TMS Co.,LTD

TSE Growth：4891

2Q FY02/2024 Financial Results

(Six months ended August 31,2023)

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Create impactful therapeutics by the power of relentless exploration and challenge

Agenda

1. Topics
2. Summary of Financial results for 2Q FY02/2024(6M)
3. TMS-007
4. TMS-008 / 009
5. Expansion of Pipelines
6. Appendix

Topics

Topics

1 TMS-007 (BIIB131)

Timeline

- Mar 10, 23 Outline of Ph2b trial was registered at ClinicalTrials.gov (estimated start date Apr 17)
- Apr 25, 23 Biogen announced it would pause and re-examine initiation of the Ph2b trial
- Apr 27, 23 Registered information at ClinicalTrials.gov was updated (estimated start date updated to Aug 21)
- Jul 25, 23 Biogen's 2Q financial results earnings call
  BIIB131 continued to be listed on the pipeline table without a specific comment
- Jul 27, 23 Registered information at ClinicalTrials.gov was updated (estimated start date updated to Dec 1)

- TMS continues to collect information through various communication lines
- Preparing for three possible scenarios
  1. Biogen moves forward to develop TMS-007/BIIB131
  2. Biogen terminates development
  3. Biogen to transfer/license/joint-develop the asset with a third party

✓ Contacted by several third parties, pending until Biogen's decision

1 TMS-007 (BIIB131)

Recent development of Biogen with new CEO

- November 2022 — Mr. Chris Viehbacher appointed as new CEO
- April 2023 — BIIB093 (large hemispheric infarction) terminated
  BIIB093 (brain contusion) terminated
  BIIB132 (spinocerebellar ataxia) terminated
  Ophthalmology field withdrew
  BIIB131 (acute ischemic stroke) paused
- July 2023 — LEQEMBI (Alzheimer's disease) officially approved by FDA
  BIIB122 (Parkinson's disease) terminated
  Announced headcount reduction of approximately 1,000
  Announced acquisition of Reata Pharmaceuticals, Inc. ($7.3 billion)
- October 2023 — Jane Grogan, Ph.D. appointed as Head of Research

2 TMS-008

- Making progress to initiate Ph1 clinical trial by the end of this fiscal year
  - Planned IND Application (PMDA) 4Q this fiscal year and completion of the Ph1 trial during the next fiscal year

3 Pipeline expansion

- Efforts to expand pipeline continue utilizing both internal and external sources. Internal projects leverage our expertise combined with external chemical libraries.

Internal projects

- New indications for TMS-008
- sEH inhibitors
- Natural product screening

Exploring external library

- Initiated evaluation of an external compound library (October 2022)
- Entered joint research agreement with the Microbial Chemistry Research Foundation (June 2023)

External projects

Option agreements with Hokkaido University

- Project 1 (July 2022)
- Project 2 (May 2023)

Summary of Financial Results

FY02/2024.2Q(6M)

Financial Results FY02/2024.2Q(6M)- Statement of Income

Although one-time non-operating expenses were recorded due to the preparation for the stock listing in the same period of the previous fiscal year, no one-time expenses were recorded in this Q2 FY02/2024, resulting in a smaller loss in both ordinary income and net income

(million of yen)

	Q2(YTD) FY02/2023	Q2(YTD) FY02/2024	Change(YoY)	
Operating revenue	-	-	-	-
Operating expenses	268	345	76	28.5%
Research and development expenses	151	213	62	41.1%
Operating income	(268)	(345)	(76)	-
Non-operating income	0	3	3	-
Non-operating expenses	200	0	(200)	(99.8%)
Ordinary income	(469)	(342)	126	-
Net income	(468)	(342)	125	-

YoY increased mainly due to the recording of expenses for TMS-008 Ph1 trial

IPO-related expenses were recorded in the Q2 FY02/2023

Expected expenses for FY02/2024

(million of yen)

Research and Development expenses	500 - 800
Other selling, general and administrative expenses	350 - 450

R&D expenses are mainly for;
- Development of TMS-008
- Research activities for pipeline expansion
- Introduction of external assets

Financial Results FY02/2024.2Q(6M)- Cash flows

Cash and cash equivalents at end of period increased 1,254 million yen from the same period of the previous fiscal year due to the issuance of new shares with IPO in November 2022

(million of yen)

	Q2(YTD) FY02/2023	Q2(YTD) FY02/2024
Cash flows from operating activities	(364)	(336)
Income before income taxes	(469)	(342)
Cash flows from investing activities	(6)	(1)
Cash flows from financing activities	(233)	1
Income from the issuance of shares	(233)	-
Net (decrease) increase in cash and cash equivalents	(604)	(336)
Cash and cash equivalents at beginning of period	2,598	3,584
Cash and cash equivalents at end of period	1,993	3,248

Financial Results FY02/2024.2Q(as of Aug. 31)- Balance sheet

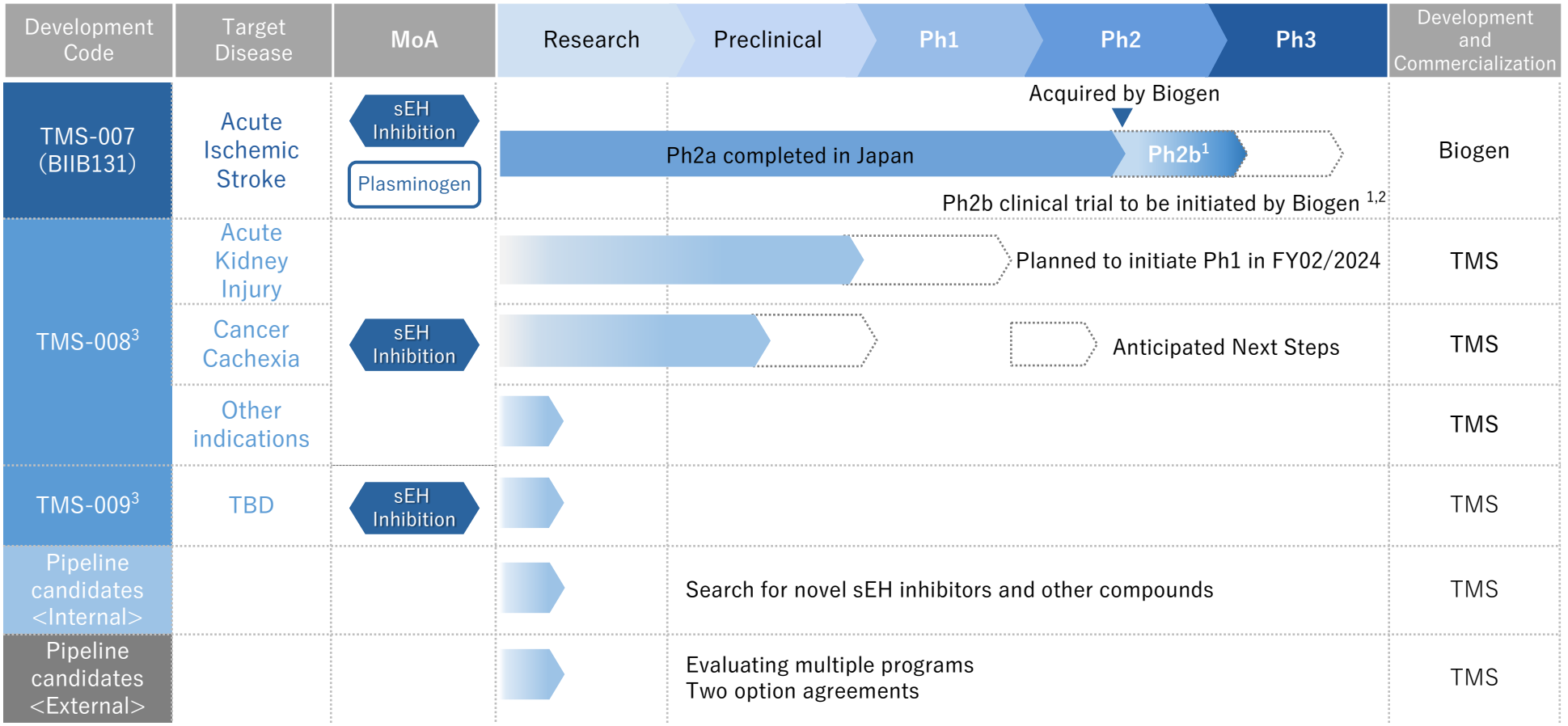
No operating revenue was recorded in Q2 FY02/2024, resulting in decreases in both total assets and total net assets

(million of yen)

	FY02/2023 (as of Feb. 28)	Q2 FY02/2024 (as of Aug. 31)	Change(YTD)	
Current assets	3,766	3,415	(350)	(9.3%)
Cash and deposits	3,584	3,248	(336)	(9.4%)
Non-current assets	23	21	(1)	(7.7%)
Total assets	3,790	3,437	(352)	(9.3%)
Current liabilities	76	61	(14)	(19.6%)
Non-current liabilities	-	-	-	-
Total liabilities	76	61	(14)	(19.6%)
Total net assets	3,714	3,376	(337)	(9.1%)
Total liabilities and net assets	3,790	3,437	(352)	(9.3%)

Growing and Differentiated Drug Pipeline

TMS-007 Ph2a completed: TMS-007 (BIIB131) is the lead pipeline which was acquired by Biogen
TMS-008 Preclinical stage: Being developed by TMS under grant-back license from Biogen



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. Biogen has registered and published detailed clinical trial information in ClinicalTrials.gov on March 10, 2023. ： https://www.clinicaltrials.gov/study/NCT05764122?cond=BIIB131&checkSpell=false&rank=1
   Biogen has announced to pause initiation of Phase 2b clinical trial and reassess whether to initiate the trial at its Q1 2023 Earnings Presentation on April 25, 2023.
2. Our development rights for TMS-008 and TMS-009, which are being developed under a free license from Biogen, are limited to certain indications, and TMS-009 is a backup compound for TMS-008.

TMS-007

Potential Next Generation Acute Ischemic Stroke Treatment

Lecture requests on SMTP focusing on TMS-007

■ The 38th Interactive Seminar for Novel Medicinal Sciences at The Pharmaceutical Society of Japan

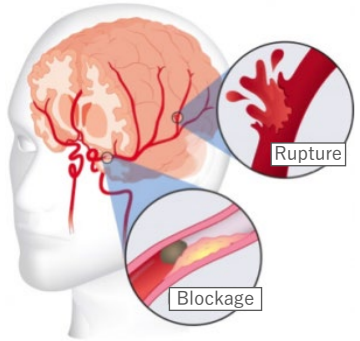
Lecture date	July 14, 2023
Lecturer	Keiji Hasumi, Ph.D., Chief Scientific Officer, Board Member
Lecture title	“Discovery and development of prothrombotic compound SMTP”
Lecture outline	Introduced stages from discovery of SMTP compound family to mechanism of action, pharmacological activity and drug development

■ The 75th Symposium at The Society for Biotechnology, Japan

Lecture date	September 4, 2023
Symposium name	“Synthetic Biology-Facilitated Next Generation Drug Discovery of Engineered Natural Products”
Lecturer	Keiji Hasumi, Ph.D., Chief Scientific Officer, Board Member
Lecturer title	“Discovery of the prothrombotic compound SMTP and its development as a drug for treatment of ischemic stroke”
Lecture outline	Introduced discovery history, mechanism of action and pharmacological activity of SMTP compound including TMS-007 and TMS-008 as well as overview of development of TMS-007 as a drug for treatment of ischemic stroke. Also presented significance of SMTP biosynthetic pathway and biosynthesis, and further to attractivity and possibility of natural product as a drug.

