TMS Co.,LTD

TSE Growth: 4891

First Half FY2025 Financial Results Presentation Material

（Fiscal Year Ending 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 H1 FY2025 (Fiscal Year Ending 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

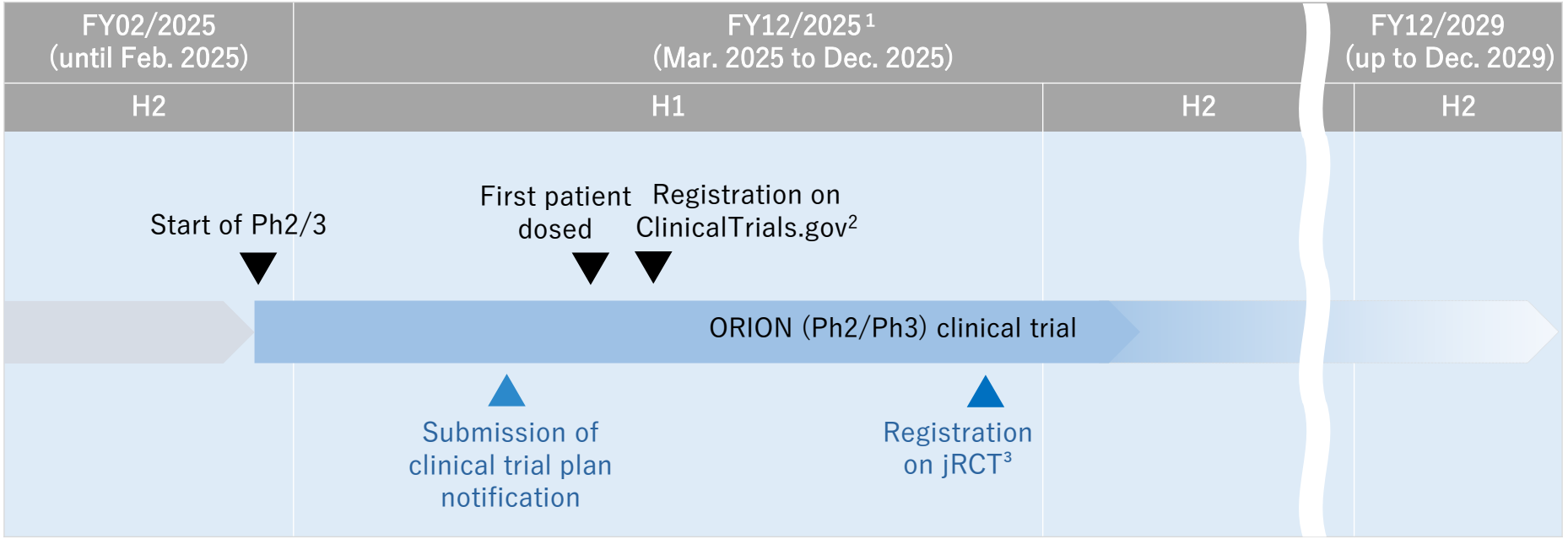
Highlights

1 Initiation of global clinical trial ORION (Ph2/Ph3) for TMS-007 (JX10)

- First patient dosed by CORXEL on May 16, 2025.
- Preparations for study initiation in Japan are underway.

[Development Progress]

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



1. From FY2025, the fiscal year-end has been changed from February to December.
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 on the Japan clinical trial database)

Highlights

TMS-007: Global Clinical Trial “ORION” (Ph2/Ph3)[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 (Ph2)	Part 2 (Ph3)
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.

Highlights

Comparison of Japan Ph2a and Global Clinical Trial ORION (Ph2/Ph3)[1]

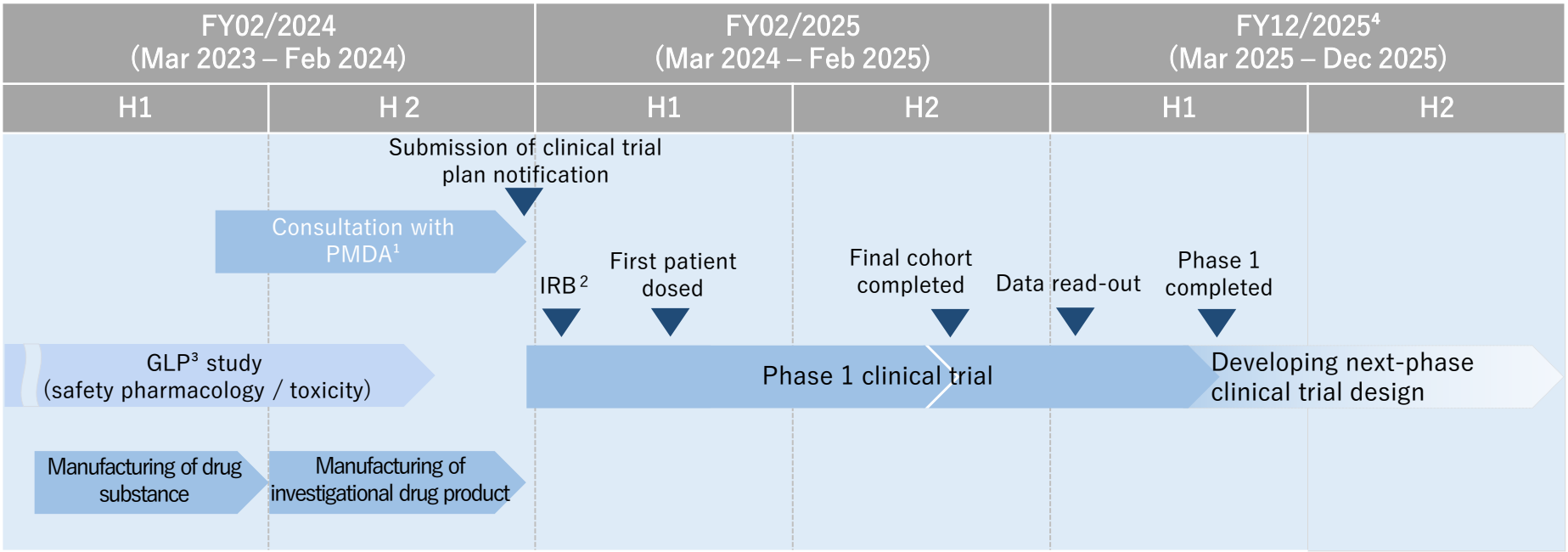
		Ph2a	ORION (Ph2/Ph3)
Basic Design		Single stage	Two stages (Part 1, Part 2)
Number of Patients		90	740 (planned)
Primary Efficacy Endpoint		Proportion of patients with mRS 0–1	Proportion of patients with mRS 0–1
Inclusion Criteria	Age	Male: 20–88 years Female: 60–88 years	18-90 years
	Time Window	Within 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).

2 Completion of TMS-008 Phase 1 Clinical Trial

- Data read-out from the Phase 1 clinical trial in April 2025.
- Clinical Study Report (CSR) finalized in June 2025.
  ⇒ Favorable safety and tolerability demonstrated
- Developing trial design for the next phase.

[Development Progress]



1. PMDA: Pharmaceuticals and Medical Devices Agency
2. IRB: Institutional Review Board
3. GLP: Good Laboratory Practice
4. From FY2025, the fiscal year-end has been changed from February to December.

Highlights

3 Status of JX09

- A Phase 1 clinical trial is ongoing in Australia conducted by CORXEL.
- There are only four clinical-stage aldosterone synthase inhibitors (ASIs) for resistant/uncontrolled hypertension (rHTN) to our knowledge, including JX09 and the two drugs noted below.

The mechanism of action of JX09, aldosterone synthase inhibition, is attracting significant attention

- Lorundrostat (Mineralys Therapeutics) and Baxdrostat (AstraZeneca) are reported to have achieved positive Ph3 results in March and July this year, respectively.[1.2]
- Both programs targeted patients with resistant/uncontrolled hypertension (rHTN), defined as patients whose blood pressure remain uncontrolled despite treatment with two or more types of antihypertensive drugs.
- Compared with placebo, blood pressure reductions of approximately 8–10 mmHg were achieved.
- AstraZeneca expects peak annual sales of baxdrostat to exceed USD 5 billion.[3]
- Mineralys' share price has more than doubled, pushing its market capitalization close to USD 3 billion (as of September 17, 2025).

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

1. From Mineralys Press Release. https://ir.mineralystx.com/news-events/press-releases/detail/60/mineralys-therapeutics-announces-positive-topline-results
2. From 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. From Reuters News dated August 30, 2025. AstraZeneca to seek approval for blood pressure drug by year-end | Reuters

Topics

1 Appointment of New Director in Charge of Development

- Appointed Naohisa Yokota, M. Pharma as EVP, Development, who joined the Company in November 2024 as Senior Director. Mr. Yokota succeeded Noriaki Inamura, PhD.
- 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 (EFPIA).

2 TMS-007 (JX10) Paper Recognized as a “Top Viewed Article”

- A paper on the Phase 1 trial of TMS-007 (JX10), published in 2023 in the *British Journal of Clinical Pharmacology (BJCP)*, was awarded “Top Viewed Article” ranking as the top 10% of most-viewed papers in 2023.

3 Pathology Associates Initiates Analyst Coverage

- Coverage has been initiated by Dr. Dion Stefan Büchner of Patrology Associates Co., Ltd. (after the end of the second quarter).

Project Outcomes and Milestones

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

2. Summary of Financial Results for H1 of FY2025 *

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

H1 FY2025 Summay of Financial Results - Income Statement

Although expenses related to the TMS-007 ORION trial were recorded, ordinary loss and net loss remained generally in line with the same period of the previous year.

(million yen)

	FY2024 H1	FY2025 H1	Change	
			Amount	Percentage
Operating revenue	-	-	-	-
Operating expenses	452	471	19	+4.4%
R&D	314	289	(15)	-5.0%
SG&A	137	173	35	+25.8%
Operating profit (loss)	**(452)**	**(471)**	(19)	-
Non-operating expenses	-	13	13	-
Ordinary profit (loss)	**(451)**	**(484)**	**(32)**	-
Extraordinary losses	**25**	**2**	(23)	-91.1%
Net Income (loss)	**(477)**	**(487)**	**(9)**	-

Recording of expenses for the TMS-007 ORION trial began

Decline in impairment losses on fixed assets

Expected expenses for the Full Fiscal Year 2025*

(million yen)

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

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.

H1 FY2025 Summay of Financial Results - Cash Flows

Cash inflows from financing activities were due to fundraising.

As a result, cash and cash equivalents at the end of the period stood at 3.0 billion yen, an increase of 0.16 billion yen from the beginning of the period.

(million yen)

	FY2024 H1	FY2025 H1
Cash flows from operating activities	**(409)**	**(476)**
Profit(loss) before income taxes	(447)	(486)
Cash flows from investing activities	**(29)**	**(2)**
Cash flows from financing activities	**0**	**640**
Proceeds from issuance of shares	0	649
Net increase(decrease) in cash and cash equivalents	(437)	161
Cash and cash equivalents at beginning of period	3,446	2,922
Cash and cash equivalents at end of period	**3,008**	**3,084**

Due to fundraising

H1 FY2025 Financial Results Financial Results - Balance Sheet

Total assets increased compared to the previous fiscal year-end due to fundraising.

