May 25, 2020

Poxel Announces Program Update and Preclinical Results on PXL770 for NASH Combinations and Other Metabolic Diseases

- **PXL770, a novel direct AMPK activator, produced additive benefits in a NASH model when combined with other late-stage agents in development**
- **PXL770 treatment was observed to improve cardio-renal disease and adrenoleukodystrophy (ALD) / adrenomyeloneuropathy (AMN) in animal models**
- **Poxel plans to further evaluate its AMPK platform for continued advancement and pipeline expansion in chronic and rare metabolic diseases**
- **Poxel concurrently announced today a capital raise of €17.7 million ($19.4 million) to accelerate advancement of PXL770 and PXL065 in NASH and to pursue development activities in other metabolic diseases for pipeline growth**
- **PXL770 PK/PD and Phase 2a studies in NASH remain on track for results in the second and third quarter of 2020, respectively**

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 new preclinical results for PXL770, the lead molecule in the Company's adenosine monophosphate-activated protein kinase (AMPK) platform. PXL770, a direct AMPK activator, was evaluated in a rodent NASH model in combination with other key agents in development, including an FXR agonist (obeticholic acid), a GLP-1 receptor agonist (semaglutide) and a thyroid receptor β agonist (MGL-3196). The results highlight PXL770 as a potentially novel NASH therapy that may also produce complementary benefits when combined with other agents with different mechanisms of action.

PXL770 was also evaluated in rodent models of diabetic kidney disease (DKD) which also assessed cardiac dysfunction and adrenoleukodystrophy (ALD) / adrenomyeloneuropathy (AMN), a deadly, inherited rare metabolic disease characterized by neurodegeneration. These results demonstrate that AMPK activation may lead to broader utility for other diseases mediated by metabolic pathway dysfunction.

Poxel conducted these studies as part of the investigation into a broader application of PXL770 in a range of metabolic diseases and in support of the Company's Phase 2 clinical trial and NASH development program.

"AMPK is a compelling pharmaceutical target that has been observed to modulate both

metabolic and inflammatory pathways and has the potential to treat several chronic and rare metabolic diseases," said David E. Moller, MD, CSO of Poxel. "Our new preclinical data highlights the potential of PXL770 to show even greater additive or synergistic benefits to treat the root causes of NASH when combined with other agents in development. We are also very excited by the new findings implicating the potential of PXL770 and, more broadly, of AMPK activation for the treatment of other serious chronic disorders ranging from common to rare monogenic metabolic disorders."

"These studies are another step forward for PXL770 and add to the growing body of data that supports the continued development of our AMPK platform. The results demonstrate PXL770's potential in NASH and also validate our hypothesis for the use of AMPK activation more broadly in additional metabolic diseases," said Thomas Kuhn, CEO of Poxel. "We look forward to the upcoming results from the PXL770 PK/PD study and the ongoing Phase 2a clinical trial for the treatment of NASH. We are also enthusiastic about the opportunity to evaluate other metabolic diseases through our AMPK platform and are committed to pursuing all options to continue to build value in our pipeline."

In parallel to the drug discovery efforts, the Company is focused on advancing its NASH studies including the ongoing Phase 2a clinical trial evaluating the efficacy and safety of PXL770 in approximately 100 likely NASH patients with results expected during the third quarter of 2020. In addition, the PK/PD trial assessing the profile of PXL770 in nonalcoholic fatty liver disease (NAFLD) patients is nearing completion with results expected during the second quarter of 2020. As Poxel's lead drug candidate for the treatment of type 2 diabetes, Imeglimin, continues to advance with preparations under way for the New Drug Application submission in Japan and a Phase 3 program in the U.S., the Company remains well-positioned to leverage its drug discovery and development expertise to expand its pipeline in the metabolic disease area. Currently, Poxel's AMPK platform includes its lead candidate, PXL770, in addition to a broader library of AMPK activator molecules. The Company also has a deuterated thiazolidinedione (TZD) platform that it is currently being investigated for metabolic diseases.

Summary of PXL770 NASH Combination Study Results

These studies evaluated a diet-induced obese (DIO) mouse model of NASH. Mice were treated with either PXL770, obeticholic acid (OCA, Intercept), Semaglutide (SMG, Novo Nordisk) or MGL-3196 (MGL, Madrigal), or paired combinations of PXL770 with each additional agent. Key findings included the following:

- PXL770 alone confirmed its efficacy potential in comparison with each of the other three agents.
- Combination treatment with PXL770 and OCA or PXL770 and SMG resulted in further improvements in several key disease-related parameters.
- PXL770 and MGL combined resulted in further improvements in liver lipid content.

These PXL770 preclinical combination study results will be submitted for publication or presentation at an upcoming scientific congress.

Summary of PXL770 Chronic and Rare Metabolic Disease Study Results

Diabetic Kidney Disease Model: In collaboration with Professor Paul Mulder (Rouen

University Medical School, Rouen, France), PXL770 was evaluated in ZSF1 rats, a model of diabetic nephropathy and metabolic disease-induced heart failure. PXL770 prevented disease progression. Compared to untreated ZSF1 rats, kidney function and albuminuria were improved, and several indices related to left ventricular diastolic cardiac dysfunction were also ameliorated. The full set of data from these studies will be presented at an upcoming scientific congress in 2020.

ALD / AMN Disease Model: In collaboration with Jaspreet Singh, PhD, (Henry Ford Health, Detroit, MI), several studies were conducted to assess the effects of direct AMPK activation in models of ALD / AMN. Human cells from patients with X-linked AMN due to mutations in the gene encoding the peroxisomal ABCD1 fatty acid transporter and an ALD / AMN animal model (ALD-KO, ABCD1 null, mice) were evaluated. In patient-derived cells, PXL770 suppressed pathologic elevated levels of very long chain fatty acids. Alternative fatty acid transporters (ABCD2 and 3) were also upregulated implicating the potential to circumvent defects in ABCD1. In ALD-KO mice, *in vivo* PXL770 treatment reduced elevated levels of very long chain fatty acids in both brain and plasma. The full set of data from these studies will be presented at an upcoming scientific congress and submitted for publication.

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 or can even result in liver failure or liver cancer. Typical risk factors for NASH include obesity, elevated levels of blood lipids (such as cholesterol and triglycerides) and type 2 diabetes. Currently no curative or specific therapies are available.

About Diabetic Nephropathy

Diabetic kidney disease (DKD) is the most common cause of chronic kidney disease and leads to substantial morbidity (dialysis, cardiac disease) and mortality. Metabolic biochemical perturbations and pro-inflammatory pathway activation are major contributing factors. AMPK is known to have a role in modulating these pathways. Very few approved therapies are available, and they are known to only partially attenuate the progression of DKD.

About ALD / AMN

ALD / AMN are X-linked monogenic metabolic diseases caused by mutations in the gene encoding the peroxisomal ABCD1 fatty acid transporter. Defective lipid metabolism leads to accumulation of very long chain fatty acids in tissues, subsequently resulting in inflammation and cellular damage. Major consequences include adrenal insufficiency, cerebral lesions with severe neurocognitive impairment, peripheral neuropathy and death in early childhood. In the U.S. alone, there are 10,000-15,000 patients (combined ALD and AMN). Currently, no specific pharmaceutical medications are available to treat or cure these diseases.

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)[1].

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 **T**rials of **IM**eglimin for **E**fficacy and **S**afety (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 targeting metabolic, specialty and rare 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.

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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 our 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.

[1] Source: Smith B. K et al., (2016) Am J Physiol Endocrinol Metab 311, E730 – E740.

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