director and has served on the institutional review board for the last 20 years.

He is the head of cerebrovascular surgery and is an expert in the surgical treatment of ruptured and unruptured cerebral aneurysms as well as other brain blood vessel abnormalities. This is also the main focus of his clinical research. He is heavily involved in the design, and execution of multiple multinational studies in the treatment vasospasm, a potentially fatal condition that follows aneurysmal subarachnoid hemorrhage. New surgical techniques are being investigated for the treatment of interventricular and intracerebral hemorrhage. He also serves as the principal investigator on many of these studies.

References

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- Vajkoczy P, et al. Journal of Neurosurgery 2005; 103:9-17.
- Roux S. et al. J Pharmacol Exp Ther 1997; 283:1110-1118.

Investor webcast

An investor conference call and webcast will be held to discuss the Global Phase 3 program, the Japanese registration program and the establishment of Idorsia Pharmaceuticals Japan. The call will start with presentations by senior management, followed by a Q&A session (live access to the speakers).

Date: Monday June 18, 2018
Time: **14:00 CEST | 13:00 BST | 08:00 EDT**

Webcast participants should visit Idorsia’s website www.idorsia.com 10-15 minutes before the webcast is due to start. Conference call participants should start calling the number below 10-15 minutes before the conference is due to start.

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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 650 highly qualified specialists dedicated to realizing our ambitious targets.

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