October 1, 2020

Poxel Announces Positive Results From Phase 2a NASH Trial With PXL770, an Oral First-in-Class Direct AMPK Activator

- **The Phase 2a trial for the treatment of NASH met its primary efficacy endpoint; PXL770-treated patients achieved statistically significant improvement in the relative decrease in liver fat mass measured by magnetic resonance imaging-estimated proton density fat fraction (MRI-PDFF) at 12-weeks with a greater response in patients with type 2 diabetes[1]**
- **Key secondary measures in PXL770-treated patients included statistically significant observed improvements in liver enzymes - alanine transaminase (ALT) and hemoglobin A1c (HbA1c)**
- **PXL770 was observed to be safe and well tolerated; profile supports further evaluation for combination use**
- **First human clinical assessment of a direct AMPK activator; results support potential for development in NASH including key high-risk subgroups (patients with type 2 diabetes) and utility of AMPK activation in other chronic and rare metabolic diseases**
- **Conference call in English scheduled today for 12:00 pm EDT (New York time) / 6 pm CEST (Paris time)**

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 positive top-line results for STAMP-NAFLD, the PXL770 Phase 2a trial. The Phase 2a trial was a 12-week, randomized, parallel group study, in 120 presumed NASH patients with or without diabetes. PXL770 is a first-in-class, oral direct adenosine monophosphate-activated protein kinase (AMPK) activator. AMPK is a master regulator of several important metabolic pathways, including lipid metabolism, glucose control and inflammation, and is a novel target for NASH and a range of other chronic and rare metabolic diseases.

“The underlying pathophysiological drivers of nonalcoholic fatty liver disease (NAFLD) and NASH are highly complex and support the need for development of novel therapies acting on different targets that can address a variety of key disease drivers,” said Vlad Ratziu, MD, PhD, Professor of Hepatology, Sorbonne University and Pitié-Salpêtrière Hospital. “AMPK activation is a differentiated approach for NASH and these results demonstrate that it could have a beneficial role in controlling key pathways that lead to liver injury. By also directly targeting inflammation and fibrogenesis, as demonstrated in preclinical models including

human cells, PXL770 has the potential to independently impact multiple disease components. As an oral agent, PXL770 also has the potential to be used in combination with other agents, which could provide for broad treatment of this disease."

Summary of STAMP-NAFLD PXL770 Phase 2a Study Results

STAMP-NAFLD was a 12-week randomized, placebo-controlled, parallel group trial in 120 presumed NASH patients, with or without diabetes, which evaluated three dosing regimens of PXL770 versus placebo. Primary enrollment criteria were evidence of hepatic steatosis (NAFLD) based on a controlled attenuation parameter (CAP) score of >300 db/m measured by MRI-PDFF. Patients were randomized into four groups: PXL770 at 250 mg once-daily (QD); 250 mg twice-daily (BID); 500 mg once-daily (QD) versus patients who received placebo.

The Phase 2a trial met its primary efficacy endpoint; PXL770 was observed to produce a statistically significant mean relative decrease of 18% in liver fat mass from baseline at 12-weeks in the 500 mg QD dose group as measured by MRI-PDFF (p=0.0036 vs. -0.7% change in placebo). A greater proportion of patients who received PXL770 also achieved a $\geq$30% relative reduction in liver fat content compared to placebo; greater liver fat content reduction (up to -85%) was also observed in more responsive patients. Although mean baseline ALT values (37-41 U/L) were near the upper range of normal, a statistically significant reduction in mean ALT was also observed in the 500 mg dose group.

In patients with type 2 diabetes (41-47% of each group), PXL770 treatment resulted in a greater mean relative reduction in liver fat content (-27% at 500 mg QD; p=0.004 versus baseline). The effects of PXL770 in this key subpopulation will be further evaluated within each treatment group. Despite nearly normal mean baseline HbA1c values (6.03-6.30%) across all groups (patients with and without diabetes), a significant reduction in mean HbA1c was also observed. A similar trend was also observed on fasting plasma glucose.

