Minoryx announces dosing of the first patient with leriglitazone in the phase 2a study in Rett syndrome (TREE study)

Barcelona, Spain – 4 March 2025 – Minoryx Therapeutics, a late-stage biotech company focused on the development of therapies for orphan central nervous system (CNS) disorders, today announces that the first patient in the TREE study has been dosed with leriglitazone. TREE is a phase 2a clinical study assessing the safety and efficacy of lead candidate leriglitazone, a novel, brain-penetrant and selective PPAR gamma agonist, to treat patients with Rett syndrome.

The TREE study will enrol 24 female patients aged 5-12y who will be dosed with leriglitazone or placebo for 36 weeks. The study will be carried out at the Neurometabolic Disorders Unit of the Hospital Sant Joan de Déu, Barcelona, Spain under the direction of Dr. Ángeles García Cazorla, Head of Research in Neurology and Head of Neurometabolic Unit.

In preclinical models[1], treatment with leriglitazone resulted in recovery of the bioenergetic alterations in human Rett fibroblasts. In a Rett mouse model, leriglitazone exerted an anti-neuroinflammatory effect, resulting in the amelioration of general condition and exploratory activity. Based on these preclinical findings, the TREE study is designed to show improved cognition with stabilisation/gain of communication skills, improved behaviour and delaying neuromuscular worsening resulting in improved motor skills.

"Following the positive results in the study NEXUS in boys with cerebral adrenoluekodystrophy (cALD) we will pursue additional orphan CNS indications with high unmet medical need," ***said Marc Martinell, CEO, Minoryx.*** *"Rett syndrome is one such indication, and we look forward to collaborating with the team of excellent physicians from Hospital Sant Joan de Déu in Barcelona."*

"We are excited to have initiated the TREE study. Leriglitazone has a mode of action relevant to the pathways associated with Rett syndrome," ***said Arun Mistry CMO, Minoryx.*** *"Thus far we have clinical safety and efficacy data in male paediatric patients, adult men and adult women from studies in X-ALD and Friedreich's ataxia and the TREE study expands to paediatric female patients with Rett syndrome."*

"The preclinical data for leriglitazone in Rett models is very encouraging as leriglitazone demonstrates effect on neuroinflammation and mitochondrial function which are hallmarks of Rett syndrome." ***said Dr. Ángeles García Cazorla, Head of Research in Neurology and Head of the Neurometabolic Disorders Unit, Hospital Sant Joan de Déu.*** *"Patients with Rett syndrome have complex clinical pictures where a new treatment that could provide improvements in cognition, behaviour and communication skills would help not just the patient to have an improved quality of life but also the family too.*

The results from the TREE study are expected during the first half of 2026 when all patients have concluded 36 weeks of treatment and 4 weeks of follow-up.

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About leriglitazone

Leriglitazone is Minoryx Therapeutics' 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 favourable safety profile. It showed robust preclinical proof-of-concept in animal models of multiple diseases including X-ALD and Rett syndrome by modulating pathways leading to mitochondrial dysfunction, oxidative stress, neuroinflammation, demyelination and axonal degeneration. In clinical trials, leriglitazone showed clinical benefit in adult and paediatric male X-ALD patients by reducing disease progression. Filing of a European MAA in cALD is scheduled for mid-2025. Leriglitazone has been granted orphan drug status for X-ALD and Friedreich's ataxia from the FDA and the EMA and Fast Track and Rare Paediatric Disease designation from the FDA for the treatment of X-ALD.

About TREE

TREE^2 is a 36-week, phase 2a, randomized 1:1, placebo-controlled study of once-daily oral leriglitazone in female paediatric patients aged 5-12 with Rett syndrome conducted at Hospital Sant Joan de Déu, Barcelona, Spain. The study will enrol 24 patients that will undergo 36 weeks of treatment and 4 weeks of follow-up. The primary endpoint is safety. In addition, the study assesses a number of secondary and exploratory endpoints including the Rett Syndrome Behavior Questionnaire (RSBQ), the Vineland Adaptive Behaviour Scale (VABS), and the Rett Syndrome Motor Evaluation Scale (RESMES) including various biomarkers.

About Rett Syndrome

Rett syndrome is a rare genetic neurological and developmental disorder that primarily affects females. It is almost exclusively caused by a de-novo genetic mutation in the MECP2 gene on the X-chromosome. The disorder causes a progressive loss of motor skills and language. Babies born with Rett syndrome initially seem to develop as expected, however they subsequently lose the skills they previously had such as the ability to crawl, walk, communicate and use their hands. Over time, these children experience increasing problems with the use of muscles that control movement, coordination and communication. Most patients also experience seizures and have intellectual disabilities. Rett syndrome affects about 1 in 10-20.000 females and natural history suggest that many patients live into middle age.

About Minoryx

Minoryx Therapeutics is a registration-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, leriglitazone (MIN-102), a novel, brain penetrant and selective PPAR gamma agonist, is being developed to treat X-linked adrenoleukodystrophy (X-ALD), Rett syndrome, and other orphan CNS diseases. The company is backed by a syndicate of experienced investors, which includes Columbus Venture Partners, CDTI Innvierte, Criteria BioVentures, 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] For Rett the preclinical models in the following article were employed: Musokhranova *et al., Journal of Translational Medicine (2023) 21:756,* https://doi.org/10.1186/s12967-023-04622-5

[2] NEXUS, a 96-week, pivotal, open-label, multicentre study for European registration (NEXUS; NCT04528706) of once-daily oral leriglitazone in paediatric patients with cALD. NEXUS has enrolled 23 patients

[2] El ensayo clínico es parte del proyecto CPP2021-008554, financiado por MCIN/AEI/10.13039/501100011033 y por la Unión Europea-NextGenerationEU/PRTR