(million yen)

	FY2024-end	FY2025 H1-end	Change	
			Amount	Percentage
Current assets	3,029	3,118	89	+3.0%
Cash and deposits	2,922	3,084	161	+5.5%
Non-current assets	3	3	0	+0.0%
Total assets	**3,032**	**3,122**	**89**	**+3.0%**
Current liabilities	216	130	(86)	-40.0%
Total liabilities	**216**	**130**	**(86)**	**-40.0%**
Share acquisition rights	23	28	4	+19.6%
Net assets	**2,815**	**2,992**	**176**	**+6.3%**
Total liabilities and net assets	**3,032**	**3,122**	**89**	**+3.0%**

Increased resulting from fundraising

Due to a decrease in accounts payable-other from the amount recorded at the end of the previous fiscal year

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.
- Initiation of the global Phase 2/3 trial, ORION, led by our partner CORXEL.
- TMS owns development and marketing rights in Japan, and the rights to receive and royalties in the rest of the world (ex-Japan).

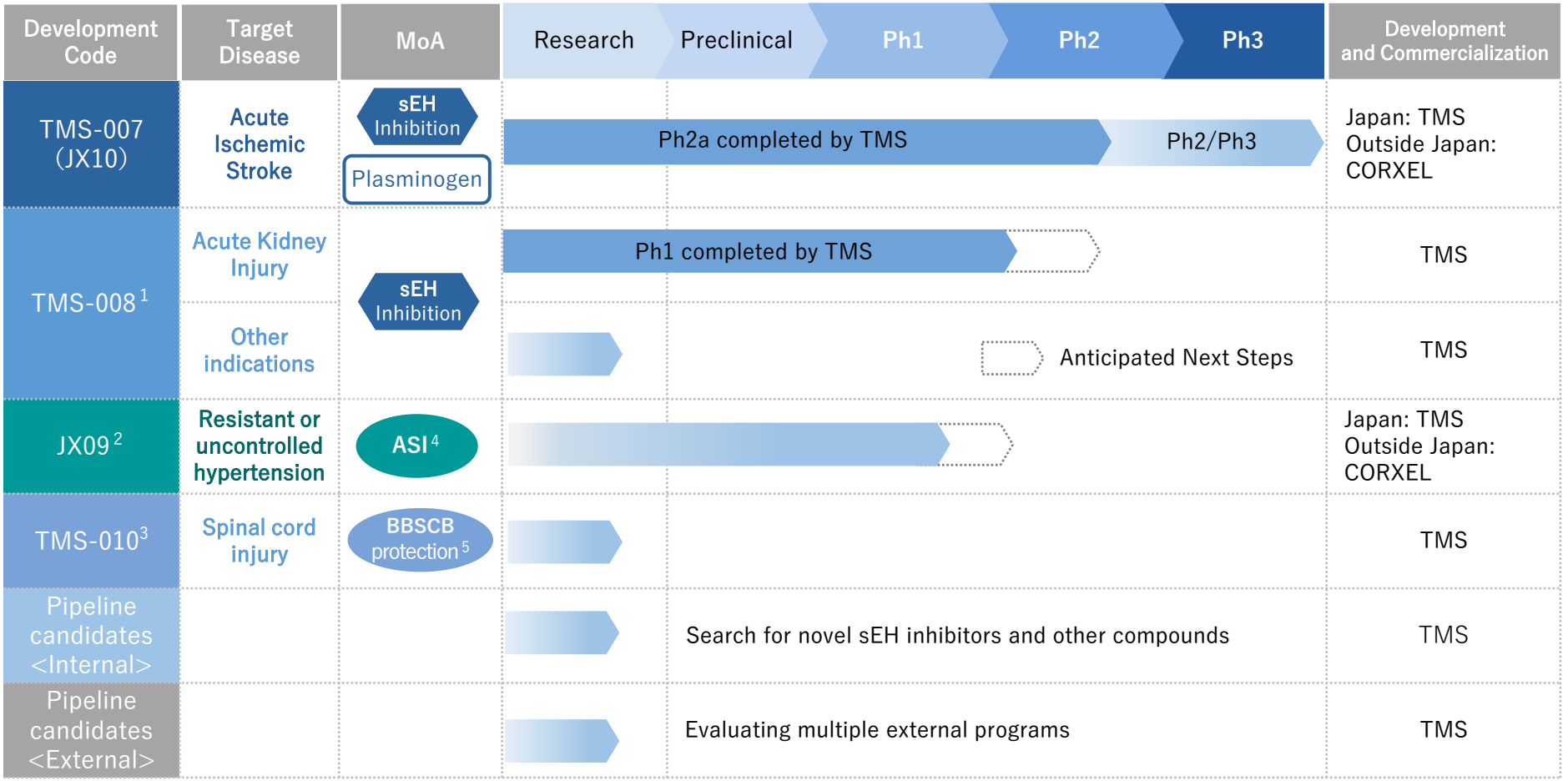
TMS-008 *(Acute kidney injury)*

- Important unmet medical needs for which no approved drug exists.
- Phase 1 trial in Japan completed in April 2025 (Favorable safety and tolerability demonstrated).
- TMS owns the rights to develop and market the product globally.

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 Pipeline



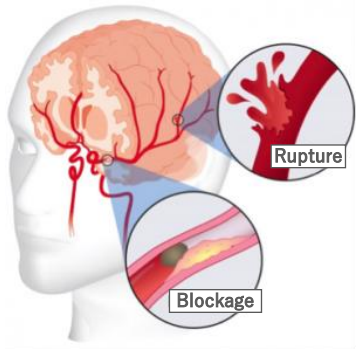
1. TMS-008 is currently under development by TMS under a free license from CORXEL.
2. Obtained free license for development and marketing rights in Japan from CORXEL (January 2024).
3. Obtained exclusive license for the candidate drug for spinal cord injury from Hokkaido University for the entire world,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

4. TMS-007

Potential Next Generation Acute Ischemic Stroke Treatment

Acute Ischemic Stroke - Important Unmet Medical Needs

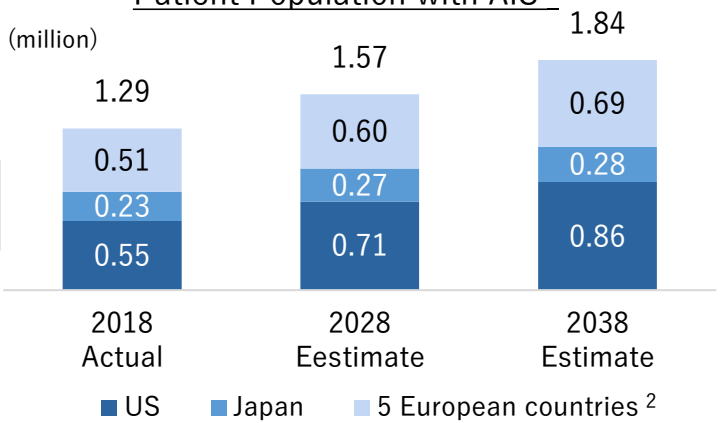
Acute Ischemic Stroke (AIS) Overview



- 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]

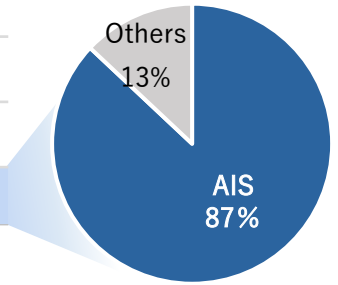


Important Unmet Medical Needs

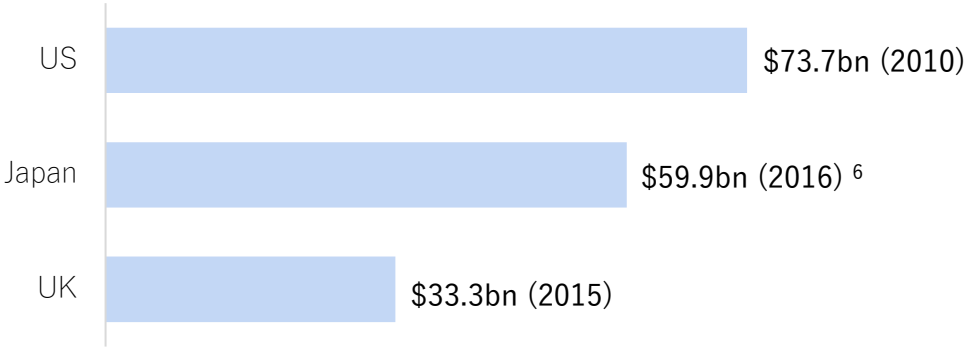
Cause of death in the US (2019) [3]

#	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]



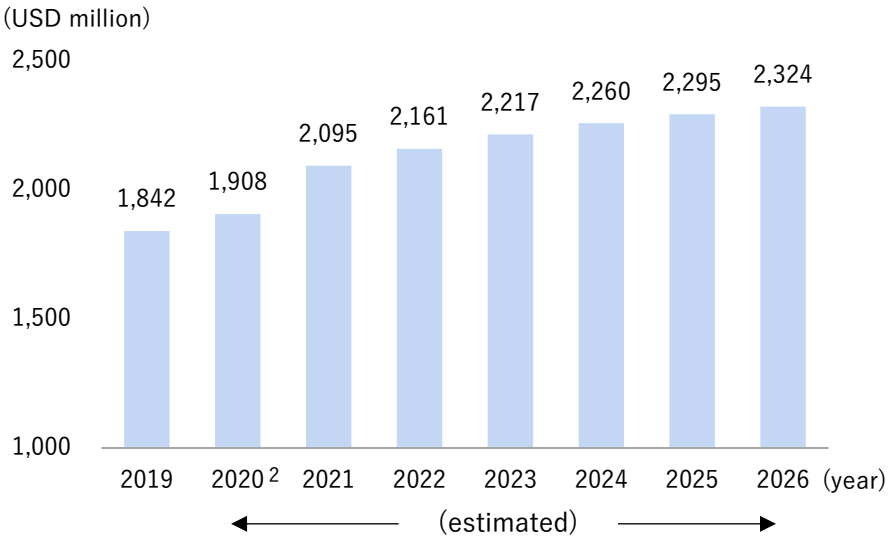
1. Datamonitor Healthcare, "Stroke Epidemiology", Ref Code:DMKC0201444, Published on 07 January 2019
2. 5 European countries are composed of five major countries: Germany, France, Italy, Spain, and United Kingdom
3. Centers for Disease Control and Prevention, "National Vital Statistics Reports volume 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]

