Note: This document has been translated from the Japanese original for reference purposes only. In the event of any discrepancy between this translated document and the Japanese original, the original shall prevail.

November 8, 2024

NEWS RELEASE

Company name :TMS Co., Ltd.
Name of representative :Takuro Wakabayashi, Chief Executive Officer
(Securities code: 4891; Growth Market)

Publication of the Phase 2a Clinical Trial Results of JX10 (TMS-007) in the American Heart Association and American Stroke Association's Stroke

TMS Co., Ltd. (TSE: 4891) (the "Company"), a clinical-stage biopharmaceutical company focused on discovering and accelerating the development of transformative medicines in areas of high unmet medical need, today announced that a paper based on the results of the Company's Phase 2a clinical trial of JX10 (TMS-007) for the potential treatment of acute ischemic stroke, was published in *Stroke*, a peer-reviewed journal published by the American Heart Association (AHA) and American Stroke Association (ASA).

"Publication of the JX10 (TMS-007) Phase 2a data in *Stroke* underscores the importance of this dataset and the potential of TMS-007 as a first-line treatment for patients suffering from an acute ischemic stroke," said Takuro Wakabayashi, Chief Executive Officer of TMS Co., Ltd. "In the Phase 2a study, JX10 (TMS-007) showed significant efficacy with an expanded therapeutic time window and no symptomatic intracranial hemorrhage reported. This publication and the 2022 Paul Dudley White International Scholar Award we received from AHA based on this dataset further validate the potential of JX10 (TMS-007) to become a long-awaited novel therapeutics for a substantially underserved AIS patient population and gives us confidence as we advance the compound to late-stage studies."

The Phase 2a clinical trial of JX10 (TMS-007) was conducted in 90 patients in Japan, and achieved excellent efficacy and safety results within 12 hours of the last known normal (LKN). This publication in *Stroke* is expected to contribute to the ongoing development of JX10 (TMS-007) by widely confirming the significance of the results of the clinical trial.
This paper is published online at *Stroke* linked here. (The link displays only the summary; a paid subscription is required to access the full article.) For the Company's previous press release related to the Phase 2a result, please visit here.

Summary

Title: Anti-Inflammatory Thrombolytic JX10 (TMS-007) in Late Presentation of Acute Ischemic Stroke

Abstract: BACKGROUND: Contemporary thrombolytics in acute ischemic stroke (AIS) are limited to administration within 4.5 hours of last known normal (LKN). JX10 (formerly TMS-007), a *Stachybotrys microspora* triprenyl phenol family member, may extend this therapeutic window.

METHODS: In this multicenter, randomized, double-blind, placebo-controlled, dose-escalation Phase 2a study, JX10 or placebo was administered as a single intravenous infusion to Japanese patients with AIS who were unable to receive tissue-plasminogen activator or thrombectomy within 12 hours of LKN. Primary endpoint was incidence of symptomatic intracranial hemorrhage with a worsening National Institutes of Health Stroke Scale (NIHSS) score of ≥4 points within 24 hours of drug administration (sICH incidence).

RESULTS: Ninety patients received either placebo (n=38; female 26.3%) or JX10 at 1, 3, or 6

mg/kg (n=6, 18, 28; female 0, 33.3, 42.9%, respectively). Median age (range) and baseline median (range) NIHSS scores were respectively 76.5 (42–87) and 8 (6–21) for the combined JX10 cohort (JX10 Cohorts) and 75.0 (34–85) and 8 (6–22) for placebo. Median (range) dosing time since LKN was 9.5 (5.0–12.1) and 10.0 (3.7–12.0) hours for JX10 Cohorts and placebo, respectively. sICH incidence was 0% (0/52; 95% confidence interval [CI] 0.0–5.6) for JX10 Cohorts vs 2.6% (1/38; 0.1–13.8) for placebo (p=0.42). Vessel patency at 24 hours (secondary endpoint) in patients with baseline arterial occlusive lesion score <3 (39/90) improved in 58.3% (14/24) of patients in JX10 Cohorts vs 26.7% (4/15) for placebo (odds ratio 4.23; 95% CI 0.99–18.07). In JX10 Cohorts, a significantly higher proportion of patients had modified Rankin Scale 0–1 score on Day 90 (secondary endpoint) vs placebo (JX10: 21/52, 40.4% vs placebo: 7/38, 18.4%; p=0.03).

