April 3, 2017

Poxel Reports Results for Fiscal Year 2016 and Provides Corporate 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, today announced the results for its fiscal year ended December 31, 2016 and provided a corporate update. As of year-end 2016, cash and cash equivalents were EUR €45.6 million (USD $48.1 million).

“We achieved significant clinical, regulatory, financial and corporate milestones during 2016. In particular, we advanced the 300-patient Phase 2b study of Imeglimin in Japan and presented promising data demonstrating the potential for cardiovascular protective properties of Imeglimin to treat diabetic cardiomyopathy and vascular dysfunction, both of which are major complications of type 2 diabetes,” said Thomas Kuhn, CEO of Poxel.

“In 2017, we anticipate several important milestones beginning with the Phase 2b data results during the second quarter. Based on the timing and outcome of these results, we plan to be in the position to initiate the Phase 3 program for Imeglimin in Japan during the fourth quarter of 2017. We will also present additional preclinical data demonstrating Imeglimin’s potential cardiovascular benefits and explore beneficial properties beyond glucose control, targeting cardiovascular function, as well as liver disease,” continued Thomas Kuhn. “For our second program, PXL770, we are making substantial progress on the preclinical work related to its metabolic pattern and anticipate that we could initiate the Phase 1 multiple ascending dose study during the second half of this year. In addition to Imeglimin and PXL770, we are actively working to further leverage our internal capabilities and are currently assessing additional development opportunities in the metabolic area.”

Poxel 2016 Highlights

Imeglimin

In preclinical and clinical studies, Imeglimin has demonstrated the potential to address the mitochondrial dysfunction at the core of type 2 diabetes pathophysiology. 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. Imeglimin has completed Phase 1 and Phase 2 in 912 subjects in the US and EU, and is currently completing a 300-patient Phase 2b clinical trial in Japan. Over the course of 2016, Imeglimin successfully completed several important milestones including:

Significant Progress in Japan

- Completed enrollment of the Imeglimin dose-ranging, randomized, double-blind, placebo-controlled Phase 2b study with approximately 300 naïve and pre-treated Japanese patients. The primary endpoint of the trial is efficacy measured by change in glycated hemoglobin A1c after 24 weeks.

Additional Benefits Beyond Glucose Control in Cardiovascular and Beta-Cell Function

- Preclinical data presented at scientific meetings demonstrated Imeglimin's benefits beyond glucose lowering, targeting cardiovascular and beta-cell function.
    - Data presented at the European Association for the Study of Diabetes Annual Meeting demonstrated Imeglimin's potential for protective effects in the early stages of vascular dysfunction, a major complication in type 2 diabetes. Cardiovascular disease affects approximately 68% of people 65 years of age and older with diabetes.[1]
    - Data presented at the 14th Annual World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease demonstrated beneficial effects on beta-cell function and Imeglimin's potential to delay the development of type 2 diabetes.
- Based on the positive preclinical cardiovascular function data, Poxel initiated a clinical study designed to demonstrate Imeglimin's benefits on endothelial dysfunction in humans. The results from this study are anticipated in the second half of 2017.
- Imeglimin has successfully completed a thorough QT/QTc (TQT) cardiac safety study in 55 healthy subjects and no evidence of QT prolongation was observed. This study assesses a drug's risk of QT prolongation and its proarrhythmic potential.

Mechanism of Action Data on Insulin Secretion

- In the American Journal of Physiology, Endocrinology and Metabolism findings from a study led by Yale School of Medicine were published demonstrating that Imeglimin primarily lowers glucose levels by increasing glucose-stimulated insulin secretion in a dedicated preclinical model. These findings highlight Imeglimin's direct effect on insulin secretion in response to glucose through amplification of mitochondrial metabolism-dependent signals. These data also help to explain the absence of hypoglycemia seen in clinical trials. Many diabetes treatments currently on the market are associated with causing hypoglycemia, which is an adverse effect when blood sugar levels are too low.
- At the American Diabetes Association meeting, preclinical data showing Imeglimin's dual mechanism of action were presented. The new discovery that Imeglimin increases the nicotinamide adenine dinucleotide (NAD) synthesis, a pivotal molecule for mitochondrial function, further elucidates Imeglimin's unique mechanism of action on insulin secretion in response to glucose. The Company has made significant progress in understanding how Imeglimin improves both insulin sensitivity and secretion, which are the two major defects that cause type 2 diabetes.

Regulatory Update

- In 2016, Poxel continued its discussions with the European Medicines Agency for the Phase 3 program in Europe, and finalized its plan for this region. In addition, the Company remained engaged with the U.S. Food and Drug Administration and has had

active interactions with the Japanese Pharmaceuticals and Medical Devices Agency on the Phase 3 program.

PXL770

PXL770 is a first-in-class direct AMPK activator, a key enzyme in energy metabolism acting as an energy sensor regulating glucose and lipid levels. AMPK activation is considered to play an important role in metabolic disorders[2], and has the potential to treat several metabolic diseases, including liver and kidney, as well as in diabetes management, especially for patients with cardiovascular and liver complications.

- At the European Association for the Study of Diabetes meeting, Poxel presented new PXL770 data showing its effect on *de novo* lipid synthesis, and on weight and fat mass loss in an animal model of diabetes and obesity.
- PXL770 is in Phase 1 development. Results from the first part of the single ascending dose study indicate that PXL770 exhibited a favorable safety and tolerability profile with no reported serious adverse events.
- During the Phase 1 study, Poxel observed a different metabolic pattern in humans, as compared to animals that were treated with PXL770. Based on regulatory guidelines, Poxel is evaluating the profile of the metabolites. The Company anticipates that it could initiate the multiple ascending dose portion of the Phase 1 study during the second half of 2017.

