



TSE Growth : 4891

## First Half FY2024 Financial Results ( Fiscal Year Ending February 28, 2025 )

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1. Highlights
2. Summary of Financial results for 1H FY2024 (Fiscal Year Ending February 28, 2025)
3. Pipeline
4. TMS-010 / [Spinal Cord Injury \(New Asset\)](#)
5. TMS-007 / [Potential Next Generation Acute Ischemic Stroke Treatment](#)
6. JX09 / [Resistant or uncontrolled hypertension](#)
7. TMS-008 / [Acute Kidney Injury](#)
8. Expansion of Pipelines
9. Appendix



# Highlights



## 1 Progress of TMS-007 (JX10)

- Preparation for the next global clinical trial is underway, led by JIXING\* (We envision it as a pivotal study).
- TMS plans to participate in the global study.
- TMS expects formal announcement from JIXING by March 2025.

(When we are able to independently announce progress, we will do so promptly.)

\* JIXING (Ji Xing Pharmaceuticals ) will change its name to CORXEL effective November 2024.

## 2 TMS-008 Ph1 Clinical Trial- Start of Administration

- Clinical Trial Notification (CTN) was submitted to the Pharmaceuticals and Medical Devices Agency (PMDA) at the end of previous fiscal year, and the first dosing was made on June 19, 2024, at The University of Tokyo Hospital.
- This is the-second FIH (First-In-Human) study for TMS, following TMS-007(JX10).
- The Ph1 trial is designed as a dose escalation study in 5 cohorts with healthy volunteers.

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

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

# Upcoming and Achieved Milestones in the Last 12 Months

| Projects  | Achievements and milestones   | Timing                |
|---|---|-----------------------|
| TMS-007<br><i>(Acute ischemic stroke)</i>               | Start of the next phase clinical trial  | Preparations underway |
|   | Transferred ex-Japan rights from Biogen to JIXING   | January 2024 ✓        |
| JX09<br><i>(Resistant or uncontrolled hypertension)</i> | First subject dosed in Ph1 study in Australia   | February 2024 ✓       |
|   | In-licensed exclusive Japan rights  | January 2024 ✓        |
| TMS-008<br><i>(Acute kidney injury)</i>                 | Report Ph1 results to confirm safety, tolerability, and pharmacokinetics                  | Q2 FY2025             |
|   | Completion of dosing to all healthy volunteers in Ph1 study                               | Q4 FY2024             |
|   | First subject dosed in Ph1 study  | June 2024 ✓           |
|   | Submission of Investigational New Drug application  | February 2024 ✓       |
| Discovery Projects                                      | Expanded pipeline by in-licensing TMS-010 as a potential treatment for spinal cord injury | July 2024 ✓           |

# Summary of Financial Results for the first half of \*FY2024

\*March 2024 – February 2025





# 1H FY2024 Financial Results - Income Statement



R&D expenses increased due to the initiation of TMS-008 Ph1 study and addition of a new asset. Overall expenses are controlled within the beginning of year plan.

|                                   | FY2023<br>1H | FY2024<br>1H | (million yen)<br>Change |            |
|-----------------------------------|--------------|--------------|-------------------------|------------|
|                                   |              |              | Amount                  | Percentage |
| Operating revenue                 | -            | -            | -                       | -          |
| Operating expenses                | 345          | 452          | 107                     | 31.0%      |
| Research and Development expenses | 213          | 314          | 100                     | 40.1%      |
| Operating income(loss)            | (345)        | (452)        | (107)                   | -          |
| Ordinary income (loss)            | (342)        | (451)        | (109)                   | -          |
| Extraordinary loss                | -            | (25)         | (25)                    | -          |
| Net income (loss)                 | (342)        | (477)        | (135)                   | -          |

R&D expenses Increased YOY mainly due to starting TMS-008 Ph1 and the addition of a new pipeline (TMS-010).

Loss on full amortization of fixed assets

Expected expenses for the Full Fiscal Year 2024 (million yen)

|  |             |
|--|-------------|
| Research and Development expenses                  | 750 - 1,100 |
| Other selling, general and administrative expenses | 300 - 400   |

# 1H FY2024 Financial Results - Cash Flows



The initiation of the Phase I clinical trial of TMS-008 and the in-licensing of TMS-010 increased the amount of negative operating cash flow.

As a result, there was a decrease in cash and cash equivalents at the end of the period.

|   | (million yen) |           |
|---|---------------|-----------|
|   | FY2023 1H     | FY2024 1H |
| Cash flows from operating activities  | (336)         | (409)     |
| Net income before tax   | (342)         | (447)     |
| Cash flows from investing activities  | (1)           | (29)      |
| Cash flows from financing activities  | 1             | 0         |
| Net increase and decrease in cash and cash equivalents (indicates decrease) | (336)         | (437)     |
| Cash and cash equivalents at beginning of period                            | 3,584         | 3,446     |
| Cash and cash equivalents at end of period                                  | 3,248         | 3,008     |

Increased costs mainly due to the start of Ph1 TMS-008 study, and the acquisition of TMS-010

# 1H FY2024 Financial Results - Balance Sheet



Total assets decreased from the beginning of the period, due to increase of expenditure of R&D cost

(million yen)

|                                  | FY2023 | FY2024<br>1H | Change |            |
|----------------------------------|--------|--------------|--------|------------|
|                                  |        |              | Amount | Percentage |
| Current assets                   | 3,551  | 3,084        | (467)  | (13.2%)    |
| Cash and deposits                | 3,446  | 3,008        | (437)  | (12.7%)    |
| Non-current assets               | 3      | 3            | 0      | 0.0%       |
| Total assets                     | 3,554  | 3,087        | (467)  | (13.1%)    |
| Current liabilities              | 97     | 99           | 1      | 1.4%       |
| Total liabilities                | 97     | 99           | 1      | 1.4%       |
| Total net assets                 | 3,457  | 2,988        | (468)  | (13.6%)    |
| Total liabilities and net assets | 3,554  | 3,087        | (467)  | (13.1%)    |

Decrease mainly due to R&D expenses including TMS-008 Ph1 clinical study and other SG&A expenses

# Pipeline



## Clinical Pipeline



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

- Excellent results achieved for both efficacy and safety in the Ph2a clinical trial.
- Preparation for next clinical trial (global study) is ongoing, led by our partner JIXING.
- TMS owns development and marketing rights for Japan, and milestones and royalties for the rest of the world.

### JX09 (*Resistant or uncontrolled hypertension*)

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

### TMS-008 (*Acute kidney injury*)

- Important unmet medical needs for which no approved drug exists.
- Ph1 clinical trial is underway in Japan.
- TMS owns the rights to develop and market the product in Japan.



## Robust Pipeline of Transformative Medicines in Areas of High Unmet Need

| Development Code               | Target Disease                         | MoA                           | Research  | Preclinical | Ph1 | Ph2 | Ph3 | Development and Commercialization   |
|--------------------------------|--|-------------------------------|---|-------------|-----|-----|-----|-------------------------------------|
| TMS-007 (JX10)                 | Acute Ischemic Stroke                  | sEH Inhibition<br>Plasminogen | Ph2a completed in Japan                             |             |     |     |     | Japan: TMS<br>Outside Japan: JIXING |
| JX09 <sup>1</sup>              | Resistant or uncontrolled hypertension | ASI <sup>4</sup>              |   |             |     |     |     | Japan: TMS<br>Outside Japan: JIXING |
| TMS-008 <sup>2</sup>           | Acute Kidney Injury                    | sEH Inhibition                |   |             |     |     |     | TMS                                 |
|                                | Other indications                      |                               |   |             |     |     |     | TMS                                 |
| New TMS-010 <sup>3</sup>       | Spinal cord injury                     | BBSCB protection <sup>5</sup> |   |             |     |     |     | TMS                                 |
| Pipeline candidates <Internal> |  |                               | Search for novel sEH inhibitors and other compounds |             |     |     |     | TMS                                 |
| Pipeline candidates <External> |  |                               | Evaluating multiple programs                        |             |     |     |     | TMS                                 |

Anticipated Next Steps



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

TMS-010

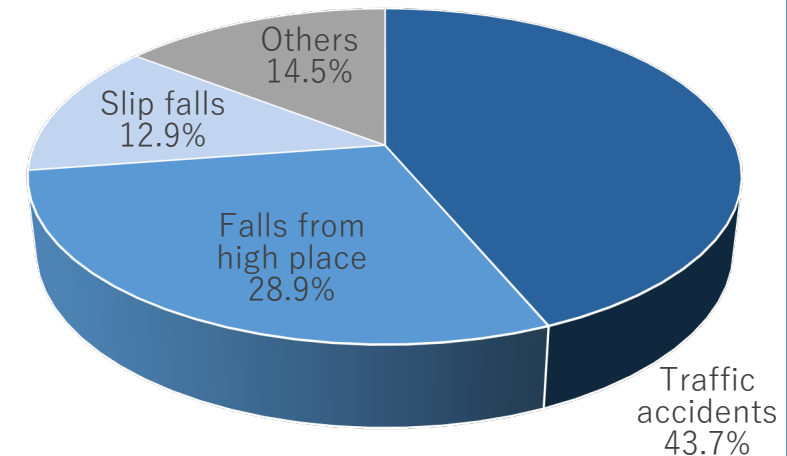
Spinal Cord Injury  
*New Asset*



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

|              |   |
|--------------|---|
| SCI          | 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. <sup>1</sup>   |
| Outline      | <p>Range of damage expands for approximately 2 weeks after SCI<sup>3</sup> (secondary damage). TMS-010 is expected to reduce symptoms caused by SCI by controlling secondary damage.</p> <div> <div> <p>Immediately after injury</p>  <p>Spinal cord</p> <p>Damage range</p> <p>Primary damage</p> </div> <div> <p>After 2 weeks</p>  <p>Expansion of damage range</p> <p>Primary damage + Secondary damage</p> </div> </div> |
| Epidemiology | <ul style="list-style-type: none"> <li>■ 5,000 incidences per year in Japan<sup>4</sup></li> <li>■ 180,000 cases per year worldwide<sup>5</sup></li> </ul>  |
| Treatment    | <ul style="list-style-type: none"> <li>■ <b>There is no approved therapeutic drug</b></li> <li>■ Steroid therapy, current standard treatment, is not considered to be sufficient.</li> </ul>  |

### Causes of Spinal Cord Injury in Japan<sup>2</sup>



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's aging population

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)

