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The Lancet Neurology publishes results from Minoryx Therapeutics Phase 2/3 ADVANCE clinical trial of leriglitazone in X-linked Adrenoleukodystrophy

Leriglitazone was well tolerated, and significant benefit was shown through clinically meaningful myelopathy endpoints and reduced progression of cerebral lesions

Mataró, Barcelona, Spain, January 19, 2023 - Minoryx Therapeutics ("Minoryx"), a Phase 3 clinical stage biotech company focused on the development of differentiating treatment options in orphan central nervous system (CNS) disorders, today announces that data from its Phase 2/3 ADVANCE clinical trial of lead candidate, leriglitazone, has been published in The Lancet Neurology. This trial, assessing the efficacy and safety of leriglitazone in male patients with adrenomyeloneuropathy, is the first and largest international study to enroll adult male X-linked adrenoleukodystrophy patients.

X-linked adrenoleukodystrophy (X-ALD) is an orphan inherited neurodegenerative disease. Adrenomyeloneuropathy (AMN) affects X-ALD patients when reaching adulthood and it is characterized by progressive deterioration of balance and sensory function, spastic paraparesis and development of incontinence. Mobility is significantly affected with progression and therefore maintaining sensorimotor balance in patients with AMN is very important[1].

X-ALD male patients (pediatric and adult) develop cerebral lesions that can evolve to progressive cerebral ALD (cALD), which is devastating and leads to death within two to four years. The potential of the development of cALD is a major concern to both patients and clinicians with regular MRI screening being recommended[2]. In cALD patients, allogenic and autologous hematopoietic stem cell transplantation (HSCT) are the only treatment options available. However, they are only possible in a limited number of patients. For AMN patients, only symptomatic supportive care is available. Therefore, a treatment is very much needed for X-ALD patients allowing early intervention to halt disease progression.

Minoryx's Phase 2/3 ADVANCE clinical trial was a pivotal multicenter, double-blind and placebo-controlled study conducted in the United States and Europe in adult male X-ALD patients with AMN. In the ADVANCE trial, of 116 patients randomized, 77 received leriglitazone and 39 received placebo. The study did not meet the primary outcome for the 6-minute walk test. However, clinical measures of body sway (assessing balance) demonstrated clinically relevant differences and favorable trends were observed for EDSS, SSPROM and quality of life. Leriglitazone was generally well tolerated.

In addition, the results also showed that leriglitazone reduces the progression of cerebral lesions and only placebo group patients developed clinically progressive cALD (6 out of 39 patients). Plasma biomarker data showed that neurofilament light levels were significantly increased at week 96 in placebo patients with cerebral lesion progression, supportive of a drug effect on reducing axonal degeneration. Treatment with leriglitazone also significantly reduced plasma levels of MMP-9, a marker of blood-brain barrier integrity. Furthermore, while at baseline, both placebo and leriglitazone groups were well balanced in terms of number of patients with a Loes severity score greater than 0, an increase in this score at week 96 was significantly greater in the placebo group.

The ADVANCE study continues as an open label extension study for three further years with on-going monitoring of both myelopathy and cerebral lesion progression. The final five-year data will read out towards the end of 2023. Moreover, a two-year pediatric study in boys with progressive cALD, called NEXUS, is due to report six-month interim data in H1 2023.

The Committee for Medicinal Products for Human Use (CHMP) for the European Medicines Agency (EMA) is currently reviewing leriglitazone's Marketing Authorization Application (MAA) that Minoryx submitted in August, 2022 for the treatment of adult male patients with X-linked adrenoleukodystrophy (X-ALD).

"Minoryx's Phase 2/3 ADVANCE study is the first international and robust study providing evidence of drug effect in this population," said Professor Wolfgang Kohler, Global Co-ordinating Investigator, University of Leipzig Medical Centre."The ADVANCE study has consolidated clinically meaningful endpoints

for AMN myelopathy with body sway assessments and also the need to treat early in the AMN time course with leriglitazone showing clinical utility in this disease with a significant unmet need."

"The finding that no patients treated with leriglitazone developed progressive cerebral ALD is very significant. The cerebral lesion stabilization seen with MRI in placebo patients who progressed in the blinded period and are now on leriglitazone is even more promising for patients with cerebral ALD," said Principal Investigator, Professor Fanny Mochel, Paris Brain Institute, Sorbonne University, Paris.

"The ADVANCE data are integral to Minoryx's Marketing Authorization Application which is now under review by the EMA," said Marc Martinell, CEO, Minoryx. "We are working together with our partner Neuraxpharm to ensure that leriglitazone reaches X-ALD patients as quickly as possible."

Leriglitazone has been granted orphan drug status for X-ALD from the FDA and the EMA; and fast track and rare pediatric disease designation from the FDA for the treatment of X-ALD.

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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 neuroinflammation, demyelination and mitochondrial dysfunction. In clinical trials, leriglitazone showed clinical benefit for X-ALD patients and clinical proof of concept in Friedreich's Ataxia patients supporting further larger studies in the future.

About X-ALD
X-ALD (X-linked adrenoleukodystrophy) is an orphan neurodegenerative disease characterized by accumulation of very long chain fatty acids. The global incidence of X-ALD is approximately 6-8/100,000 live births. X-ALD patients reaching adulthood develop adrenomyeloneuropathy (AMN), characterized by progressive deterioration of balance and sensory function, spastic paraparesis and development of incontinence, due to spinal cord degeneration. A large proportion of X-ALD patients can also develop cerebral lesions that can evolve into progressive cerebral ALD (cALD), characterized by severe cognitive and motor impairment, often leading to permanent disability and death within 2-4 years. Progressive cALD typically affects boys with an age of onset between 4-8 years although recent literature indicates that up to 60% of adult X-ALD patients will also develop progressive cALD. There is currently no pharmacological treatment available for X-ALD. In progressive cALD, hematopoietic stem cell transplantation can arrest the disease when performed early enough, however, it is an aggressive procedure and only available for a portion of patients. In adults, experience in HSCT is very limited and the intervention is often not recommended in patients with advanced myeloneuropathy.

About Minoryx
Minoryx is a registration 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, brain penetrant and selective PPAR gamma agonist, is being developed in X-linked Adrenoleukodystrophy (X-ALD) and other orphan CNS diseases. The company is backed by a syndicate of experienced investors, which includes Columbus Venture Partners, CDTI Innvierte, Caixa Capital Risc, Fund+, Ysios Capital, Roche Venture Fund, Kurma Partners, Chiesi Ventures, S.R.I.W, Idinvest Partners / Eurazeo, SFPI-FPIM, HealthEquity, Sambrinvest and Herrecha, 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 €120 million.
For more information, please visit www.minoryx.com.

[1] van Ballegoij WJC et al (2020) Postural Body Sway as Surrogate Outcome for Myelopathy in Adrenoleukodystrophy. Front. Physiol. 11:786. doi: 10.3389/fphys.2020.00786
[2] Marc Engelen, MD PhD et al (2022) International Recommendations for the Diagnosis and Management of Patients With Adrenoleukodystrophy: A Consensus-Based Approach . Neurology. doi: 10.1212/WNL.0000000000201374