Dilaforette presents results from exploratory Phase I/II clinical trial in uncomplicated malaria

STOCKHOLM, SWEDEN – May 30, 2014. Today, Dilaforette AB announced the results from an exploratory Phase I/II clinical trial in malaria with its candidate drug sevuparin. Sevuparin was studied in adult patients with uncomplicated falciparum malaria as adjunct treatment and was found to be safe and well tolerated. The study results indicates important early anti-adhesive effects with a potential to improve the outcome for patients with severe malaria, even though the primary efficacy endpoint was not met. Karolinska Development owns 69 percent of Dilaforette.

The study was conducted by Dilaforette in close collaboration with The Mahidol Oxford Tropical Medicine Research Unit (MORU), at the Mae Sot and Mae Ramat Hospitals in Thailand.

”The effect seen in this study is promising and warrants quick assessment whether sevuparin should be added to the treatment regime in severe malaria”, says Professor Arjen Dondorp, Coordinating Principal Investigator, Department Head and Deputy Director of the MORU.

Sevuparin is a potential novel adjunctive treatment for severe malaria pre-clinically developed in the laboratory of Professor Mats Wahlgren, one of the co-founders of Dilaforette, at Karolinska Institutet. The aim of the present trial was to study sevuparin in adult patients with uncomplicated *falciparum* malaria prior to studies in patients with severe malaria. The trial was divided into two parts, the objective of the first part was to assess safety and tolerability of sevuparin. The objective of the second part was, in addition to safety, to measure reversal of sequestration of mature parasitized red blood cells in the smallest blood vessels. In the second part of the trial, which was open labeled, the patients were randomized into two groups; one group received standard-of-care (SoC), atovaquone/proguanil, and the other group received a combination of SoC and sevuparin.

Due to slow recruitment and in order to progress the program into severe malaria, it was decided to prematurely terminate the study when a total of 53 of the planned 89 patients had been treated. Among the 53 patients that were treated, 23 patients received SoC and 30 patients received SoC plus sevuparin. The study results showed that sevuparin is safe and well-tolerated in adult patients with uncomplicated *falciparum* malaria. The study did not reach statistical significance on its primary efficacy endpoint, i.e. an increase in appearance of mature parasitized red blood cells into the blood circulation over the first 11 hours after start of sevuparin treatment. However, due to the premature termination of the trial, the results do not suffice as the basis for conclusive determination of the effect of sevuparin.

Furthermore, exploratory analyses indicates a higher number of mature parasites in the circulating blood already one hour after the first dose of sevuparin. This observation is consistent with the intended effect of sevuparin, which is to reverse blockage of blood vessels by mature parasitized red blood cells which normally stick to the vessel wall and obstruct the blood flow. In addition, the number of young parasitized cells consistently decreased over the early time period after the initial sevuparin injection which is in line with the assumed capacity of sevuparin to block parasite invasion into red blood cells. As patients with uncomplicated malaria have a much lower parasite load than patients with severe disease, the exploratory analysis supports further clinical studies in severe malaria with the aim to show that sevuparin can reverse the binding, which should improve blood flow and clinical outcome.

”Based on these findings, we intend to approach relevant stakeholders in the malaria community with the aim to progress the program into the intended patient group, patients with severe malaria”, says Christina Herder, CEO, Dilaforette.

”These data with sevuparin indicates its potential to improve microvascular blood flow and thereby address unmet medical needs for several diseases including severe malaria and sickle cell disease”, says Torbjörn Bjerke, CEO, Karolinska Development.

The Indian part of the clinical development program will due to unforeseen changes in local legislation not continue.

For further information, please contact:
Christina Herder, CEO, Dilaforette AB
Phone: +46 (0)70 374 71 56, e-mail: christina.herder @dilaforette.se

Torbjörn Bjerke, CEO, Karolinska Development AB
Phone: +46 (0)72 744 41 23, e-mail: torbjorn.bjerke@karolinskadevelopment.com

Benjamin Nordin, IRO, Karolinska Development AB
Phone: +46 (0)73 093 60 80, e-mail: benjamin.nordin@karolinskadevelopment.com

TO THE EDITORS

About Dilaforette
Dilaforette is a Swedish drug development company developing sevuparin, a heparan sulfate mimetic, for the treatment of severe malaria and vaso-occlusive crisis in sickle cell disease.

Despite improved prevention and treatment in malaria, there are still about 1 million deaths per year, mostly in children in Africa. In severe malaria, the blood circulation is hampered due to massive obstruction of parasitized red blood cells that stick to the wall of the smallest blood vessels and to uninfected red blood cells. This constitutes the central feature in the severe disease development and is a direct cause of coma and death. There is today no drug available that reverses the obstruction of the small blood vessels. Sevuparin is a potential new adjunctive treatment of severe malaria that acts by preventing and reversing the parasitized red blood cells ability to block blood vessels.

Sickle cell disease is a genetic life-shortening disorder where one main feature is the vaso-occlusive crisis caused by sickle cell shaped red blood cells that obstruct blood flow in capillaries, resulting in ischemia and severe pain.

For more information, please visit www.dilaforette.se

About sevuparin
Dilaforette's drug candidate, sevuparin, is a proprietary polysaccharide drug derived from heparin. It has been designed to retain the anti-adhesives effects, while reducing the anti-coagulant properties. Sevuparin, has the potential to be of clinical use in several therapeutic conditions.

About Mahidol – Oxford Tropical Medicine Research Unit (MORU)
The MORU, supported by the Wellcome Trust of Great Britain, was founded in 1979 as a research collaboration between the Faculty of Tropical Medicine, Mahidol University and the University of Oxford. The main research interests are the epidemiology, diagnosis, pathophysiology and treatment of malaria and other tropical infections. For more information, please visit www.tropmedres.ac

About Karolinska Development
Karolinska Development aims to create value for patients, researchers, and investors by developing innovations from world class science into products that can be sold or out-licensed with high returns. The business model is to: SELECT the most commercially attractive medical innovations; DEVELOP innovations to the stage where the greatest return on investment can be achieved; and COMMERCIALIZE the innovations through the sale of companies or out-licensing of products. An exclusive deal flow agreement with Karolinska Institutet Innovations AB, along with other cooperation agreements with leading Nordic universities, delivers a continuous flow of innovations. Today, the portfolio consists of 34 projects, of which 17 are in clinical development. For more information, please visit www.karolinskadevelopment.com

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