

Minoryx gains FDA approval to initiate a Phase 3 clinical trial in patients with cerebral adrenoleukodystrophy

US trial with leriglitzazone to commence in mid-2023 providing an FDA-approved route to US market whilst EMA evaluates European Marketing Authorization Application (MAA)

Mataró, Barcelona, Spain, May 31, 2023 - Minoryx Therapeutics, a registration stage biotech company focused on the development of therapies for orphan central nervous system (CNS) disorders, today announces the US Food and Drug Administration (FDA) approval of its Phase 3 clinical trial (CALYX) of lead candidate leriglitzazone, to treat adult male X-linked Adrenoleukodystrophy (X-ALD) patients with cerebral adrenoleukodystrophy (cALD).

The CALYX protocol has received both FDA and central IRB approval. Significant preparations for the trial commencement have been completed and patient recruitment is expected to start by the end of Q2 2023 with results anticipated by late 2025.

"Minoryx is focused on bringing therapeutic options to X-ALD patients and we now have an agreed route to the US market with a Phase 3 trial designed to confirm the disease modifying potential of leriglitzazone." **said Marc Martinell, CEO, Minoryx and added:** "CALYX will be funded from the Series C financing together with proceeds from our European strategic collaboration with Neuraxpharm. We look forward to initiating this trial which could provide an important therapeutic option for patients suffering from this devastating orphan disease with a major unmet medical need."

CALYX will enroll 40 adult male X-ALD patients with progressive cALD defined by the presence of gadolinium enhancing brain lesions. A pre-screening campaign will be initiated across participating sites in order to identify adult patients with brain lesions. The trial is placebo controlled with 1:1 randomization, and the primary endpoint is "time to death" or "bedridden with permanent ventilatory support". The trial has an adaptive duration with an initial pre-specified efficacy read at 18 months and if needed subsequent efficacy assessments at 27 and 36 months, respectively with the option to complete the study at any of the three time points once statistical significance is reached. Adult cALD patients with gadolinium enhancing lesions have a rapid cognitive deterioration and survival of 3-4 years.

The design of CALYX builds upon the results from the ADVANCE and NEXUS trials and from the on-going compassionate use program where leriglitzazone has demonstrated the ability to halt lesion progression. The NEXUS interim analysis (recently disclosed at AAN[1] conference) showed that after 24 weeks of treatment all patients were clinically stable and, radiologically, demonstrated disease arrest or lesion growth stabilization. Radiological changes were similar to those attained with Hematopoietic Stem Cell Transplant (HSCT) or ex-vivo gene therapy, hence it is expected that leriglitzazone could provide a comparable clinical benefit to cALD patients.

CALYX will be conducted across selected centers of excellence in the US and South America and Minoryx has appointed Dr Ali Fatemi at the Kennedy Krieger Institute in Baltimore, US as the Global Principal Investigator for CALYX.

"There is a major unmet medical need for a treatment that can halt or slow the disease progression in cALD as the majority of patients, and particularly adults, do not have any treatment option" **said Dr Ali Fatemi, Global Principal Investigator of CALYX, and added:** "Leriglitzazone results are so far very encouraging and with CALYX the objective is to confirm the clinical benefit of leriglitzazone and provide cALD patients with a treatment that can arrest or slow-down their neurological decline and prolong their lives".

[1] Abstract number 1159 entitled **"Interim Results from the NEXUS Open-Label Phase 2 Study on the Safety and Efficacy of Leriglitzazone in the Treatment of Childhood Cerebral Adrenoleukodystrophy"** presented at the 2023 Annual Meeting of the American Academy of Neurology by Professor Eric Mallack

About CALYX

CALYX will enroll 40 adult male X-ALD patients with progressive cALD defined by the presence of *gadolinium-enhancing* brain lesions, and where HSCT (haematopoietic stem cell transplantation) is not recommended or refused by the patient. Patients will be randomized either to leriglitazone or placebo with 1:1 randomization. The key exclusion criteria involve a Loes Score greater than 12, and patients that previously received HSCT or gene therapy. The trial has an adaptive duration with an initial efficacy read at 18 months and if needed subsequent efficacy assessments at 27 and 36 months respectively with the option to complete the study at any of the three time points once statistical significance is reached. Statistical analysis will, at all timepoints, be carried out using 0.05 one-sided alpha. The primary endpoint is "time to death" or "bedridden with permanent ventilatory support". Secondary endpoints include a key secondary endpoint of radiological progression through the Loes Score, clinical endpoints including Major Functional Disability, activities of daily living and major neurocognitive impairment, and biomarkers in plasma such as neurofilament light chain. There will also be safety and PK measurements.

About leriglitazone

Leriglitazone (MIN-102) is Minoryx's novel orally bioavailable and selective PPAR γ agonist with a potential first-in-class and best-in-class profile for CNS diseases. It has demonstrated 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. 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.

About X-ALD

X-ALD (X-linked adrenoleukodystrophy) is an orphan neurodegenerative disease. The global incidence of X-ALD is approximately 6-8/100,000 live births. ALD patients, boys and adult men, at any point in their lifetime can develop cALD, characterized by demyelinating brain lesions that rapidly progress, leading to acute neurological decline and death. These lesions can produce severe symptoms such as loss of voluntary movements, inability to swallow, loss of communication, cortical blindness and total incontinence and death with a mean survival of 3 to 4 years. cALD occurs in 31-35% of ALD patients in childhood with onset typically between the age of 2 and 12 years. A majority of adult ALD men, i.e., up to 60%, also develop cALD over time. cALD ultimately affects 2/3 of all male ALD patients (1/3 in pediatric age and another 1/3 in adulthood). All X-ALD patients reaching adulthood develop adrenomyeloneuropathy (AMN), characterized by progressive spastic paraparesis, as well as progressive deterioration of balance and sensory function, and development of incontinence. This form progresses chronically with onset of symptoms typically in adulthood, affecting both men and women, and has poor prognosis. There is currently no pharmacological treatment available for X-ALD. In childhood, allogeneic hematopoietic stem cell transplantation (HSCT) and the FDA-approved ex-vivo gene therapy eli-cel can arrest the disease, 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.

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 Invierte, Caixa Capital Risc, Fund+, Ysios Capital, Roche Venture Fund, Kurma Partners, Chiesi Ventures, S.R.I.W, Idivest 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 <https://www.minoryx.com/>.