Acute Ischemic Stroke - Important Unmet Medical Needs

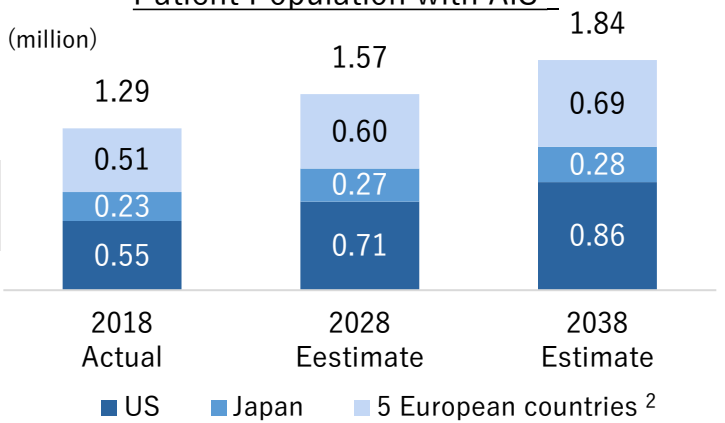
Acute Ischemic Stroke (AIS) Overview



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

Patient Population with AIS [1]

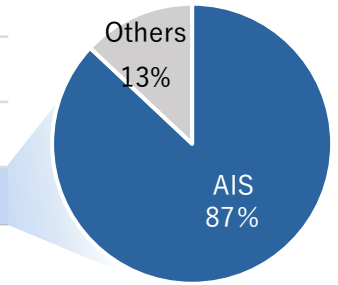


Important Unmet Medical Needs

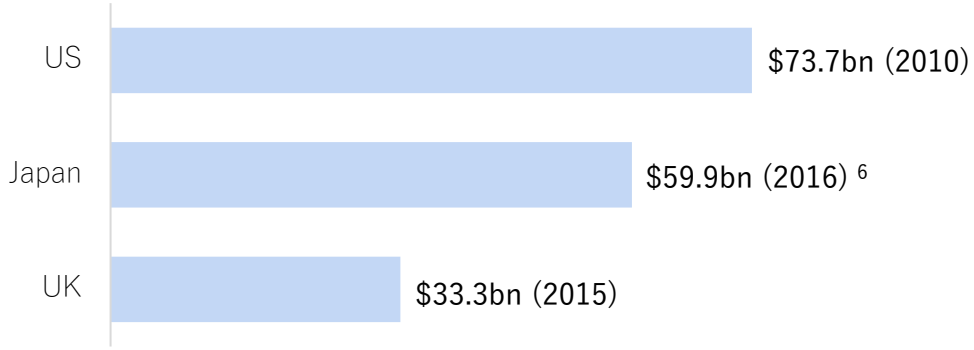
Cause of death in the US (2019) [3]

#	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]



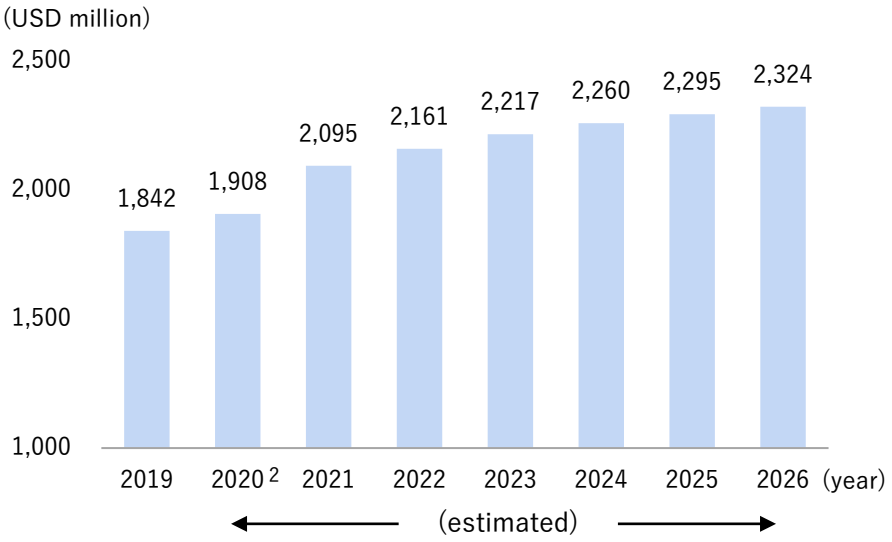
1. Datamonitor Healthcare, "Stroke Epidemiology", Ref Code:DMKC0201444, Published on 07 January 2019
2. 5 European countries are composed of five major countries: Germany, France, Italy, Spain, and United Kingdom
3. Centers for Disease Control and Prevention, "National Vital Statistics Reports volume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

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



Challenges of the existing drug

Incidence rate of fatal intracranial hemorrhage [3,5]

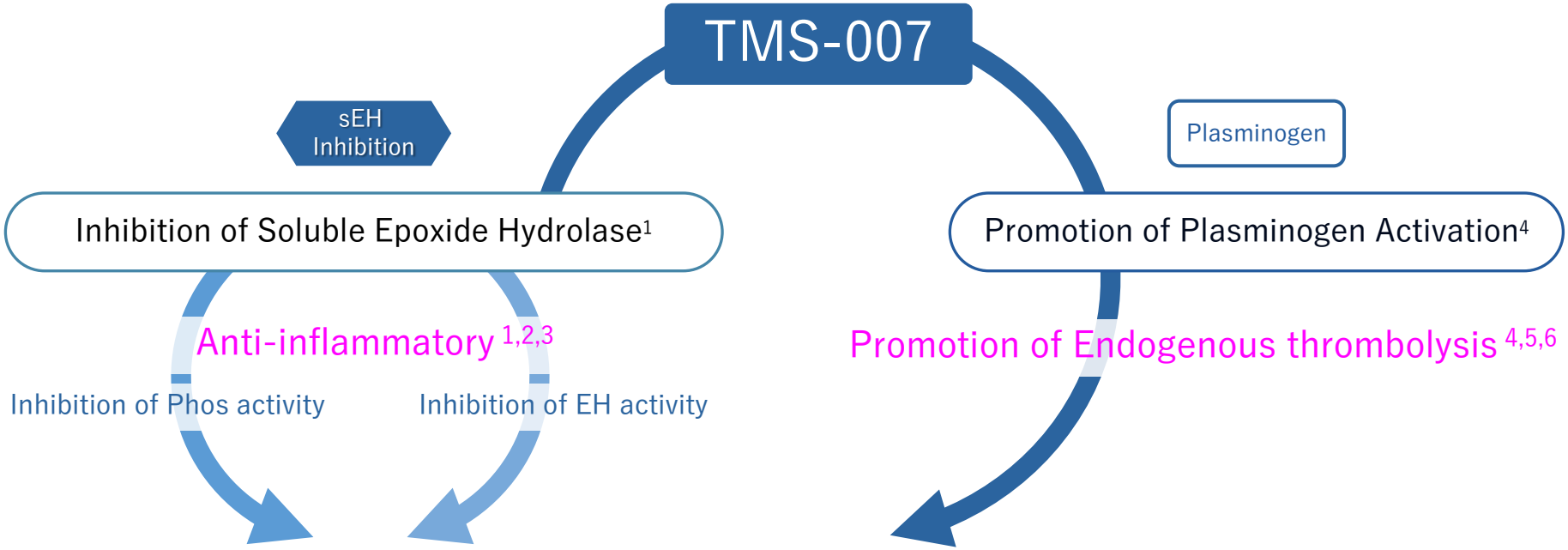
Mortality [4,5]

- 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 – "Anti-inflammatory" and "Thrombolytic" activities



Our SMTP-based small molecule analogues with unique therapeutic properties

Anti-inflammatory and thrombolytic activities

Ideal profile for acute ischemic stroke treatment

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

TMS-007 (BIIB131): Acquired by Biogen, the U.S. Biotech Company

Biogen exercised its option to acquire all IP and assets related to TMS-007 and SMTP compound in May 2021 [1]

Oct, 2015	Nov, 2017	Jun, 2018	May, 2021	Aug, 2021
TMS completed Ph1 Clinical Trial	TMS started Ph2a Clinical Trial	Option Agreement with Biogen Signed	Biogen Exercises Option Rights	TMS Completed Ph2a Clinical Trial

Received

Upfront Payment	Upfront Payment
$4mn	$18mn

Milestone Revenues ~$335mn + Royalties

Next Step [2]	Biogen initiates Ph2b Clinical Trial [3]	Biogen initiates Ph3 Clinical Trial	Biogen completes Ph3 Clinical Trial	・Submit Application for New Drug Approval ・New Drug Approval ＋Insurance Coverage	Sales

Potential Receipt	Potential Receipt	Potential Receipt
Development Milestone $60mn	Development Milestone ~$105mn	Commercial Milestone ~$170mn

Completion of the first dosing of the fifth patient in Ph3 Clinical Trial in US

Phased Royalties on TMS-007 Drug sales [5]
High single-digit ~ low-teens percentages

Biogen MA Inc.

