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Metavant and Poxel Announce Positive Topline Safety and PK/PD Results of Imeglimin in Patients with Type 2 Diabetes and Chronic Kidney Disease Stages 3b/4

- Trial met its primary objective with imeglimin observed to have a favorable safety and tolerability profile in patients with type 2 diabetes and chronic kidney disease stages 3b/4
- Pharmacokinetics (PK) and pharmacodynamics (PD) data are consistent with previous Poxel data
- Metavant aims to initiate a Phase 3 program in patients with type 2 diabetes and chronic kidney disease (CKD) stages 3b/4 in the US and Europe
- These results follow two positive readouts for Phase 3 trials in Japan conducted by Poxel and Sumitomo Dainippon Pharma

NEW YORK & BASEL, Switzerland & LYON, France--(BUSINESS WIRE)-- Metavant Sciences, a clinical-stage biopharmaceutical company committed to developing innovative therapies for metabolic disorders, and 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 positive topline results from a PK/PD clinical trial for imeglimin, an investigational oral therapy for the treatment of type 2 diabetes. The Metavant study evaluated the safety, tolerability and PK/PD of imeglimin in individuals with type 2 diabetes and chronic kidney disease (CKD) stages 3b/4. Imeglimin met the primary objective of being well-tolerated in this specific patient population, confirming the safety profile observed to date and demonstrating its potential in this patient population. This completes one of the key activities to prepare for a Phase 3 program in the US and Europe.

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Paul Strumph, M.D., Metavant's Chief Medical Officer, noted: "Patients with type 2 diabetes and CKD have few treatment options to improve glycemic control, and those that are available may be associated with an increased risk of hypoglycemia or lactic acidosis. This study improved our understanding of imeglimin drug levels in this population, thereby facilitating our plan to work with regulatory authorities to initiate a Phase 3 program to develop imeglimin as a treatment option in these patients with the goal of improving glycemic control with a favorable safety and tolerability profile."

PK/PD Study Design and Results
The primary objective of the 28-day, randomized, placebo-controlled, parallel design study in individuals with type 2 diabetes and CKD stages 3b/4 was to evaluate the safety, tolerability and pharmacokinetics of imeglimin. Exploratory objectives included measures of glycemic control. A total of 49 subjects with HbA1c levels ranging from 6.0% to 12.0% were assigned to one of four treatment groups (500 mg twice a day, 1500 mg once a day, 1000 mg twice a day, or placebo) for 28 days.

There were no serious adverse events reported and no cases of lactic acidosis were observed. All treatment-related adverse events were mild or moderate, with the most common being diarrhea (18.2% in placebo group, 10.5% in the total imeglimin treated group). Imeglimin PK was as predicted from modeling previously performed by Poxel. Data from this study will inform dosing for the Phase 3 program in subjects with type 2 diabetes and CKD stages 3b/4. Multiple measures of glycemic control in this new population with type 2 diabetes were consistent with previous Poxel data.

“Type 2 diabetes is the leading cause of chronic kidney disease and these data demonstrate imeglimin’s potential in a patient population where the disease is advanced and treatment options for blood glucose control are significantly reduced. The results are consistent with our Phase 2 data in the US and Europe and Phase 2b and Phase 3 data in Japan, in which imeglimin was observed to demonstrate similar safety and efficacy in patients with impaired renal function compared to patients with normal renal function,” said Christophe Arbet-Engels, M.D., Ph.D., Chief Medical Officer, Executive Vice President Late Development and Medical Affairs at Poxel. “To date, imeglimin has been studied in 28 clinical trials in over 2,500 subjects, which support imeglimin’s improved glycemic control and favorable side effect profile.”

On February 12, 2018, Roivant Sciences and Poxel announced a strategic development and license agreement for imeglimin in the U.S., Europe and all other countries not covered by Poxel’s existing agreement with Sumitomo Dainippon Pharma in East and Southeast Asia[1].

About Imeglimin
Imeglimin is the first clinical candidate in a new chemical class of agents called glimins. Imeglimin acts on the three key organs which play an important role in the current anti-diabetic treatment paradigm: the liver, muscles, and the pancreas. In several studies conducted to-date, imeglimin has demonstrated potential glucose-lowering effects through increased insulin secretion in response to glucose, increased insulin sensitivity, and suppression of gluconeogenesis. Imeglimin’s mechanism of action also has the potential to provide protective effects on endothelial and beta cell survival and function. Imeglimin has been evaluated in a total of 28 clinical trials in over 2,500 subjects with type 2 diabetes in the U.S., Europe, and Japan. The trials have consistently met their primary objective, which demonstrated improved glycemic control in patients with type 2 diabetes with a favorable side effect profile observed.

About Poxel SA
Poxel uses its development expertise in metabolism to advance a pipeline of drug candidates focused on the treatment of metabolic disorders, including type 2 diabetes and non-alcoholic steatohepatitis (NASH). We have successfully completed the Phase 2 clinical program for our first-in-class lead product, Imeglimin, which targets mitochondrial

dysfunction, in the U.S., Europe and Japan. Together, with our partner Sumitomo Dainippon Pharma, we are conducting the Phase 3 Trials of Imeglimin for Efficacy and Safety (TIMES) program for the treatment of type 2 diabetes in Japan. Our partner Roivant Sciences is responsible for Imeglimin's development and commercialization in countries outside of Poxel's 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 in Phase 1 and being developed for the treatment of NASH. Poxel also has additional earlier-stage programs, including deuterated drug candidates for metabolic, specialty and rare diseases. We intend to generate further growth through strategic partnerships and pipeline development. (Euronext: POXEL, www.poxelpharma.com)

About Metavant Sciences
Metavant Sciences, a member of the Roivant family of companies, is a clinical-stage biopharmaceutical company committed to developing innovative therapies for metabolic disorders. For more information, please visit the company's website at www.metavant.com.

About Roivant Pharma
Roivant Pharma is the biopharmaceutical business unit of Roivant Sciences. Roivant Pharma is focused on end-to-end biopharmaceutical company creation, launch, and oversight. Roivant Pharma companies include Altavant, Aruvant, Axovant, Dermavant, Enzyvant, Genevant, Immunovant, Metavant, Myovant, Respivant, Urovant, and Arbutus.

About Roivant Sciences
Roivant aims to improve health by rapidly delivering innovative medicines and technologies to patients. Roivant does this by building Vants – nimble, entrepreneurial biotech and healthcare technology companies with a unique approach to sourcing talent, aligning incentives, and deploying technology to drive greater efficiency in R&D and commercialization. For more information, please visit www.roivant.com.

Forward-Looking Statements
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. The Poxel and Roivant Sciences agreement includes all countries other than those covered under the Poxel and Sumitomo Dainippon Pharma agreement, which includes Japan, China, the Republic of Korea, Taiwan, 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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