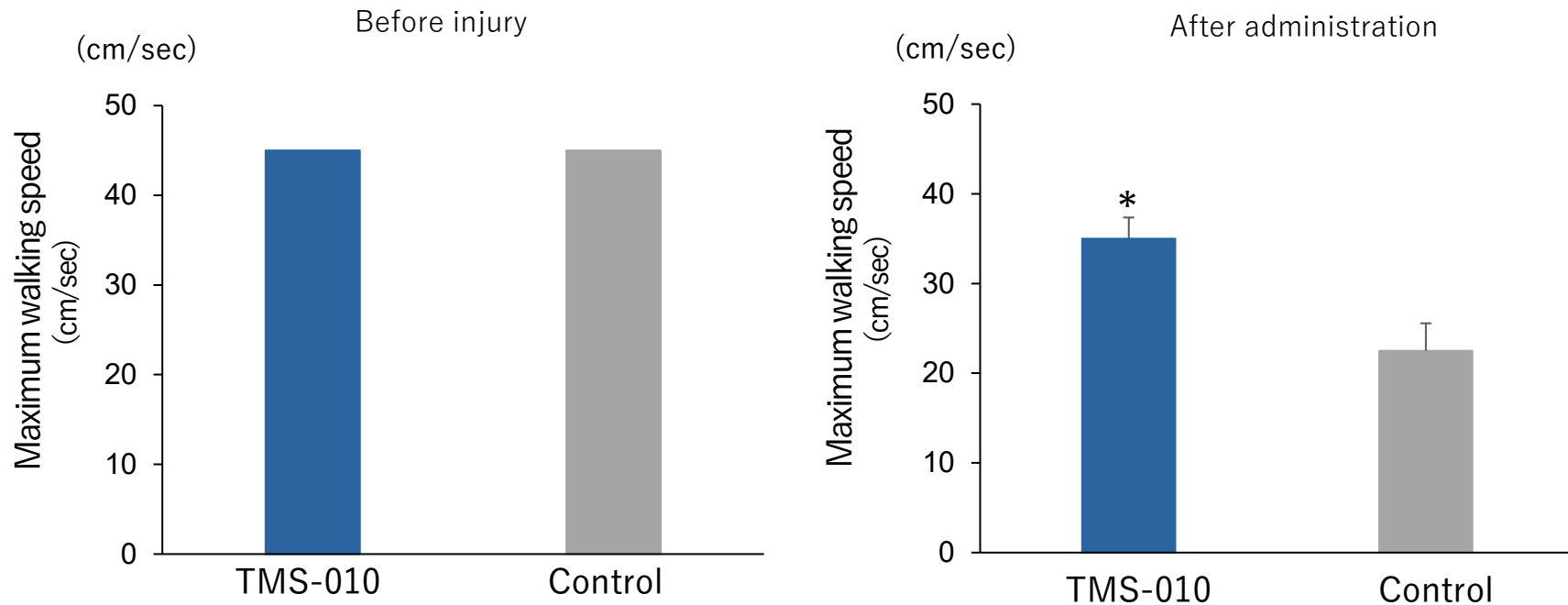
4. Miyakoshi N, et al. A nationwide survey on the incidence and characteristics of traumatic spinal cord injury in Japan in 2018. Spinal Cord 59(6), 626-634 (2021)

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)

## Promising preclinical data from multiple animal studies

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

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



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

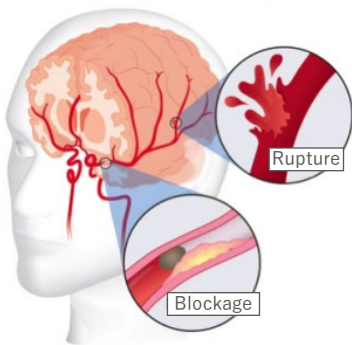
TMS-007

Potential Next Generation  
Acute Ischemic Stroke  
Treatment

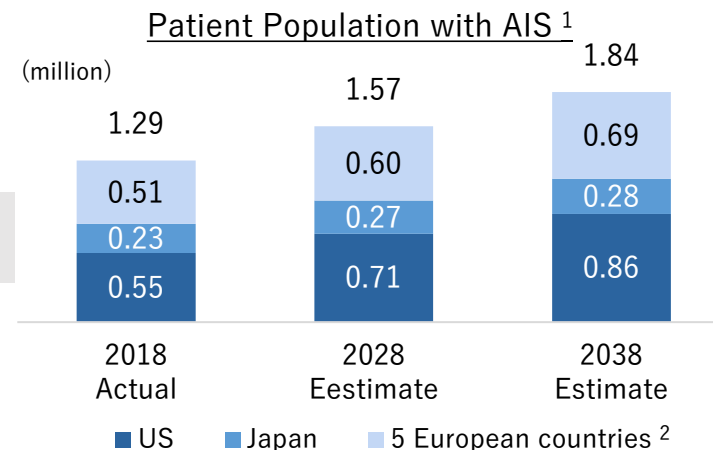




## Acute Ischemic Stroke (AIS) Overview



- AIS is caused by blockages of blood supply to the brain
- Potentially leads to **permanent brain damage** :  
hemiplegia, memory loss, speech problems, reading and comprehension difficulties and other complications
- The number of patients with Ischemic Stroke: approx. 1.3 million/year (total of 7 major countries) and it is expected to increase



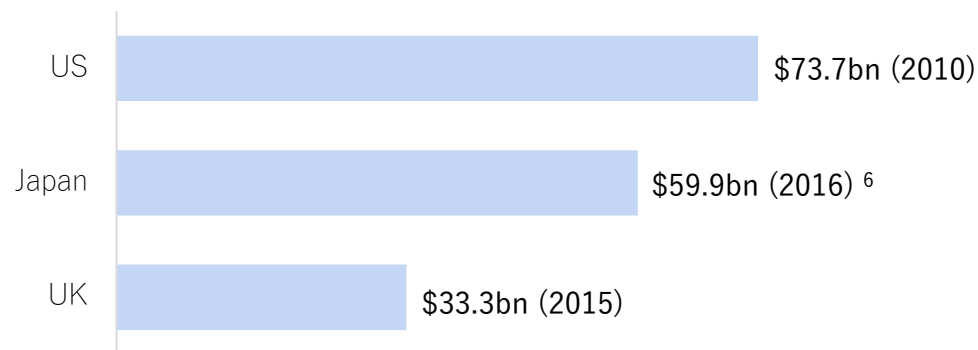
## Important Unmet Medical Needs

### Cause of death in the US (2019) <sup>3</sup>

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

Breakdown of Stroke <sup>4</sup>

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



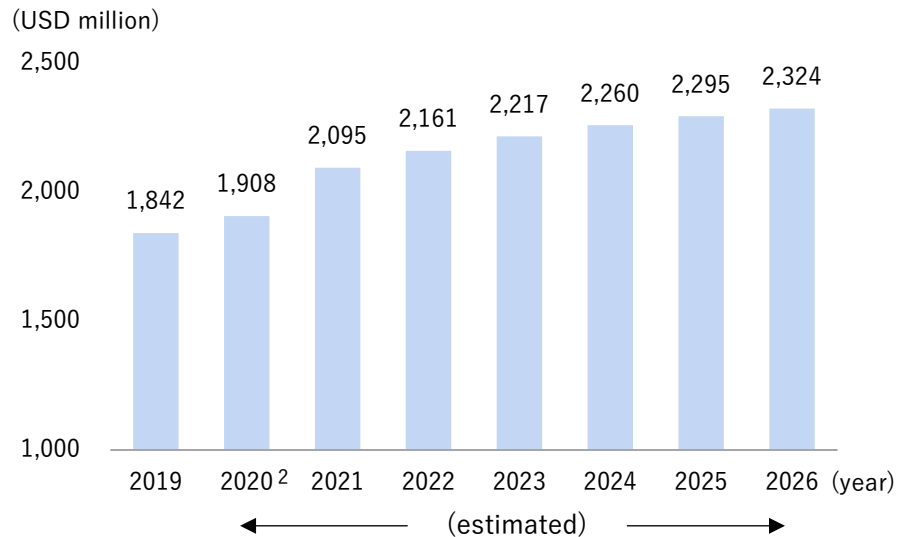
1. Datamonitor Healthcare, "Stroke Epidemiology", Ref Code:DMKC0201444, Published on 07 January 2019  
 2. 5 European countries are composed of five major countries: Germany, France, Italy, Spain, and United Kingdom  
 3. Centers for Disease Control and Prevention, "National Vital Statistics Reports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

No drug has been approved since 1996 in the US

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

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



## Challenges of the existing drug

Incidence rate of fatal intracranial hemorrhage <sup>3,5</sup>



Mortality <sup>4,5</sup>



- 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** <sup>6</sup>

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

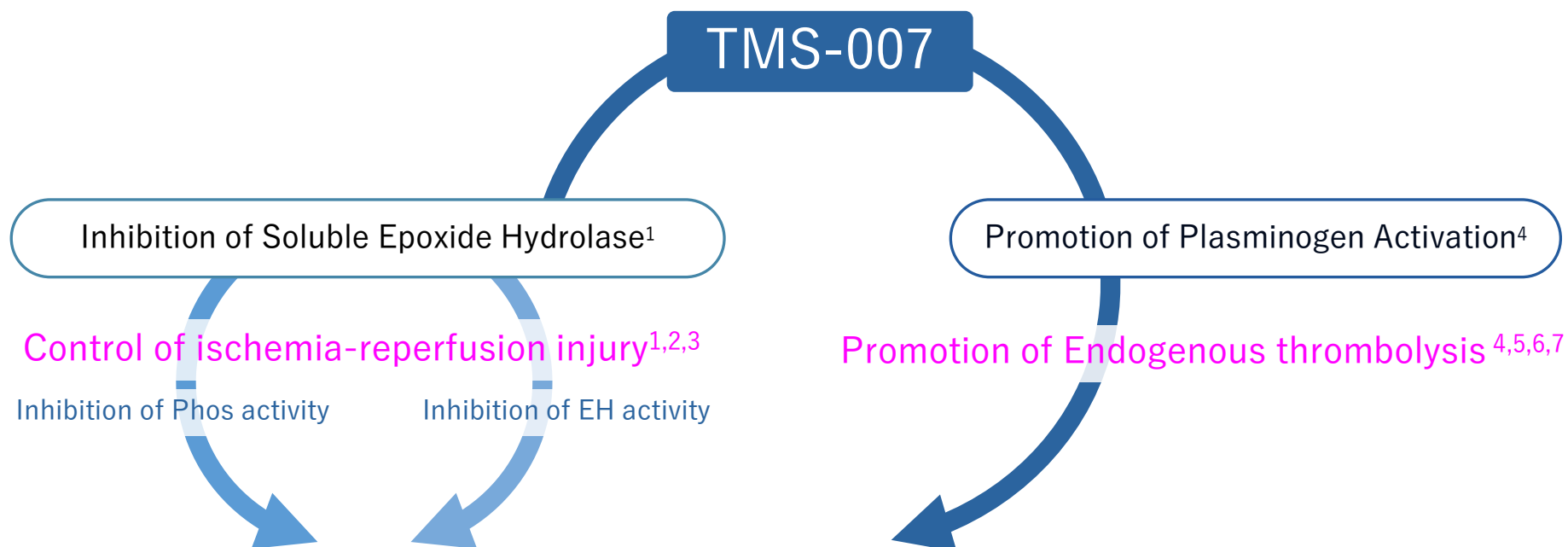
3. Incidence rate at 7 days

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

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



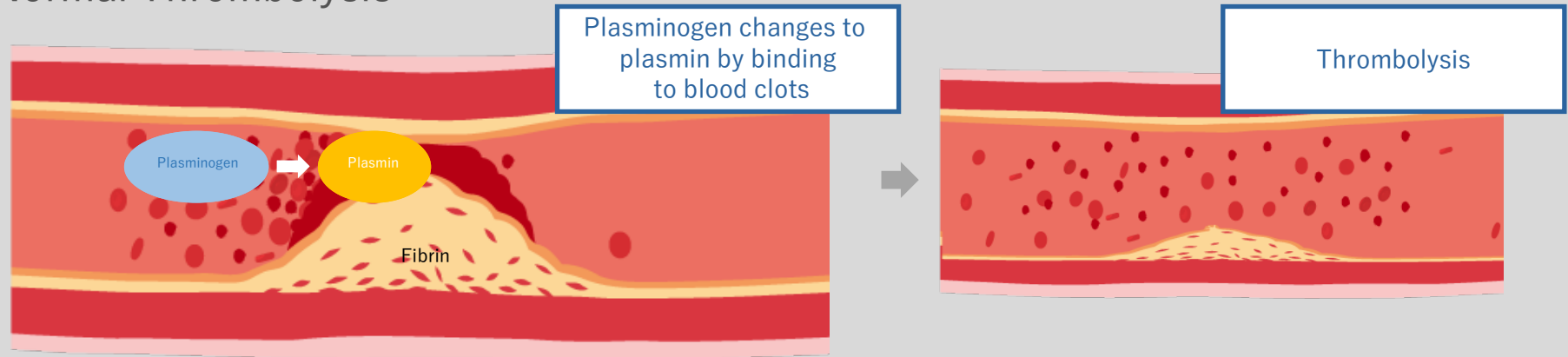
Our SMTP-based small molecule analogues with unique therapeutic properties

