March 24, 2021

Poxel Reports Financial Results for Full Year 2020 and Provides Corporate Update

- **Imeglimin Japanese New Drug Application (J-NDA) under review following submission by Poxel's partner, Sumitomo Dainippon Pharma, with product launch anticipated in 2021[1]**
- **Successful completion of PXL770 Phase 2a STAMP-NAFLD trial in NASH with new data demonstrating greater response in high-risk patients with co-existing type 2 diabetes (T2DM), estimated to affect about 50% of NASH patients[2]**
- **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 expected to commence in H2 2021**
- **PXL065 Phase 2 study underway with topline data readout expected mid-2022**
- **Financial position strengthened through capital increase of EUR 17.7 million in May 2020 and EUR 6 million in October 2020 in non-dilutive funding in the form of a French Government Guarantee Loan (Prêts Garantis par l'Etat or PGE) in the context of the COVID-19 pandemic. This loan has an initial term of one year, with a five-year extension option. The Company already decided to activate the extension option**
- **As of December 31, 2020, cash and cash equivalents were EUR 40.2 million (USD 49.4 million)**

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 results for the year ended December 31, 2020 and provided a corporate update.

"Looking back, 2020 was a strong year for Poxel in which we achieved critical clinical milestones to advance our key programs PXL770 and PXL065 into late-stage development with promising data readouts, and further asserted ourselves as an industry leader in metabolic diseases," commented Thomas Kuhn, CEO of Poxel. "Further, with the submission of the J-NDA for Imeglimin for the treatment of T2DM we are in a strong position and moving toward a potential market launch in Japan in 2021[2]. We were also able to present additional results from our Phase 3 TIMES 2 and TIMES 3 clinical trials at the 56th EASD Annual Meeting, highlighting Imeglimin's unique position and strong therapeutic profile both as a monotherapy and in combination with standard of care available in Japan, including DPPIV inhibitors, a notable feature considering that this drug class is the market leader in Japan and is prescribed to approximately 80% of treated T2DM patients[3]. In

parallel with this, we are pursuing the development of our two NASH candidates, PXL770 and PXL065. Results from our Phase 2a trial with PXL770 showed consistently greater response in patients with coexisting T2DM, highlighting its potential in this high-risk and underserved patient population. Despite the pandemic, recruitment for the PXL065 Phase 2 trial has been progressing as planned. Taken together, all of these achievements show the tremendous potential of the pipeline we are proud to build upon and the future we are headed toward as we expand our AMPK activation and TZD platforms."

"2021 will be a very special year for Poxel. We have built the Company to bring novel treatments to patients with chronic metabolic disorders and this vision will become a reality once Imeglimin is approved in Japan, anticipated this year. We will also complete PXL065 Phase 2 recruitment and are planning to initiate a Phase 2b study for PXL770 in biopsy-proven NASH patients. We remain committed to advancing our programs alone and together with partners in an effort to bring tangible solutions to patients living with metabolic diseases," continued Mr. Kuhn.

Clinical Development Updates

Imeglimin (Type 2 Diabetes)

- In November 2020, Poxel announced that, for strategic reasons, its partner 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. Poxel regained all rights to Imeglimin at the end of January 2021.
- In September 2020, Poxel presented Imeglimin Phase 3 TIMES results at the 56th European Association for the Study of Diabetes Annual Meeting. Phase 3 TIMES 2 and TIMES 3 trial results demonstrated Imeglimin met its primary endpoints and objectives and was observed to exhibit a favorable safety and tolerability profile.
- In July 2020, Poxel announced the submission of the Imeglimin J-NDA for the treatment of T2DM by its partner, Sumitomo Dainippon Pharma. The submission triggered a JPY500 million (EUR 4.1 million, USD 4.7 million)[4] development milestone payment to Poxel with the potential for a JPY 1.75 billion (approximately EUR 13.8 million, USD 16.9 million)[5] milestone payment upon product approval. The target product launch date is anticipated in 2021[6] which will trigger the potential for sales-based payments and escalating double-digit royalties on product sales.
- In April 2020, Poxel announced the publication of Imeglimin clinical study results in *Clinical Pharmacokinetics*. The two clinical studies evaluated the potential for drug-drug interactions of Imeglimin with two widely prescribed medications, metformin or sitagliptin. Imeglimin was observed to be safe and well-tolerated in both studies.

