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Poxel Presents New Preclinical Imeglimin Data Demonstrating Improvement of Both Peripheral and Coronary Vascular Function at the European Society of Cardiology Congress

- Additional data from metabolic syndrome model support protective effects of Imeglimin on diabetic cardiomyopathy, a significant cardiovascular complication in diabetic patients

LYON, France--(BUSINESS WIRE)-- POXEL SA (Euronext – POXEL - FR0012432516), a biopharmaceutical company focused on the development of innovative treatments for metabolic disorders, including type 2 diabetes, announced today that preclinical Imeglimin data showed a benefit in peripheral and coronary vascular function that was associated with an improvement of cardiac function (diastolic dysfunction), in a rat model of metabolic syndrome. Over the weekend, these data were presented in poster P577 in the chronic heart failure session at the European Society of Cardiology (ESC) Congress at the Fira Gran Via Conference Center in Barcelona, Spain. These results positively reinforce the data recently presented at the American Diabetes Association (ADA) Scientific Session and further strengthen Imeglimin's profile as a novel treatment for type 2 diabetes.

"This is the first time Imeglimin has shown a benefit on peripheral and coronary vascular function in addition to a concomitant protective effect for diabetic cardiomyopathy. Furthermore, the reduced oxidative stress and the increase in nitric oxide bioavailability, two key components involved in vasodilation of coronary and peripheral arteries, may contribute to Imeglimin's protective effect on cardiac function," said Thomas Kuhn, CEO of Poxel. "Diabetic cardiomyopathy is a significant cardiovascular complication with limited treatment options. It affects approximately 40 percent of the type 2 diabetic patients and is associated with an increase in morbidity and mortality[1]. These exciting data demonstrate that Imeglimin may have the potential to reduce the burden of this prominent cardiovascular complication in type 2 diabetes patients."

Imeglimin Results

The preclinical study in a rat model of metabolic syndrome was designed to investigate Imeglimin's protective effects on diabetic cardiomyopathy. Obese Zucker fa/fa rats, which are known to develop cardiac dysfunction very similar to cardiomyopathy observed in type 2 diabetes patients, were treated with150 mg/kg Imeglimin twice-daily for 9 and 90 days. The

effects of Imeglimin were evaluated through key parameters of both left ventricular (LV) function (echocardiography, MRI) and hemodynamics (LV catheterization). Endothelium-dependent relaxation of coronary and peripheral arteries was also evaluated. The study demonstrated that very early in the course of treatment, Imeglimin significantly improved vascular function, which was strongly impaired in this rat model. Concomitantly, all the parameters of LV diastolic dysfunction as well as myocardial perfusion were improved compared to the untreated controls, suggesting a clear beneficial effect on the progression of diabetic cardiomyopathy. In addition, Imeglimin was also shown to improve glucose tolerance in this model.

These demonstrated effects on diastolic dysfunction, in a model of metabolic syndrome, further strengthen Imeglimin's therapeutic profile in type 2 diabetes, where heart failure remains a key complication with limited therapeutic options. The results are consistent with Imeglimin's mechanism of action and with previous data in another diabetic model showing protective effects on endothelial dysfunction, an early sign of diabetic cardiovascular complication (EASD 2016).

The poster presented at the ESC Congress titled, "Short- and long-term Imeglimin treatment reduces metabolic syndrome-related diabetic cardiomyopathy," is available on the Company's website under "Scientific Publications" or by using the following link http://www.poxelpharma.com/en_us/product-pipeline/posters.

Imeglimin has successfully completed Phase 1 and Phase 2 development in over 1,200 subjects in the U.S., EU and Japan.

About Imeglimin

Imeglimin is the first clinical candidate in a new chemical class of oral agents called the Glimins. Imeglimin has a unique mechanism of action (MOA) that targets mitochondrial bioenergetics. Imeglimin acts on the three main target organs involved in glucose homeostasis: the liver, muscle, and the pancreas. This MOA has the potential for glucose lowering benefits, as well as the potential to prevent endothelial dysfunction, which can provide protective effects on micro- and macro-vascular defects induced by diabetes. The additional protective effect on beta-cell survival and function may lead to a delay in disease progression. This unique mode of action, compared to existing treatments for type 2 diabetes, makes Imeglimin a prime candidate in all stages of the current anti-diabetic treatment paradigm, including monotherapy or as an add-on to other glucose lowering therapies for the treatment of patients with type 2 diabetes.

About Poxel SA

Poxel uses its development expertise in metabolism to advance a pipeline of drug candidates focused on the treatment of metabolic disorders, including type 2 diabetes. We have successfully completed our Phase 2 clinical program for our first-in-class lead product, Imeglimin, which targets mitochondrial dysfunction, in the U.S., EU and Japan. Our second program, PXL770, a direct AMPK activator, is in Phase 1 development. We intend to generate further growth through strategic partnerships and pipeline development. (Euronext: POXEL, www.poxel.com)

[1] Fitchett et al. European Journal of Heart Failure (2017)

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Poxel SA
Jonae R. Barnes, +1-617-818-2985
Senior Vice President, Investor Relations and Public Relations
jonae.barnes@poxelpharma.com
or
Investor relations / Media - EU/US
MacDougall Biomedical Communications
Gretchen Schweitzer or Stephanie May, +49 89 2424 3494 or +49 175 571 1562
smay@macbiocom.com
or
Investor relations / Media - France
NewCap
Florent Alba/Nicolas Mérigeau, + 33 1 44 71 98 55
poxel@newcap.fr

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