PXL770 was observed to be generally safe and well tolerated. The number of patients with treatment-emergent adverse events in each group were similar to placebo and these events were mainly mild-to-moderate. The safety results from the Phase 2a trial are consistent with the PXL770 PK/PD trial and Phase 1 program.

	Placebo	PXL770 250 mg QD	PXL770 250 mg BID	PXL770 500 mg QD
Patients	31	30	30	29
Relative % change in liver fat content (per protocol)	-0.7	-2.3	-13.9*	-18.0*
Relative % change in liver fat content (patients with diabetes)	-6.0	+1.2	-16.7	-27.2*
% patients with $\geq$30% relative reduction in liver fat content	6.5	13.3	13.3	27.6$^{\Delta}$
Absolute reduction in ALT	+1.0	0.0	+0.3	-6.3*
Absolute change in HbA1c (%)	+0.05	-0.08	-0.18	-0.24*

*statistically significant vs. baseline ($p < 0.05$); Δ p=0.051

"Along with previous data from our PK/PD trial where AMPK target engagement

(suppression of *de novo* lipogenesis) and insulin sensitization were observed, the Phase 2a results are encouraging and further characterize this novel molecule and mechanism. Looking at the aggregate picture of preclinical and clinical results obtained to-date as well as published literature in the field, we believe that PXL770 has the potential to improve the underlying root causes of the disease, such as insulin resistance, dysregulation of lipid and glucose metabolism and inflammation," commented Pascale Fouqueray, MD, PhD, Executive Vice President, Clinical Development and Regulatory Affairs at Poxel. "These results support continued advancement of PXL770, which could include longer-term assessment of important histological endpoints such as inflammation and fibrosis and exploring subpopulations for further differentiation."

"AMPK is a compelling pharmaceutical target. In addition to the potential to further pursue PXL770 in NASH, clinical evidence of target engagement - including effects on glycemia - suggest that PXL770 and AMPK activation could provide utility to treat a broader range of other metabolic diseases, such as diabetic nephropathy and certain rare diseases," said David E. Moller, MD, Executive Vice President and Chief Scientific Officer of Poxel. "We are currently evaluating our library of AMPK targeted molecules, which could have the potential to expand our pipeline into programs for other chronic and rare metabolic diseases, and we look forward to publishing additional data supporting PXL770 and our AMPK platform later this year."

The Phase 2a results will be submitted for presentation at an upcoming scientific meeting.

In addition to Poxel's development program for PXL770, the Company announced on September 2, 2020, initiation of DESTINY 1 (Deuterium-stabilized R-pioglitazone [PXL065] Efficacy and Safety Trial In NASH), the single dose-ranging Phase 2 trial of PXL065 for the treatment of NASH. PXL065 is a novel, proprietary deuterium-stabilized R-stereoisomer of pioglitazone.

DESTINY 1 is a Phase 2 36-week, randomized, dose-ranging, double-blind, placebo-controlled, parallel group study that will assess efficacy and safety of PXL065 in approximately 120 noncirrhotic biopsy-proven NASH patients across multiple clinical sites in the US. The primary endpoint of the study will measure the relative change in the percentage of liver fat content based on magnetic resonance imaging-estimated proton density fat fraction (MRI-PDFF). The study will also assess the effects of PXL065 on liver histology and other metabolic and non-metabolic biomarkers. Results from the Phase 2 study are anticipated in the first half of 2022.

Conference Call Information

Poxel will host a conference call to discuss the results later today. To access the call, please use the dial-in numbers below or click this link or refer to Poxel's website.

US: +1 (646) 722-4916
UK: +44 20 7194 3759
France: +33 1 72 72 74 03
PIN: 16970470#

Replay:
US: +1 (646) 722-4969

UK: +44 20 3364 5147
France: +33 1 70 71 01 60
Access code: 418952943#

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 NASH

Non-alcoholic steatohepatitis (NASH) is a metabolic disease with no clear disease origin that is quickly becoming a worldwide epidemic. It is characterized by the accumulation of fat in the liver causing inflammation and fibrosis. The disease can be silent for a long period of time, but once it accelerates, severe damage and liver cirrhosis can occur, which can significantly impact liver function and can even result in liver failure or hepatocellular cancer. Typical risk factors for NASH include obesity, elevated levels of blood lipids (such as cholesterol and triglycerides) and diabetes. Currently no curative or specific therapies are available.

