



Financial Results for FY02/2025

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Create impactful therapeutics by the power of relentless exploration and challenge

### Agenda



- 1. Highlights
- 2. Summary of Financial Results for FY02/2025
- 3. Pipeline
- 4. TMS-007 / Potential Next Generation Acute Ischemic Stroke Treatment
- 5. JX09 / Resistant or Uncontrolled Hypertension
- 6. TMS-008 / Acute Kidney Injury
- 7. TMS-010 / Spinal Cord Injury (New Asset)
- 8. Pipeline Expansion
- 9. Appendix

# Highlights





### 1

#### Initiation of Global Phase 2/3 Trial for TMS-007 (JX10)

- Initiation of global registrational trial "ORION" led by CORXEL\*.
- TMS is preparing to participate in ORION as the Japanese partner for this global trial.

#### **Timeline**

- June 5, 2018 TMS and Biogen signed the Option Agreement
- May 11, 2021 Biogen exercised its option
- Apr 25, 2023 Biogen announced pausing of TMS-007 Ph2b study
- Jan 11, 2024 Biogen assigned the Option Agreement to CORXEL\*
   BIIB131 is renamed JX10.
- Feb 5, 2025 CORXEL announced initiation of Clinical Trial ORION (Phase 2/3)
- \* JIXING (Ji Xing Pharmaceuticals) changed its name to Corxel Pharmaceuticals (CORXEL) effective November 2024.

#### 2

### TMS-008 Ph1 Clinical Trial- Administration • Dosing and Observation Completed

- First dosing in a healthy participant at the University of Tokyo Hospital was conducted in June 2024. TMS-008 is the Company's second clinical-stage program from internal source.
- Dosing and observation for all participants completed in December 2024.
  - Topline results reported in April 2025 (after end of FY2024): favorable safety and tolerability demonstrated.

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### 3 Enhancing Corporate Capabilities

- Strengthening our team by hiring experienced professionals capable of supporting global business operations in line with business expansion:
  - Established a Business Development Department and appointed a Senior Director of Business Development.
  - Recruited a Senior Director of Clinical Development to support global clinical trials.

### Financing Initiative (after end of FY2024)

■ To bolster our financial foundation and ensure we are fully prepared for the initiation of the Phase 2/3 ORION trial for TMS-007 (JX10), a third-party allotment of stock acquisition rights were issued in March 2025.

[Issuance of Stock Acquisition Rights through Third-Party Allotment]

Allotment Date: March 31, 2025

Number of Stock Acquisition Rights Issued: 80,000 (equivalent to 8 million potential shares)

Initial Exercise Price: ¥192 (minimum exercise price: ¥100)

### Acquired a New Pipeline Asset for Spinal Cord Injury Treatment from Hokkaido University

- TMS licensed in a drug candidate for spinal cord injury from Hokkaido University on July 3, 2024, which the company has been evaluating since July 2022.
- This program is designated as TMS-010.

### Highlights



### Publication of TMS-007 (JX10) Study in *Stroke* and Presentation at ISC 2025

- A paper describing the Phase 2a trial results of TMS-007 (JX10), "Anti-Inflammatory Thrombolytic JX10 (TMS-007) in Late Presentation of Acute Ischemic Stroke" was published in Stroke, an official journal published by the American Heart Association (AHA) and American Stroke Association (ASA) in November 2024
- TMS-007 (JX10) related presentation was made by CORXEL's Chief Medical Officer at the International Stroke Conference 2025 (ISC 2025) in February 2025.

### 7 Dividend Received from CORXEL

 TMS received a stock dividend payment of approximately \$2.25 million (¥342 million) from CORXEL in February 2025.

### 8 Change in Fiscal Year-End (after end of FY2024)

 To align with global standards, TMS is changing its fiscal year-end starting from FY2025, subject to shareholders' meeting resolution.

Current: March 1 – February 28 New : January 1 – December 31

<sup>\*</sup> FY2025 will be from March 1, 2025 to December 31, 2025 (10 months).

### **Project Outcomes and Milestones**



Programs	Achievements and Upcoming Milestones	Timing
	Next-phase clinical trial ORION (Phase 2/3) initiated	Q4 FY2024
TMS-007 (Acute ischemic stroke)	First-patient-in (FPI) for ORION (Phase 2/3)	FY2025
	Initiation of the Japan cohort in the ORION (Phase 2/3) trial	FY2025
JX09 (Resistant or uncontrolled hypertension)	Completion of Phase 1 clinical trial by CORXEL	FY2025
	First subject dosed in Ph1 study	Q2 FY2024
TMS-008	Completed dosing to all healthy volunteers in Ph1 study	Q4 FY2024
(Acute kidney injury)	Readout of Ph1 results on safety, tolerability, and pharmacokinetics	Q1 FY2025
	Completion of next-phase clinical trial design	FY2025
Discovery	Pipeline expansion by in-licensing TMS-010 as a potential treatment for spinal cord injury	Q2 FY2024

Summary of Financial Results for FY02/2025



### Financial Results FY02/2025 - Statement of Income



Operating expenses remained generally in line with the previous fiscal year.

Ordinary income (loss) and net income (loss) narrowed compared to the previous fiscal year due to the receipt of dividends from CORXEL.

vidends from CORXEL.

	FY02/2024 FY02/2025		Change		
			Amount	Percentage	
Operating revenue	-		-	-	
Operating expenses	943	907	(35)	-3.8%	
R&D	607	621 <sup>1</sup>	13	+2.2%	
SG & A	335	286 <sup>1</sup>	(48)	-14.6%	
Operating income(loss)	(943)	(907)	35	-	
Non-operating income	3	342	339	-	
Non-operating expenses	3	67	64		
Ordinary income (loss)	(943)	(633)	310	-	
Extraordinary loss	15	26	10	+69.3%	
Net income (loss)	(960)	(660)	299	-	

While costs increased due to the introduction and development of TMS-010, this was offset by a timing shift in the recognition of clinical and CMC expenses for TMS-008, keeping overall R&D expenses generally in line with the previous fiscal year.

Dividend income from CORXEL

Distribution of dividend income as royalties and compensations

Loss on full amortization of fixed assets

#### Expected expenses for the Full Fiscal Year 2025<sup>2</sup>

(million yen)

(million yen)

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Research and Development expenses	550	- 800	
Other selling, general and administrative expenses	260	- 350	

Mainly development costs for each pipeline, including TMS-007 (JX10) and TMS-008, and exploration and introduction costs for expanding the pipeline

<sup>1.</sup> Note: R&D expenses for the fiscal year ending February 2025, as announced at the beginning of the fiscal year, were projected to be between ¥750 million and ¥1,100 million, while other SG&A expenses were projected to be between ¥300 million and ¥400 million.

<sup>2.</sup> Note: Due to the change in fiscal year end, the next fiscal year will be a 10-month period ending December 31, 2025.

Annualized (12-month) expenses are expected to be R&D expenses, ¥660-960 million, and other SG&A expenses, ¥312-420 million.

### Financial Results FY02/2025 - Cash Flows



Mainly due to the receipt of dividend income, cash outflows from operating activities decreased. As a result, cash and cash equivalents at end of period stood at ¥2.9 billion, down ¥0.5 billion from the previous fiscal year-end.

(million yen)

	FY02/2024	FY02/2025
Cash flows from operating activities	(822)	(493)
Net income before tax	(959)	(660)
Cash flows from investing activities	(3)	(30)
Cash flows from financing activities	688	0
Proceeds from issuance of shares	688	0
Net increase and decrease in cash and cash equivalents (indicates decrease)	(138)	(523)
Cash and cash equivalents at beginning of period	3,584	3,446
Cash and cash equivalents at end of period	3,446	2,922

The receipt of dividend income from CORXEL reduced cash outflows.

