



Poxel Announces Positive Pharmacokinetic (PK) / Pharmacodynamic (PD) Study Results for PXL770, a Direct AMPK Activator for the Treatment of NASH

- The study met its key objectives; PXL770 was observed to demonstrate a consistent PK profile in the likely-NASH patient population and was observed to be safe and well-tolerated
- Results demonstrate target engagement and efficacy signals that support the potential for PXL770 in NASH and for the AMPK platform in other chronic and rare metabolic diseases
- Efficacy and safety results from the PXL770 Phase 2a study for the treatment of NASH are anticipated late Q3 2020

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 results from a PXL770 four-week placebo-controlled PK/PD study in 16 likely-NASH patients with insulin resistance. The primary objective of the study was to assess the full pharmacokinetic (PK) profile of PXL770 as well as to evaluate safety and tolerability. PXL770 is a first-in-class direct adenosine monophosphate-activated protein kinase (AMPK) activator, which is being evaluated for the treatment of NASH. 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.

In the results observed from the PK/PD trial, PXL770 met its study objectives showing a PK profile in likely-NASH patients that was similar to the one observed in healthy volunteers in the Company's Phase 1 program. In the PK/PD trial, PXL770 was also observed to be safe and well-tolerated. PXL770 induced a statistically significant suppression of *de novo* lipogenesis (DNL) known to be one of the important contributors to the progression of NASH. A statistically significant effect was also observed on glucose tolerance during a glucose challenge test (OGTT) in this population of non-diabetic patients. This trial confirmed the target engagement of PXL770 on the AMPK pathway and the potential of the drug in other metabolic diseases.

"We are pleased with these results in likely-NASH patients; they confirm that target engagement in patients has been achieved and that some of the effects observed with

PXL770 in various preclinical models can be translated in the clinic. They also support the role of AMPK as an important player in the NASH pathophysiology as suggested in published literature,” commented Pascale Fouqueray, MD, PhD, Executive Vice President, Clinical Development and Regulatory Affairs at Poxel.

“These results support our hypothesis that AMPK activation could have a beneficial role in controlling key pathways that lead to liver injury and NASH, and these data provide additional understanding of this novel mechanism,” said Thomas Kuhn, CEO of Poxel. “We look forward to the upcoming results from the Phase 2a study, which is evaluating PXL770 in approximately 100 likely-NASH patients. Topline results from the study are expected toward the end of the third quarter in 2020.”

“AMPK is a compelling pharmaceutical target and we are encouraged by the outcome of this study. Not only does the data further demonstrate the potential for PXL770 in NASH, the positive effects on DNL and OGTT suggest that AMPK activation may be useful in addressing a broader range of other diseases mediated by metabolic pathway dysfunction,” said David E. Moller, MD, Chief Scientific Officer of Poxel. “Thus, we are also 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.”

About the PXL770 PK/PD Study

The four-week PK/PD study was conducted to assess the full PK profile, and safety and tolerability of PXL770 in 16 likely-NASH patients with insulin resistance. Primary enrollment criteria were evidence of hepatic steatosis (NAFLD) based on a controlled attenuation parameter (CAP) score of >300 db/m measured by transient elastography (FibroScan®) along with a HOMA-IR (calculated measure of insulin resistance) score >2.5. Patients were randomized into two groups; twelve patients were administered PXL770 at 500 mg once-daily versus four patients who received placebo. The study assessed the effect of PXL770 on several target pathways, including hepatic DNL, glucose tolerance, as well as other fasting biomarkers.

The observed PK profile of PXL770 at the dose of 500 mg once-daily in these likely-NASH patients was consistent with results obtained in the Company’s Phase 1 program in healthy subjects.

Relative to baseline measurements, PXL770 treatment was observed to produce statistically significant ($p=0.0045$) suppression of DNL along with a statistically significant ($p\leq 0.03$) improvement in glycemia (total and incremental glucose AUC) following an oral glucose challenge test (OGTT). Neither dynamic test was affected in subjects who received placebo. A statistically significant reduction ($p=0.0134$) in HOMA-IR was also observed in PXL770 treated subjects, suggesting improved insulin sensitivity. Since mean values for a number of parameters were within the normal range of healthy individuals at baseline and the study duration was limited, as expected, additional secondary endpoints including alanine aminotransferase (ALT), circulating lipids, or markers of inflammation were unaffected by PXL770 treatment.

The safety results from the PK/PD trial are consistent with the PXL770 Phase 1 program that included 132 subjects and evaluated the safety, tolerability and PK of PXL770 administered once- or twice-daily after single or 10-day repeated administration ranging from 30 mg to

500 mg. In both the Phase 1 studies and this PK/PD trial, there were no serious adverse events or adverse events leading to withdrawal. In the PK/PD trial, the overall incidence of patients presenting with treatment emergent adverse events was lower in the PXL770 group versus the placebo group.

The efficacy and safety of PXL770 is currently being evaluated in a Phase 2a twelve-week, multicenter, randomized, double-blind, placebo-controlled, parallel group trial. This trial is expected to evaluate approximately 100 diabetic and non-diabetic likely-NASH patients in the U.S. and will investigate three doses of PXL770 versus placebo. The primary endpoint of the trial will measure the change in liver fat content based on magnetic resonance imaging-estimated proton density fat fraction (MRI-PDFF), an imaging-based biomarker that allows fat mapping of the entire liver. The trial will also assess the effects of PXL770 on other metabolic and non-metabolic biomarkers as well as safety and tolerability. Results from the Phase 2a trial are expected late in the third quarter of 2020.

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 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 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. Together, with its partner Sumitomo Dainippon Pharma, Poxel successfully completed the Phase 3 Trials of **IMeglimin for Efficacy and Safety (TIMES)** program for the treatment of type 2 diabetes in Japan. 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 mitochondrial pyruvate carrier (MPC) inhibitor, is advancing into a Phase 2 clinical trial for the treatment of NASH. Poxel also has additional earlier-stage programs from its AMPK activator and 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 has undertaken a full review of the impact of the outbreak on its business. Considering the rapidly evolving situation, the Company is updating this assessment on a regular basis.

The Company anticipates that the COVID-19 pandemic could have a 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 have been implemented by the authorities. In addition, the deteriorating market conditions may impact the Company's ability to raise additional funding and/or to enter into partnerships. Particularly, delays in the supply of drug substance or drug products, in pre-clinical 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. The Company will continue to proactively monitor the situation.

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