CONCLUSION: JX10 was well tolerated and may expand the AIS therapeutic window as a novel thrombolytic agent.

Author: Kuniyasu Niizuma, MD[*1–3], Naoko Nishimura, PhD[*4], Keiko Hasegawa, BSc[4], Takashi Moritoyo, MD[5], Kohsuke Kudo, MD[6], Josh Bell, MD[7], Michael Wald, PhD[7], Yoshifumi Umeda, MSc[8], Kazuhiko Kuribayashi, PhD[9], Yasuo Toda, MD[9], Teiji Tominaga, MD[1], Keiji Hasumi, PhD[4,10]

[*]Co-first authors

[1] Department of Neurosurgery, Tohoku University Graduate School of Medicine, Sendai, Japan

[2] Department of Neurosurgical Engineering and Translational Neuroscience, Graduate School of Biomedical Engineering, Tohoku University, Sendai, Japan

[3] Department of Neurosurgical Engineering and Translational Neuroscience, Tohoku University Graduate School of Medicine, Sendai, Japan

[4] Department of Research and Development, TMS Co. Ltd., Fuchu, Japan

[5] Clinical Research Promotion Center, The University of Tokyo Hospital, Japan

[6] Department of Diagnostic Imaging, Faculty of Medicine, Hokkaido University, Sapporo, Japan

[7] Biogen Inc., Cambridge, MA, USA

[8] PPD-SNBL, Kagoshima, Japan

[9] Biogen Japan Ltd., Tokyo, Japan

[10] Department of Applied Biological Science, Tokyo University of Agriculture and Technology, Japan

Publication journal: Stroke※

Publication date: November 7, 2024

※ Stroke publishes reports of clinical and basic investigation of any aspect of the cerebral circulation and its diseases from many disciplines, including anesthesiology, critical care medicine, epidemiology, internal medicine, neurology, neuro-ophthalmology, neuropathology, neuropsychology, neurosurgery, nuclear medicine, nursing, radiology, rehabilitation, speech pathology, vascular physiology, and vascular surgery.

About JX10 (TMS-007)

JX10 (TMS-007) is a small molecule being developed for the treatment of acute ischemic stroke (AIS) by Ji Xing Pharmaceuticals and TMS Co., Ltd. It is considered that the compound possesses two distinct mechanisms of actions: rapid blood flow restoration through thrombolysis by altering the structure of plasminogen without affecting coagulation homeostasis and reduction of ischemia-reperfusion injury through anti-inflammatory effects driven by soluble epoxide hydrolase (sEH) inhibition. This unique combination could position JX10 (TMS-007) as a potential next generation thrombolytic for individuals with AIS with the aim to provide an extended treatment window as compared to currently approved thrombolytic agents. JX10 (TMS-007) demonstrated efficacy and safety in its Phase 2a clinical trial in patients with AIS, which was evaluated in a multi-center, single-administration, double-blinded, randomized, placebo-controlled, ascending dose trial.

About TMS Co., Ltd.

TMS Co., Ltd. is a clinical-stage biopharmaceutical company focused on the discovery and development of transformative medicines for the treatment of serious diseases in areas of high unmet medical need. The Company's pipeline consists of a family of small molecule compounds called SMTPs (Stachybotrys Microspora Triprenyl

Phenols) derived from a fungus. TMS' lead program, TMS-007 (JX10), has demonstrated efficacy and safety in its Phase 2a study for the treatment of acute ischemic stroke. The Company's robust pipeline also includes programs in resistant or uncontrolled hypertension, acute kidney injury, and spinal cord injury. TMS continues to explore new pipeline products by leveraging its established partnerships with leading academic institutions in Japan, with the intention to build a bridge between academic discoveries and the global pharmaceutical market. For more information about TMS, please visit https://www.tms-japan.co.jp/.

Investor and Media Contact:
ir@tms-japan.co.jp

End