- Parent Company (Biogen Inc.) is listed on NASDAQ (BIIB) with a market capitalization of approx. $37bn [4]
- One of the first global biotech companies in the world
- Primary targets are neurological diseases

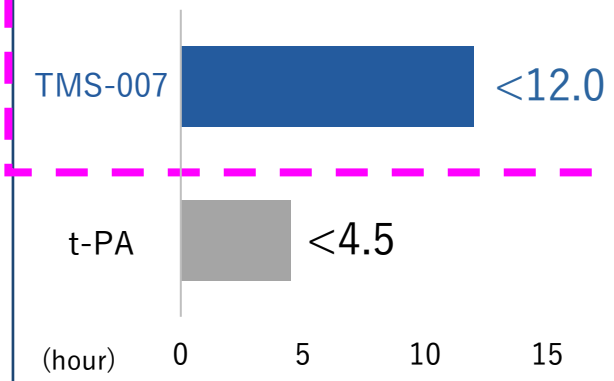
1. TMS and Biogen joint press release (May 12, 2021)
2. All future development, manufacturing and commercialization costs and expenses will be borne by Biogen.
3. Biogen has announced to pause initiation of Phase 2b clinical trial and reassess whether to initiate the trial at its Q1 2023 Earnings Presentation on April 25, 2023.
4. Biogen Inc (BIIB) market capitalization as of September 30, 2023
5. A percentage of worldwide annual sales of TMS-007 (under certain circumstances, payment may decrease due to changes in the cap)

TMS-007: Ph2a clinical trial showed good results

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

Time Window

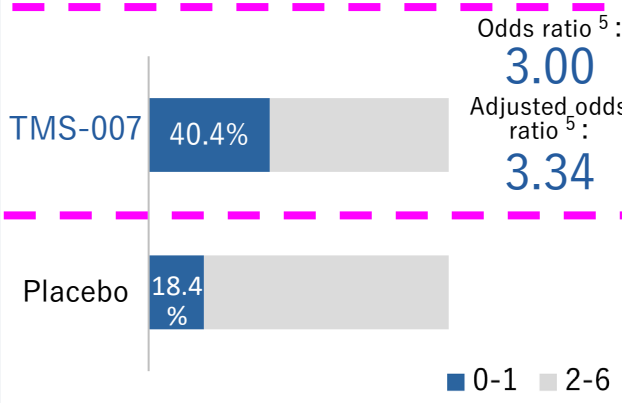
Therapeutic time window



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

Efficacy

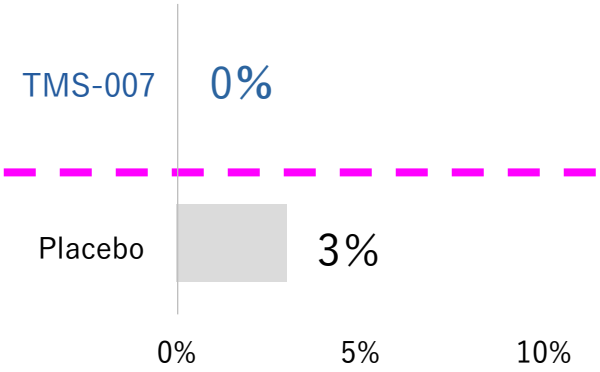
mRS [2] 0-1 ratio at 90 days
Gold-standard Endpoint



- 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 Intracerebral hemorrhage risk [3,4]



- TMS-007 showed the potential to overcome the biggest problem of t-PA.

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)

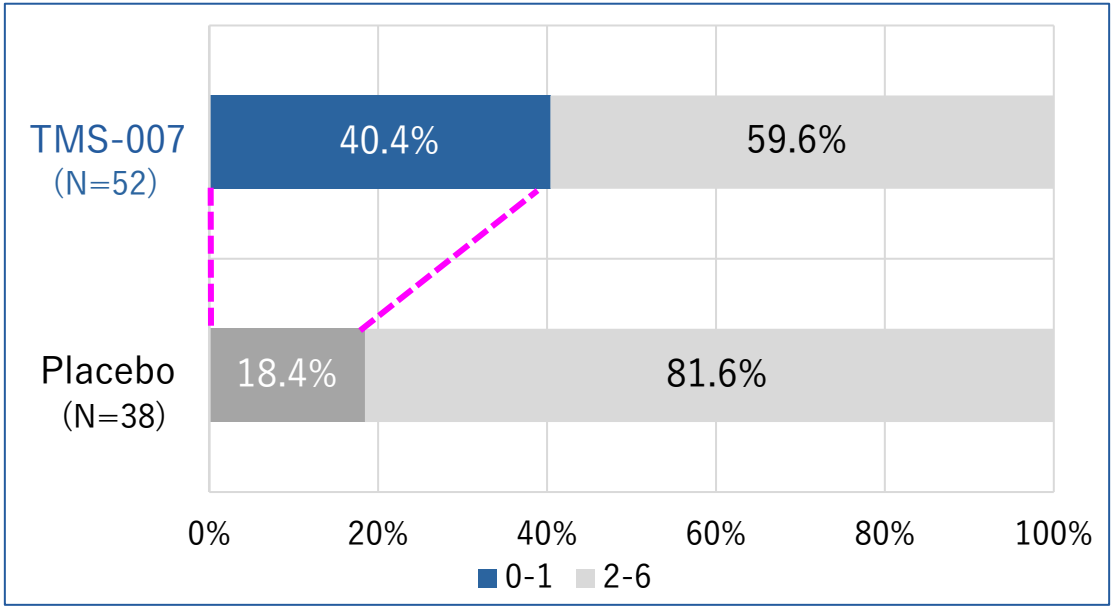
TMS-007: Ph2a clinical results　Achieved the “Gold-standard” Endpoint

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[1]



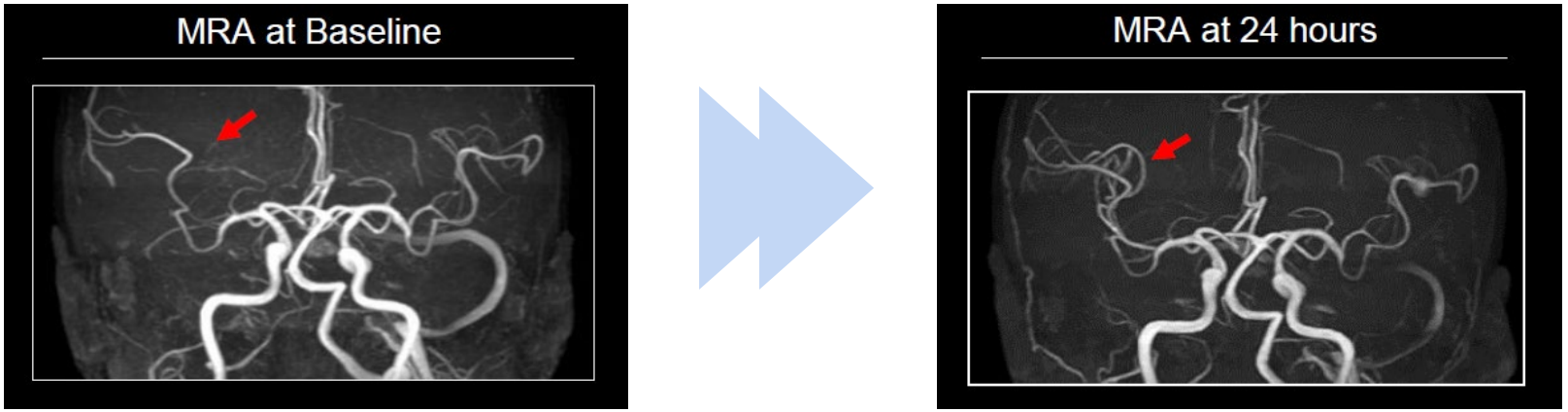
mRS (modified Rankin Scale)		
	0	No symptoms
	1	No significant disability, despite symptoms; able to perform all usual duties and activities
	2	Slight disability; unable to perform all previous activities but able to look after own affairs without assistance
	3	Moderate disability; requires some help, 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: Ph2a clinical results　Efficacy - Vessel Recanalization

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

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



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

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

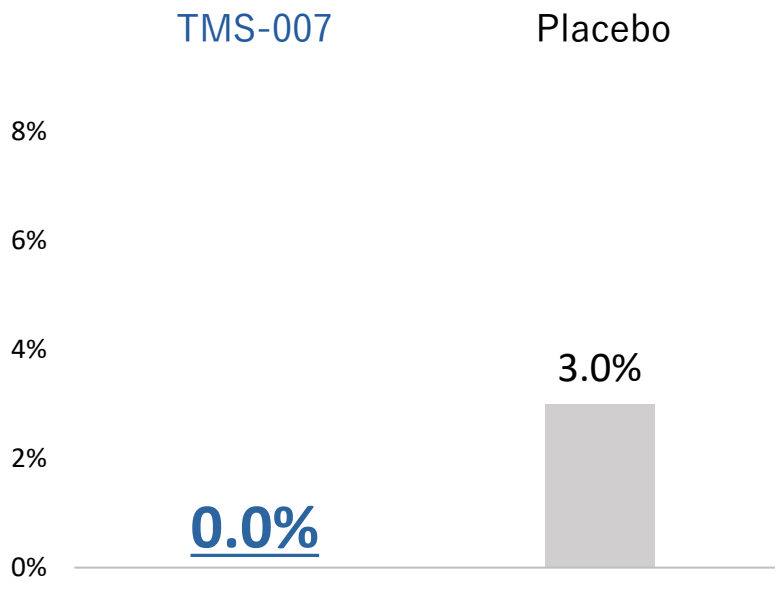
1. Biogen, Investor Day Material (September 21, 2021), Q4 and Full Year 2021: Financial Results and Business Update

TMS-007: Ph2a clinical results　Safety

In terms of safety, the biggest concern of t-PA, TMS-007 demonstrated reduced risk of the incidence of symptomatic Intracerebral Hemorrhage (sICH) [1]

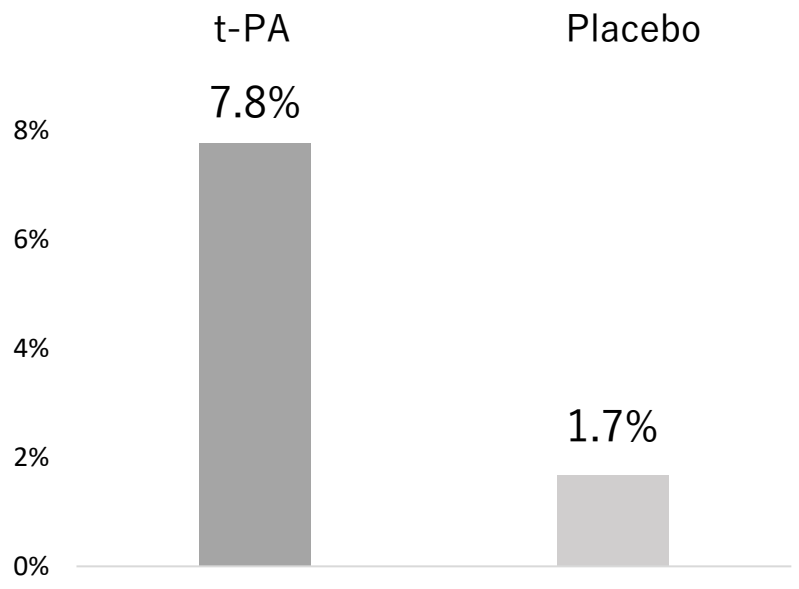
Incidence rate of sICH[1]