### Financial Results FY02/2025 - Balance sheet



### Total assets declined compared to the previous fiscal year-end, primarily due to R&D expenditures.

(million yen)

	FY02/2024 FY	EV02/2025	Change		
	F 102/2024	FY02/2024 FY02/2025		Percentage	
Current assets	3,551	3,029	(522)	-14.7%	
Cash and deposits	3,446	2,922	(523)	-15.2%	
Non-current assets	3	3	0	+0.0%	
Total assets	3,554	3,032	(522)	-14.7%	
Current liabilities	97	216	119	+121.9%	
Total liabilities	97	216	119	+121.9%	
Subscription rights to shares	11	23	11	+101.2%	
Total net assets	3,457	2,815	(641)	-18.6%	
Total liabilities and net assets	3,554	3,032	(522)	-14.7%	

Primarily due to R&D expenditures, including Phase 1 costs for TMS-008, as well as other SG&A expenses.

Primarily due to increases in accrued expenses for subcontracting costs related to TMS-008 and in unpaid patent royalties and compensations to be paid from dividend income.

# **Pipeline**



### TMS Clinical Pipeline



### Clinical Pipeline



#### TMS-007/JX10 (Acute ischemic stroke)

- Novel thrombolytic with the potential to be first line treatment for AIS
- Demonstrated excellent efficacy and safety results in the Phase 2a clinical trial.
- Initiation of the global Phase 2/3 trial, ORION, led by our partner CORXEL.
- TMS owns development and marketing rights for Japan, and milestones and royalties for the rest of the world.

#### JX09 (Resistant or uncontrolled hypertension)

- Aldosterone synthase inhibitor with best-in-class potential.
- Ph1 clinical trial underway in Australia by CORXEL.
- TMS owns the rights to develop and market the product in Japan.

### TMS-008 (Acute kidney injury)

- Important unmet medical needs for which no approved drug exists.
- Dosing and observation of Phase 1 clinical trial conducted in Japan completed.
- Data read-out in April 2025; favorable safety and tolerability demonstrated
- TMS owns the rights to develop and market the product globally.

### **TMS Pipeline**



Development Code	Target Disease	MoA	Research	Preclinical	Ph1	Ph2	Ph3	Development and Commercializatio
TMS-007 (JX10)	Acute Ischemic Stroke	sEH Inhibition		Ph2a completed	d in Japan	<u> </u>	Ph2/Ph3	Japan: TMS Outside Japan: CORXEL
JX09 <sup>1</sup>	Resistant or uncontrolled hypertension	ASI <sup>4</sup>			<u> </u>			Japan: TMS Outside Japan: CORXEL
TNAC 0002	Acute Kidney Injury	sEH						TMS
TMS-008 <sup>2</sup>	Other indications	Inhibition						TMS
TMS-010 <sup>3</sup>	Spinal cord injury	BBSCB protection 5						TMS
Pipeline candidates <internal></internal>				Search for n	ovel sEH inhib	itors and other o	compounds	TMS
Pipeline candidates <external></external>				Evaluating m	nultiple progran	ns		TMS

- 1. Obtained free license for development and marketing rights in Japan from CORXEL (January 2024).
- 2. TMS-008 which were being developed under a free license from Biogen, continue to be developed under a free license from CORXEL.
- 3. Obtained exclusive license for the candidate drug for spinal cord injury from Hokkaido University for the entire world, including Japan (July 2024).
- 4. ASI: Aldosterone synthase inhibitor.
- 5. BBSCB(Blood-brain spinal cord barrier) protection

## **TMS-007**

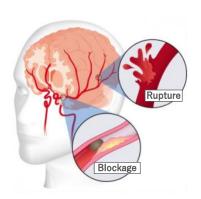
Potential Next Generation Acute Ischemic Stroke Treatment



### Acute Ischemic Stroke - Important Unmet Medical Need



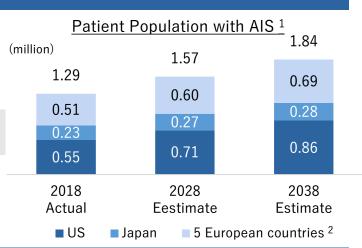
### Acute Ischemic Stroke (AIS) Overview



- AIS is caused by blockages of blood supply to the brain
- Potentially leads to permanent brain damage :

hemiplegia, memory loss, speech problems, reading and comprehension difficulties and other complications

 The number of patients with Ischemic Stroke: approx. 1.3 million/year (total of 7 major countries) and it is expected to increase



#### **Important Unmet Medical Needs**

#### Cause of death in the US (2019) 3

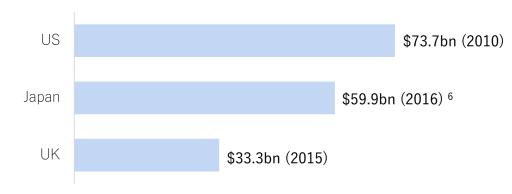
#	Disease	Ratio	Breakdown of Stroke 4
1	Heart Disease	23.1%	Others
:	:	:	13%
4	CLRD	5.5%	
5	Stroke	<u>5.3%</u>	AIS 87%
6	Alzheimer	4.3%	5.77

#### 1. Datamonitor Healthcare, "Stroke Epidemiology", Ref Code:DMKC0201444, Published on 07 January 2019

3. Centers for Disease Control and Prevention, "National Vital Statistics Reports volume 70"

 Tsao et al. (2022) Heart Disease and Stroke Statistics—2022 Update: A Report From the American Heart Association

#### Stroke causes significant economic loss <sup>5</sup>



- National Stroke Association, Explaining stroke 101, 2011; Current, future and avoidable cost of stroke in the UK, 2017; Yamaga et al. (2016), "Cost of illness in cerebrovascular disease" Calculation based on exchange rates; USD/JPY=110, USD/GBP=1.3
- Estimated COI based on direct and indirect costs related to stroke for 1 year until November 2015

<sup>5</sup> European countries are composed of five major countries: Germany, France, Italy, Spain, and United Kingdom

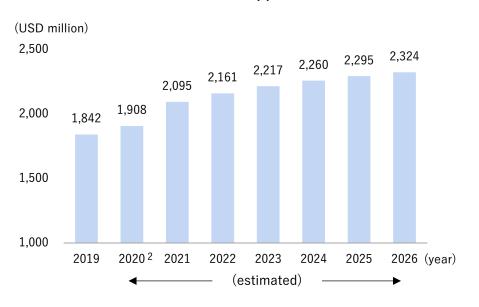
### t-PA - The Only FDA-Approved Drug for AIS



#### No drug has been approved since 1996 in the US

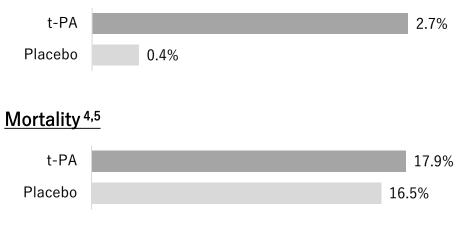
#### Market size <sup>1</sup> of the existing drug

