

July 12, 2021



Poxel Announces New Strategic Direction with Increasing Focus on Rare Metabolic Diseases Following Recent Achievements

- **Following the recent approval of TWYMEEG® (Imeglimin) in Japan and associated potential future revenues, Poxel to accelerate and expand rare metabolic disease programs leveraging existing platforms and proven capabilities**
- **Poxel to advance its deuterated thiazolidinediones (dTZD) and direct adenosine monophosphate-activated protein kinase (AMPK) activator platforms in rare metabolic diseases with initiation of PXL065 and PXL770 Phase 2a clinical Proof-of-Concept (POC) studies in X-linked adrenoleukodystrophy (ALD) in early 2022; data expected in Q4 2022**
- **Continued commitment to non-alcoholic steatohepatitis (NASH) through PXL065 DESTINY Phase 2 trial with results expected in Q3 2022; reassessment of PXL770 future development in NASH pending results from PXL065 Phase 2 trial and both Phase 2a POC studies in ALD**
- **Webcast and conference call on Monday, July 12, at 6:00pm CEST (in French), 1:15pm ET (in English)**

LYON, France--(BUSINESS WIRE)-- [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 disorders, today announced a new strategic direction to focus its pipeline on high value, rare metabolic indications and NASH, with the goal of creating pipeline synergies, maximizing resources, and driving shareholder value.

"Based on the recent approval of TWYMEEG® (Imeglimin) in Japan with the associated infusion of cash and potential for future royalty and sales-based payments, we completed a strategic pipeline evaluation focused on determining the optimal value-creating opportunities for our technologies," said Thomas Kuhn, CEO of Poxel. "Following our recent achievements and a thorough review of the Company's programs, we are excited to announce a new strategic direction for Poxel, with an increasing focus on rare metabolic indications that represents the intersection of high unmet medical needs, promising pre-clinical and clinical data, opinion leader enthusiasm, significant commercial opportunity, and attractive time horizons. Moreover, we believe that by leveraging our existing platforms and proven capabilities to develop products in rare metabolic diseases in addition to NASH, we can be more efficient with our resources and more expediently deliver novel medicines to patients with an even stronger potential to create significant value for the benefit of our shareholders.

We also anticipate expanding our rare disease pipeline with additional internal and external clinical opportunities.”

“Our first rare disease development program targets ALD, a serious monogenic disorder with no approved pharmaceutical therapy, where both direct AMPK activation and non-genomic pathways modulated by TZDs have been implicated as therapeutic opportunities,” commented David E. Moller, MD, Chief Scientific Officer of Poxel. “Our recent preclinical data demonstrates that both approaches have substantial efficacy potential. This includes the reversal of pathology in patient-derived cells and improvements in the phenotype of the classical rodent animal model. Moreover, since there are strong preclinical biomarker signals, we believe that our pending Phase 2a studies will provide meaningful near-term results that could then lead to a pivotal trial.”

Based on results from the ongoing PXL065 DESTINY Phase 2 NASH trial and the planned Phase 2a POC biomarker studies for PXL065 and PXL770 in ALD, the Company intends to select one program, either PXL065 or PXL770, to advance in NASH and one program to advance in ALD. In parallel with the Company’s efforts in ALD, another important goal is to launch an additional rare disease development program in 2022. The Company believes that this strategy will expand the addressable market opportunity for its development programs and offers stakeholders a more diversified clinical pipeline.

As a result of the review process and portfolio prioritization, the Company is announcing the following clinical development program updates:

- In ALD, Phase 2a clinical POC biomarker studies of PXL065 and PXL770 are planned to initiate in early 2022, with data expected by year end 2022. The initial focus will be on patients with adrenomyeloneuropathy (AMN), the largest subtype of ALD. Two identical studies will enroll adult male AMN patients and assess the effect of PXL065 and PXL770 over 12 weeks of treatment on pharmacokinetics, safety, and efficacy using relevant biomarkers, including the impact on elevated very long-chain fatty acids (VLCFA), the hallmark plasma marker of disease.
- In NASH, PXL065, deuterium-stabilized *R*-pioglitazone, is in a streamlined Phase 2 trial (DESTINY). Patient screening is finished and enrollment is now expected to complete in Q3 2021, with topline data anticipated approximately one year later. This Phase 2 36-week trial in noncirrhotic biopsy-proven NASH patients will assess three doses of PXL065 compared to placebo in at least 120 patients. The results of this trial will be used to help identify the dose or doses for a Phase 3 registration trial.
- Initiation of the NASH Phase 2b trial for PXL770, a first-in-class, oral direct AMPK activator, will be postponed, pending results from the ongoing PXL065 Phase 2 trial in NASH and both Phase 2a POC biomarker studies in AMN. In the STAMP-NAFLD Phase 2a trial, completed at the end of 2020, PXL770 was observed to produce significant improvements in liver fat content and liver enzymes with a greater response in patients with co-existing Type 2 diabetes mellitus (T2DM); in these patients, additional improvements in glycemia were observed. PXL770 was observed to be safe and well tolerated.

