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# Poxel Presents Imeglimin Phase 3 TIMES Results and PXL770 Preclinical Cardio-Renal Results at the 56th European Association for the Study of Diabetes Annual Meeting

- **Phase 3 TIMES 2 and TIMES 3 trial results demonstrate that Imeglimin met its primary endpoints and objectives and was observed to exhibit a favorable safety and tolerability profile**
- **PXL770, a direct AMPK activator, was observed to improve renal and cardiac disease in a preclinical model demonstrating utility for NASH co-morbidities and additional indications driven by metabolic dysfunction**

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 that it presented Imeglimin Phase 3 results for TIMES 2 and TIMES 3 and new preclinical results for PXL770 in a cardio-renal disease model at the 56$^{th}$ European Association for the Study of Diabetes (EASD) Annual Meeting, which is being held virtually. The poster presentations can be accessed on Poxel's website using the following link: https://www.poxelpharma.com/en_us/product-pipeline/posters.

In two presentations, Phase 3 results from the Imeglimin TIMES 2 and TIMES 3 (**T**rials of **IM**eglimin for **E**fficacy and **S**afety) trials were presented. The TIMES program in Japan was a joint development effort between Poxel and Sumitomo Dainippon Pharma Co., Ltd. and it included three pivotal trials in over 1,100 patients. In all three trials, Imeglimin met its primary endpoints and objectives and was observed to exhibit a favorable safety and tolerability profile. In July 2020, a New Drug Application (NDA) was submitted by Sumitomo Dainippon Pharma in Japan and is currently under review by the Pharmaceuticals and Medical Devices Agency (PMDA) to request approval for the manufacturing and marketing of Imeglimin for the treatment of type 2 diabetes.

"Across all three TIMES trials, Imeglimin was observed to demonstrate the ability to safely and significantly reduce HbA1c as a monotherapy and in combination with insulin and other existing therapies," said Pascale Fouqueray, MD, PhD, EVP, Clinical Development and Regulatory Affairs at Poxel. "In the TIMES 2 trial, we observed clinically meaningful HbA1c reductions when Imeglimin was added to other oral approaches. The greatest efficacy

observed was an HbA1c reduction of 0.92% as an add-on to DPP4 inhibitors, suggesting that this combination of mechanisms could be a particularly important treatment option. In the TIMES 3 trial, Imeglimin also demonstrated meaningful efficacy as an add-on to insulin in patients who were not well controlled. In addition to placebo-like overall tolerability, no signal of severe hypoglycemia was observed in either trial. Based on these results, we believe that Imeglimin has the potential to treat type 2 diabetes at multiple disease stages."

In a poster session focusing on PXL770, a direct AMPK activator, results from a cardio-renal syndrome preclinical model demonstrated observed improvements in diabetic nephropathy and in diastolic cardiac dysfunction that are consistent with the prevention of disease progression in both the kidney and heart. These results demonstrate that PXL770 and direct AMPK activation may lead to broader utility for organ diseases mediated by metabolic pathway dysfunction.

"This study adds to the growing body of data that supports the continued development of our AMPK platform in both chronic and rare metabolic diseases," said David E. Moller, MD, EVP and Chief Scientific Officer at Poxel. "These results highlight PXL770's potential to treat co-morbidities related to NASH, such as cardiac diastolic dysfunction, and importantly, the potential to also target significant residual unmet medical need in patients with diabetic kidney disease. These data further validate our hypothesis for the use of AMPK activation more broadly in additional chronic metabolic diseases."

**About Imeglimin TIMES 2 and TIMES 3 Results**

**The TIMES 2 trial** evaluated Imeglimin in combination with several approved anti-hyperglycemic therapies, and as a monotherapy, for the treatment of type 2 diabetes in Japan. The 52-week, open-label, parallel-group trial, evaluated the long-term safety and efficacy of Imeglimin in 714 Japanese patients. During the trial, 1,000 mg of Imeglimin was orally administered twice-daily as an add-on to stable doses of existing approved drug classes that were both oral and injectable. Details of the combination study arms with several other oral agents are featured in the EASD presentation. These included the following (with respective changes in mean HbA1c values): DPP-4 inhibitors (-0.92%), thiazolidinediones (-0.88%), alpha-glucosidase inhibitors (-0.85%), glinides (-0.70%), metformin (a biguanide; -0.67%), SGLT-2 inhibitors (-0.57%), sulphonylureas (-0.56%). The observed robust efficacy benefits in combination with DPP-4 inhibitors are notable given that this drug class is the market leader in Japan and is prescribed to approximately 80% of treated type 2 diabetes patients.[1]