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

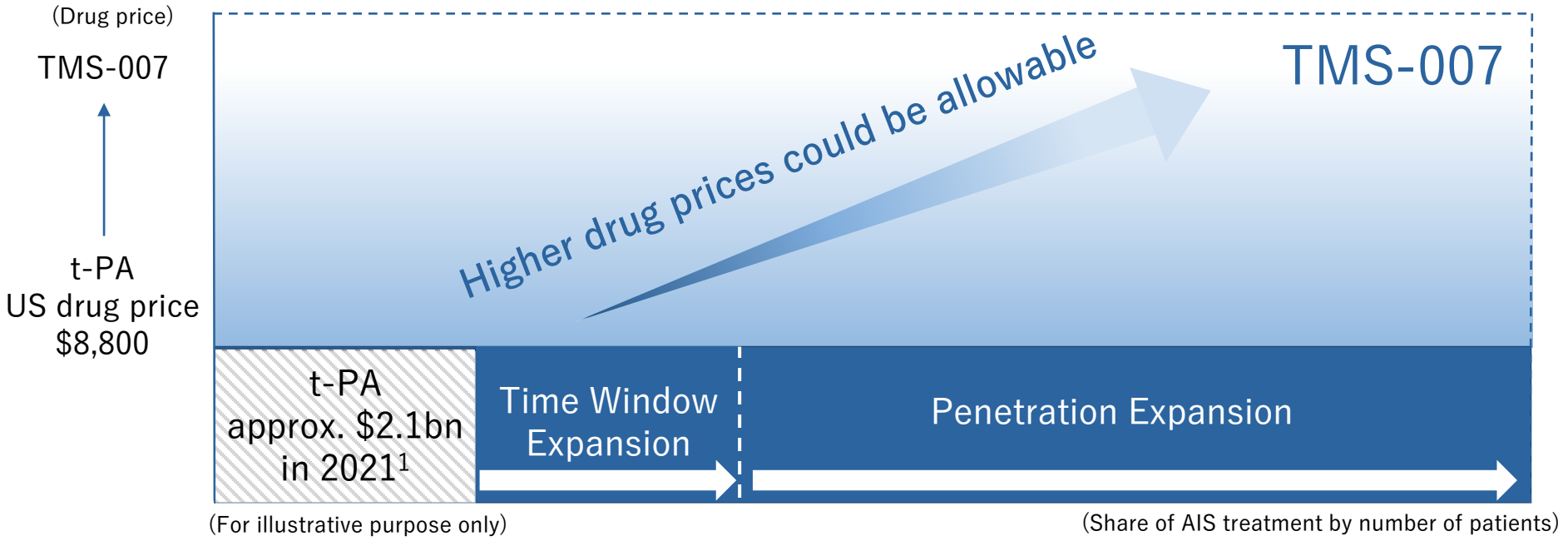


	t-PA	Placebo
N	3,384	3,330
Prehospital time	Within 6h	

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

Potential of TMS-007: Potential Market Size

Potential Market Size for TMS-007 with possible outstanding Efficacy and Safety



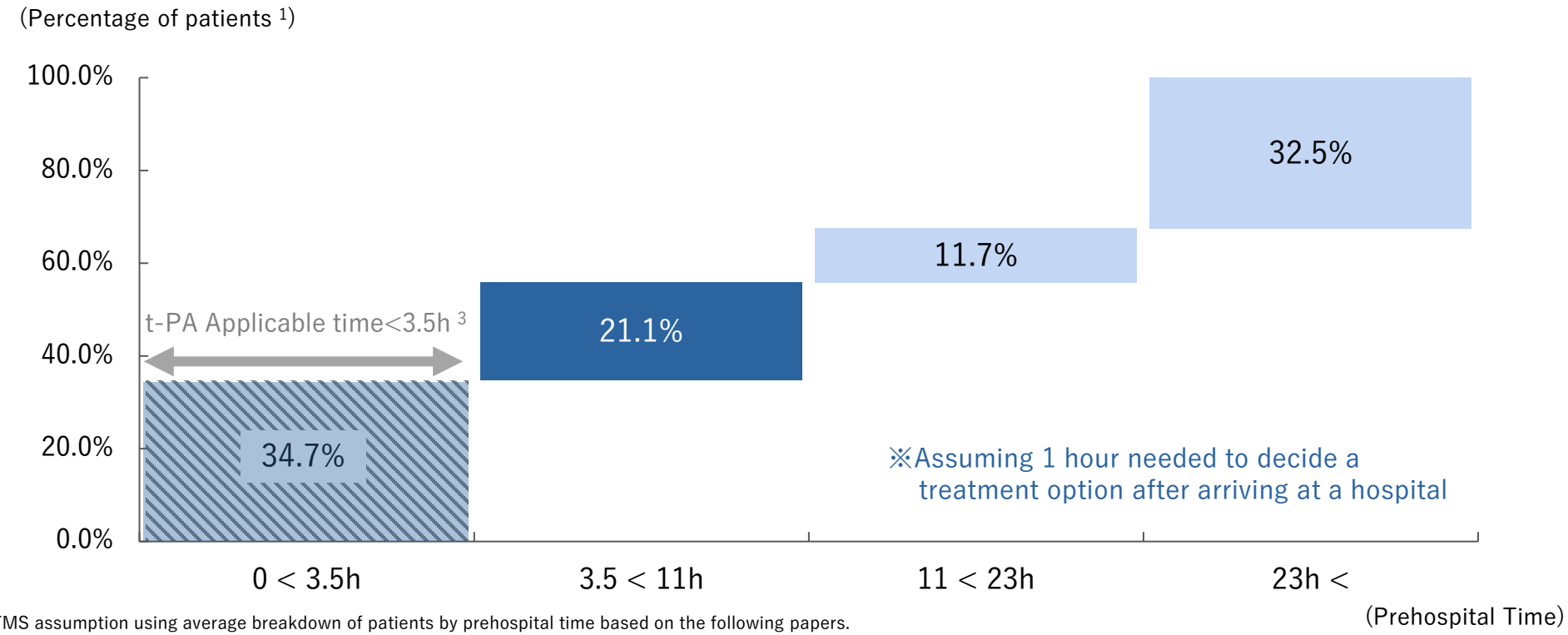
- TMS-007 has potential to realize the expansion of time window
  ⇒ Total addressable patients of TMS-007 may expand significantly
- If TMS-007 can achieve higher efficacy and safety than t-PA, higher drug price could be expected (sales of t-PA estimated to be approx. $2.1bn in 2021 [1])
- In clinical trial TIMELESS to test the use of tenecteplase, a potential alternative to t-PA, for ischemic stroke patients within 4.5 to 24 hours from symptom onset, there was no significant difference between tenecteplase and the placebo group on a measure of autonomy at 90 days which is a primary efficacy endpoint [2]

1. For 2021, Informa; calculated as the sum of estimated sales of Activase® and Actilyse® in 2021. Actual market size may differ from the estimate due to the limitations peculiar to such statistical data and publications in terms of their accuracy
2. Source："ESOC 2023: Large Clinical Trials Session", American Heart Association Blogs, June 5, 2023, DOI: 10.1161/blog.20230605.574378, Ana Ponciano, MD MSc

Potential of TMS-007: Expanding Time Window

Relationship between Prehospital Time and treatment [1]

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

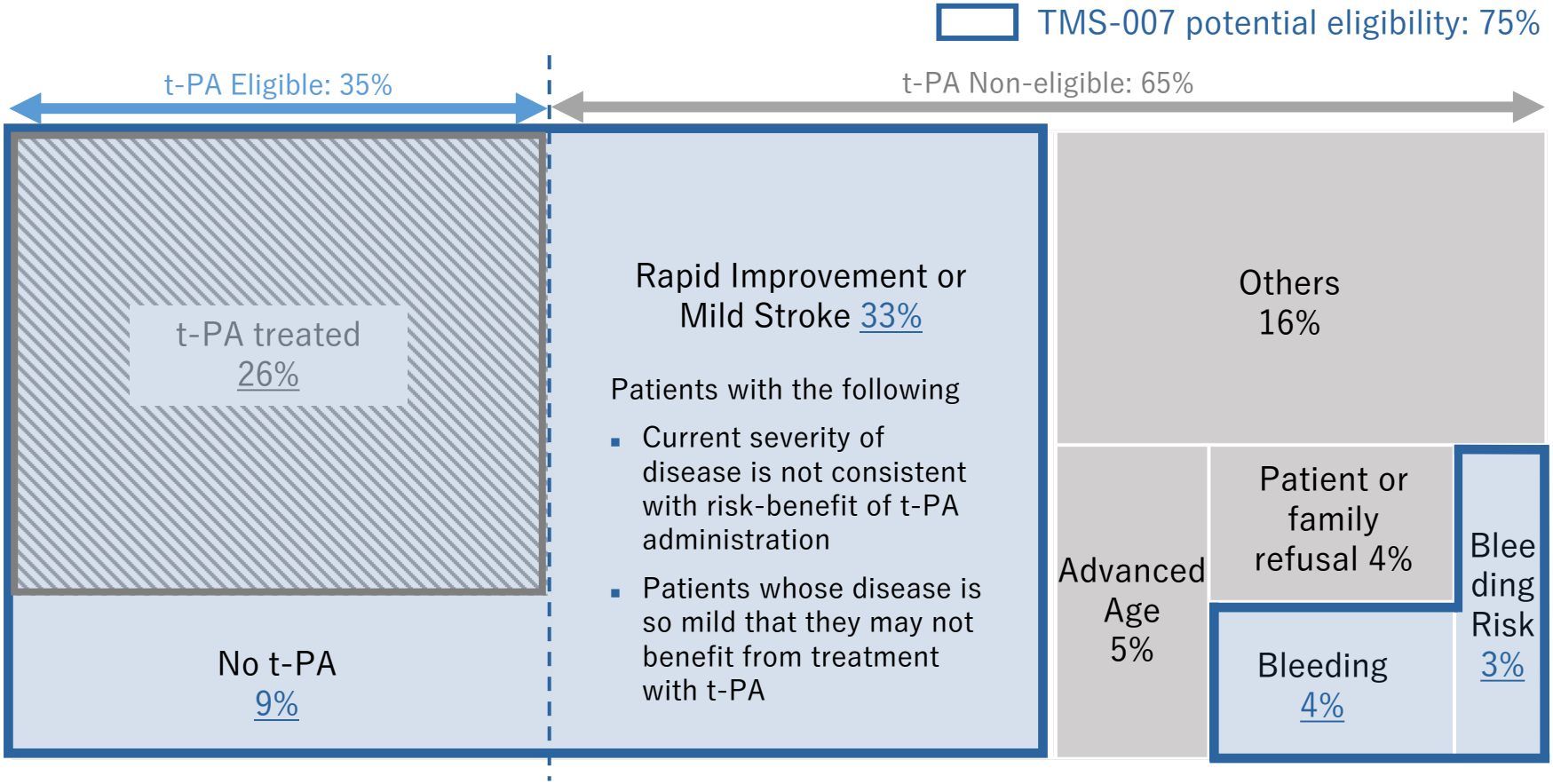


1. TMS assumption using average breakdown of patients by prehospital time based on the following papers. Please note that the company's estimate above is based on various assumptions and beliefs stated herein, including the available dose window, disregard certain significant conditions such as the eligibility 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. Expantion of time window over 12 hours (maximum 24 hours) is based on the registered and pubished information by Biogen on ClinicalTrials.gov on March 10, 2023.
3. Assuming 1 hour needed to decide a treatment option after arriving at a hospital

