December 14, 2020

Poxel Announces Additional Positive Phase 2a Results, and Phase 2b Plan for PXL770, an Oral First-in-Class AMPK Activator, in NASH

- **New results from the Phase 2a STAMP-NAFLD trial show consistently greater response in high-risk patients with coexisting type 2 diabetes (T2DM), estimated to be approximately 50% of NASH patients[1]**
- **Clinically meaningful improvements ($p<0.05$) in liver fat content, liver enzymes alanine transaminase (ALT) and aspartate transaminase (AST), fasting glucose and hemoglobin A1c (HbA1c) were observed in PXL770-treated patients with T2DM**
- **New preclinical results demonstrated PXL770 produced direct beneficial effects on human cells which mediate fibrosis (stellate cells) and inflammation (macrophages)**
- **Poxel plans to conduct a 52-week Phase 2b trial evaluating up to two doses of PXL770 in up to 120 patients per study arm with biopsy-proven NASH and pre-diabetes or T2DM; primary endpoint to measure NASH resolution with no worsening of fibrosis**
- **Poxel to host virtual NASH investor event today from 8:30-10:00 am EST / 2:30-4:00 pm CET featuring presentations from Kenneth Cusi, MD, Chief of the Division of Endocrinology, Diabetes & Metabolism in the Department of Medicine at the University of Florida and Stephen A. Harrison, MD, Director, Summit Clinical Research and company management**

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 an update on results from the PXL770 Phase 2a STAMP-NAFLD trial in NASH. The STAMP-NAFLD trial was a 12-week, randomized, parallel group study in 120 presumed NASH patients with or without type 2 diabetes (T2DM). The Company additionally announced new preclinical results and plans for a Phase 2b trial focused on patients with noncirrhotic biopsy-proven NASH and coexisting prediabetes or T2DM. 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 additional chronic and rare metabolic diseases.

Summary of New PXL770 Phase 2a Study Results

The STAMP-NAFLD study was a 12-week, randomized, controlled trial in 120 presumed NASH patients, with or without T2DM, which evaluated three dosing regimens of PXL770 versus placebo. Primary enrollment criteria were hepatic steatosis (NAFLD) based on a controlled attenuation parameter (CAP) score of >300 db/m measured by MRI-PDFF. In patients with T2DM (41-47% of each group), the results observed showed treatment with PXL770 resulted in a -27% mean relative reduction in liver fat content at 500 mg QD (p=0.004) versus baseline. In a new analysis of the T2DM subpopulation patients, findings included: a significant increase in the proportion of responders (≥30% reduction in liver fat); dose-responsive and significant mean decreases in alanine transaminase (ALT) and aspartate transaminase (AST) levels were achieved despite only slightly elevated mean baseline ALT levels (36-47 IU/L; normal range ≤41 IU/L). In the T2DM patients, baseline fasting glucose (121-144 mg/dL) and HbA1c (6.6-7.1%) levels were well controlled, and in this context, significant placebo-adjusted decreases were observed in both glycemic parameters along with improvements in commonly used fasting indexes of insulin sensitivity (HOMA-IR and QUICKI scores). In the T2DM subpopulation, PXL770 was generally safe and well tolerated and was similar to the whole trial population.

Selected Clinical Parameters in Patients with Type 2 Diabetes at 12 Weeks

	Placebo	PXL770 250 mg QD	PXL770 250 mg BID	PXL770 500 mg QD
Relative % change in liver fat content	-6.1	+1.2	-16.7	-27.2**
% responders (≥30% relative reduction in liver fat content)	7.1	15.4	21.4	58.3*
Absolute reduction in ALT (IU/L)	+2.1	-2.2	-3.8	-12.8*
Absolute reduction in AST (IU/L)	-0.8	-3.7	-0.9	-10.7*
Placebo adjusted change in HbA1c (%)	-	-0.24	-0.43	-0.64*
Placebo adjusted change in fasting glucose (mg/dL)	-	-0.3	-14.9	-21.3*
Change from baseline in HOMA-IR / QUICKI scores	+1.2 / -0.01	+1.0 / -0.01	0 / -0.004	-1.7^ / + 0.005^

statistically significant vs. placebo* or baseline** ($p < 0.05$) ^($p = 0.08$; 0.052)

“There is a sizable overlap in the NASH patient population such that approximately 50% of NASH patients also have co-existing type 2 diabetes. PXL770 is one of the only therapies in development that has demonstrated the potential to treat NASH with specific use in patients with coexisting type 2 diabetes that are at higher risk for faster disease progression and for co-morbidities, including cardiovascular complications,” commented Pascale Fouqueray, MD, PhD, Executive Vice President, Clinical Development and Regulatory Affairs at Poxel. “AMPK activation has the potential to improve the underlying root causes of NASH, such as insulin resistance, the dysregulation of lipid and glucose metabolism and inflammation. We believe PXL770 has the potential to be a much-needed and differentiated therapeutic option for NASH and could be particularly important for the high-risk population with type 2 diabetes.”