PXL770 (NASH)

- In December 2020, Poxel announced additional positive Phase 2a results showing greater response in high-risk patients with coexisting T2DM, and a Phase 2b Plan for PXL770, an oral first-in-class AMPK activator, in NASH[7].
- In November 2020, Poxel presented new preclinical data for PXL770 at the AASLD The Liver Meeting® 2020. PXL770 revealed the potential for direct effects on key components of NASH as both a mono- and combination therapy producing anti-inflammatory effects in mouse liver and adipose tissue and in human immune cells as

well as specific biomarkers related to improvements involving mitochondria in mouse liver.

- In October 2020, Poxel announced positive results from its Phase 2a NASH trial with PXL770. The trial met its primary efficacy endpoint and was observed to be safe and well tolerated.
- In September 2020, Poxel presented PXL770 preclinical cardio-renal results at the 56th European Association for the Study of Diabetes Annual Meeting. PXL770 was observed to improve renal and cardiac disease in a preclinical model which revealed its utility for not only NASH co-morbidities but also additional indications driven by metabolic dysfunction.
- In June 2020, Poxel announced positive pharmacokinetic (PK) / pharmacodynamic (PD) study results for PXL770.

PXL065 (NASH)

- PXL065 is currently being evaluated in DESTINY-1, a Phase 2 study in biopsy-proven NASH patients, which seeks to identify the optimal dose or doses for a Phase 3 registration trial.
- The recruitment for the DESTINY-1 Phase 2 study is expected to be completed in 2021.
- In November 2020, Poxel presented Phase 1b clinical results for PXL065 at the AASLD The Liver Meeting® 2020. Analysis of results from the study predicts efficacy at 15 mg once-daily is equivalent to 45 mg Actos®8, with little to no PPARγ-related side effects, such as weight gain.

Early Stage Development

- In November 2020, at ALD Connect, the Company presented new results in cell-based and *in vivo* preclinical models of adrenoleukodystrophy. These data showed that both PXL770 and PXL065 produced significant improvements in disease-associated pathology, providing a rationale to pursue this indication with next generation molecules derived from both platforms.
- The potential of PXL770 and PXL065 with other agents in development continues to be assessed in preclinical studies. Further preclinical studies are ongoing to evaluate direct adenosine monophosphate-activated protein kinase (AMPK) activation and mitochondrial pyruvate carrier (MPC) inhibition in additional metabolic, specialty and rare diseases.

Corporate Updates

- In October 2020, Poxel received EUR 6 Million in non-dilutive financing guaranteed by the French government.
- In May 2020, Poxel successfully raised EUR 17.7 million in a capital increase. The proceeds will enable the acceleration of development plans for PXL770 and PXL065 for treatment of NASH, the pursuit of development activities in other metabolic diseases and will be used for general corporate purposes.
- In January 2020, Poxel appointed David E. Moller, MD, as CSO. Dr. Moller is an industry leader in the discovery and development of new therapeutic agents, particularly in diabetes and metabolic disorders.

Significant Events after the Period

- In February 2021, Poxel announced the resolution of the arbitration procedure with Merck Serono.
- In January 2021, Poxel regained Imeglimin rights from Metavant. Metavant has returned all rights to Imeglimin to Poxel in addition to all data, materials and information, including FDA regulatory filings, related to the program. Metavant is not entitled to any payments from Poxel as part of the return.
- Imeglimin'sinnovative MOA and Phase 2b/3 results in Japan were published in peer reviewed journals.

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*Actos is the branded version of pioglitazone and a registered trademark of Takeda Chemical Industries, Ltd.