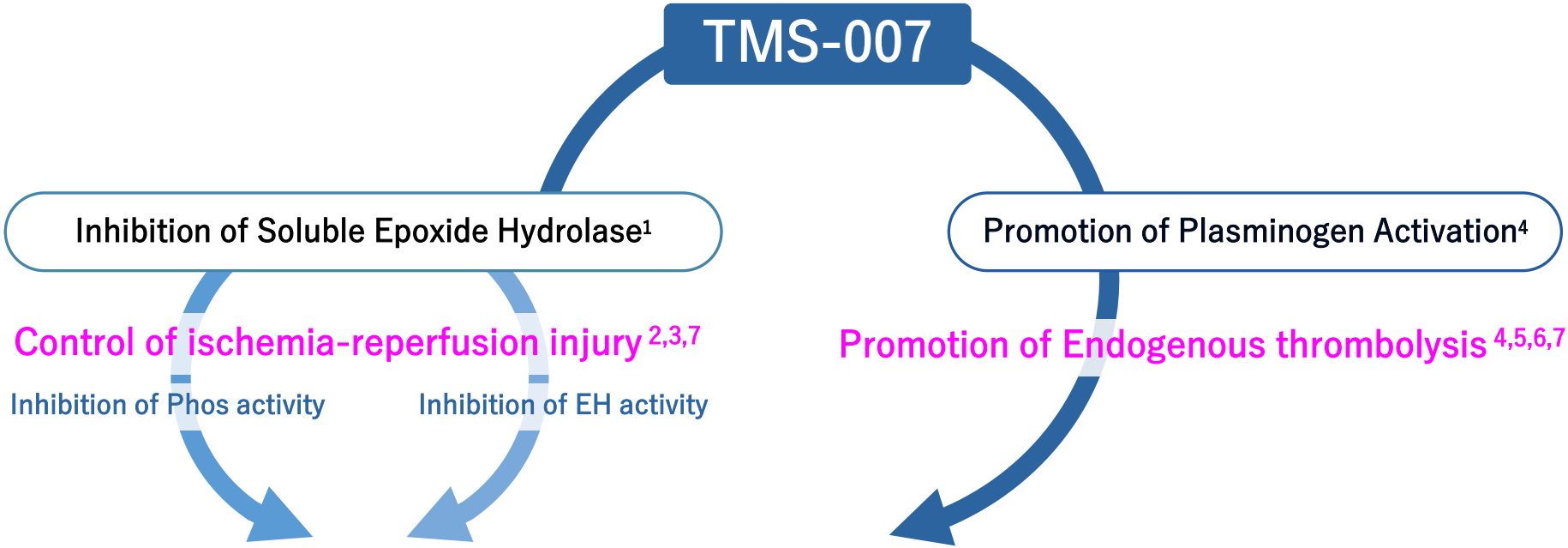
Mortality [4,5]

- 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

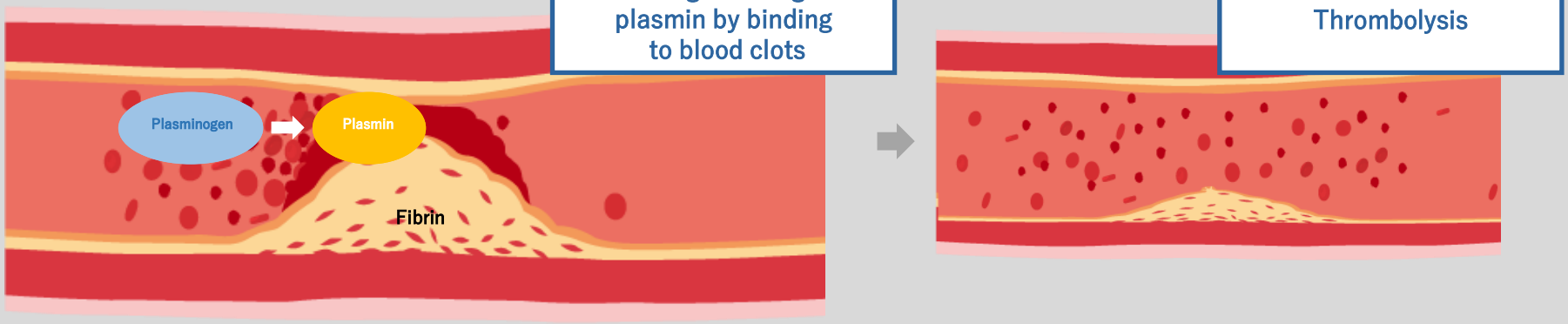
Thrombolysis effect and Inhibitory control of ischemia-reperfusion injury effect (based on anti-inflammatory activities)

Ideal profile for treatment of acute ischemic stroke

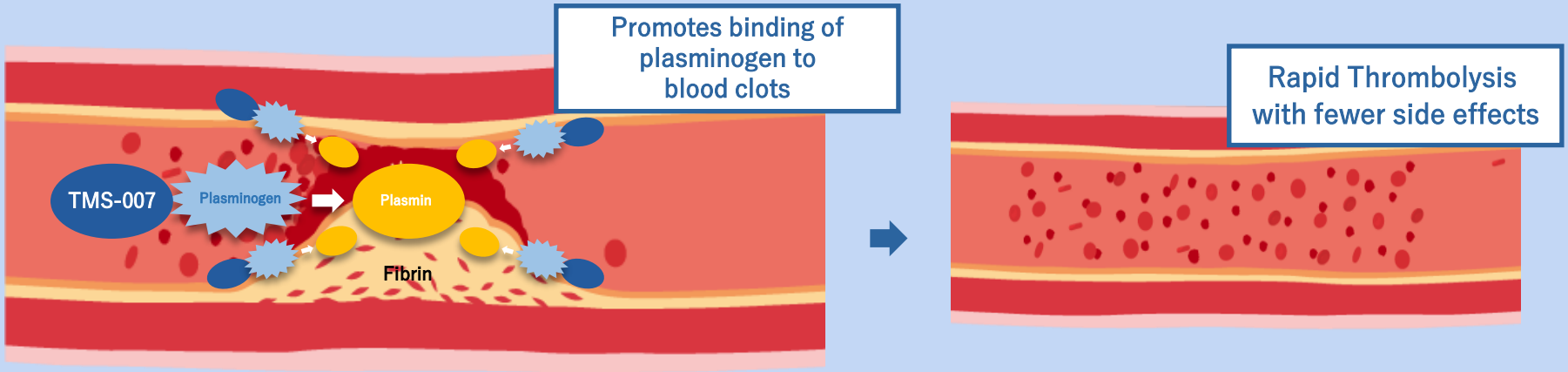
1. Matsumoto et al. (2014) J Biol Chem
2. Shibata et al. (2011) N-S Arch Pharmacol
3. Ito et al. (2014) Brain Res
4. Hasumi et al. (2010) FEBS J
5. Hu et al. (2012) Thrombosis J
6. Miyazaki et al. (2011) Stroke
7. Hasumi & Suzuki (2021) Int J Mol Sci

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

Normal Thrombolysis



Thrombolysis promotion by administration of TMS-007



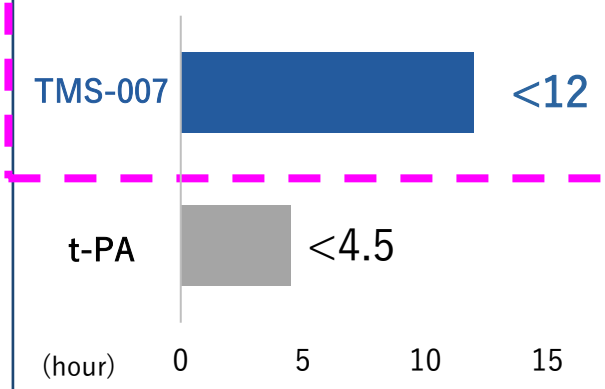
1. For illustrative purposes only

TMS-007：Ph2a Clinical Trial Showed Excellent Results

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

Time Window

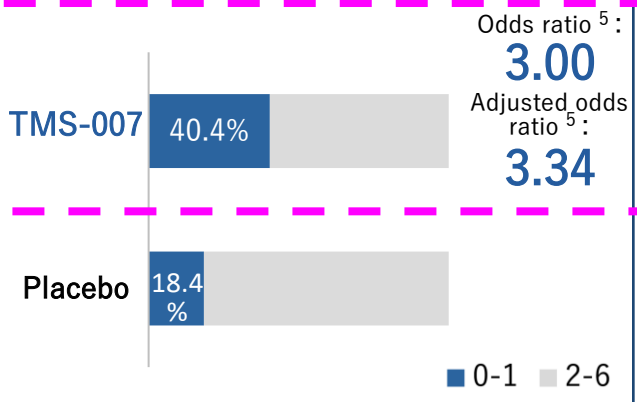
Therapeutic time window



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

Efficacy

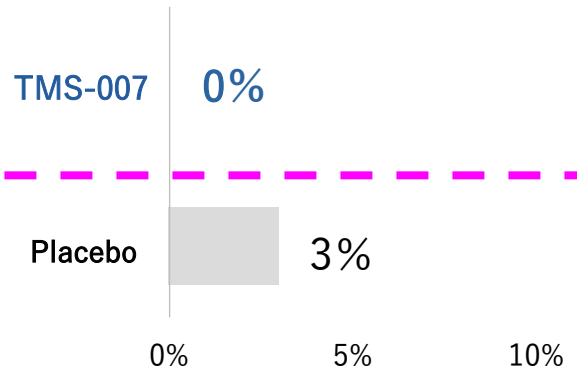
mRS [2] 0-1 ratio at 90 days
Gold-standard Endpoint



- 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)

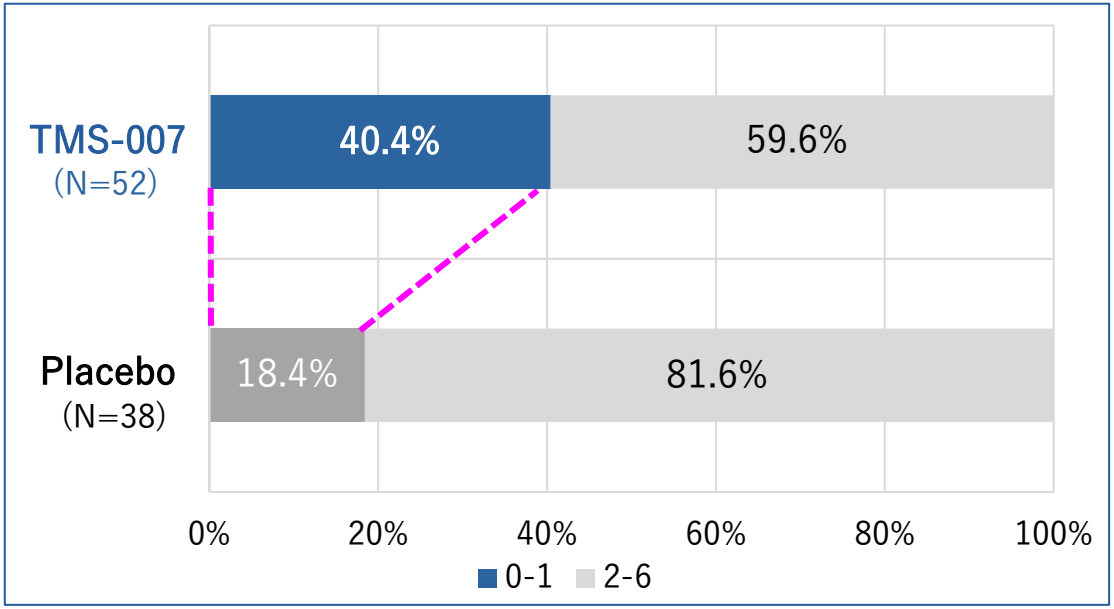
TMS-007：Ph2a Clinical Results Achieved “Gold-standard” Endpoint

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]