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

Summary of New PXL770 Preclinical Results

In recent *in vitro* experiments with human macrophages, incubation with PXL770 resulted in significant suppression of cytokine (IL-6, TNFα, MCP-1) release. In collaboration with Dr. Gregory Steinberg (McMaster University, Ontario, Canada), activation of human stellate cells was observed to be strongly inhibited by incubation with PXL770. These results are consistent with the potential for PXL770 to have direct effects leading to reduced inflammation and fibrosis in NASH.

“We are very encouraged by the consistency of PXL770’s preclinical results, which are beginning to translate into meaningful clinical outcomes as observed in our Phase 2a trial,” said David E. Moller, MD, Executive Vice President and Chief Scientific Officer. “Interestingly, the greater response rate in NASH-related measures observed in the type 2 diabetes subpopulation aligns with published literature, which shows low endogenous AMPK tone in the context of hyperglycemia and greater degrees of metabolic dysfunction. To fully understand the benefits of AMPK, including direct effects on inflammation and fibrosis, which were not measured in the Phase 2a trial, histology measures will be included in the Phase 2b trial in order to further confirm the preclinical findings.”

Summary of Plans for PXL770 Phase 2b Trial in NASH

Based on the results of the Phase 2a trial, as well as other results and published literature, Poxel plans to initiate a 52-week Phase 2b trial in noncirrhotic biopsy-proven NASH patients with coexisting prediabetes or T2DM. The trial will evaluate up to two oral daily doses of PXL770 compared to placebo in up to 120 patients per study arm in clinical sites located in the U.S. and in Europe. The primary endpoint of the trial will be NASH resolution with no worsening of fibrosis assessed on histology. The Phase 2b trial will also evaluate efficacy on other histology endpoints (fibrosis), assessment of metabolic and non-metabolic parameters, pharmacokinetic assessment as well as safety and tolerability. The Phase 2b trial is expected to begin during the second half of 2021.

NASH Investor Event Information

Poxel will host a virtual NASH investor event today, December 14, 2020 from 8:30-10:00 am EST / 2:30-4:00 pm CET.

The event will feature members of the Poxel management team and NASH key opinion leaders, Kenneth Cusi, MD, Chief of the Division of Endocrinology, Diabetes & Metabolism in the Department of Medicine at the University of Florida and Stephen A. Harrison, MD, Director, Summit Clinical Research. The agenda for the event will include:

- Detailed results from the Phase 2a STAMP-NAFLD study of PXL770 for the treatment of NASH;
- The Phase 2b plan for PXL770; and
- The status of PXL065, Poxel’s deuterium-stabilized R-pioglitazone for NASH.

A live webcast of the event will be available on Poxel’s website at https://www.poxelpharma.com/en_us/news-media/events under Events. To participate

by phone, please use the following dial-in number: 1 (847) 944-7134, Confirmation Number: 50030660. A replay of the event will be available on Poxel's website following the presentation.

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. **PXL770**, a first-in-class direct adenosine monophosphate-activated protein kinase (AMPK) activator, has successfully completed a Phase 2a proof-of-concept trial for the treatment of NASH. The Phase 2a trial met its primary endpoint and study objectives. PXL770 could also have the potential to treat additional metabolic diseases. **PXL065** (deuterium-stabilized R-pioglitazone), a MPC inhibitor, is in a streamlined 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%; approximately 26% of T2DM patients have NASH; clinical and economic burden of NASH in T2DM greater than with either disease alone (Younossi ZM et al, *Hepatology* 2016, 64, 73–84; Cusi K, *Diabetes Care* 2020, 43:275-79; Younossi ZM et al,*Diabetes Care* 2020, 43:283–89

View source version on businesswire.com:
https://www.businesswire.com/news/home/20201213005014/en/

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

Source: Poxel SA