Potential of TMS-007: Expanding Penetration

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

- Due to its high 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



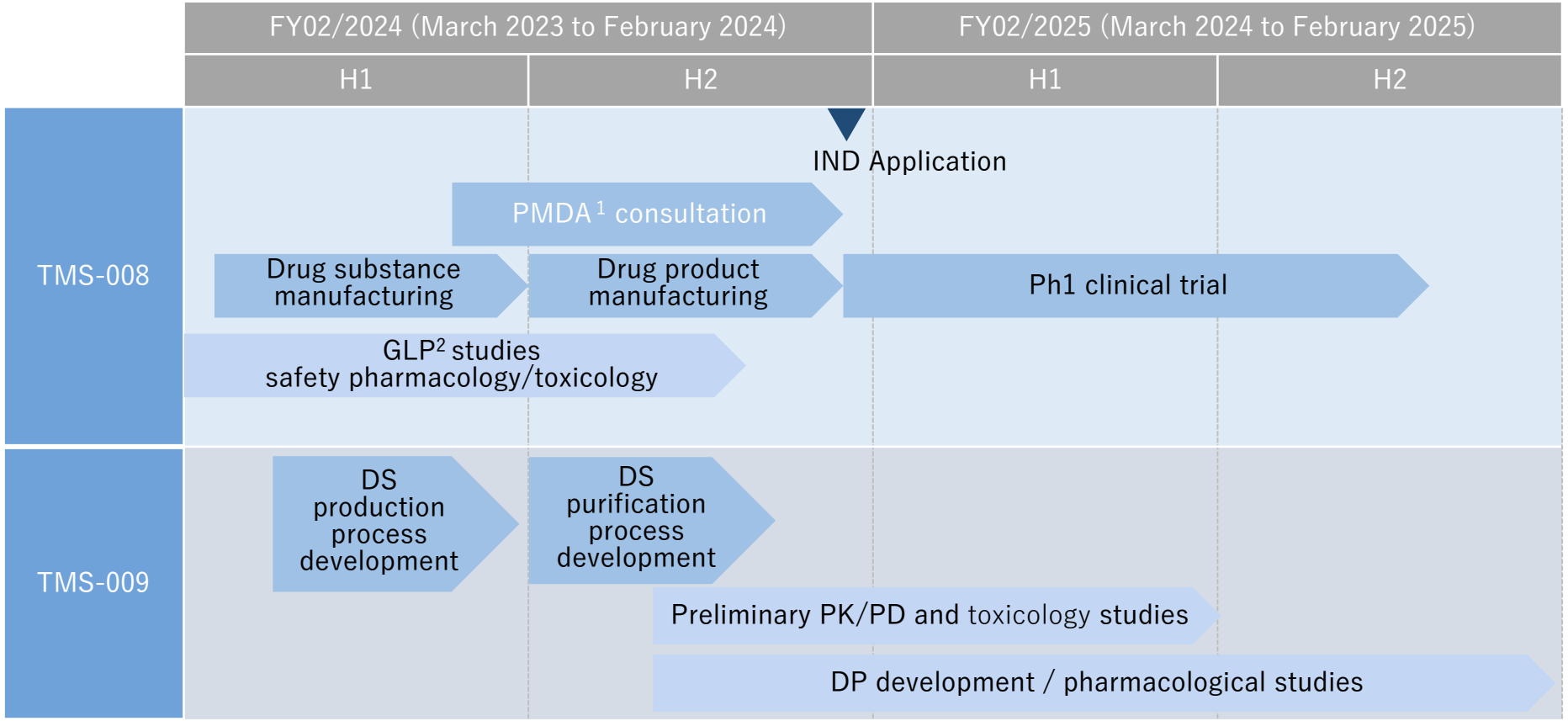
1. Messe (2016), "Why are acute ischemic stroke patients not receiving IV t-PA"

TMS-008/009

Acute Kidney Injury
and other indications

Progress of TMS-008/TMS-009

TMS-008：IND (PMDA[1]) filing in H2 FY02/2024 and Ph1 completion during FY02/2025 planned
TMS-009：GMP manufacturing process development and preliminary PK/PD/TOX studies ongoing



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 Medica Devices Agency
2. GLP refers to Good Laboratory Practice

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

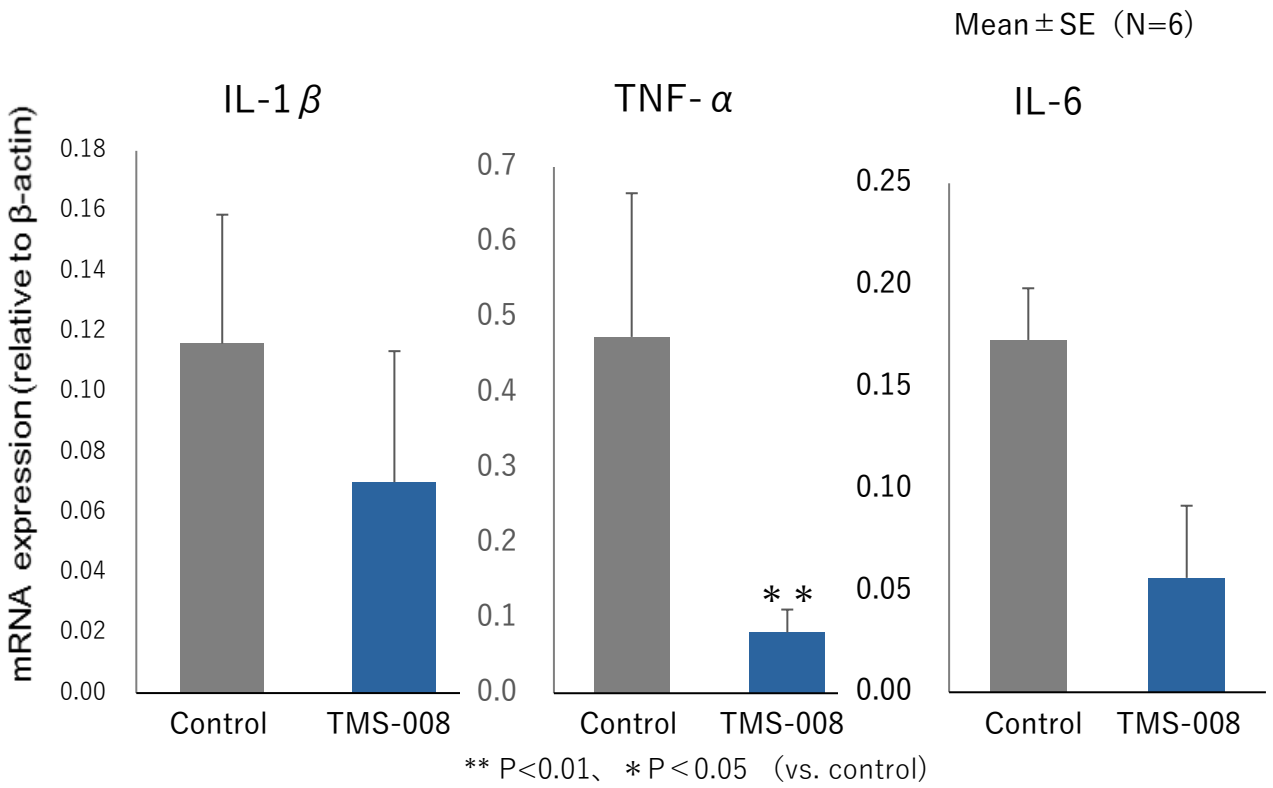
Potent sEH inhibitor with high anti-inflammatory and antioxidant activity

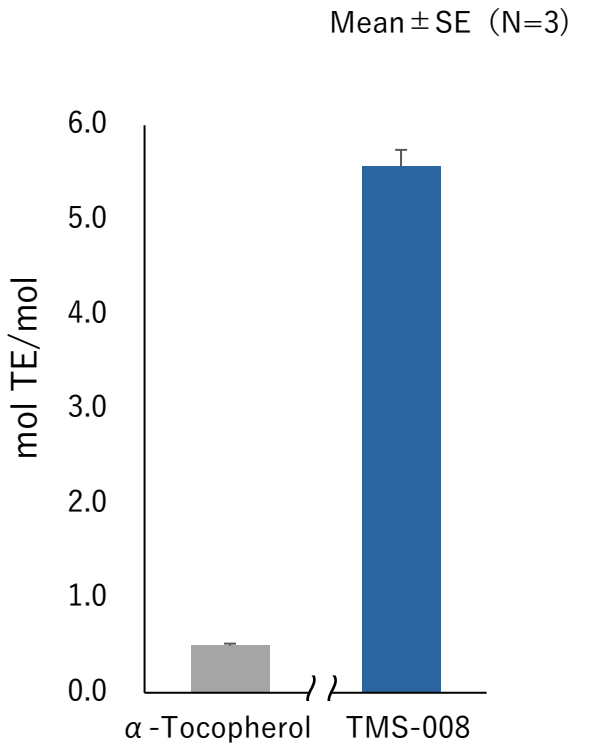
Inflammation-related parameter using AIS model mouse [1]

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

Antioxidant activity test [1,2]

- H-ORAC： hydrophilic oxygen radical absorbance capacity method





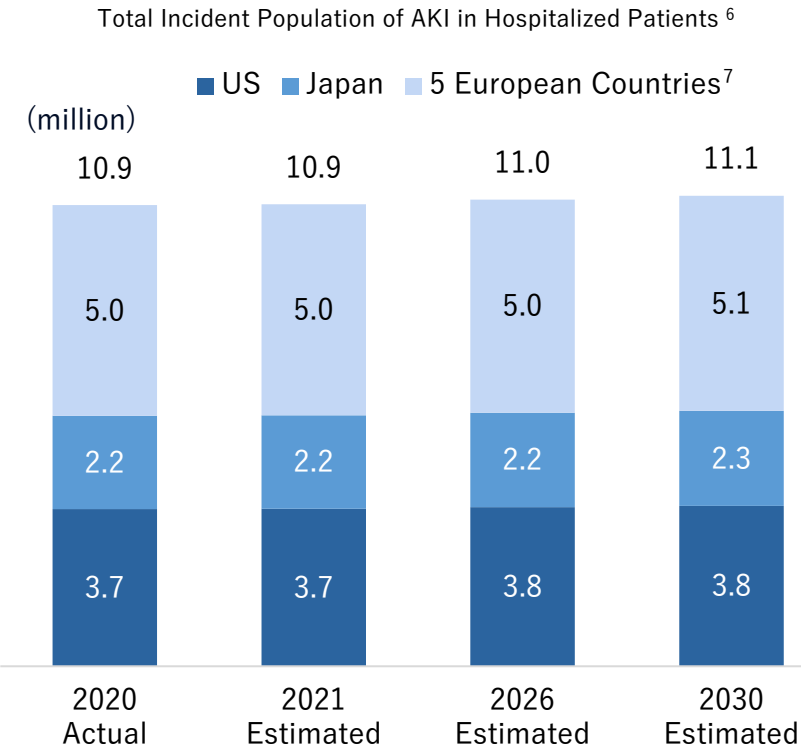
1. SourceEuropean Journal of Pharmacology Volume 818, 5 January 2018, “Evaluation of the effects of a new series of SMTPs in the acetic acid-induced embolic cerebral infarct mouse model” Publication number：WO 2011/004620
2. Results are shown in Trolox equivalents (TE). α-Tocopherol ORAC Values are for reference (Huang et al., J. Agric. Food Chem., 50, 1815-1821 (2002)).

