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Poxel Announces Positive Results from a Preclinical Study for PXL065, a Proprietary Deuterium-Stabilized R-Stereoisomer of Pioglitazone, in Hypertrophic Cardiomyopathy

- Hypertrophic cardiomyopathy (HCM) is the most common human genetic cardiac disorder and can lead to serious complications including heart failure and sudden cardiac death
- The preclinical study was financed through a grant by DZHK¹ and conducted at the TUM University Hospital German Heart Center under a research collaboration² between Poxel and the TUM University Hospital German Heart Center
- PXL065 demonstrated significant benefits in a HCM mouse model preventing pathological myocardial remodeling, including hypertrophy and fibrosis in the heart
- The top-line results from this mouse model support the clinical development of PXL065 as a potential disease-modifying treatment for symptomatic and asymptomatic HCM

LYON, France--(BUSINESS WIRE)-- Regulatory News:

[POXEL SA](#) (Euronext : POXEL - FR0012432516), a clinical stage biopharmaceutical company developing innovative treatments for chronic serious diseases with metabolic pathophysiology, including metabolic dysfunction-associated steatohepatitis (MASH) and rare metabolic disorders, today announces the positive top-line results for PXL065 from a preclinical study conducted in a mouse model of hypertrophic cardiomyopathy. PXL065 is a novel, proprietary deuterium-stabilized R-stereoisomer of pioglitazone which is known to reduce inflammation and fibrosis, improve mitochondrial function, and restore metabolic balance.

Thomas Kuhn, CEO of Poxel, stated: *"We are very pleased with these top-line results, which illustrate the potential of PXL065 for treating hypertrophic cardiomyopathy, the most common genetic cardiac disorder. Current therapeutic options for this disease are limited, with either low efficacy, a difficult safety profile or addressing a limited patient population. There is therefore a high medical need for novel, effective and well-tolerated treatments that would prevent disease progression and help to avoid invasive procedures such as heart*

surgery. We look forward to initiating the clinical development of PXL065 in this indication based on these promising results.”

Prof. Dr. Cordula Wolf, Director of the Center for Rare Congenital Heart Diseases at the TUM University Hospital German Heart Center, added: *“The findings of the pre-clinical study conducted in collaboration with Poxel represent a major step in the development of a novel therapeutic approach to treat hypertrophic cardiomyopathy, a severe and progressive disease that can lead to life-threatening cardiac events. Results obtained during this preclinical study showed that PXL065 may have the potential to improve the clinical outcomes for patients suffering from this genetic condition by reducing left ventricular hypertrophy, decreasing cardiac fibrosis and improving the underlying pathophysiological mechanisms. The profile of PXL065 also compares well versus standard of care, including mavacamten, with a highly differentiated mechanism of action. Building on the data package available for this novel compound, in our view the study results support the development of PXL065 as a disease modifier and long-term treatment for HCM patients.”*

Hypertrophic Cardiomyopathy (HCM) is a genetic disorder marked by myocardial hypertrophy, cardiac fibrosis, ventricular dysfunction, arrhythmias, and an increased risk of sudden cardiac death. It is caused by mutations in sarcomere protein genes, leading to altered cell metabolism, including oxidative stress and mitochondrial dysfunction. The estimated prevalence of HCM is 0.2%, or 1/500 adults, and its incidence is around 5 per 100,000 person-years.

In connection with the mechanism of action of PXL065 on the inhibition of the mitochondrial pyruvate carrier (MPC) and on the inhibition of Acyl CoA Synthetase 4 (ACSL4) thus acting on oxidative stress, inflammation and fibrosis, PXL065 was tested in an established mouse model of hypertrophic cardiomyopathy. After 10 weeks of treatment, a significant reduction in myocardial hypertrophy associated with a significant reduction in cardiac fibrosis was demonstrated, highlighting the potential of PXL065 in this pathology.

This preclinical study was funded by the German Center for Cardiovascular Research (DZHK) and conducted at the TUM University Hospital German Heart Center by leading HCM expert Prof. Dr. Cordula Wolf. Poxel and the TUM University Hospital German Heart Center collaborated on the pre-clinical study based on Poxel’s existing data and patent portfolio on PXL065 and prior research conducted by Prof. Dr. Cordula Wolf and her group on the disease mechanisms and therapeutic use of TZD’s in HCM. The top-line results available indicate that PXL065 prevents pathological myocardial remodeling in a HCM mouse model, including hypertrophy and cardiac fibrosis. A detailed analysis of the transcriptome and proteomics will help evaluate the mechanistic pathways of PXL065. The deuterium-stabilized R-Pioglitazone may thus provide a promising therapeutic approach for the long-term treatment of HCM.

The full results of this preclinical study have been submitted for presentation at an upcoming scientific meeting.

In parallel of finalizing the analysis of this study and pending additional financing, Poxel plans to define the best patient population for HCM that could benefit from PXL065 based on the data available and its mechanism of action and also to elaborate the associated clinical development and regulatory plan under advice from leading HCM experts including Prof. Dr. Cordula Wolf.

About Poxel SA

Poxel is a **clinical stage biopharmaceutical company** developing **innovative treatments for chronic serious diseases with metabolic pathophysiology**, including **metabolic dysfunction-associated steatohepatitis (MASH)** and rare disorders. For the treatment of MASH, **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 now 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. 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 *DZHK: German Center for Cardiovascular Research (Deutsches Zentrum für Herz-Kreislauf-Forschung)*

² *The research collaboration between Poxel and the TUM University Hospital German Heart Center currently entails evaluating the potential of PXL065 for the treatment of HCM in pre-clinical studies under a research grant obtained from DZHK*

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