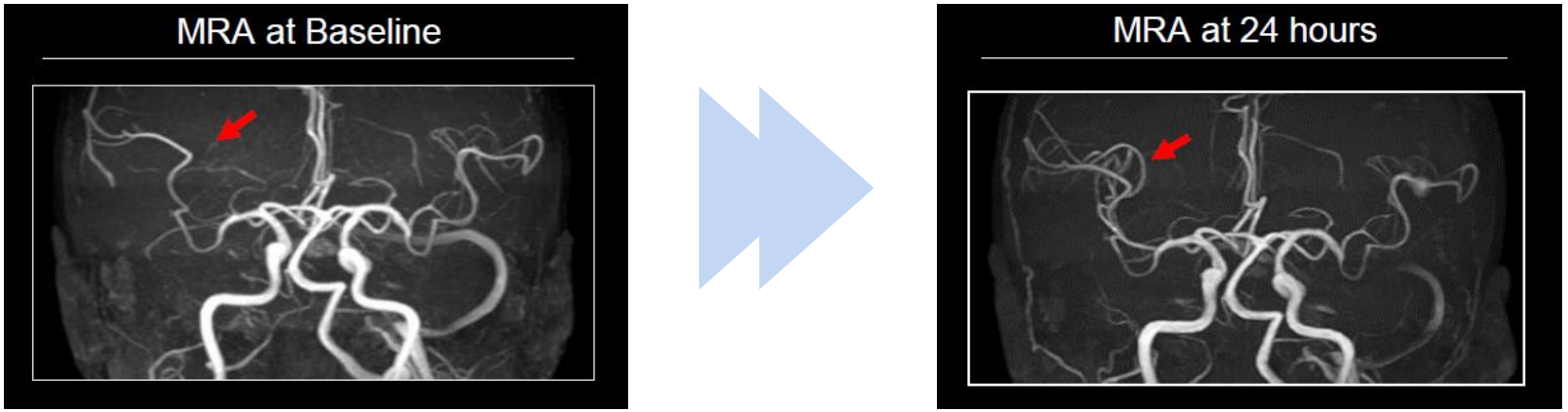


mRS (modified Rankin Scale)		
	0	**No symptoms**
	1	**No significant disability, despite symptoms;** able to perform all usual duties and activities
	2	**Slight disability;** unable to perform all previous activities but able to look after own affairs without assistance
	3	**Moderate disability;** requires 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'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

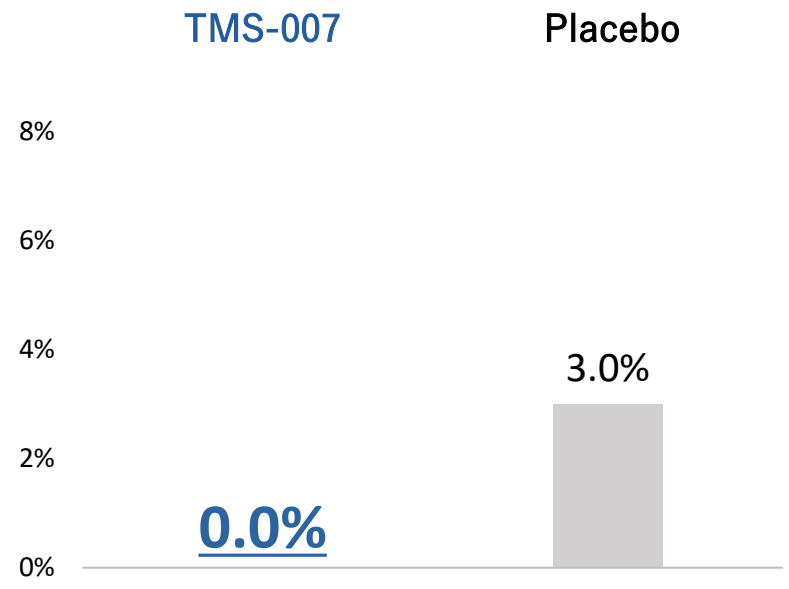
1. Biogen, Investor Day Material (September 21, 2021), Q4 and Full Year 2021: Financial Results and Business Update

TMS-007：Ph2a 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 Ph2a TMS-007 study demonstrated a reduced risk of the incidence of sICH.

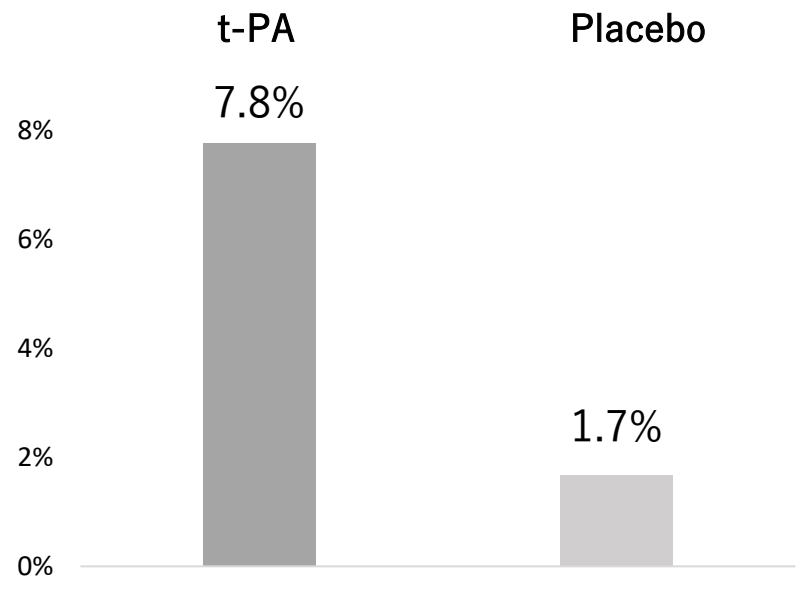
Incidence rate of sICH[1]

TMS-007 vs Placebo [2] — Ph2a



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

t-PA vs Placebo [3] — Meta-analysis



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

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."

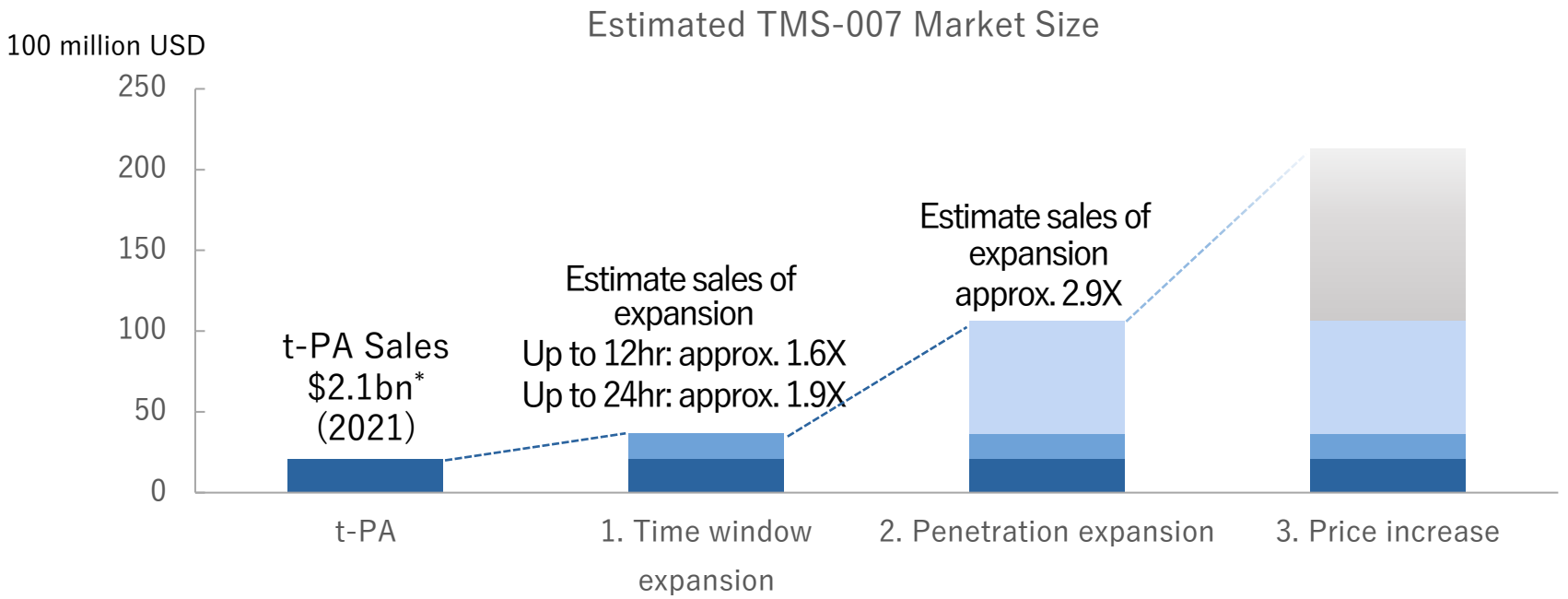
* In clinical trials for acute ischemic stroke (AIS), the proportion of patients with an mRS (modified Rankin Scale) score of 0–1 at Day 90 is considered the gold-standard endpoint.

Company	Product Name	Mechanism of Action	Modality	Development Status	Partner
Corxel / TMS	**JX10/TMS-007**	**Thrombolysis Anti-inflammatory effect Antioxidant effect**	**Small molecule**	**Ph2/3**	**-**
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	Ph3 (Approved in India)	Sun Pharmaceutical
NoNO	Nerinetide (NA-1)	Inhibits cell death Anti-inflammatory effect	Peptide	Ph3	-
Healios	Multistem	Anti-inflammatory effect	Cell therapy	Ph3	-
DiaMedica Therapeutics	DM199	Anti-inflammatory effect	Protein	Ph2/3	Fosun Pharma
Shionogi & Co., Ltd.	Redasemtide (S-005151)	Regenerative induction Anti-inflammatory effect	Peptide	Ph2b	StemRIM
Lumosa Therapeutics	Oldatrotide (LT3001)	Thrombolysis Antioxidant effect	Peptide + small molecule	Ph2	Shanghai Pharmaceuticals

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



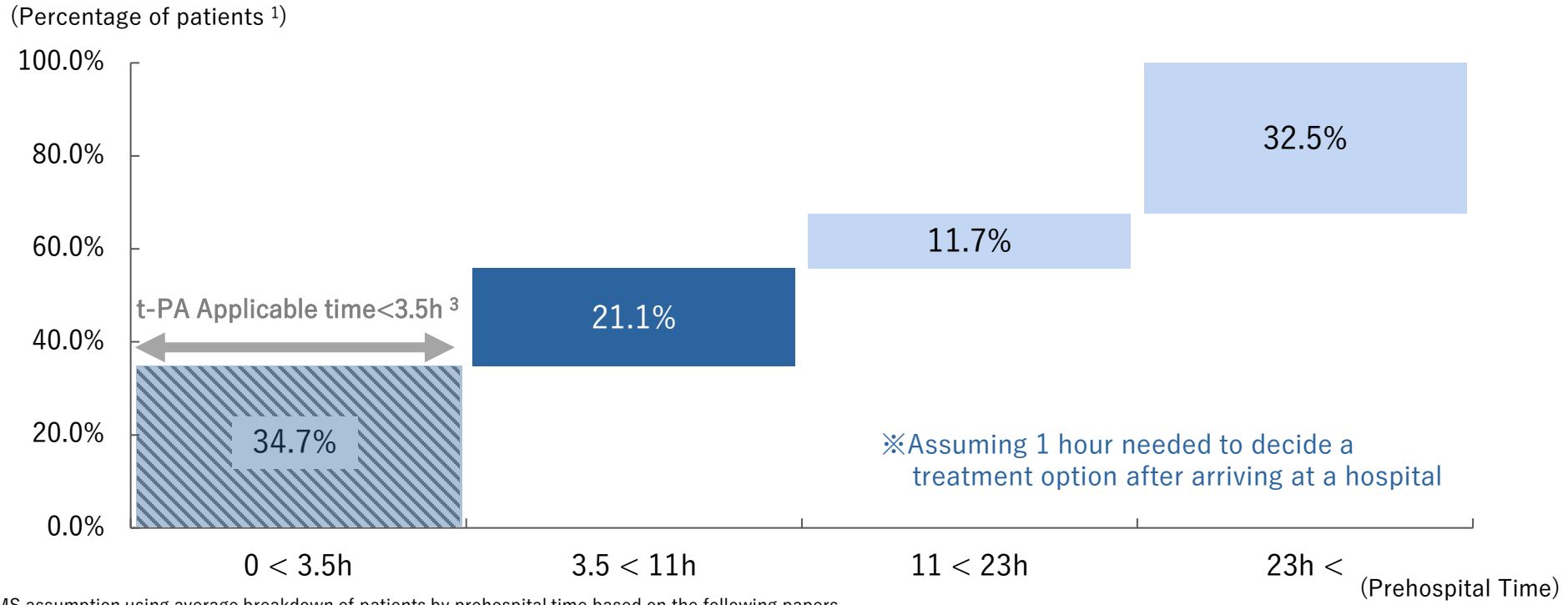
1. Novel thrombolytic with the potential to be first line treatment for AIS
   - Possibility to expand time window after onset (12hr or 24hr)
   - Possibility to expand penetration due to excellent safety
2. Higher pricing can be expected if higher efficacy and safety than t-PA are achieved

