Leriglitazone halts disease progression in adult patients with early cerebral adrenoleukodystrophy in compassionate-use study published in *Brain*

In a French early-access program study, 10 of 13 patients were clinically and radiologically stable

Mataró, Barcelona, Spain, 11 June, 2024 - Minoryx Therapeutics ("Minoryx"), a late-stage biotech company focused on the development of therapies for orphan central nervous system (CNS) disorders, today announce that results from a compassionate use study of leriglitazone for treatment of progressive cerebral adrenoleukodystrophy (cALD) in adult male patients, published[1] in the peer-reviewed journal *Brain*.

The compassionate-use study was led by Fanny Mochel, MD, Ph.D., professor at the Hôpital Universitaire La Pitié-Salpêtrière (Paris, France), as part of an early-access program through the French national drug agency (ANSM) that allows for the use of innovative treatments with favorable safety profiles under a Compassionate Access Authorization protocol (ATU)[2].

The publication describes 13 adult male patients with progressive cALD, a fatal neurodegenerative disorder that is characterized by growing, demyelinating brain lesions. The patients were either awaiting hematopoietic stem cell transplantation (HSCT) – the only treatment option for progressive cALD today – or ineligible for HSCT.

Among the 13 patients treated with leriglitazone, the disease stabilized clinically and in radiological tests in 10 patients through up to two years of follow-up. Five patients that had originally presented with gadolinium enhancement (active neuroinflammation) lesions in the corticospinal tract that usually lead to poor HSCT outcomes all became gadolinium negative. Importantly, the lesion load was reduced in four of these patients. Moreover, plasma neurofilament light chain levels (a biomarker for neurodegeneration) stabilized in all 10 patients and correlated with lesion load. The two patients who continued to deteriorate were both over 60 years of age with prominent cognitive impairment at baseline, while one patient died from Covid-19 a few months after initiating treatment. Leriglitazone was well tolerated in all patients, with minimal weight gain in most patients and moderate leg edema in only two patients.

These results are in contrast with the natural history for patients with progressive cALD, which predicts rapid lesion progression leading to acute neurological decline, with death occurring typically within 3-4 years of onset.

"This cohort study shows that leriglitazone can halt neuroinflammation and disease progression in adult patients with cALD at early disease stages, as evidenced by clinical, radiological, and biological stability for up to two years of treatment," **said Prof. Mochel.** *"All five patients who initiated treatment while on the waiting list for stem cell transplant have now been taken off, on the basis of the positive results observed with leriglitazone."*

"*The results are very encouraging and support the efficacy of leriglitazone that we have observed in our clinical trials, ADVANCE[3] and NEXUS[4],"* **said Marc Martinell, CEO, Minoryx**. *"In these studies in adult and pediatric patients with cALD, leriglitazone is able to reduce further lesion development and stabilize patients clinically and radiologically. These results from Hôpital Universitaire La Pitié-Salpêtrière further confirm the effect of leriglitazone."*

In consultation and alignment with the U.S. Food and Drug Administration, Minoryx has launched a phase 3 clinical trial (CALYX[5]) in patients with adult progressive cALD that have a profile similar to those treated at Hôpital Universitaire La Pitié-Salpêtrière. CALYX is currently recruiting adult patients with progressive cALD in the U.S., Brazil, and Argentina.

Brain has provided a video summary of the study on their video channel[6].

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About NEZGLYAL® (leriglitazone)

NEZGLYAL® (leriglitazone) is Minoryx Therapeutics'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, NEZGLYAL® showed clinical benefit in both adult X-ALD patients in ADVANCE and pediatric X-ALD patients in NEXUS. Data from ADVANCE showed that NEZGLYAL® reduces the progression of lesions and the development of progressive cALD. Results on radiological stabilization 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 NEZGLYAL® could provide a comparable clinical benefit to cALD patients. NEZGLYAL® 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. In Europe, NEZGLYAL® is exclusively licensed to Neuraxpharm.

About X-ALD and cALD

X-linked adrenoleukodystrophy (X-ALD) is an orphan neurodegenerative disease. The global incidence of X-ALD is approximately 6-8/100,000 live births. Boys and adult men with X-ALD can, at any point in their lifetime, develop cALD, which is characterized by demyelinating brain lesions that may become rapidly progressive, 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.

Progressive cALD occurs in 31-35% of ALD patients in childhood with typical onset between the age of 2-12 and up to 60% of adult patients with X-ALD will develop progressive cALD over time. There is currently no pharmacological treatment available for cALD. In childhood, Hematopoietic Stem Cell Transplantation (HSCT) 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.

In addition, 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.

About Minoryx

Minoryx Therapeutics is a late-stage biotech company focusing on the development of novel therapies for orphan central nervous system (CNS) diseases with high unmet medical needs. The company's lead program, NEZGLYAL® (leriglitazone), a novel, brain penetrant and selective PPAR gamma agonist, is being developed to treat 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 https://www.minoryx.com/

[1] Marianne Golse, Isabelle Weinhofer, Bernardo Blanco, Magali Barbier, Elise Yazbeck, Camille Huiban, Boris Chaumette, Bertrand Pichon, Ali Fatemi, Silvia Pascual, Marc Martinell, Johannes Berger, Vincent Perlbarg, Damien Galanaud, Fanny Mochel, Leriglitazone halts disease progression in adult patients with early cerebral adrenoleukodystrophy, Brain, 2024;, awae169, https://doi.org/10.1093/brain/awae169

[2] https://ansm.sante.fr/tableau-acces-derogatoire/min-102

[3] ADVANCE, a pivotal phase 2/3 randomized, double-blind, placebo-controlled, clinical study with an open-label extension, was designed to assess the efficacy and safety of leriglitazone in adult male patients with X-ALD.

[4] NEXUS, a phase 2/3, open-label clinical study that designed to assess the efficacy and safety of leriglitazone in male pediatric patients with early stage cALD.

[5] CALYX, a phase 3, multicenter, randomized (1:1), double-blind, placebo-controlled, clinical study, has been designed to assess the efficacy and safety of leriglitazone in male adult patients with progressive cALD.

[6] Leriglitazone halts disease progression in adult patients with early cerebral adrenoleukodystrophy https://www.youtube.com/watch?app=desktop&v=5QUUZhw4PSg