#### Sales of t-PA is estimated to be approx. \$2.1bn in 2021



#### Challenges of the existing drug

#### Incidence rate of fatal intracranial hemorrhage 3,5

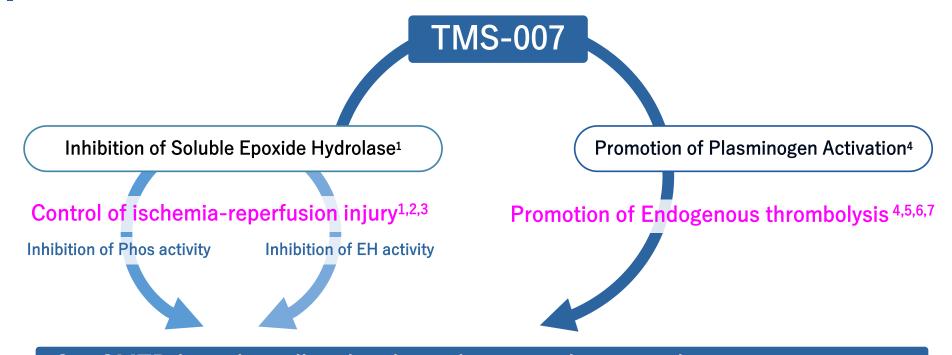


- t-PA (tissue Plasminogen Activator): the only FDA-approved drug for AIS (thrombolytic agent)
- t-PA generally needs to be administered within 4.5 hours from symptom onset and is used for <10% of patients 6
  - 1. Informa; estimated as the sum of sales of Activase® and Actilyse® for each year
  - 2. As Actilyse® sales in 2020 is not available, Actilyse® sales in 2019 is used for estimation for 2020
  - 3. Incidence rate at 7 days
  - I. Mortality at 90 days
  - 5. Emberson et al. (2014), "Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials"
  - 6. Audebert et al. Nat. Rev. Neurol. 10.675-676, 2014 'Time is brain' after stroke, regardless of age and severity

### TMS-007: Mechanism of Action



Dual mechanism – "thrombolytic" and "Inhibitory control of ischemia-reperfusion injury" activities



### Our SMTP-based small molecule analogues with unique therapeutic properties

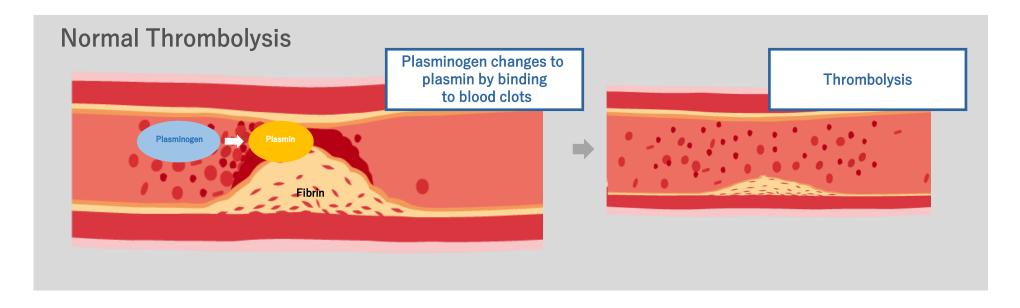
Thrombolysis effect and Inhibitory control of ischemia-reperfusion injury effect (based on anti-inflammatory activities)

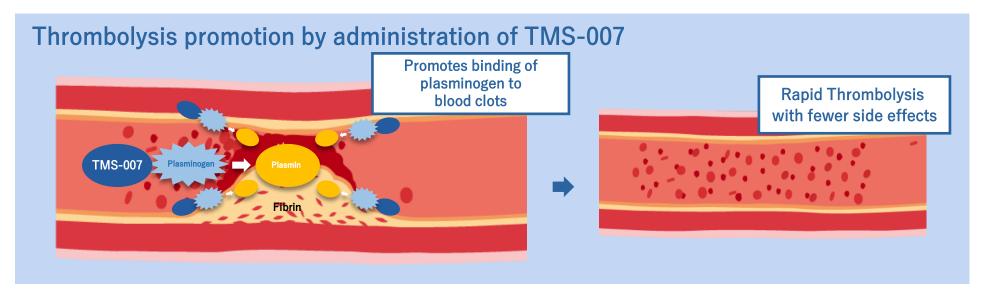
Ideal profile for treatment of acute ischemic stroke

- 1. Matsumoto et al. (2014) J Biol Chem
- Shibata et al. (2011) N-S Arch Pharmacol
- 3. Ito et al. (2014) Brain Res
- 4. Hasumi et al. (2010) FEBS J
- 5. Hu et al. (2012) Thrombosis J
- 6. Miyazaki et al. (2011) Stroke
- 7. Hasumi & Suzuki (2021) Int J Mol Sci

### Mechanism of Action of TMS-007: Image of Thrombolysis <sup>1</sup>





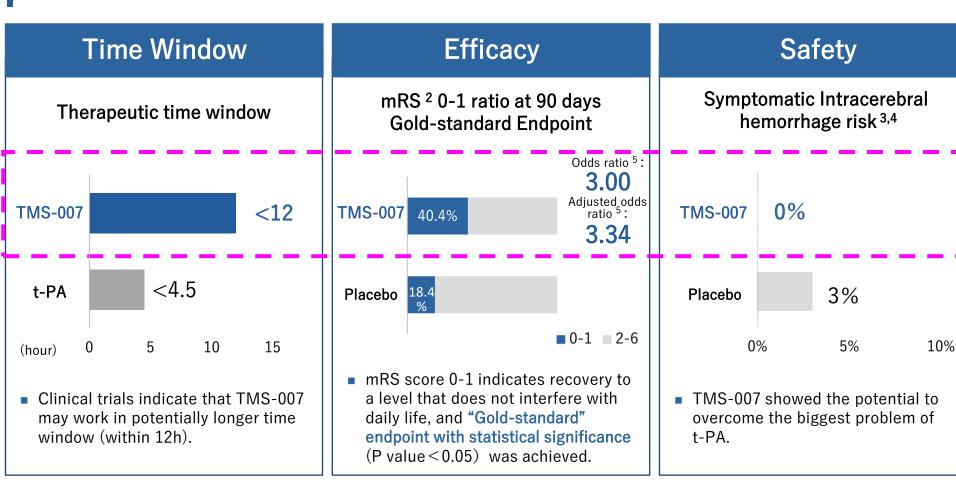


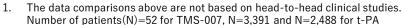
For illustrative purposes only

### TMS-007: Ph2a Clinical Trial Showed Excellent Results



### TMS-007 has the potential to become the first line AIS treatment <sup>1</sup>





<sup>2.</sup> mRS indicates modified Rankin Scale, and it refers to degree of independence in daily life

<sup>3.</sup> Biogen, Investor Day Material (September 21, 2021), Q4 and Full Year 2021: Financial Results and Business Update

<sup>4.</sup> Wardlaw et al. (2012), "Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated systematic review and meta-analysis". N=2.488

<sup>.</sup> Calculation of each odds ratio; TMS-007: odds ratio 3.0=(40.4%/59.6%)/(18.4%/81.6%), adjusted odds ratio 3.34, (statistically adjusted to control for other predictor variables; Source; ISC2022 Poster)

### TMS-007: Ph2a Clinical Results Achieved "Gold-standard" Endpoint

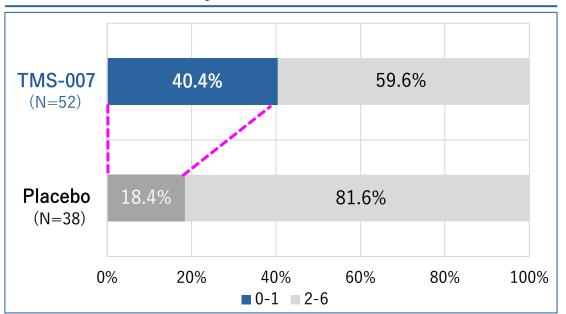


# TMS-007 achieved <u>statistically significant improvement</u> on mRS 0-1 ratio at 90 days, one of the most important indicators

	Placebo	TMS-007
Number of patients (N)	38	52
Number of patients scored mRS 0-1	7	21
mRS 0-1 ratio	18.4%	40.4%

