Minoryx announces enrollment of first patients with cerebral Adrenoleukodystrophy (cALD) in US Phase 3 clinical trial, CALYX

As part of CALYX, Minoryx is conducting an extensive pre-screening MRI-based campaign aimed at identifying eligible adult X-ALD patients with cerebral Adrenoleukodystrophy (cALD)

Mataró, Barcelona, Spain, November 16, 2023 - Minoryx Therapeutics, a registration stage biotech company focused on the development of therapies for orphan central nervous system (CNS) disorders, today announces the first patients have been enrolled in its US Phase 3 clinical trial (CALYX) of lead candidate leriglitazone, to treat adult male X-linked Adrenoleukodystrophy (X-ALD) patients with cerebral Adrenoleukodystrophy (cALD), an orphan indication with no alternative therapeutic options.

"CALYX has been designed as a Phase 3 trial to confirm the disease modifying potential of leriglitazone that we detected in the previous ADVANCE and NEXUS trials," ***said Arun Mistry, CMO, Minoryx.*** *"The initiation of enrollment will enable Minoryx to take the final steps towards US approval of leriglitazone for treatment of X-ALD patients."*

"Minoryx has begun an extensive pre-screening program aimed at identifying additional eligible patients. This will push the Phase 3 CALYX trial forward and bring leriglitazone to patients as quickly as possible," ***said Sílvia Pascual, VP Clinical Development, Minoryx.*** *"In patients with cALD, appearance of gadolinium-enhancing lesions typically precedes a phase with pronounced lesion growth and rapid clinical deterioration. Minoryx therefore wants to encourage adult X-ALD patients to participate in the pre-screening program to have cALD diagnosed as early as possible."*

CALYX is a double-blind randomized placebo-controlled phase 3 clinical trial that will recruit 40 adult male patients with cALD across selected centers of excellence in the US and South America. The primary endpoint measuring survival, and secondary endpoints include the Loes score, major functional disabilities, activities of daily living and major neurocognitive impairment. Centers in the US are already enrolling patients and results are anticipated by early 2026.

"The X-ALD patient community is very excited to have a study commencing in adult cALD where few options are currently available," ***said Kathleen O'Sullivan-Fortin, Co-Founder, ALD Connect.*** *"This study will help increase the understanding of cALD and raise disease awareness among both patients and physicians."*

In Europe, review of the Marketing Authorization Application (MAA) is currently ongoing at EMA. Neuraxpharm, a leading CNS specialist company and Minoryx's strategic partner in Europe, is preparing for commercial launch of leriglitazone.

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 (hematopoietic 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 disabilities, 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 gamma 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. Radiological changes seen in NEXUS after 24 weeks of treatment were similar to those attained with Hematopoietic Stem Cell Transplant (HSCT) or ex-vivo gene therapy, hence it is expected that leriglitazone could provide a comparable clinical benefit to cALD 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 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.

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