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

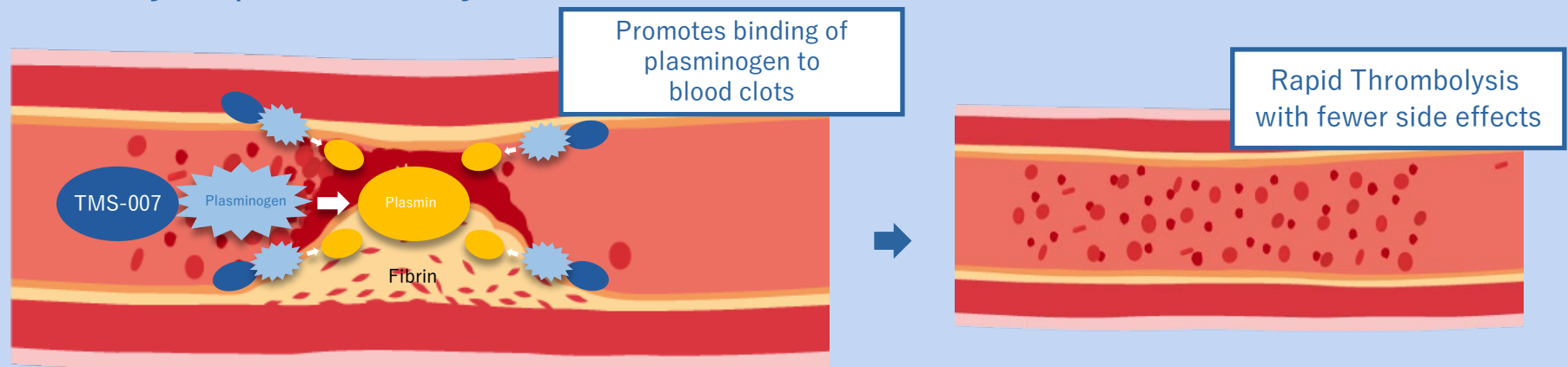
Ideal profile for treatment of acute ischemic stroke

1. Matsumoto et al. (2014) J Biol Chem
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

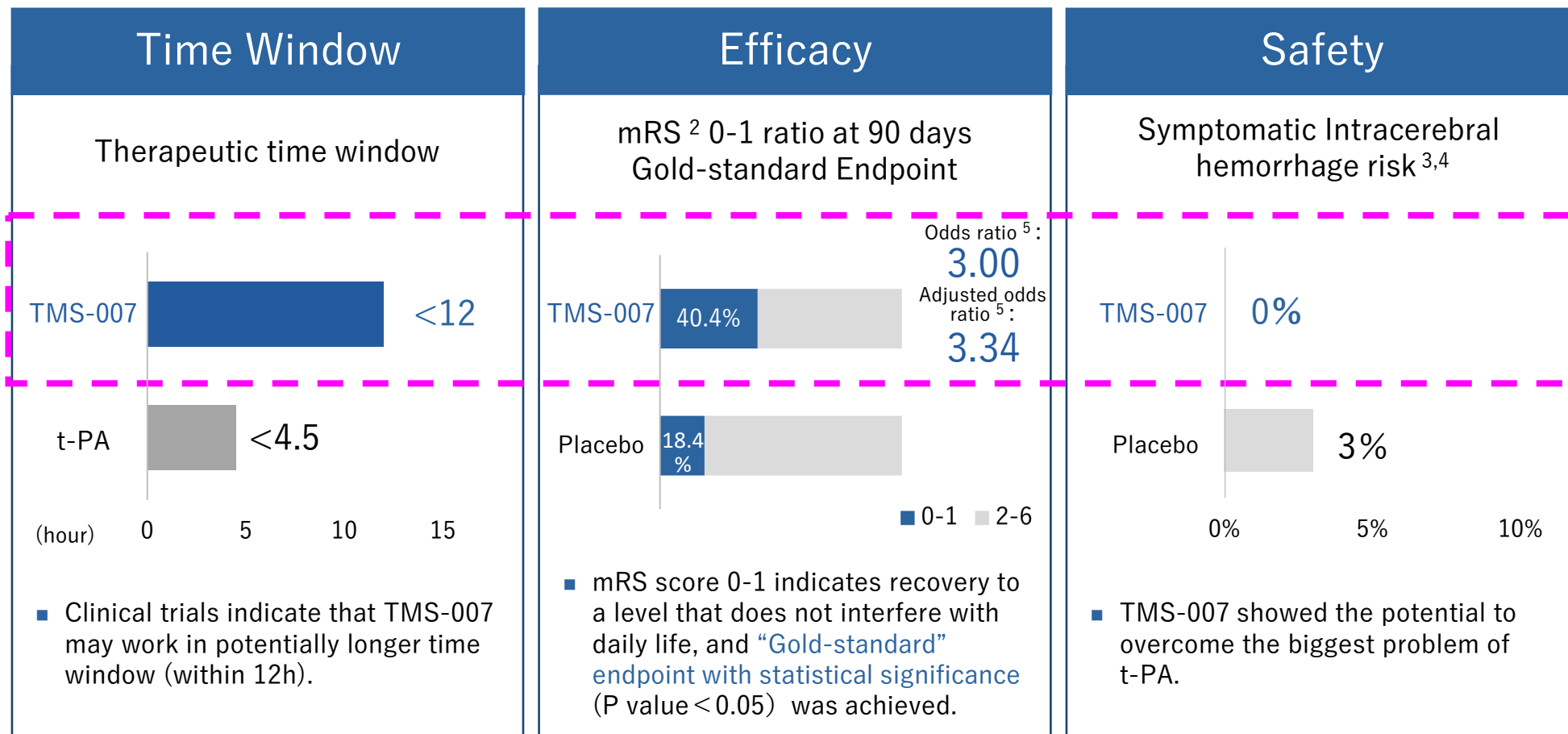
## Normal Thrombolysis



## Thrombolysis promotion by administration of TMS-007



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



1. The data comparisons above are not based on head-to-head clinical studies.

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)

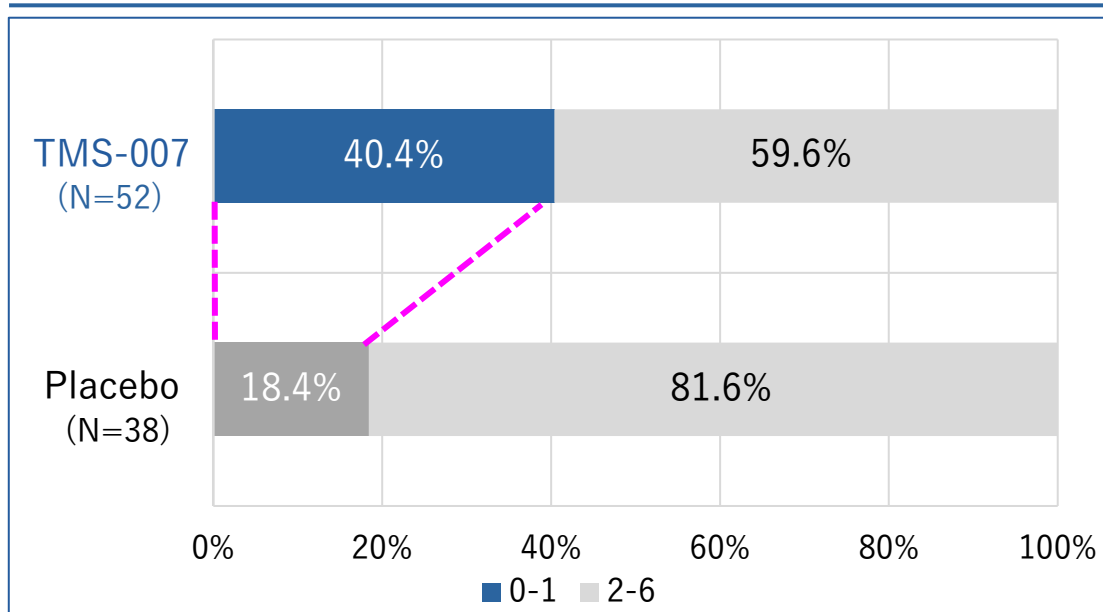






TMS-007 achieved statistically significant improvement on mRS 0-1 ratio at 90 days, one of the most important indicators

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

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

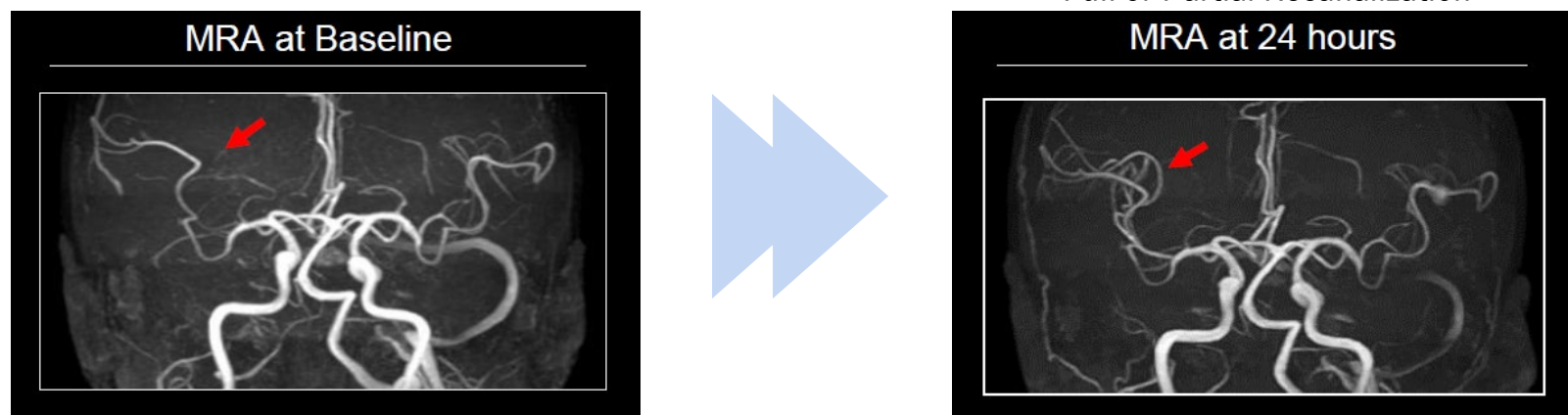
mRS 0-1 ratio at 90 days<sup>1</sup>



| mRS (modified Rankin Scale)   |   |   |
|---|---|---|
|    | 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   |

