Media Release
June 28, 2021

Ad hoc announcement pursuant to Art. 53 LR

Idorsia initiates the Phase 3 registration study with selatogrel for the treatment of acute myocardial infarction

- Idorsia to host an investor webcast to discuss the Phase 3 study today at 14:30hrs CEST

Allschwil, Switzerland – June 28, 2021
Idorsia Ltd (SIX: IDIA) today announced the initiation of the Phase 3 registration study "SOS-AMI" to evaluate the efficacy and safety of self-administered subcutaneous selatogrel, Idorsia's $P2Y_{12}$ receptor antagonist, in suspected acute myocardial infarction (AMI).

An AMI, or heart attack, is a life-threatening condition that occurs when blood flow to the heart muscle (myocardium) is suddenly decreased or completely cut off by a blood clot in one or more of the coronary vessels. An AMI requires immediate treatment, as any delay in intervention can result in irreversible damage to the heart muscle and adverse clinical outcomes. According to the US Centers for Disease Control and Prevention, each year more than 800,000 persons living in the US will suffer a heart attack.[1]

Although the management of AMI has improved in recent decades, morbidity and mortality associated with AMI remain high. The majority of deaths occur outside the hospital.[2,3] Early action is crucial for survival and to preserve heart muscle.

Besides aspirin, there are no treatment options currently available for the critical time from onset of AMI symptoms to first medical contact. The development of selatogrel in an autoinjector aims to fulfill this medical gap: upon symptoms suggestive of a heart attack, patients would self-inject selatogrel as early as possible and immediately call for emergency medical help.

Martine Clozel, MD and Chief Scientific Officer at Idorsia, commented:
"From the moment that symptoms start, the clock is ticking. Thrombus formation is progressing, and ischemia is rapidly causing irreversible damage to the heart. In the initial stages of thrombus formation, platelet aggregation dominates – a process in which the platelet $P2Y_{12}$ receptor plays a key role. If left untreated, the thrombus will become fibrin rich, at which point platelets have a more limited role in thrombus formation. This suggests that a fast-acting $P2Y_{12}$ receptor antagonist could cut short the thrombus formation in the initial stages of thrombus formation. Our drug discovery team has created a compound with unique properties which might fill this important therapeutic gap."

Dr Deepak L. Bhatt, MD, MPH, Executive Director of Interventional Cardiovascular Programs at Brigham and Women's Hospital, Professor of Medicine at Harvard Medical School, and Chair of the Steering Committee for SOS-AMI, commented:
"$P2Y_{12}$ receptor antagonists have been used in the treatment of millions of patients globally, and their safety and efficacy profiles are well established. Despite the success of chronic treatment with this class and other effective interventions, patients are still suffering recurrent heart attacks. The idea for patients to self-inject early in the onset of symptoms is truly innovative. The subcutaneous route of administration could overcome the onset delay observed with oral compounds from the same class."

To be effective, any antithrombotic treatment for use at the onset of AMI symptoms should be rapidly absorbed and potent, acting quickly to inhibit thrombus formation at an early stage. Inhibition should be reversed after a few hours to avoid interfering with later patient management decisions. It must also have an appropriate safety profile for use prior to formal diagnosis of AMI. Selatogrel has the potential to satisfy these necessary conditions.

Selatogrel administered subcutaneously is a potent, highly selective, fast-acting, reversible $P2Y_{12}$ receptor antagonist. Two published Phase 2 studies, one in patients with chronic coronary syndromes and one in patients with AMI showed fast and reversible inhibition of platelet aggregation. Subcutaneous administration of selatogrel 16 mg has demonstrated a rapid onset of action, within 15 minutes, with the magnitude of the effect extending over approximately eight hours. Selatogrel was safe and well tolerated in both studies.[6,7]

About the Antares Pharma integrated drug delivery device

In late 2019, Idorsia entered into a global development agreement with Antares Pharma, a US-based leader in autoinjector and rescue pen technologies, to design and customize an autoinjector for selatogrel. The Antares autoinjector was selected for its robustness, reliability, ease-of-use and emergency-ready capabilities – key characteristics necessary due to the nature of AMI. Idorsia has confirmed the usability of the Antares autoinjector through human factor validation studies.

