July 30, 2020

Poxel Announces Submission of Imeglimin Japanese New Drug Application for the Treatment of Type 2 Diabetes by Sumitomo Dainippon Pharma

- **Japanese New Drug Application (J-NDA) for Imeglimin is supported by an extensive preclinical and clinical program, including positive results from the Phase 3 TIMES program in over 1,100 patients in Japan**
- **Imeglimin is a first-in-class drug candidate with a unique dual mechanism of action with the potential to treat type 2 diabetes across several stages of the current treatment paradigm, both as a monotherapy or as an add-on to other glucose lowering therapies**
- **J-NDA submission triggers a ￥500 million (€4.1 million, $4.7 million)* development milestone payment to Poxel with the potential for a ￥1.75 billion (approximately €14.2 million, $16.6 million)* milestone payment upon product approval**
- **Pending an average J-NDA review period, Imeglimin's target product launch is anticipated in fiscal year 2021[1]**

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 that Sumitomo Dainippon Pharma has submitted a Japanese New Drug Application (J-NDA) to the Pharmaceuticals and Medical Devices Agency (PMDA) to request approval for the manufacturing and marketing of Imeglimin for the treatment of type 2 diabetes. The Imeglimin J-NDA is supported by numerous preclinical and clinical trials, including the Phase 3 TIMES (**T**rials of **IM**eglimin for **E**fficacy and **S**afety) program in Japan led by Poxel, which included three pivotal trials to evaluate Imeglimin's efficacy and safety in over 1,100 patients. In all three trials, Imeglimin met its primary endpoints and objectives and was observed to exhibit a favorable safety and tolerability profile.

"The Imeglimin J-NDA submission represents a significant milestone for Poxel and the culmination of several years of clinical development work. It also serves as a strong validation of our R&D capabilities and the international footprint that we have established. Our vision as a company is focused on developing innovative drugs for metabolic diseases, including type 2 diabetes. We are now one step closer to fulfilling this goal with Imeglimin and we will continue to work closely with Sumitomo Dainippon Pharma throughout the regulatory review process. In addition, we will continue to support Metavant in advancing

Imeglimin into a Phase 3 program in the US and Europe," said Thomas Kuhn, CEO of Poxel. “Going forward, our efforts are now focused on our two first-in-class programs for the treatment of NASH, PXL770 and PXL065, as well as advancing earlier-stage opportunities from our AMPK activator and deuterated TZD platforms.”

The Phase 3 TIMES program was a joint development effort between Poxel and Sumitomo Dainippon Pharma. The companies entered into a strategic partnership in October 2017 for the development and commercialization of Imeglimin in Japan, China, South Korea, Taiwan and nine other Southeast Asian countries.[2] The J-NDA submission triggered a ￥500 million (€4.1 million, $4.7 million) development milestone payment to Poxel. In addition, Poxel is entitled to receive a ￥1.75 billion (approximately €14.2 million, $16.6 million) milestone payment upon product approval. Furthermore, after product launch, Poxel will receive escalating double-digit royalties on net sales and sales-based payments of up to ￥26.5 billion (approximately €210 million, $250 million)* in accordance with sales goals.

“We believe that Imeglimin can be an important addition to our existing diabetes franchise through its differentiated dual mechanism of action and favorable safety and tolerability profile. Based on the clinical data, we believe that it has the potential for use as a monotherapy, and in combination with other existing therapies; thus, it provides the opportunity for greater flexibility in treatment regimens for diabetes patients,” said Koichi Kozuki, Executive Officer, Drug Development Division of Sumitomo Dainippon Pharma. “We are committed to delivering new therapeutic options to help patients manage their disease.”

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 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. Poxel also established a partnership with Roivant Sciences for Imeglimin’s

development and commercialization in countries outside of the 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 in 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) inhibitor, is advancing into a Phase 2 clinical 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.

Based on this review, and as of the date of this press release, the Company has identified one significant impact of the COVID-19 outbreak related to the initiation of the Phase 2 study enrollment for its drug candidate PXL065, which the Company initially planned during the second quarter of 2020 and is now anticipated in the second half of 2020, contingent on a safe and stable environment for patient recruitment and the availability of clinical trial sites during the COVID-19 outbreak. As of the date of this press release, and based on publicly available information, the Company has not identified the occurrence of other material negative effects on its business due to the COVID-19 pandemic. 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 proactively 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.

*****Converted at the exchange rate as of July 28, 2020.

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

[2] Including Indonesia, Vietnam, Thailand, Malaysia, The Philippines, Singapore, Republic of the Union of Myanmar, Kingdom of Cambodia and Lao People's Democratic Republic.

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Source: Poxel SA