Financial Statements for Full Year 2020 (IFRS Standards)

Revenue

Poxel reported revenues of EUR 6.8 million for the year ended December 31, 2020, as compared to EUR 26.6 million during the corresponding period in 2019.

The revenues for 2020 include the JPY 500 million (EUR 4.0 million) 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 millions)	**FY 2020 12 months**	**FY 2019 12 months**
Roivant Agreement	18	276
Sumitomo Agreement	6,787	26,179
Other	1	101
Total revenues	**6,806**	**26,556**

The audit procedures have been performed and the issuance of the audit report is in process.

Income Statement

Poxel devotes the bulk of its resources to research and development (R&D) activities. R&D expenses totaled EUR 26.7 million in 2020, as compared to EUR 40.2 million in 2019. R&D expenses in 2020 primarily reflected the clinical costs incurred for the ongoing Phase 2

programs of PXL770 and PXL065, the Company's two compounds for the treatment of NASH. To a lesser extent, they also included the residual clinical study costs incurred for Imeglimin Phase 3 TIMES program over the period, which were mostly re-invoiced to Sumitomo Dainippon Pharma. The decrease in R&D costs was mostly driven by the completion of the TIMES program in Japan, for which expenses of EUR 1.3 million were incurred in 2020, compared to EUR 20 million in 2019.

R&D costs are net of the R&D Tax Credit (CIR) that resulted in income of EUR 2.5 million in 2020, as compared to EUR 4.4 million in 2019.

General and administrative expenses totaled EUR 9.9 million in 2020, as compared to EUR 11.1 million in 2019. The decrease in G&A costs reflects non-recurring costs incurred in 2019, partially offset by increasing personnel costs in 2020, reflecting recruitments to support the continuous growth and development of the company.

The financial income amounted to a loss of EUR 2 million in 2020, as compared to a loss of EUR 1.1 million in 2019. The financial loss in 2020 includes interest expenses for EUR 1.3 million, a EUR 1.3 million non-cash income reflecting the change in IPF warrants fair value and a EUR 1.7 million exchange rate loss, mostly reflecting year-end reevaluation of deposit in Dollar.

The net result for the financial period ending December 31, 2020 was a net loss of EUR 31.9 million, as compared to a net loss of EUR 25.7 million in 2019.

Condensed Income Statement

EUR (in thousands)	**FY 2020 12 months**	**FY 2019 12 months**
Revenue	6,806	26,557
Net research and development expenses**	(26,718)	(40,177)
General and administrative expenses	(9,935)	(11,051)
Operating gain (loss)	(29,847)	(24,671)
Financial income (expenses)	(1,975)	(1,071)
Income tax	(36)	(1)
Net income (loss)	**(31,858)**	**(25,743)**

***Net of R&D tax credit*

The audit procedures have been performed and the issuance of the audit report is in process.

Cash

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 lease and derivative debts)

were EUR 17.1 million as of December 31, 2020, as compared to EUR 27.4 million as of December 31, 2019.

The management team will host a conference call on Thursday, March 25th in English at 9:30 am EDT (New York time) / 2:30 pm CET (Paris time). A presentation will be available in the *Investors section* of the Poxel website.

To register for the video-conference:
https://us02web.zoom.us/webinar/register/WN_X5epv0UiQPyA6NRZRo3t_A

The replay of the video conference will be available on Poxel's website:
https://www.poxelpharma.com/en_us/investors/company-information/corporate-presentations

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

- Mitochondria-Targeted Drug Development Summit, April 27-29
- Kempen Life Sciences Conference, May 5
- Japan Diabetes Society, May 20-21

Next Financial Press Release: First Quarter 2021 Financial Update, April 21, 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[9] . 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)[10]. 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 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.

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

[2] 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).

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

[4] IQVIA data FY2016 and NDB data FY2016.

[5] Converted at the exchange rate as of July 28, 2020.

[6] Based on the JPY/EUR exchange rate at December 31, 2020.

[7] Sumitomo Dainippon Pharma's Fiscal Year, from April 2021 to March 2022.

[8] 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).

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

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

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