About Selatogrel Outcome Study in suspected Acute Myocardial Infarction "SOS-AMI"

Idorsia is initiating an international, multi-center, double-blind, randomized, placebo-controlled, parallel-group, Phase 3 study to assess the clinical efficacy and safety of 16 mg selatogrel when self-administered (on top of standard-of-care) upon occurrence of symptoms suggestive of an acute myocardial infarction. The primary efficacy endpoint is the occurrence of death from any cause, or non-fatal AMI after any study treatment self-administration. The study will enroll approximately 14,000 patients who are at high risk of recurrent AMI, at around 250 sites in about 30 countries.

A Special Protocol Assessment has been agreed with the FDA. This indicates the FDA is in agreement with the adequacy and acceptability of specific critical elements of overall protocol design (e.g., entry criteria, dose selection, endpoints and planned analyses) for a study intended to support a future marketing application.

In December 2020, the FDA designated the investigation of selatogrel for the treatment of a suspected AMI in adult patients with a history of AMI as a "fast-track" development program. This designation is intended to promote communication and collaboration between the FDA and pharmaceutical companies for drugs that treat serious conditions and fill an unmet medical need.

Guy Braunstein, MD and Head of Global Clinical Development at Idorsia, added:
"Selatogrel has a pharmacokinetic and pharmacodynamic profile that results in a fast onset, and short duration of action - making it suitable for administration at the onset of symptoms. It is potent and highly selective for the $P2Y_{12}$ receptor and was well-tolerated in the Phase 2 studies. Further to these properties, selatogrel is suitable for subcutaneous administration, giving rise to the real innovation in SOS-AMI: self-administration as early as possible after onset of symptoms of a suspected AMI. We are now ready to put selatogrel in the hands of patients and I am looking forward to seeing SOS-AMI progress in the course of the next 2-3 years."

SOS-AMI has been designed as a patient-centric study in collaboration with patients. Patients participating in SOS-AMI will be trained by qualified professionals appointed at each study site, on how to recognize AMI symptoms, on how and where to self-inject treatment, and to call for emergency medical help immediately. Trainers will use standardized material mirrored across all countries, which

has been developed with the support of education experts, feed-back from post-MI patients, and in alignment with current guidelines. The patient is empowered through focused education to take action. In addition, regular interaction is performed by telephone with the designated site trainer, minimizing the burden on the patient, particularly during times of a global pandemic.

Dr Mary Mooney, Assistant professor at the School of Nursing and Midwifery, Trinity College Dublin, and Member of the Steering Committee for SOS-AMI, commented:
"I am passionate about patient education and involving patients in their own care. SOS-AMI pushes the boundaries of heart attack care provision. It puts the patient at the center of the study and empowers them to manage their heart attack symptoms. This means that our success will be heavily dependent on patients' responses, but I believe patients are ready for this challenge. For our part, we are educating patients on how to recognize the symptoms of AMI, how to use the study autoinjector, and to call emergency services after using the study autoinjector. We should strive for a world where slowing or stopping of a heart attack is as simple as a self-injection. We know the potential is there, we just need to see if it can be realized."

Jean-Paul Clozel, MD and Chief Executive Officer, concluded:
"Self-administration is currently used to treat a number of emergent medical conditions – why not AMI? Anyone can have a good idea, but drug innovation happens when a great team with a great compound, takes a great idea and runs with it. With our integrated drug delivery device, the potential to self-administer selatogrel in the critical time period immediately following onset of suspected AMI symptoms could be revolutionary for patients."

Notes to the editor

Investor webcast

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

Date: **Monday June 28, 2021**
Time: **14:30 CEST | 13:30 BST | 08:30 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.