＊ 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]

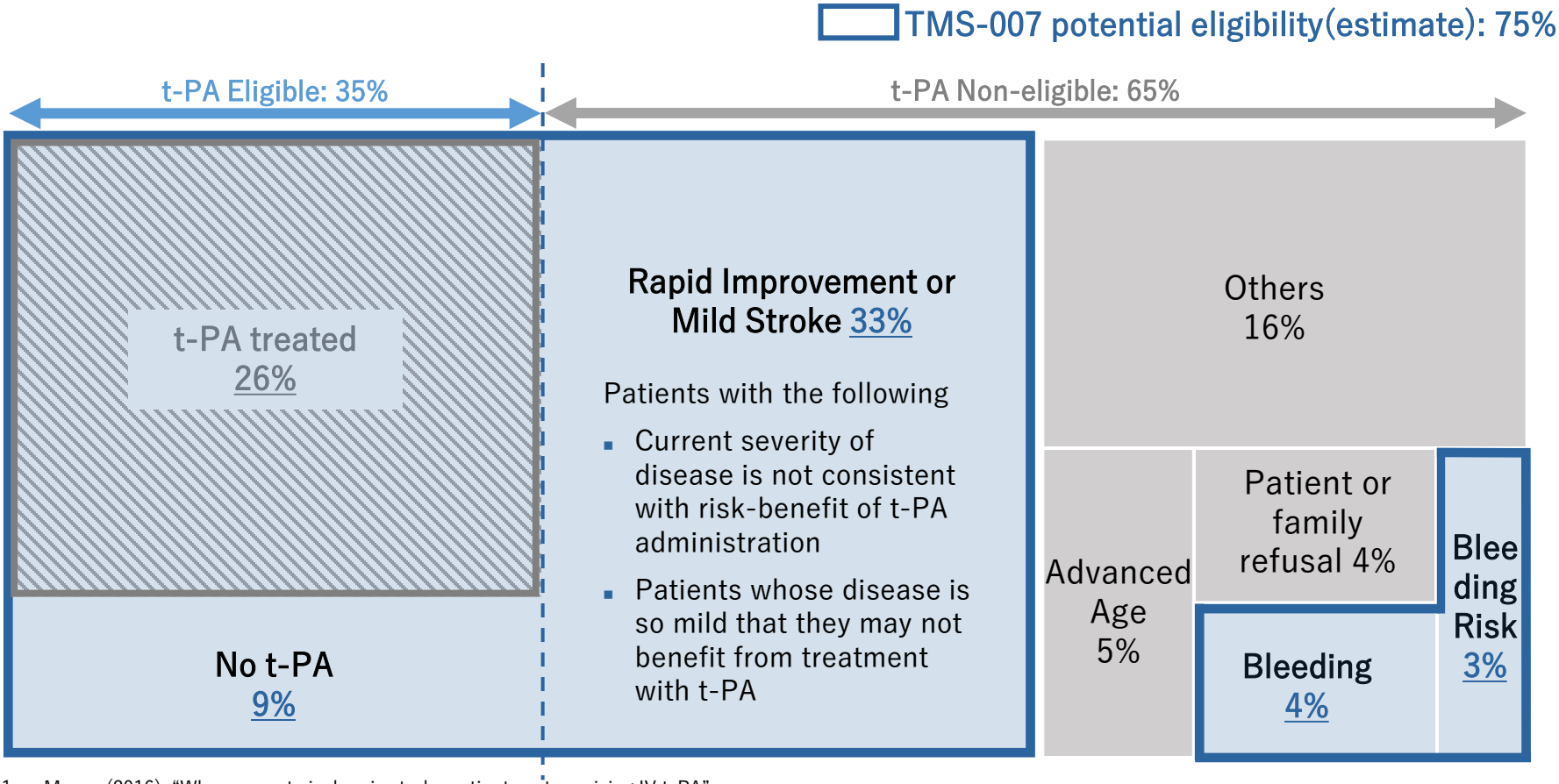


1. TMS assumption using average breakdown of patients by prehospital time based on the following papers. Please note that the company's estimate above is based on various assumptions and beliefs stated herein, including applicable time, disregard certain conditions such as the eligibility of the patients 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



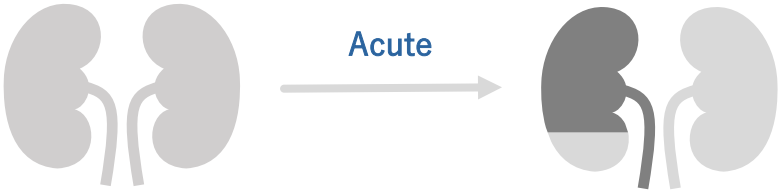
1. Messe (2016), “Why are acute ischemic stroke patients not receiving IV t-PA”

5. TMS-008

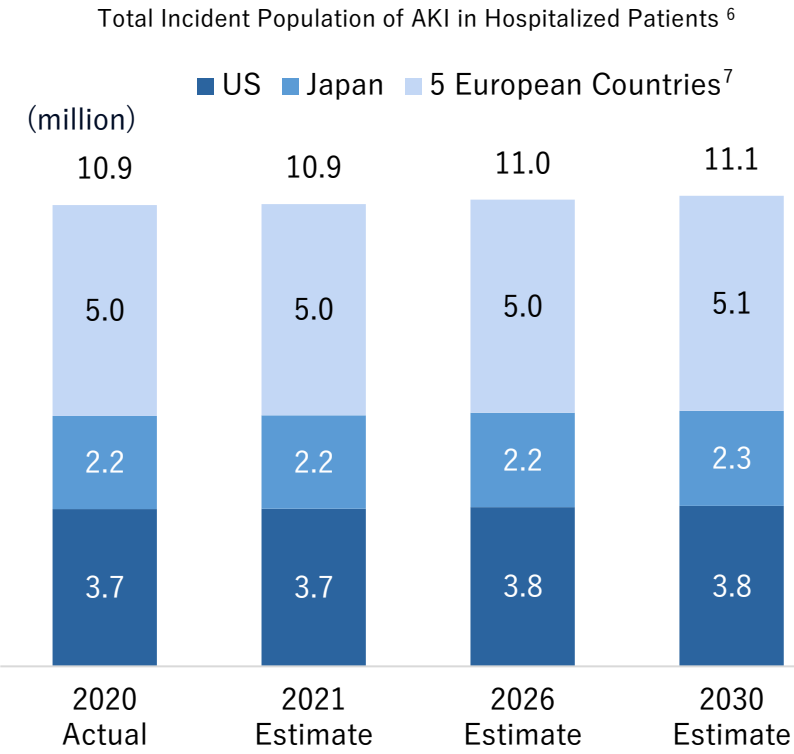
Acute Kidney Injury

TMS-008：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

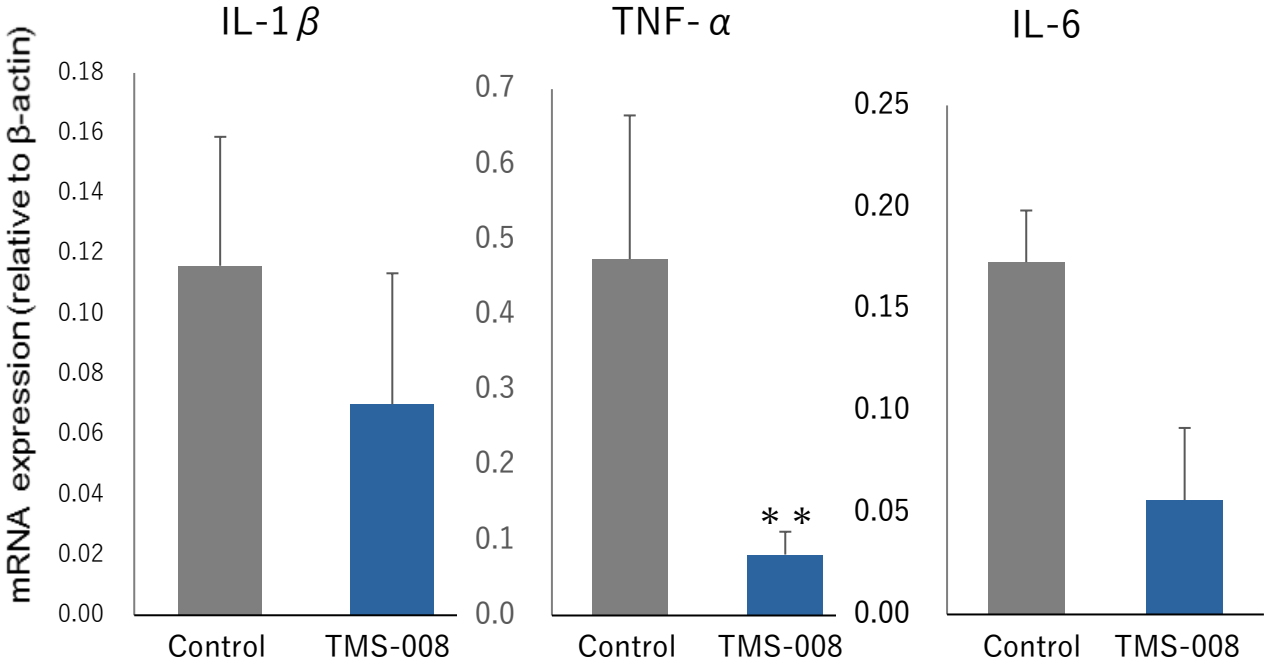
TMS-008：Anti-inflammatory activities with potential for broad indications

Potent sEH inhibitor with high anti-inflammatory and antioxidant activity

Inflammation-related parameter using AIS model mouse [1]

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

Mean ± SE（N=6）



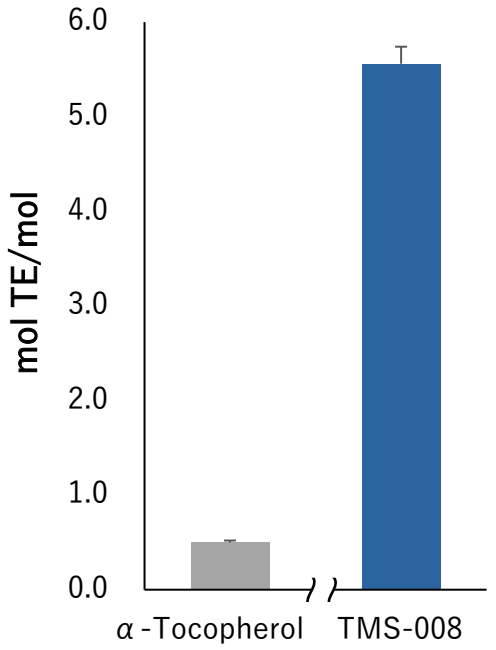
** P<0.01、＊P＜0.05 （vs. control）

Antioxidant activity test [1, 2]

- H-ORAC： hydrophilic oxygen radical absorbance capacity method

(The results are expressed as Trolox Equivalents (TE). The ORAC value for α -tocopherol is a reference value.)

