February 12, 2021

Poxel Reports Financial Update for Cash and Revenue for the Full Year 2020 and Provides Corporate Update

- **As of December 31, 2020, cash and cash equivalents were EUR 40.2 million (USD 49.4 million)**
- **New results from the PXL770 Phase 2a STAMP-NAFLD trial for the treatment of NASH showed consistently greater response in high-risk patients with coexisting type 2 diabetes (T2DM), which is estimated to affect approximately 50% of NASH patients[1]**
- **Poxel announced plans to conduct a 52-week Phase 2b trial evaluating up to two doses of PXL770 in approximately 100 patients per study arm with biopsy-proven NASH and pre-diabetes or T2DM; primary endpoint to measure NASH resolution with no worsening of fibrosis**
- **Imeglimin Japanese New Drug Application (J-NDA) under review following submission by Poxel's partner Sumitomo Dainippon Pharma in July 2020, with a target product launch anticipated in 2021[2]; following Metavant's decision, for strategic reasons, not to move forward with the Imeglimin development program at the end of 2020, Poxel regained all rights to Imeglimin in January 2021**
- **In October 2020, Poxel received EUR 6 million of non-dilutive funding in the form of state-guaranteed loans (*Prêts Garantis par l'Etat*, or PGE, in France) in the context of the COVID-19 pandemic**

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 its cash position and revenue for the twelve months ended December 31, 2020 and provided a corporate update.

"Despite the challenges posed by the COVID-19 pandemic, Poxel ended 2020 on a strong note, having accomplished several important corporate and clinical milestones and positioning the Company for an exciting 2021. We continued working closely with our partner Sumitomo Dainippon Pharma to further advance the review of the Japanese New Drug Application for Imeglimin following its submission in July 2020. Sumitomo Dainippon Pharma is actively preparing the product launch, anticipated in its fiscal year 2021," said Thomas Kuhn, CEO of Poxel. "Additionally, we announced positive clinical results for PXL770 for the treatment of NASH. Our Phase 2a STAMP-NAFLD trial met its primary endpoint demonstrating that PXL770-treated patients experienced a statistically significant improvement in the relative decrease in liver fat mass at 12-weeks, with an even greater

response in patients with type 2 diabetes. These encouraging results support PXL770's development in this high-risk, underserved patient population. For PXL065, deuterium-stabilized R-pioglitazone, we continued to make progress with the enrollment of DESTINY 1, a streamlined dose-ranging Phase 2 trial for the treatment of NASH."

"Our corporate achievements included strengthening the Company's financial position by EUR 6 million during the fourth quarter 2020 through financing in the form of French state-guaranteed loans, related to the COVID-19 pandemic," added Thomas Kuhn. "Throughout 2021, the Company expects to achieve several important milestones, including the Imeglimin J-NDA approval[3], which would entitle us to a milestone payment, sales-based payments and escalating double-digit royalties on product sales. We would also be able to draw down EUR 13.5 million for the third tranche of the IPF loan, which is contingent on obtaining marketing authorization of Imeglimin in Japan. In early 2021, we regained the full rights for Imeglimin in countries not covered by our partnership with Sumitomo Dainippon Pharma. We are currently exploring various options to advance Imeglimin, and we plan to provide an update on our progress during the year. For our two NASH programs, we expect to finalize the recruitment for the Phase 2 trial for PXL065, and to launch the Phase 2b trial for PXL770 during the second half of the year," continued Thomas Kuhn, CEO of Poxel.

As of December 31, 2020, total cash and cash equivalents were EUR 40.2 million (USD 49.4 million), as compared to EUR 37.2 million (USD 41.8 million) as of December 31, 2019. Cash and cash equivalents net of financial liabilities (excluding IFRS16 impacts and derivative debts) were EUR 17.2 million as of December 31, 2020, as compared to EUR 27.4 million as of December 31, 2019.

