EMBARGOED UNTIL Monday, June 16th, 7.30 am CET

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Poxel's Investigational Oral Agent - Imeglimin - Shows Unique Anti-diabetic Profile in Preclinical and Clinical Studies

- Imeglimin induces glucose-stimulated insulin secretion by improving beta cell glucose sensitivity in Type 2 diabetic patients
- Imeglimin normalizes glucose tolerance and insulin sensitivity by improving mitochondrial function in a diabetic pathophysiological model
- Imeglimin has a unique mechanism of action targeting the mitochondria bioenergetics

LYON, France, June 16, 2014 – Poxel SA presented data from human and animal studies with its novel anti-diabetic agent – Imeglimin – currently in phase 2b clinical development, during the 74th Scientific Sessions of the American Diabetes Association. The data demonstrate Imeglimin's dual activity on both insulin sensitizing and insulin secretion defects of Type 2 Diabetes, featuring the innovative profile of this new anti-diabetic agent.

"These Phase 2 clinical trial and preclinical study results confirm that Imeglimin is the first treatment to act on the two key defects of Type 2 Diabetes, namely insulin sensitizing and secretion," said Thomas Kuhn, CEO of Poxel. "Imeglimin acts directly on the three main organs affected by Type 2 Diabetes: the pancreas, the liver and the muscle. Our recent data confirm that Imeglimin acts – at the organ level - in a different manner from metformin and sitagliptin, evidencing its combination potential already seen in two add-on trials in humans. These results validate that Imeglimin is unique among current anti-diabetic agents."

An oral communication entitled "*Imeglimin Increases Glucose-Dependent Insulin Secretion and Improves Beta-cell Function in Patients with Type 2 Diabetes*" described the glucose-dependent insulin secretion effect of Imeglimin administered to Type 2 Diabetes patients, using a hyperglycemic clamp technique. Imeglimin significantly raises insulin response to glucose (p=0.035); achieving this primary endpoint. Imeglimin increases significantly 1st and 2nd phase insulin secretion rates (p=0.034 and 0.031, respectively) and improves beta cell glucose sensitivity (p=0.034). Imeglimin has no effect on plasma glucagon, in contrast to DPP-4 inhibitors.

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Michael Roden, MD (Institute for Clinical Diabetology, German Diabetes Center, Department of Endocrinology and Diabetology, University Hospital Düsseldorf, Düsseldorf, Germany) who presented the work stated: "*Imeglimin improves glucose sensing of the pancreatic beta cell and increases glucose-stimulated insulin secretion, which contributes to the glucose lowering action of Imeglimin. Given the activity of Imeglimin on both liver and muscle demonstrated in preclinical studies, Imeglimin has a unique mechanism of action that could represent a new way of addressing the pathophysiology underlying Type 2 Diabetes".*

A second oral communication entitled "*Imeglimin Normalizes Glucose Tolerance and Insulin Sensitivity in Improving Mitochondrial Function in a High-Fat-High Sucrose Diet Mice Model*" described Imeglimin's benefit on glucose tolerance, insulin sensitivity and insulin signaling in both liver and muscle in a nutrient-overload Type 2 diabetic model. Imeglimin adapts mitochondrial functioning to this overload, leading to fat utilization. As a result, Imeglimin decreases liver steatosis, improves insulin signaling and decreases insulin resistance, one of the two key defects of Type 2 diabetic disease.

Dr. Vidal (INSERM U160, Faculté de Médecine Lyon-Sud, European Center for Nutrition and Health) who headed the work commented: "*we are very pleased to have achieved this important result in understanding the mechanism by which Imeglimin exhibits insulin sensitizing effects and so contribute to its anti-diabetic activity".*

A poster entitled "*Imeglimin Decreases Hepatic Glucose Production through a Unique Mitochondrial Mechanism of Action*" was presented to ADA audience. The aim was to identify the underlying mechanisms by which Imeglimin decreases gluconeogenesis in primary rat hepatocytes in comparison to metformin. Imeglimin's unique mechanism of action targets the mitochondrial bioenergetics by inducing an increase in redox potential and a decrease in membrane potential without modifying mitochondrial respiration by contrast to metformin.

Pr Eric Fontaine (INSERM U1055, Université de Grenoble France) whose team is broadly involved in mitochondrial bioenergetics investigations stated: "*these results are key to understand Imeglimin's innovative mechanism of action. Imeglimin inhibits gluconeogenesis without affecting respiratory flux, thereby preventing Imeglimin from inducing lactic acidosis in contrast to metformin."*

About Type 2 Diabetes

Type 2 Diabetes is the most common type of diabetes. It usually occurs in adults, but is increasingly seen in children and adolescents. In Type 2 Diabetes, the body is able to produce insulin but it is either not sufficient or the body is not responding to its effects, leading to a build-up of glucose in the blood. Type 2 Diabetes is a major cause of both cardiovascular and kidney diseases.

The number of people with Type 2 Diabetes is rising rapidly worldwide. This rise is associated with economic development, ageing populations, increasing urbanization, dietary changes, reduced physical activity and changes in other lifestyle patterns.

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The International Diabetes Federation estimates that in 2011, 366 million people around the world have diabetes. This total is expected to rise to 552 million in 2030. Each year a further 7 million people develop diabetes. The current market is dominated by few product classes and significant unmet needs remain for both physicians and patients.

The worldwide pharmaceutical market for Type 2 Diabetes, 60% of which is represented by oral anti-diabetics, is expected to increase from $31 billion in 2012 to $48.8 billion in 2021 (source IMS audits).

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 and has therefore a distinct mode of action compared to existing treatments for Type 2 Diabetes. In that, it looks like the best partner to complement other treatments. Imeglimin phase 2a monotherapy results were published in *Diabetes, Obesity and Metabolism* in April 2012. In October 2011, Poxel reported phase 2 results of Imeglimin as add-on therapy to metformin in patients inadequately controlled with metformin monotherapy. This study achieved its primary end-point of superiority in HbA1c reduction versus placebo ($p<0.001$). The study results are published in *Diabetes Care*. In November 2012, Poxel reported phase 2 results of Imeglimin as add-on therapy to sitagliptin in patients inadequately controlled with sitagliptin monotherapy. This study achieved its primary end-point of superiority in HbA1c reduction versus placebo ($p<0.001$). The study results are published in *Diabetes Care*.

About Poxel SA

Poxel, founded in 2009, is a biopharmaceutical company developing innovative first-in-class drugs, with a primary focus on Type 2 Diabetes. The company develops novel treatments before seeking pharmaceutical industry partners. Poxel was spun out from Merck Serono and now operates independently as a lean organization with strong in-house drug development and business expertise.

Poxel's product pipeline consists of several first-in-class Type 2 Diabetes candidates, including Imeglimin in phase 2b clinical development and a direct activator of AMPK, close to phase 1 development for the treatment of Type 2 Diabetes.

For more information, please visit www.poxel.com

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