TMS Co.,LTD

TSE Growth: 4891

FY2025 Financial Results Presentation Material

(Fiscal Year December 31, 2025)

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Corporate Mission

Create impactful therapeutics by the power of relentless exploration and challenge

Agenda

1. Highlights & Topics
2. Summary of Financial Results for FY2025 (Fiscal Year December 31, 2025)
3. Pipeline
4. TMS-007 / Potential Next Generation Acute Ischemic Stroke Treatment
5. TMS-008 / Acute Kidney Injury
6. JX09 / Resistant or Uncontrolled Hypertension
7. TMS-010 / Spinal Cord Injury
8. Pipeline Expansion
9. Appendix

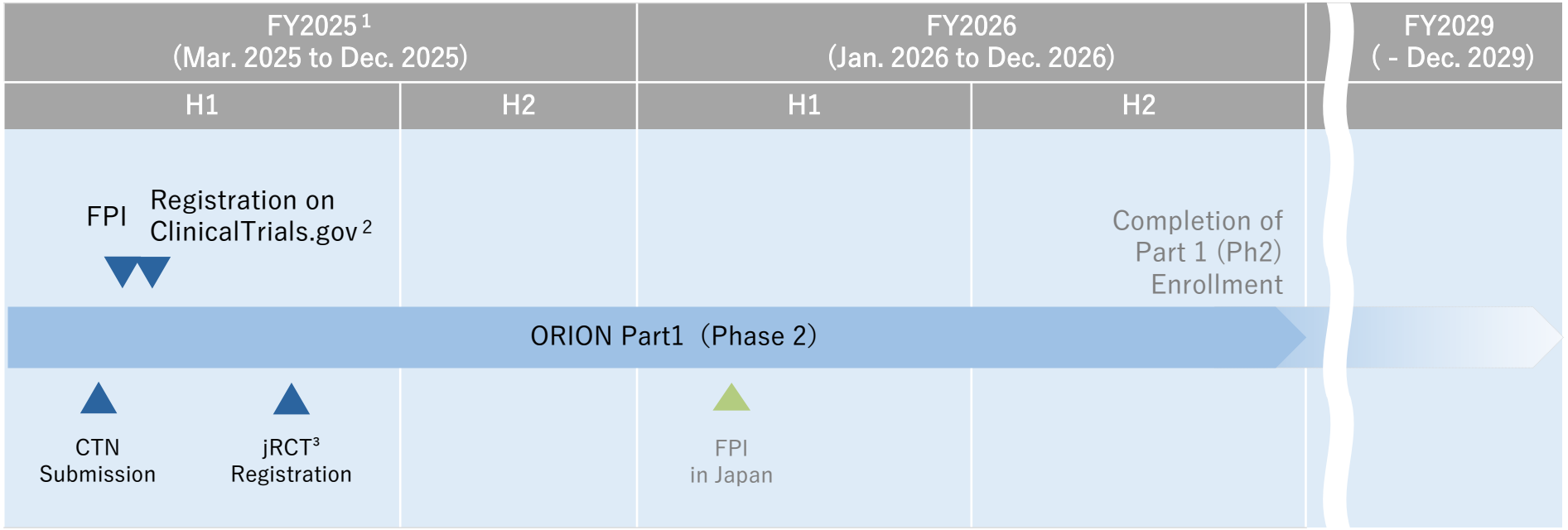
1. Highlights & Topics

1 Global Clinical Trial ORION (Phase 2/3) for TMS-007 (JX10) Underway

- Dosing of the first patient in the global clinical trial on May 16, 2025
- Preparations for initiating dosing in Japan are currently underway at TMS
- Patient inclusion status announced on December 8, 2025: 59 patients in total ➤ Enrollment has progressed substantially beyond this level as of today
- Completion of Part 1 (Phase 2) inclusion is expected during 2026 (TMS estimate)

Forecasted Timeline

The upper row shows global status; the lower row shows status in Japan



1. From FY2025, the fiscal year-end has been changed from February to December. As a result, FY2025 is a transitional fiscal year covering a 10-month period.
2. ClinicalTrials.gov: U.S. clinical trial database (https://clinicaltrials.gov/study/NCT06990867)
3. jRCT: Japan Registry of Clinical Trials (https://jrct.mhlw.go.jp/latest-detail/jRCT2021250014) (registration in the Japan clinical trial database)

Highlights: TMS-007 Recap

- **The first ischemic stroke drug candidate with two distinct MoA: thrombolysis and brain cytoprotection**

- **The deal size with Biogen in 2018 was the largest ever in the ischemic stroke space[1]**
  - Total upfront of USD 355 million plus royalties
  - The program has since been succeeded by CORXEL in a modified form, and a global Phase 2/3 clinical trial is underway
  - RTW, which founded CORXEL and continues to hold a majority equity stake, is regarded as one of the world's top three crossover investors (investing in both public and private companies), in terms of quality, performance, and scale (our opinion)

- **The deal size with Biogen in 2018 ranks fourth among Japanese biotech startups, regardless of therapeutic area[2]**
  - Among agreements that remain in effect, it ranks second (first is the Carna Biosciences – Gilead deal)

- **Results from the Phase 2a clinical trial conducted in Japan showed a significant difference from the placebo group, representing exceptionally strong outcomes for an acute ischemic stroke clinical trial (our opinion)**
  - For the most critical efficacy endpoint, the proportion of patients with mRS score of 0–1, TMS-007 demonstrated a high degree of superiority over placebo, with an odds ratio of 3.34 (unadjusted odds ratio: 3.00), achieving statistical significance ($P < 0.05$)
  - The proportion of patients with mRS score of 0–2 also showed favorable results (unadjusted odds ratio of 2.00)

- **Participation in the global clinical trial ORION, which is highly exceptional for a Japanese biotech**
  - Planned enrollment of 740 patients, spanning across 150 sites in 20 countries (based on publicly disclosed information: 76 sites in 17 countries are already registered)
  - The Steering Committee is composed of world-class physicians in the field of ischemic stroke

1. Based on the views of TMS using search results from the Cortellis™ database.
2. Based on the views of TMS using search results from Nikkei BP's "Nikkei Biotechnology & Business" database.

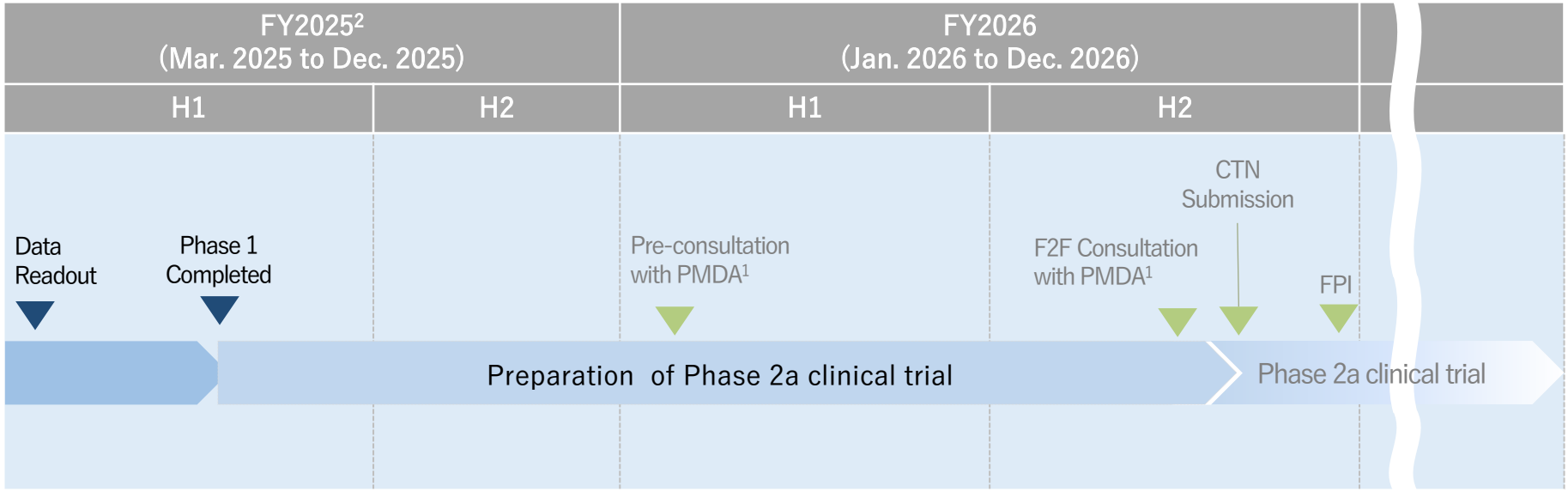
2 TMS-008: Phase 1 Clinical Trial Completed; Advancing to a Phase 2a Clinical Trial in Acute Kidney Injury (AKI)

- June 2025: Finalization of the Phase 1 Clinical Study Report (CSR)
- H2 2026: Submission of the Clinical Trial Notification (CTN) for the Phase 2a trial [a,b] (planned)
- H2 2026: First patient dosed (planned)

a. A clinical study designed to evaluate safety and the rate of suppression of acute kidney injury (AKI) in patients undergoing cardiac surgery.

b. Postoperative AKI, particularly AKI following cardiac surgery, is a critical risk factor that significantly affects patient prognosis. Although there is a strong unmet need for therapeutic agents, no approved drugs are currently available. The onset of postoperative AKI involves ischemia–reperfusion injury followed by inflammation. TMS-008 possesses antioxidant activity and anti-inflammatory effects mediated by soluble epoxide hydrolase (sEH) inhibition, and it is demonstrated to be effective in animal models in improving these pathological conditions.

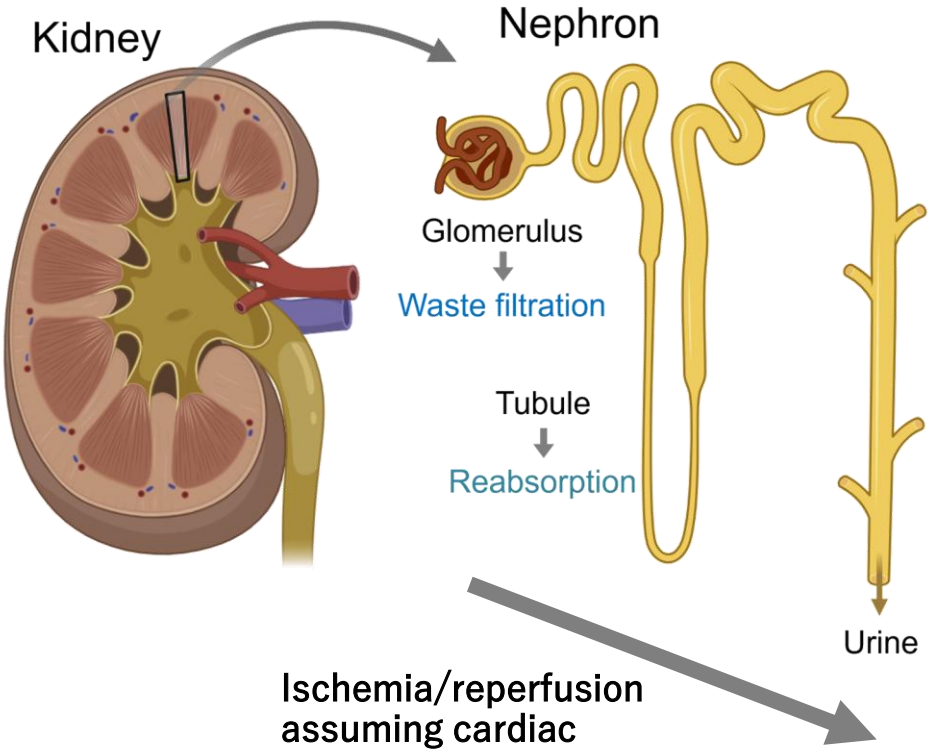
Forecasted Timeline



1. PMDA: Pharmaceuticals and Medical Devices Agency
2. From FY2025, the fiscal year-end has been changed from the end of February to December.

Highlights: Nonclinical Data for TMS-008

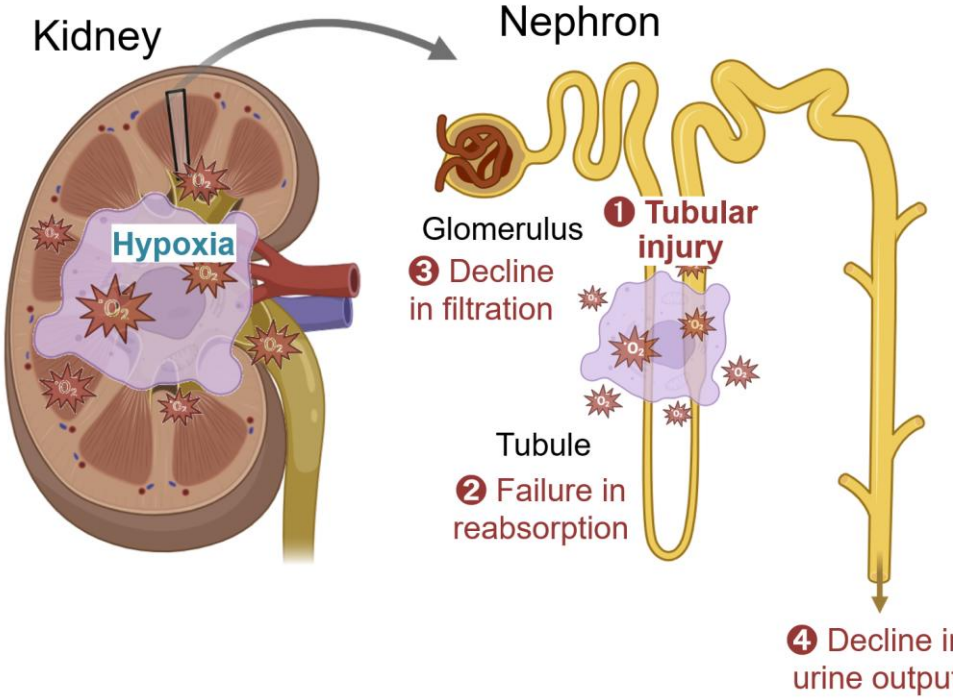
Acute kidney injury (AKI) mouse model:
Significant efficacy demonstrated using a dosing regimen assuming clinical application