EUR (in thousands)	**Q4 2020**	**Q4 2019**
Cash	15,588	18,161
Cash equivalents	24,615	19,026
Total cash and cash equivalents*	**40,203**	**37,187**

Unaudited data.
**Cash and cash equivalents net of financial liabilities (excluding IFRS 16 impacts and derivative debts) were EUR 27.4 million at the end of Q4 2019 and EUR 17.2 million at the end of Q4 2020.*

FY20 Revenue

Poxel reported revenues of EUR 6.7 million for the year ended December 31, 2020, as compared to EUR 26.6 million during the corresponding period in 2019.

The revenues for 2021 include the JPY 500 million (EUR 4.0 million[4]) milestone payment that Poxel received from Sumitomo Dainippon Pharma for the submission of the Imeglimin J-NDA. To a lesser extent, it also includes an allocated portion of the EUR 36.0 million upfront payment received from Sumitomo Dainippon Pharma relating to the strategic corporate partnership announced on October 30, 2017, as well as the residual Imeglimin Phase 3 program costs in Japan incurred in 2020 that were re-invoiced to Sumitomo Dainippon Pharma. Both the allocated portion of the upfront payment and the re-invoiced costs of the Phase 3 **T**rials of **IM**eglimin for **E**fficacy and **S**afety (TIMES) program have been recognized based on the accounting percentage of the completion of this program, which has been fully

completed, and therefore led to the decrease in revenue in 2020.

EUR (in thousands)	**FY 2020 12 months**	**FY 2019 12 months**
Roivant Agreement	18	276
Sumitomo Agreement	6,708	26,179
Other	1	101
Total revenues	**6,727**	**26,556**

Unaudited data.

Clinical & Additional Development Update

Imeglimin

- Poxel continues to support its partner, Sumitomo Dainippon Pharma, in all activities related to the ongoing regulatory review of the J-NDA, following its submission in July 2020. Target product launch is anticipated in 2021[5].
- In October 2020, results for Imeglimin focused on safety were presented at the 63rd JDS meeting. In the Phase 2b and Phase 3 TIMES trials, Imeglimin was observed to have a favorable safety profile at the 1,000 mg dose with similar frequency and types of adverse events as seen in placebo-treated patients; specifically, Imeglimin appeared to be unlikely to cause hypoglycemia.
- In November 2020, Poxel announced that, for strategic reasons, Metavant would not be moving forward with the Imeglimin development program. This decision was not based on any efficacy, safety or other data generated through the partnership. In January 2021, Poxel announced that Metavant would return all rights to Imeglimin to Poxel, as well all data, materials, and information, including FDA regulatory filings, related to the program, effective January 31, 2021. Metavant is not entitled to any payment from Poxel as part of the return of the program.

PXL770

- In October 2020, Poxel announced that the Phase 2a STAMP-NAFLD trial for the treatment of NASH met its primary efficacy endpoint. PXL770-treated patients achieved statistically significant improvements in the relative decrease in liver fat mass and alanine aminotransferase (ALT) levels at 12-weeks with a greater response in patients with T2DM.
- In November 2020, several preclinical studies supporting the efficacy of PXL770 in NASH and other metabolic diseases were presented at the American Association for the Study of Liver Disease (AASLD) The Liver Meeting® 2020.
- In December 2020, Poxel announced that *in vitro* experiments with human immune cells and stellate cells demonstrated the potential of PXL770 to mediate independent direct effects leading to reduced inflammation and fibrosis in NASH.
- In December 2020, additional Phase 2a data from the PXL770 STAMP-NAFLD trial

was presented at a virtual NASH investor event, featuring members of the Poxel management team and NASH key opinion leaders, Kenneth Cusi, MD, Chief of the Division of Endocrinology, Diabetes & Metabolism in the Department of Medicine at the University of Florida and Stephen A. Harrison, MD, Director, Summit Clinical Research. The results showed a consistently greater response in high-risk subpopulation patients with coexisting T2DM, estimated to affect approximately 50% of NASH patients[6]. Poxel also announced plans to pursue a Phase 2b development strategy focused on NASH patients with T2DM. PXL770's mechanism of action could be particularly beneficial for this patient population as it has the potential to improve the underlying root causes of the disease, such as insulin resistance, dysregulation of lipid and glucose metabolism and inflammation.
- Poxel plans to initiate a Phase 2b 52-week trial in noncirrhotic biopsy-proven NASH patients with coexisting prediabetes or T2DM. The trial will evaluate up to two oral daily doses of PXL770 compared to placebo in approximately 100 patients per study arm in clinical sites located in the US and EU. The primary endpoint of the trial will be NASH resolution with no worsening of fibrosis assessed by histology. The Phase 2b trial is expected to begin during the second half of 2021.

