



Press Release

Unique Mitochondria-targeting Mechanism of Action Confirmed for Poxel's Oral Agent Imeglimin

Presentation of data at the Berlin World Congress on Targeting Mitochondria shows:

- **Imeglimin targets two aspects of mitochondria bioenergetics: the mitochondrial respiratory chain and the mitochondrial permeability transition pore (mPTP). This leads to**
 - **An improvement in insulin sensitivity and insulin secretion, thereby improving glucose control**
 - **The protection of beta and endothelial cells from oxidative stress-induced apoptosis, delaying disease progression and protecting cells against micro- and macrovascular complications**
- **Imeglimin has the potential to innovate type 2 diabetes management**

LYON, France, October 30, 2015 – POXEL SA (Euronext: POXEL), a biopharmaceutical company developing innovative drugs to treat type 2 diabetes today announced presentation of preclinical data on Imeglimin, the Company's first-in-class oral anti-diabetic agent, at the 6th World Congress on Targeting Mitochondria held October 28-30, 2015, in Berlin, Germany. Imeglimin has been proven to have a beneficial effect on both insulin sensitizing and insulin secretion defects in type 2 diabetes. The new data demonstrate the drug candidate's positive impact on the mitochondrial respiratory chain, providing critical insights to Imeglimin's molecular mechanism of action. In detail, the data demonstrate Imeglimin's ability to improve mitochondria respiratory chain the functioning, triggering an improvement of insulin and glucose sensing in the target tissues, muscle, liver and pancreas, which translates into an improvement of both insulin sensitizing and insulin secretion defects in patients suffering from type 2 diabetes.

"These results clearly demonstrate Imeglimin's innovative mechanism of action and illustrate the benefits of targeting the mitochondria to treat type 2 diabetes," said Sébastien Bolze, Ph.D., EVP Non-Clinical Development and CSO of Poxel. *"Our data confirm again that Imeglimin's profile is unique among current anti-diabetic agents."*

In the recent years, type 2 diabetes has been recognized to be a mitochondrial disease. In an oral presentation titled *"Imeglimin, a New Mitochondria Targeted Agent for Type 2 Diabetes Treatment"* the Poxel team described Imeglimin's potential to increase the mitochondrial capacity to oxidize fatty acids by favoring complex 2 substrate oxidation, while preventing the subsequent overproduction of

ROS linked to the reverse transfer of electrons. Imeglimin has thus been shown to target mitochondrial dysfunction, restoring the impaired electron flux along the respiratory chain.

This results in metabolic benefits to patients, namely improved insulin action in peripheral tissues and insulin secretion, in a glucose-dependent manner. These benefits translate into a significant reduction of Hemoglobin A1c and other glycemic parameters such as fasting and post-prandial glucose, as Poxel has demonstrated in seven Phase 2 trials to date.

The data presented at the World Congress on Targeting Mitochondria also demonstrate Imeglimin's ability to delay opening of the mitochondrial permeability transition pore (mPTP), preventing apoptotic cell death induced by various forms of oxidative stress including excess glucose, as shown in endothelial cells and human pancreatic islet cells exposed to high glucose concentrations.

Addressing mitochondrial dysfunction as an underlying, disease-causing element of type 2 diabetes, these improvements are likely to provide long-term benefits with respect to microvascular and macrovascular complications, some of the most important causes of morbidity and mortality in this devastating disease. Imeglimin with its mitochondria-targeting properties represent a unique approach to delaying type 2 diabetes progression and the occurrence of disease complications.

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 the mitochondria 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 Poxel

Poxel uses its unique development expertise in metabolism to advance a pipeline of truly novel products currently focused on type 2 diabetes. Our first-in-class lead product, Imeglimin, targeting mitochondrial dysfunction, has successfully completed Phase 2 development in the US and EU and has entered clinical development in Japanese subjects. We are advancing our second program, PXL770, a direct AMPK activator, through clinical proof-of-concept. We will generate further growth through strategic partnerships and pipeline development.

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