Corporate Update

- To support this new strategic direction and following the recent approval of TWYMEEG in Japan, which completes a significant chapter in Poxel's development, the composition of Poxel's Board of Directors has evolved with the appointment of Dr. John Kozarich as a director during the June 23, 2021 general assembly meeting, who also becomes the chair of the scientific committee of the Board, and the departure of Bpifrance Participations as Board observer, effective July 9, 2021.
- In addition, the approval of TWYMEEG in Japan enabled Poxel to draw down the third and final tranche of EUR 13.5 million from the IPF loan, which was received on June 30, 2021.

The Poxel executive management team will host a conference call to present the new strategic plan. The call will be led by Thomas Kuhn, Chief Executive Officer of Poxel, who will be joined by external experts in ALD and by members of the executive management team to answer questions.

The conference calls will be held on July 12th:

- In **French**, at **12:00 pm ET** (New York) / **6:00 pm CEST** (Paris time).

To register for the webcast:

https://us02web.zoom.us/webinar/register/WN_I5qp1FHkSkm9WNOBjfGHOg

- In **English**, at **1:15 pm ET** (New York) / **7:15 pm CEST** (Paris time).

To register for the webcast:

https://us02web.zoom.us/webinar/register/WN_VVZYJ6JIQgqEdlQcT8HTlw

A presentation will be available in the [Investors section](#) of the Poxel website. The replay of the video conference will be available on Poxel's website:

https://www.poxelpharma.com/en_us/investors/company-information/corporate-presentations

About NASH

Non-alcoholic steatohepatitis (NASH) is a metabolic disease with no clear disease origin that is quickly becoming a worldwide epidemic. It is characterized by the accumulation of fat in the liver causing inflammation and fibrosis. The disease can be silent for a long period of time, but once it accelerates, severe damage and liver cirrhosis can occur, which can significantly impact liver function or can even result in liver failure or liver cancer. Typical risk factors for NASH include obesity, insulin resistance, elevated levels of blood lipids (such as cholesterol and triglycerides) and type 2 diabetes. Type 2 diabetes is also a frequent co-morbid condition (estimated to be present in up to 50% of NASH patients). Currently no curative or specific therapies are available.

About ALD

X-linked adrenoleukodystrophy (ALD) is an orphan neurometabolic disease caused by mutations in the ABCD1 gene which encodes for a key protein that is required for metabolism of very long chain fatty acids (VLCFA) by peroxisomes (cellular organelles).

ALD is the most common leukodystrophy with a prevalence similar to hemophilia – up to 1/10,000 individuals in the general population have ALD [<https://rarediseases.org>]. Forms of this disease include cerebral ALD (C-ALD) and adrenomyeloneuropathy (AMN) which is the most common form – typically occurring in adolescence through adulthood. AMN is characterized by chronic and progressive distal axonopathy involving the long tracts of the spinal cord and to a lesser extent the peripheral nerves resulting in progressive stiffness and weakness in the legs, impaired gait and balance, incontinence, and loss of sensation. All men are affected and many women also present with features of AMN with a later onset. C-ALD is characterized by inflammatory demyelination of cells in the brain and typically afflicts children, but many men with AMN may also develop cerebral disease; these white matter brain lesions lead to severe neurologic deficits and death. There are no approved medicines for ALD (other than glucocorticoid supplements for associated adrenal insufficiency). C-ALD when first detected in early childhood, can be treated with hematopoietic stem cell transplantation. HSCT is currently limited to early stage of CALD and this procedure is at risk of severe adverse reactions.

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). 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. In 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 for the treatment of type 2 diabetes in Japan. With this approval, Poxel is entitled to receive milestones, sales-based payments and royalties 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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