Ischemia/reperfusion assuming cardiac surgery

Ischemia-reperfusion injury simulating cardiac surgery in a mouse model

1. Tubular injury
2. Reabsorption failure
3. Filtration failure
4. Decline in urine output



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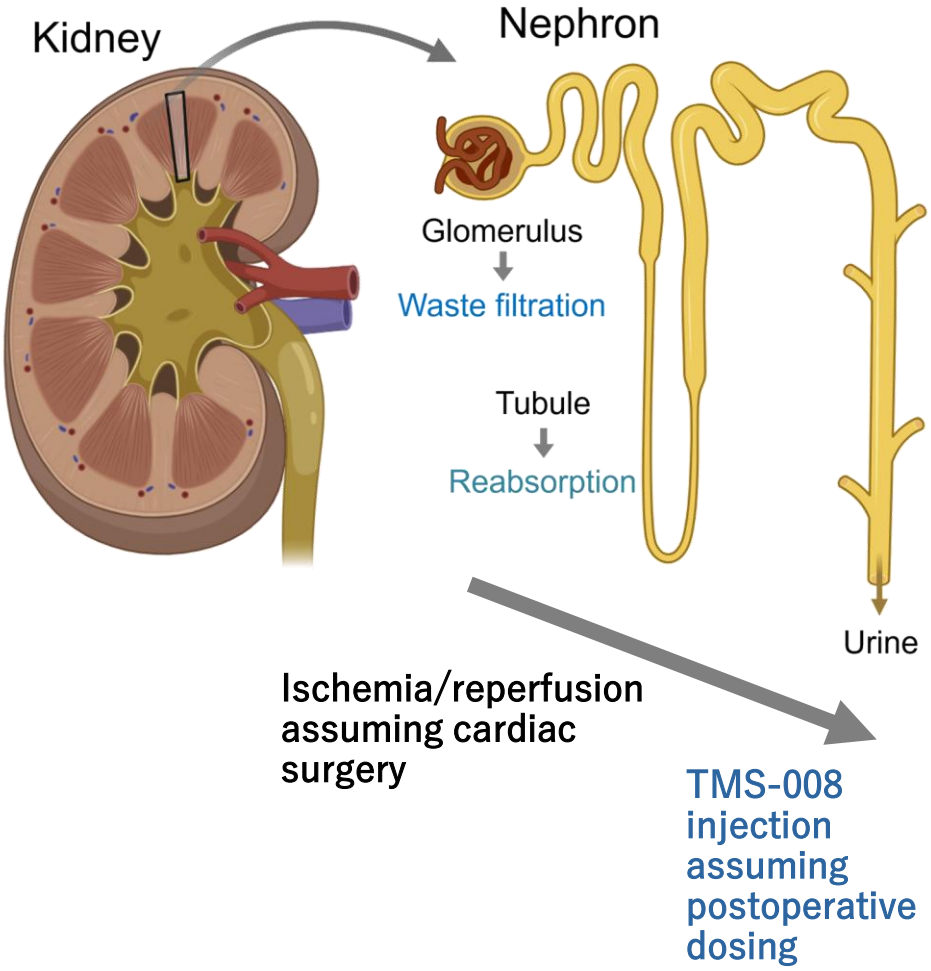
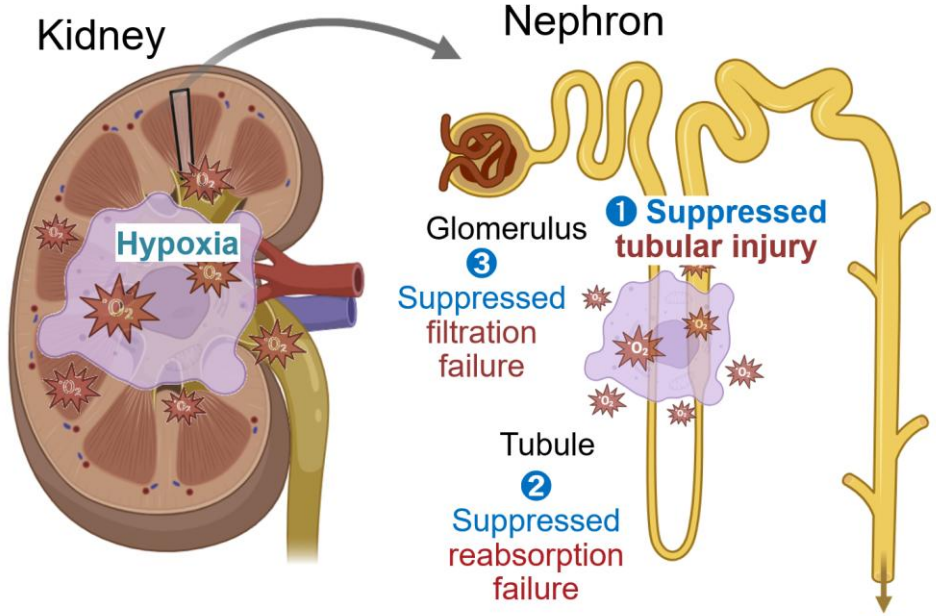


TMS-008 administration following ischemia-reperfusion injury simulating cardiac surgery in a mouse model

1. Suppressed tubular injury
2. Suppressed reabsorption failure
3. Suppressed filtration failure
4. Maintained urine output



Created in BioRender. Hasumi, K. (2026)

3 Status of JX09

- Phase 1 clinical trial is currently being conducted by CORXEL in Australia.
- According to our research, there are only four aldosterone synthase inhibitors (ASIs) in clinical development for resistant/uncontrolled hypertension (rHTN), including JX09 and the two drugs noted below.
- Phase 1 data readout is expected in 2026 (our estimate).

The mechanism of action of JX09, aldosterone synthase inhibition, has attracted significant attention

- In 2025, Mineralys Therapeutics (U.S.) announced positive Phase 3 results for lorundrostat, and AstraZeneca (U.K.) announced similarly strong Phase 3 results for baxdrostat.[1,2]
- The trials targeted patients whose blood pressure remained inadequately controlled despite treatment with two or more antihypertensive agents.
- Compared with placebo, blood pressure reductions of approximately 8–10 mmHg were achieved.
- AstraZeneca has reportedly stated that peak annual sales of baxdrostat could exceed USD 5 billion.[3]
- Mineralys' valuation reached nearly $2.5b (as of January 30, 2026), expected to file NDA in 2026.

1. Source: Mineralys press release https://ir.mineralystx.com/news-events/press-releases/detail/60/mineralys-therapeutics-announces-positive-topline-results
2. Source: AstraZeneca press release https://www.astrazeneca.com/media-centre/press-releases/2025/baxdrostat-demonstrated-statistically-significant-clinically-meaningful-reduction-sbp-patients-hard-control-hypertension-baxhtn-phase-iii-trial.html
3. Source: Reuters, August 30, 2025 AstraZeneca to seek approval for blood pressure drug by year-end

4 CORXEL Financing[1] (After Year-End)

- CORXEL announced completion of a financing round, raising USD 287 million, on January 22, 2026.
  - Equivalent to approximately ¥45.3 billion (USD/JPY exchange rate of 158).
  - There were only six larger financings[2] completed among U.S. private biotech companies in 2025, indicating that this was a large-scale financing even by the U.S. standard.
  - Proceeds will be used for development of CX11, therapeutic candidate for obesity, as well as JX10 (TMS-007) and JX09.
- This financing will provide positive momentum for development of TMS-007 (JX10).
- In addition to RTW Investments, a broad group of well-known institutional investors participated in the financing.
  - Existing shareholders: RTW Investments, Hengdian Group
  - New investors: SR One, TCG Crossover (TCGX), RA Capital Management, HBM Healthcare Investments, SymBiosis, Adage Capital Management, Invus, SilverArc Capital, among others

1. CORXEL press release: https://www.corxelbio.com/en/press-releases/corxel-announces-287-million-series-d1-financing-to-further-advance-its-cardiometabolic-pipeline-including-oral-small-molecule-glp-1-receptor-agonist/
2. Based on the Company's research using Labiotech database

Topics

1 In-License of Novel Resolvin Analogues from Hokkaido University

- In November 2025, TMS in-licensed novel stable-form of resolvin-analogues from Hokkaido University. Application of Resolvins, lipid mediators with anti-inflammatory activities, in medicine has been hindered due to low in vivo stability.

2 New Collaborative Research with Tokushima University and Akita University, Continued Collaborative Research with Tokyo University of Agriculture and Technology, Showa Medical University, and Teikyo University

- Collaborative research projects ongoing to investigate pharmacological efficacy and mechanism of sEH inhibitors.

3 Appointment of New Head of Development

- Appointed Naohisa Yokota, MPharma as EVP, Head of Development, who joined the Company in November 2024 as Senior Director. Mr. Yokota succeeded Noriaki Inamura, Ph.D.
- Mr. Yokota has top-level experience at major global pharmaceutical companies, including seven years as Head of R&D at Sanofi K.K. He also has extensive experience in industry associations, such as Chair of the Technical Committee of the European Federation of Pharmaceutical Industries and Associations Japan (EFPIA-Japan).

4 Initiation of Coverage by Pathology Associates

- Pathology Associates Co., Ltd., an independent investment advisory firm, initiated coverage of TMS in September 2025 (analyst Dr. Dion Stéfan Büchner, M.D.).

5 Launch of the Official Blog “TMS Tsushin”

- To provide broader insight into the Company’s initiatives and activities, TMS launched its official blog, “TMS Tsushin” (Japanese only). URL:https://www.tms-japan.co.jp/ja/blog.html

6 Publications of Collaborative Research Projects on SMTP Compounds

Diabetic neuropathy

Journal of Pharmacological Sciences
Volume 159, Issue 1, September 2025, Pages 25-34

SMTP-44D prevents negative symptoms of diabetic neuropathy by inhibiting sciatic nerve apoptosis

Ayaka Aoki [a b], Keita Shibata [a b] ✉, Ryosuke Shinouchi [a b], Keiji Hasumi [c d], Koji Nobe [a b]

Journal of Diabetes and its Complications
Volume 39, Issue 7, July 2025, 109061

Antioxidant and anti-inflammatory effects of SMTP-44D in a streptozotocin-induced diabetic neuropathy mouse model

Ryosuke Shinouchi [a b] ✉, Keita Shibata [a b], Taiju Nagatsuka [c], Keiji Hasumi [d e], Koji Nobe [a b]

Diabetic nephropathy

Journal of Pharmacological Sciences
Volume 159, Issue 2, October 2025, Pages 87-93

Therapeutic potential of SMTP-27 in attenuating diabetic nephropathy with anti-inflammatory activity

Keita Shibata [a b] ✉, Taiki Awane [a b], Takashi Takaki [c], Keiji Hasumi [d e], Koji Nobe [a b]

Diabetic retinopathy

Journal of Pharmacological Sciences
Volume 157, Issue 2, February 2025, Pages 57-64

SMTP-44D alleviates diabetic retinopathy by suppressing inflammation and oxidative stress in *in vivo* and *in vitro* models

Mio Ishibashi [a b], Keita Shibata [a b] ✉, Michishige Terasaki [c], Yuta Saito [d], Sho-ichi Yamagishi [c], Keiji Hasumi [e f], Koji Nobe [a b]

Pulmonary fibrosis

American Journal of Respiratory and Critical Care Medicine

SMTP-44D, a Novel Soluble Epoxide Hydrolase Inhibitor, Ameliorates Bleomycin-induced Pulmonary Fibrosis in Mice

K. Murakami [1], S. Sato [1], Y. Isomura [1], P.T.H. Trang [1], N. Bando [1], R. Suzue [1], N.-E. Danzan [1], Y. Yamashita [1], H. Bando [1], K. Haji [1], N. Naito [1], K. Kagawa [1], H. Kawano [1], N. Inamura [2], K. Hasumi [2], Y. Nishioka [1]

FY2026 Projections & Milestones

Programs	Achievements and Upcoming Milestones	Timing
TMS-007 *(Acute ischemic stroke)*	Initiation of dosing in the Japan cohort for Part 1 of the global ORION (Phase 2/3) clinical trial	Q1 FY2026
	Completion of dosing for Part 1 of the global ORION (Phase 2/3) clinical trial	H2 FY2026
	Data read-out for Part 1 of the global ORION (Phase 2/3) clinical trial	H1 FY2027
	Completion of the global ORION (Phase 2/3) clinical trial	H2 FY2029
TMS-008 *(Acute kidney injury)*	Completion of the design of the next-phase (Phase 2a) clinical trial	H1 FY2026
	Submission of the Phase 2a clinical trial notification	H2 FY2026
	Dosing of the first patient in the Phase 2a clinical trial	H2 FY2026
JX09 *(Resistant or uncontrolled hypertension)*	Completion of the Phase 1 clinical trial conducted by CORXEL	H1 FY2026
New Oral sEH Inhibitor (R002)	Completion of pharmacology studies; evaluation of indications and CMC	H2 FY2026

The information above includes forward-looking statements based on the Company's judgment using currently available information. These statements are subject to various risks and uncertainties, and actual development results may differ materially from these projections.

2. Summary of Financial Results for FY2025*

*The fiscal year-end has been changed.
The current fiscal year covers a 10-month period ending December 31, 2025.

FY2025 Financial Results - Income Statement

Operating expenses came in below the range projected at the beginning of the fiscal year.
12 month-equivalent operating loss improved by 71m yen YoY.

(million yen)

	FY2024 (Mar.2024 to Feb.2025)	FY2025 (Mar.2025 to Dec.2025)	Change	
			Amount	Percentage
Operating revenue	-	-	-	-
Operating expenses	907	696 [1]	(210)	-23.2%
R&D	621	456 [1]	(264)	-26.4%
SG&A	286	240 [1]	(46)	-16.3%
Operating profit (loss)	**(907)**	**(696)**	**(210)**	-
Non-operating income	342	0	(342)	-100.0%
Non-operating expenses	67	14	(53)	-78.5%
Ordinary profit (loss)	**(633)**	**(711)**	**(78)**	-
Extraordinary losses	26	3	(22)	-86.0%
Profit (loss)	**(660)**	**(716)**	**(55)**	-

Expenses remained at a relatively low level, and due to the 10-month transitional fiscal year, results declined by 23.2%.

12 month-equivalent operating loss for the FY2025 amounted to 835m yen.

Dividend income from CORXEL shares was recorded in FY2024.

1. The expense outlook for the fiscal year ended December 31, 2025 announced at the beginning of the fiscal year was ¥810–1,150 million, comprising R&D expenses of ¥550–800 million and other SG&A expenses of ¥260–350 million.

Expected expenses for the Full Fiscal Year 2026*

(million yen)

Operating expenses	900 - 1,300
Research and Development expenses	600 - 900
Other selling, general and administrative expenses	300 - 400

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

Note: Due to a change in the fiscal year end, the current fiscal year will be a 10-month period ending on December 31, 2025.
Annualized (12-month) expenses are expected to be R&D expenses, at 660-960 million yen, and other SG&A expenses, at 312-420 million yen.

FY2025 Financial Results - Cash Flows

Cash inflows from financing activities were attributable to fundraising. Cash and cash equivalents at the end of the period amounted to 2.7b yen, representing a decrease of 0.14b yen from the beginning of the fiscal year.

(million yen)

	FY2024 (Mar.2024 to Feb.2025)	FY2025 (Mar.2025 to Dec.2025)
Cash flows from operating activities	**(493)**	**(779)**
Profit(loss) before income taxes	(660)	(715)
Cash flows from investing activities	**(30)**	**(2)**
Cash flows from financing activities	**0**	**640**
Proceeds from issuance of shares	0	649
Payments for issuance of share acquisition rights	0	(9)
Net increase(decrease) in cash and cash equivalents	(523)	(141)
Cash and cash equivalents at beginning of period	3,446	2,922
Cash and cash equivalents at end of period	**2,922**	**2,781**

Mainly expenditures for R&D costs, including TMS-007 (JX10)

Due to fundraising

FY2025 Financial Results - Balance Sheet

Total assets slightly decreased compared with the end of the previous fiscal year, primarily due to lossed made by R&D activities.

(million yen)

	FY2024 (Mar.2024 to Feb.2025)	FY2025 (Mar.2025 to Dec.2025)	Change	
			Amount	Percentage
Current assets	3,029	2,863	(165)	-5.5%
Cash and deposits	2,922	2,781	(141)	-4.9%
Non-current assets	3	1	(1)	-45.0%
Total assets	**3,032**	**2,865**	**(166)**	**-5.5%**
Current liabilities	216	94	(122)	-56.6%
Total liabilities	**216**	**94**	**(122)**	**-56.6%**
Share acquisition rights	23	35	12	+51.8%
Net assets	**2,815**	**2,771**	**(44)**	**-1.6%**
Total liabilities and net assets	**3,032**	**2,865**	**(166)**	**-5.5%**

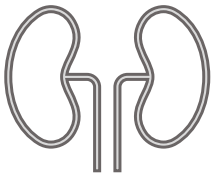
Primarily due to a decrease in accounts payable and accrued expenses.

3. 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.
- A global clinical trial, ORION Phase 2/3, is currently underway under the leadership of CORXEL.
  Completion of dosing for Part 1 (Phase 2) is expected during FY2026 (TMS estimate)
- TMS owns development and marketing rights in Japan, and the rights to receive and royalties in the rest of the world (ex-Japan).



