August 26, 2019

Poxel Reports Financial Results for First Half 2019 and Provides Corporate Update

- **Positive Phase 3 top-line results were reported for Imeglimin TIMES 1 and TIMES 3 16-week portion of the trial for the treatment of type 2 diabetes in Japan; Results from TIMES 2 and TIMES 3 36-week open label portion of the trial are expected around the end of 2019**
- **Positive top-line results were reported from Imeglimin Metavant trial in patients with type 2 diabetes and chronic kidney disease (CKD) stages 3b/4; Metavant aims to initiate a Phase 3 program in patients with type 2 diabetes and CKD stages 3b/4 in the U.S. and Europe**
- **A Phase 2a program for PXL770 was initiated for the treatment of NASH; PK/PD results are expected in Q4 2019 and Phase 2a efficacy and safety results are expected in Q2 2020**
- **A Phase 1a trial reported 15 mg of PXL065 was observed to have the potential to provide an improved therapeutic profile over 45 mg Actos® (pioglitazone); a Phase 1b multiple ascending dose trial for PXL065 is expected to be initiated in Q3 2019 with results expected in Q4 2019. PXL065 is being developed for the treatment of NASH**
- **Poxel will meet with U.S. FDA in Q4 2019 to discuss next steps for PXL065, including a registration program and use of Actos® data for a 505(b)(2) registration pathway**

Poxel will host an investor conference call today to discuss the Half Year 2019 results at 2:00 pm EDT (7:00 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: 63877744#. For a replay of the call, please use: US: +1 646-722-4969 FR: +33 (0)1 70710160 UK: +44 203364 5147 Access Code: 418869005#.

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 results for the period ended June 30, 2019. As of June 30, 2019, cash and cash equivalents were EUR 49.8 million (USD 56.7 million), as compared to EUR 66.7 million (USD 76.4 million) as of December 31, 2018. Cash and cash equivalents net of financial liabilities were EUR 41.1 million as of June 30, 2019, as compared to EUR 52.5 million as of December 31, 2018.

“Substantial progress continues to be made in the development of Imeglimin for the treatment of type 2 diabetes in Japan, the U.S. and Europe. We achieved two significant milestones when we reported positive top-line results for Imeglimin from both the Phase 3 TIMES 1 and TIMES 3 trials in Japan. Preparation for the Japanese New Drug Application with our partner, Sumitomo Dainippon Pharma, continues and is targeted for 2020, with a product launch anticipated for 2021,” said Thomas Kuhn, CEO of Poxel. “Metavant is also making progress advancing Imeglimin in the U.S. and Europe and positive top-line results were recently reported from a trial in patients with type 2 diabetes and chronic kidney disease stages 3b/4. Metavant aims to advance Imeglimin into a Phase 3 program in this specific patient population.”

“In parallel, using our extensive expertise in metabolic drug development, we are making progress advancing our two clinical programs for the treatment of NASH. A Phase 2a program for PXL770 is underway to further demonstrate its potential in NASH and validate our hypothesis for AMPK activation more broadly,” said Thomas Kuhn, CEO of Poxel. “In addition, we will meet with the U.S. Food and Drug Administration in the fourth quarter to discuss next steps for PXL065 in the treatment of NASH, including a registration program and the use of Actos® data for a 505(b)(2) registration pathway, which has the potential for an expediated development timeline.”

Clinical Development Highlights

Imeglimin Update (Type 2 Diabetes)

- During the second quarter of 2019, Poxel and Sumitomo Dainippon Pharma reported positive top-line results for the Phase 3 TIMES 1 (**T**rials of **Im**eglimin for **E**fficacy and **S**afety), and TIMES 3 16-week portion of the trial for the treatment of type 2 diabetes in Japan.