TMS-007's promising efficacy is potentially backed by good recanalization outcome <sup>1</sup>

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



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

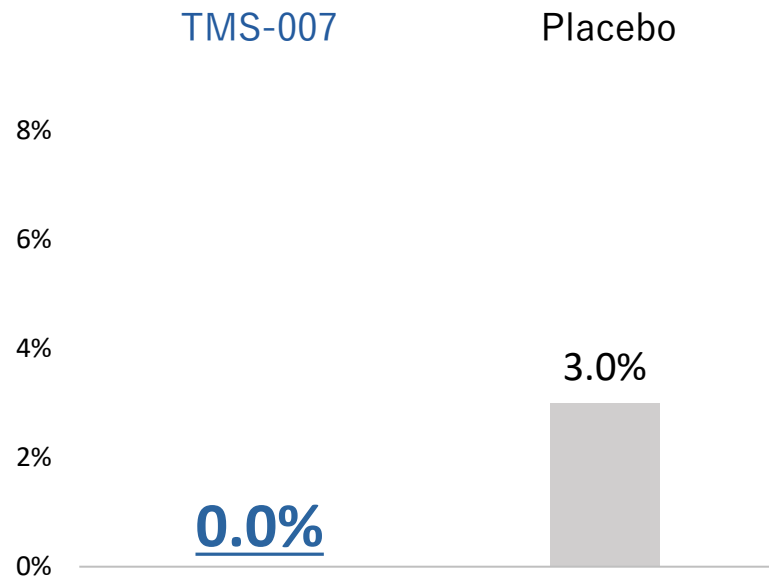
|   | Placebo Pooled | TMS-007 Pooled |
|---|----------------|----------------|
| Number of patients (N)                      | 15 (100)       | 24 (100)       |
| Number of patients with recanalization      | 4 (26.7)       | 14 (58.3)      |
| Estimate of odds ratio (TMS-007 vs placebo) | -       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

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

## Incidence rate of sICH<sup>1</sup>

### TMS-007 vs Placebo <sup>2</sup>

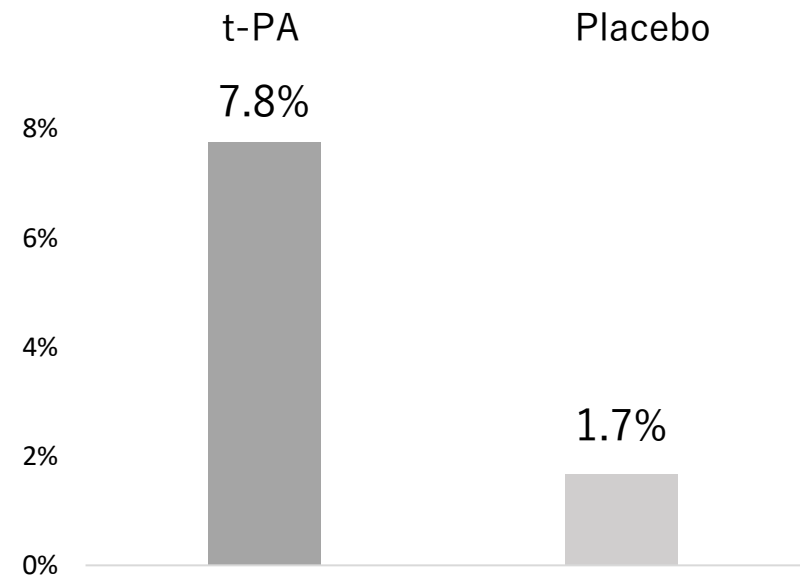
Ph2a



| N                | 52                | 38                |
|------------------|-------------------|-------------------|
| Prehospital time | 9.5h<br>(Average) | 9.3h<br>(Average) |

### t-PA vs Placebo <sup>3</sup>

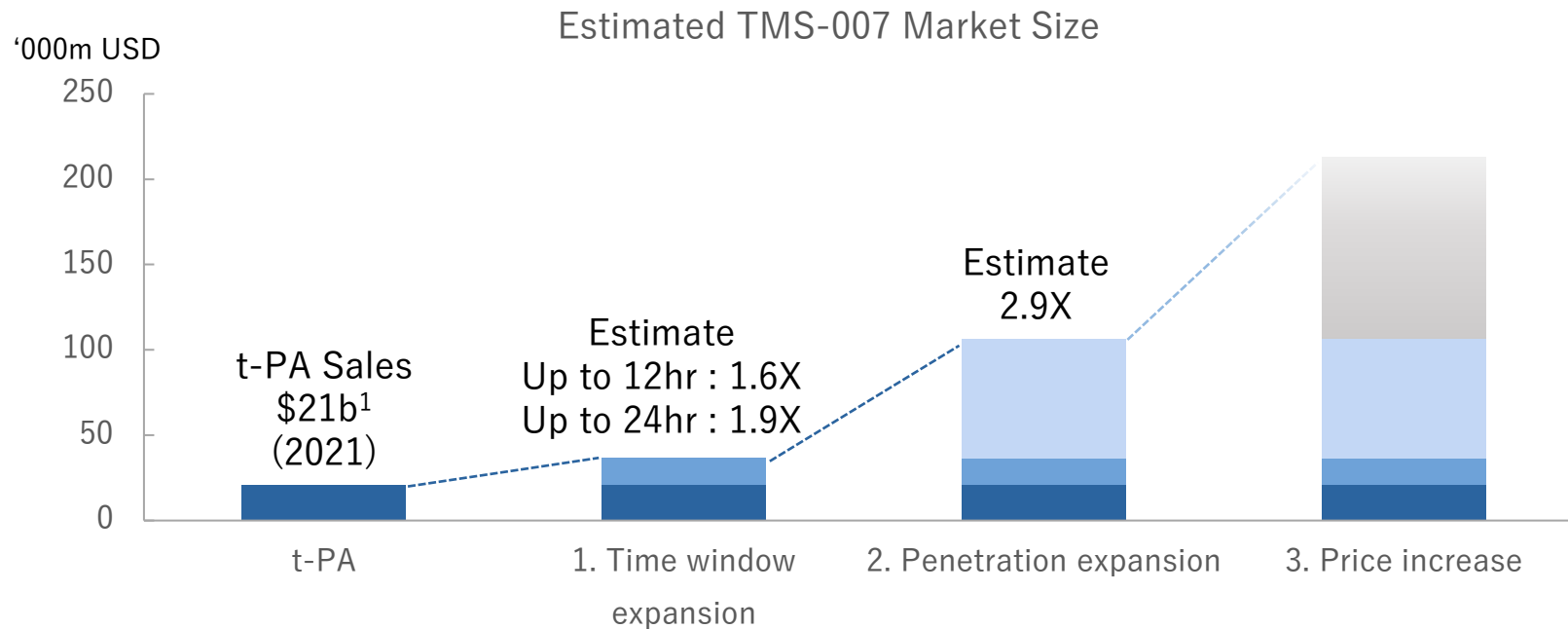
Meta-analysis



| N                | 3,384     | 3,330 |
|------------------|-----------|-------|
| Prehospital time | Within 6h |       |

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

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



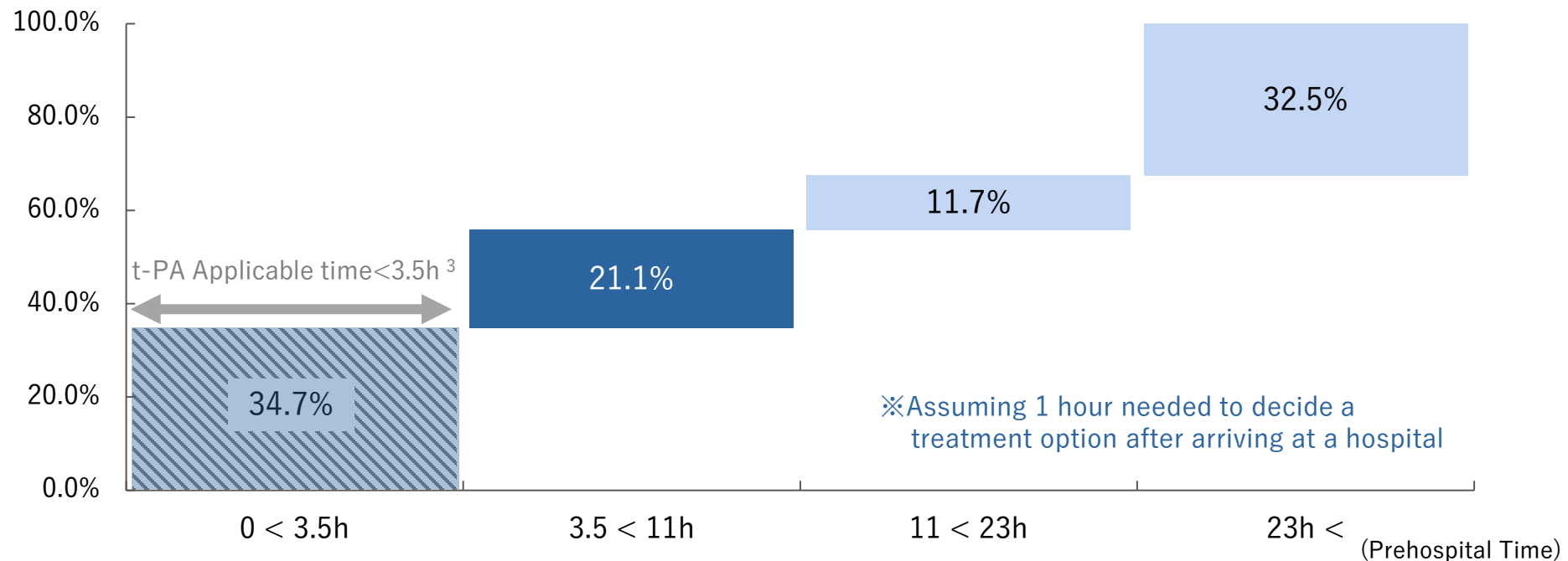
1. Possibility to expand time window after onset (12hr or 24hr)
2. Possibility to expand penetration due to excellent safety
3. Possibility to claim higher pricing if higher efficacy and safety than t-PA are achieved

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

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

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

(Percentage of patients <sup>1</sup>)



