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Poxel Initiates Pharmacokinetic (PK)/ Pharmacodynamic (PD) Study as part of the Phase 2a Clinical Program for PXL770, a Direct AMPK Activator for the Treatment of NASH

- **Study will assess full PK profile and PD effect on target pathways and metabolic parameters in parallel with the ongoing Phase 2a efficacy and safety study**
- **Data results from the PK/PD study are anticipated in Q4 2019, Phase 2a efficacy and safety results are anticipated in Q2 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 initiation of a PK/PD study, which is part of the Phase 2a clinical program for PXL770, a first-in-class direct adenosine monophosphate-activated protein kinase activator (AMPK), for the treatment of NASH.

“NASH is a multifactorial and complex disease state and AMPK activation could play a beneficial role in the metabolic and inflammatory pathways leading to liver injury. The clinical program was designed to confirm in likely NASH patients the potential of PXL770 observed in preclinical models and to correlate PXL770's activity to its PK profile,” said Pascale Fouqueray, MD, PhD, EVP, Translational Medicine and Early Clinical Development at Poxel. “By targeting the underlying root causes of nonalcoholic fatty liver disease, we believe that PXL770 has the potential to improve the key components of this disease, which include liver steatosis, inflammation, ballooning and fibrosis. PXL770 may also provide benefits to known co-morbidities, including those related to cardiovascular disease.”

“This study is another step forward for PXL770 as we use our extensive expertise in metabolic drug development to pursue proof-of-concept with this program to further demonstrate PXL770’s potential in NASH and validate our hypothesis for AMPK activation more broadly,” said Thomas Kuhn, CEO of Poxel. “AMPK is a major regulator of energy metabolism and we continue to believe in its activation as a mechanism to treat a wide range of chronic metabolic diseases, including NASH.”

The four-week PK/PD study of PXL770 is expected to enroll approximately 16 patients per

dose, with the primary objective to assess the full PK profile of PXL770 in nonalcoholic fatty liver disease (NAFLD) patients, who likely have NASH, as well as evaluate the safety and tolerability. The study will also evaluate the effect of PXL770 on its two main targeted metabolic pathways, which include hepatic de novo lipogenesis (DNL) and lipolysis. It will also assess several other glycemic and lipidic metabolic parameters as well as non-metabolic biomarkers. Data results from the PK/PD study are expected during the fourth quarter of 2019.

Concurrently, PXL770 is being evaluated in an ongoing efficacy and safety Phase 2a twelve-week, multicenter, randomized, double-blind, placebo-controlled, parallel group study. This study is expected to enroll approximately 100 NAFLD patients in the U.S. who likely have NASH and will investigate three doses of PXL770 versus placebo. The primary endpoint of the study will measure the change in liver fat mass 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 study will also assess the effects of PXL770 on other metabolic and non-metabolic biomarkers as well as safety and tolerability. Data results from the Phase 2a study are anticipated in the second 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 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 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 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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