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Poxel and Sumitomo Dainippon Pharma Announce Positive Topline Phase 3 Results from TIMES 2 Trial of Imeglimin for the Treatment of Type 2 Diabetes in Japan and Successful Completion of the Pivotal TIMES Clinical Development Program

- **Imeglimin met its key efficacy endpoint of HbA1c reduction, demonstrating how its unique dual mechanism of action was observed to show added efficacy benefits in combination with existing hypoglycemic agents**
- **In particular, Imeglimin was observed to demonstrate robust efficacy benefits in combination with DPP-4 inhibitors, the market leader in Japan and prescribed to approximately 80% of treated type 2 diabetes patients[1]**
- **Imeglimin was observed to exhibit a favorable safety and tolerability profile across all treatment arms, consistent with prior trials**
- **TIMES 2 was the third and final pivotal registration trial from Phase 3 TIMES program**
- **Imeglimin Japanese New Drug Application targeted for 2020[2] with a product launch anticipated in 2021[2]**

LYON, France & OSAKA, Japan--(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), and Sumitomo Dainippon Pharma Co., Ltd (Head Office: Osaka, Japan; Representative Director, President and CEO: Hiroshi Nomura; Securities Code: 4506, First Section of TSE), today announced positive topline results from TIMES 2, a Phase 3 trial evaluating Imeglimin in combination with approved hypoglycemic therapies, and as a monotherapy, for the treatment of type 2 diabetes in Japan. These results mark the successful conclusion of the Phase 3 program in Japan, referred to as TIMES (**T**rials of **IM**eglimin for **E**fficacy and **S**afety), which included three pivotal trials to evaluate Imeglimin's efficacy and safety in over 1,100 patients.

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"Type 2 diabetes is a progressive disease and involves the need for additional agents over

time. Successful management of type 2 diabetes patients who are no longer controlled by one therapy will progress to combination therapy using agents with complementary mechanisms of action," said Prof. Kohei Kaku, MD, PhD, Department of Internal Medicine, Kawasaki Medical School, Okayama, Japan. "In the Phase 3 TIMES 2 trial, Imeglimin was observed to demonstrate added efficacy benefits as add-on therapy to a DPP-4 inhibitor as well as other standard of care agents with different mechanisms, including metformin. The added efficacy benefits observed for Imeglimin in combination with other agents in the TIMES 2 trial combined with its favorable safety and tolerability profile, highlight Imeglimin's potential as an innovative new treatment option to complement other existing hypoglycemic therapies."

The TIMES 2 trial further strengthens Imeglimin's differentiated profile showcasing that its dual mechanism of action of increasing insulin secretion in response to glucose and improving insulin sensitivity was observed to show added efficacy benefits, especially with agents that have complementary mechanisms of action. In the 52-week, open-label, parallel-group trial, which evaluated the long-term safety and efficacy of Imeglimin in 714 Japanese patients with type 2 diabetes, 1,000 mg of Imeglimin was orally administrated twice daily in combination with existing hypoglycemic agents, including a DPP-4 inhibitor, a thiazolidine, an alpha-glucosidase inhibitor, a glinide, a biguanide, a SGLT-2 inhibitor, a sulphonylurea, and an injectable GLP1 receptor agonist or as monotherapy. The TIMES 2 trial, which was open-label and not placebo-controlled, was observed to show a glycated hemoglobin A1c (HbA1c) decrease from baseline at the end of the 52-week treatment (LS mean) period of:

- -0.92% versus baseline with Imeglimin as an add on to a DDP-4 inhibitor
- -0.88% versus baseline with Imeglimin as an add on to a thiazolidine
- -0.85% versus baseline with Imeglimin as an add on to an alpha-glucosidase inhibitor
- -0.70% versus baseline with Imeglimin as an add on to a glinide
- -0.67% versus baseline with Imeglimin as an add on to a biguanide
- -0.57% versus baseline with Imeglimin as an add on to a SGLT2 inhibitor
- -0.56% versus baseline with Imeglimin as an add on to a sulphonylurea
- -0.12% versus baseline with Imeglimin as an add on to a GLP1 receptor agonist
- -0.46% versus baseline with Imeglimin as monotherapy

In addition, the TIMES 2 trial met another important efficacy endpoint and was observed to show a decrease in fasting plasma glucose (FPG) that was consistent with the reduction in HbA1c, except in the GLP1 group, which showed a stronger reduction in FPG when compared to the observed decrease in HbA1c.

In addition, the HbA1c and FPG decrease for Imeglimin as monotherapy were similar to previous studies in this population when measured from baseline (not placebo controlled), such as the Phase 2b trial in Japan.

In this trial, Imeglimin demonstrated a favorable safety and tolerability profile that was observed across all arms of the study. In addition, the adverse event profile was consistent with what was observed in the TIMES 1 monotherapy trial, the TIMES 3 trial in combination with insulin and prior clinical studies of Imeglimin.