Mean ± SE（N=3）



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

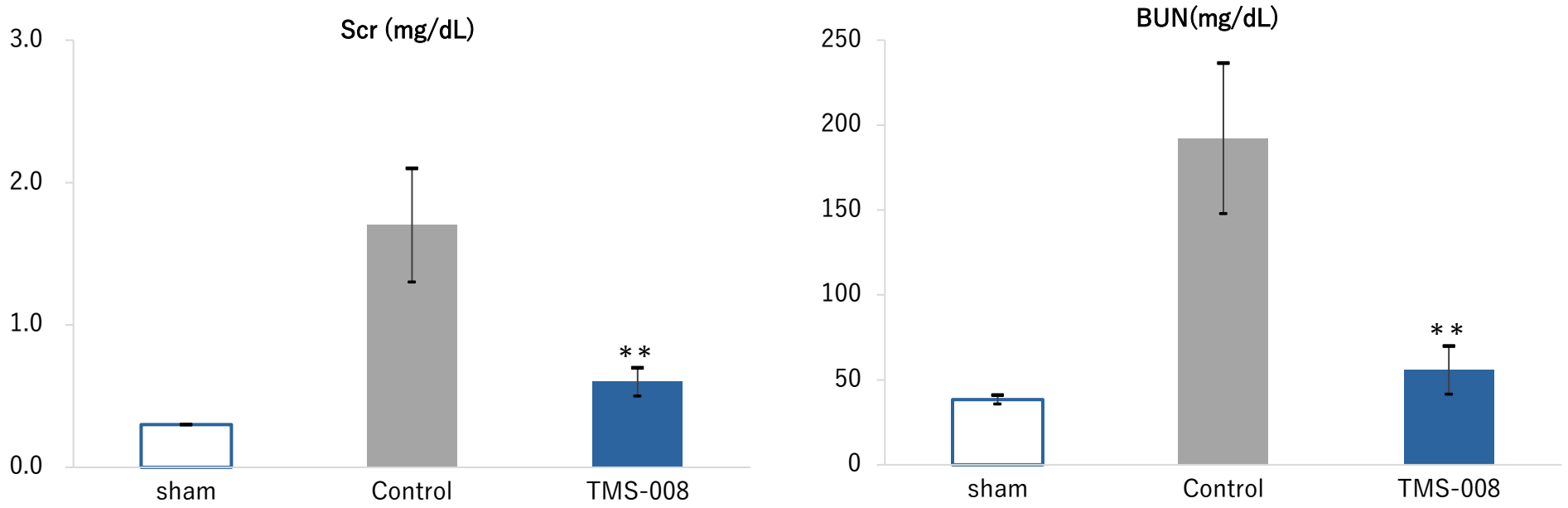
TMS-008：Target Disease_ Acute Kidney Injury (AKI)

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 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 [1]



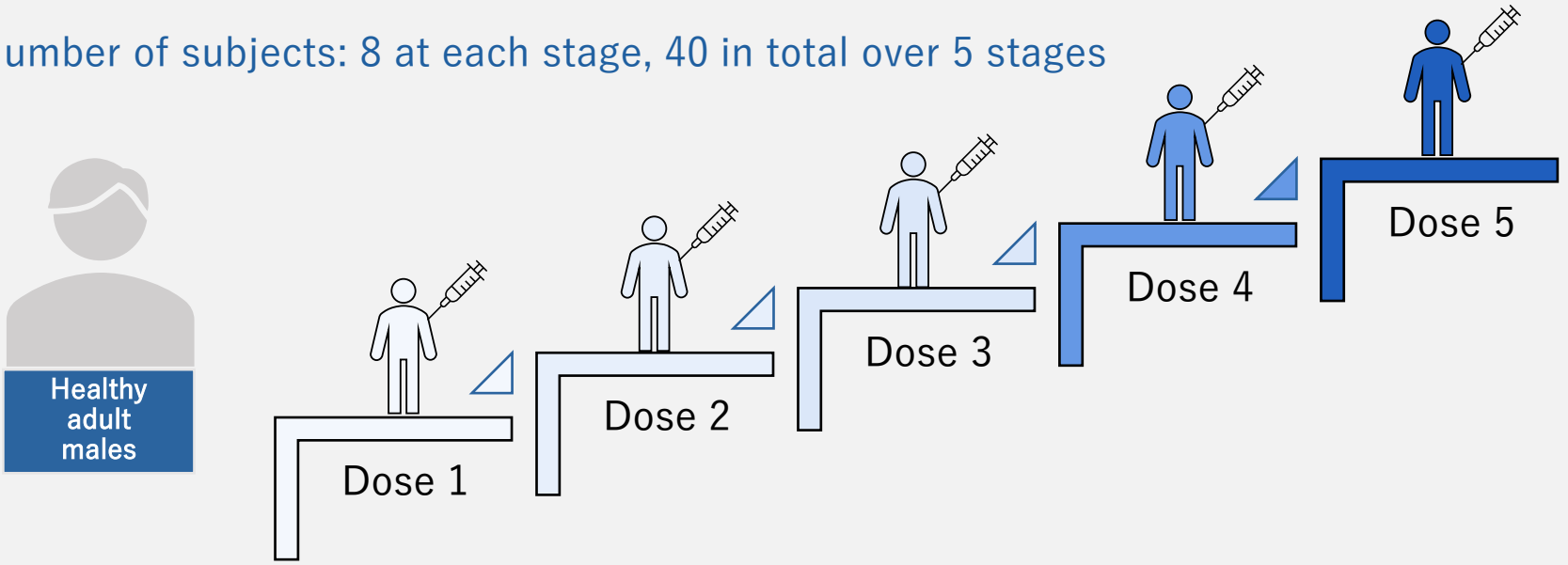
1. Mean ± SE (n = 6), *p value < 0.05 and **p value < 0.01 when compared with control groups by using ANOVA with Bonferroni specimen

TMS-0008：Overview of Ph1 Clinical Trials

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
- ◆ Design ：Randomized, placebo-controlled, double-blind, dose-escalation, single-dose study
- ◆ Results ：Favorable safety and tolerability demonstrated