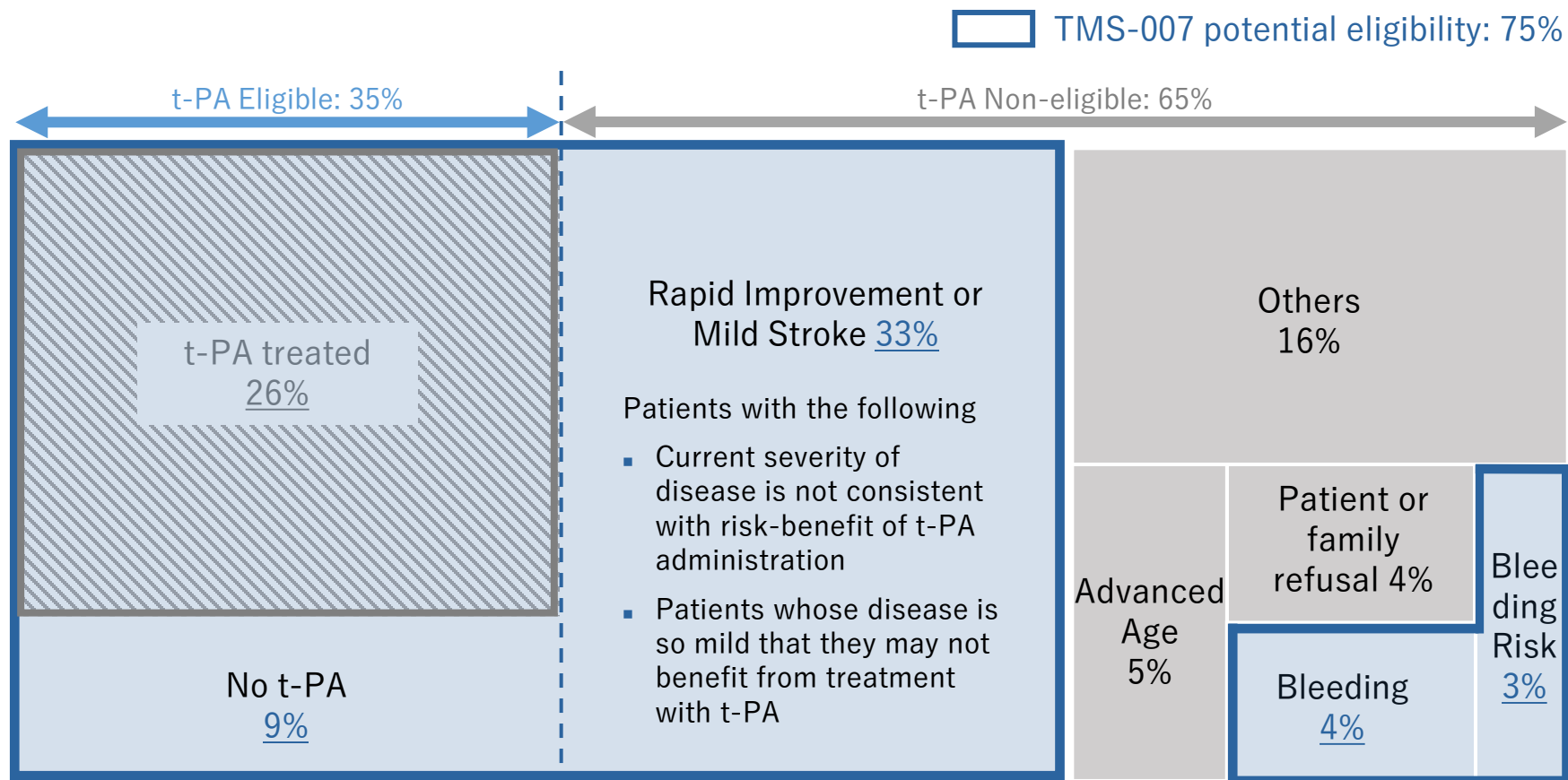
1. TMS assumption using average breakdown of patients by prehospital time based on the following papers. Please note that the company's estimate above is based on various assumptions and beliefs stated herein, including the available dose window, disregard certain significant conditions such as the eligibility of the patients and may not be supported by any clinical data;  
 Tong et al. (2012), "Times From Symptom Onset to Hospital Arrival in the Get With The Guidelines-Stroke Program 2002 to 2009"  
 Harraf (2002), "A multicenter observational study of presentation and early assessment of acute stroke"  
 Kim (2011), "Stroke awareness decreases prehospital delay after acute ischemic stroke in Korea"  
 Matsuo (2017), "Association Between Onset-to-Door Time and Clinical Outcomes After Ischemic Stroke"

2. Expansion of time window over 12 hours (maximum 24 hours) is based on the registered and published 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



How t-PA is treated for patients arriving within 2 hours from symptom onset <sup>1</sup>

- 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"

JX09

Resistant or uncontrolled  
hypertension

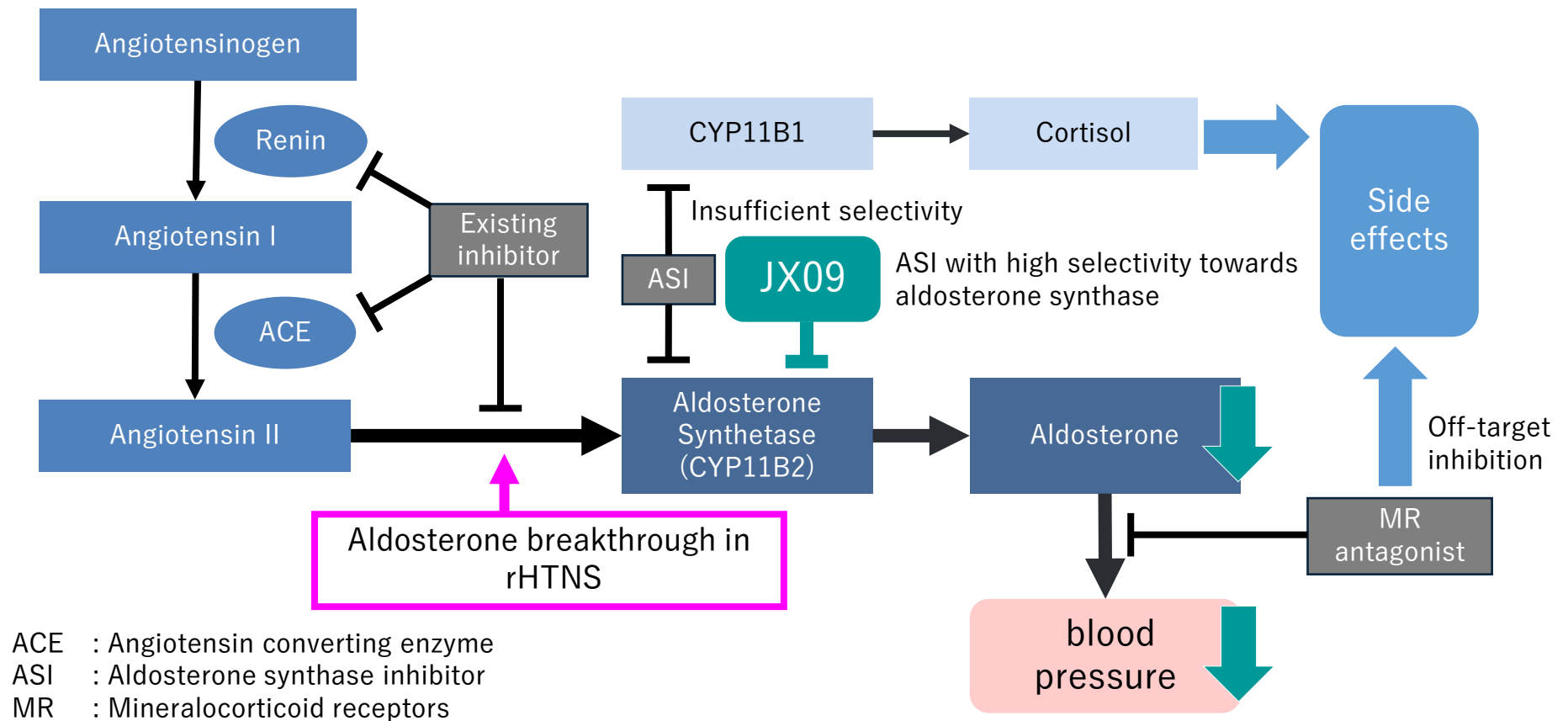


- Therapeutic candidate for “resistant/uncontrolled hypertension” (rHTN), a condition with high unmet medical needs
- 10-20% of treated hypertension patients are believed to be resistant<sup>1</sup>.
- Oral, small molecule aldosterone synthesis inhibitor (ASI)
- Highly selective inhibition of aldosterone synthase (CYP11B2) over structurally similar CYP11B1 is crucial for effective ASI. JX09 has very high selectivity.
  - ▣ > 300 fold selectivity for CYP11B2 over CYP11B1 (*in vitro*), suggesting selectivity higher than baxdrostat (<100 fold) <sup>2</sup>
  - ▣ Achieved >90% aldosterone lowering with no increase in CYP11B1 precursor steroids (*in vivo*, non-human primates) <sup>2</sup>
- Phase I clinical trial was initiated in Feb 2024 by JIXING.

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

2. Source JIXING website March 2023 "[JIXING Presents the Latest Research Data of Cardiovascular Asset JX09 at the American College of Cardiology Annual Congress 2023](#)"

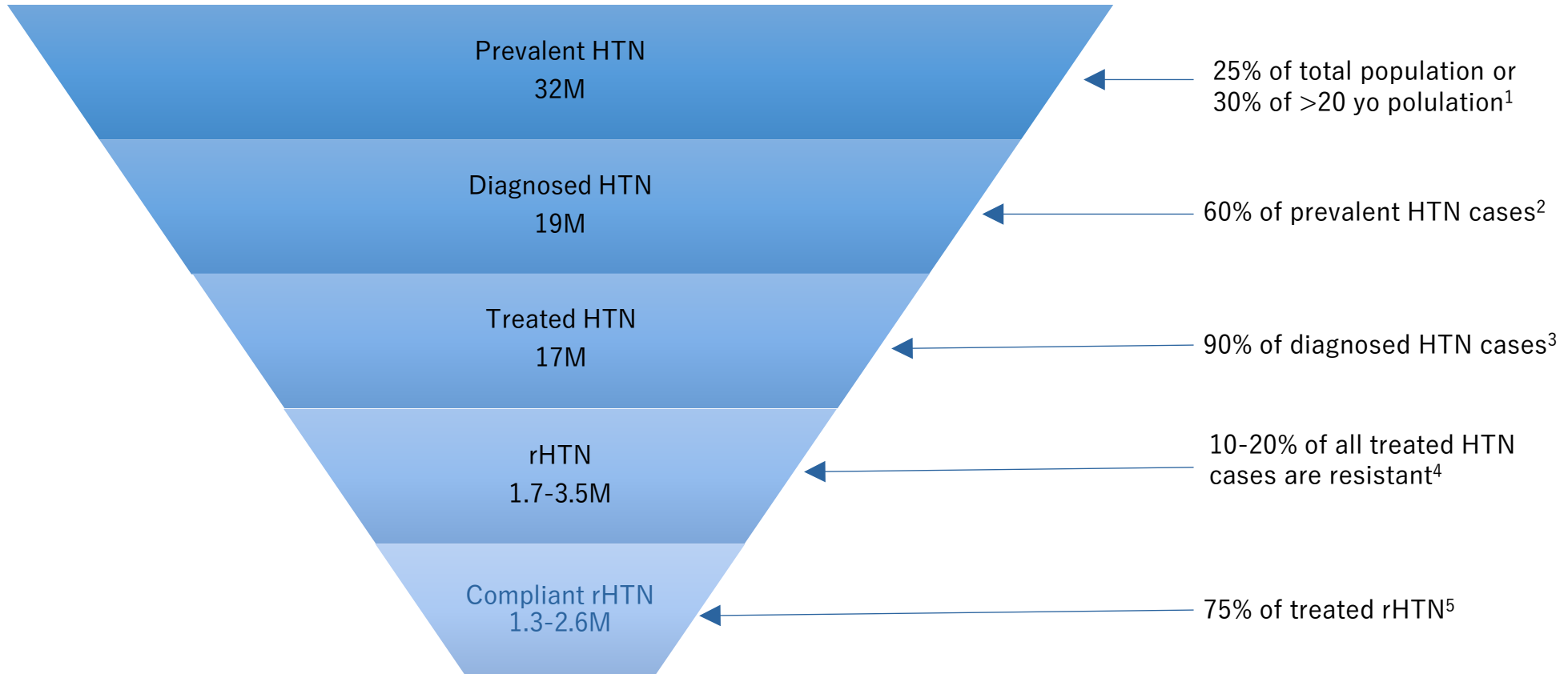
Highly selective inhibition: Inhibits aldosterone synthase (CYP11b2)<sup>1</sup> more selectively than the structurally similar CYP11b1



### Position of aldosterone synthesis inhibitors among hypertension drugs

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

JX09 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).

