

Minoryx's clinical candidate leriglitzzone shows clinical benefit in a proof of concept Phase 2 study in Friedreich's ataxia

Study demonstrates leriglitzzone improves relevant disease biomarkers and ataxia resulting in clinical benefit in this orphan disease

Mataró, Barcelona, Spain, December 15, 2020 - [Minoryx Therapeutics](#), a Phase 3 clinical stage biotech company focused on the development of differentiating treatment options in orphan central nervous system (CNS) disorders, today announces topline results from the Phase 2 FRAMES clinical trial. The study evaluates leriglitzzone, a novel, selective PPAR γ agonist, in patients with Friedreich's ataxia (FRDA). FRDA is a life-threatening disease characterized by neurodegeneration and results in a loss of coordination, muscle strength and cardiomyopathy.

The Phase 2 clinical trial was a proof of concept, multicenter, double-blind and placebo-controlled study. 39 patients were enrolled, with 32 completing the study. Treatment with leriglitzzone resulted in PPAR γ engagement, within the target range, in all patients as assessed by the relevant biomarker (adiponectin). Results of the trial show modulation of the Frataxin pathway and restoration of the bioenergetics deficits by leriglitzzone in Friedreich's ataxia patients. These signals are consistent with the mechanism of action of leriglitzzone, recently published by the journal [Neurobiology of Disease \(Rodríguez-Pascau et al. 2021\)](#).

“Minoryx's lead clinical candidate, the PPAR γ agonist leriglitzzone, can target multiple CNS diseases. Friedreich's ataxia is a potentially fatal neurodegenerative condition that has severe and worsening symptoms for sufferers. Developing therapeutic options for this condition is vital for patients,” said Marc Martinell, CEO, Minoryx. “We believe that the Phase 2 FRAMES trial data shows promising proof of concept as a therapy for Friedreich's ataxia, despite the inconclusive results of the primary endpoint, and provide a clear demonstration of the mechanism of action of leriglitzzone. We intend to initiate discussions with regulatory agencies to define the clinical development path forward to deliver this therapy to Friedreich's ataxia patients as quickly as possible.”

Key preliminary results include:

- Leriglitzzone significantly prevented an accumulation of iron in the brain when compared with placebo (ANCOVA $p = 0.050$). Iron accumulation is linked to Frataxin deficiency and was assessed by Quantitative Susceptibility Mapping (QSM). These results demonstrate that leriglitzzone directly modulates the frataxin pathway.
- Magnetic Resonance Spectroscopy (MRS) shows an improvement in the metabolic biomarkers related to mitochondrial function in the spinal cord.
- Composite Cerebellar Function Severity scale (CCFS) showed that leriglitzzone prevented decline in upper limb ataxia when compared with placebo. This effect is aligned with the observed MRS and QSM changes and patients treated with leriglitzzone showed a consistent improvement in these three quantitative objective assessments (O'Brien test, Wilcoxon $p = 0.043$).
- A determination of changes in the spinal cord area, the primary outcome, were inconclusive in results from the study, as no progression was observed in patients on placebo.

- Overall, Leriglitzone was well tolerated in Friedreich's ataxia patients. As expected, based on the mechanism of action of the compound, weight gain and edema were the most frequent adverse events. Importantly, no events indicating increased cardiac risk were detected in this population known to suffer from accompanying cardiomyopathy.

“Clinical results from the Minoryx Phase 2 FRAMES clinical trial are promising. Specifically, the reduction in decline in upper limb ataxia in Friedreich's ataxia patients demonstrate the potential of meaningful benefit in tackling this neurodegenerative condition,” said Professor Alexandra Durr, the principal investigator and coordinator of the FRAMES study, from the Brain and Spine Institute of La Pitié-Salpêtrière University Hospital (ICM), Paris.

Minoryx designed the Phase 2 FRAMES study to enable the identification of a FRDA patient population that would most benefit from treatment with leriglitzone. Full and detailed results from the study will be presented in the next few months. The study data are being used to design an additional confirmatory study. Minoryx plans to discuss this new study with the FDA and the EMA. Minoryx previously received orphan drug status from the FDA and the EMA and rare pediatric disease designation from the FDA for leriglitzone as a treatment for FRDA. FRAMES has received the support of the Region Wallonia, Belgium (SPW-EER).

About Minoryx

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, leriglitzone (MIN-102), a novel, selective PPAR γ agonist, is currently being evaluated in X-linked Adrenoleukodystrophy (X-ALD) and Friedreich's ataxia. The company is backed by a syndicate of experienced investors, which includes Caixa Capital Risc, Roche Venture Fund, Ysios Capital, Kurma Partners, Fund+, Chiesi Ventures, S.R.I.W, Idinvest, SFPI-FPIM, HealthEquity and Sambrinvest, 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 €85M.

www.minoryx.com

About leriglitzone

Leriglitzone (MIN-102) is a novel bioavailable and selective PPAR γ agonist with a potential 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 mitochondrial dysfunction, oxidative stress, neuroinflammation, demyelination and axonal degeneration. Leriglitzone has successfully completed a Phase 1 clinical trial showing good safety, tolerability and CNS engagement of PPAR γ receptors at levels equivalent to those required for efficacy in preclinical models. Leriglitzone has the potential to treat several CNS disorders, including orphan diseases, and is currently being evaluated in a registration enabling Phase 2/3 study in Adrenomyeloneuropathy (AMN), a registration enabling Phase 2 in cerebral ALD (cALD) and in a Phase 2 in Friedreich's ataxia.

About Friedreich's ataxia

Friedreich's ataxia is a devastating, orphan genetic disease characterized by loss of coordination and muscle strength, resulting from the degeneration of nerves caused by a genetic defect. The

disease is characterized by frataxin deficiency leading to mitochondrial dysfunction; symptoms range from the inability to coordinate movements to imbalance, muscle weakness and tremors. Within 10-15 years after disease onset, patients lose their ability to stand, sit and walk. Friedreich's ataxia is fatal, mainly due to cardiac failure. It affects approximately one in 40,000 people worldwide. There is currently no curative therapy available; existing treatments solely address symptoms.

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