Dial-in: **CH: +41 44 580 6522 | UK: +44 20 3009 2470 | US: +1 877 423 0830**
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About acute myocardial infarction (AMI)

An AMI, or heart attack, is a life-threatening condition that occurs when blood flow to the heart muscle (myocardium) is suddenly decreased or completely cut off. It is usually caused by a blood clot or blockage in one or more of the coronary vessels supplying blood to the heart muscle. An AMI requires immediate treatment and medical attention, as any delay in intervention can result in irreversible damage to the heart muscle. According to the US Centers for Disease Control and Prevention, each year more than 800,000 persons living in the US will suffer a heart attack.[1]

The need for an early intervention has been highlighted by the guidelines of the European Society of Cardiology, which identified the prehospital phase as the most critical for high-risk patients and reiterated that efforts must be made to reduce the delay in initiation of treatment in order to reduce death.[4,5]

Data supporting selatogrel in suspected AMI

Idorsia has completed a multicenter, double blind, randomized, placebo-controlled study assessing the pharmacodynamics, pharmacokinetics, tolerability and safety of a single subcutaneous injection of selatogrel in adults with chronic coronary syndrome. In this study, 346 patients receiving conventional background oral antiplatelet therapy (e.g. acetylsalicylic acid, $P2Y_{12}$ receptor antagonists) were randomized to receive either selatogrel 8 mg, 16 mg or placebo. The primary objective of the study was to characterize inhibition of platelet aggregation relative to placebo after a single subcutaneous injection of selatogrel either in the thigh or in the abdomen at 2 different doses in patients with chronic coronary syndromes.[6]

Idorsia has also completed a multi-center, open-label, randomized, exploratory study to assess the onset of platelet aggregation inhibition after a single subcutaneous injection of selatogrel in adults with acute myocardial infarction. In this study, 48 patients with confirmed diagnosis of AMI and time from onset of symptoms of more than 30 min and less than 6 hours were randomized to receive either selatogrel 8 mg or 16 mg in addition to conventional antithrombotic treatment (e.g., acetylsalicylic acid, oral $P2Y_{12}$ receptor antagonists, anticoagulants). The primary objective of the study was to assess the inhibition of platelet aggregation 30 minutes after a single subcutaneous injection of selatogrel in patients with AMI.[7]

About $P2Y_{12}$ receptor antagonism

Platelet adhesion, activation and aggregation play a pivotal role in atherothrombosis. An essential element in the platelet activation process is the interaction of adenosine diphosphate (ADP) with the platelet $P2Y_{12}$ receptor. This platelet activation and aggregation can be inhibited by antagonizing the platelet $P2Y_{12}$ receptor. This prevents the binding of ADP to the receptor, which reduces platelet aggregation and the reaction of platelets to stimuli of thrombus aggregation.

About Dr Deepak L. Bhatt

Deepak L. Bhatt MD, MPH, FACC, FAHA, FSCAI, FESC, is Executive Director of Interventional Cardiovascular Programs at Brigham and Women's Hospital and Professor of Medicine at Harvard Medical School.

After graduating as valedictorian from Boston Latin School, Dr Bhatt obtained his undergraduate science degree as a National Merit Scholar at MIT while also serving as a research associate at Harvard Medical School. He received his medical doctorate from Cornell University and a Master of Public Health with a concentration in clinical effectiveness from Harvard University. His internship and residency in internal medicine were at the Hospital of the University of Pennsylvania, and his cardiovascular training was at Cleveland Clinic. He also completed fellowships in interventional cardiology and cerebral and peripheral vascular intervention and served as Chief Interventional Fellow at Cleveland Clinic, where he spent several years as an interventional cardiologist and an Associate Professor of Medicine. He served for many years as Director of the Interventional Cardiology Fellowship, Associate Director of the Cardiovascular Medicine Fellowship, and Associate Director of the Cardiovascular Coordinating Center. He was then recruited to be the Chief of Cardiology at VA Boston Healthcare System and served in that role for several years. He was a Senior Investigator in the TIMI Study Group for over a decade. He was selected by Brigham and Women's Hospital as the 2014 Eugene Braunwald Scholar. He has been listed in Best Doctors in America from 2005 to 2020. He received the Eugene Braunwald Teaching Award for Excellence in the Teaching of Clinical Cardiology from Brigham and Women's Hospital in 2017, ACC's Distinguished Mentor Award in 2018, and AHA's Distinguished Scientist Award in 2019.