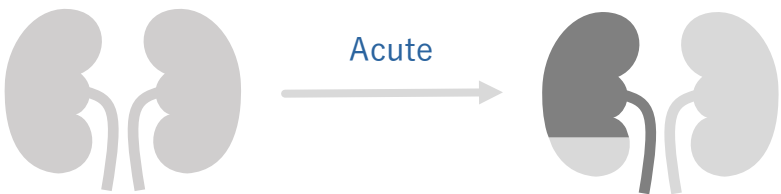
TMS-008

Acute Kidney Injury

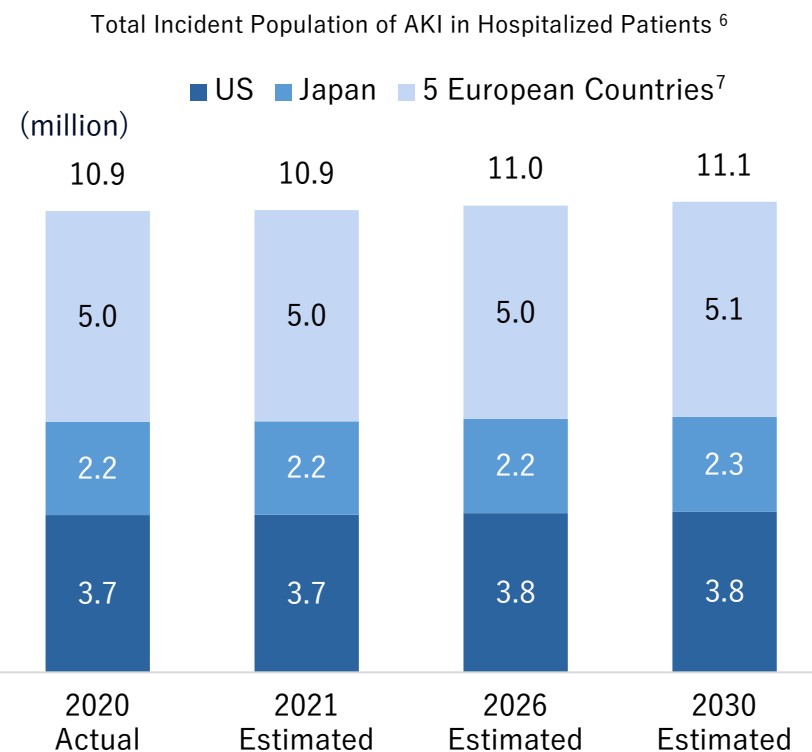




TMS-008 development is directed to take advantage of its strong anti-inflammatory properties

|                    |   |
|--------------------|---|
| Indication         | <p>No protein leakage<br/>Appropriate toxin excretion</p>  <p>Decreased renal function adversely affects heart and other organs</p>   |
| Overview           | <ul style="list-style-type: none"> <li>■ Acute Kidney Injury (AKI) is a rapid decline in renal function over a period of hours to days</li> <li>■ 20-25% mortality rate in hospitalized AKI patients</li> <li>■ AKI causes chronic kidney disease (CKD) and end-stage renal disease (ESRD)</li> </ul> |
| Number of patients | <ul style="list-style-type: none"> <li>■ 5 European countries: ~5,080,000</li> <li>■ United States: ~3,800,000</li> <li>■ Japan: ~2,300,000</li> </ul> <p>(Patients assumptions for year 2030 as of 2020)</p>   |
| Treatment method   | <ul style="list-style-type: none"> <li>■ No approved therapeutic drug <sup>5</sup></li> </ul>   |

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



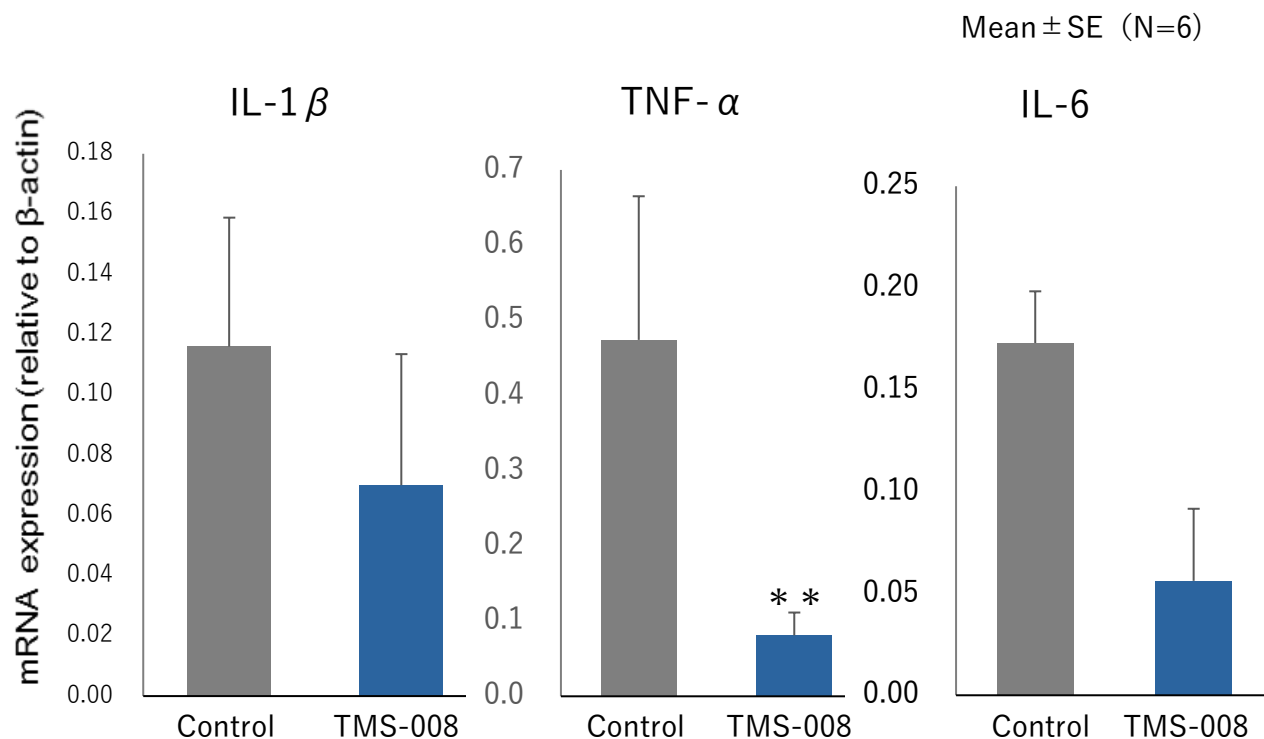
1. Nature Reviews Nephrology volume 16, pages747–764 (2020)  
 2. Adv Chronic Kidney Dis. 2017;24(4):194-204  
 3. Nephron. 2017 ; 137(4):297–301  
 4. Delveinsight, “Acute Kidney Injury - Market Insights, Epidemiology, and Market Forecast—2030”

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 includes Germany, France, Italy, Spain, and the UK

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

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

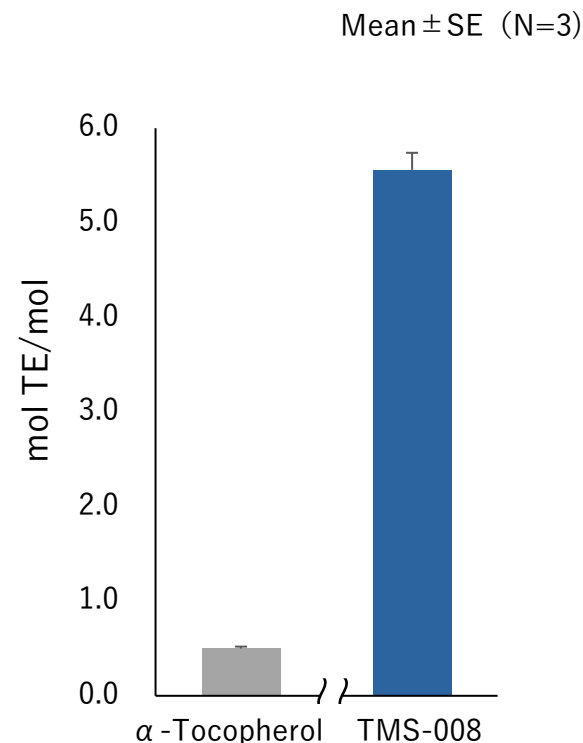
- One hour after the start of ischemia, 10 mg/kg was administered continuously intravenously for 30 minutes. Brain slices at 24 hours were evaluated by RT-PCR method.



