Press Release

Poxel Reports Financial Update for Cash and Revenue for the Full Year 2021 and Provides Corporate Update

- **As of December 31, 2021, cash and cash equivalents were EUR 32.3 million (USD 36.6 million)**
- **Company reports revenues of EUR 13.4 million for the year ended December 31, 2021**
- **Results of PXL065 Phase 2 (DESTINY-1) trial in NASH expected in Q3 2022**
- **Fast Track Designation (FTD) granted to PXL065 for adrenoleukodystrophy (ALD); Phase 2a clinical Proof-of-Concept (POC) biomarker program now anticipated to start midyear, with results to follow in early 2023**

For more details on this publication, a video interview of Thomas Kuhn, CEO of Poxel, is available here.

LYON, France, February 16, 2022 – 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 its cash position and revenue for the twelve months ended December 31, 2021 and provided a corporate update.

"2021 has been another productive year for Poxel. We supported our partner Sumitomo Dainippon Pharma, a leading company in the diabetes field in Japan, across all steps that led to the Japanese approval of TWYMEEG® (Imeglimin) in June followed by its launch in September. Sumitomo has a track record of success and we look forward to their further activities in Japan and other territories to maximize TWYMEEG's commercial performance," said Thomas Kuhn, CEO of Poxel.

"The year also marked the beginning of our strategic transition into rare diseases where we believe we can become a leading player due to our novel, first-in-class products, combined with our team's expertise. Our first effort in this area involves two planned Phase 2a clinical POC biomarker studies for PXL065 and PXL770 in X-linked ALD and we are thrilled that the FDA has granted Fast Track Designation to PXL065 for this important program," continued Thomas Kuhn, CEO of Poxel. "While we are very pleased with the progress of the preparatory activities for our development program in ALD, we now believe our clinical program in ALD will initiate midyear,

followed by results in early 2023. Overall, for 2022, we remain committed to executing our strategic plan and are excited to share topline results from DESTINY-1, our Phase 2 trial in NASH for PXL065, which are expected in Q3."

As of December 31, 2021, total cash and cash equivalents were EUR 32.3 million (US$ 36.6 million), as compared to EUR 40.2 million (US$ 49.4 million) as of December 31, 2020. Net financial debt (excluding IFRS16 impacts and derivative debts) was EUR 2.6 million as of December 31, 2021, as compared to EUR -17.2 million as of December 31, 2020.

EUR (in thousands)	**Q4 2021**	**Q4 2020**
Cash	28,753	15,588
Cash equivalents	3,534	24,615
Total cash and cash equivalents*	**32,287**	**40,203**

Unaudited data.
**Net financial debt (excluding IFRS 16 impacts and derivative debts) was EUR 2.6 million at the end of Q4 2021 and were EUR -17.2 million at the end of Q4 2020.*

FY21 revenue

Poxel reported revenues of EUR 13.4 million for the year ended December 31, 2021, as compared to EUR 6.8 million during the corresponding period in 2020.

EUR (in thousands)	**2021 Q1 3 months**	**2021 Q2 3 months**	**2021 Q3 3 months**	**2021 Q4 3 months**	**FY 2021 12 months**	**FY 2020 12 months**
Roivant Agreement	-	-	-	-	-	18
Sumitomo Agreement	-	13,274	-	103	13,377	6,787
Other	-	-	-	20[1]	20	1
Total revenues	-	13,274	-	123	**13,397**	**6,806**

Unaudited data.

The revenues for 2021 include the following payments from Sumitomo Dainippon Pharma (Sumitomo) under the Sumitomo license agreement:

- JPY 1.75 billion (EUR 13.2 million) milestone payment for the approval of TWYMEEG in Japan on June 23, 2021, and
- JPY 7.5 million (EUR 58 thousand) of royalty revenue which represents 8% of TWYMEEG net sales in Japan.

In accordance with the Sumitomo license agreement, Poxel is entitled to receive escalating royalties of 8 - 18% on net sales of TWYMEEG and sales-based payments

[1] Other revenue includes a payment from ENYO Pharma SA related to Vonafexor (EYP001), an FXR agonist that was licensed from Poxel in 2015.

of up to JPY 26.5 billion (approximately EUR 200 million)[2]. Based on the current forecast, Poxel expects to receive 8% royalties on TWYMEEG net sales in Japan through the Sumitomo fiscal year 2022 (April 2022 to March 2023)[3].

As part of the Merck Serono licensing agreement[4], Poxel will pay Merck Serono a fixed 8% royalty based on the net sales of Imeglimin, independent of the level of sales.

