Minoryx publishes mechanism of action of leriglitazone in X-ALD in Science Translational Medicine journal

Published data highlights therapeutic potential for all forms of X-ALD as well as other neurodegenerative and neuroinflammatory diseases

Mataró, Barcelona, Spain, June 3, 2021 - Minoryx Therapeutics, a Phase 3 clinical stage biotech company focused on the development of differentiating treatment options in orphan central nervous system (CNS) disorders, today announces the publication of mechanism of action data of its lead candidate leriglitazone, a novel, selective and brain penetrant PPARγ agonist.

Published results show efficacy in both adrenomyeloneuropathy (AMN) and cerebral ALD (cALD) related models. The data demonstrate the potential of leriglitazone to treat the whole spectrum of the X-linked adrenoleukodystrophy (X-ALD) condition as well as other neurodegenerative and neuroinflammatory conditions. The paper has been published in *Science Translational Medicine*, a peer-reviewed journal: https://stm.sciencemag.org/content/13/596/eabc0555.

The publication of these data follows the disclosure of results from Minoryx's Phase 2/3 ADVANCE clinical trial in adult male patients with AMN, showing that leriglitazone reduces the progression of cerebral lesions and myelopathy symptoms. These data also support Minoryx's ongoing NEXUS study, an open-label phase 2 trial assessing leriglitazone in male pediatric patients with early stage cALD.

The publication provides details of the molecular mechanism of action of leriglitazone, modulating multiple pathways involved in the pathophysiology of X-ALD by delaying or stopping the progression of AMN and cALD. The study results reinforce the first in class potential of leriglitazone as a novel brain-penetrant drug candidate with an improved profile over other PPARγ agonists, including pioglitazone. Importantly, these data validate the concept of treatment of neurodegeneration and neuroinflammation with a brain penetrant PPAR gamma agonist and provides further evidence to support the development of leriglitazone in X-ALD.

The published studies show that leriglitazone modulates the key hallmarks in X-ALD in several in vitro and in vivo models. In those models, leriglitazone exerts neuroprotective and antioxidant effects, improves mitochondrial function and reduces microglial activation. Leriglitazone also increases myelin debris clearance and oligodendrocyte survival and myelination, thus promoting remyelination. Finally, leriglitazone reduces neuroinflammation and prevents the endothelial damage disrupting the blood-brain barrier (BBB) that characterizes the early stages of cALD. The publication also reports phase 1 data showing CNS exposure and PPARγ engagement in humans at levels that were efficacious in preclinical models.

"The results generated by Minoryx are aligned with those obtained in our recent study in adult X-ALD patients and reinforce the potential use of leriglitazone in this condition as well as a broader range of neurodegenerative and neuroinflammatory diseases with a high unmet medical need," said Marc Martinell, CEO, Minoryx. "We would like to thank all co-authors for their contribution to this key publication."

X-ALD is an orphan neurodegenerative disease. The most common form of X-ALD is AMN, which is a chronic disease affecting all male and female X-ALD patients reaching adulthood. There is currently no approved treatment. X-ALD patients can also develop an acute form, cALD. This results in brain inflammation and leading to permanent disability and death within 2-4 years. cALD typically affects boys with an age of onset between 4-8 years. However, adult males with AMN can also develop this aggressive phenotype. For cALD the only available treatments are based on Hematopoietic stem cell transplantation (HSCT), but even if such treatments stop cALD progression, they still do not prevent the development of AMN.

Leriglitazone has been granted orphan drug status *for X-linked adrenoleukodystrophy* from the FDA and the EMA and fast track and rare pediatric disease designation from the FDA for the treatment of X-ALD. Minoryx is currently completing documentation to be submitted to regulatory authorities for discussions for approval of leriglitazone for AMN patients.

Minoryx is also developing leriglitazone in Friedreich's Ataxia, where after showing clinical benefit in a phase 2 proof of concept study (FRAMES) the company is preparing a phase 3 study.

About Minoryx
Minoryx is a clinical stage biotech company focusing on the development of novel therapies for orphan CNS diseases with high unmet medical needs. The company's lead program, leriglitazone (MIN-102), a novel, selective PPARγ agonist, is currently being evaluated in X-linked Adrenoleukodystrophy (X-ALD) and Friedreich's Ataxia. The company is backed by a syndicate of experienced investors, which includes Caixa Capital Risc, Roche Venture Fund, Ysios Capital, Kurma Partners, Fund+, Chiesi Ventures, S.R.I.W, Idinvest, SFPI-FPIM, HealthEquity and Sambrinvest, and has support from a network of other organizations. Minoryx was founded in 2011, is headquartered in Spain with Belgian facilities and has so far raised more than €85 million. www.minoryx.com

About leriglitazone
Leriglitazone (MIN-102) is Minoryx's novel orally bioavailable and selective PPARγ agonist with a potential first-in-class and best-in-class profile indicated for CNS diseases. It has demonstrated sufficient brain penetration and a favorable safety profile. It showed robust preclinical proof-of-concept in animal models of multiple diseases by modulating pathways leading to mitochondrial dysfunction, oxidative stress, neuroinflammation, demyelination and axonal degeneration. In clinical trials, leriglitazone showed clinical benefit both for X-ALD and Friedreich's Ataxia patients.

About X-ALD
X-ALD (X-linked adrenoleukodystrophy) is an orphan neurodegenerative disease. The global incidence of X-ALD is approximately 6.2/100,000 live births and AMN and cALD are the two most common phenotypes. AMN affects all patients reaching adulthood and is characterized by progressive spastic paraparesis, sensory dysfunction and incontinence. This form progresses chronically with onset of symptoms typically in adulthood, affecting both men and women and has poor prognosis. cALD typically affects boys with an age of onset between 4-8 years, although recent literature suggests that up to 60% of adult AMN patients develop cALD in an average time of 10 years since onset of myelopathy. Untreated cALD patients progress quickly, as severe neurological function impairment appears 6-24 months after disease onset, often leading to permanent disability and death within 2-4 years. There is currently no approved treatment available for AMN. The only available treatments for cALD

are based on hematopoietic stem cell transplantation (HSCT). However, HSCT requires a very aggressive procedure and there is no evidence that it prevents patients from progressing to AMN later in their lives.

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