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

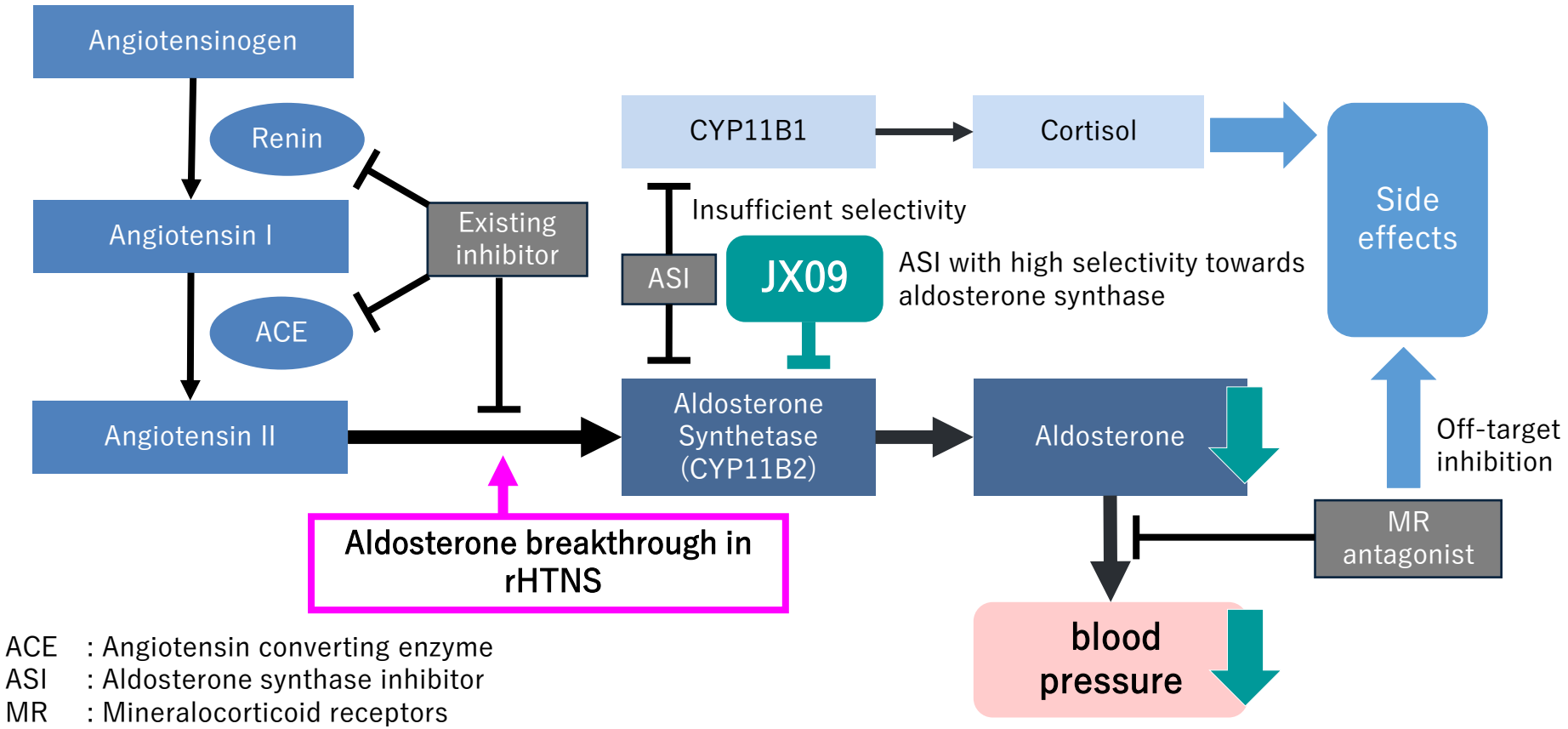
Resistant or uncontrolled hypertension

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



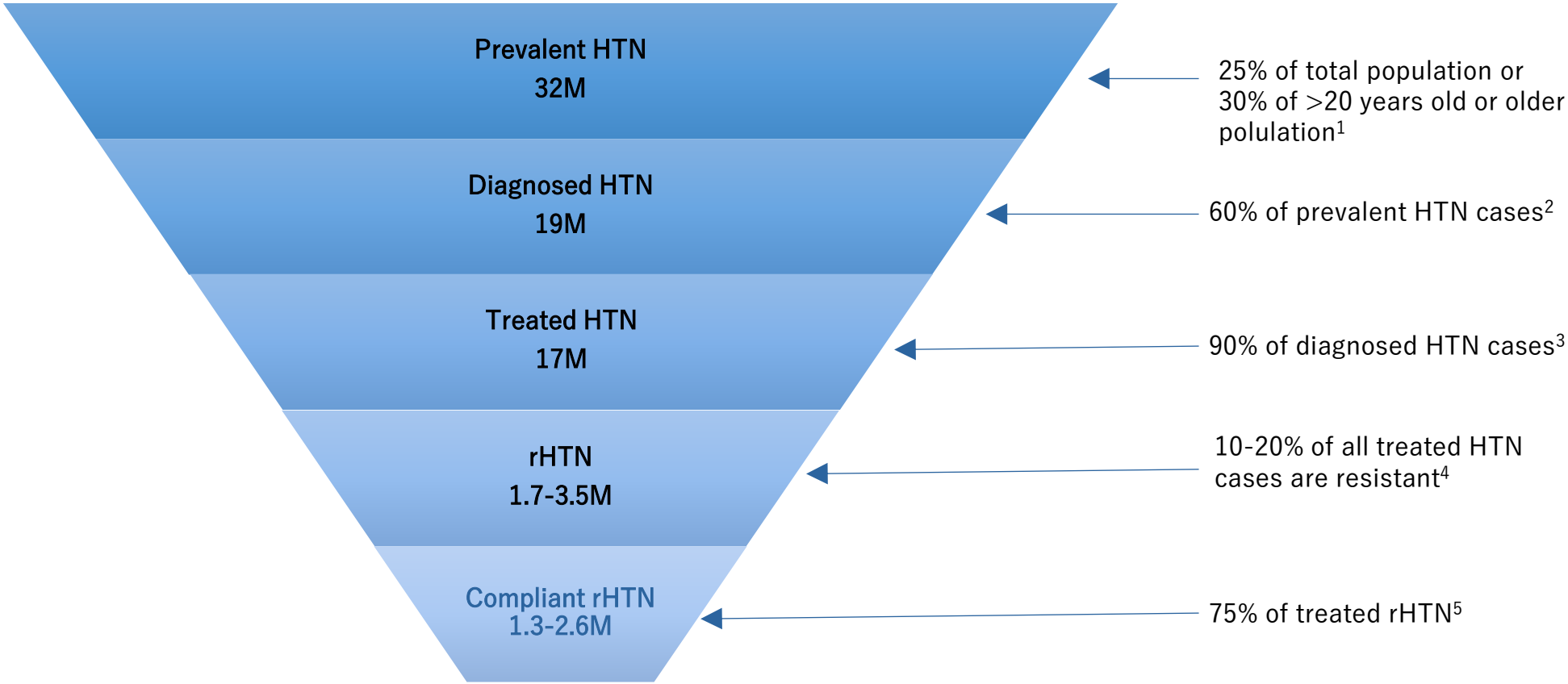
ACE : Angiotensin converting enzyme
ASI : Aldosterone synthase inhibitor
MR : Mineralocorticoid receptors

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



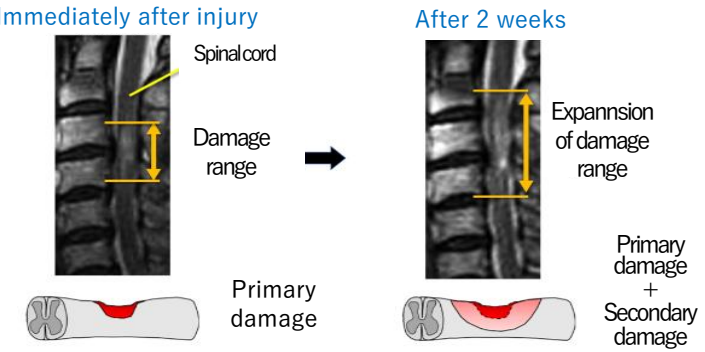
1：Estimated with data from Health Service Bureau, MHLW "National Health and Nutrition Survey 2019“: https://www.mhlw.go.jp/english/database/compendia.html
2：Saito et al. (2015): We find that there are much higher rates of undiagnosed hypertension in Japan (44.3%) than in the U.S. (11.9%)
3：Used the same 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

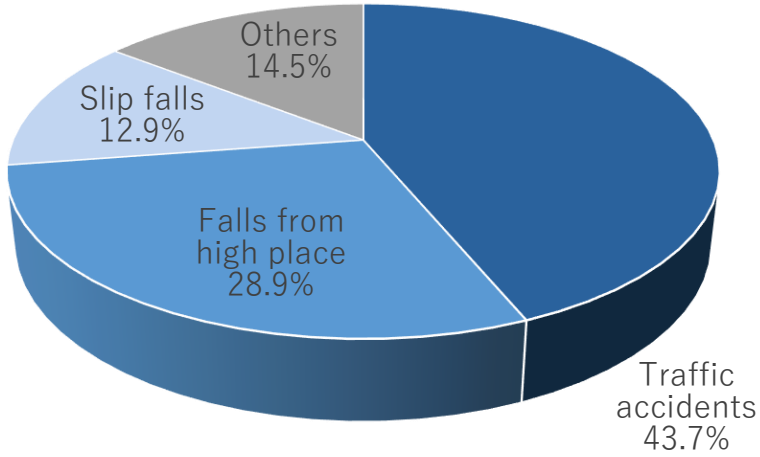
Spinal Cord Injury

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, sensory paralysis, and excretion disturbances.[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.

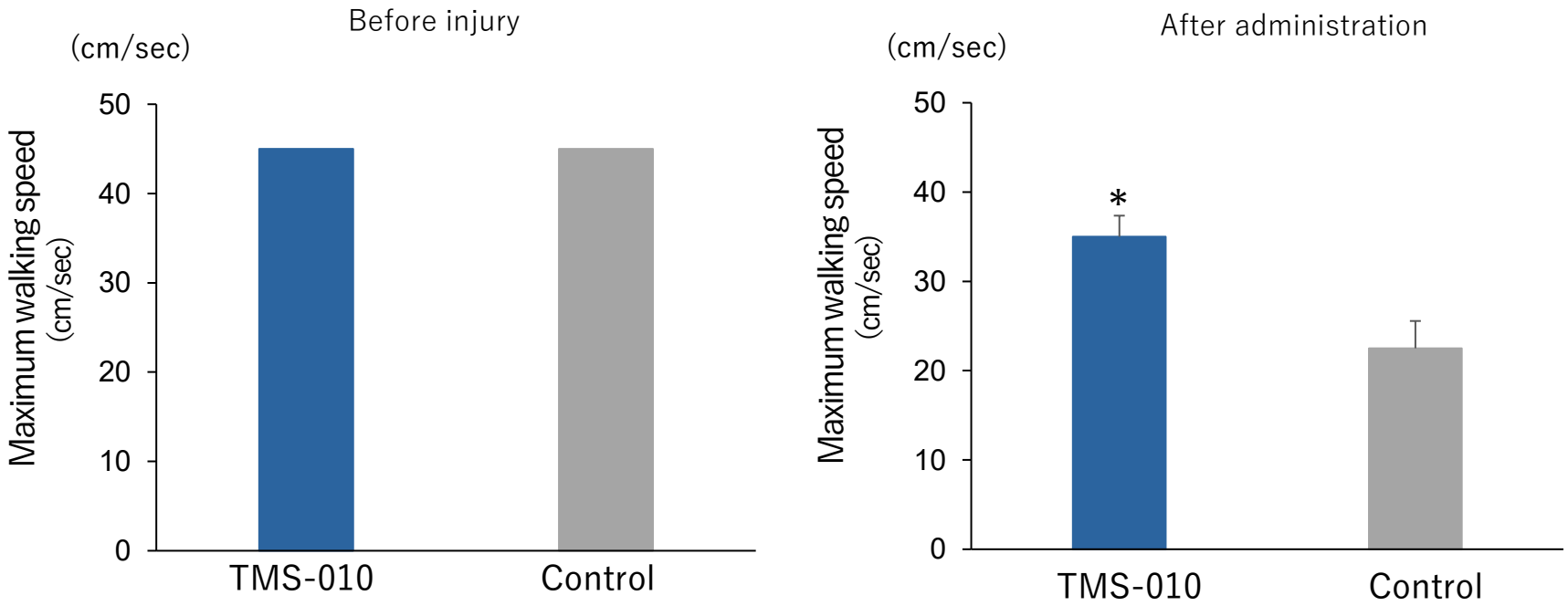
1,2. Neurospinal Society of Japan website (https://www.neurospine.jp/original62.html)
3. Ahuja CS, et al. Traumatic spinal cord injury. Nat Rev Dis Primers. 27(3), 17018 (2017)
4. Miyakoshi N, et al. A nationwide survey on the incidence and characteristics of traumatic spinal cord injury in Japan in 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

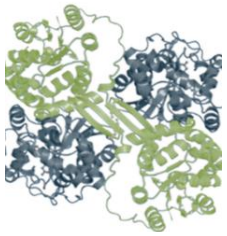
Pursue internal and external paths for pipeline expansion, leveraging knowledge and experience cultivated through SMTP compounds development

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



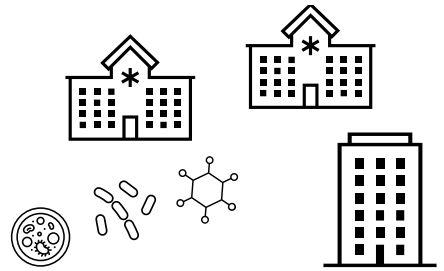
Human sEH

- 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.