- Odds ratio 3.00, Adjusted odds ratio 3.34
- P value < 0.05

#### mRS 0-1 ratio at 90 days<sup>1</sup>



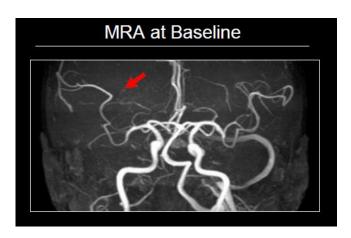
mRS (modified Rankin Scale)				
<b>†</b>	0	No symptoms		
	1	No significant disability, despite symptoms; able to perform all usual duties and activities		
11	2	Slight disability; unable to perform all previous activities but able to look after own affairs without assistance		
•	3	Moderate disability; requires some help, but able to walk without assistance		
<b>K</b> E	4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance		
<b>_</b>	5	Severe disability; bedridden, incontinent and requires constant nursing care and attention		
	6	Death		

### 

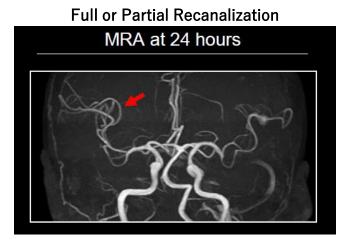


TMS-007's promising efficacy is potentially backed by good recanalization outcome 1

Effect of vessel recanalization confirmed for patients with full or partial vascular occlusion - MRA image







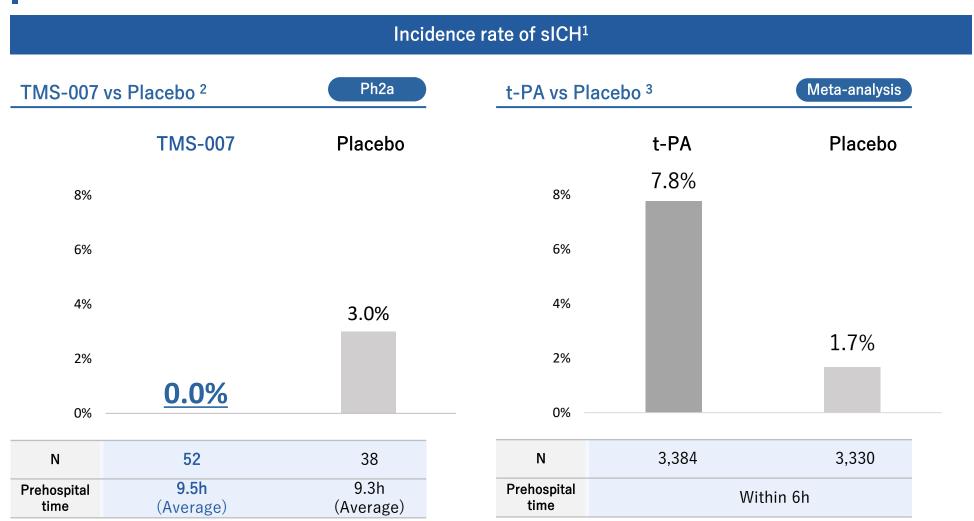
The percentage of subjects receiving TMS-007 achieving recanalization was greater than those treated with placebo

	Placebo Pooled	TMS-007 Pooled
Number of patients (N)	15 (100)	24 (100)
Number of patients with recanalization	4 (26.7)	14 (58.3)
Estimate of odds ratio (TMS-007 vs placebo)	-	4.23
95% CI for the odds ratio	-	0.99, 18.07

### TMS-007: Ph2a Clinical Study Result Achieved a Safety Profile



In terms of safety, the biggest concern of t-PA was the incidence of symptomatic Intracerebral Hemorrhage (sICH). The Ph2a TMS-007 study demonstrated a reduced risk of the incidence of sICH.



The data comparisons below are not based on head-to-head clinical studies. N=52 for TMS-007, N=3,384 for t-PA

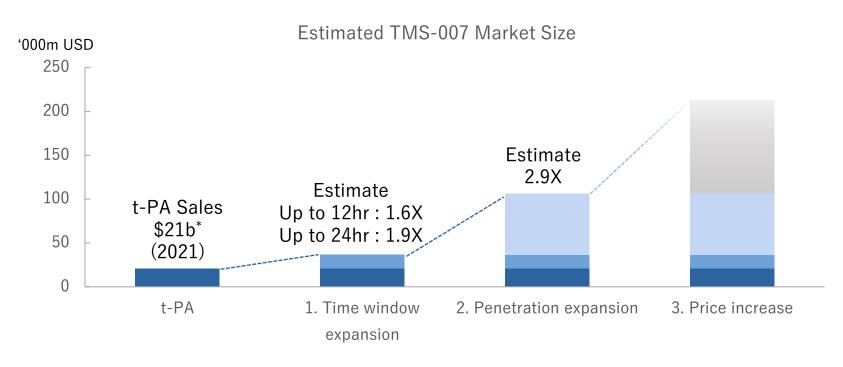
<sup>2.</sup> Biogen, Investor Day Material (September 21, 2021), Q4 and Full Year 2021: Financial Results and Business Update

Wardlaw et al. (2012), "Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated systematic review and meta-analysis"

### Potential of TMS-007: Estimated Market Size



#### Estimated market size for TMS-007 with excellent efficacy and safety potential



- Novel thrombolytic with the potential to be first line treatment for AIS
  - Possibility to expand time window after onset (12hr or 24hr)
  - Possibility to expand penetration due to excellent safety
- 2. Higher pricing can be expected if higher efficacy and safety than t-PA are achieved

<sup>\*</sup> Data for 2021 from Informa

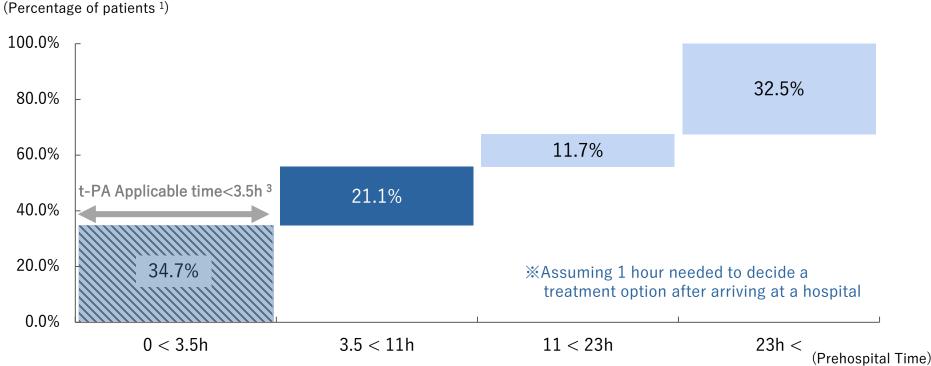
Calculated as the sum of estimated 2021 sales of Activase® and Actilyse®. Actual market size may differ from estimate due to the limitations peculiar to such statistical data and publications in terms of their accuracy

### Potential of TMS-007: Expanding Time Window



#### Relationship between Prehospital Time and treatment <sup>1</sup>

- Number of t-PA treated patients is only a part of entire patient population arriving at a hospital
- Time window expansion for TMS-007 could expand the target patient population 2



