Axoltis Pharma presents promising results from phase 1b clinical trial of innovative drug candidate for neurodegenerative diseases

- **Good safety profile and significant pharmacological effects confirm NX210c drug candidate properties and potential to address broad range of neurodegenerative diseases**
- **Biomarkers reveal significant and sustained effects confirming NX210c's action on integrity and repair of Blood Brain Barrier (BBB), as well as fundamental pathways in neuroprotection and neurotransmission**
- **In 2024, Axoltis plans to initiate phase 2 trial in patients with Amyotrophic Lateral Sclerosis (ALS) and conduct phase 1b trial in Parkinson's Disease (PD) while performing *in silico* modeling to further evaluate and optimize potential of NX210c more broadly in neurodegenerative diseases**

Clermont-Ferrand and Lyon, France, December 12, 2023 - Axoltis Pharma, a French biopharmaceutical company dedicated to developing therapeutic solutions for neurodegenerative diseases, today announces promising results from its phase 1b clinical trial evaluating NX210c, a patented peptide drug candidate.

These results follow a single-ascending dose phase 1a study carried out in 2020, which had demonstrated a good safety profile for NX210c in healthy volunteers.

The phase 1b trial was a multiple ascending-dose study aimed at evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics of NX210c in healthy volunteers aged over 55 years (NCT05827653). During Q1, 2023, Axoltis enrolled 29 healthy volunteers (12 with 5mg/kg, 11 with 10mg/kg and 6 receiving a placebo) in a single-center, randomized, double-blind, placebo controlled, dose escalation study conducted at the Centre for Human Drug Research, Leiden (The Netherlands). NX210c was administrated in a ten-minute infusion via an intravenous route, three times a week for four weeks.

The findings confirm that NX210c is safe and well-tolerated at all tested doses, any related adverse events observed were mild. Additionally, the specific neurologic safety profile of NX210c was strengthened by applying Neurocart® (a series of central nervous system tests) and included an extensive EEG signal review.

"This trial confirms the excellent safety and tolerability profile of NX210c. Moreover, we are excited to observe significant pharmacodynamic effects on blood and cerebrospinal fluid biomarkers, especially those important for BBB integrity, neuroprotection and neurotransmission. The results are very promising and provide a strong foundation to build on the NX210c drug development strategy," said Dr. Annette Janus, neurologist and chief medical officer at Axoltis.

Axoltis recently presented these phase 1b results, combined with encouraging findings from the company's preclinical studies, at Neuroscience 2023, the annual meeting of the Society for Neuroscience (SfN) in Washington DC (USA). In addition, Axoltis has been selected to deliver an oral presentation at AD/PD™ in Lisbon (Portugal) in March 2024.

By using a computational modeling approach based on the clinical dataset, Axoltis was also able to show an NX210c pharmacokinetics-pharmacodynamics (PKPD) relationship for several biomarkers, strengthening its therapeutic approach.

"We are very pleased with our preclinical and clinical studies, which strengthen Axoltis' position to become a key leader in BBB repair. Among our target applications is the initiation of a phase 2 trial for NX210c in patients living with amyotrophic lateral sclerosis, as BBB deterioration may be a trigger in the progression of this terrible disease," said Dr. Yann Godfrin, chief executive officer of Axoltis.

In parallel to this study in ALS, Axoltis Pharma has already obtained authorization to extend its phase 1b study in the Netherlands with a cohort of Parkinson's Disease patients. Additionally, Axoltis is partnered with InSilicoTrials, Milan (Italy), experts in *in silico* modeling, to explore the potential effects of NX210c in neurodegenerative disease models.

About the Blood Brain Barrier (BBB)

On a physiological level, the BBB separates the brain from the blood compartment, protecting it from circulating toxins and inflammatory blood components. When the BBB is no longer fully functional, these undesirable blood components can permeate the barrier and reach the brain. This plays a role in the progression of neurodegenerative diseases; it can even trigger them. For example, it has been recently shown in ALS that the BBB is damaged at the very early stage of the disease, probably even before clinical signs have become clear.

About NX210c

A large glycoprotein (SCO-spondin) produced by the subcommissural organ (SCO) plays crucial roles in neurogenesis and axonal guidance during embryogenesis. Only remnants of the SCO subsist in adults, thereby halting the production of SCO-spondin, which may account for a lack of regeneration and recovery in patients with neurological disorders. In this context, Axoltis is developing NX210c, a cyclic peptide of 12 amino acids designed from the most conserved sequence of the type 1 thrombospondin repeats of the SCO-spondin, as an innovative therapy for neurodegenerative diseases and traumas. NX210c is protected by seven patents fully owned by Axoltis Pharma, including one for composition of matter. In 2022, the FDA granted Orphan Drug Designation for NX210c in ALS.

For more details: https://www.axoltis.com/our-product/properties/

About Axoltis Pharma

Axoltis Pharma, a French biopharma company, develops innovative drugs for neurodegenerative and neurotraumatic diseases with a high unmet medical need. Headquartered in Clermont-Ferrand, with offices in Lyon, (France), Axoltis has established several partnerships with internationally recognized academic and private labs to develop its lead product, NX210c. The team is highly experienced in drug development, especially for neurological applications.

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