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Poxel Announces Publication of Imeglimin Clinical Study Results in Clinical Pharmacokinetics

- **Two drug-drug interaction studies assessed the effect of repeated co-administration of commonly prescribed medications, metformin or sitagliptin (Januvia®; Merck & Co.), with Imeglimin**
- **Repeated co-administration of Imeglimin with both medications did not result in clinically relevant changes in drug exposure levels in healthy subjects**
- **Imeglimin was observed to be safe and well tolerated in both studies**

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 and non-alcoholic steatohepatitis (NASH), today announced the publication of results from two clinical studies that evaluated the potential for drug-drug interactions of Imeglimin with two widely prescribed medications, metformin or sitagliptin. The manuscript titled, “Imeglimin Does Not Induce Clinically Relevant Pharmacokinetic Interactions When Combined with Either Metformin or Sitagliptin in Healthy Subjects,” is available online in the life sciences journal, *Clinical Pharmacokinetics* published by *Springer Nature.* To access the manuscript, please use the following link: https://rdcu.be/b3uZT.

The primary objective for the two drug-drug interaction studies was to assess the effect of repeated co-administration of metformin or sitagliptin with Imeglimin on metformin or sitagliptin pharmacokinetic parameters in healthy subjects. The secondary objectives for both studies were safety and tolerability. The results from both clinical studies demonstrated that Imeglimin was observed to be safe and well tolerated and did not show clinically relevant changes in systemic drug exposure levels.

“Type 2 diabetes is a progressive disease and involves the need for additional therapeutic agents over time. Successful management of type 2 diabetes patients who are no longer controlled by one therapy will typically progress to combination therapy using agents with complementary mechanisms of action,” said David E. Moller, MD, Chief Scientific Officer of Poxel. “The safety and tolerability profile observed with Imeglimin co-administered with metformin or sitagliptin in these studies has been consistent across several other studies evaluating Imeglimin’s use with different agents, including the pivotal Phase 3 TIMES 2 trial and two prior Phase 2 studies, which also showed the potential for additive efficacy benefits. These results highlight Imeglimin’s potential as an innovative new treatment option to complement existing anti-diabetic therapies.”

“We are committed to working with our Imeglimin partners to bringing this innovative therapy to the market. In Japan, and more broadly in Asia, we are working with Sumitomo Dainippon Pharma, and in the US and Europe, we are working with Metavant to advance Imeglimin into a Phase 3 program. Preparations are underway for the New Drug Application submission for Imeglimin in Japan, which is anticipated during the third quarter of 2020 with a target launch in 2021,” said Thomas Kuhn, CEO of Poxel. “We believe that, with its differentiated dual mechanism of action and favorable safety and tolerability profile, Imeglimin has the potential to be an important new therapeutic option to help patients manage type 2 diabetes in multiple stages of the disease.”

“Imeglimin is the first drug candidate in a new class of oral drugs targeting the mitochondrial respiratory chain, which is where the cell produces energy. These results show that Imeglimin does not induce a clinically relevant change in the pharmacokinetic profile of two important medications in the diabetes treatment armamentarium. These results are consistent with prior preclinical and longer-term clinical studies,” said Sebastien Bolze, PhD, Chief Operating Officer, Executive Vice President, Non-Clinical and Manufacturing Operations at Poxel.

Imeglimin Drug-Drug Interaction Study Designs

Study 1: Imeglimin Metformin Drug–Drug Interaction Study

In this study, 16 subjects received metformin (850 mg) twice daily (BID) together with placebo from days 1 to 6, and metformin BID together with Imeglimin (1500 mg BID) from days 7 to 12. Plasma sampling (full 24-hour profiles) occurred at several intervals from pre-dose through day 12. Urine samples were also obtained and analyzed.

Study 2: Imeglimin Sitagliptin Drug–Drug Interaction Study

In this study, 16 subjects received sitagliptin (100 mg) once daily with placebo BID from days 1 to 6, and daily sitagliptin with Imeglimin (1500 mg BID) from days 7 to 12. Plasma sampling (full 24-hour profiles) occurred at several intervals from pre-dose through day 12. Urine samples were also obtained and analyzed.