Corporate

- In July 2016, Poxel completed a private placement of 3,400,000 new ordinary shares, which raised net proceeds of €24.1 million. Prominent US and European institutional investors participated in this financing.
- In December 2016, ENYO Pharma SA reported that they had initiated a Phase 1 program for EYP001 for the treatment of Hepatitis B. They also announced that the next phase of the Phase 1 clinical program is anticipated to begin in 2017 and will test the safety, PK and initial antiviral activity. EYP001 is an FXR agonist licensed to ENYO Pharma by Poxel.

Financial Statements for Fiscal Year 2016 (IFRS standards)

Poxel devotes the bulk of its resources to research and development (R&D). The corresponding R&D costs included below are net of the R&D Tax Credit (CIR) that resulted in income of €3.2 million in 2016. The variance from 2015 to 2016 (approximately €11 million) is mainly driven by clinical activities for Imeglimin, particularly the Phase 2b study in Japan, and the increased R&D costs for PXL770. The increase in general and administrative (G&A) costs were mainly from non-recurrent costs directly related to financing activities, which ended up resulting in net proceeds of €24.1 million from a successful private placement, and increased personnel costs related to the Company's ongoing R&D programs, particularly in Japan and in the U.S. In 2016, financial charges were mainly driven by interest expenses linked to the venture loan and interests rates of conditional advances. The net result for the financial period ending December 31, 2016 was a net loss of €24.5 million, as expected, compared to a net loss of €12.2 million in the previous year. On December 31,

2016, cash and cash equivalents were €45.6 million compared to €42.4 million on December 31, 2015.

Condensed Income Statement (consolidated) *In thousand €*

	31 Dec 2016	**31 Dec 2015**
Turnover	**70**	**59**
Net research and development expenses*	(17 675)	(7 319)
General and administrative expenses	(6 678)	(4 462)
Operating loss	**(**24 282**)**	**(**11 721**)**
Financial expenses/Financial income	(201)	(520)
Net loss	**(24 482)**	**(12 241)**

*Excludes R&D tax credit

Number of shares and voting rights as of December 31, 2016:

Month	Date	Total number of shares outstanding	Total of theoretical voting rights (1)	Total of exercisable voting rights (2)
December	12/31/2016	22,950,228	22,950,228	22,933,528

(1) The total number of theoretical voting rights (or “gross” voting rights) is used as the basis for calculating the crossing of shareholding thresholds. In accordance with Article 223-11 of the AMF General Regulation, this number is calculated on the basis of all shares to which voting rights are attached, including treasury shares whose voting rights have been suspended.
(2) The total number of exercisable voting rights (or “net” voting rights) is calculated without taking into account the treasury shares with suspended voting rights, in this case, shares held by the Company in the context of a liquidity contract agreement with ODDO.

Next financial press release: Q1-turnover and cash position May 4, 2017.

About Imeglimin

Imeglimin is the first clinical candidate in a new chemical class of oral agents called the Glimins. Imeglimin has a unique mechanism of action (MOA) that targets mitochondrial bioenergetics. Imeglimin acts on the three main target organs involved in glucose homeostasis: the liver, muscle, and the pancreas. This MOA has the potential for glucose lowering benefits, as well as the potential to prevent endothelial dysfunction, which can provide protective effects on micro- and macro-vascular defects induced by diabetes. The additional protective effect on beta-cell survival and function may lead to a delay in disease

progression. This unique mode of action compared to existing treatments for type 2 diabetes makes Imeglimin a prime candidate in all stages of the current anti-diabetic treatment paradigm, including monotherapy or as an add-on to other glucose lowering therapies for the treatment of patients with type 2 diabetes.

About PXL770

PXL770 is a first-in-class direct adenosine monophosphate-activated protein kinase AMPK activator, a key enzyme in energy metabolism acting as an energy sensor regulating glucose and lipid levels. AMPK activation is considered to play an important role in metabolic disorders, and has the potential to treat several metabolic diseases, including liver and kidney, as well as in diabetes management, especially for patients with cardiovascular and liver complications.

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. We have successfully completed our Phase 2 clinical program for our first-in-class lead product, Imeglimin, which targets mitochondrial dysfunction, in the U.S. and EU and have fully enrolled a Phase 2b clinical study in Japan. Our second program, PXL770, a direct AMPK activator, is in Phase 1 development. We intend to generate further growth through strategic partnerships and pipeline development. (Euronext: POXEL, www.poxel.com)

[1] American Heart Association updated November 4, 2016.
http://www.heart.org/HEARTORG/Conditions/More/Diabetes/WhyDiabetesMatters/CardiovascDisease-Diabetes_UCM_313865_Article.jsp/#.WNvMQzLMyqA

[2] Source: Srivastava, R. A et al., (2012) Journal of Lipids Research 53, 2490- 2514

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Poxel SA
Jonae R. Barnes, +1 617 818 2985
Senior Vice President, Investor Relations and Public Relations
jonae.barnes@poxelpharma.com
or
Investor relations / Media - EU/US
MacDougall Biomedical Communications
Gretchen Schweitzer or Stephanie May
+49 89 2424 3494 or + 49 175 571 1562
smay@macbiocom.com
or
Investor relations / Media - France
NewCap
Florent Alba/Nicolas Merigeau
+33 1 44 71 98 55
poxel@newcap.fr

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