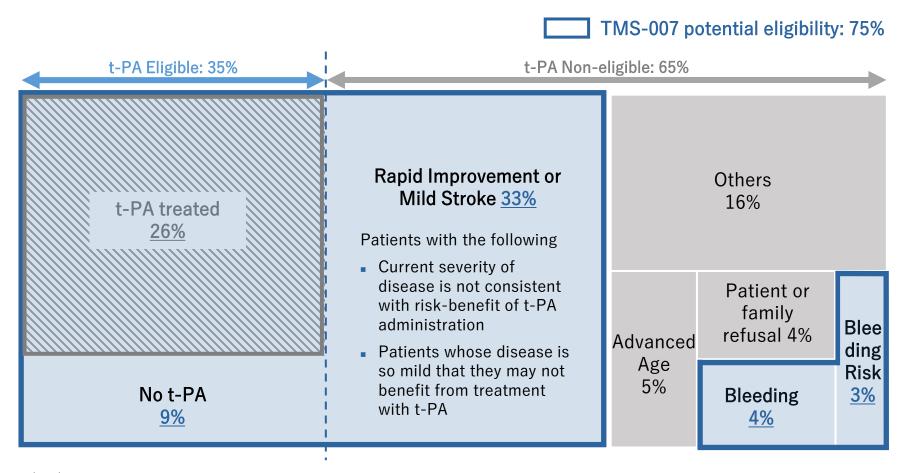
- TMS assumption using average breakdown of patients by prehospital time based on the following papers. Please note that the company's estimate above is based on various assumptions and beliefs stated herein, including the available dose window, disregard certain significant conditions such as the eligibility of the patients and may not be supported by any clinical data;
  - Tong et al. (2012), "Times From Symptom Onset to Hospital Arrival in the Get With The Guidelines–Stroke Program 2002 to 2009"
  - Harraf (2002), "A multicenter observational study of presentation and early assessment of acute stroke" Kim (2011), "Stroke awareness decreases prehospital delay after acute ischemic stroke in Korea" Matsuo (2017), "Association Between Onset-to-Door Time and Clinical Outcomes After Ischemic Stroke"
- 2. Expantion of time window over 12 hours (maximum 24 hours) is based on the registered and pubished information by Biogen on ClinicalTrials.gov on March 10, 2023.
- 3. Assuming 1 hour needed to decide a treatment option after arriving at a hospital

### Potential of TMS-007: Expanding Penetration



#### How t-PA is treated for patients arriving within 2 hours from symptom onset 1

- Due to its favorable safety profile, TMS-007 has a potential to <u>expand its penetration</u>
- It is estimated that TMS-007 may be used for <u>up to 75%</u> of patients, within the dosing window



## JX09

Resistant or uncontrolled hypertension



### JX09: A Potential Best-In-Class Therapeutic for rHTN



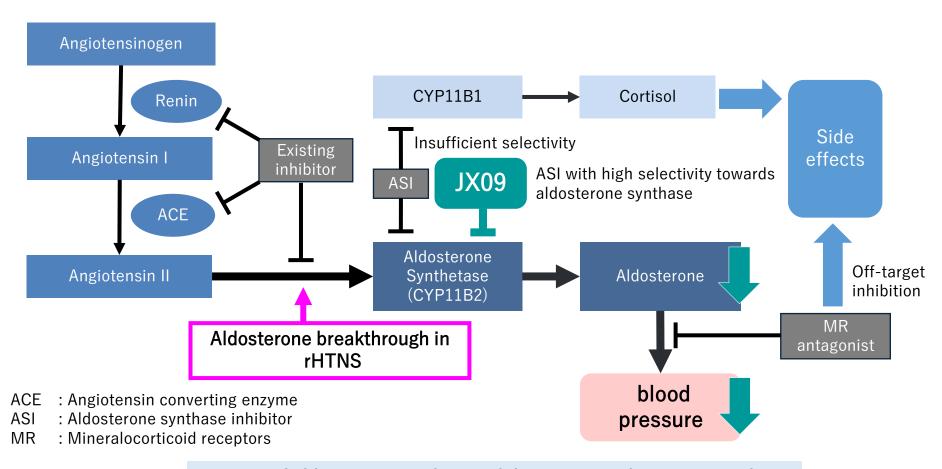
- Therapeutic candidate for "resistant/uncontrolled hypertension" (rHTN), a condition with high unmet medical needs
- 10-20% of treated hypertension patients are believed to be resistant<sup>1</sup>
- JX09, an oral, highly selective, small molecule aldosterone synthesis inhibitor (ASI)
- Selective inhibition of aldosterone synthase (CYP11B2) over structurally similar CYP11B1 is crucial for effective ASI.
  - JX09 has demonstrated > 300-fold selectivity for CYP11B2 over CYP11B1 (*in vitro*), suggesting selectivity higher than baxdrostat (<100 fold)  $^2$
  - JX09 achieved >90% aldosterone lowering with no increase in CYP11B1 precursor steroids (*in vivo*, non-human primates)<sup>2</sup>
- The Phase 1 clinical trial is currently underway in Australia (CORXEL)

<sup>1.</sup> Dudenbostel et al (2017): Resistant hypertension (rHTN) is relatively common with an estimated prevalence of 10-20% of treated hypertensive patients

<sup>2.</sup> Source CORXEL website March 2023 "JIXING Presents the Latest Research Data of Cardiovascular Asset JX09 at the American College of Cardiology Annual Congress 2023"



# Highly selective inhibition: Inhibits aldosterone synthase (CYP11b2)<sup>1</sup> more selectively than the structurally similar CYP11b1



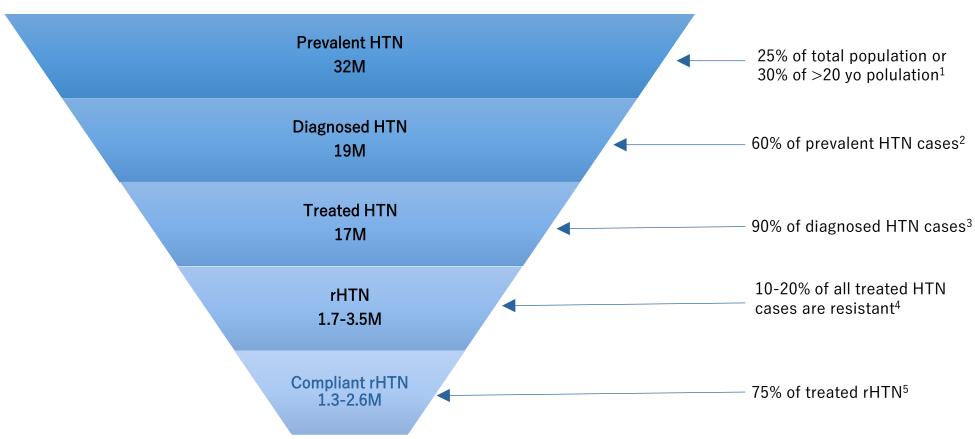
Position of aldosterone synthesis inhibitors among hypertension drugs

1. Lee J, et al, Abstract 121: The Selective Aldosterone Synthase Inhibitor PB6440 Normalizes Blood Pressure In A Human Aldosterone Synthase-Transgenic Mouse Model Of Hypertension, Hypertension 2022; 79:A121

### JX09: Japan Market



# JX09 targets treatment-resistant hypertension, which is expected to affect 1.3 to 2.6 million patients in Japan alone



<sup>1:</sup> Estimated with data from Health Service Bureau, MHLW "National Health and Nutrition Survey 2019": https://www.mhlw.go.jp/english/database/compendia.html

3: Used the same treatment rate as in China, as per Zhang (2022): diagnosed but untreated ~10% in 2018

<sup>2:</sup> Saito et al. (2015): We find that there are much higher rates of undiagnosed hypertension in Japan (44.3%) than in the U.S. (11.9%)

<sup>4:</sup> Dudenbostel et al (2017): Resistant hypertension (RHTN) is relatively common with an estimated prevalence of 10-20% of treated hypertensive patients

<sup>5:</sup> Siddiqui et al (2019): Among patients with RHTN, multiple studies have reported high rates of poor medication adherence. Strauch et al (2013): Our main finding is a surprisingly low compliance with drug treatment in out-patients with resistant hypertension (23% partially noncompliant and 24% totally noncompliant – in total, 47% prevalence of noncompliance).