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

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

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 hours to days ■ 20-25% mortality rate in hospitalized AKI patients ■ AKI causes chronic kidney disease (CKD) and end-stage renal disease (ESRD)
Number of patients	■ 5 European countries: ~5,080,000 ■ United States: ~3,800,000 ■ Japan: ~2,300,000 (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 includes Germany, France, Italy, Spain, and the UK

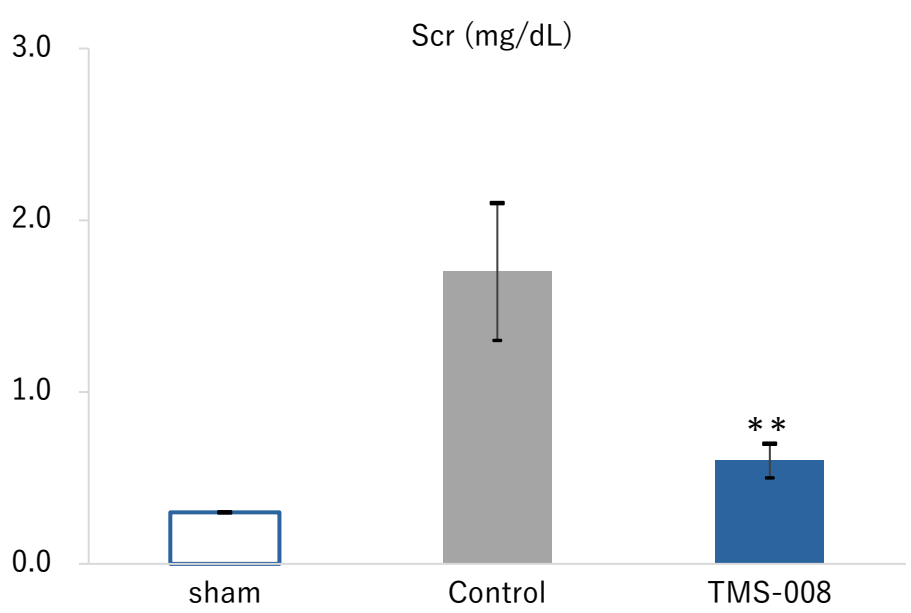
TMS-008 Indication: Acute Kidney Injury (AKI)

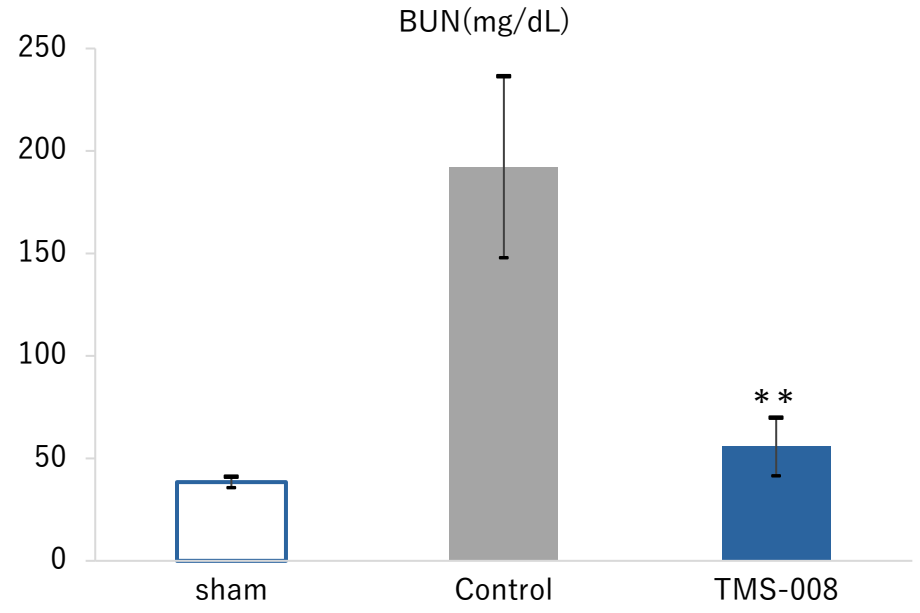
Preclinical studies in collaboration with Japanese university using AKI mouse models confirmed its potential as a new treatment for AKI

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

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

AKI model mouse experiment at Showa University [1]





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

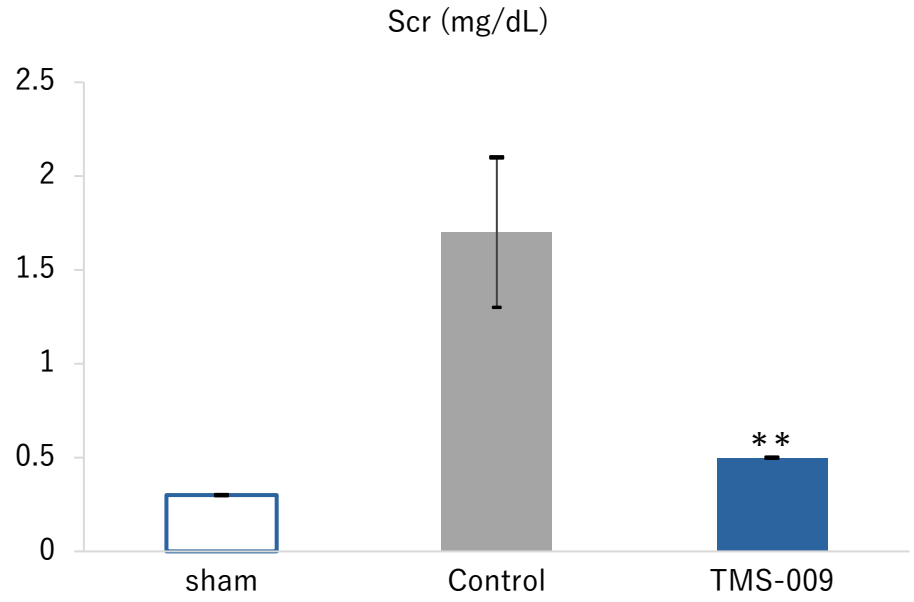
TMS-009: Backup for TMS-008

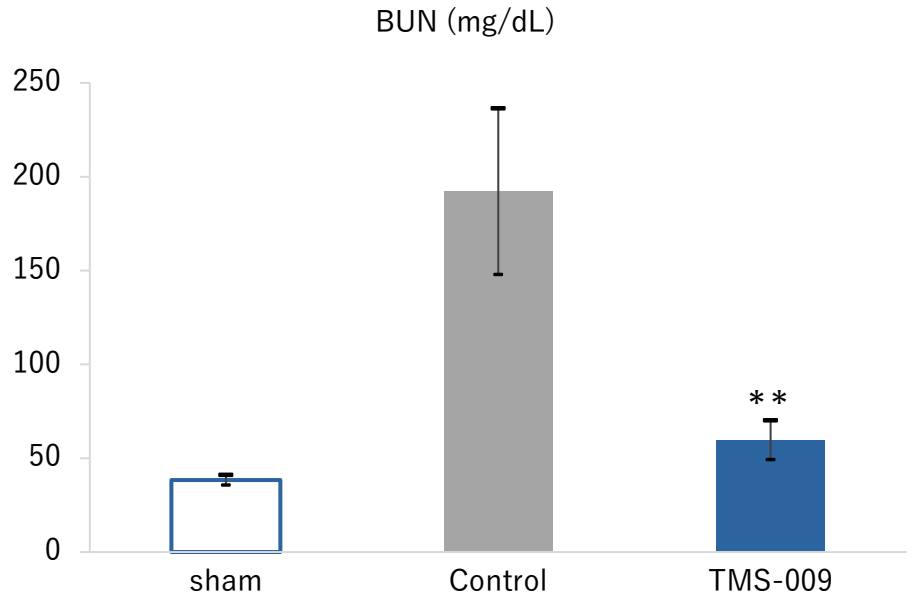
TMS-009 showed compelling potential as an anti-inflammatory agent with strong sEH [1] inhibition observed

TMS-009 is protective of renal function in a mouse model of AKI

- Demonstrated equivalent pharmacological activity as TMS-008 in vitro [2] and in vivo [3] studies
- Designated as a backup clinical candidate by taking advantage of dissimilar chemical structure and safety profile to TMS-008

AKI model mouse experiment at Showa Univ





1. sEH refers to soluble epoxide hydrolase
2. in vitro refers to a medical experiment which uses human or animal tissue to detect drug responses within the confines of a test tube or laboratory dish
3. in vivo refers to a medical experiment that detects drug responses in living organisms or cells, such as a laboratory animal or human

Expansion of Pipelines

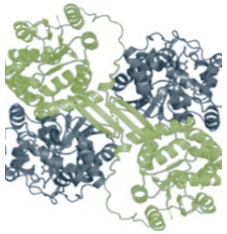
Pipeline expansion efforts both internally and externally

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

R&D and business development capabilities cultivated through SMTP compounds

Internal programs

- Novel small molecule compounds
  - New indications for TMS-008
  - sEH inhibitors
  - Natural product screening



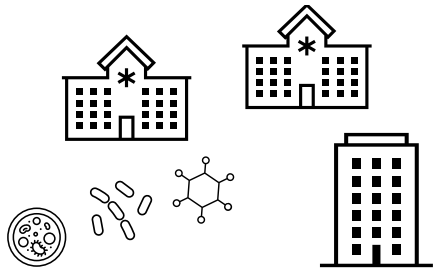
Human sEH

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

Program acquisition

Collaborative research

External programs (Academia and others)



Deploy

Licensing, etc.

