Minoryx Therapeutics doses first patient with leriglitazone in registration-enabling cALD NEXUS trial

Pediatric Investigational Plan (PIP) for leriglitazone in X-ALD approved by EMA, allowing Minoryx to file Marketing Authorization Application (MAA) in Europe based on NEXUS

Timelines for other ongoing trials not impacted by COVID-19 pandemic

Mataró, Barcelona, Spain and Charleroi, Belgium, May 12, 2020 – Minoryx Therapeutics, a company that specializes in the development of innovative treatments for orphan Central Nervous System (CNS) diseases, today announces the initiation of the registration-enabling Phase 2 NEXUS trial to evaluate the safety and efficacy of leriglitazone in pediatric patients with early-stage cerebral ALD (cALD), the acute form of X-linked adrenoleukodystrophy (X-ALD).

In addition the European Medicines Agency (EMA) approved the proposed PIP for leriglitazone for the treatment of X-ALD, allowing the company to file for an MAA in Europe based on the Phase 2 NEXUS trial, subject to positive results. Minoryx received a deferral for completion of its pediatric plan until after EMA approval of adrenomyeloneuropathy (AMN).

Leriglitazone (MIN-102), a novel, brain penetrant, orally bioavailable and selective PPARγ agonist, is currently in late-stage development for the treatment of severe orphan CNS disorders, including both forms of X-ALD (cALD and AMN) and Friedreich's Ataxia. Leriglitazone obtained Orphan Drug Designation in X-ALD from the European Commission and the FDA, and has been awarded the FDA fast-track procedure in X-ALD.

"With newborn screening currently being implemented, it is now possible to diagnose patients with early stage cALD, an orphan neurodegenerative disorder characterized by rapid cerebral demyelination and inflammation of the brain, leading to death within a few years of diagnosis. There is an urgent need for alternative treatments that are less invasive than the current standard of care, which is based on hematopoietic stem cell transplantation," said Dr. Patricia Musolino, principal investigator of the study and Assistant Professor in Neurology at the Harvard Medical School. "The first patient, a ten-year-old boy, has been enrolled in the NEXUS trial at the Hospital Sant Joan de Déu in Barcelona. We look forward to further supporting the company and to bringing this much needed innovation to pediatric patients suffering from this devastating disease."

María Pascual, Chief Regulatory Officer of Minoryx, added: "This EMA approval of the PIP, based on the NEXUS trial, marks an important milestone for the company. It highlights the importance of making alternative safe and effective treatments available for children with early cALD. It not only provides a clear path for faster registration of leriglitazone in childhood cerebral ALD but also paves the way for submission of the MAA in Europe for leriglitazone in adrenomyeloneuropathy, following successful completion of the ongoing Phase 2/3 ADVANCE trial."

"We are pleased that the first patient has been enrolled in the NEXUS trial and expect to report results in 2021, with the potential for preliminary results as soon as this year," said Marc Martinell, Chief Executive Officer of Minoryx.
"Despite the current COVID-19 pandemic, the timelines of the other ongoing trials with leriglitazone in adrenomyeloneuropathy and Friedrich's Ataxia have not been impacted. Always putting the safety and needs of our patients first, we continue to work diligently with the study sites and our CRO to complete these trials. We still expect to report results for both trials by the end of 2020."

About the NEXUS trial and the PIP
The NEXUS registration-directed Phase 2 clinical trial is an open-label study designed to assess the efficacy and safety of leriglitazone in male pediatric patients with early stage cerebral X-linked adrenoleukodystrophy (cALD). In addition to Spain, the trial has also been approved by ethical committees and the regulatory agencies in France and Germany. Alongside to the Barcelona study site under the supervision by Dr Angeles García-Cazorla, other recruitment sites include the University Medical Center Hamburg-Eppendörf, with Dr Anette Bley, the University Hospital Göttingen under the supervision of Dr Hendrik Rosewich and the Bicêtre Hospital in Paris with Dr Caroline Sevin.
The NEXUS trial will recruit up to 13 cALD patients with early cerebral MRI lesions. All patients will receive leriglitazone and will be carefully monitored for safety, clinical symptoms and changes in cerebral MRI lesions. The study has been designed with input from both the EMA and the FDA, clinical experts in X-ALD in Europe and the US, and patient advocacy groups. The trial is partially funded by the European Union's Horizon 2020 research and innovation programme (SME instrument) under grant agreement No 822968.
The PIP for leriglitazone is based on the NEXUS trial and has been approved by the EMA following positive opinion from its Pediatric Committee (PDCO). The PIP includes a deferral in completion of the trial until after the approval of the MAA for leriglitazone in adrenomyeloneuropathy (AMN), the most common form of X-ALD. With successful completion of the agreed PIP, leriglitazone will be eligible for two additional years of marketing exclusivity, on top of the ten-year market exclusivity after market approval.

About X-ALD and cALD
X-ALD (X-linked adrenoleukodystrophy) is the most prevalent peroxisomal disease. It is caused by mutations in the ABCD1 gene. It has an estimated incidence of 1:17,000 newborns worldwide. Although it primarily affects males, heterozygous women may also develop the disease in later life. X-ALD is characterized by the accumulation of very long chain fatty acids (VLCFA), leading to a neurodegenerative disorder where the most affected tissues are the spinal cord, the brain and the adrenal cortex. The CNS-related effects lead to two main phenotypes: adrenomyeloneuropathy (AMN), characterized by progressive motor dysfunction, and cerebral ALD (cALD), characterized by severe neuroinflammation leading to early death. The only alternative to manage cALD is hematopoietic stem cell transplantation (HSCT) but this approach does not prevent the development of AMN during adulthood, for which there is currently no approved treatment option available.

About leriglitazone
Leriglitazone (MIN-102) is a novel, brain penetrant, orally bioavailable and selective PPARγ agonist that engages the target receptor at the levels required for efficacy within the central nervous system (CNS). It has demonstrated efficacy in animal models of multiple disease modulating pathways leading to mitochondrial dysfunction, oxidative stress, neuroinflammation, demyelination and axonal degeneration. Leriglitazone has the potential to treat several CNS disorders, including orphan diseases, such as X-ALD (X-linked adrenoleukodystrophy) and Friedreich's Ataxia. A Phase 1 clinical study was successfully completed confirming that leriglitazone is well tolerated and is able to cross the blood brain barrier and engage PPARγ within the central nervous system at an equivalent level as in preclinical studies. Leriglitazone has completed enrolment in ADVANCE, a two-year double-blind, placebo-controlled, pivotal Phase 2/3 study in adult patients with adrenomyeloneuropathy (AMN) and recruitment is ongoing in NEXUS, a pivotal open-label study in pediatric cALD patients. Leriglitazone has also completed enrolment in FRAMES, a one year double-blind, placebo-controlled Phase 2 study in patients with Friedreich's Ataxia. Results from ADVANCE and FRAMES are expected by the end of 2020 and results from NEXUS are expected in 2021. Leriglitazone has obtained Orphan Drug Designation from the European Commission and the FDA in X-ALD and Friedreich's Ataxia.

About Minoryx Therapeutics
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-ALD and Friedreich's Ataxia. The company is backed by a syndicate of experienced investors, which includes Ysios Capital, HealthEquity, Kurma Partners, Chiesi Ventures, Roche Venture Fund, Caixa Capital Risc, Idinvest Partners, Fund+, S.R.I.W, Sambrinvest and SFPI-FPIM, and has support from a network of other organizations. Minoryx was founded in 2011, has operations in Spain and Belgium and has so far raised a total of more than €50M.
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