PXL065

- In November 2020, Poxel presented Phase 1b clinical results for PXL065 at the AASLD The Liver Meeting® 2020. The results showed a dose-proportional pharmacokinetic profile with a substantially altered ratio of R- vs. S-pioglitazone stereoisomers.
- In December 2020, the ongoing DESTINY 1 Phase 2 study was reviewed during Poxel's virtual NASH investor event.
- The recruitment for the DESTINY 1 Phase 2 study is expected to be completed in the second half of 2021.

Corporate Events

- In October, Poxel received approval from BNP Paribas, Bpifrance and CIC Lyonnaise de Banque for EUR 6 million in non-dilutive financing in the form of a French Government Guarantee Loan (PGE Loan). The initial term is one-year, with a five-year extension option.
- After almost five years as part of the Poxel management team, Jonae Barnes, Senior Vice President, Investor Relations, Corporate Communications and Public Relations has moved on from the Company to pursue a new opportunity. Poxel would like to thank Ms. Barnes for her dedication over the years and wishes her well in her future endeavors. Poxel has launched a recruitment effort to fill this position, which is based in the US.

Planned Presentations and Participation at the Following Upcoming Events (virtual)

- H.C. Wainwright Global Life Sciences Conference, March 9-10
- 2021 NASH Tag conference, March 11- 13
- Mitochondria-Targeted Drug Development Summit, April 27-29
- Kempen Life Sciences Conference, May 5
- Japan Diabetes Society, May 20-22

- Jefferies Global Healthcare Conference, June 8-10

Next Financial Press Release: 2020 Annual Results, March 25, 2021

About Imeglimin
Imeglimin is a new chemical substance classified as a tetrahydrotriazine compound, and the first clinical candidate in a chemical class. Imeglimin has a unique dual mechanism of action (MOA) that targets mitochondrial bioenergetics. Imeglimin acts on all three key organs which play an important role in the treatment of type 2 diabetes: the pancreas, muscles, and the liver, and it has demonstrated glucose lowering benefits by increasing insulin secretion in response to glucose, improving insulin sensitivity and suppressing gluconeogenesis. This MOA has the potential to prevent endothelial and diastolic dysfunction, which can provide protective effects on micro- and macro-vascular defects induced by diabetes. It also has the potential for protective effect on beta-cell survival and function. This unique MOA offers the potential opportunity for Imeglimin to be a candidate for the treatment of type 2 diabetes in almost all stages of the current anti-diabetic treatment paradigm, including monotherapy or as an add-on to other glucose lowering therapies.

About NASH
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 PXL770
PXL770 is a first-in-class 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 NASH.

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 and has demonstrated “resolution of NASH without worsening of fibrosis” in a Phase 4 trial[7]. Pioglitazone is the only drug recommended for biopsy-proven NASH patients by the Practice Guidelines published by the AASLD and the European Association for the Study of the Liver (EASL)[8]. 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, we stabilized each stereoisomer and characterized their different pharmacological properties. In *in vitro* studies, PXL065 has been shown to target mitochondrial pyruvate carrier (MPC) as an inhibitor. In preclinical animal models, PXL065 exhibits the anti-inflammatory and NASH activity associated with pioglitazone with

little or no weight gain or fluid retention, side effects which are associated with the S-stereoisomer. Based upon preclinical and Phase 1 results to date, Poxel believes that PXL065 may have a better therapeutic profile than pioglitazone for NASH.

