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Poxel Presents Complete PXL770 Phase 1 Results, Cardiac Safety Profile and Preclinical Efficacy Data in NASH at AMPK - From Mechanisms to New Therapies Scientific Congress

- **Phase 1 clinical program for PXL770 was observed to have a favorable pharmacokinetic, tolerability and safety profile**
- **PXL770 was observed to have a favorable cardiac safety profile in both healthy subjects and in animal models**
- **PXL770 was observed to show efficacy in a diet-induced obese-NASH mice model**

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 the presentation of PXL770 data at AMPK - From Mechanisms to New Therapies Scientific Congress held in Niagara-on-the-Lake, Ontario, Canada, September 30 - October 4, 2018. The PXL770 results were presented in two poster presentations and an oral presentation. The data presented emphasized the favorable pharmacokinetic, tolerability and safety profile of PXL770 in the Phase 1 program as well as a favorable cardiac and electrocardiography (ECG) safety profile in both healthy subjects and animal models. In addition, mechanistic and efficacy data in a diet-induced obese (DIO)-NASH mouse model were also presented. Poxel previously announced data results from the Phase 1b multiple ascending dose trial and a drug-drug interaction study of PXL770, a direct adenosine monophosphate-activated protein kinase activator (AMPK), in a [press release](#) on July 18, 2018. Based on these results, the Company is advancing PXL770 into a Phase 2a proof-of-concept study in nonalcoholic fatty liver disease (NAFLD) patients who likely have NASH in early 2019.

“We are very pleased to have the opportunity to present the complete data results from our Phase 1 program to the scientific AMPK community and key experts. AMPK is a major regulator of energy metabolism and its activation is expected to show beneficial effects in metabolic and cardiovascular diseases,” said Sophie Bozec, PhD, Senior Vice President, Research and Development Pharmacology at Poxel. “Supported by positive preclinical mechanistic and efficacy results in a DIO-NASH model, we believe that PXL770 is uniquely

positioned to treat the underlying root causes of fatty liver diseases, including liver steatosis, inflammation and fibrosis, as well as provide benefits for co-morbidities, including those related to cardiovascular disease.”

“We are looking forward to advancing PXL770 into a Phase 2a proof-of-concept program for NASH in early 2019,” said Thomas Kuhn, CEO of Poxel. “With our recent acquisition of DeuteRx’s drug candidate, PXL065, we are rapidly expanding our presence in NASH and are one of only a few biotech companies with two clinical programs in development in this therapeutic area. The underlying pathophysiological mechanisms that contribute to the development and progression of NAFLD and NASH are highly complex and support the need for the development of novel therapies acting on different targets. Both of our programs have the potential to be developed as a monotherapy or in combination together or with other agents.”

In a poster presentation, results from the two Phase 1 studies including single and multiple ascending dose administrations of PXL770 investigated in healthy male subjects (n=124), were presented. The safety profile was good across the dose range tested with no serious adverse events nor adverse effects leading to discontinuation. A good tolerability profile was also observed up to the highest dose tested of 500 mg, both as single or multiple administrations, with no changes in the electrocardiogram observed. The maximum tolerated dose was not reached. Pharmacokinetic assessment demonstrated that PXL770 plasma exposure (C_{max} and AUC) increased in a dose dependent manner following single administration. After multiple administrations, the pharmacokinetics (C_{max} and AUC) of PXL770 were shown to be linear with a trend for saturation at the highest dose tested. These results suggest that PXL770 is well positioned to enter Phase 2 development.

In a second poster presentation, cardiac safety was evaluated in an extensive *in vivo* program. A pharmacological study performed in a rat model demonstrated that PXL770 administration (75 mg/kg bid) did not induce cardiac hypertrophy after 16 weeks of treatment in toxicological studies and no adverse effects of cardiac hypertrophy or accumulation of glycogen in the myocardium were detected at 1000 mg/kg dosing during 13 weeks of PXL770 treatment. These results were replicated in the 13-week treatment study in dogs with no increase in cardiac glycogen content (Shiff periodic acid staining) observed. A twenty-four-hour Holter-ECG recording performed in the 13-week study in dogs showed no rhythm or conduction disorders. Lastly, regulatory safety pharmacological studies (hERG binding assay, hERG voltage clamp assay and radiotelemetry in dogs) dedicated to cardiac assessment (cardiac repolarization and electrocardiographic parameters, blood pressure) did not raise any safety concerns. The favorable cardiac safety is reinforced by the absence of adverse effects observed on extensive ECG recordings after a shorter period of PXL770 administration in healthy subjects evaluated in the Phase 1 program.

In addition, an oral presentation summarizing PXL770 and its preclinical profile as a direct AMPK activator, specifically in a diet-induced (high fat, fructose and cholesterol for 45 weeks) obesity NASH (DIO-NASH) mouse model, was presented. The results highlighted the beneficial effect of AMPK activation in the NASH model and the potential of PXL770 as a promising novel treatment option in NAFLD and, in particular, NASH acting on the three main characteristics of the physiopathology: steatosis, inflammation and fibrosis.

The posters titled “PXL770, a direct AMPK activator, shows a favorable cardiac safety profile” and “PXL770, a direct AMPK activator for the treatment of NASH, shows a favorable

PK, tolerability and safety profile in humans” are available on the Company’s website under “Posters” or by using the following link http://www.poxelpharma.com/en_us/product-pipeline/posters.

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 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 uses its development expertise in metabolism to advance a pipeline of drug candidates focused on the treatment of metabolic disorders, including type 2 diabetes and non-alcoholic steatohepatitis (NASH). We have successfully completed the Phase 2 clinical program for our first-in-class lead product, Imeglimin, which targets mitochondrial dysfunction, in the U.S., Europe and Japan. Together, with our partner Sumitomo Dainippon Pharma, we are conducting the Phase 3 Trials of IMeglimin for Efficacy and Safety (TIMES) program for the treatment of type 2 diabetes in Japan. Our partner Roivant Sciences is responsible for Imeglimin’s development and commercialization in countries outside of Poxel’s 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 advancing into 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), is in Phase 1 and being developed for the treatment of NASH. Poxel also has additional earlier-stage programs, including deuterated drug candidates for metabolic, specialty and rare diseases. We intend to generate further growth through strategic partnerships and pipeline development. (Euronext: POXEL, www.poxelpharma.com)

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