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Poxel Announces Fourth Quarter and Full Year 2018 Financial Update

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 its cash position and revenue for the fourth quarter and the twelve months ended December 31, 2018.

As of December 31, 2018, cash and cash equivalents were EUR 66.7 million (USD 76.4 million).

Poxel reported revenues of EUR 19.6 million for the quarter ended December 31, 2018 and EUR 74.6 million for the twelve months ended December 31, 2018 compared with revenues of EUR 5.3 million during the same period in 2017.

EUR millions	Q1 2018	Q2 2018	Q3 2018	Q4 2018	**FY 2018 12 months**	Q1 2017	Q2 2017	Q3 2017	Q4 2017	**FY 2017 12 months**
Roivant Agreement	8.1	-	-	.1	**8.2**	-	-	-	-	**-**
Sumitomo Agreement	10.2	19.2	17.5	19.5	**66.4**	-	-	-	5.3	**5.3**
Total revenues	18.3	19.2	17.5	19.6	**74.6**	-	-	-	5.3	**5.3**

Unaudited data

The revenue reflects a portion of the EUR 36 million upfront payment received from Sumitomo Dainippon Pharma relating to the strategic corporate partnership announced on October 30, 2017 and the USD 35 million (EUR 28 million) upfront payment associated with the corporate partnership announced with Roivant Sciences on February 12, 2018, net of Poxel's financial contribution to Roivant. In addition, the revenue also reflects the Imeglimin Phase 3 program costs in Japan incurred during the twelve months ended December 31, 2018 that were re-invoiced to Sumitomo Dainippon Pharma. Both the upfront payment from Sumitomo Dainippon Pharma and re-invoiced costs of the Phase 3 **T**rials of **IM**eglimin for **E**fficacy and **S**afety (TIMES) program are recognized according to the percentage of completion for this program.

"I am very pleased to report that we made substantial progress advancing the Company in 2018. Our significant accomplishments include signing an agreement with Roivant Sciences

for Imeglimin in the US, Europe and the rest of the world not covered in the agreement with Sumitomo Dainippon Pharma, fully enrolling all three Imeglimin Phase 3 TIMES trials with over 1,100 patients in Japan, advancing PXL770 for the treatment of NASH and acquiring PXL065, a second clinical-stage program for the treatment of NASH," said Thomas Kuhn, CEO of Poxel.

"This year will be very important for Imeglimin beginning early in the second quarter with the Phase 3 TIMES 1 monotherapy double-blind placebo-controlled randomized efficacy top-line results, which will be followed by top-line data for the TIMES 3 16-week double-blind placebo-controlled randomized part of the study expected mid-year. For the TIMES 2 and the full TIMES 3 data, including the additional 36-week open-label part of the study, top-line results are anticipated during the fourth quarter of 2019. In parallel to leading the Phase 3 TIMES program, we have been working very closely with our partner Sumitomo Dainippon Pharma in preparing for the Japanese New Drug Application for Imeglimin for the treatment of type 2 diabetes, which is targeted for 2020," said Thomas Kuhn, CEO of Poxel. "For the United States and Europe, we are collaborating with Roivant Sciences and Metavant, a company formed by Roivant Sciences to develop innovative therapies for metabolic disorders, on advancing the Imeglimin clinical program. This program will initially target patients with type 2 diabetes and moderate-to-severe chronic kidney disease (CKD stages 3b/4) and includes a dedicated clinical trial that is currently ongoing."

"In addition, PXL770 for the treatment of NASH is expected to enter a Phase 2a program during the first quarter of 2019. For PXL065, we plan to initiate the Phase 2 program for the treatment of NASH during second half of 2019 following the completion of the Phase 1 program," continued Thomas Kuhn. "We have expanded our presence in NASH and are one of only a few biotech companies with two clinical programs in development in this therapeutic area. The underlying pathophysiological mechanisms that contribute to the development and progression of nonalcoholic fatty liver disease and NASH are highly complex and support the need for the development of novel therapies acting on different targets. Both of our programs have the potential to be developed as a monotherapy or in combination together or with other agents."

Planned Presentations and Participation at the Following Upcoming Events
BIO Asia, March 5-6, 2019, Tokyo, Japan
Oppenheimer 29th Annual Healthcare Conference, March 19-20, 2019, New York City

Next Financial Press Release: Full Year 2018 Financial Statement expected on March 21, 2019

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 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 study 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 will include other standard glycemic and non-glycemic parameters.

TIMES 2: A Phase 3, 52-week, open-label, parallel-group study to assess the long-term safety and efficacy of Imeglimin in Japanese patients with type 2 diabetes. In this study, 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 study 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 PXL770
PXL770 is a first-in-class direct adenosine monophosphate-activated protein kinase (AMPK) activator. AMPK is a central regulator of multiple metabolic pathways leading to the control of lipid metabolism, glucose homeostasis and inflammation. Based on its central metabolic role, targeting AMPK offers the opportunity to pursue a wide range of indications to treat chronic metabolic diseases, including diseases that affect the liver, such as non-alcoholic steatohepatitis (NASH)[1].

About PXL065
PXL065, formerly DRX-065, is deuterium-stabilized R-pioglitazone. Pioglitazone is the most extensively studied drug for NASH and has demonstrated “resolution of NASH without worsening of fibrosis” in a Phase 4 trial[2]. Pioglitazone is the only drug recommended for biopsy-proven NASH patients by the Practice Guidelines published by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL).[3] Pioglitazone’s use for NASH, however, has been limited due to the PPARγ-related side effects, which include weight gain, bone fractures and fluid retention.

Pioglitazone is a 1:1 mixture of two mirror-image compounds (R- and S-stereoisomers) that interconvert *in vivo*. Using deuterium, DeuteRx stabilized each stereoisomer and characterized their dramatically different pharmacological properties. In *in vitro* studies, PXL065 has been shown to target MPC as an inhibitor. In preclinical models, PXL065 exhibits the anti-inflammatory activity and NASH efficacy associated with pioglitazone with little or no weight gain or fluid retention, side effects which are associated with the S-stereoisomer. Based upon preclinical and Phase 1 results to date, PXL065 is expected to

exhibit a better therapeutic profile than pioglitazone for NASH.

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 **T**rials of **IM**eglimin for **E**fficacy and **S**afety (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 advancing into 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)

1. Source: Smith B. K et al., (2016) Am J Physiol Endocrinol Metab 311, E730 – E740
2. Cusi, *et al*., Ann Intern Med. 2016, 165(5), 305-315
3. J Hepatol. 2016, 64(6),1388-402; Hepatology 2018, 67, 328-357

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