Lys therapeutics

# Lys Therapeutics announces positive preclinical results for its drug candidate in synergy with gold standard treatments for ischemic stroke

## Lys Therapeutics demonstrates synergy-driven efficacy of its monoclonal antibody in combination with reference thrombolytics, and marks a significant maturity of its technology

**Lyon & Caen, France, September 26, 2023 –** Lys Therapeutics announces new positive preclinical results in ischemic stroke with its drug candidate featuring a unique mechanism of action restoring the functionality of the blood-brain barrier (BBB) through antagonism of the tPA-NMDAr interaction. Lys Therapeutics' monoclonal antibody has demonstrated synergistic therapeutic efficacy in combination with reference thrombolytic treatments, whether alteplase (rtPA) or tenecteplase (TNK), with a significant reduction in neuronal death and the risk of hemorrhagic transformation. Improved recanalization/reperfusion of the main vessels involved in ischemia, and better functional recovery compared with the gold standard treatment used alone were also observed. Finally, by preventing the interaction of rtPA and TNK with NMDA receptors, the time window for administering these treatments has been extended well beyond their current clinical and regulatory limitations (0h-3h post-stroke for the FDA / 0h-4h30 post-stroke for the EMA).

These results, generated in collaboration with Prof. Denis Vivien's teams (INSERM, University and Hospital of Caen-Normandy, and the Blood & Brain @Caen-Normandy Institute), were the subject of a plenary oral presentation at the European Stroke Organisation Congress (ESOC 2023) held in Munich, Germany in May 2023. Further results will be presented at the World Stroke Congress (WSC 2023) in Toronto, Canada, in October 2023.

The monoclonal antibody developed by Lys Therapeutics counteracts the pathological mechanisms associated with elevated plasma levels of endogenous tPA and its binding to endothelial NMDA receptors involved in BBB disruption, a phenomenon widely observed in various neurological diseases.

Specifically in the context of ischemic stroke, the potential positioning of Lys Therapeutics' drug candidate as an add-on to the two main thrombolytics derived from endogenous tPA allows synergistic improvement to their benefit-risk profiles by blocking the side effects due to their off-target binding to NMDA receptors, notably those linked to the increased risk of hemorrhagic transformations. Also, since the short therapeutic window for these two thrombolytics means that only a minority of patients (less than 15%) are eligible, there is an urgent need to provide a solution for patients who cannot currently receive these treatments.

It has been shown that blocking the mechanisms involved in BBB disruption can limit the inflammatory, excitotoxic and neurodegenerative cascades associated to neuronal death and thereby improving post-stroke functional recovery. By confirming the positioning of its drug candidate and its efficacy, either used alone or as an add-on to the gold standard treatment (rtPA, alteplase) or its recent variant (TNK, tenecteplase) in an extended treatment window, and also taking into account the most common comorbidities such as diabetes as recommended by the stroke drug development guidelines

established in the USA by the *Stroke Treatment Academic Industry Roundtable* ("STAIR"), Lys Therapeutics is opening up new therapeutic prospects for ischemic stroke patients, regardless of the nature of their associated comorbidities or treatments.

Prof. Denis Vivien, University Professor and Hospital Practitioner, Director of the INSERM Unit "PhIND" and Scientific Director of Lys Therapeutics and the Blood and Brain @Caen-Normandy Institute, comments: "This work once again demonstrates the involvement of the tPA-NMDAr interaction in alterations to BBB homeostasis and associated hemorrhagic and inflammatory processes. Preclinical data demonstrating the synergy of our antibody with the gold standard stroke treatments mean that it can be positioned in combination with thrombolysis and thrombectomy, while also being used alone for patients who are ineligible for these treatments. By targeting mechanisms widely implicated in ischemic stroke, and in particular those linked to disruption of the BBB, we hope to be able to offer patients, in addition to existing treatments, a real benefit in terms of neuroprotection, reduced risk of bleeding, and cognitive and functional recovery after stroke."

Dr. Manuel Blanc, President and co-founder of Lys Therapeutics, adds: "We are delighted with these scientific data which confirm the very strong therapeutic potential of our antibody in ischemic stroke. Lys Therapeutics is demonstrating that its product is effective when administered alone, by targeting the disruption of the BBB linked to high levels of endogenous tPA, but also in combination with the reference treatment, recombinant tPA, by enhancing its efficacy while reducing its side effects. In addition, our new results generated in combination with tenecteplase, a thrombolytic commonly used in hospitals yet not officially approved for the treatment of ischemic stroke, demonstrate the complementarity of our drug candidate with the evolution of treatments. Earlier this year, we were the only company invited to present preclinical data in a plenary session at the ESOC, one of the world's leading scientific meetings on the subject of strokes. This attests to the quality and particularly promising nature of the work carried out by Lys Therapeutics and its partners."

## About Lys Therapeutics

*First-in-class biotherapies against neurological diseases.*

**Lys Therapeutics** is a biotechnology company pioneering a revolutionary approach to treat unmet medical needs in patients suffering from neurovascular or neurodegenerative disorders by targeting blood-brain barrier (BBB) dysfunction.

In the pathophysiology of several neurological diseases, such as **ischemic stroke**, **multiple sclerosis**, and **Parkinson's disease**, hyperactivation of **endothelial NMDA receptors** (NMDAr) by **overexpressed tissue plasminogen activator** (tPA) leads to tight junction degradation and BBB dysfunction, allowing transmigration of inflammatory cells to the brain parenchyma resulting in severe **neuroinflammation**, a primary cause of **neuronal cell death.**

Lys Therapeutics' main drug candidate is a **first-in-class monoclonal antibody** displaying a groundbreaking mechanism of action counteracting these mechanisms by specifically preventing inside blood vessels **the binding of tPA on NMDAr**, without blocking the physiological function of NMDA receptors. By inhibiting this interaction, NMDA receptors can operate normally, haltering downstream deleterious cellular pathways. Tight junctions are reestablished, endothelial cells return to their healthy state and the BBB function is restored, **protecting the brain from further neuroinflammatory and subsequent neurodegenerative cascades**.

Lys therapeutics

Targeting neuroinflammation to tackle neurodegeneration.

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