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. Poxel has a strategic partnership with Sumitomo Dainippon Pharma for Imeglimin in Japan, China, South Korea, Taiwan and nine other Southeast Asian countries. A Japanese new drug application (J-NDA) is under review by the Pharmaceuticals and Medical Devices Agency (PMDA) to request approval for the manufacturing and marketing of Imeglimin for the treatment of type 2 diabetes. After successfully completing a Phase 2a proof-of-concept trial for the treatment of NASH, which met its primary endpoint and study objectives, for **PXL770**, a first-in-class direct adenosine monophosphate-activated protein kinase (AMPK) activator, Poxel plans to initiate a Phase 2b program in the second half of 2021. PXL770 could also have the potential to treat additional metabolic diseases. **PXL065** (deuterium-stabilized R-pioglitazone), a MPC inhibitor, is in a streamlined Phase 2 trial for the treatment of NASH. Poxel also has additional earlier-stage programs from its AMPK activator and deuterated TZD platforms targeting chronic and rare metabolic 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.

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 is regularly reviewing the impact of the outbreak on its business.

As of the date of this press release, and based on publicly available information, the Company has not identified the occurrence of any material negative effect on its business due to the COVID-19 pandemic that remains unresolved. However, the Company anticipates that the COVID-19 pandemic could have further material negative impact on its 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 are implemented by the authorities. In addition, COVID-19 may impact market conditions and the Company's ability to seek additional funding or enter into partnerships. Particularly, delays in the supply of drug substance or drug products, in the initiation or the timing of results of preclinical 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 and partnered programs. The Company will continue to actively monitor the situation.

All statements other than statements of historical fact included in this press release about future events are subject to (i) change without notice and (ii) factors beyond the Company's control. These statements may include, without limitation, any statements preceded by, followed by or including words such as "target," "believe," "expect," "aim," "intend," "may," "anticipate," "estimate," "plan," "project," "will," "can have," "likely," "should," "would," "could"

and other words and terms of similar meaning or the negative thereof. Forward-looking statements are subject to inherent risks and uncertainties beyond the Company's control that could cause the Company's actual results or performance to be materially different from the expected results or performance expressed or implied by such forward-looking statements

[1] Prevalence of T2DM in patients with NASH estimated to be 47%; approximately 26% of T2DM patients have NASH; clinical and economic burden of NASH in T2DM greater than with either disease alone (Younossi ZM et al, *Hepatology* 2016, 64, 73–84; Cusi K, *Diabetes Care* 2020, 43:275-79; Younossi ZM et al, *Diabetes Care* 2020, 43:283–89).

[2] Year noted is Fiscal Year from April 2021 to March 2022, which is Sumitomo Dainippon Pharma's Fiscal Year.

[3] Expected during Sumitomo Dainippon Pharma's 2021 Fiscal Year, which is from April 2021 to March 2022.

[4] Exchange rate at the filing date.

[5] Year noted is Fiscal Year from April 2021 to March 2022, which is Sumitomo Dainippon Pharma's Fiscal Year.

[6] Prevalence of T2DM in patients with NASH estimated to be 47%; approximately 26% of T2DM patients have NASH; clinical and economic burden of NASH in T2DM greater than with either disease alone (Younossi ZM et al, *Hepatology* 2016, 64, 73–84; Cusi K, *Diabetes Care* 2020, 43:275-79; Younossi ZM et al, *Diabetes Care* 2020, 43:283–89).

[7] Cusi, et al., Ann Intern Med. 2016, 165(5), 305-315.

[8] J Hepatol. 2016, 64(6),1388-402; Hepatology 2018, 67, 328-357.

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Poxel SA
Aurélie Bozza
Investor Relations & Communication Director
aurelie.bozza@poxelpharma.com
+33 6 99 81 08 36

Investor relations / Media - EU/US
Trophic Communications
Stephanie May or Valeria Fisher
poxel@trophic.eu
+49 171 185 56 82 or +49 175 804 1816

Investor relations / Media - France
NewCap
Emmanuel Huynh or Arthur Rouillé
poxel@newcap.eu

+33 1 44 71 94 94

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