Commercial Update

TWYMEEG® (Imeglimin)

- As of December 31, 2021, royalty revenue to Poxel based on TWYMEEG net sales in Japan under the Sumitomo license agreement has been limited following TWYMEEG's recent commercial launch on September 16, 2021. TWYMEEG's initial commercial uptake has been impacted by prescribing restrictions for new products during the first year of sales and COVID-19 conditions. This has reduced the frequency of physician visits and limited the significant market education efforts required for an innovative new product with a new mechanism of action. However, due to Sumitomo's comprehensive launch activities and promotional efforts, TWYMEEG has high awareness amongst prescribing physicians.
- Following Metavant's decision to return all US and European rights for Imeglimin to Poxel, the Company conducted and completed a comprehensive evaluation of partnering options in 2021 and does not expect to enter into a broad strategic partnership for these geographies in the near term. The Company is now considering opportunities to leverage the Imeglimin data package in specific territories, including those resulting from inbound interest.
- Results from two Phase 3 clinical trials of Imeglimin were recently published in the medical journal *Diabetes Obesity and Metabolism*:
    - The TIMES 2 publication titled, "Long-term safety and efficacy of Imeglimin as monotherapy or in combination with existing antidiabetic agents in Japanese patients with type 2 diabetes (TIMES 2): A 52-week, open-label, multicentre phase 3 trial" was published in December 2021.
    - The TIMES 3 publication titled, "Efficacy and safety of Imeglimin add-on to insulin monotherapy in Japanese patients with type 2 diabetes (TIMES 3): A randomized, double-blind, placebo-controlled phase 3 trial with a 36-week open-label extension period" was published in January 2022.

[2] Converted at the exchange rate at the date of the agreement (30 Oct 2017).
[3] Corresponding to Sumitomo Dainippon Pharma's Fiscal Year.
[4] As described in the "2.3.1. Merck Serono Agreement" section of the Poxel 2020 Document d'Enregistrement Universel.

Clinical Updates

NASH (PXL065 and PXL770)

- The PXL065 Phase 2 trial (DESTINY-1) in NASH with 123 noncirrhotic biopsy-proven NASH patients across multiple clinical sites in the US is a 36-week, randomized, double-blind, placebo-controlled, parallel group, dose-ranging study designed to assess efficacy and safety; completion of enrollment occurred in September 2021. Results from this Phase 2 study are anticipated in Q3 2022. The goal of DESTINY-1 is to identify the optimal dose or doses of PXL065 to advance into a Phase 3 registration trial for the treatment of noncirrhotic biopsy-proven NASH patients.
- Last November, Poxel presented new clinical analysis on PXL065 DESTINY-1 screening data at the AASLD The Liver Meeting® 2021.
- Future development of PXL770, a first-in-class, oral direct AMPK activator, in NASH will be assessed pending results from the PXL065 Phase 2 trial in NASH and both Phase 2a POC studies in ALD.

Rare metabolic diseases (PXL065 and PXL770)

- The U.S. Food and Drug Administration (FDA) recently granted Fast Track status to PXL065 for ALD in patients with adrenomyeloneuropathy (AMN). Fast Track Designation (FTD) is awarded by FDA to investigational drugs which treat a serious or life-threatening condition, and which fill an unmet medical need. FDA notes that 'the purpose [of the Fast Track program] is to get important new drugs to the patient earlier'.[5]
- The Phase 2a clinical Proof-of-Concept (POC) biomarker program in X-linked adrenoleukodystrophy (ALD) is now anticipated to begin midyear, followed by results in early 2023.
- On December 6, 2021, as part of its strategy to increase its focus on rare diseases, Poxel announced the formation of its Scientific Advisory Board (SAB) for rare metabolic diseases The first meeting of this SAB, in 2021, included productive discussions that informed the design of the upcoming ALD POC Phase 2a studies and provided insights into pivotal trial concepts.
- During Q4 2021, Poxel participated in several scientific and patient advocacy conferences related to X-linked adrenoleukodystrophy (ALD) and presented its programs, including the comprehensive preclinical pharmacological package, targeting this severe orphan neurometabolic disease with no approved therapies. This included presentations at two major advocacy organizations, Alex The Leukodystrophy Charity in the United Kingdom and ALD Connect in the U.S.

[5] https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/fast-track

Planned Presentations and Participation at the Following Upcoming Events

- Jefferies Global Healthcare Conference, June 8-10
- JMP Securities 2022 Life Sciences Conference, June 15-16

Next Financial Press Release: 2021 Annual Results on March 23, 2022

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. Poxel has clinical and earlier-stage programs from its adenosine monophosphate-activated protein kinase (AMPK) activator and deuterated TZD platforms targeting chronic and rare metabolic diseases. For the treatment of NASH, **PXL065** (deuterium-stabilized *R*-pioglitazone) is in a streamlined Phase 2 trial (DESTINY-1). **PXL770**, a first-in-class direct AMPK activator, has successfully completed a Phase 2a proof-of-concept trial for the treatment of NASH, which met its objectives. For the rare inherited metabolic disorder, adrenoleukodystrophy (ALD), the company intends to initiate Phase 2a proof of concept studies with PXL065 and PXL770 in patients with adrenomyeloneuropathy (AMN). **TWYMEEG®** (Imeglimin), Poxel's first-in-class lead product that targets mitochondrial dysfunction, has been approved and launched for the treatment of type 2 diabetes in Japan. Poxel expects to receive royalties and sales-based payments from Sumitomo Dainippon Pharma. Poxel has a strategic partnership with Sumitomo Dainippon Pharma for Imeglimin in Japan, China, South Korea, Taiwan and nine other Southeast Asian countries. 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

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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