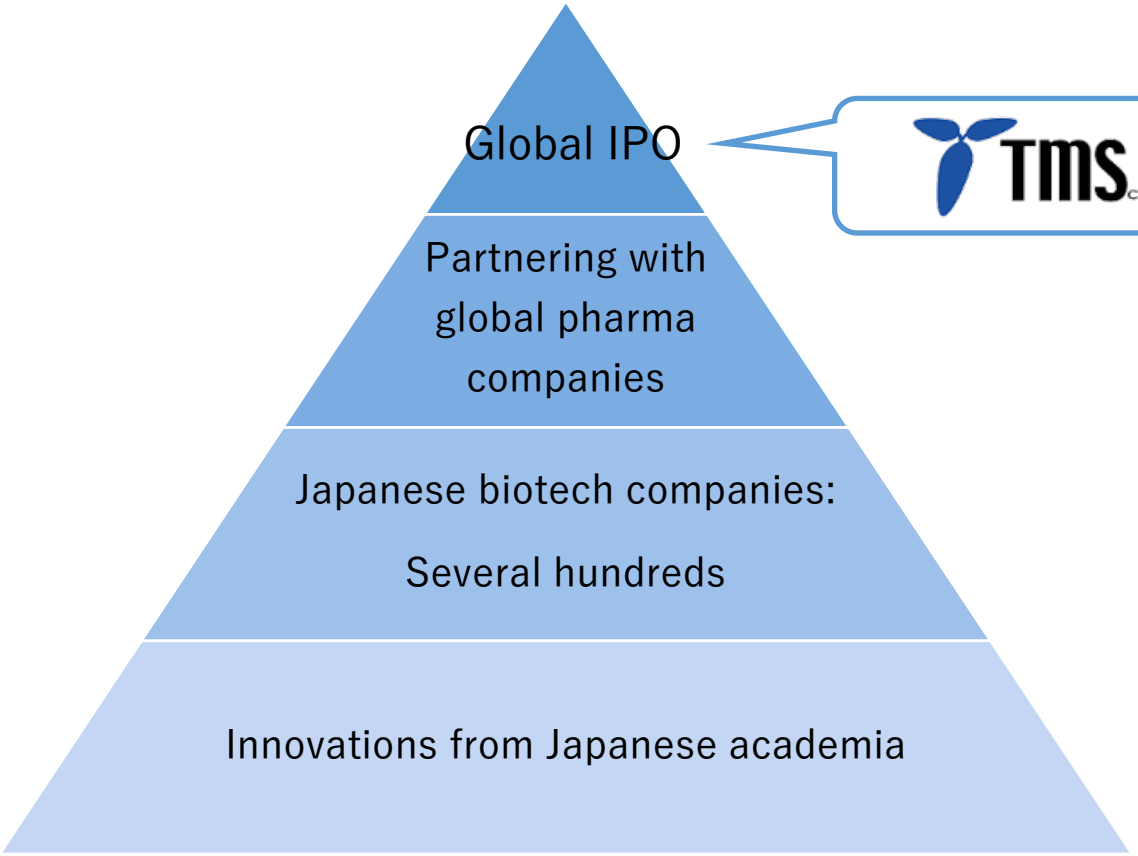
Global Market

* Global market is >10 times larger than Japanese market

Bridging innovation in Japanese academia to global market

Value creation on academic innovations by leveraging our unique capability as a Japanese biotech

- Positions well to bring academic innovation to market based on TMS-007 experience
- Global experience: global partnering and global IPO
- Pursuing business opportunities through bridging local innovation to global market



Global innovations from Japan

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

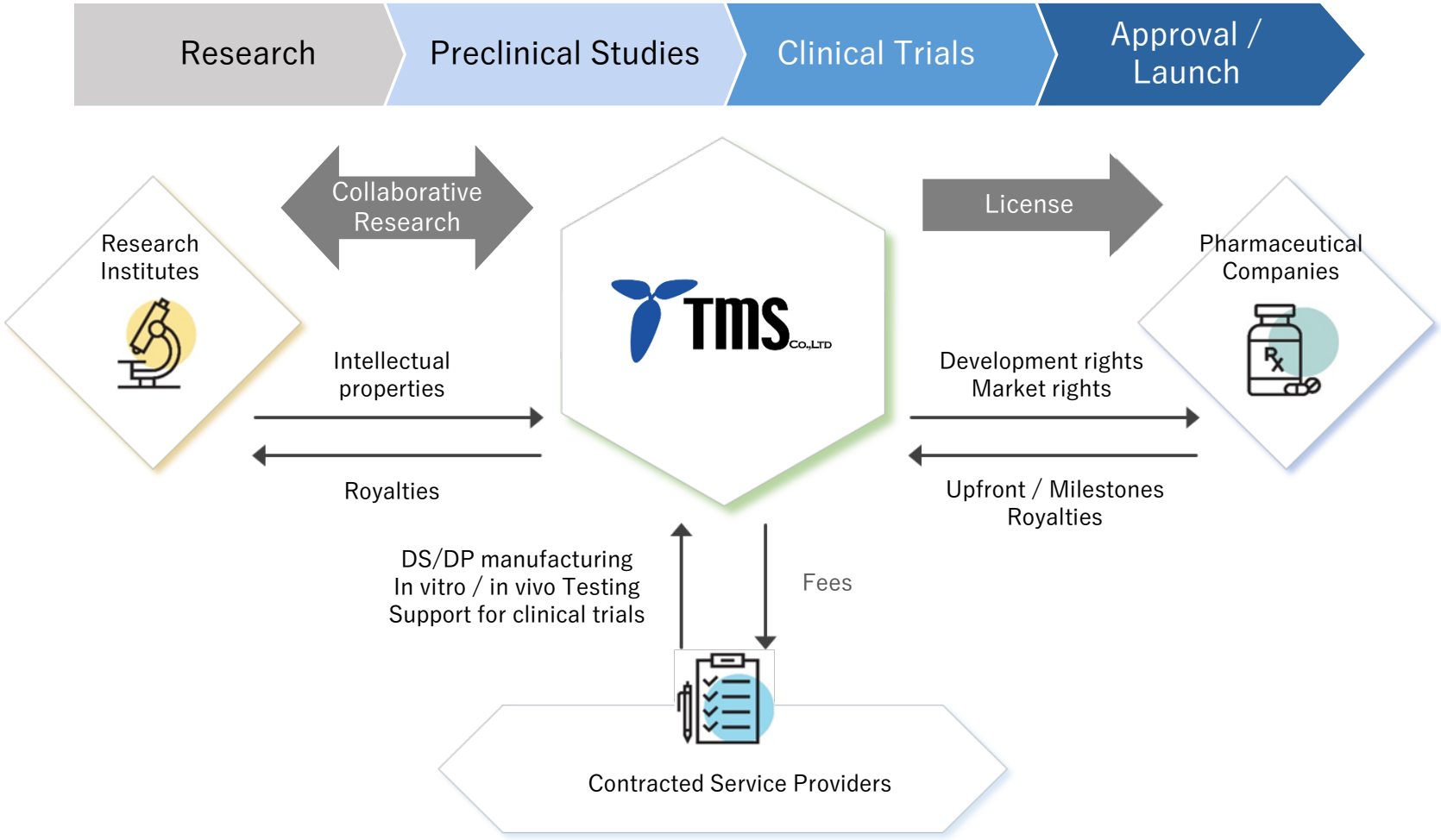
Appendix

Corporate Profile

Name	TMS Co., Ltd. (Stock Code: 4891)
Established	February 17, 2005
Closing month	February
Representative Directors	Takuro Wakabayashi Chief Executive Officer
Address	Headquarters: 1-9-11F, Fuchu-cho, Fuchu-shi, Tokyo JAPAN
Business Field	Research and development of drug products
Management	Board Member: 6 Audit & Supervisory Board Member: 4
Number of employee	14 (as of February 28, 2023)

	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
Oct. 2014	Started Phase I clinical trial of TMS-007
Oct. 2015	Completed Phase I clinical trial of TMS-007
Feb. 2018	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)

Business Model



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

History of TMS Co., Ltd.

SMTP

Stachybotrys
Microspora
Triprenyl
Phenol

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

Keiji Hasumi

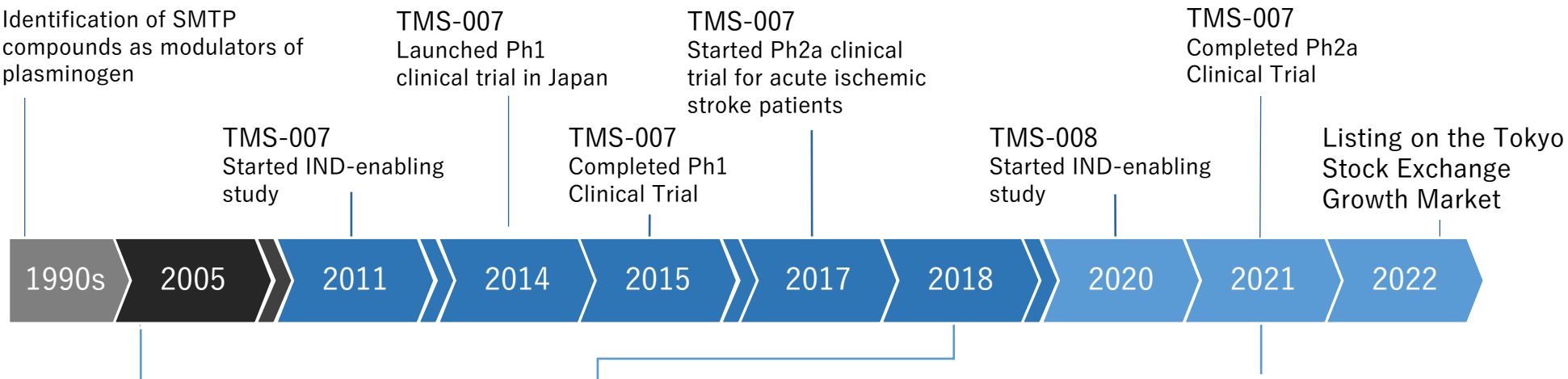
Ph.D.
Founder
Chief Scientific Officer

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

Dr. Akira Endo

Distinguished Professor Emeritus of Tokyo University of Agriculture and Technology

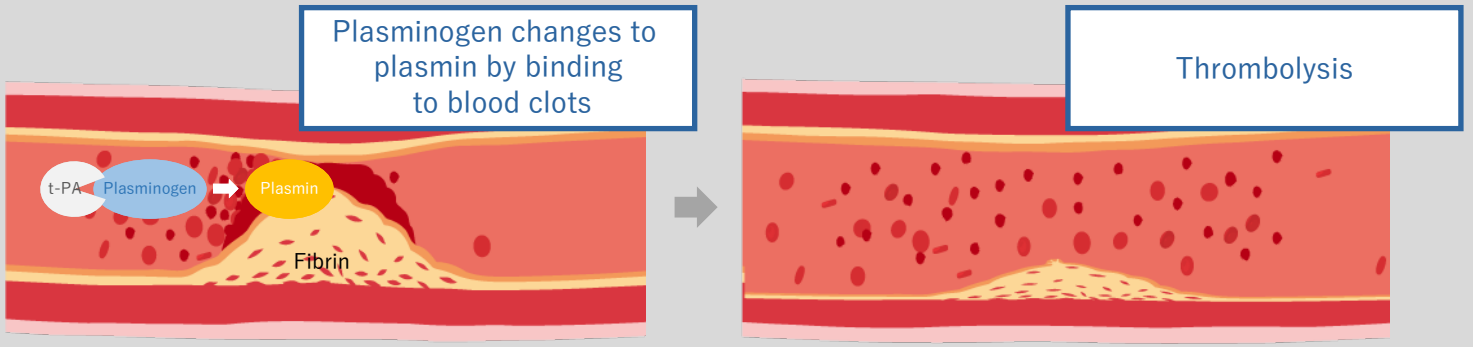
Invention of the hyperlipidemia drug statin (HMG-CoA reductase inhibitor), one of the best-selling category of drugs in history.



