Matrix Therapy for Regeneration

OTR4132 in patients with ischemic stroke meets primary efficacy endpoint

Paris, France, June 29, 2026 – OTR3, a biotechnology company, announces today that the primary endpoint was met in its clinical trial MATRISS II.

MATRISS II investigated the efficacy and safety of OTR4132 administered intra-arterially immediately after successful endovascular thrombectomy, in patients with acute ischemic stroke.

The MATRISS II study was a randomized, double-blinded and placebo-controlled phase II trial that recruited 60 subjects from 11 major stroke centres in France. A single dose of OTR4132 selected from pre-clinical studies and from the prior escalating-dose clinical trial MATRISS was tested *versus* placebo. The study protocol was registered on ClinicalTrials.gov - NCT 06700824 and conducted according to ICH good clinical practices.

The primary endpoint for the study was defined as the "Baseline-Adjusted 24-Hour NIHSS score" which is considered a strong predictor of long-term disability.

Results were statistically significant on the primary endpoint in the intention to treat analysis (p=0.047).

Even if not powered to demonstrate statistical significance, all secondary endpoints concurred to support the primary endpoint particularly on NIHSS score and up to 3 months, 24h-NIHSS responders' rate, "0 or 1" mRS at 3 months, rate of haemorrhagic transformations at 24 hours, change in stroke lesion volume, length of hospital stay. Tolerability and safety were notably better in the treated group.

Detailed results will be published in a scientific medical journal.

OTR3 is actively preparing the next steps that will require additional funding.

"Results are very encouraging and consistent with pre-clinical and first in human studies. They suggest acceleration of recovery in the few days after stroke. There is a consensus that shorter delay to clinical improvement after stroke is strongly related to better chances of a long-term good outcome." said **Prof. Olivier Detante, Principal Investigator of the study, CHU de Grenoble, Neurology, France.**

"I am very excited by the MATRISS II results. I have always been convinced that matrix therapy could represent a new branch of regenerative medicine, especially for neurological diseases." said **Denis Barritault, co-inventor of the technology, founder and president of OTR3.**

"We are very happy with these results; however, a larger trial is mandatory to confirm acceleration of recovery and demonstrate a better long-term outcome." said **Frédéric Sedel, MD, PhD, Chief Medical Officer and vice president of OTR3.**

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About Ischemic Stroke

Stroke is the third leading cause of death and disability globally. Ischemic stroke accounts for approximately 85% of all strokes. It is a medical emergency caused by decreased blood flow to the brain. During the acute phase, the treatment objective is the restoration of blood flow and the prevention of subsequent clots. Current therapies remain exclusively limited to intravenous thrombolysis and endovascular thrombectomy. The rates of functional independence achieved even after highly effective reperfusion treatments are just below 50%, showing an unmet clinical need for adjunctive neuroprotective treatments.

Significant effort has been made to minimize neuronal damage following stroke with the use of neuroprotective agents, however, these treatments have yet to show clinical efficacy and no treatment has been approved so far in Europe and the USA in this indication.

About OTR3 proprietary RGTA® technology.

OTR3 is a privately held French biotechnology company founded by Denis Barritault and Jean-Pierre Caruelle from University of Paris-Est-Creteil (https://www.otr3.com). The ReGeneraTing Agents (RGTA®) technology is based on the central role of the extracellular matrix (ECM) in tissue and organ repair and regeneration. This regenerative process is regulated by specific signalling molecules—communication peptides/growth factors—present in the extracellular space. These molecules are normally stored, protected, and retained by a family of polysaccharides known as heparan sulfates (HS). Together with matrix proteins such as collagen, laminin and elastin, they form the structural scaffold of the ECM. Following tissue injury, enzymes are released that degrade these ECM components, including HS. As a result, communication peptides and growth factors are no longer protected and undergo accelerated degradation. RGTA® are polysaccharides that act as structural and functional biomimetics of natural HS, while being resistant to enzymatic degradation. The primary mechanism of action of RGTA® is to replace degraded HS and thereby restore the ECM scaffold through direct physical interactions with matrix proteins. Restoration of this scaffold protects communication peptides/growth factors and is conductive to tissue regeneration.

About OTR4132

OTR4132 is a RGTA® intended to be administered in situ, just after endovascular thrombectomy to improve functional outcomes in patients with acute ischemic stroke. The safety of OTR4132 was evaluated in multiple *in vitro* and *in vivo* models from which it could be concluded that it is likely to have a positive benefit/risk ratio in ischemic stroke (Khelif et al., 2018, https://pmc.ncbi.nlm.nih.gov/articles/PMC6299437/pdf/thnov08p5814.pdf).

A first-in-human escalating dose trial ("MATRISS") performed in 19 patients showed no serious adverse event attributable to the device at any of 6 tested doses. The rate of severe intracranial haemorrhages at 24 hours was even lower in the higher doses groups suggesting a protective effect on the blood brain barrier. Furthermore, efficacy data (including functional scores and volumetric measurements) suggested acceleration of recovery at higher doses.

Results were published in "clinical drug investigation" by Barreau et al. (https://pmc.ncbi.nlm.nih.gov/articles/PMC12535512/pdf/40261_2025_Article_1487.pdf).

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