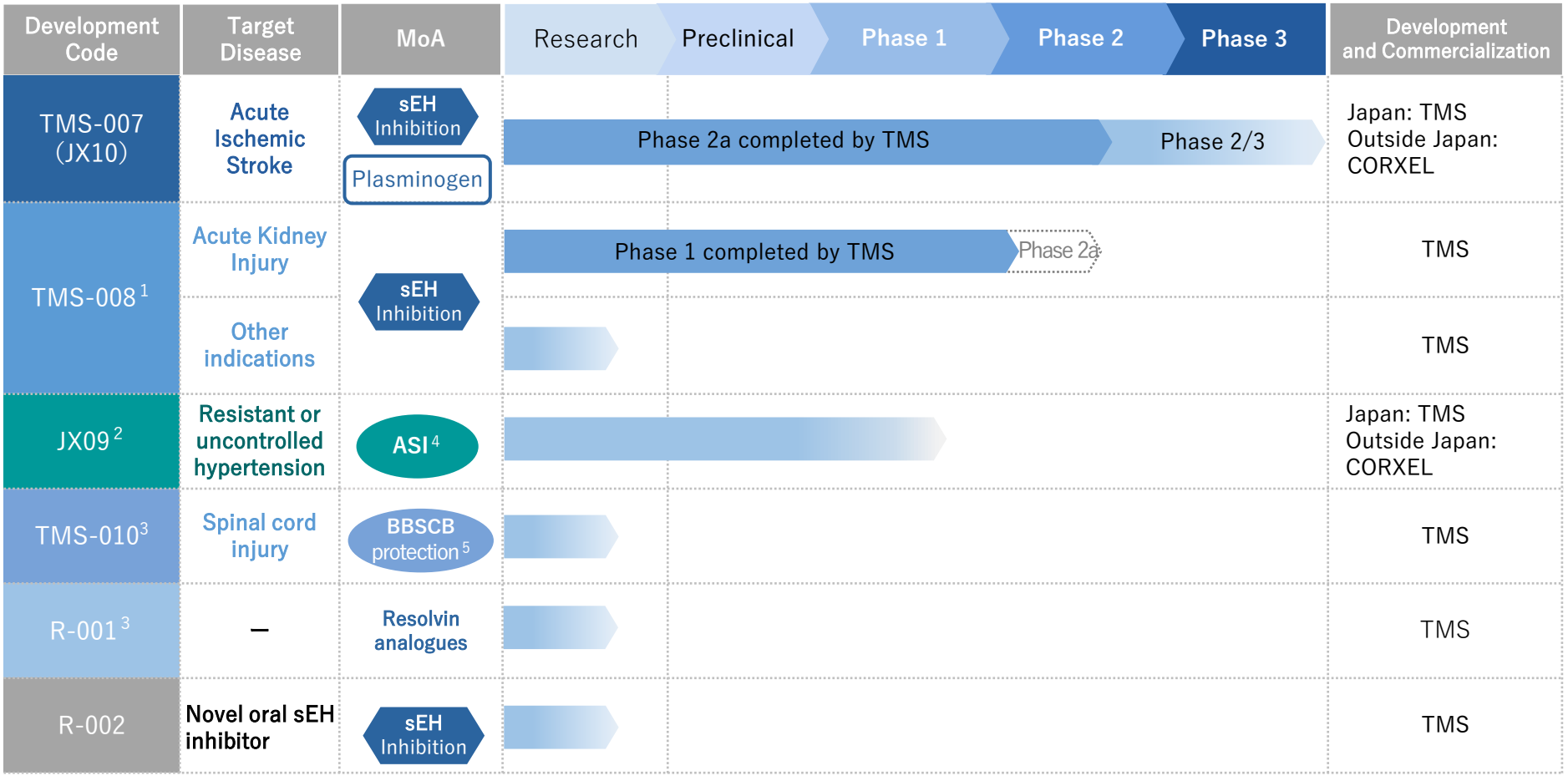
TMS-008 *(Acute kidney injury)*

- Important unmet medical needs for which no approved drug exists.
- The Phase 1 clinical trial in Japan was completed in April 2025, confirming safety and tolerability.
- Initiation of a Phase 2a clinical trial is planned for FY2026.
- TMS owns the rights to develop and market the product globally.

JX09 *(Resistant or uncontrolled hypertension)*

- Aldosterone synthase inhibitor with best-in-class potential.
- Phase 1 clinical trial underway in Australia by CORXEL.
- TMS owns the rights to develop and market the product in Japan

TMS Pipeline



The information above includes forward-looking statements based on the Company's judgment using currently available information. These statements are subject to various risks and uncertainties, and actual development results may differ materially from these projections.

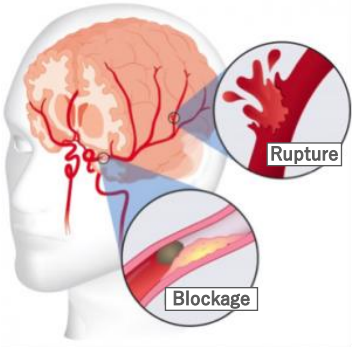
1. TMS-008 is currently under development by TMS under a free license from CORXEL.
2. Obtained free license for development and marketing rights in Japan from CORXEL (January 2024).
3. TMS-010 was in-licensed in July 2024, and R-001 was in-licensed in November 2025, with exclusive worldwide rights (including Japan) obtained from Hokkaido University.
4. ASI：Aldosterone synthase inhibitor.
5. BBSCB(Blood-brain spinal cord barrier) protection

4. TMS-007

Potential Next Generation Acute Ischemic Stroke Treatment

Acute Ischemic Stroke - Important Unmet Medical Needs

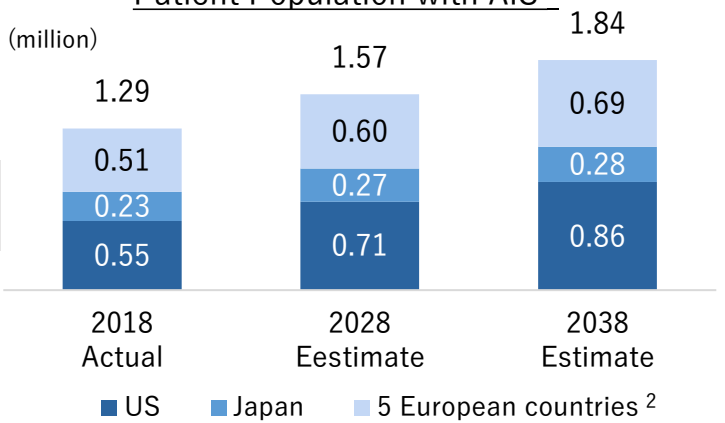
Acute Ischemic Stroke (AIS) Overview



- 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 per year (total of 7 major countries) and it is expected to increase

Patient Population with AIS [1]

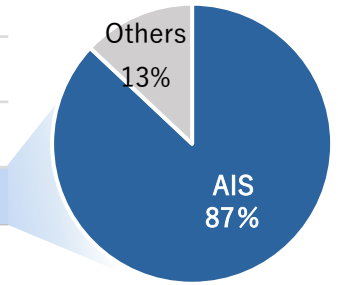


Important Unmet Medical Needs

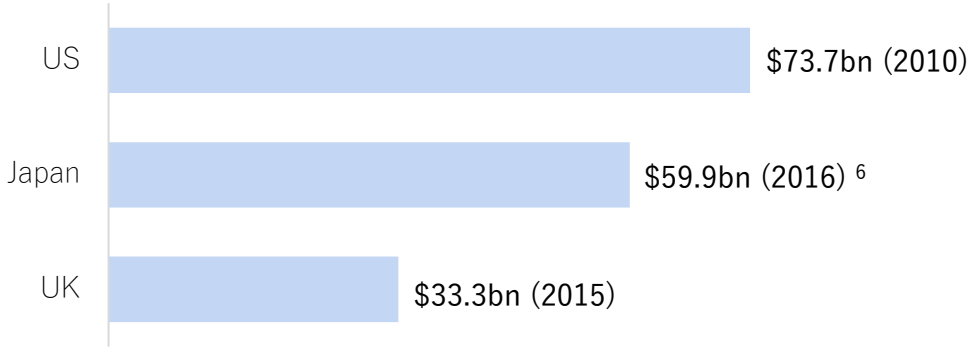
Cause of death in the US (2019) [3]

#	Disease	Ratio
1	Heart Disease	23.1%
:	:	:
4	CLRD	5.5%
5	Stroke	5.3%
6	Alzheimer	4.3%

Breakdown of Stroke [4]



Stroke causes significant economic loss [5]



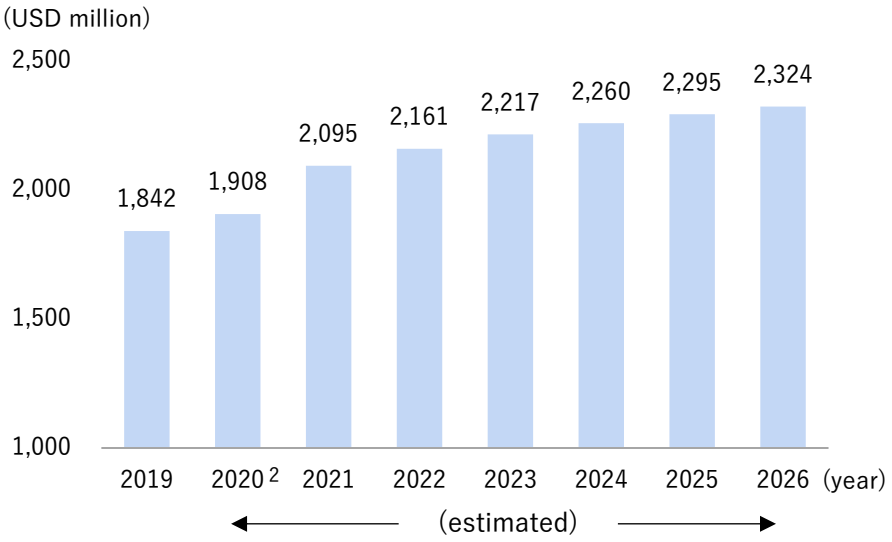
1. Datamonitor Healthcare, "Stroke Epidemiology", Ref Code:DMKC0201444, Published on 07 January 2019
2. 5 European countries are composed of five major countries: Germany, France, Italy, Spain, and United Kingdom
3. Centers for Disease Control and Prevention, "National Vital Statistics Reports volume 70"
4. Tsao et al. (2022) Heart Disease and Stroke Statistics—2022 Update: A Report From the American Heart Association
5. 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
6. Estimated COI based on direct and indirect costs related to stroke for 1 year until November 2015

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

No drug has been approved since 1996 in the US

Market size [1] of the existing drug

Market size 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]

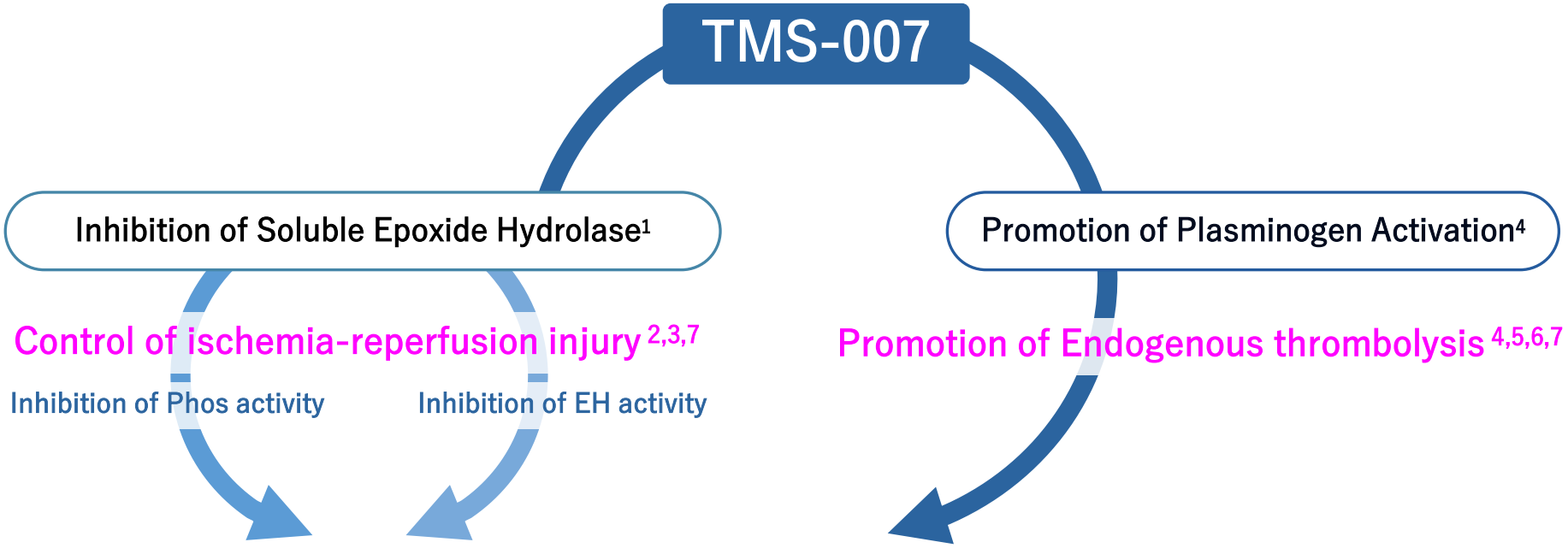
Mortality [4,5]

- 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
4. 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 compound with unique mechanism of action

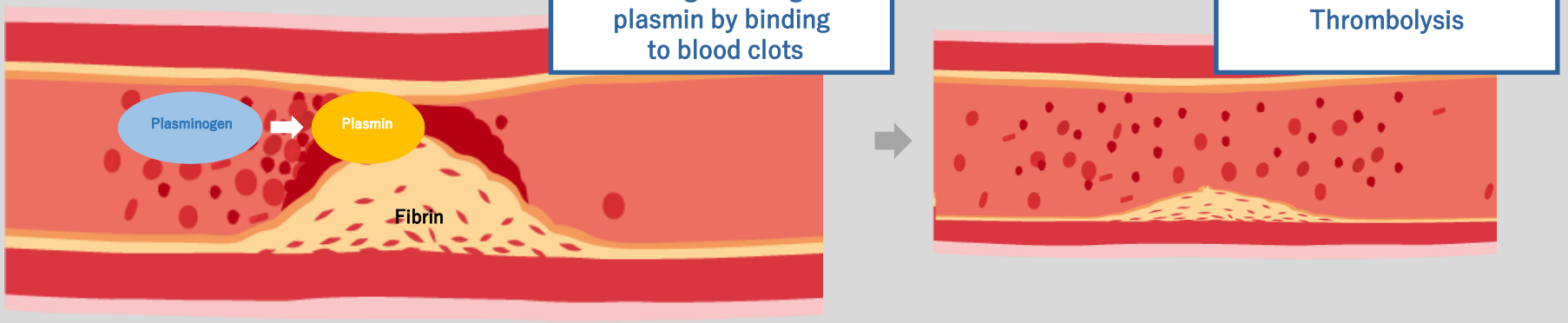
Thrombolysis effect and Inhibitory control of ischemia-reperfusion injury effect (based on anti-inflammatory activities)

Ideal profile for treatment of acute ischemic stroke

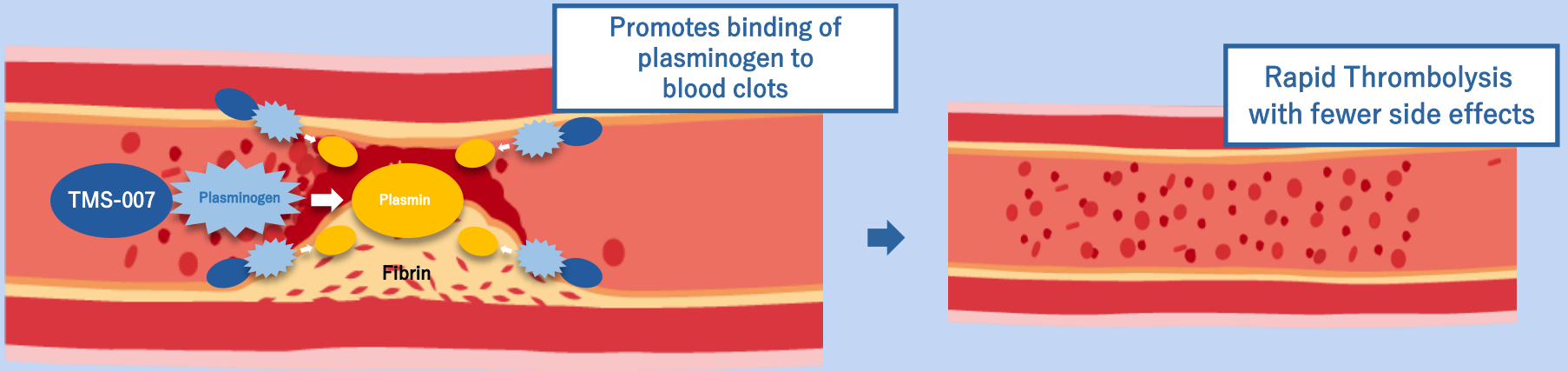
1. Matsumoto et al. (2014) J Biol Chem
2. Shibata et al. (2011) N-S Arch Pharmacol
3. Ito et al. (2014) Brain Res
4. Hasumi et al. (2010) FEBS J
5. Hu et al. (2012) Thrombosis J
6. Miyazaki et al. (2011) Stroke
7. Hasumi & Suzuki (2021) Int J Mol Sci

