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Poxel Announces Additional Positive Results for Imeglimin Phase 2b Study in Japan for the Treatment of Type 2 Diabetes

- **Imeglimin Phase 2b trial in 299 Japanese patients achieved statistically significant results for its primary and secondary endpoints**
- **Significant improvement in liver function and similar safety and efficacy in patients with chronic kidney disease compared to patients with normal renal function**
- **Imeglimin Phase 2b results from the study in Japan have been accepted for presentation at the European Association for the Study for Diabetes 53rd Annual Meeting in September 2017**
- **Imeglimin Phase 3 program in Japan is anticipated to be initiated in the fourth quarter of 2017**
- **The Japanese diabetes market is fast-growing and anticipated to reach approximately $6B by 2020***

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 additional results from the Imeglimin Phase 2b study conducted in Japan. In addition to the highly statistically significant ($p<0.0001$) top-line results for the primary and key secondary endpoint, the Company is reporting additional data from this study. This press release is being issued in conjunction with a corporate presentation at the Jefferies global healthcare conference today at 4 pm ET. To access the webcast, please use the following link **http://wsw.com/webcast/jeff105/poxel.pa**.

The Phase 2b randomized, double-blind, placebo-controlled study tested three doses of Imeglimin (500 mg, 1000 mg and 1500 mg) administered twice-daily for 24 weeks in 299 Japanese patients for the treatment of type 2 diabetes. In this study, a statistically significant ($p<0.0001$) decrease in the primary endpoint of HbA1c was observed along with consistent, statistically significant ($p<0.0001$) decreases in the key secondary endpoints of fasting plasma glucose, glycated albumin and percentage of patients reaching a target HbA1c of less than 7%. A statistically significant dose dependent (500 mg $p=0.008$,1000 mg $p=0.0008$, and 1500 mg $p<0.0001$) improvement of the homeostasis model assessment of beta-cell

function (HOMA-B), a marker of beta cell function in fasting condition, was also observed and is consistent with previously published data. In addition, there was a significant decrease in two of the most relevant liver enzymes, alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT), which are considered biomarkers in liver disease. The ALT and GGT results reflect an improvement of liver function and are consistent with previously published data in animal models. These data support Imeglimin's unique dual mechanism of action of improving both insulin secretion and sensitivity, which are the two key defects that cause type 2 diabetes.

In this study, Imeglimin was safe and well tolerated and the adverse event profile was consistent to what was observed in the U.S. and EU Phase 1 and 2 programs. No serious adverse events related to Imeglimin were reported. There was no difference in the overall incidence of patients presenting with at least one treatment emergent adverse event between treatment and placebo groups. Of particular note, in this study, the safety and efficacy of Imeglimin in patients with mild to moderate chronic kidney disease was similar to patients with normal renal function. Furthermore, no weight gain from Imeglimin was observed.

"Imeglimin's effect on beta cell function through HOMA-B is very meaningful. We believe that Imeglimin could be particularly well-suited for Japanese patients with type 2 diabetes and this effect may be an important contributor to the robust efficacy seen in our Phase 2b study in Japanese patients," said Pascale Fouqueray, MD, PhD, Executive Vice President, Early Development & Translational Medicine of Poxel. "The additional data demonstrating a decrease in liver enzymes are promising and could represent an added benefit to type 2 diabetes patients who are at a high risk for liver disease."

As previously reported, the primary endpoint of the trial achieved statistical significance ($p<0.0001$) for the change from baseline in HbA1c versus placebo in all treatment groups at 24 weeks. In the study, placebo adjusted HbA1c reduction was 0.52%, 0.94% and 1.00% for the 500 mg, 1000 mg and 1500 mg dose twice-daily, respectively.

The Company anticipates meeting with the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan during the third quarter of this year, and pending feedback from the meeting, the Company anticipates advancing Imeglimin into a Phase 3 program in Japan during the fourth quarter of 2017.

"Japan is a key focus and an integral part of our business strategy, especially with the unique treatment paradigm for innovative new therapies. Given Imeglimin's novel mechanism of action coupled with the results of this Phase 2b trial, we believe Imeglimin is a prime candidate for first-line therapy either as monotherapy or as an add-on to other glucose lowering therapies for the treatment of patients with type 2 diabetes," said Thomas Kuhn, CEO of Poxel. "We look forward to advancing Imeglimin into a Phase 3 program in 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 a 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)

* Source: Oppenheimer & Co. estimates

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