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Poxel Presents New Data on Imeglimin and PXL770 at the European Association for the Study of Diabetes Annual Meeting

Imeglimin Demonstrates Improvement in Vascular Dysfunction in Type 2 Diabetes Model Showing the Potential for Protective Effects in the Treatment of Type 2 Diabetes

PXL770 Demonstrates Potent Inhibition of *De Novo* Lipogenesis Through an AMPK-Dependent Pathway and Beneficial Effects on Fat Mass and Body Weight in Models of Type 2 Diabetes

LYON, France--(BUSINESS WIRE)-- POXEL SA (Euronext – POXEL - FR0012432516), a biopharmaceutical company focused on the development of innovative treatments to treat type 2 diabetes, today announced the presentation of novel data on its lead drug candidate, Imeglimin, and its direct adenosine monophosphate-activated protein kinase (AMPK) activator, PXL770, at the European Association for the Study of Diabetes (EASD) Annual Meeting in Munich, Germany. The data discussed in an oral presentation and during two poster sessions highlight important new insights on the potential of each compound for the treatment of type 2 diabetes as well as related metabolic diseases.

“These exciting results for Imeglimin represent significant progress in further understanding the benefits beyond glycemic control that Imeglimin can deliver, specifically the potential for beneficial protective effects in the early stages of vascular dysfunction, which is key in the treatment of type 2 diabetes,” commented Thomas Kuhn, CEO of Poxel. “In addition, we are very enthusiastic about the AMPK target and the data for PXL770, which have been consistent in a variety of animal models. Our studies highlight the therapeutic potential of AMPK activation by PXL770 for the treatment of type 2 diabetes, especially for patients with cardiovascular risk and other metabolic disorders, such as hepatic steatosis and metabolic syndrome.”

Imeglimin has completed Phase 2 development in over 850 subjects in the US and EU and is currently being studied in a 300-patient Phase 2b clinical trial in Japan. PXL770, a first-in-class direct AMPK activator, which regulates cellular energy metabolism and is considered to mimic the effects of long-term exercise, is in Phase 1 clinical development.

Imeglimin

The Imeglimin preclinical study in diabetic mice was designed to investigate the compound's effect on endothelial dysfunction, which is the first step in the development of vascular diseases and a contributing factor to atherosclerosis in type 2 diabetes. To measure

endothelial function, pressure or acetylcholine induced vasodilatation was assessed in diabetic mice treated with an increasing dose of Imeglimin. The study demonstrated that one week of treatment with 150mg/kg Imeglimin prevents endothelial dysfunction induced by severe hyperglycemia in the mice suggesting that Imeglimin could provide protective effects on micro and macro-vascular defects induced by diabetes. These results further strengthen Imeglimin's therapeutic profile as vascular diseases remains a key complication of type 2 diabetes.

PXL770

The two studies conducted on PXL770 evaluated the effects of the direct AMPK activator on fat metabolism and body weight in several model systems. In the first study, presented in an oral presentation on September 14th, 5-week old mice fed with a high fat or normal diet were treated with 75mg/kg PXL770 or a control vehicle. Mice on a high fat diet treated with PXL770 gained less weight than pair-fed control animals despite identical caloric intake. Furthermore, an increase in total energy expenditure and a significant increase in fat oxidation could be observed in the PXL770 group compared to the high fat control animals. Finally, over the 4 to 5-week treatment period, PXL770 significantly improved fasting glycemia and glucose tolerance by 32% ($p < 0.001$) and significantly reduced fat mass by 53% ($p < 0.0001$) compared to control animals, confirming the results seen in previous studies.

In the second study, the inhibitory potency of PXL770 on *de novo* lipogenesis was evaluated in primary mouse and human hepatocytes as well as *in vivo* in nine-week-old mice. PXL770 dose dependently decreased liver *de novo* lipogenesis with a high potency in all model systems. The results are consistent with previous studies showing a decrease in fatty acid synthesis following PXL770 treatment confirming the role of AMPK in this metabolic pathway.

Overall, both studies solidify PXL770's potential to treat type 2 diabetes and other cardiovascular risk factors, such as lipid disorders and obesity, and also its potential to improve the treatment of hepatic lipid metabolism disorders.

PXL770 is currently in Phase 1. In the first part of the Phase 1 study, the results indicate that PXL770 exhibits a favorable safety and tolerability profile with no safety signals. During the Phase 1 study, Poxel observed a different metabolic pattern in humans compared to animals that were treated with PXL770. Therefore, based on regulatory guidelines, Poxel will need to further evaluate the profile of the metabolites, which may be pharmacologically active, prior to starting the second part of the Phase 1 study. As a result of this additional preclinical work, the start of the second part of the Phase 1b study will be delayed until 2017.

The posters and oral presentation presented at the EASD Annual Meeting are available on the Company's website under "Scientific Publications" or by using the link <http://poxel.com/our-science/scientific-publications.php>.

- *Imeglimin Improves Vascular Dysfunction in Type 2 Diabetes Animal Models*
- *PXL770, a novel direct AMPK activator, inhibits hepatic de novo lipogenesis for the treatment of metabolic disorders*
- *PXL770, a novel direct AMPK activator, improves metabolic disorders in diet induced mice model of obesity and diabetes*

About Imeglimin

Imeglimin is the first in a new chemical class of oral anti-diabetic agents, the Glimins. Imeglimin acts on three main target organs involved in glucose homeostasis: the liver, muscle, and the pancreas. Imeglimin's unique mechanism of action targets mitochondrial bioenergetics. This distinct mode of action compared to existing treatments for type 2 diabetes makes Imeglimin a prime candidate in monotherapy and to complement other treatments such as metformin or sitagliptin.

About PXL770

PXL770 directly activates adenosine monophosphate-activated protein kinase (AMPK), an enzyme that acts as an energy sensor and regulator, maintaining cellular homeostasis, thus playing an important role in the management of diabetes. In addition to its anti-diabetic properties, PXL770 has the potential to treat lipid-related abnormalities, which are present in a vast majority of diabetic patients and are the cause of cardiovascular incidents among this population, as well as other metabolic disorders.

About Poxel SA

Poxel uses its development expertise in metabolism to advance a pipeline of drug candidates focused on the treatment of 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. and EU and have fully enrolled a Phase 2b clinical study in 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

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