- Full data results from the Phase 3 TIMES 1 trial will be presented at the 55th Annual Meeting of the European Association for the Study of Diabetes in a symposium presentation on September 18, 2019.
- Imeglimin Phase 3 results for TIMES 2 and TIMES 3 36-week open-label period of the trial are expected around the end of 2019.
- For Imeglimin's development in the U.S. and Europe, positive top-line results were reported in July 2019 from a Metavant trial in patients with type 2 diabetes and chronic kidney disease (CKD) stages 3b/4. Imeglimin was observed to demonstrate a favorable safety and tolerability profile and the pharmacokinetics (PK) and pharmacodynamics (PD) data were consistent with previous Poxel data.
- Metavant plans to work with regulatory authorities and aims to initiate a Phase 3 program in patients with type 2 diabetes and CKD stages 3b/4 in the U.S. and Europe.

PXL770 Update (NASH)

- The Phase 2a 12-week, multicenter, randomized, double-blind, placebo-controlled, parallel group trial for PXL770 was initiated in April 2019. It will include efficacy and safety assessment in approximately 100 patients who likely have NASH. Results are expected during the second quarter of 2020.
- A separate four-week PK/PD study of PXL770 was recently initiated. The trial is expected to enroll approximately 16 patients per dose with the primary objective to assess the full PK profile of PXL770 in nonalcoholic fatty liver disease (NAFLD) patients who likely have NASH as well as evaluate the safety and tolerability. Results are expected in the fourth quarter of 2019.

PXL065 Update (NASH)

- A NASH TAG presentation in January 2019 highlighted data in which PXL065 was observed to have a more favorable profile versus pioglitazone and other thiazolidinediones (TZDs).
- A Phase 1a study in April 2019 reported that 15 mg of PXL065 was observed to show the potential to provide an improved therapeutic profile over 45 mg Actos®.
- A Phase 1b multiple ascending dose trial for PXL065 is expected to be initiated in the third quarter of 2019 with results expected in the fourth quarter of 2019.
- Poxel will meet with the U.S. FDA in the fourth quarter of 2019 to discuss next steps in the development of PXL065, including a registration program and the use of Actos® data for a 505(b)(2) registration pathway.

Early Stage Development (Other metabolic, specialty and rare diseases)

- Poxel is evaluating direct adenosine monophosphate-activated protein kinase (AMPK) activation and mitochondrial pyruvate carrier (MPC) inhibition for additional metabolic, specialty and rare diseases.

Corporate Update

- During the first half of 2019, Poxel established a U.S. subsidiary, Poxel Incorporated, with offices in the Boston area, as it continues to expand its presence in the U.S.
- Poxel recently appointed Iman Barilero, PharmD, PhD, as Senior Vice President Global Head of Regulatory Affairs based in Boston.

Financial Statements for First Half 2019 (IFRS Standards)

Revenue
Poxel reported revenues of EUR 23.2 million for the first half of 2019, as compared with EUR 37.5 million during the same period in 2018.

EUR (in thousand)	**H1 2019**	**H1 2018**	**Variance**
Roivant Agreement	155	8,148	(7.993)
Sumitomo Agreement	22,914	29,315	(6.401)
Other	100	0	100
Total revenues	**23,169**	**37,463**	**(14,294)**

Revenue for the first half of 2019 primarily 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. The revenue also reflects the Imeglimin Phase 3 TIMES program costs in Japan incurred during the first half of 2019 that were re-invoiced to Sumitomo Dainippon Pharma. Both the Sumitomo Dainippon Pharma upfront payment and re-invoiced costs of the Phase 3 TIMES program are recognized according to the percentage of completion of this

program. The decrease in revenue from Sumitomo Dainippon Pharma in 2019 compared to the same period in 2018 is due to the advanced stage of the Phase 3 program, which corresponds to less re-invoicing and, therefore, revenues received. In addition, the upfront payment received from Roivant for the agreement for Imeglimin announced on February 12, 2018 was fully reported as revenue of EUR 8 million in 2018.