Mechanism of Action of TMS-007：Image of Thrombolysis [1]

Normal Thrombolysis



Thrombolysis promotion by administration of TMS-007



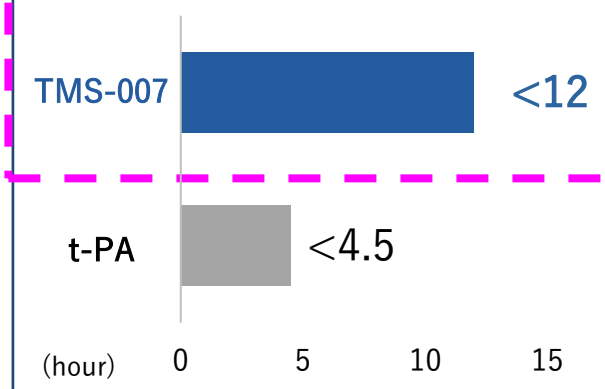
1. For illustrative purposes only

TMS-007：Phase 2a Clinical Trial Showed Excellent Results

TMS-007 has the potential to become the first line AIS treatment [1]

Time Window

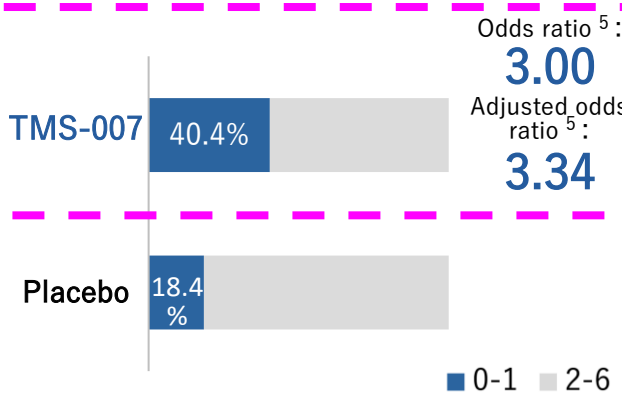
Therapeutic time window



- Clinical trials indicate that TMS-007 may work in potentially longer time window (within 12hr).

Efficacy

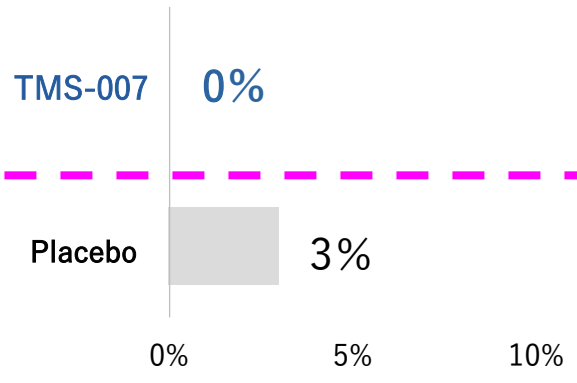
mRS [2] 0-1 ratio at 90 days
Gold-standard Endpoint



- mRS score 0-1 indicates recovery to a level that does not interfere with daily life, and **"Gold-standard" endpoint with statistical significance** (P value＜0.05) was achieved.

Safety

Symptomatic Intracranial hemorrhage risk [3,4]



- TMS-007 showed the potential to overcome the biggest problem of t-PA, which is safety.

1. The data comparisons above are not based on head-to-head clinical studies of TMS-007 versus t-PA.
   Number of patients(N)=52 for TMS-007, N=3,391 and N=2,488 for t-PA
2. mRS indicates modified Rankin Scale, and it refers to degree of independence in daily life
3. Biogen, Investor Day Material (September 21, 2021), Q4 and Full Year 2021: Financial Results and Business Update
4. Wardlaw et al. (2012), "Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated systematic review and meta-analysis", N=2,488
5. 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)

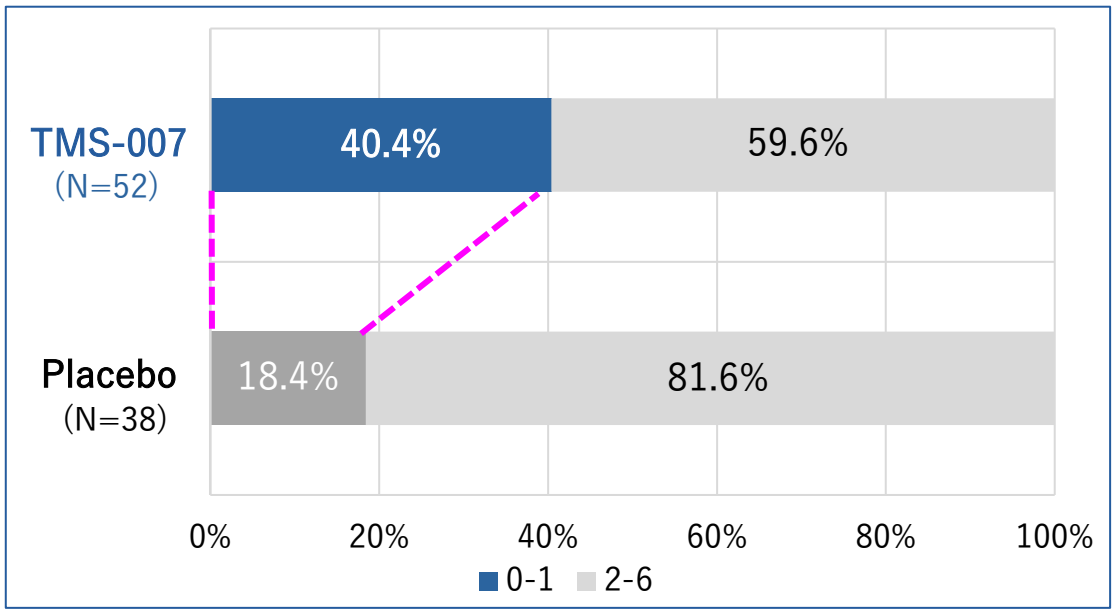
TMS-007：Phase 2a Clinical Results Achieved “Gold-standard” Endpoint

TMS-007 achieved statistically significant efficacy 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[1]



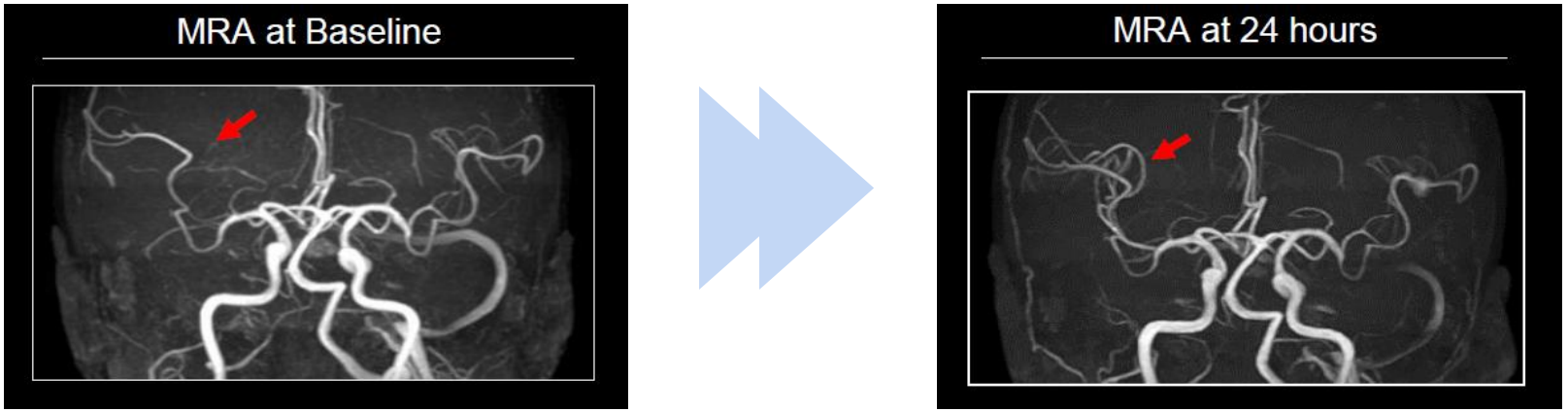
mRS (modified Rankin Scale)		
	0	No symptoms
	1	**No significant disability, despite symptoms;** able to perform all usual duties and activities
	2	**Slight disability;** unable to perform all previous activities but able to look after own affairs without assistance
	3	**Moderate disability;** requires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

1. Biogen, Investor Day Material (September 21, 2021), Q4 and Full Year 2021: Financial Results and Business Update

TMS-007：Phase 2a Clinical Results Efficacy of Favorable-Vessel Recanalization

TMS-007's promising efficacy is 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	TMS-007
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

1. Biogen, Investor Day Material (September 21, 2021), Q4 and Full Year 2021: Financial Results and Business Update

Overview of the ORION (Phase 2/3) Trial

TMS-007: Global Clinical Trial “ORION” (Phase 2/3)[1]

Overview

- Design: Multicenter, double-blind, placebo-controlled, randomized, parallel-group study
- Study period: May 15, 2025 (actual) – December 31, 2029 (planned)
- Planned enrollment: 740 patients (total across Part 1 and Part 2)

Key Inclusion Criteria

- Age: 18–90 years
- Acute ischemic stroke patients within 4.5–24 hours from last known well (LKW)
- Patients with salvageable tissue confirmed by imaging analysis
- NIHSS pre-treatment score[2] ≥ 5 (patients with severe stroke are also eligible)

Primary Endpoints

- Proportion of patients with mRS 0–1 at Day 90
- Incidence of symptomatic intracranial hemorrhage (sICH) within 36 hours

Part 1 (Phase2)	Part 2 (Phase3)
Dose-finding study in 240 patients Doses: 1 mg/kg, 3 mg/kg, or placebo	Efficacy confirmation in 500 patients Comparison between the optimal dose selected in Part 1 and placebo

1. This slide was created by the Company based on information registered by CORXEL on ClinicalTrials.gov (https://clinicaltrials.gov/study/NCT06990867?cond=Stroke%20Acute&term=JX10&rank=1) and information registered by the Company on jRCT (https://jrct.mhlw.go.jp/latest-detail/jRCT2021250014).
2. NIHSS (National Institutes of Health Stroke Scale) is a standardized clinical assessment scale developed to evaluate the severity of acute stroke. It consists of 11 items assessing level of consciousness, motor function, language, vision, articulation, and others. Higher scores indicate greater stroke severity. 0–4 points: Minor stroke, 5–15 points: Moderate stroke, 16–42 points: Severe stroke.

Overview of ORION (Phase 2/3) clinical trial Comparative trial with Phase 2a clinical trial conducted in Japan

Comparison of Japan Phase 2a and Global Clinical Trial ORION (Phase 2/3)[1]

		Phase 2a	ORION (Phase 2/3)
Basic Design		Single stage	Two stages (Part 1, Part 2)
Number of Patients		90	740 (planned)
Primary Efficacy Endpoint		Proportion of patients with mRS 0–1	Proportion of patients with mRS 0–1
Inclusion Criteria	Age	Male: 20–88 years Female: 60–88 years	18-90 years
	Time Window	Within 12 hours of onset	4.5–24 hours from onset
	Radiographic Evidence	—	Confirmation of salvageable tissue in ischemic area
	Endovascular Therapy	Excluded	Patients undergoing endovascular therapy also eligible
	NIHSS Score at Baseline	6–23 (moderate)	≥ 5 (patients with severe stroke also eligible)

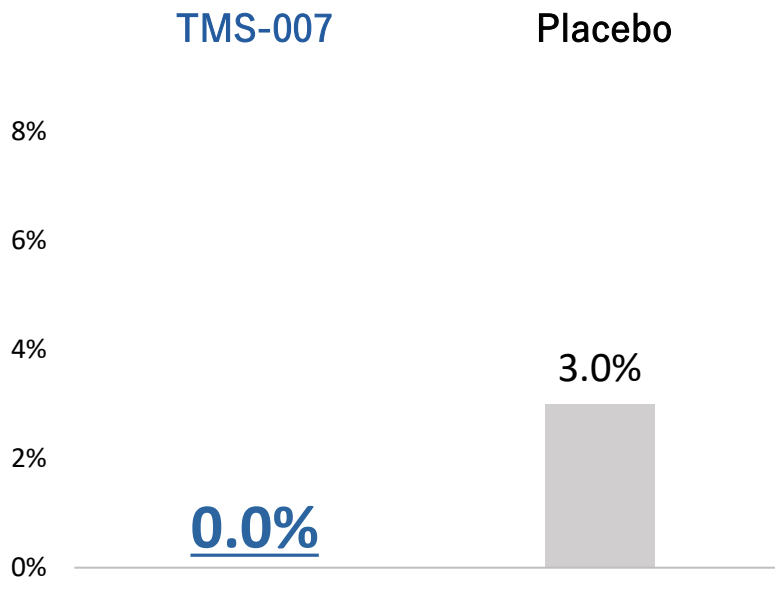
1. This table was created by the Company based on information registered by CORXEL on ClinicalTrials.gov (https://clinicaltrials.gov/study/NCT06990867?cond=Stroke%20Acute&term=JX10&rank=1) and information registered by the Company on jRCT (https://jrct.mhlw.go.jp/latest-detail/jRCT2021250014).

TMS-007：Phase 2a Clinical Study Result Achieved a Safety Profile

In terms of safety, the biggest concern of t-PA was the incidence rate [1] of symptomatic Intracranial Hemorrhage (sICH). The Phase 2a TMS-007 study demonstrated a reduced risk of the incidence of sICH.

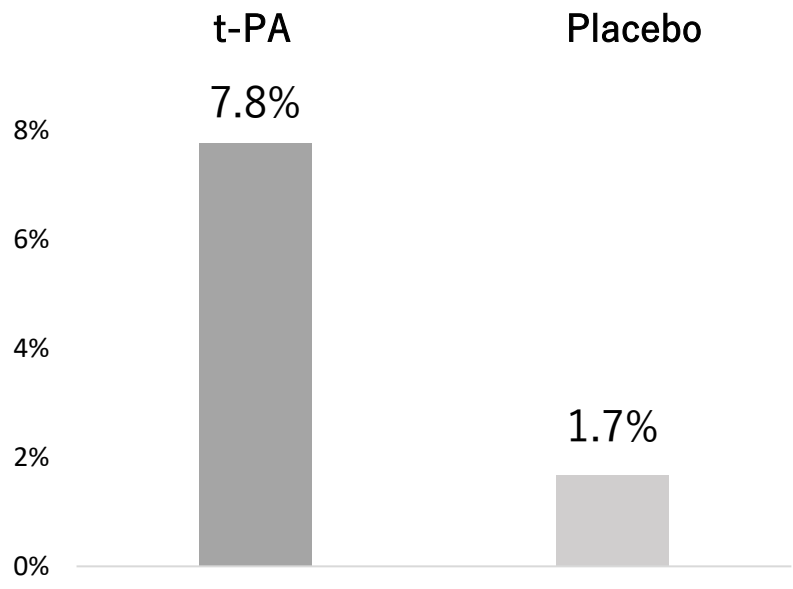
Incidence rate of sICH[1]

TMS-007 vs Placebo [2] — Phase 2a



	TMS-007	Placebo
N	52	38
Prehospital time	9.5hr (Average)	9.3hr (Average)

t-PA vs Placebo [3] — Meta-analysis



	t-PA	Placebo
N	3,384	3,330
Prehospital time	Within 6hr	

1. The data comparisons below are not based on head-to-head clinical studies of TMS-007 versus t-PA. N=52Financial Results and Business Update
2. Wardlaw et al. (2012), “Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated for TMS-007, N=3,384 for t-PA
3. Biogen, Investor Day Material (September 21, 2021), Q4 and Full Year 2021: systematic review and meta-analysis”

TMS-007: Development Status of Other Companies' Stroke Drug Candidates[1-7]

- Apart from the approved drug t-PA, TMS-007 is the only candidate to have achieved statistical significance for "mRS score 0–1 outcome ratio."

