March 21, 2019

Poxel Reports Financial Results for Full Year 2018 and Provides Corporate Update

- **Executed strategic agreement for Imeglimin with Roivant Sciences; potential for up to USD 600 million in regulatory and development milestone payments and sales-based payments plus royalties on net sales**
- **Roivant concurrently invested USD 15 million (approximately EUR 12 million) in Poxel through subscription in newly-issued ordinary shares at EUR 8.5 per share**
- **Phase 3 TIMES program for Imeglimin in Japan with partner Sumitomo Dainippon Pharma on track with initial data results anticipated beginning early second quarter 2019**
- **Expanded metabolic pipeline through acquisition of PXL065 (DRX-065), a novel, clinical-stage drug candidate for NASH, and other programs from DeuteRx LLC**
- **PXL770 and PXL065, clinical-stage programs for the treatment of NASH, continue to advance in development**

Poxel will host an investor conference call today to discuss the Full Year 2018 results at 2:30 pm EDT (7:30 pm CET). To participate in the call, please use the dial-in numbers: US: +1 646-722-4916 France: +33 (0) 172727403 UK: + 442071943759 Access Code: 89356541#. For a replay of the call, please use: US: +1 646-722-4969 FR: +33 (0)1 70710160 UK: +44 203364 5147 Access Code: 418836924#

LYON, France--(BUSINESS WIRE)-- POXEL S.A. (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), announced today its results for the year ended December 31, 2018 and provided a corporate update.

“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 Poxel. There will be several significant milestones that have the potential for substantial value creation. For Imeglimin, key milestones include the

announcement of Phase 3 data results beginning early second quarter with the TIMES 1 results and further Phase 3 data from the TIMES 2 and TIMES 3 studies, which will be reported on throughout 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 a significant milestone targeted for 2020 with product launch anticipated in 2021," said Thomas Kuhn, CEO of Poxel.

"For our two clinical-stage programs for the treatment of NASH, key milestones include, initiation of a Phase 2a program for PXL770, which will include efficacy and safety assessment as well as a separate pharmacokinetic and pharmacodynamic study. Data results from these studies are anticipated to be announced beginning later this year," continued Thomas Kuhn. "For PXL065, we plan to initiate a pivotal Phase 2 program for the treatment of NASH in the fourth quarter or early 2020 following completion of the Phase 1 program mid-year to third quarter 2019."

Poxel 2018 Highlights

Imeglimin

Imeglimin is the first orally available drug candidate that simultaneously targets all three key organs affected by diabetes: the pancreas, the liver and the muscles. It has completed Phase 1 and Phase 2 development in over 1,200 subjects in the U.S., Europe and Japan and is in Phase 3 development in Japan. Over the course of 2018, Imeglimin successfully completed several important milestones.

Strategic Partnership Signed for Imeglimin in the U.S., Europe and Additional Countries Worldwide

- The strategic agreement with Roivant for the development and commercialization of Imeglimin in the U.S., Europe and additional countries worldwide will support Imeglimin's development and commercialization in the U.S., Europe and other countries outside of Poxel's partnership with Sumitomo Dainippon Pharma.
- To support the initiation of the Phase 3 program, activities in 2018 with Metavant, a subsidiary of Roivant, include an ongoing study in type 2 diabetes patients with moderate-to-severe chronic kidney disease, as well as manufacturing of the drug product for use in the Phase 3 program.
- The goal is for Metavant to initiate the Phase 3 program in 2019.

Progression of the Phase 3 TIMES Program

- Referred to as TIMES (**T**rials of **IM**eglimin for **E**fficacy and **S**afety), the Imeglimin Phase 3 program in Japan enrolled three pivotal trials to evaluate Imeglimin's efficacy and safety in over 1,100 patients.
- Phase 3 data results for the TIMES program are expected to be announced in 2019 beginning with TIMES 1 top-line results, which are expected early second quarter. The TIMES 3 16-week, double-blind, placebo controlled, randomized part of the study is anticipated to report top-line data mid-year and the TIMES 2 and full results from the

TIMES 3 trials are anticipated in the fourth quarter of 2019.

- The TIMES 1 trial is a multicenter, double-blind, placebo-controlled, randomized, monotherapy study in over 200 Japanese patients with type 2 diabetes. The TIMES 2 trial is an open-label study to assess the long-term safety and efficacy of Imeglimin administered as a monotherapy or combination therapy with existing hypoglycemic agents in approximately 700 Japanese patients with type 2 diabetes. The TIMES 3 trial is a double-blind, placebo-controlled, randomized study with an open-label extension period to evaluate the efficacy and safety of Imeglimin in combination with insulin in over 200 Japanese patients with type 2 diabetes and inadequate glycemic control on insulin therapy.

Data at the American Diabetes Association 78th Scientific Sessions

- Data on Imeglimin's effect on pancreatic beta-cell protection was presented at the American Diabetes Association 78th Scientific Sessions. Imeglimin was observed to protect and preserve human beta-cells from cell death from fructose- and glucose-induced toxicity by inhibiting mitochondrial Permeability Transition Pore opening (mPTP). This data highlights Imeglimin's potential to delay type 2 diabetes disease onset and progression through the preservation of beta-cell mass.

PXL770

PXL770 is a first-in-class direct adenosine monophosphate-activated protein kinase (AMPK) activator. AMPK plays a key role as a master regulator of cellular energy and modifying its activity offers the opportunity to pursue a wide range of indications to treat chronic metabolic diseases, including diseases that affect the liver, such as NASH.

