Poxel's Anti-diabetic Imeglimin Confirms Its Unique Mechanism of Action in Type 2 Diabetic Patients

Imeglimin improves glucose-stimulated insulin secretion, confirming Imeglimin potential to be combined to current diabetes treatments

Lyon, France, 7 October 2013, - Poxel SA, today announced that during a human hyperglycemic clamp trial, Imeglimin, a novel compound in development to treat Type 2 diabetes, increases insulin secretion in response to glucose, confirming previous preclinical and clinical results. Imeglimin acts directly on the three main organs affected by type 2 diabetes: the pancreas, the liver and the muscle. This mechanism makes Imeglimin unique among the current anti-diabetic agents available to physicians.

Poxel's objective was to confirm, in diabetic patients, Imeglimin's impact on glucose-stimulated insulin secretion, using the reference method of hyperglycemic clamp technique, including arginine stimulation to assess maximal secretory capacity. This clinical pharmacology trial was a randomized, double-blind, placebo-controlled, parallel-group study investigating insulin secretion after Imeglimin chronic treatment. The trial included 30 patients; 15 per group. Results showed that Imeglimin met the primary and secondary endpoints, with a statistically significant increase in the incremental area under the curve of insulin response to glucose ($iAUC_{0\text{-}45min}$ insulin) and a statistically significant increase in the incremental area under the curve of C-peptide and proinsulin response ($iAUC_{0\text{-}45min}$ C-peptide, $iAUC_{0\text{-}45min}$ proinsulin), in comparison to placebo.

Professor Michael Roden, Poxel Scientific Board member, commented, *"Imeglimin is a very interesting new agent as the analysis of the data showed that the increase in glucose-stimulating insulin secretion, 1st and 2nd phases, is triggered by an improvement in the glucose sensitizing properties of the beta cell, contributing to Imeglimin's anti-hyperglycemic activity . Given Imeglimin's activity on both the liver and the muscle, these data confirm that Imeglimin has a unique mechanism of action that could represent a new way of addressing the Type 2 diabetes pathophysiology".*

Thomas Kuhn, CEO of Poxel added, *"These positive data reinforce Imeglimin's fully differentiated profile as a new anti-diabetic agent. No other single agent impacts the three main organs involved in this chronic disease, which means Imeglimin can be combined with any current diabetes treatments. This potential was already evidenced in two clinical trials in combination with the two most important molecules on the market today, metformin and sitagliptin. Combining treatments to control glycaemia is now at the cornerstone of Type 2 diabetes management".*

The full study results will be submitted soon to a diabetes peer-reviewed journal.

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, presented at ADA meeting in Chicago this year, are under review by a diabetes peer-reviewed journal.

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 urbanisation, dietary changes, reduced physical activity and changes in other lifestyle patterns.

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 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 II development. A direct activator of AMPK is close to phase1 development for the treatment of Type 2 diabetes.

For more information, please visit www.poxel.com

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