\*\* P<0.01, \* P<0.05 (vs. control)

### Antioxidant activity test <sup>1,2</sup>

- H-ORAC : hydrophilic oxygen radical absorbance capacity method



#### References:

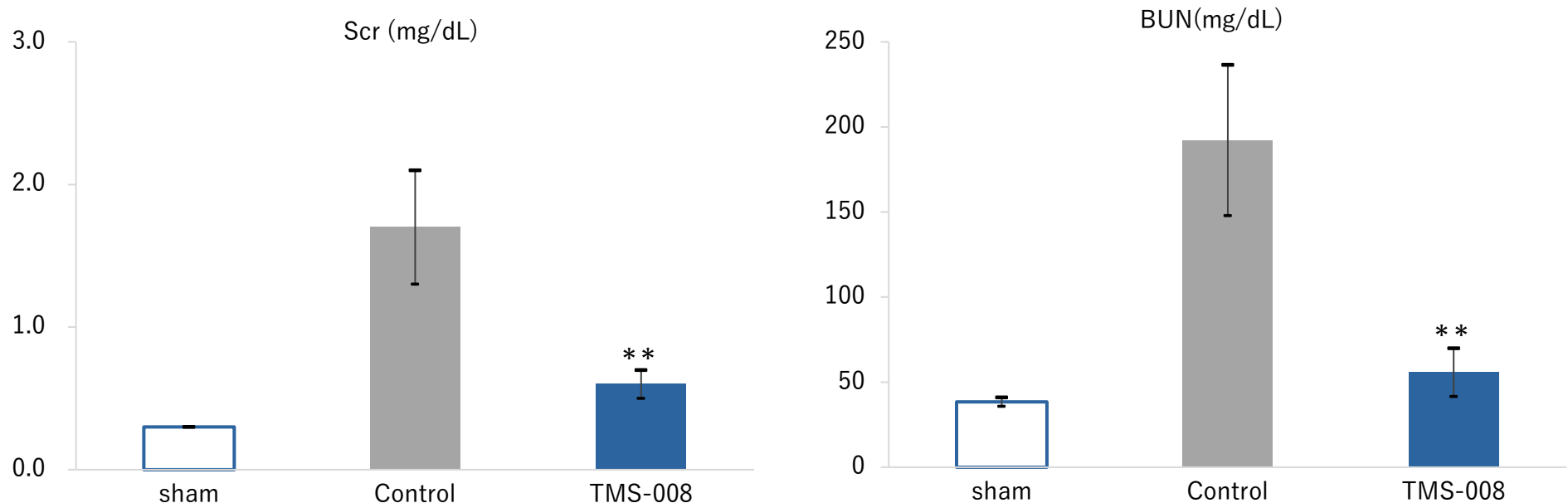
- Shibata et al. (2018) Eur J Pharmacol
- Hasumi & Suzuki (2021) Int J Mol Sci

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

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

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

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

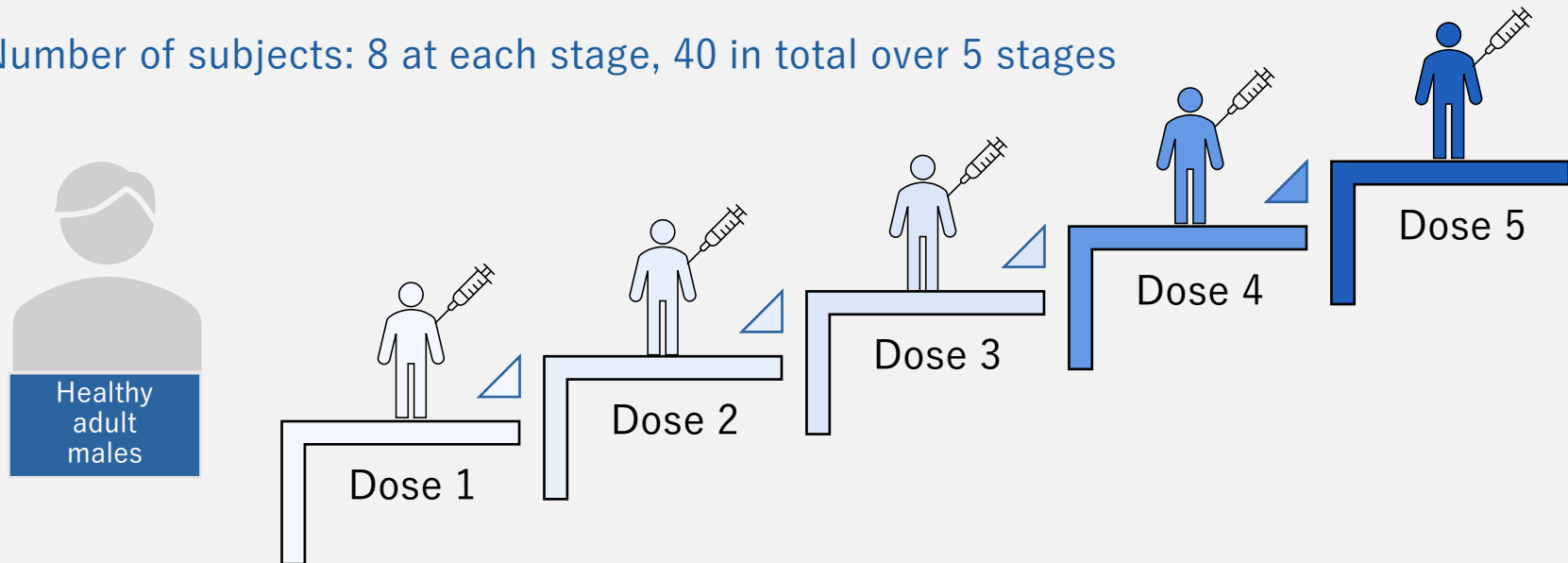


1. Mean  $\pm$  SE (n = 6), \*p value < 0.05 and \*\*p value < 0.01 as compared with control groups by using ANOVA with Bonferroni correction

## Ph1 Clinical Trial Design

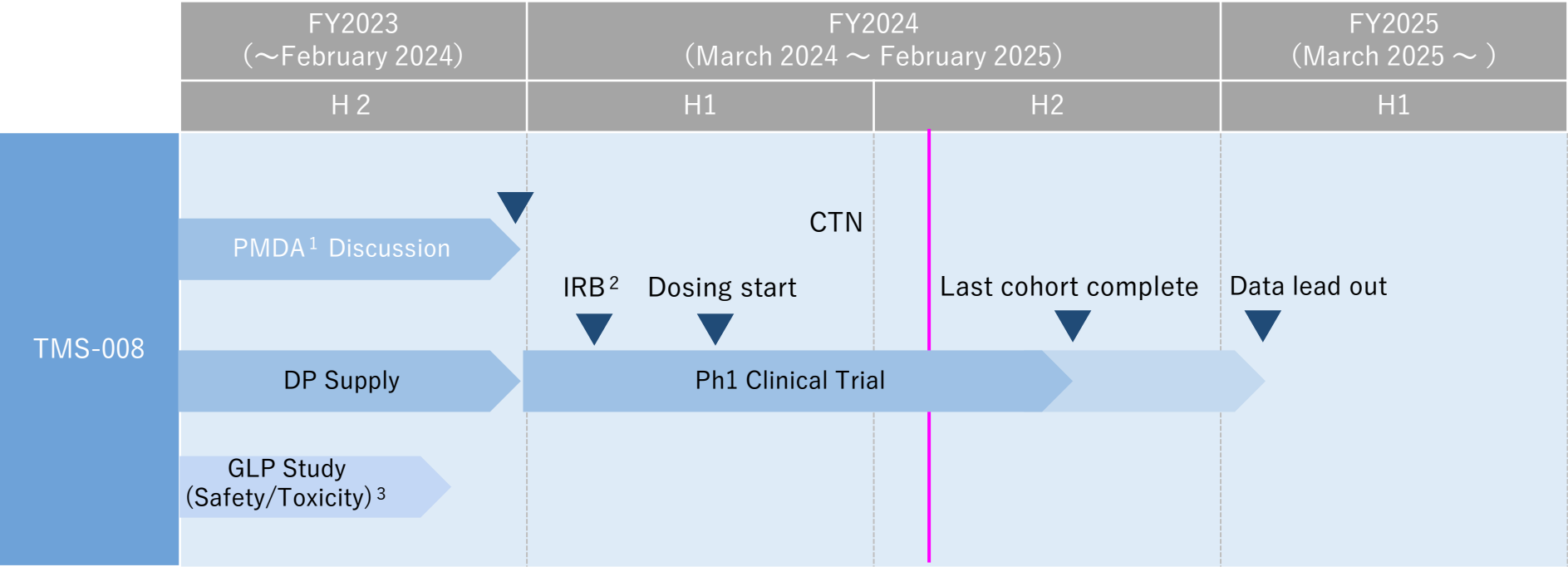
- ◆ Objective : To confirm pharmacokinetics, tolerability, and safety of a single dose of TMS-008 administered to a healthy adult male as a First-In-Human study
- ◆ Design : Randomized, placebo-controlled, double-blind, dose-escalation, single-dose study

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.

Ph1 clinical trial was initiated in the first half of FY2024  
Future plan : All cohorts administered and observed by the end of FY2024  
Data read-out in the first quarter of FY2025



Now here

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

1. PMDA refers to Pharmaceuticals and Medical Devices Agency

2. IRB refers to Institutional Review Board

3. GLP refers to Good Laboratory Practice

# Expansion of Pipeline



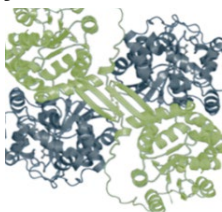
Pursue internal and external paths for pipeline expansion, leveraging knowledge and experience through SMTP compounds development



R&D and business development capabilities cultivated through SMTP compounds

## Internal projects

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



Human sEH

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

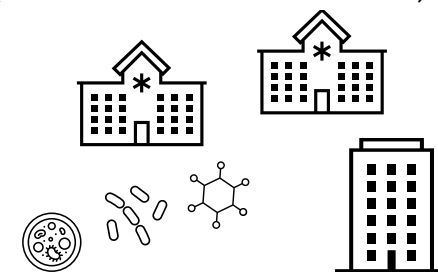
Program acquisition

Collaborative research

Deploy

Licensing, etc.