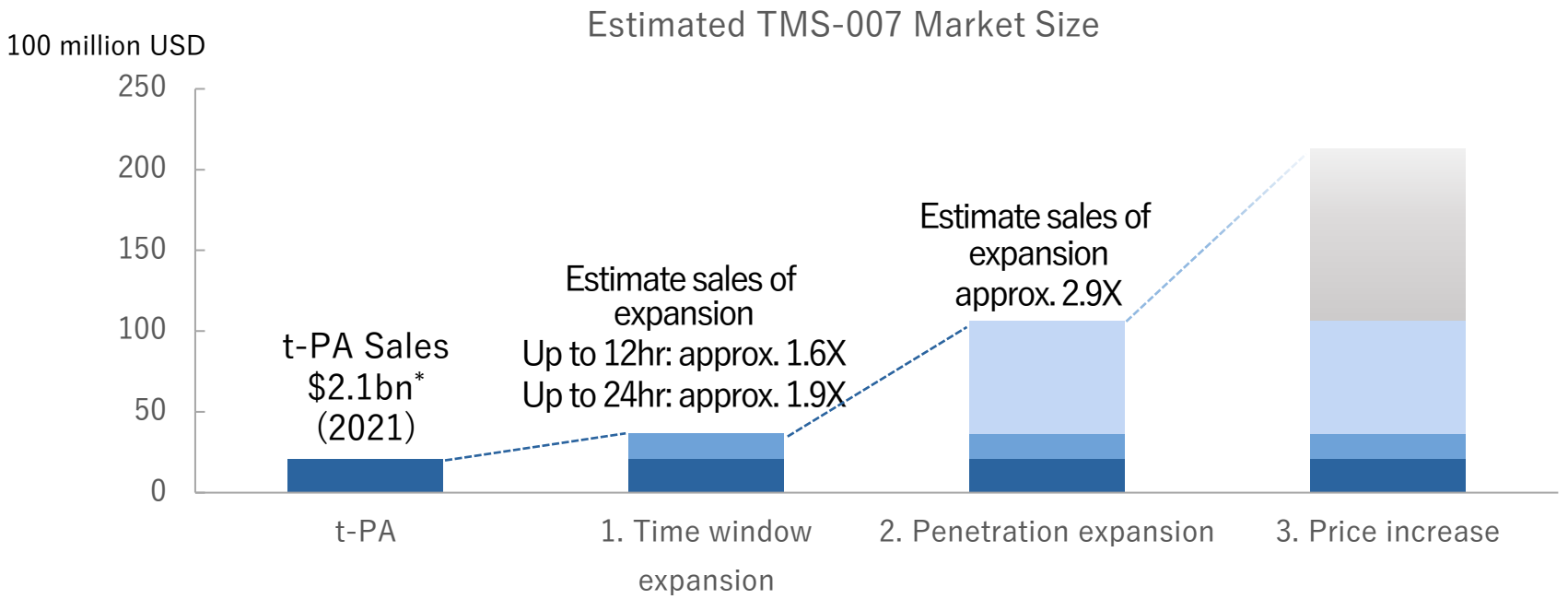
* In clinical trials for acute ischemic stroke (AIS), the proportion of patients with an mRS (modified Rankin Scale) score of 0–1 at Day 90 is considered the gold-standard endpoint.

Company	Product Name	Mechanism of Action	Modality	Development Status	Partner
Corxel / TMS	**JX10/TMS-007**	**Thrombolysis Anti-inflammatory effect Antioxidant effect**	**Small molecule**	**Phase 2/3**	**-**
Genentech	Activase, Actilyse, etc.	Thrombolysis	Protein (t-PA)	Approved	Boehringer Ingelheim, etc.
Genentech	TNKase®	Thrombolysis	Protein (t-PA)	Approved	Boehringer Ingelheim
Pharmazz, Inc.	Sovateltide (PMZ-1620)	Increases blood flow Inhibits cell death Neurorepair	Peptide	Phase 3 (Approved in India)	Sun Pharmaceutical
NoNO	Nerinetide (NA-1)	Inhibits cell death Anti-inflammatory effect	Peptide	Phase 3	-
Healios	Multistem	Anti-inflammatory effect	Cell therapy	Phase 3	-
DiaMedica Therapeutics	DM199	Anti-inflammatory effect	Protein	Phase 2/3	Fosun Pharma
Shionogi & Co., Ltd.	Redasemtide (S-005151)	Regenerative induction Anti-inflammatory effect	Peptide	Phase 2b	StemRIM
Lumosa Therapeutics	Oldatrotide (LT3001)	Thrombolysis Antioxidant effect	Peptide + small molecule	Phase 2	Shanghai Pharmaceuticals
Jiangsu Hengrui	HRS-7450	Thrombolysis Anti-inflammatory effect Antioxidant effect	Small molecule	Phase2	-

1. Polta et al. (2022), "Tenecteplase vs. alteplase for acute ischemic stroke: a systematic review"
2. Company websites
3. Hill et al. (2020), "Efficacy and safety of nerinetide for the treatment of acute ischaemic stroke (ESCAPE NA1): a multicentre, double blind, randomised controlled trial"
4. DiaMedica press release (April 17, 2024)
5. Pharmazz, Inc. company introduction (March 2024)
6. Shionogi & Co., Ltd. press release (April 10, 2023)
7. Lumosa Therapeutics press release (February 2, 2024)

Potential of TMS-007：Estimated Market Size

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



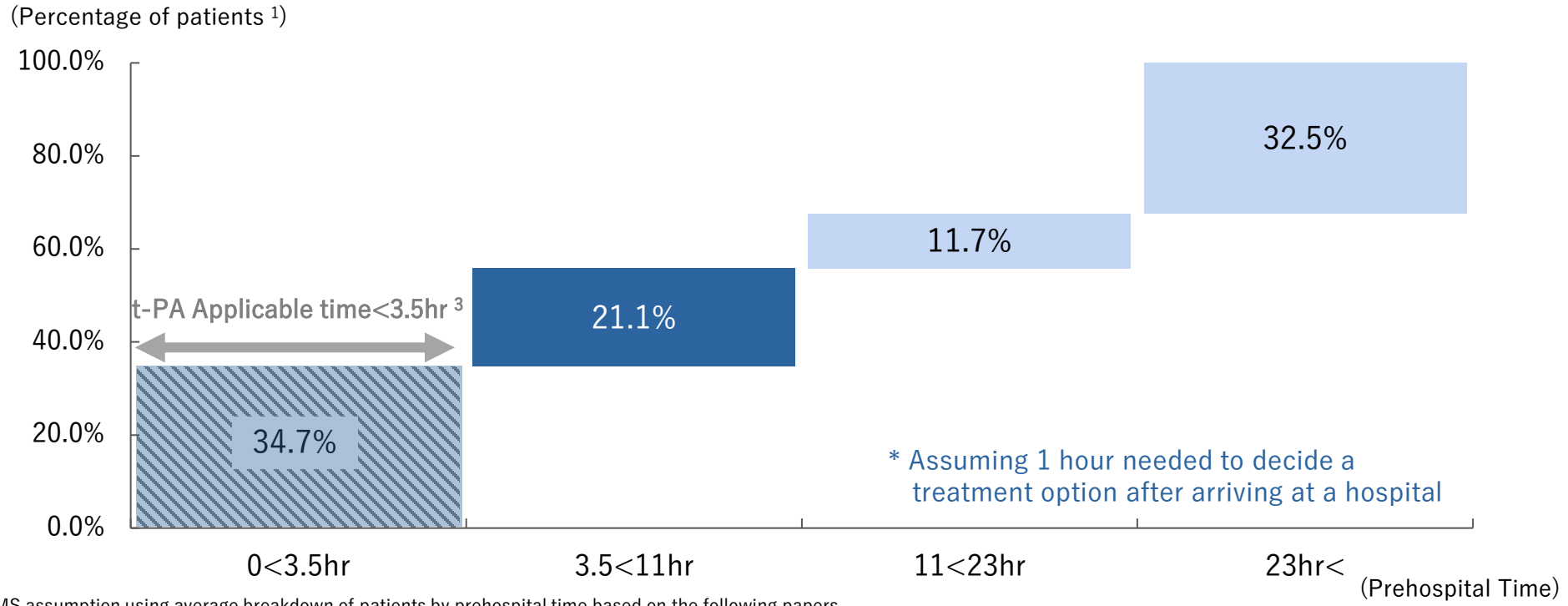
1. Novel thrombolytic with the potential to be first line treatment for AIS
   - Possibility to expand time window after onset (12hr or 24hr)
   - Possibility to expand penetration due to excellent safety
2. Higher pricing can be expected if higher efficacy and safety than t-PA are achieved

＊ 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 in accuracy of statistical data and publications.

Potential of TMS-007：Expanding Time Window after Onset

Relationship between Prehospital Time and treatment [1]

- Number of patients able to be treated by 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]

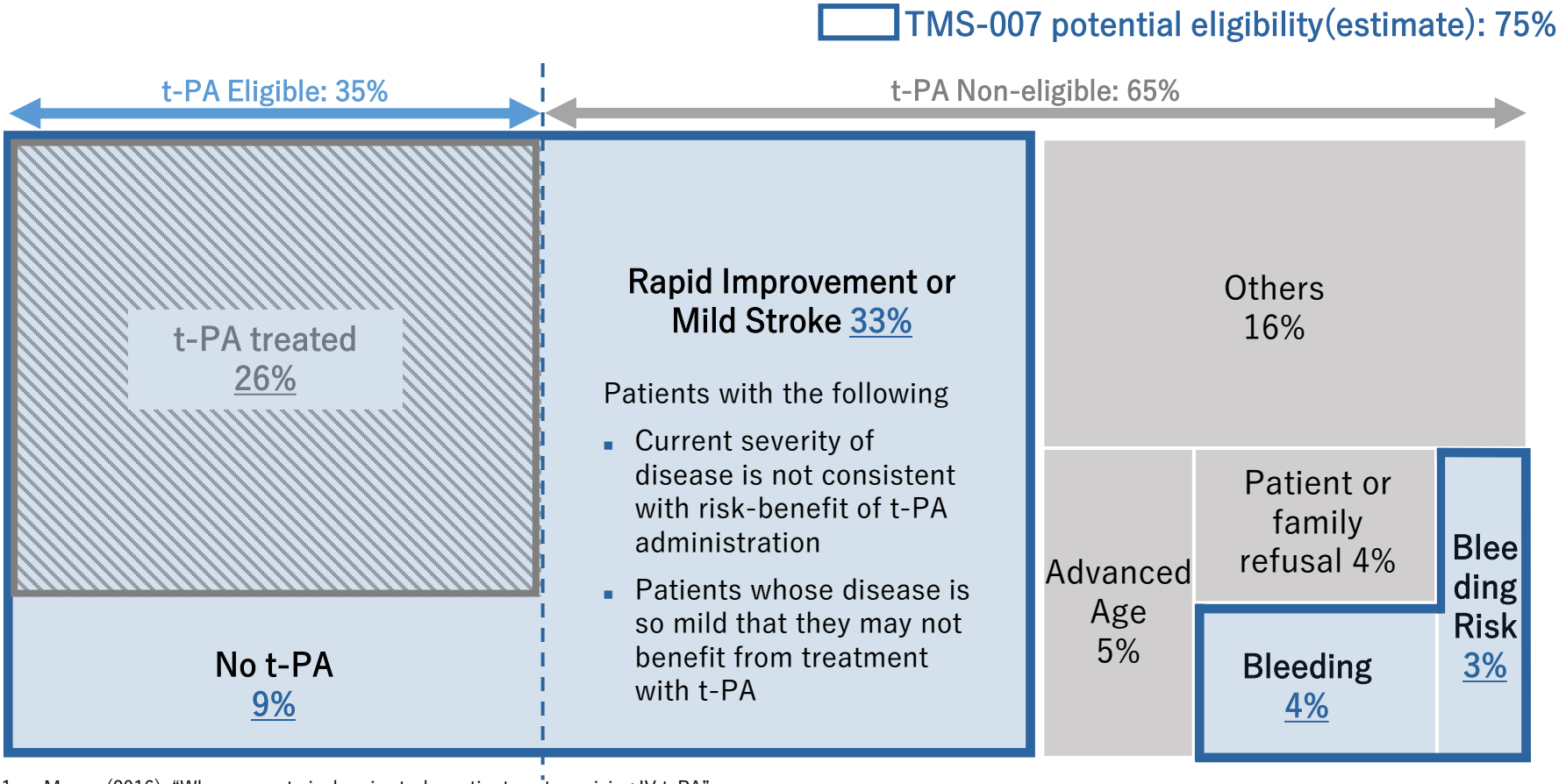


1. TMS assumption using average breakdown of patients by prehospital time based on the following papers. Please note that the company's estimate above is based on various assumptions and beliefs stated herein, including applicable time, disregard certain conditions such as the eligibility of the patients and are not confirmed 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 Time Window

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

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



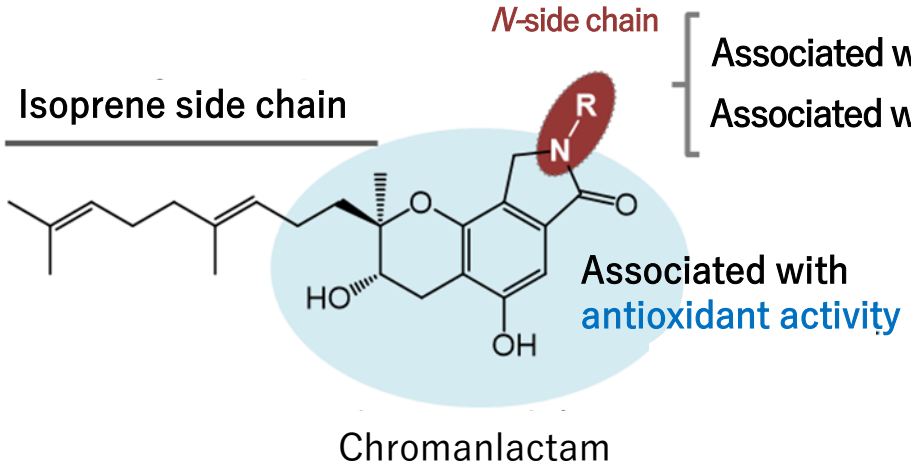
1. Messe (2016), “Why are acute ischemic stroke patients not receiving IV t-PA”