Dr Bhatt has authored or co-authored over 1650 publications and has been listed by the Web of Science Group as a Highly Cited Researcher from 2014 to 2020. He is the Editor of Cardiovascular Intervention: A Companion to Braunwald's Heart Disease and of Opie's Cardiovascular Drugs: A Companion to Braunwald's Heart Disease. He is Senior Associate Editor for News and Clinical Trials for ACC.org. He is the Editor of the peer-reviewed Journal of Invasive Cardiology and Editor-in-Chief of the Harvard Heart Letter for patients. Dr Bhatt receives funding paid to Brigham and Women's Hospital from Idorsia for his role as the Chair of the Steering Committee for SOS-AMI.

About Dr Mary Mooney

Dr Mary Mooney (PhD, MSc, RGN, RM, RNT, MA, Higher. Diploma Cardiovascular Studies) is an assistant professor in the School of Nursing and Midwifery, Trinity College Dublin. Her research areas focus predominantly on cardiac-related aspects of patient care and nurse education. Her research experience encompasses qualitative and quantitative research methods, including randomized controlled trials. Mary's PhD was a randomized controlled trial that comprised delivering an educational intervention to patients with Acute Coronary Syndrome. This Health Research Board (HRB) funded study was the first RCT in the world to target and successfully reduce patient pre-hospital delay time and its groundbreaking effect has been renowned for its effectiveness in reducing patient delay in the presence of heart attack symptoms. Dr Mooney has many publications, is widely cited, and her work has contributed to the development of further international research with which she is currently actively engaged.

In terms of research funding, Mary has been Principal Investigator or a co-applicant across a range of projects, from a variety of funding sources. She has wide national and international collaborates with whom she is actively engaged in research. Mary maintains a clinical remit in cardiology, in addition to her academic role, and is an external examiner for post-graduate programs in other universities. As an elected committee member for the Irish Nurses Cardiovascular association (INCA), she contributes to the delivery of cardiovascular education of nurses in Ireland. She is actively engaged in research, most of which is concerned with cardiovascular or critical care. She has worked as a researcher and clinical advisor to an Irish Enterprise, funded by Enterprise Ireland She has been an invited speaker and presenter across a range of national and international events. Dr Mooney serves as a consultant to Idorsia.

About Antares Pharma Inc. (NASDAQ: ATRS)

Antares Pharma, Inc. is a specialty pharmaceutical company focused primarily on the development and commercialization of pharmaceutical products and technologies that address unmet needs in targeted therapeutic areas such as urology and endocrinology. The Company has a portfolio of proprietary and partnered commercial products with several product candidates in various stages of development, as well as significant strategic alliances with industry leading pharmaceutical companies.

Key literature

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2. Adnet F, et al. Incidence of acute myocardial infarction resulting in sudden death outside the hospital. Emerg Med J. 2011;28(10):884–6.
3. Norris RM. Fatality outside hospital from acute coronary events in three British health districts, 1994-5. United Kingdom Heart Attack Study Collaborative Group. BMJ 1998;316(7137):1065–70.
4. Ibanez B, et al. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2018;39(2):119–77
5. Neumann FJ, et al. 2018 ESC/EACTS guidelines on myocardial revascularization. Eur Heart J 2019;40(2):87–165
6. Storey R. F, et al. Pharmacodynamics, pharmacokinetics, and safety of single-dose subcutaneous administration of selatogrel, a novel $P2Y_{12}$ receptor antagonist, in patients with chronic coronary syndromes. Eur Heart J 2019;0, 1-9, doi:10.1093/eurheartj/ehz807
7. Sinnaeve P, et al. Subcutaneous Selatogrel Inhibits Platelet Aggregation in Patients With Acute Myocardial Infarction. J Am Coll Cardiol. 2020 May 26;75(20):2588-2597. doi: 10.1016/j.jacc.2020.03.059. PMID: 32439008.
8. Juif P, et al. Clinical Pharmacology of the Reversible and Potent $P2Y_{12}$ Receptor Antagonist ACT-246475 After Single Subcutaneous Administration in Healthy Male Subjects. The Journal of Clinical Pharmacology 2019, 59(1): 123-130. doi:10.1002/jcph.1296

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 900 highly qualified specialists dedicated to realizing our ambitious targets.

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