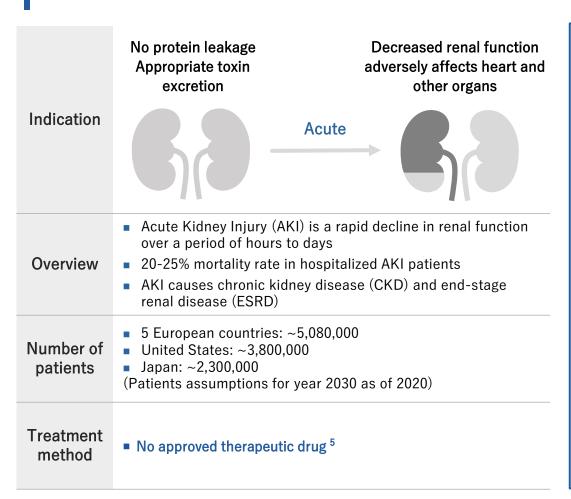
TMS-008

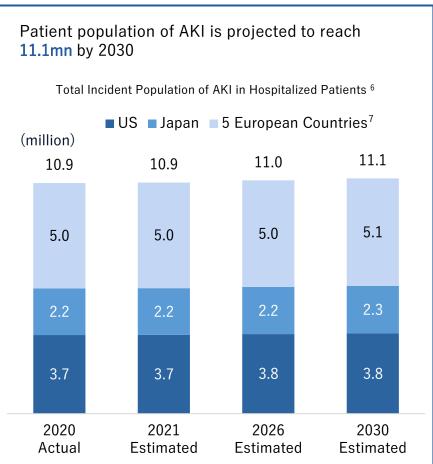
**Acute Kidney Injury** 





### TMS-008 development is directed to take advantage of its strong anti-inflammatory properties





- 1. Nature Reviews Nephrology volume 16, pages747–764 (2020)
- 2. Adv Chronic Kidney Dis. 2017;24(4):194-204
- 3. Nephron. 2017; 137(4):297-301
- Delveinsight, "Acute Kidney Injury Market Insights, Epidemiology, and Market Forecast—2030"
- 5. Perioperative renal protection, Current Opinion in Critical Care December 2021 Volume 27 Issue 6 pages 676-685
- 6. Delveinsight, "Acute Kidney Injury Market Insights, Epidemiology, and Market Forecast—2030"
- 7. 5 European countries includes Germany, France, Italy, Spain, and the UK

### TMS-008: Anti-inflammatory activities with potential for broad indications



### Potent sEH inhibitor with high anti-inflammatory and antioxidant activity

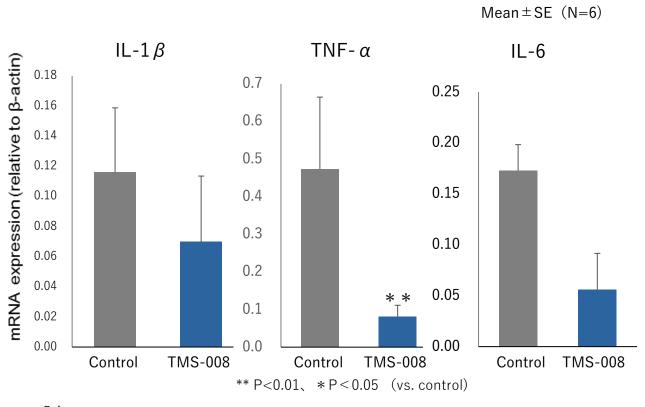
#### Inflammation-related parameter using AIS model mouse <sup>1</sup>

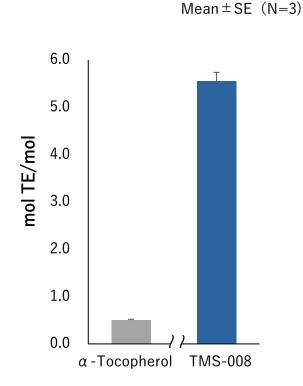
 One hour after the start of ischemia, 10 mg/kg was administered continuously intravenously for 30 minutes.
 Brain slices at 24 hours were evaluated by RT-PCR method.

### H-ORAC: hydrophili

Antioxidant activity test 1,2

 H-ORAC: hydrophilic oxygen radical absorbance capacity method





#### References

- 1. Shibata et al. (2018) Eur J Pharmacol
- 2. Hasumi & Suzuki (2021) Int J Mol Sci

### TMS-008: Acute Kidney Injury (AKI)

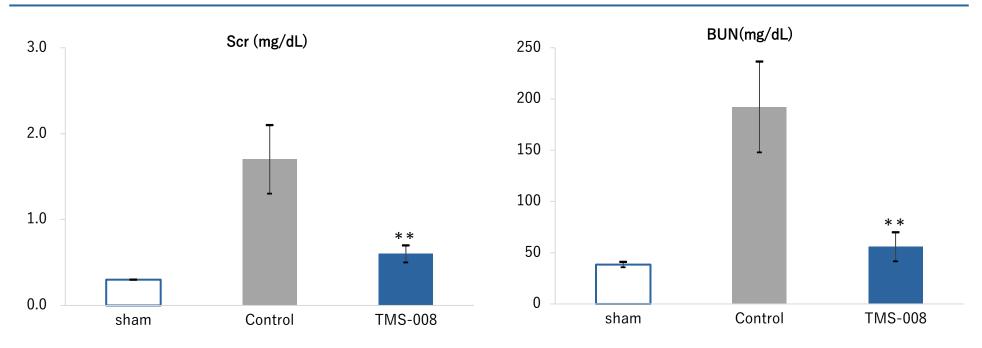


Preclinical studies in collaboration with Japanese university using AKI mouse models confirmed its potential as a new treatment for AKI

Preclinical studies confirmed efficacy in two animal models, indicating the feasibility of TMS-008 for practical use

 Improvement on Scr (serum creatine) and BUN (blood urea nitrogen), which are parameters of renal function, has been observed

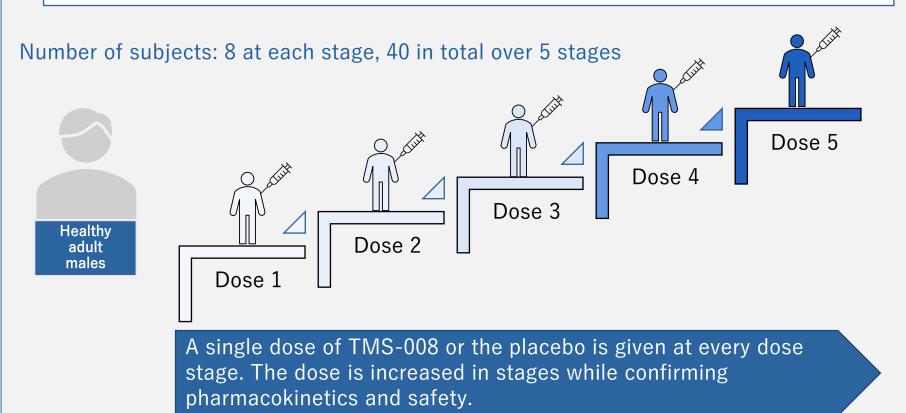
#### AKI model mouse experiment at Showa University <sup>1</sup>





#### Ph1 Clinical Trial Design

- Objective: To confirm pharmacokinetics, tolerability, and safety of a single dose of TMS-008 administered to a healthy adult male as a First-In-Human study
- ◆ <u>Design</u>: Randomized, placebo-controlled, double-blind, dose-escalation, single-dose study

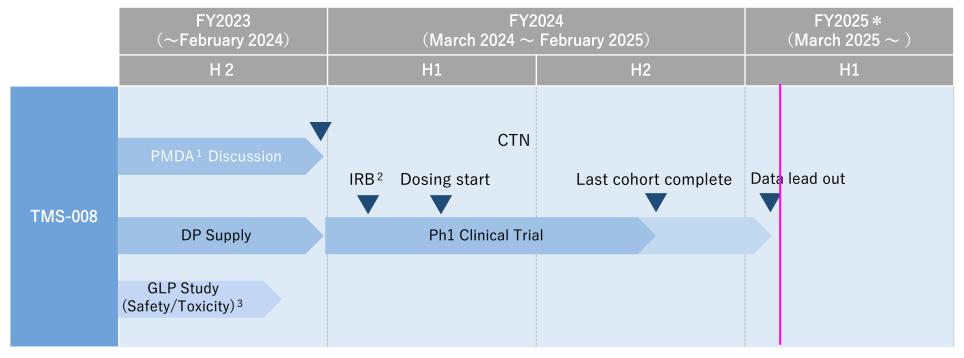


# TMS-008: Progress Status



First patient dosed in the Phase 1 clinical trial in the first half of 2024, with all dosing and observation completed by February 2025.