About Poxel SA

Poxel is a **dynamic biopharmaceutical company** that uses its extensive expertise in developing **innovative drugs for metabolic diseases**, with a focus on **type 2 diabetes** and **non-alcoholic steatohepatitis (NASH)**. In its mid-to-late stage pipeline, the Company is currently advancing three drug candidates as well as earlier-stage opportunities. **Imeglimin**, Poxel's first-in-class lead product, targets mitochondrial dysfunction. Poxel has a strategic partnership with Sumitomo Dainippon Pharma for Imeglimin in Japan, China, South Korea, Taiwan and nine other Southeast Asian countries. A Japanese new drug application (J-NDA) is under review by the Pharmaceuticals and Medical Devices Agency (PMDA) to request approval for the manufacturing and marketing of Imeglimin for the treatment of type 2 diabetes. Poxel also established a partnership with Roivant Sciences for Imeglimin's development and commercialization in countries outside of the 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 MPC inhibitor, is in a single Phase 2 trial for the treatment of NASH. Poxel also has additional earlier-stage programs from its AMPK activator and deuterated TZD platforms targeting chronic and rare metabolic diseases. The Company intends to generate further growth through strategic partnerships and pipeline development. Listed on Euronext Paris, Poxel is headquartered in Lyon, France, and has subsidiaries in Boston, MA, and Tokyo, Japan. For more information, please visit: www.poxelpharma.com.

In the context of the COVID-19 outbreak, which was declared a pandemic by the World Health Organization (WHO) on March 12, 2020, the Company is regularly reviewing the

impact of the outbreak on its business.

As of the date of this press release, and based on publicly available information, the Company has not identified the occurrence of any material negative effect on its business due to the COVID-19 pandemic that remains unresolved. However, the Company anticipates that the COVID-19 pandemic could have further material negative impact on its business operations. The worldwide impact of COVID-19 may notably affect the Company's internal organization and efficiency, particularly in countries where it operates and where confinement measures are implemented by the authorities. In addition, COVID-19 may impact market conditions and the Company's ability to seek additional funding or enter into partnerships. Particularly, delays in the supply of drug substance or drug products, in the initiation or the timing of results of preclinical and/or clinical trials, as well as delays linked to the responsiveness of regulatory authorities could occur, which could potentially have an impact on the Company's development programs and partnered programs. The Company will continue to actively monitor the situation.

All statements other than statements of historical fact included in this press release about future events are subject to (i) change without notice and (ii) factors beyond the Company's control. These statements may include, without limitation, any statements preceded by, followed by or including words such as "target," "believe," "expect," "aim," "intend," "may," "anticipate," "estimate," "plan," "project," "will," "can have," "likely," "should," "would," "could" and other words and terms of similar meaning or the negative thereof. Forward-looking statements are subject to inherent risks and uncertainties beyond the Company's control that could cause the Company's actual results or performance to be materially different from the expected results or performance expressed or implied by such forward-looking statements.

[1] Prevalence of type 2 diabetes in patients with NASH estimated to be 47% (Younossi ZM et al, *Hepatology 64*, 73–84, 2016)

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

Aurélie Bozza
Investor Relations & Communication Director
aurelie.bozza@poxelpharma.com
+33 6 99 81 08 36

Investor relations / Media - EU/US
Trophic Communications
Stephanie May or Valeria Fisher
may@trophic.eu or fisher@trophic.eu
+49 171 185 56 82 or +49 175 804 1816

Investor relations / Media - France

NewCap
Emmanuel Huynh or Arthur Rouillé
poxel@newcap.eu
+33 1 44 71 94 94

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