Income Statement
Poxel devotes the bulk of its resources to research and development (R&D) activities. R&D expenses totaled EUR 24.2 million for the first half of 2019, as compared to EUR 27.4 million for the corresponding period in 2018. R&D expenses for the first half of 2019 primarily reflect the EUR 16.6 million clinical study costs incurred in respect of the Imeglimin Phase 3 TIMES program over the period. To a lesser extent, they also reflect the clinical study costs incurred for PXL770 and PXL065, Poxel's two clinical-stage programs for the treatment of NASH.

R&D expenses are net of the R&D Tax Credit (CIR) that resulted in income of EUR 1.6 million for the first half of 2019 as compared to EUR 1.5 million for the corresponding period of 2018.

General and administrative expenses totaled EUR 4.9 million for the first half of 2019, as compared to EUR 3.6 million for the first half of 2018.

The financial income amounted to EUR 0.1 million for the first half of 2019, as compared to EUR 0.8 million for the first half of 2018, which primarily reflected foreign exchange fluctuations.

The net result for the financial period ending June 30, 2019 was a net loss of EUR 5.8 million, as compared to a net income of EUR 7.3 million in the corresponding period in 2018.

Condensed Income Statement

EUR (in thousand)	**H1 2019**	**H1 2018**	**Variance**
Revenue	23.169	37.463	(14.294)
Net research and development expenses*	(24.164)	(27.442)	3.278
General and administrative expenses	(4.868)	(3.614)	(1.254)
Operating gain (loss)	**(5.864)**	**6.406**	**(12.270)**
Financial income (expenses)	71	850	(779)
Net income (loss)	**(5.792)**	**7.256**	**(13.049)**

*Net of R&D tax credit

Cash
As of June 30, 2019, cash and cash equivalents were EUR 49.8 million (USD 56.7 million), as compared to EUR 66.7 million (USD 76.4 million) as of December 31, 2018. Cash and cash equivalents net of financial liabilities were EUR 41.1 million as of June 30, 2019 and EUR 52.5 million at the end of Q4 2018.

Next Financial Press Release: 2019 third quarter and nine months, October 7, 2019

Planned Presentations and Participation at the Following Upcoming Events:

- 55th Annual Meeting of the European Association for the Study of Diabetes, September 16-20, 2019, Symposium Presentation for TIMES 1 September 18th, Barcelona, Spain
- HC Wainwright 21st Healthcare Conference, September 8-10, 2019 New York City, NY
- Licensing Executives Society (LES) 2019 Annual Meeting, October 20-23, 2019, Phoenix, AZ
- BioNetwork Partnering Summit, October 23-25, 2019, Laguna Niguel, CA
- AASLD 2019 The American Association for the Study of Liver Diseases, Poster Presentation for PXL065, November 8-12, 2019, Boston, MA
- Bio-Europe, November 11-13, 2019, Hamburg, Germany
- Jefferies Global Healthcare Conference, November 20-21, 2019 London, UK
- World Congress on Insulin Resistance, Diabetes and Cardiovascular Disease, December 4-7, 2019, Los Angeles, CA

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. 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 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. The TIMES 2 results are expected around the end of 2019.

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. The TIMES 3 16-week portion of the trial met its primary endpoint with a favorable safety and tolerability profile observed and the top-line data was reported on June 25, 2019. The TIMES 3 36-week open label results are expected around the end of 2019.

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).

About PXL065
PXL065 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. 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). 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, we 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 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)

*Actos is the branded version of pioglitazone and a registered trademark of Takeda Chemical Industries, Ltd.

1. 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20190826005443/en/

Poxel SA
Jonae R. Barnes
Senior Vice President, Investor Relations and Public Relations
jonae.barnes@poxelpharma.com
+1 (617) 818-2985

Investor relations / Media - EU/US
Trophic Communications
Stephanie May or Joanne Tudorica
may@trophic.eu or tudorica@trophic.eu
+49 89 238 877 34 or +49 171 185 56 82

Investor relations / Media - France
NewCap
Alexia Faure/Arthur Rouillé
poxel@newcap.eu
+33 1 44 71 98 55

Source: POXEL SA