About Imeglimin

Imeglimin is a new chemical substance classified as a tetrahydrotriazine compound, and the first clinical candidate in this chemical class. Imeglimin has a unique mechanism of action (MOA) that targets mitochondrial bioenergetics. Imeglimin acts on all three key organs which play an important role in the treatment of type 2 diabetes: the pancreas, muscles, and the liver, and it has demonstrated glucose lowering benefits by increasing insulin secretion in response to glucose, improving insulin sensitivity and suppressing gluconeogenesis. This MOA has the potential to prevent endothelial and diastolic dysfunction, which can provide protective effects on micro- and macro-vascular defects induced by diabetes. It also has the potential for protective effect on beta-cell survival and function. This unique MOA offers the potential opportunity for Imeglimin to be a candidate for the treatment of type 2 diabetes in almost all stages of the current anti-diabetic treatment paradigm, including monotherapy or as an add-on to other glucose lowering therapies.

About Poxel SA

Poxel is a **dynamic biopharmaceutical company** that uses its extensive expertise in developing **innovative drugs for metabolic diseases**, with a focus on **type 2 diabetes** and **non-alcoholic steatohepatitis (NASH)**. In its mid-to-late stage pipeline, the Company is currently advancing three drug candidates as well as earlier-stage opportunities. **Imeglimin**, Poxel's first-in-class lead product, targets mitochondrial dysfunction. Together, with its partner Sumitomo Dainippon Pharma, Poxel successfully completed the Phase 3 **T**rials of **IM**eglimin for **E**fficacy and **S**afety (TIMES) program for the treatment of type 2 diabetes in Japan. Poxel also established a partnership with Roivant Sciences for Imeglimin's development and commercialization in countries outside of the partnership with Sumitomo Dainippon Pharma, including the U.S. and Europe. **PXL770**, a first-in-class direct adenosine monophosphate-activated protein kinase (AMPK) activator, is in a Phase 2a proof-of-concept program for the treatment of NASH. PXL770 could also have the potential to treat additional metabolic diseases. **PXL065** (deuterium-stabilized R-pioglitazone), a mitochondrial pyruvate carrier (MPC) inhibitor, is advancing into a Phase 2 clinical trial for the treatment of NASH. Poxel also has additional earlier-stage programs targeting metabolic, specialty and rare diseases. The Company intends to generate further growth through strategic partnerships and pipeline development. Listed on Euronext Paris, Poxel is headquartered in Lyon, France, and has subsidiaries in Boston, MA, and Tokyo, Japan. For more information, please visit: www.poxelpharma.com.

In the context of the COVID-19 outbreak, which was declared a pandemic by the World Health Organization (WHO) on March 12, 2020, the Company has undertaken a full review of the impact of the outbreak on its business. Considering the rapidly evolving situation, the Company is updating this assessment on a regular basis.

The Company anticipates that the COVID-19 pandemic could have a material negative impact on our business operations. The worldwide impact of COVID-19 may notably affect the Company's internal organization and efficiency, particularly in countries where it operates and where confinement measures have been implemented by the authorities. In addition, the deteriorating market conditions may impact the Company's ability to raise additional funding and/or to enter into partnerships. Particularly, delays in the supply of drug substance or drug products, in pre-clinical and/or clinical trials, as well as delays linked to the responsiveness of regulatory authorities could occur, which could potentially have an impact on the Company's development programs. The Company will continue to proactively monitor the situation.

All statements other than statements of historical fact included in this press release about future events are subject to (i) change without notice and (ii) factors beyond the Company's control. These statements may include, without limitation, any statements preceded by, followed by or including words such as "target," "believe," "expect," "aim," "intend," "may," "anticipate," "estimate," "plan," "project," "will," "can have," "likely," "should," "would," "could" and other words and terms of similar meaning or the negative thereof. Forward-looking statements are subject to inherent risks and uncertainties beyond the Company's control that could cause the Company's actual results or performance to be materially different from the expected results or performance expressed or implied by such forward-looking statements.

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