October 12, 2022

Poxel to Present DESTINY-1 Phase 2 Results for PXL065 in NASH at AASLD The Liver Meeting® 2022

- **Late-Breaking Abstract Selected for Oral Presentation, November 7th**
- **Phase 2 for PXL065 in NASH achieved the primary efficacy endpoint for liver fat content reduction for all doses and showed strong improvement in fibrosis without worsening of NASH**

LYON, France--(BUSINESS WIRE)-- POXEL SA (Euronext : POXEL - FR0012432516), a clinical stage biopharmaceutical company developing innovative treatments for chronic serious diseases with metabolic pathophysiology, including non-alcoholic steatohepatitis (NASH) and rare metabolic disorders, today announced that its late-breaking abstract describing the results from its Phase 2 study of PXL065 in NASH (DESTINY-1) has been selected for an oral presentation at The Liver Meeting® 2022, hosted by the American Association for the Study of Liver Diseases (AASLD), being held on November 4-8, 2022 in Washington, D.C.

Details of the presentation are as follows:

Abstract 5010: *PXL065 (Deuterium-Stabilized R-enantiomer of pioglitazone) Reduces Liver Fat Content and Improves Liver Histology without PPARγ-mediated Side Effects in Patients with NASH: Analysis of a 36 Week Placebo-Controlled Phase 2 Trial (DESTINY-1)*

Presenter: Stephen Harrison, MD, President, Summit Clinical Research

Date and Time: Monday, November 7, 2022, 2:15 PM ET

Summary of Phase 2 NASH (DESTINY-1) PXL065 Study Results

DESTINY-1 was a Phase 2, 36-week, randomized, dose-ranging, double-blind, placebo-controlled, parallel group study designed to assess the efficacy and safety of PXL065 in patients with noncirrhotic biopsy-proven NASH across multiple clinical sites in the US. The primary endpoint of the study measured the relative change in the percentage of liver fat content based on magnetic resonance imaging-estimated proton density fat fraction (MRI-PDFF). The study also assessed the effects of PXL065 on liver histology and other metabolic and non-metabolic biomarkers.

117 subjects were randomized to one of 4 daily (QD) treatment arms (7.5 mg, 15 mg, 22.5 mg, placebo). Analysis of histologic changes was based on paired liver biopsies in PXL065

vs. placebo-treated NASH patients before and after the 36-week treatment period.

Top line results included:

- The primary efficacy endpoint was achieved: PXL065-treated patients achieved statistically significant improvements in the relative decrease in liver fat content at 36-weeks for all doses.
- Fibrosis improvement by ≥1 stage without worsening of NASH, an endpoint recognized by FDA for approval, occurred in 31-50% patients in the PXL065 study arms vs. 17% with placebo. Across all PXL065 treatment arms (pooled data), 39% of patients had fibrosis improvement by ≥1 stage without worsening NASH (%) vs. 17% with placebo.
- PXL065 was observed to be safe and well tolerated with no dose-dependent increase in body weight and no increased lower extremity edema vs. placebo.

About PXL065

PXL065 is a novel, proprietary deuterium-stabilized R-pioglitazone. Although pioglitazone is not approved by the FDA for the treatment of NASH, it is the most extensively studied drug for NASH; in multiple prior trials, improvements in liver histology, including reductions in fibrosis, were demonstrated[1,2]. Pioglitazone is the only drug recommended for biopsy-proven NASH patients by the Practice Guidelines published by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL)[3]. Pioglitazone's off-label use for NASH, however, has been limited due to the PPARγ-related side effects, which include weight gain, bone fractures and fluid retention.

Pioglitazone is a 1:1 mixture of two mirror-image compounds (R- and S-stereoisomers) that interconvert *in vivo*. Using deuterium, Poxel stabilized each stereoisomer and characterized their different pharmacological properties. In *in vitro* studies, PXL065 has been shown to target non-genomic pathways including mitochondrial pyruvate carrier (MPC) and acyl-CoA synthetase 4 (ACSL4). In preclinical animal models, PXL065 exhibits the NASH efficacy associated with pioglitazone with no significant weight gain or fluid retention, side effects which are associated with the S-stereoisomer[4]. NASH Phase 2 (DESTINY 1 trial) results available to-date show statistically significant effects of PXL065 on liver fat content, biomarkers related to liver fibrogenesis-fibrosis risk, as well as positive effects on fibrosis and other key parameters based on histology analysis. Relative to published data for pioglitazone, reduced potential for weight gain and edema was also evident. Based upon preclinical, Phase 1 and Phase 2 results, Poxel believes that PXL065 may have a better therapeutic profile than pioglitazone for NASH and may also have suitable properties for further development in other indications including adrenoleukodystrophy (ALD).

[1] Cusi, et al., Ann Intern Med. 2016, 165(5), 305-315.
[2] Musso et al. Hepatology 2017; 65: 1058-1061.
[3] J Hepatol. 2016, 64:1388-402; Hepatology 2018, 67: 328-357.
[4] Jacques et al. Hepatol Comm 2021; 5:1412-1425.

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 Poxel SA

Poxel is a **clinical stage biopharmaceutical company** developing **innovative treatments for chronic serious diseases with metabolic pathophysiology**, including **non-alcoholic steatohepatitis (NASH)** and rare disorders. For the treatment of NASH,**PXL065** (deuterium-stabilized *R*-pioglitazone) met its primary endpoint in a streamlined Phase 2 trial (DESTINY-1). In rare diseases, development of **PXL770**, a first-in-class direct adenosine monophosphate-activated protein kinase (AMPK) activator, is focused on the treatment of adrenoleukodystrophy (ALD) and autosomal dominant polycystic kidney disease (ADPKD). **TWYMEEG®** (Imeglimin), Poxel's first-in-class product that targets mitochondrial dysfunction, is now marketed for the treatment of type 2 diabetes in Japan by Sumitomo Pharma and Poxel expects to receive royalties and sales-based payments. Poxel has a strategic partnership with Sumitomo Pharma for Imeglimin in Japan, China, and eleven other Asian countries. 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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