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Poxel Initiates Phase 2a Program for PXL770, a Direct AMPK Activator for the Treatment of NASH

- **The Phase 2a program will include two separate studies**
- **Phase 2a efficacy and safety study for PXL770 is underway with data results anticipated 1H 2020**
- **Pharmacokinetic (PK)/pharmacodynamic (PD) study for PXL770 is expected to initiate 2Q 2019 with results anticipated 2H 2019**

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 the Phase 2a program for PXL770, a direct adenosine monophosphate-activated protein kinase activator (AMPK), for the treatment of NASH.

The Phase 2a twelve-week, multicenter, randomized, double-blind, placebo-controlled, parallel group study, which will assess efficacy and safety, has been initiated. In this study, three doses of PXL770 versus placebo will be administered. Approximately 100 nonalcoholic fatty liver disease (NAFLD) patients who likely have NASH are expected to be included in this study across clinical sites in the US. 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), a novel 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. In addition, the effect of PXL770 on hepatic *de novo* lipogenesis (DNL) and glucose tolerance, will be investigated. Data results from the Phase 2a study are anticipated in the first half of 2020.

In addition to the Phase 2a study, a separate four-week PK/PD study is expected to be initiated during the second quarter of 2019. During this study, PXL770 will be administered to approximately 32 patients. This study will assess the PK profile of PXL770 in NAFLD patients and its effects on hepatic and metabolic parameters in the target population. Data results from this study are expected during the second half of 2019.

“AMPK is a major regulator of energy metabolism and its activation is expected to show beneficial effects in metabolic diseases, such as NASH,” said Pascale Fouqueray, MD, PhD, EVP, Translational Medicine and Early Clinical Development 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 as

well as to specifically target each step of the pathophysiology of the disease, including liver steatosis, inflammation, ballooning and fibrosis. PXL770 may also provide benefits for co-morbidities, including those related to cardiovascular disease."

"By targeting the master regulator of cellular energy, PXL770 has a unique and differentiated profile compared to other drug candidates in development for the treatment of NASH," said Thomas Kuhn, CEO of Poxel. "With the acquisition of PXL065, a mitochondrial pyruvate carrier inhibitor, we have expanded our presence in NASH, and we are one of only a few biotechnology companies with two clinical programs in development for this disease. 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 that act on different targets. Both of our programs have the potential to be developed as monotherapy or in combination together or with other agents."

Poxel previously announced data results from a Phase 1b multiple ascending dose trial and a drug-drug interaction study of PXL770 in a press release titled, "Poxel Announces Favorable Results for PXL770 Phase 1b Multiple Ascending Dose Trial and Drug-Drug Interaction Study."

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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