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# Poxel and Sumitomo Dainippon Pharma Announce Positive Top-Line Results for Imeglimin Phase 3 Trial (TIMES 1) in Japan for the Treatment of Type 2 Diabetes

- **Imeglimin Phase 3 trial (TIMES 1) met its primary and main secondary endpoints**
- **Imeglimin Phase 3 TIMES 3 16-week, double-blind, placebo controlled, randomized part of the trial is expected to report data mid-year and TIMES 2 and full results from the TIMES 3 trials are anticipated to report top-line results 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 1 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.

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"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 Kohjiro Ueki, MD, PhD, Director, Diabetes Research Center, the National Center for Global Health and Medicine, Tokyo, Japan. "Imeglimin's safety profile combined with its unique mechanism of action that targets very important deficiencies occurring in diabetes, namely beta-cell function, as well as insulin resistance, could be helpful for Japanese patients to manage their disease."

The TIMES 1 randomized, double-blind, placebo-controlled monotherapy trial orally administered 1,000 mg of Imeglimin twice-daily versus placebo for 24 weeks in 213 Japanese patients. The TIMES 1 trial demonstrated robust efficacy and achieved statistical significance ($p<0.0001$) for its primary endpoint, defined as a change of glycated hemoglobin A1c (HbA1c) versus placebo at week 24, with an HbA1c placebo-corrected mean change from baseline of -0.87%.

For the trial's main secondary endpoint of a decrease from baseline in fasting plasma glucose (FPG), Imeglimin achieved statistical significance ($p<0.0001$) versus placebo at week 24, with a FPG placebo-corrected mean change from baseline of -19 mg/dL. Analyses of data for the additional secondary endpoints are ongoing. In this trial, the overall safety and tolerability of Imeglimin was similar to placebo and the adverse event profile was consistent with what was observed in the Phase 2b trial in Japan and the U.S. and European Phase 1 and 2 programs.

"This is a significant milestone for Poxel and for the development of our most advanced drug candidate. The TIMES 1 results confirm the robust efficacy combined with favorable safety observed in the Phase 2b trial in Japan and the potential benefits that Imeglimin can bring to type 2 diabetes patients globally," said Thomas Kuhn, CEO of Poxel. "The TIMES 1 data is the first major step towards filing the Japanese New Drug Application in 2020. Japan represents the second largest single market for type 2 diabetes and, Asia, in broader terms, is considered the most important geographic location with regards to treating the diabetes pandemic in the future."

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 TIMES 1 data results and to be working closely with Poxel on the TIMES clinical trials,” said Nobuhiko Tamura, 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 data results from the Phase 3 (TIMES 1) 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.

**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. (URL: 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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