5. TMS-008

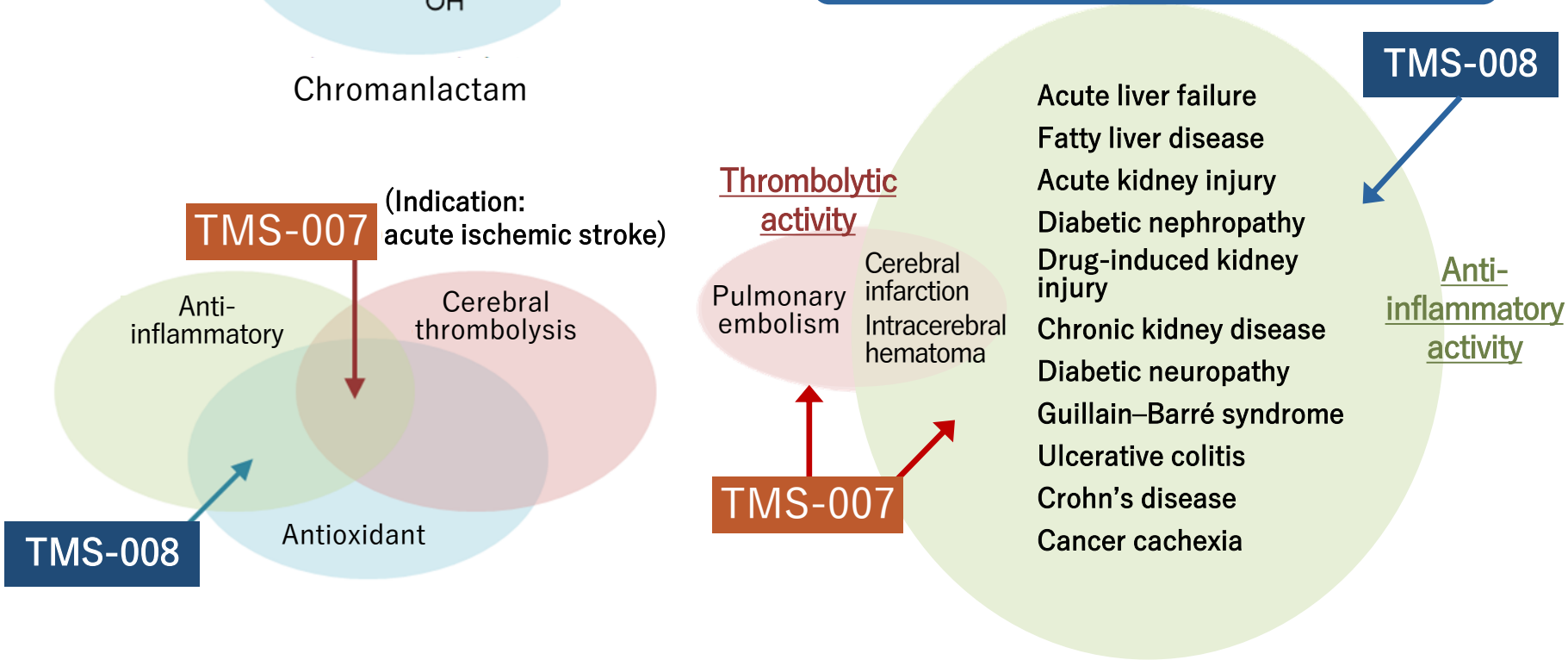
Acute Kidney Injury

TMS-008: An Anti-Inflammatory Compound with Potential for Broad Indications

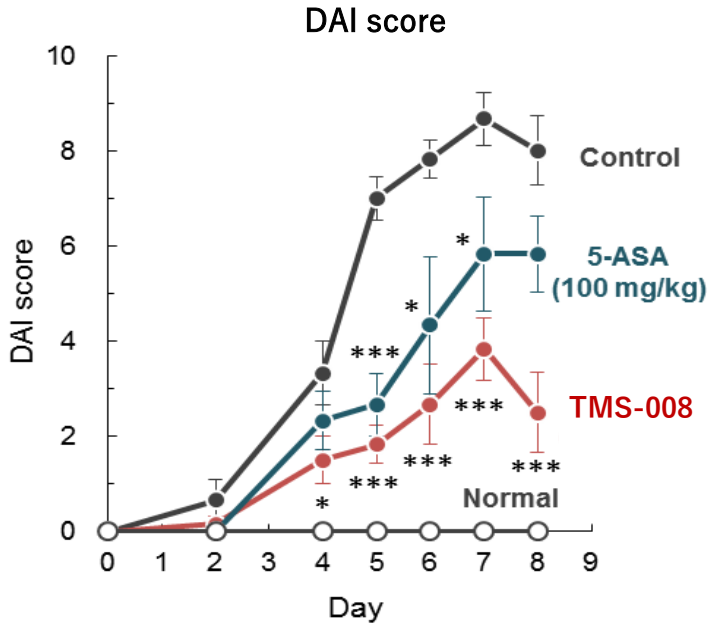
Exhibits both anti-inflammatory and antioxidant activities

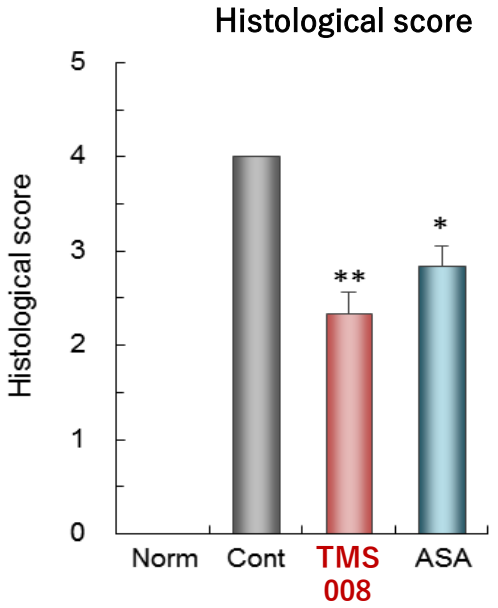


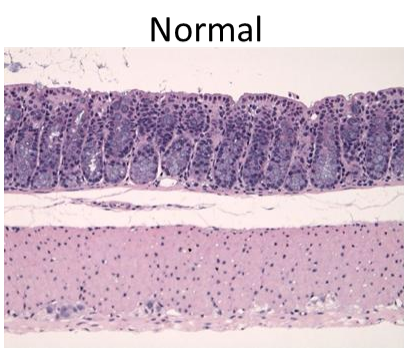
Effects of SMTP Demonstrated in Animal Models
(Disease/pathology models shown below)

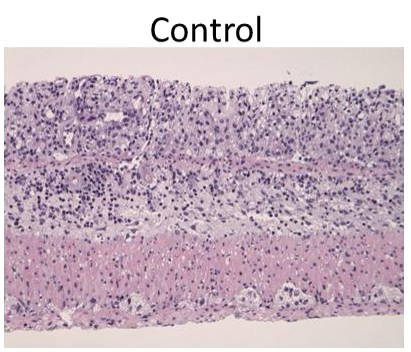


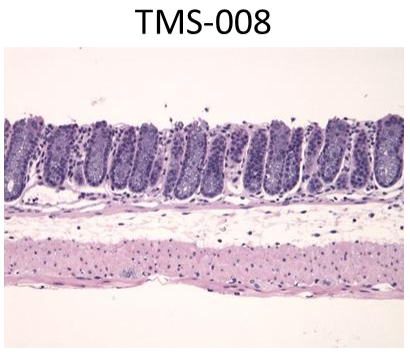
Crohn's disease model (TNBS model)





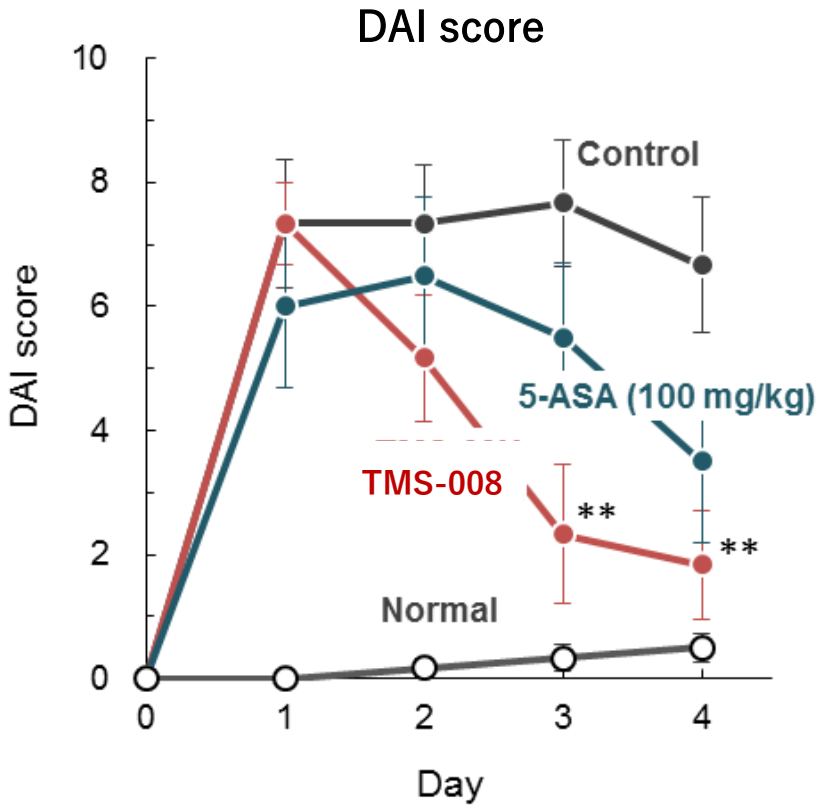


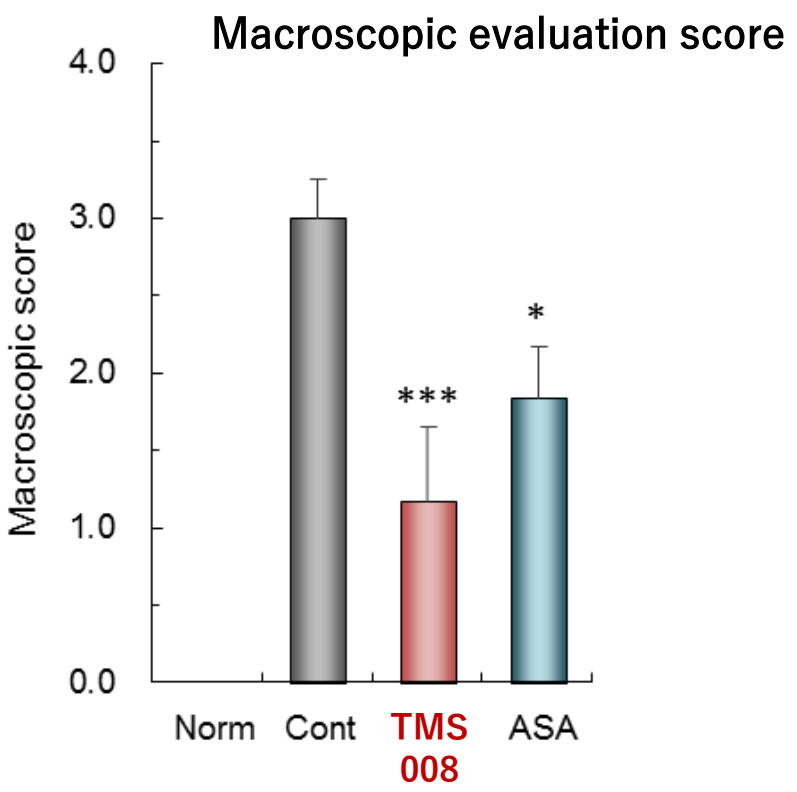




TMS-008: Anti-Inflammatory Activity with Potential for Broad Indications

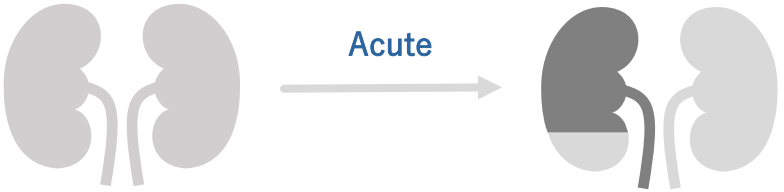
Ulcerative colitis model (DSS model)



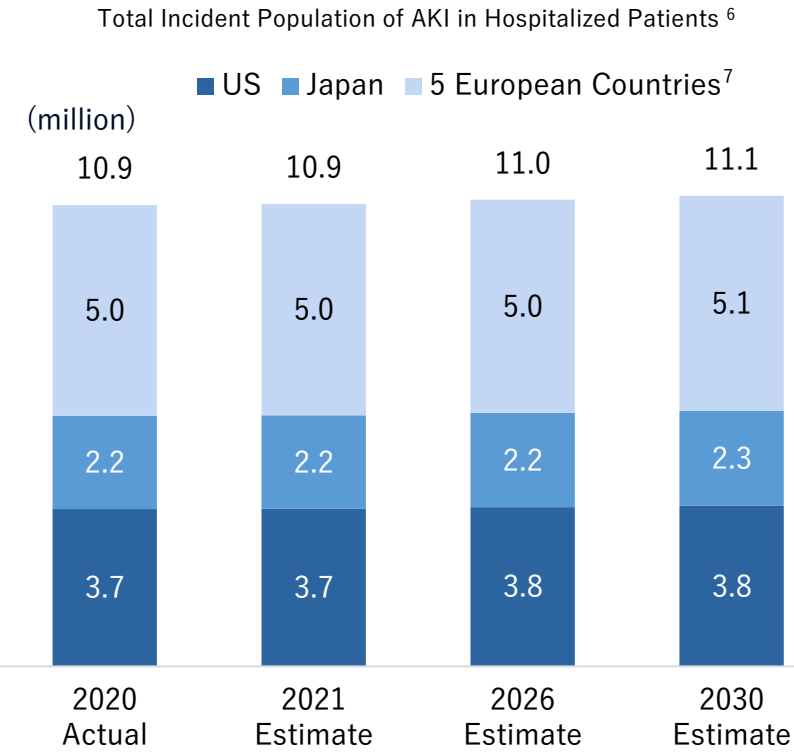


TMS-008：Target Disease_ Acute Kidney Injury (AKI) [1,2,3,4]

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

Indication	No protein leakage Appropriate toxin excretion  Acute Decreased renal function adversely affects heart and other organs
Overview	■ Acute Kidney Injury (AKI) is a rapid decline in renal function over a period of several hours to days ■ 20-25% mortality rate in hospitalized AKI patients ■ Caused by various factors including cardiopulmonary bypass and nephrotoxicity ■ AKI causes chronic kidney disease (CKD) and end-stage renal disease (ESRD)
Number of patients	■ 5 European countries: ~5,080,000 at a maximum ■ United States: ~3,800,000 at a maximum ■ Japan: ~2,300,000 at a maximum (Patients assumptions for year 2030 as of 2020)
Treatment method	■ No approved therapeutic drug [5]

Patient population of AKI is projected to reach **11.1mn** by 2030



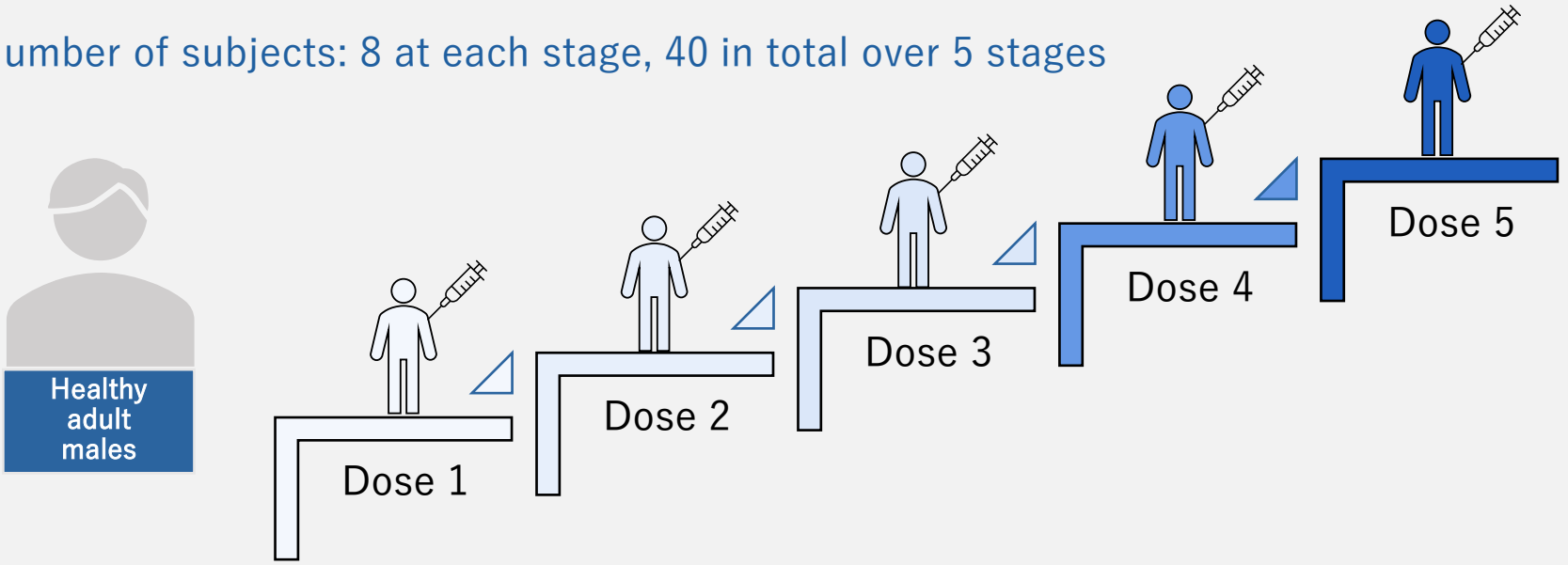
1. Nature Reviews Nephrology volume 16, pages747–764 (2020)
2. Adv Chronic Kidney Dis. 2017;24(4):194-204
3. Nephron. 2017 ; 137(4):297–301
4. Delveinsight, “Acute Kidney Injury - Market Insights, Epidemiology, and Market Forecast—2030”
5. Perioperative renal protection, Current Opinion in Critical Care 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 indicates Germany, France, Italy, Spain, and the UK

TMS-0008：Overview of Phase 1 Clinical Trial

Phase 1 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
- ◆ Design ：Randomized, placebo-controlled, double-blind, dose-escalation, single-dose study
- ◆ Results ：**Safety and tolerability observed**

Number of subjects: 8 at each stage, 40 in total over 5 stages



A single dose of TMS-008 or the placebo is given at every dose stage. The dose is increased in stages while confirming pharmacokinetics and safety.