## External projects (Academia and others)



## Global Market

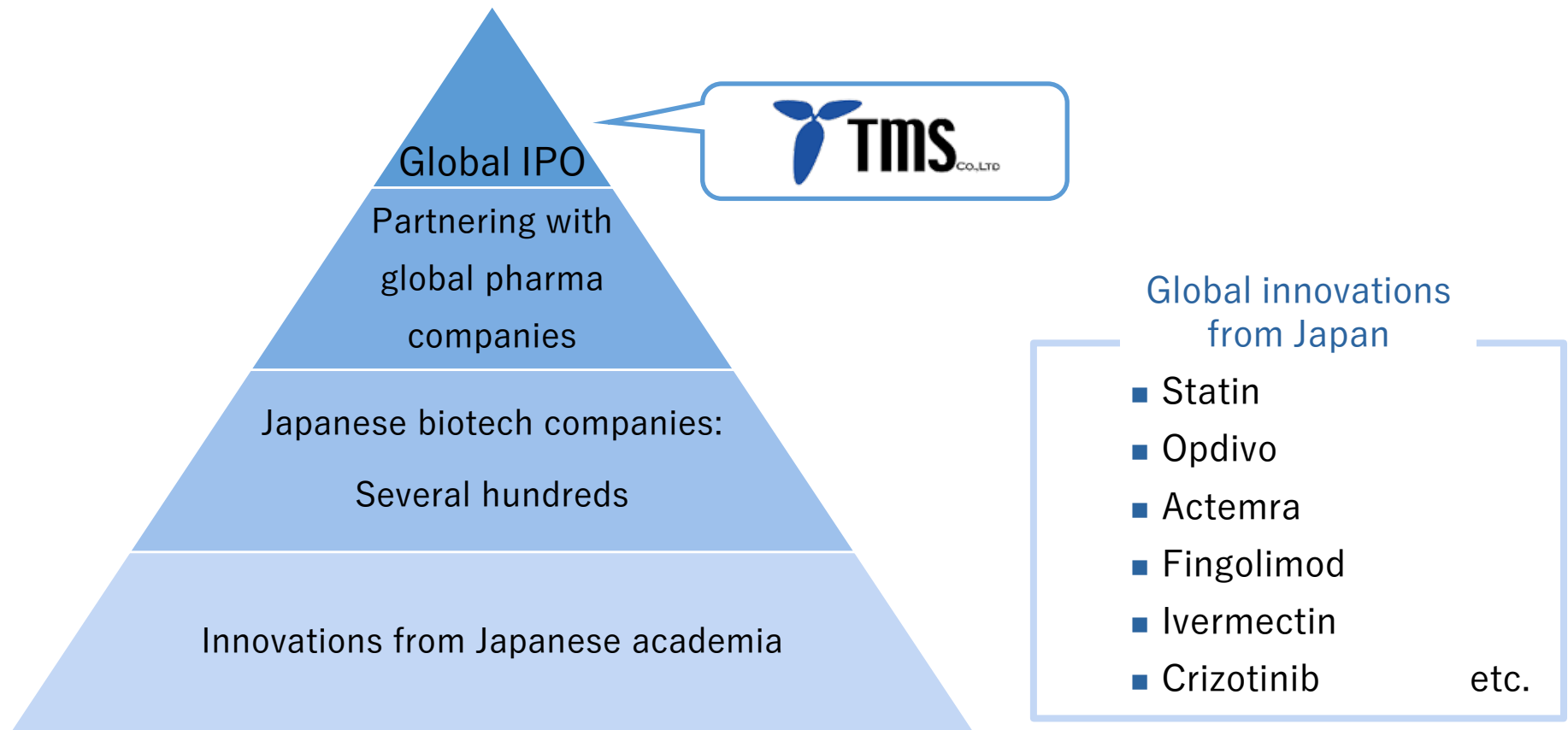


\* Global market is >10 times larger than Japanese market



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

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

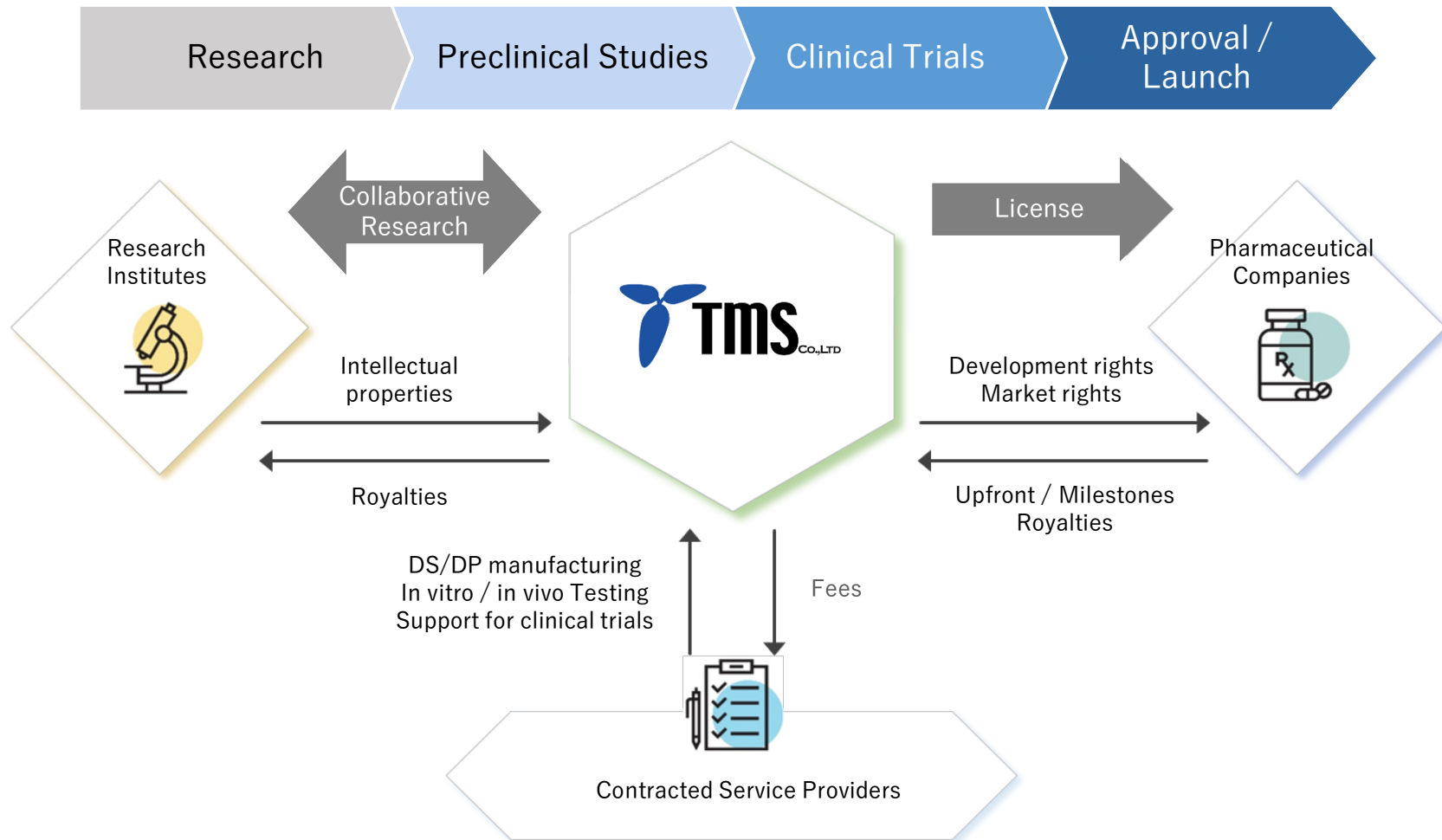


# Appendix



|                          |  |
|--------------------------|--|
| Name                     | TMS Co., Ltd.<br>(Stock Code: 4891)                            |
| Established              | February 17, 2005  |
| Closing month            | February   |
| Representative Directors | Takuro Wakabayashi<br>Chief Executive Officer                  |
| Address                  | Headquarters:<br>1-9-11F, Fuchu-cho, Fuchu-shi, Tokyo<br>JAPAN |
| Business Field           | Research and development of drug products                      |
| Management               | Board Member: 6<br>Audit & Supervisory Board Member: 4         |
| Number of employee       | 14 (as of February 31, 2024)                                   |

|             | 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 |
| Nov. 2011   | Started IND-enabling study of TMS-007  |
| Aug. 2014   | Started Phase I clinical trial of TMS-007  |
| Oct. 2015   | Completed Phase I clinical trial of TMS-007  |
| Nov. 2017   | Started phase IIa clinical trial of TMS-007 for ischemic stroke patients   |
| Jun. 2018   | Option agreement with Biogen on TMS-007  |
| May. 2021   | Biogen exercised an option to acquire TMS-007  |
| Aug. 2021   | Completed phase IIa clinical trial of TMS-007  |
| Nov. 2022   | Listing on the Tokyo Stock Exchange Growth Market (Stock code: 4891)   |
| Jan. 2024   | Biogen transferred TMS-007 rights to JIXING<br>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)   |



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

## 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.

Identification of SMTP compounds as modulators of plasminogen

TMS-007  
Launched Ph1 clinical trial in Japan

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

TMS-007  
Completed Ph2a Clinical Trial

TMS-008  
Started administration of Ph1 clinical trial

TMS-007  
Started CTN-enabling study

TMS-007  
Completed Ph1 Clinical Trial

TMS-008  
Started CTN -enabling study

TMS-008  
CTN-Submission

1990s 2005 FY2011 FY2014 FY2015 FY2017 FY2018 FY2020 FY2021 FY2022 FY2023 FY2024

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

Spinoff from Tokyo University of Agriculture and Technology

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

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

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

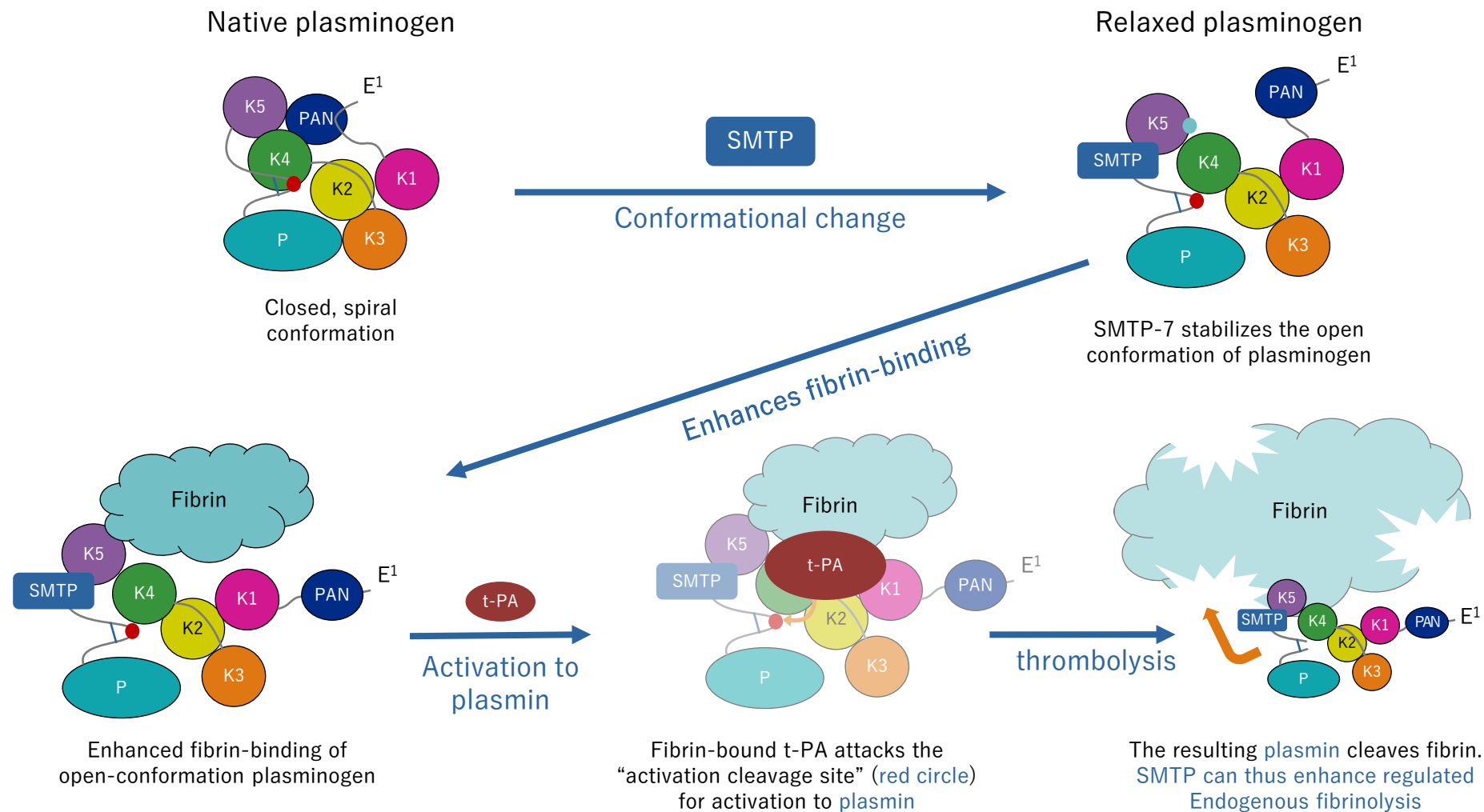
Transferred all IP and assets related to TMS-007 and SMTP to Biogen.

Rights transferred from Biogen<sup>1</sup> to JIXING

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

1. The contract party is Biogen MA Inc.

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



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](http://www.tms-japan.co.jp)