Data read-out in April 2025: Favorable safety and tolerability demonstrated.



#### Now here

\*Note: The fiscal year-end is scheduled to change to December starting from FY2025.

The above information contains forward-looking statements based on our judgement in light of the information currently available to us. Therefore, please be aware that the above information is subject to various risks and uncertainties, and actual development may differ significantly from these projections.

<sup>1.</sup> PMDA: Pharmaceuticals and Medica Devices Agency

<sup>2.</sup> IRB: Institutional Review Board

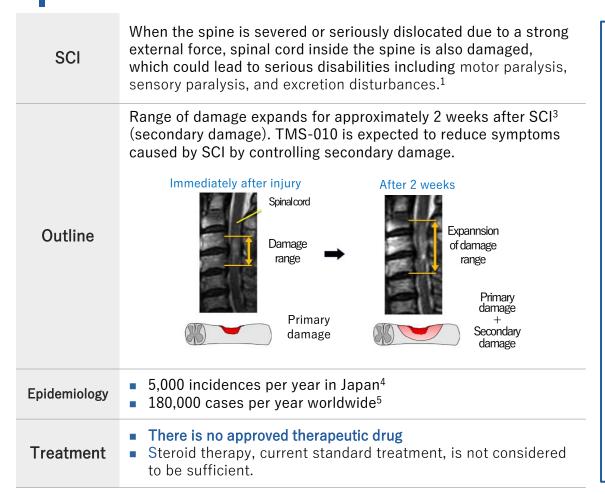
TMS-010
Spinal Cord Injury
New Asset

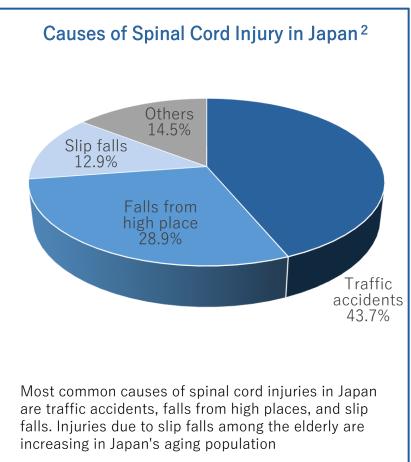


# TMS-010: Spinal Cord Injury (SCI)



# Novel program for an indication for which no approved drug exists





<sup>1,2.</sup> Neurospinal Society of Japan website (<a href="https://www.neurospine.jp/original62.html">https://www.neurospine.jp/original62.html</a>)

<sup>3.</sup> Ahuja CS, et al. Traumatic spinal cord injury. Nat Rev Dis Primers. 27(3), 17018 (2017)

<sup>4.</sup> Miyakoshi N, et al. A nationwide survey on the incidence and characteristics of traumatic spinal cord injury in Japan in 2018. Spinal Cord 59(6), 626-634 (2021)

<sup>5.</sup> Lee BB., et al. The global map for traumatic spinal cord injury epidemiology: update 2011, global incidence rate. Spinal Cord 52(2), 110-116 (2014)

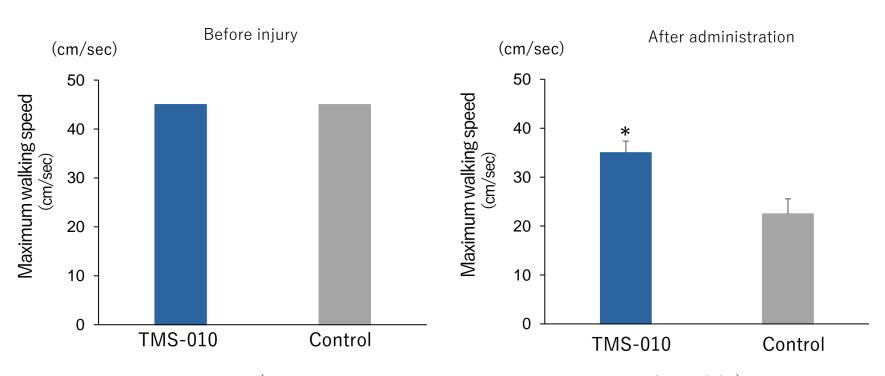
# TMS-010: Spinal Cord Injury (SCI)



## Currently advancing efforts toward entering the clinical trial

In this nonclinical study, maximum walking speed significantly improved in rats administered TMS-010 after spinal cord injury. Improvement was confirmed by a histopathological examination as well.

#### Maximum walking speed: thoracic vertebrae spinal cord injury rat model (Hokkaido Univ.)



(Mean value + Standard error is shown in the graph, n=8,\* p<0.05)

# Expansion of Pipeline



# Pipeline Expansion Efforts Both Internally and Externally



Pursue internal and external paths for pipeline expansion, leveraging knowledge and experience through SMTP compounds development



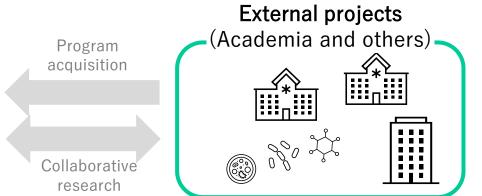
R&D and business development capabilities cultivated through SMTP compounds

#### Internal projects

- New indications for TMS-008
- Oral sEH inhibitor
- Consideration / evaluation of new targets
- Study of the SMTP field



- Brought TMS-007 all the way from research to clinical development
- Partnering experience with a global biopharma company



Deploy

Licensing, etc.



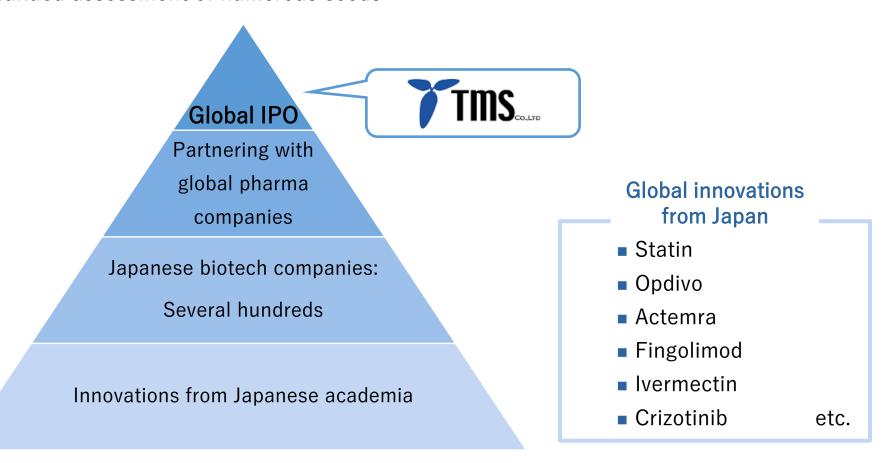
\* Global market is >10 times larger than Japanese market 42

