August 7, 2024

Sumitomo Pharma and Poxel Announce Topline Results from Post-Marketing Clinical Study on TWYMEEG® for the Treatment of Type 2 Diabetes in Japan

- **Safety and tolerability profile observed, consistent with prior clinical studies in the general type 2 diabetes population**
- **Based on the results, Sumitomo Pharma is planning to conduct discussions with the regulatory authorities in Japan, on revising TWYMEEG® package insert in fiscal 2024 for patients with renal impairment with eGFR less than 45 mL/min/1.73m^2**

OSAKA, Japan & LYON, France--(BUSINESS WIRE)-- Regulatory News:

Sumitomo Pharma Co., Ltd. (Head Office: Osaka, Japan; Representative Director, President and CEO: Toru Kimura) and 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, announced today topline results obtained from a post-marketing clinical study, TWINKLE (**TW**YMEEG® in d**i**abetic patients with re**n**al impairment: A post-mar**k**eting **l**ong-t**e**rm study) ("**the Study**"), in Japanese type 2 diabetic patients with renal impairment for TWYMEEG® Tablets 500 mg (generic name: imeglimin hydrochloride, "**the Drug**") being sold in Japan, based on the Risk Management Plan.

The Study was an open-label, uncontrolled, long-term study in 60 Japanese type 2 diabetic patients with renal impairment, who had no experience of type 2 diabetes treatment other than diet and exercise therapy or insufficient glycemic management in monotherapy with a hypoglycemic agent excluding insulin formulation.

The Drug was administered at 500 mg twice-daily to patients with moderate and severe renal impairment, characterized by an estimated glomerular filtration rate (eGFR) between 15 mL/min/1.73 m^2 or higher to less than 45 mL/min/1.73 m^2, or at 500 mg once-daily to patients with end-stage renal disease, characterized by an eGFR less than 15 mL/min/1.73m^2, in monotherapy or in combination therapy with a hypoglycemic agent excluding insulin formulation, to evaluate safety and tolerability when administered orally for 52 weeks.

The Drug was observed to be safe and well tolerated in Japanese type 2 diabetic patients

with renal impairment and no significant differences were found in the incidence of adverse events, their types and severities in this study from previous clinical studies.

Specifically, most of the adverse events were mild or moderate in severity. The incidence of serious adverse events was 16.7% (10 of 60 subjects) and causality with the Drug could be ruled out in all cases. Incidence of adverse events leading to study treatment discontinuation was also limited (4 of 60 subjects).

At present, administration of the Drug is not recommended for patients with renal impairment with eGFR less than 45 mL/min/1.73m^2. Based on the results of the Study, Sumitomo Pharma is planning to conduct discussions with the regulatory authorities in Japan, on revising the package insert in fiscal 2024[1] for patients with renal impairment with eGFR less than 45 mL/min/1.73m^2.

About TWYMEEG®

TWYMEEG® is the first agent in a class of tetrahydrotriazine-containing molecules. It is thought that the Drug shows a glucose lowering effect by both a pancreatic action that promotes glucose concentration-dependent insulin secretion and an extra-pancreatic action that improves glucose metabolism in the liver and skeletal muscle (suppression of gluconeogenesis and improvement of glucose uptake), through acting on mitochondria. The Drug has the potential to prevent endothelial and diastolic dysfunction, which could provide protective effects on micro- and macrovascular defects induced by diabetes. It may also have protective effects on pancreatic β cell survival and function. Owing to its unique mechanism of action, the Drug is widely used for glucose lowering in the treatment of type 2 diabetes, either as monotherapy or as an add-on to other therapies for this purpose.

In October 2017, Sumitomo Pharma concluded a development and commercialization partnership agreement for Japan, Chinese mainland, Taiwan, Korea and nine Southeast Asian countries with Poxel SA (Head Office: Lyon, France; CEO: Thomas Kuhn) and started selling the Drug in Japan in September 2021.

About Sumitomo Pharma Co., Ltd.

Sumitomo Pharma Group defines its Mission as "To broadly contribute to society through value creation based on innovative research and development activities for the betterment of healthcare and fuller lives of people worldwide." By pouring all our efforts into the research and development, the Group aims to provide innovative and valuable pharmaceutical and healthcare solutions to people in Japan and around the world in order to realize its Mission. The Group will remain committed to research and development with the aim of continually discovering excellent pharmaceuticals, regenerative medicine/cell therapy, non-pharmaceutical products, and others with a focus on the Psychiatry & Neurology and Oncology as priority disease areas.

For more detail, please visit our website. (https://www.sumitomo-pharma.com)

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 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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[1] *Sumitomo Pharma fiscal year 2024 ends March 31, 2025.*

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