The TIMES 2 trial further strengthens Imeglimin's differentiated profile by showcasing that its dual mechanism of action of increasing insulin secretion in response to glucose and improving insulin sensitivity can result in added efficacy benefits when combined with a broad range of agents that have complementary mechanisms of action. Imeglimin was also observed to exhibit a favorable safety and tolerability profile across all treatment arms, consistent with prior trials.

**The TIMES 3 trial** evaluated Imeglimin in combination with insulin. In TIMES 3, Imeglimin was studied in a 16-week, double-blind placebo-controlled randomized period. In this portion of the trial, a mean HbA1c placebo-corrected change from baseline of -0.60% ($p<0.0001$; primary endpoint) was observed.

In the open-label extension period of TIMES 3, which was not placebo-controlled, 208 Japanese patients who completed the first 16 weeks of the study were orally administered Imeglimin 1,000 mg twice-daily as well as insulin therapy for the next 36 weeks. The HbA1c decrease observed at the end of the open-label extension period was:

- -0.64% versus baseline in patients receiving Imeglimin and insulin for 52 weeks (Imeglimin and insulin for 16 weeks followed by Imeglimin and insulin for 36 weeks).
- -0.54% versus baseline in patients receiving Imeglimin and insulin for the last 36 weeks only (placebo and insulin for 16 weeks followed by Imeglimin and insulin for 36 weeks).

Overall, the safety and tolerability profile of Imeglimin was observed to be favorable for the entire 52-week trial. In the first 16-week double-blind placebo-controlled treatment period, the incidence of treatment emergent adverse events was similar to the placebo group. In the 36-week extension period, the safety and tolerability profile was consistent with the first part of the trial. There were no episodes of severe hypoglycemia events and the majority of the hypoglycemia events reported were mild.

Sumitomo Dainippon Pharma and Poxel entered into a strategic partnership in October 2017 for the development and commercialization of Imeglimin in Japan, China, South Korea, Taiwan and nine other Southeast Asian countries.[2]

**About PXL770 Preclinical Cardio-Renal Results**

In collaboration with Professor Paul Mulder (Rouen University Medical School, Rouen, France), PXL770 was evaluated in ZSF1 rats, a model of diabetic nephropathy and metabolic disease-induced cardiac dysfunction. In this trial, PXL770 was observed to prevent disease progression. Compared to untreated ZSF1 rats, kidney function (GFR) was improved and albuminuria (urine albumin-creatinine ratio) was normalized; several indices related to left ventricular diastolic cardiac dysfunction were also ameliorated.

**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. Poxel has a strategic partnership with Sumitomo Dainippon Pharma for Imeglimin in Japan, China, South Korea, Taiwan and nine other Southeast Asian countries. A Japanese new drug application (J-NDA) is under review by the Pharmaceuticals and Medical Devices Agency (PMDA) to request approval for the manufacturing and marketing of Imeglimin for the treatment of type 2 diabetes. 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 MPC inhibitor, is in a single Phase 2 trial for the treatment of NASH. Poxel also has additional earlier-stage programs from its AMPK activator and deuterated TZD platforms targeting chronic and rare metabolic 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 is regularly reviewing the impact of the outbreak on its business.

As of the date of this press release, and based on publicly available information, the Company has not identified the occurrence of any material negative effect on its business due to the COVID-19 pandemic that remains unresolved. However, the Company anticipates that the COVID-19 pandemic could have further material negative impact on its 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 are implemented by the authorities. In addition, COVID-19 may impact market conditions and the Company's ability to seek additional funding or enter into partnerships. Particularly, delays in the supply of drug substance or drug products, in the initiation or the timing of results of preclinical 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 and partnered programs. The Company will continue to actively 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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[1] IQVIA data FY2016 and NDB data FY2016

[2] including Indonesia, Vietnam, Thailand, Malaysia, The Philippines, Singapore, Republic of the Union of Myanmar, Kingdom of Cambodia and Lao People's Democratic Republic.

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