6. JX09

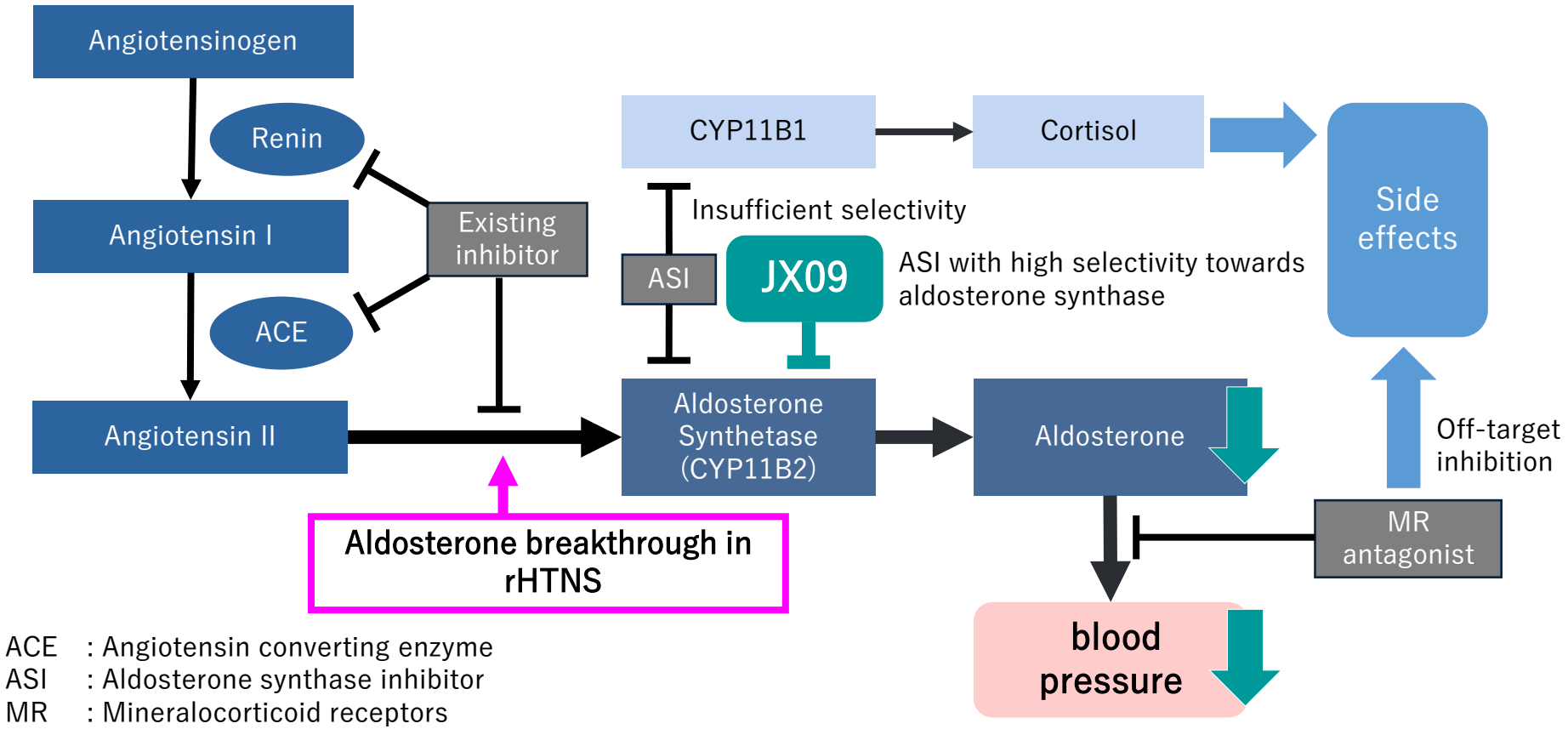
Resistant or uncontrolled hypertension

A potential "best-in-class" therapeutic for "resistant/uncontrolled hypertension" (rHTN) from COREXL

- 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[1]
- 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. JX-09 is highly selective and has potential to be best-in-class.
  - JX09 has demonstrated > 300-fold or more selectivity for CYP11B2 over CYP11B1 (*in vitro*), suggesting selectivity higher than baxdrostat (<100 fold or less) [2]
  - JX09 achieved >90% or more aldosterone lowering with no increase in CYP11B1 precursor steroids (*in vivo*, non-human primates) [2]
- The Phase 1 clinical trial is currently underway in Australia （CORXEL）

1. Dudenbostel et al (2017): Resistant hypertension (rHTN) is relatively common with an estimated prevalence of 10-20% of treated hypertensive patients
2. 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)[1] more selectively than the structurally similar CYP11B1

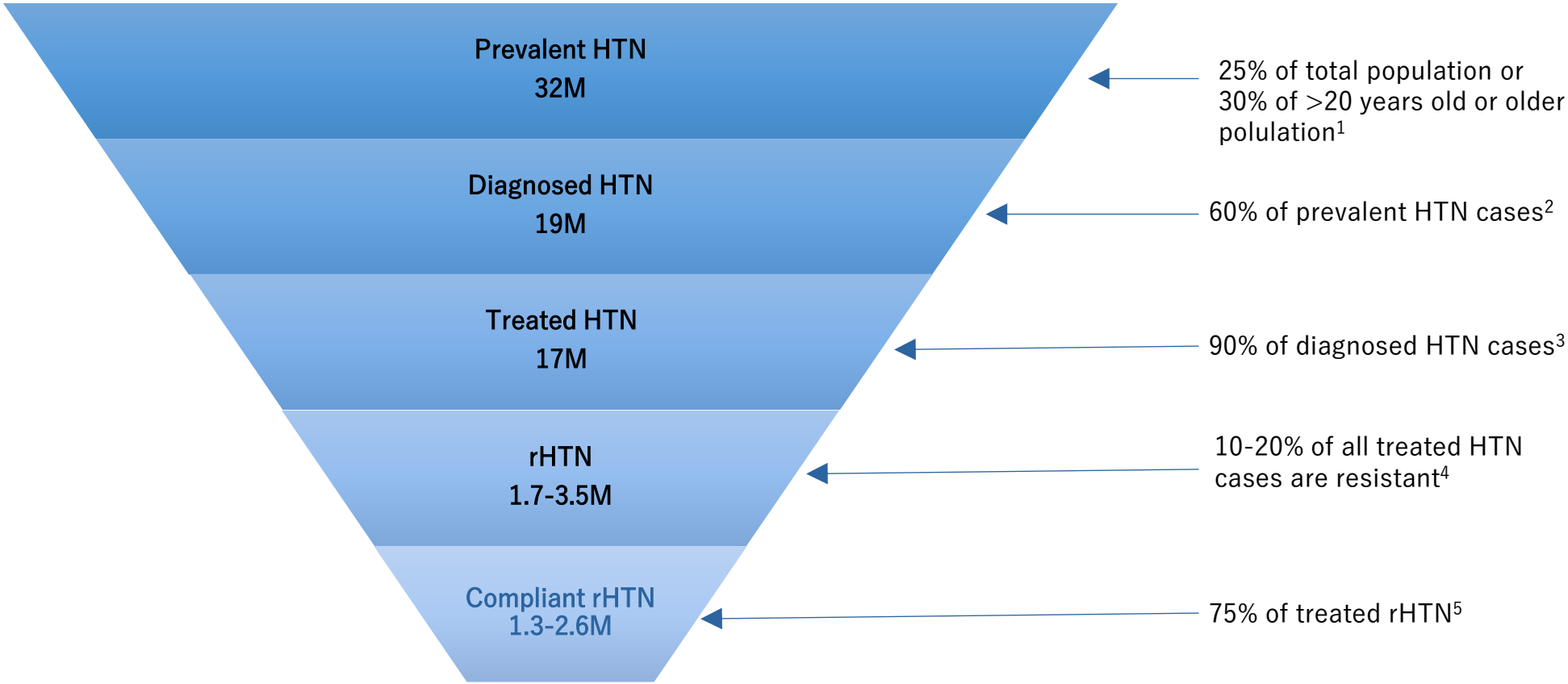


Position of aldosterone synthesis inhibitors among hypertension drugs

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



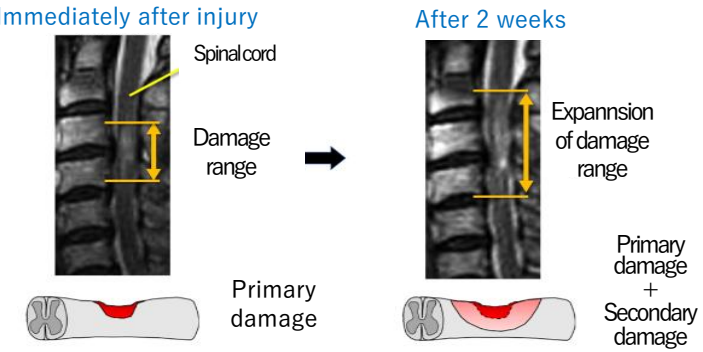
1：Estimated with data from Health Service Bureau, MHLW "National Health and Nutrition Survey 2019“: https://www.mhlw.go.jp/english/database/compendia.html
2：Saito et al. (2015): We find that there are much higher rates of undiagnosed hypertension in Japan (44.3%) than in the U.S. (11.9%)
3：Used the same treatment rate as in China, as per Zhang (2022): diagnosed but untreated ~10% in 2018
4：Dudenbostel et al (2017): Resistant hypertension (RHTN) is relatively common with an estimated prevalence of 10-20% of treated hypertensive patients
5：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).

7. TMS-010

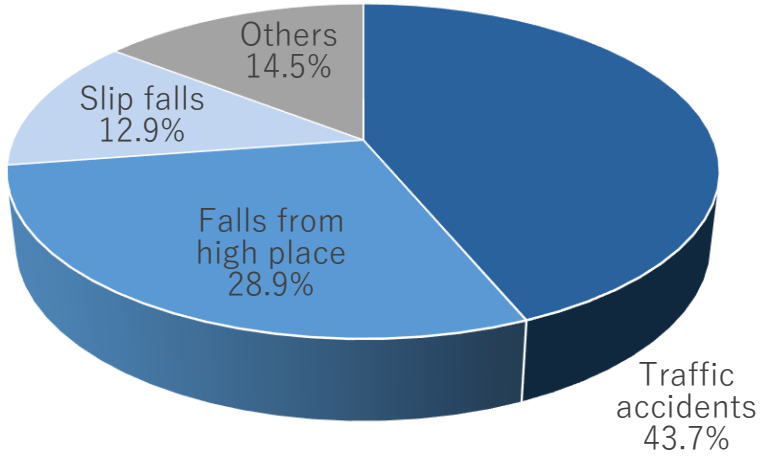
Spinal Cord Injury

TMS-010：Target Disease_ Spinal Cord Injury (SCI)

Novel program for an indication for which no approved drug exists

Symptom	When the spine is severed or seriously dislocated due to a strong external force, spinal cord inside the spine is also damaged, which could lead to serious disabilities including motor paralysis and sensory paralysis.[1]
Outline	Range of damage expands for approximately 2 weeks after SCI[3] (secondary damage). TMS-010 is expected to reduce symptoms caused by SCI by controlling secondary damage. 
Number of patients	■ 5,000 patients per year in Japan[4] ■ 180,000 patients per year worldwide[5]
Treatment	■ There is no approved therapeutic drug ■ Steroid therapy, current standard treatment, is not considered to be sufficient.

Causes of Spinal Cord Injury in Japan[2]



Most common causes of spinal cord injuries in Japan are traffic accidents, falls from high places, and slip falls. Injuries due to slip falls among the elderly are increasing in Japan where the populations is aging.

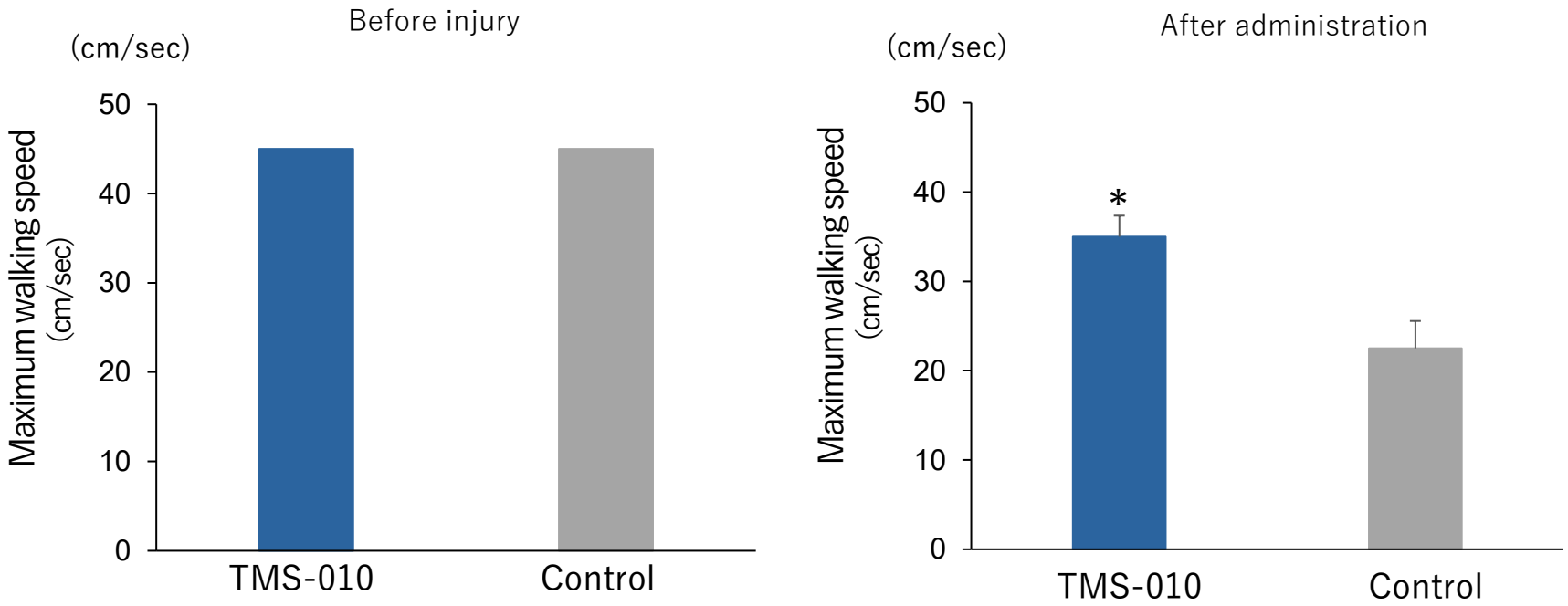
1,2. Neurospinal Society of Japan website (https://www.nsj-official.jp/general/diseasename/08_damage/sekizui.html)
3. Ahuja CS, et al. Traumatic spinal cord injury. Nat Rev Dis Primers. 27(3), 17018 (2017)
4. Miyakoshi N, et al. A nationwide survey on the incidence and characteristics of traumatic spinal cord injury in Japan in 2018. Spinal Cord 59(6), 626-634 (2021)
5. 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：Target Disease_ 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: high cervical vertebrae spinal cord injury rat model (Hokkaido Univ.)