"The TIMES 2 results represent a significant milestone for Imeglimin, with the completion of our robust Phase 3 program in Japan. Across all three pivotal TIMES trials, Imeglimin was observed to demonstrate the ability to safely and significantly reduce HbA1c, as a

monotherapy, in combination with insulin and now in combination with other existing therapies," said Thomas Kuhn, CEO of Poxel. “Taken together, these results feature Imeglimin’s potential to treat type 2 diabetes at multiple stages of the disease. We are working very closely with our partner Sumitomo Dainippon Pharma in activities to complete and submit the Japanese New Drug Application in 2020[3], and to deliver this promising drug candidate to patients in 2021[3].”

The TIMES program is a joint development effort between Poxel and Sumitomo Dainippon Pharma. The companies 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 and East Asian countries.[4]

“These positive results reinforce our observations from the TIMES 1 and TIMES 3 studies, and continue to demonstrate the efficacy benefits of Imeglimin, especially in combination with other approved therapies that have complementary mechanisms of action,” said Nobuhiko Tamura, Member, Board of Directors, Senior Executive Officer; Drug Development Division of Sumitomo Dainippon Pharma. “We believe that Imeglimin has the potential with its differentiated dual mechanism of action and favorable safety and tolerability profile to be an important addition to our existing diabetes franchise and could specifically complement our DDP-4 inhibitor and biguanide. We are committed to delivering new therapeutic options to help patients manage their disease.”

Poxel anticipates submitting the full data results from the Phase 3 TIMES 2 trial for presentation at a scientific meeting 2020.

Conference Call Information:
Poxel will host a conference call to discuss the results later today. To access the information please click this link or refer to Poxel’s website.

About the TIMES Program
TIMES (**T**rials of **Im**eglimin for **E**fficacy and **S**afety), the Phase 3 program for Imeglimin for the treatment of type 2 diabetes in Japan, consists of three pivotal trials involving over 1,100 patients. The TIMES program includes the following three trials performed using the dose of 1,000 mg twice daily:

TIMES 1: A Phase 3, 24-week, double-blind, placebo-controlled, randomized, monotherapy trial that assessed the efficacy, safety and tolerability of Imeglimin in Japanese patients with type 2 diabetes, using the change in HbA1c as the primary endpoint. Secondary endpoints of the trial included fasting plasma glucose, other standard glycemic and non-glycemic parameters. The TIMES 1 trial met its primary and secondary endpoints and the topline results were reported on April 9, 2019.

TIMES 2: A Phase 3, 52-week, open-label, parallel-group trial that assessed the long-term safety and efficacy of Imeglimin in Japanese patients with type 2 diabetes. In this trial, Imeglimin was administrated orally as combination therapy with existing hypoglycemic agents, including a DPP-4 inhibitor, a SGLT2 inhibitor, a biguanide, a sulphonylurea, a glinide, an alpha-glucosidase inhibitor, a thiazolidine and a GLP1 receptor agonist or as monotherapy.

TIMES 3: A Phase 3, 16-week, double-blind, placebo-controlled, randomized trial with a 36-

week open-label extension period that evaluated the efficacy and safety of Imeglimin in combination with insulin in Japanese patients with type 2 diabetes and inadequate glycemic control on insulin therapy. The TIMES 3 16-week portion of the trial met its primary endpoint and the topline results were reported on June 25, 2019. The TIMES 3 36-week open-label extension period met its primary objective and the topline results were reported on November 26, 2019.

About Imeglimin

Imeglimin is a new chemical substance classified as a tetrahydrotriazine compound, and the first clinical candidate in a 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 is conducting 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.

About Sumitomo Dainippon Pharma
Sumitomo Dainippon Pharma defines its corporate mission as "to broadly contribute to society through value creation based on innovative research and development activities for the betterment of healthcare and fuller lives of people worldwide". By pouring all our efforts into the research and development of new drugs, we aim to provide innovative and effective pharmaceutical solutions to people not only in Japan but also around the world in order to

realize our corporate mission. Sumitomo Dainippon Pharma aims to create innovative pharmaceutical products in the Psychiatry & Neurology area, the Oncology area and Regenerative Medicine & Cell Therapy, which have been designated as the focus research areas. Sumitomo Dainippon Pharma has also positioned Psychiatry & Neurology, Diabetes and Specialty as our focus marketing areas in Japan. For more detail, please visit our website. (URL:https://www.ds-pharma.com)

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] Year noted is Fiscal Year from April to March, which is Sumitomo Dainippon Pharma's Fiscal Year.

[3] Year noted is Fiscal Year from April to March, which is Sumitomo Dainippon Pharma's Fiscal Year.

[4] 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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