February 16, 2022

Poxel Announces PXL065 Granted FDA Fast Track Designation for X-linked Adrenoleukodystrophy

- **Phase 2a clinical Proof-of-Concept biomarker study for PXL065 in adrenoleukodystrophy (ALD) now anticipated to start midyear, with results to follow in early 2023**

LYON, France--(BUSINESS WIRE)-- POXEL SA (Euronext: POXEL - FR0012432516), a clinical stage biopharmaceutical company developing innovative treatments for serious chronic diseases with metabolic pathophysiology, including non-alcoholic steatohepatitis (NASH) and rare metabolic disorders, is pleased to announce that the U.S. Food and Drug Administration (FDA) has granted Fast Track Designation (FTD) to PXL065 for the treatment of patients with adrenomyeloneuropathy (AMN), the most common form of X-linked adrenoleukodystrophy (ALD). PXL065 is a novel, proprietary deuterium-stabilized R-stereoisomer of pioglitazone that is preparing to enter into a Phase 2a clinical Proof-of-Concept (POC) biomarker study midyear.

Poxel CEO, Thomas Kuhn, commented: "By awarding Fast Track Designation to PXL065, the FDA recognizes the drug's potential to address a significant unmet medical need for patients with ALD, where no approved therapies currently exist. This is a very powerful acknowledgement and good news for patients waiting to be treated. Fast Track Designation confers multiple benefits that are of great value and have the potential to substantially accelerate the approval timeline for PXL065 in ALD. We look forward to working closely with the FDA as we prepare to embark on our Phase 2a clinical study for PXL065 now planned to begin midyear, followed by results in early 2023."

Fast Track Designation (FTD)

- FTD is designed to expedite development of pharmaceutical products which demonstrate the potential to address unmet medical needs in serious or life-threatening conditions.
- FTD provides Poxel with substantially enhanced access to FDA, including opportunities for face-to-face meetings and written consultations throughout the remaining development of PXL065.
- Drugs with FTD are eligible to apply for Accelerated Approval and Priority Review at the time of a New Drug Application (NDA) submission, which may result in faster product approval.
- FTD also allows for 'rolling review', whereby Poxel may submit completed sections of the NDA as they become available, rather than at the end of development.

Next Steps

The Phase 2a clinical POC biomarker study for PXL065 in X-linked ALD is anticipated to begin midyear**,** followed by results in early 2023.

Fast Track Designation

Introduced under the FDA Modernization Act (1997), Fast Track Designation (FTD) may be awarded by the FDA to investigational drugs which treat a serious or life-threatening condition, and which fill an unmet medical need. Filling an unmet medical need is defined as providing a therapy where none exists or providing a therapy which may be potentially better than available therapy. The FDA notes that "the purpose of the Fast Track program is to get important new drugs to the patient earlier[1]". FTD must be requested by the sponsor company and must be accompanied by a detailed review of both preclinical and clinical data.

The key benefits of FTD comprise enhanced access to the FDA, with regular and more frequent opportunities for consultation and discussion. In addition, drugs with FTD may be eligible for Accelerated Approval, in which a new medicine is approved prior to the availability of definitive data, and Priority Review, in which the standard 10-month review process is reduced to six months. Drugs with FTD may also enter a 'rolling review' of their NDA submission, in which sections are submitted and reviewed as they become available, substantially expediting the approval process.

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. Nearly all men with a diagnosis of ALD will develop AMN, 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 C-ALD 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-1). **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. For 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 and launched for the treatment of type 2 diabetes in Japan. Poxel expects to receive royalties and sales-based payments 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

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[1] https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/fast-track

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