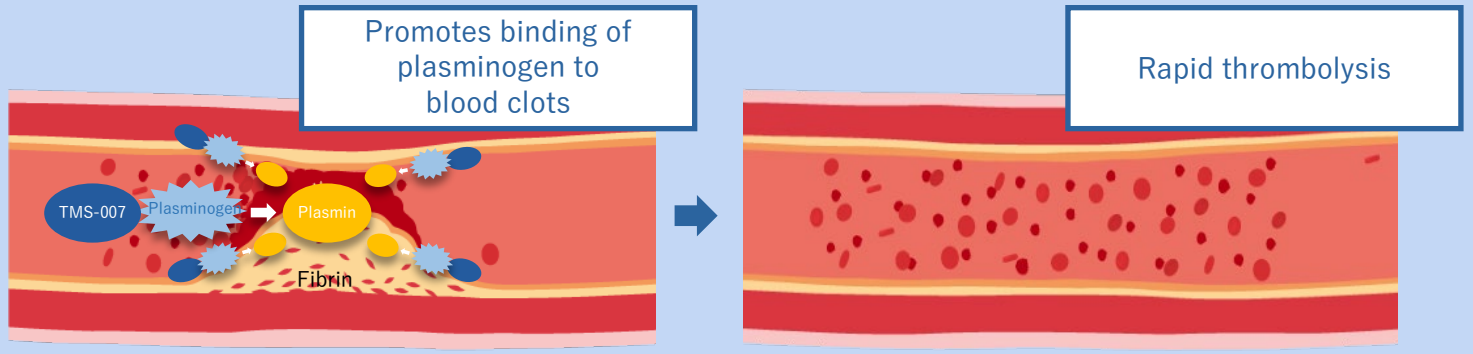
1. The contract party is Biogen MA Inc.

TMS-007 Mechanism of Action: Mechanism of thrombolysis[1] (1)

General



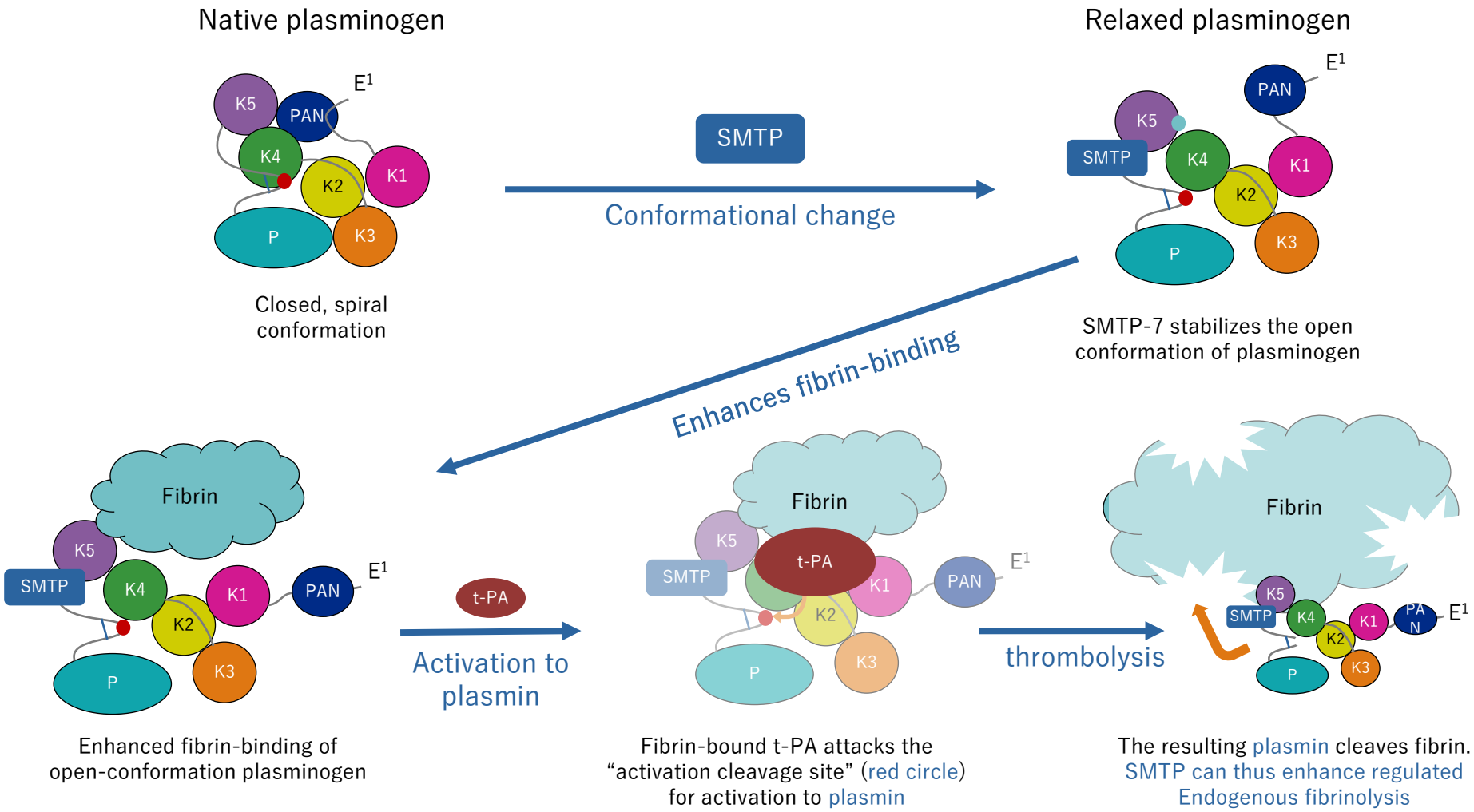
TMS-007



1. For illustrative purposes only

TMS-007 Mechanism of Action: Mechanism of thrombolysis (2)

TMS-007 promotes binding of fibrin to 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

TMS-007 (BIIB131): Outline of Ph2b Clinical Trial (DAISY) [1]

Summarized information, based on the publicly available information registered by Biogen [2]

Outline

- Multicenter, operationally seamless, double-blind, dose-ranging, placebo-controlled, randomized, parallel-group
- Estimated enrollment: 760 participants
- Estimated duration: Dec. 2023 – July 2025

Key Inclusion Criteria

- "Patients with thrombus site confirmed by imaging" [3] or "Patients with an estimation of penumbra [4] volume to be ≧10ml" [5]
- Presentation and treatment start are within 4.5 - 24 hours of LKW [6]
- No statement regarding limitations with or without endovascular therapy
- Age 18 – 85 years

Part 1

4 groups: Low, Medium and High dose, and Placebo

Primary Outcome Measures

- Arterial revascularization [7]
- Reduction of at least 90% of the area presumed to be penumbra for patients in whom the occlusion cannot be located[8]

Part 2

2 groups: a single dose specified in Part1 and Placebo

Primary Outcome Measures

- modified Rankin Scale (mRS) score at 90 days

1. Biogen has announced to pause initiation of Phase 2b clinical trial and reassess whether to initiate the trial at its Q1 2023 Earnings Presentation on April 25, 2023. As of October 18, 2023, it is not clear if the Phase 2b clinical trial will resume.
2. The above information are summarized by TMS Co., Ltd., based on the information registered and published in ClinicalTrials.gov (https://www.clinicaltrials.gov/study/NCT05764122?cond=BIIB131&checkSpell=false&rank=1) by Biogen. Therefore, the accuracy of the information cannot be assured.
3. Patients with CTA or MRA showing symptomatic intracranial occlusion, at one of the following locations: intracranial internal carotid, M1, M2 or distal branches of the middle cerebral artery (MCA), anterior cerebral artery (ACA), or posterior cerebral artery.
4. Penumbra is an area of brain, in the early (hyperacute) phase of cerebral infarction, where blood flow is reduced but cells have not yet become necrotic, and rapid vascular recanalization is expected to prevent the area from transition to infarction.
5. Patients with the volume of Tmax>6s to be ≥10 mL on perfusion imaging.
6. LKW: Last Know Well, meaning the last time patient was confirmed to be normal before symptoms started.
7. Patients with an AOL score of 2 or 3 at 4 ± 2 hours post-treatment (or at the time of the first angiogram for patients undergoing endovascular therapy).
8. For patients with no visible occlusion at baseline, >90% reduction of Tmax > 6s at 4 ± 2 hours after treatment completion.

TMS-007 (BIIB131): Ph2b (DAISY) [1] / Ph2a comparison

Summarized information, based on the publicly available information registered by Biogen [2]		
	Ph2a	Ph2b
Basic design	1 stage	2 stages (Part 1、Part 2)
Enrollment	90	760（Estimated）
Primary efficacy endpoint	mRS 0-1 ratio	Part 1・Arterial revascularization ・Reduction of at least 90% of penumbra Part 2・mRS score
Ages eligible for trial	Male: 20 - 88 years Female: 60 - 88 years	18 - 85 years
Time window	Within 12 hours after on set	Within 4.5 - 24 hours of LKW
Endovascular therapy (EVT)	Only for patients without EVT	May include patients undergoing EVT
Pre-treatment score of NIHSS	6 - 23 （Patients with moderate symptoms）	≧5 (Severe patients are also eligible)

1. Biogen has announced to pause initiation of Phase 2b clinical trial and reassess whether to initiate the trial at its Q1 2023 Earnings Presentation on April 25, 2023. As of October 18, 2023, it is not clear if the Phase 2b clinical trial will resume.
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