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

8. Expansion of Pipeline

Pipeline Expansion Efforts Both Internally and Externally

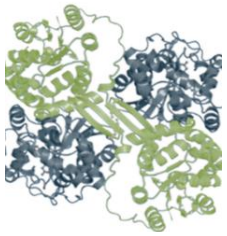
Pursue internal and external paths for pipeline expansion, leveraging knowledge and experience cultivated through SMTP compounds development

TMS Co.,LTD

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 peripheral field



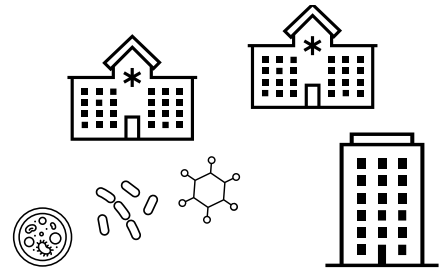
Human sEH

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

Program acquisition

Collaborative research

External projects (Academia and others)



Deploy

Licensing, etc.

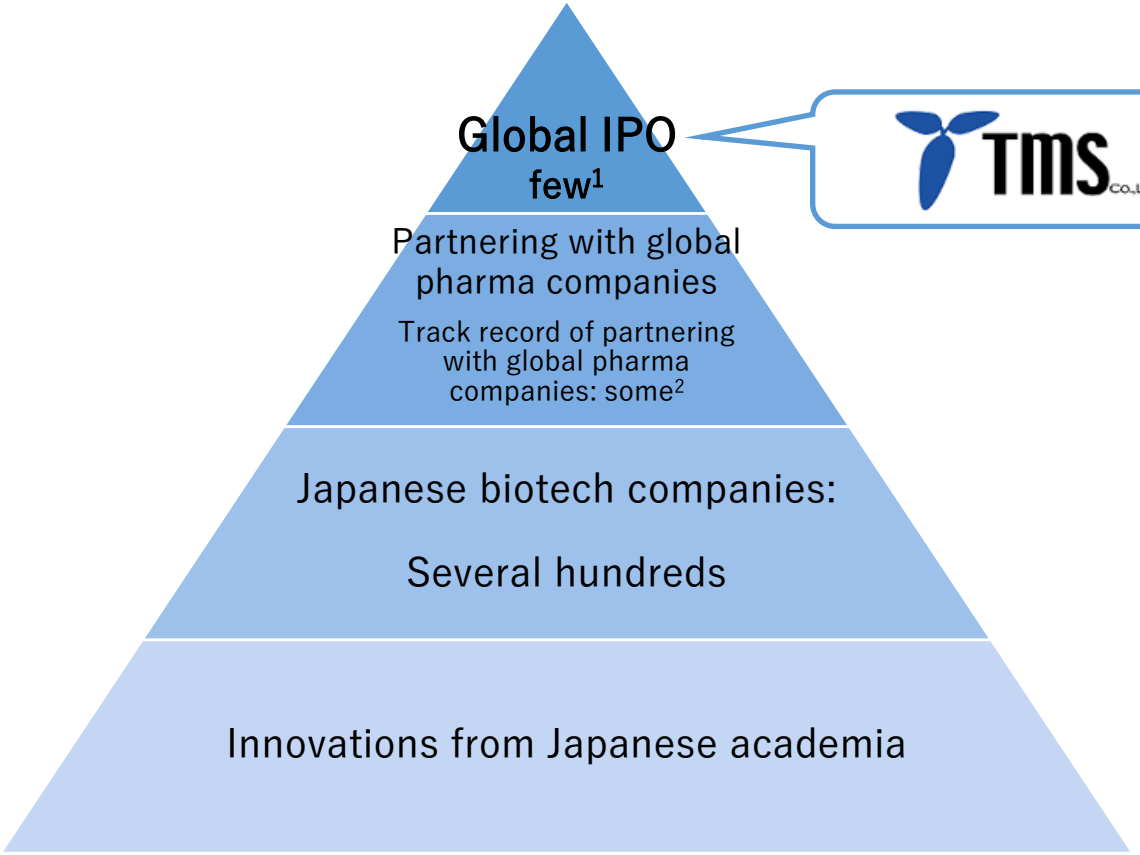
Global Market

* Global market is >10 times or larger than Japanese market

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



Global innovations from Japan

- Statin
- Opdivo
- Actemra
- Fingolimod
- Ivermectin
- Crizotinib etc.

1, As of the end of October 2024, only one other Japanese biotech venture besides our company has conducted a global IPO (according to our research).
2. According to our research (as of the end of February 2024)

9. Appendix

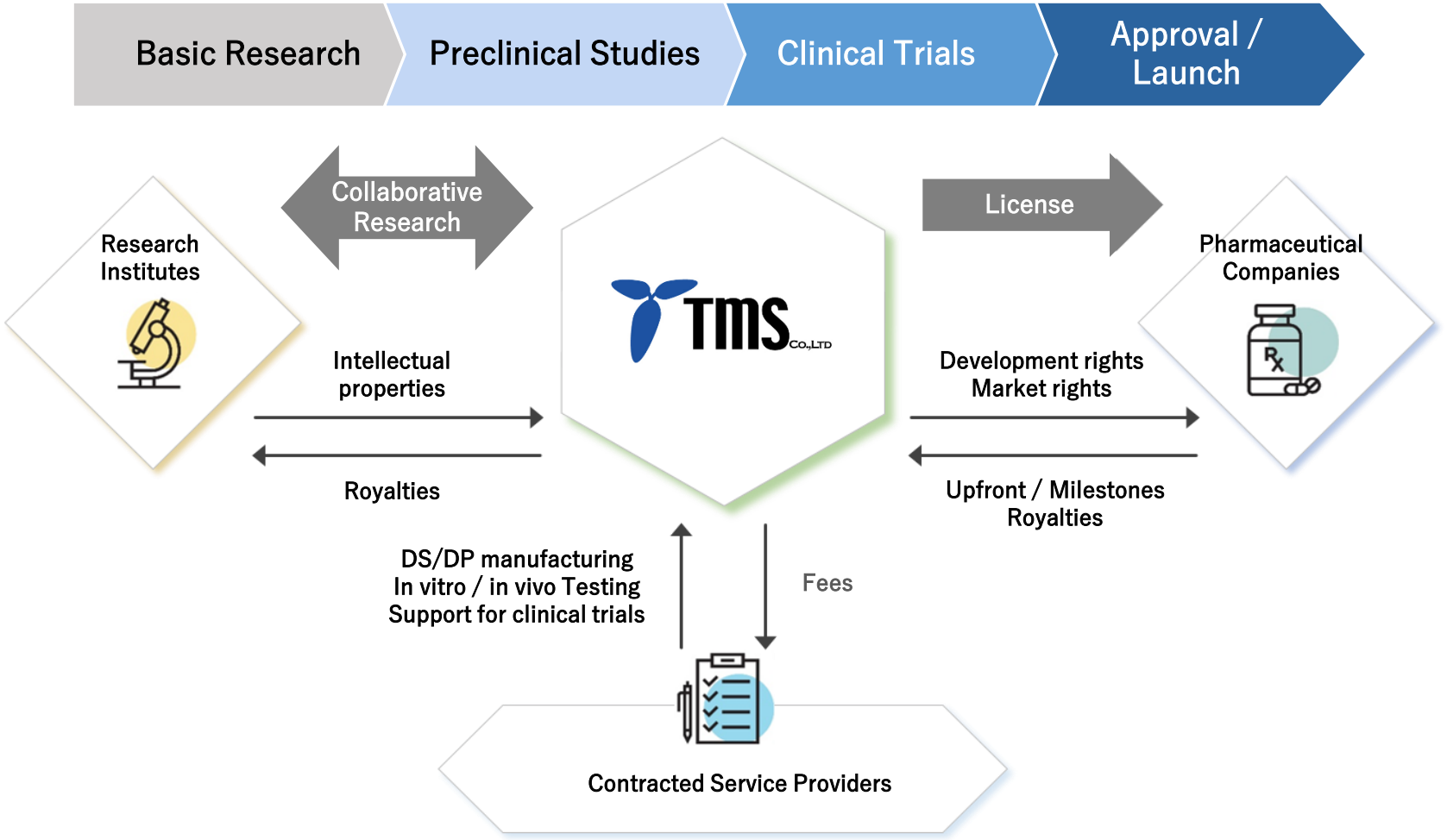
Corporate Profile & History

Name	TMS Co., Ltd. (Stock Code: 4891)
Established	February 17, 2005 (Venture company originating from Tokyo University of Agriculture and Technology)
Fiscal Year End	December *
Representative Directors	Takuro Wakabayashi Chief Executive Officer
Address	Headquarters: 11th floor,1-9 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 employees	18 (as of December 31, 2025) *Excluding temporay workers

* Note: From FY2025, the fiscal year-end has been changed to December.

	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 in Japan
Oct. 2015	Completed Phase I clinical trial of TMS-007 in Japan
Nov. 2017	Started phase IIa clinical trial of TMS-007 for ischemic stroke patients in Japan
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 in Japan
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
Jun. 2025	Completed Phase 1 clinical trial of TMS-008 in Japan

Business Model



- The basic model is that TMS Co., Ltd. conduct drug development from the seed exploration to the early clinical stage in collaboration with research institutions and contracted service providers and partner with domestic and foreign pharmaceutical companies for commercialization.
- Depending on the disease area, TMS Co., Ltd. may execute commercialization 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

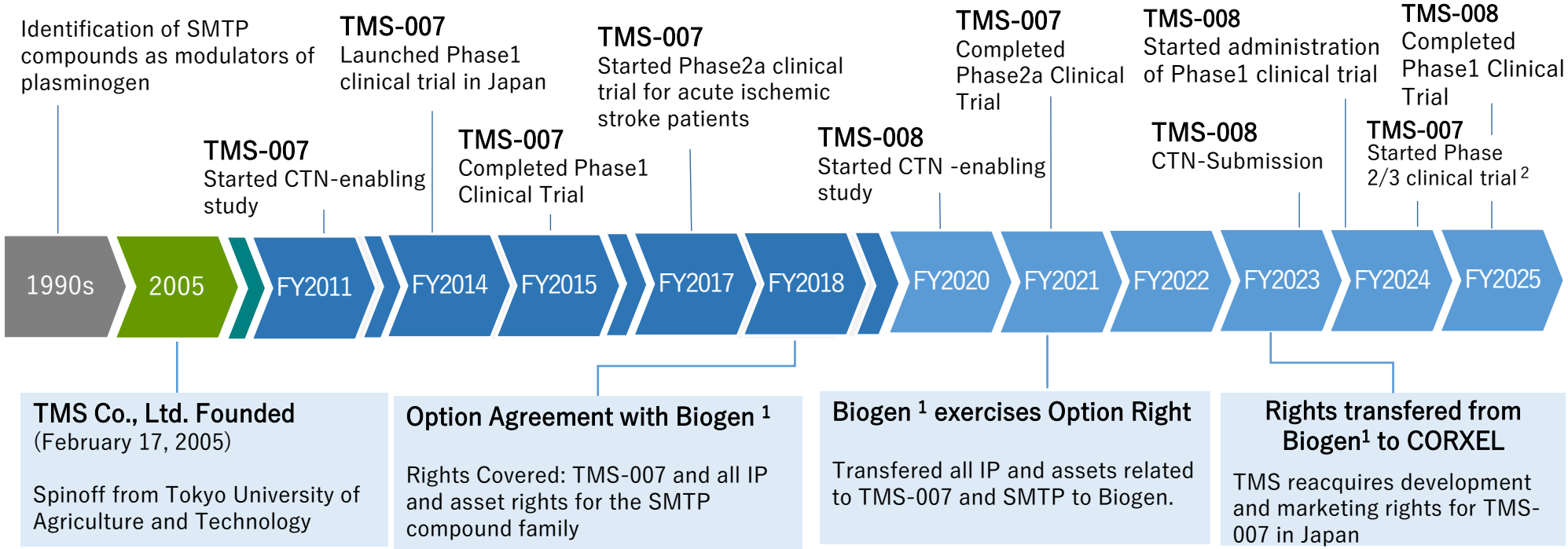
Ph.D.
Founder
Chief Scientific Officer

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

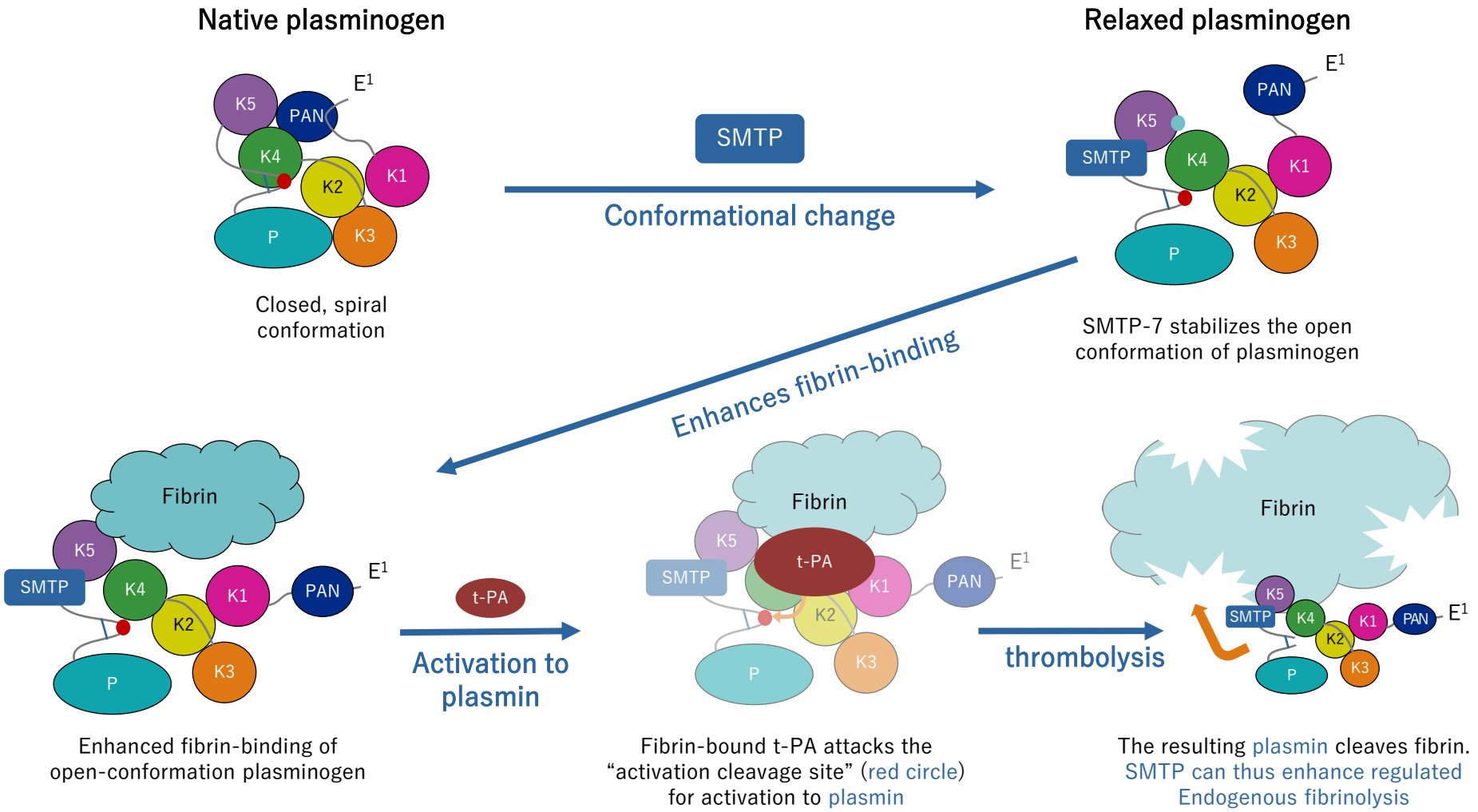
Invention of the hyperlipidemia drug statin (HMG-CoA reductase inhibitor), one of the best-selling category of drugs in history.



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 plasminogen to fibrin and blood clots[1]



1. 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