June 25, 2019

Poxel and Sumitomo Dainippon Pharma Announce Second Positive Top-Line Results for Imeglimin Phase 3 Trial (TIMES 3) in Japan for the Treatment of Type 2 Diabetes

- **Imeglimin in combination with insulin Phase 3 TIMES 3 16-week, double-blind, placebo-controlled, randomized part of the trial met its primary endpoint with a favorable safety and tolerability profile**
- **TIMES 3 16-week data is the second positive readout from the three pivotal trials of the TIMES program in Japan**
- **Phase 3 results from the TIMES 2 and 36-week open-label extension part of TIMES 3 are anticipated around the end of 2019**
- **Imeglimin Japanese New Drug Application (JNDA) targeted for 2020**
- **The Japanese diabetes market is fast-growing and anticipated to reach approximately $6B by 2020[1]**

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), announced today positive top-line Phase 3 data results for the Imeglimin TIMES 3 16-week, double-blind, placebo-controlled, randomized part of the trial for the treatment of type 2 diabetes in Japan. Referred to as TIMES (**T**rials of **IM**eglimin for **E**fficacy and **S**afety), the Imeglimin Phase 3 program in Japan includes three pivotal trials to evaluate Imeglimin's efficacy and safety in over 1,100 patients.

"I am very excited to contribute to the development of a new and innovative potential treatment option for Japanese patients with type 2 diabetes," said Professor Hirotaka Watada, MD, PhD, Professor, Department of Medicine, Metabolism and Endocrinology, Juntendo University Graduate School of Medicine, Tokyo, Japan. "Imeglimin's safety profile combined with its unique mechanism of action that targets very important deficiencies occurring in diabetes, could be helpful for Japanese patients treated with insulin to further manage their advanced disease."

The TIMES 3 16-week, double-blind, placebo-controlled, randomized part of the trial

evaluated efficacy and safety of Imeglimin in 215 patients. In this trial, Imeglimin 1,000 mg was orally administered twice-daily in combination with insulin in Japanese patients with type 2 diabetes and inadequate glycemic control on insulin therapy versus patients administered placebo and insulin. The TIMES 3 trial was observed to demonstrate efficacy and achieved statistical significance ($p<0.0001$) for its primary endpoint, defined as a change of glycated hemoglobin A1c (HbA1c) from baseline versus placebo at week 16, with a mean HbA1c placebo-corrected change from baseline of -0.60%.

In this trial, the overall safety and tolerability of Imeglimin was similar to placebo. A similar number of patients experienced hypoglycemia with Imeglimin compared to the placebo group with a fixed insulin daily dose as defined in the protocol. There were no severe hypoglycemia events and the majority of the hypoglycemia events reported were mild. In addition, the adverse event profile was similar to placebo and consistent with what was observed in the Phase 3 TIMES 1 monotherapy trial and other Imeglimin clinical trials. Additional analyses of the trial, including secondary endpoints, is ongoing and the results of the 36-week open-label extension part of TIMES 3 are anticipated around the end of 2019.

"Despite efforts to manage type 2 diabetes with diet and oral agents, many patients transition to insulin therapy as a natural part of the disease progression. For patients with type 2 diabetes who are inadequately controlled on insulin alone, TIMES 3 data show that Imeglimin has the potential to be a new treatment option that could significantly reduce HbA1c with a favorable safety and tolerability profile," said Christophe Arbet-Engels, MD, PhD, Chief Medical Officer, Executive Vice President Late Development and Medical Affairs at Poxel. “The TIMES 3 16-week results are the second positive readout from the three pivotal trials in the TIMES program and follow the positive TIMES 1 monotherapy results announced in April 2019. We are working very closely with our partner Sumitomo Dainippon Pharma in preparing for the Japanese New Drug Application and these results bring us one step closer to achieving that goal.”

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.[2]

“Our commitment to diabetes patients is to continue to innovate and provide new therapeutic options to help them manage their disease. We are very pleased with the positive results for TIMES 1 and the TIMES 3 16-week part of the trial, and to be working closely with Poxel on the TIMES clinical trials,” said Nobuhiko Tamura, Member, Board of Directors, Senior Executive Officer; Drug Development Division of Sumitomo Dainippon Pharma. “Diabetes is a significant area for our company in Japan and we believe that Imeglimin will be a very important addition to our existing diabetes franchise.”

Poxel anticipates presenting full data results from the Phase 3 TIMES 3 16-week portion of the trial at an upcoming scientific meeting.

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 that will be performed using the dose of 1,000 mg twice daily:

TIMES 1: A Phase 3, 24-week, double-blind, placebo-controlled, randomized, monotherapy trial to assess 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 include fasting plasma glucose, other standard glycemic and non-glycemic parameters. The TIMES 1 trial met its primary and secondary endpoints and the top-line data was reported on April 9, 2019.

TIMES 2: A Phase 3, 52-week, open-label, parallel-group trial to assess the long-term safety and efficacy of Imeglimin in Japanese patients with type 2 diabetes. In this trial, Imeglimin will be administrated orally as a monotherapy or combination therapy with existing hypoglycemic agents, including a DPP4 inhibitor, SGLT2 inhibitor, biguanide, sulphonylurea and GLP1 receptor agonist.

TIMES 3: A Phase 3, 16-week, double-blind, placebo-controlled, randomized trial with a 36-week open-label extension period to evaluate the efficacy and safety of Imeglimin in combination with insulin in Japanese patients with type 2 diabetes and inadequate glycemic control on insulin therapy.

About Imeglimin
Imeglimin is the first clinical candidate in a new chemical class of oral agents called Glimins by the World Health Organization. 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 liver, muscles and the pancreas, 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 uses its development expertise in metabolism to advance a pipeline of drug candidates focused on the treatment of metabolic disorders, including type 2 diabetes and non-alcoholic steatohepatitis (NASH). We have successfully completed the Phase 2 clinical program for our first-in-class lead product, Imeglimin, which targets mitochondrial dysfunction, in the U.S., Europe and Japan. Together, with our partner Sumitomo Dainippon Pharma, we are conducting the Phase 3 Trials of IMeglimin for Efficacy and Safety (TIMES) program for the treatment of type 2 diabetes in Japan. Our partner Roivant Sciences is responsible for Imeglimin’s development and commercialization in countries outside of Poxel’s 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 in Phase 1 and

being developed for the treatment of NASH. Poxel also has additional earlier-stage programs, including deuterated drug candidates for metabolic, specialty and rare diseases. We intend to generate further growth through strategic partnerships and pipeline development. (Euronext: POXEL, 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. (https://www.ds-pharma.com/)

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[1]Source: Oppenheimer & Co. estimates.

[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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