# **External Projects Approach**



## Leveraging TMS's track record to globally expand the discoveries from Japanese academia

- Pursuing business opportunities by connecting outstanding life science innovations from the local to global markets
- Continued assessment of numerous seeds



# **Appendix**



# **Corporate Profile**

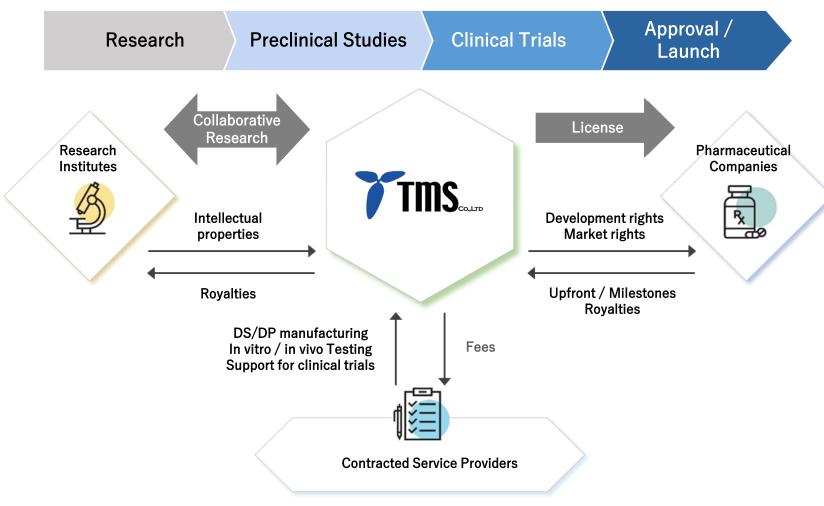


Name	TMS Co., Ltd. (Stock Code: 4891)
Established	February 17, 2005
Closing month	February*
Representative Directors	Takuro Wakabayashi Chief Executive Officer
Address	Headquarters: 1-9-11F, Fuchu-cho, Fuchu-shi, Tokyo JAPAN
Business Field	Research and development of drug products
Management	Board Member: 6 Audit & Supervisory Board Member: 4
Number of employee	18 (as of February 28, 2025)

<sup>\*</sup>Note: The fiscal year-end is scheduled to change to December starting from FY2025.

	History
Feb. 2005	TMS Co., Ltd. founded
2005 - 2011	Demonstrated thrombolytic and anti-inflammatory activities of SMTP ameliorate ischemic stroke in pharmacological studies of SMTP
Aug. 2014	Started Phase I clinical trial of TMS-007
Oct. 2015	Completed Phase I clinical trial of TMS-007
Nov. 2017	Started phase IIa clinical trial of TMS-007 for ischemic stroke patients
Jun. 2018	Option agreement with Biogen on TMS-007
May. 2021	Biogen exercised an option to acquire TMS-007
Aug. 2021	Completed phase IIa clinical trial of TMS-007
Nov. 2022	Listing on the Tokyo Stock Exchange Growth Market (Stock code: 4891)
Jan. 2024	Biogen transferred TMS-007 rights to CORXEL Acquired development and marketing rights for TMS-007 and JX09 in Japan
Jun. 2024	Started Phase I clinical trial for TMS-008 in Japan
Jul. 2024	In-licensed spinal cord injury drug candidate from Hokkaido University (TMS-010)
Feb.2025	The global Phase 2/3 clinical trial "ORION" for TMS-007 (JX10) initiated





- The basic model is that TMS Co., Ltd. conduct drug development from the discovery and research stage to the early clinical stage in collaboration with research institutions and contracted service providers, and partner with pharmaceutical companies from late development stage to commercialization.
- Depending on the disease area, TMS Co., Ltd. may execute late-stage clinical development, obtaining regulatory approval, and even marketing.

# **History of SMTP Compounds**



**SMTP** 



Stachybotrys Microspora Triprenyl Phenol

A small molecule compound produced by Stachybotrys microspore, a type of fungus



Keiji Hasumi

Ph.D. Founder Chief Scientific Officer

Worked alongside Dr. Akira Endo for 17 years
Succeeded Dr. Endo's lab in 1997

#### The late Dr. Akira Endo

Distinguished Professor Emeritus of Tokyo University of Agriculture and Technology

Invention of the hyperlipidemia drug statin (HMG-CoA reductase inhibitor), one of the best-selling category of drugs in history.

TMS-008

Identification of SMTP compounds as modulators of plasminogen

TMS-007 Started CTN-enabling study

TMS-007 Launched Ph1 clinical trial in Japan

> TMS-007 Completed Ph1 Clinical Trial

TMS-007 Started Ph2a clinical trial for acute ischemic stroke patients

> TMS-008 Started CTN -enabling study

TMS-007 Completed Ph2a Clinical Trial

> TMS-008 CTN-Submission

TMS-007 Started Phase 2/3 clinical trial<sup>2</sup>

1990s

**F**Y2011

FY2014

FY2015

FY2018

FY2017

FY2020

FY2021

FY2022

FY2023 FY2024

Started administration

of Ph1 clinical trial

TMS Co., Ltd. Founded (February 17, 2005)

Spinoff from Tokyo University of Agriculture and Technology

2005

Option Agreement with Biogen <sup>1</sup>

Rights Covered: TMS-007 and all IP and asset rights for the SMTP compound family

Biogen <sup>1</sup> exercises Option Right

Transfered all IP and assets related to TMS-007 and SMTP to Biogen.

Rights transfered from Biogen<sup>1</sup> to CORXEL

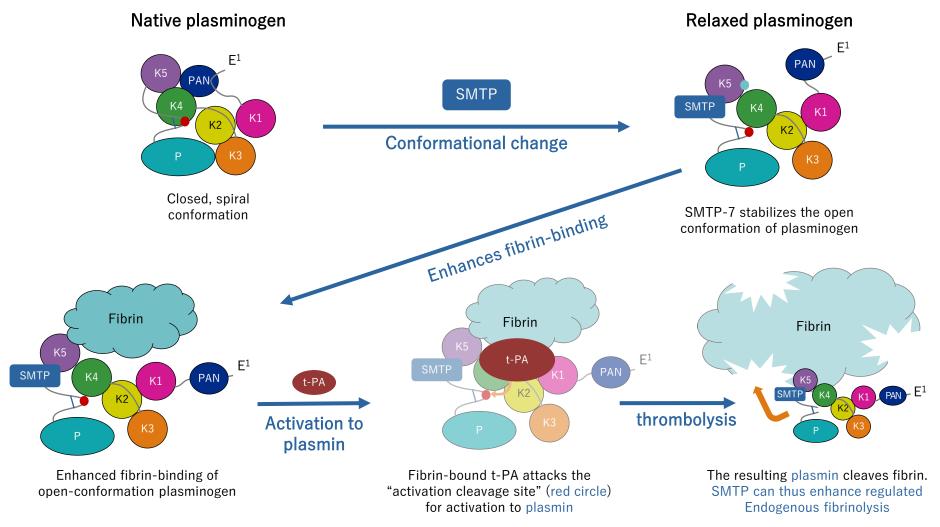
TMS reacquires development and marketing rights for TMS-007 in Japan

- 1. The contract party is Biogen MA Inc.
- 2. Named "ORION" in February 2025 and initiated by CORXEL.

# TMS-007 Mechanism of Action: Mechanism of thrombolysis



# TMS-007 promotes binding of fibrin to blood clots<sup>1</sup>



<sup>1.</sup> Hasumi & Suzuki (2021), "Impact of SMTP Targeting Plasminogen and Soluble Epoxide Hydrolase on Thrombolysis, Inflammation, and Ischemic Stroke" Diagrams shown above have been modified by the Company from the original versions. For illustrative purposes only





www.tms-japan.co.jp