- Preclinical proof-of-concept data presented at the Global NASH Congress 2018 highlighted PXL770 as a novel therapeutic approach in non-alcoholic fatty liver diseases (NAFLD), improving core disease symptoms. PXL770 was observed to significantly reduce liver steatosis and NAS score following eight weeks of treatment vs control and significantly reduce expression of a panel of key genes associated with fibrosis.
- Data presented at the American Association for the Study of Liver Diseases (AASLD) meeting in November 2018 showed a beneficial effect for PXL770 on both the adipose tissue and liver through direct activation of AMPK in a DIO-NASH model.
- Data presented at the AMPK - From Mechanisms to New Therapies Scientific Congress in October 2018 showed PXL770 was observed to have a favorable pharmacokinetic, tolerability and safety profile in the Phase 1 clinical program and demonstrated a favorable cardiac safety profile in animal models.
- The Phase 2a program for PXL770 is expected to begin during the first quarter of 2019. The twelve-week Phase 2a efficacy and safety study will measure the change in liver fat mass based on magnetic resonance imaging-estimated proton density fat fraction (MRI-PDFF) and assess the effects of PXL770 on key metabolic pathways involved in the physiopathology of NASH, as well as safety and other metabolic and non-metabolic parameters in approximately 100 patients who likely have NASH.
- Also included in the Phase 2a program will be a separate pharmacokinetic and

pharmacodynamic study that is expected to be initiated during the second quarter of 2019.

PXL065 (DRX-065)

PXL065 (deuterium-stabilized R-pioglitazone) is a mitochondrial pyruvate carrier (MPC) inhibitor. PXL065 is the R-stereoisomer (single isomer) of pioglitazone.

- On August 30, 2018, Poxel acquired from DeuteRx exclusive, worldwide ownership of PXL065 (deuterium-stabilized R-pioglitazone), as well as additional programs, including deuterated drug candidates for metabolic, specialty and rare diseases. PXL065 is a clinical-stage program for the treatment of NASH.
- Poxel paid DeuteRx an upfront payment composed of EUR 6.8 million (USD 8 million) in cash plus 1.29 million in new ordinary shares of Poxel common stock, representing 4.99 percent of Poxel's issued capital. DeuteRx is also eligible to receive development, regulatory and sales-based milestone payments and royalties on net sales.
- Data presented for PXL065 at the AASLD meeting in November 2018 suggest the potential for similar efficacy with a reduced side effect profile from pioglitazone for NASH.
- On November 26, 2018, Poxel initiated Part 2 of the Phase 1a study for PXL065. The second part of the Phase 1a study enrolled six healthy subjects per group, with a primary objective to assess safety and tolerability and a secondary objective to assess dose proportionality.
- Following the completion of the Phase 1 program, which will include a multiple ascending dose study, Poxel plans to advance PXL065 into a pivotal Phase 2 program for the treatment of NASH in the fourth quarter of 2019 or early 2020.

Corporate Update

- In September 2018, Poxel appointed Takashi Kaneko, MD, PhD, as Senior Vice President Medical and President of Poxel Japan K.K. In addition, Poxel also established a Japanese subsidiary in Tokyo.

Financial Statements for Full Year 2018 (IFRS Standards) Revenue

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

Revenues in 2018 were comprised of 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 a 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 required USD 25 million (EUR 20.5 million) financial contribution to Roivant, as well as 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.

Income Statement

Poxel devotes the bulk of its resources to research and development (R&D) activities. R&D expenses totaled EUR 54.5 million in 2018, as compared to EUR 21.0 million in 2017. R&D expenses in 2018 mainly reflected the EUR 46 million clinical study costs incurred for the Imeglimin Phase 3 TIMES program over the period, which were mostly re-invoiced to Sumitomo Dainippon Pharma. To a lesser extent, they also reflect the clinical study costs incurred for PXL770 and PXL065, the Company's two clinical-stage programs for NASH. The 160% increase in R&D expenses in 2018, as compared to 2017, is primarily driven by the Phase 3 TIMES program that was initiated in late December 2017.

R&D costs are net of the R&D Tax Credit (CIR) that resulted in income of EUR 3.6 million in 2018, as compared to EUR 3.1 million in 2017.

General and administrative expenses totaled EUR 7.5 million in 2018, as compared to EUR 6.2 million in 2017.

The financial income amounted to a gain of EUR 1.1 million in 2018, as compared to a loss of EUR 0.4 million in 2017. The gain in financial income in 2018 reflects foreign exchange fluctuations and income from financial investments.

The net result for the financial period ending December 31, 2018 was a net income of EUR 13.5 million, as compared to a net loss of EUR 22.3 million in 2017.

Condensed Income Statement *In thousand €*

	FY18	**FY17**
Turnover	**74,605**	**5,290**
Net research and development expenses*	(54,540)	(20,973)
General and administrative expenses	(7,527)	(6,219)
Operating gain (loss)	12,538	(21,902)
Financial income (expenses)	1,064	(396)
Income Tax	(77)	
Net income (loss)	**13,525**	**(22,298)**

*Net of R&D tax credit

The audit procedures have been performed and the certification report is in process.

Cash

As of December 31, 2018, cash and cash equivalents were EUR 66.7 million (USD 76.4 million), as compared to EUR 53.4 million (USD 64.1 million) as of December 31, 2017.

This figure includes the upfront payment and investment proceeds received from Roivant Sciences in February 2018 for a total amount of USD 50 million, as well as the acquisition of the deuterated drug candidates from DeuteRx for a USD 8 million upfront payment.

Next financial press release: Q1-turnover and cash position April 8, 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 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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