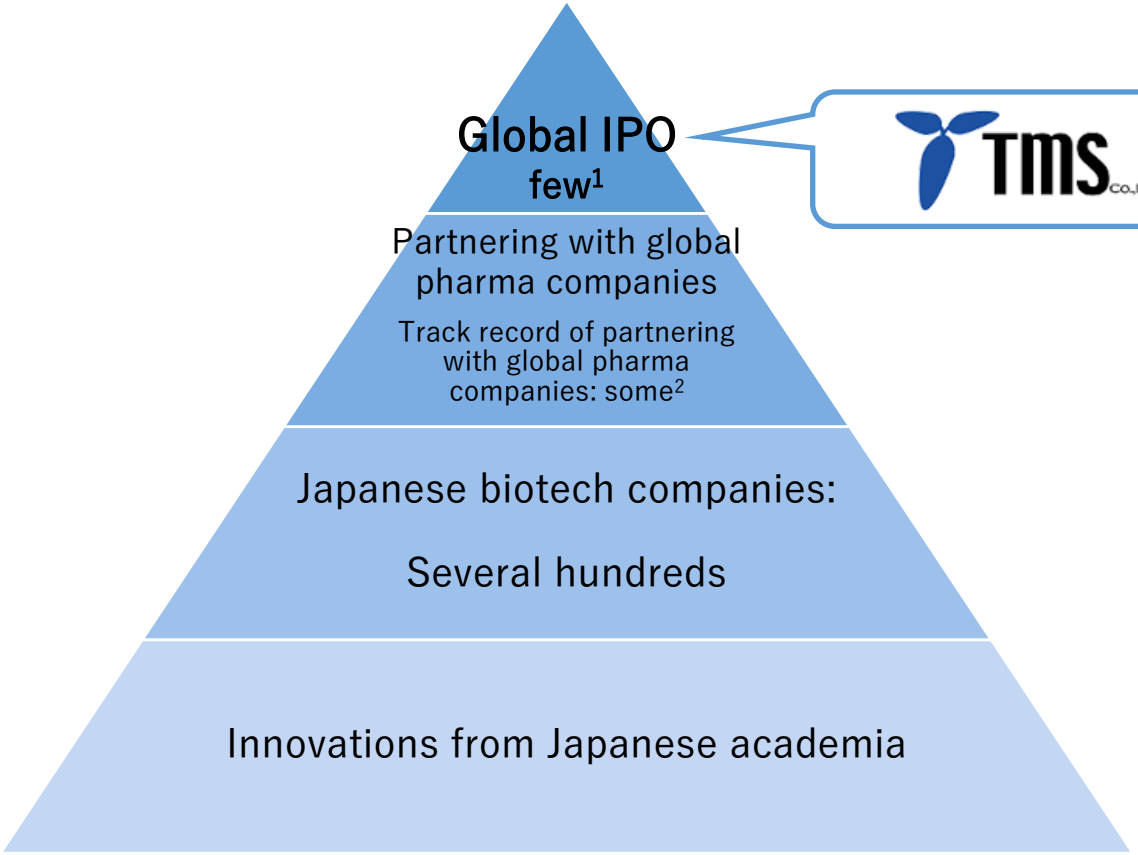
Global Market

* 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

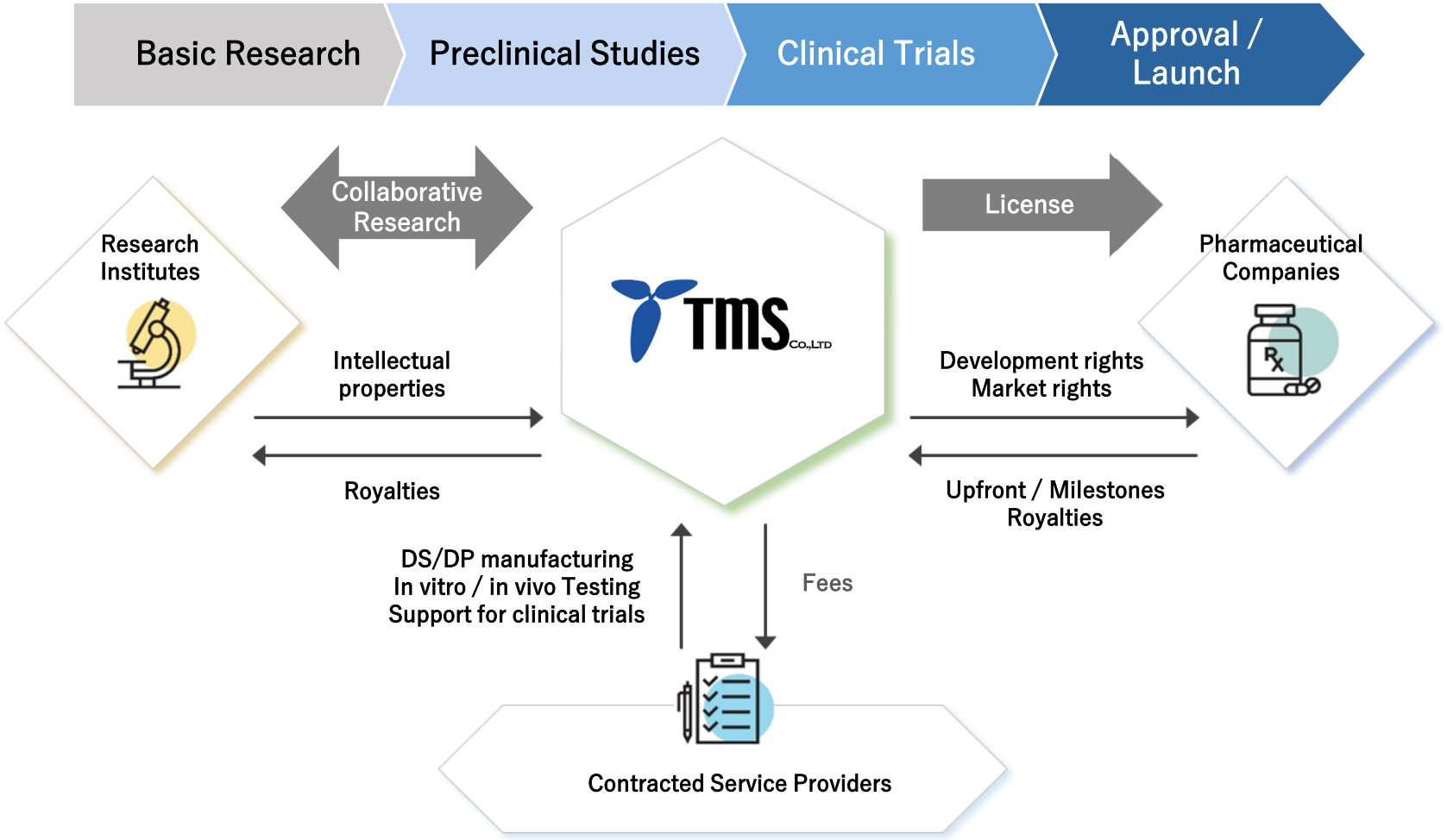
Corporate Profile & History

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 February 28, 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

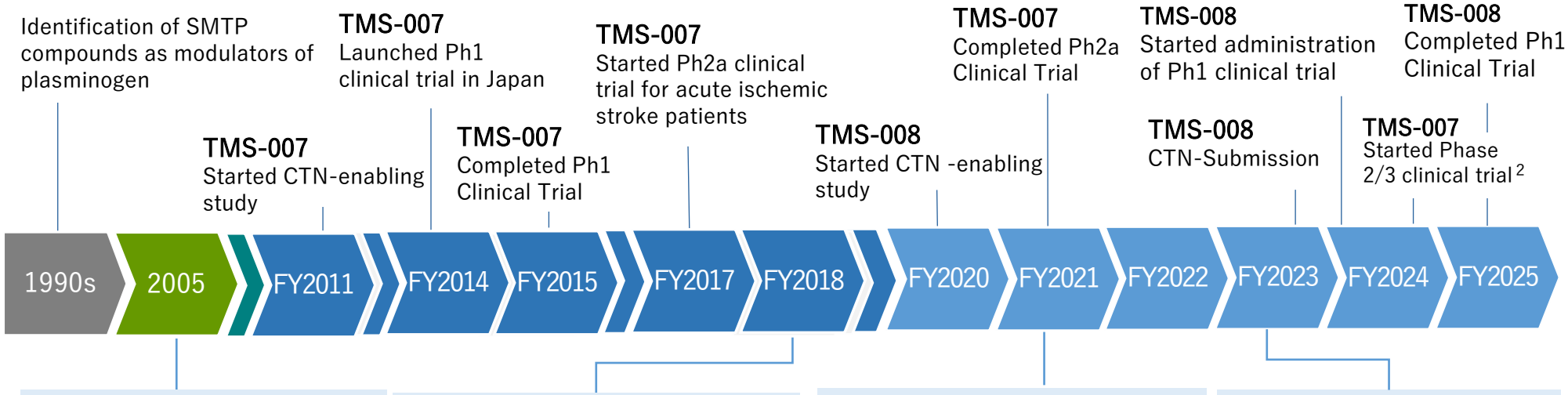
Ph.D.
Founder
Chief Scientific Officer

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.



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

Spinoff from Tokyo University of Agriculture and Technology

Option Agreement with Biogen [1]

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

Biogen [1] exercises Option Right

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

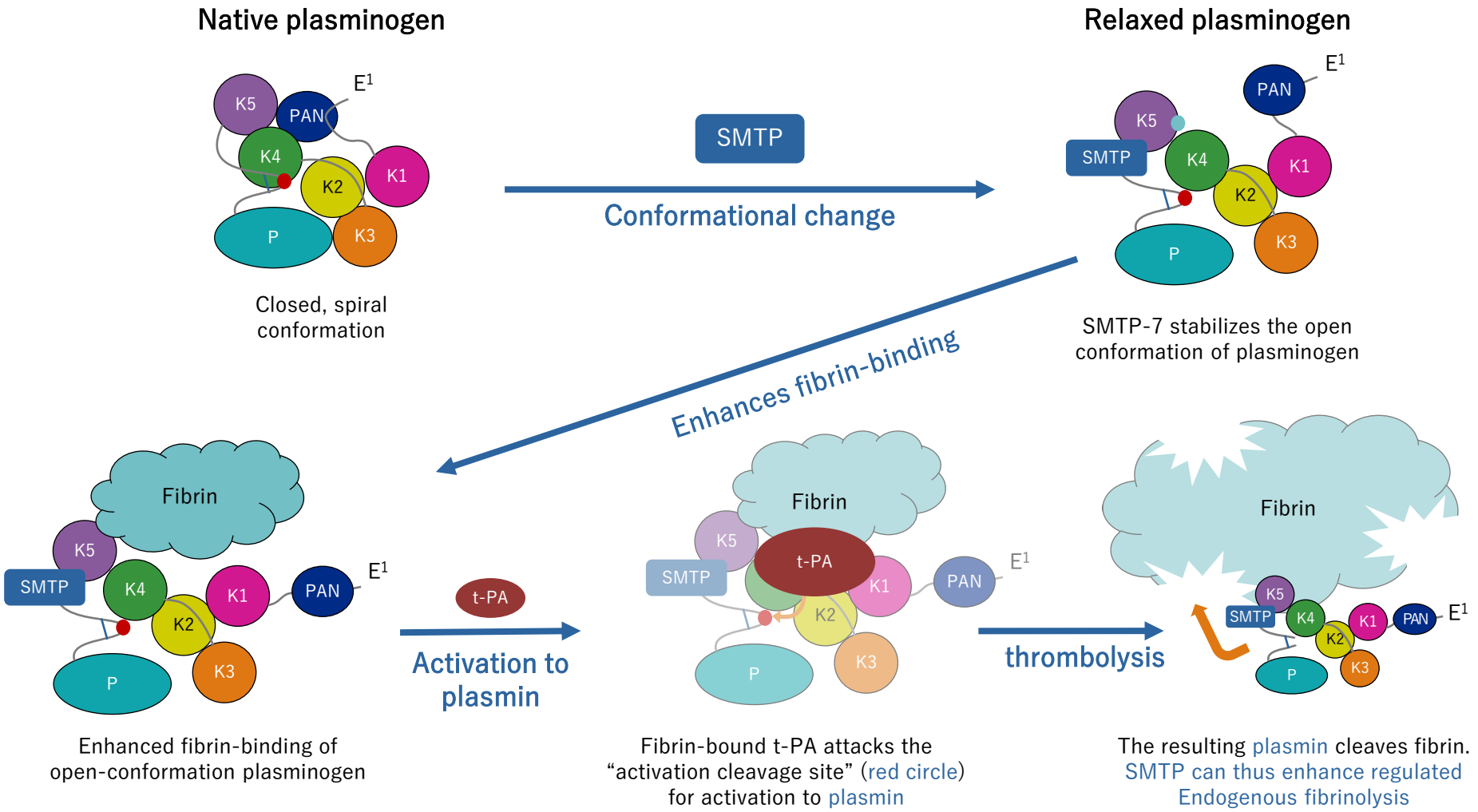
Rights transfered from Biogen[1] to CORXEL

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 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