SanBio

Pioneering Regenerative Medicine

# Financial Results for the 2nd Quarter of the Fiscal Year Ending January 31, 2021

September 15, 2020

## SanBio Company Limited

(TSE Mothers: 4592)

# Table of contents



* TBI: Traumatic Brain Injury

# 1. Financial Results

# Consolidated Income Statement

**R&D costs fell by JP¥214 million YoY due to lower clinical trial expenses, despite a rise in manufacturing-related expenses.**

| Unit: Million yen | 1H FY2020.1 Results (A) | 1H FY2021.1 Results (B) | (B)-(A) | FY2021.1 Forecast |
|---|---|---|---|---|
| Revenue | 427 | - | -427 | - |
| R&D cost | 2,013 | 1,798 | -214 | 3,757 |
| Operating expenses | 2,812 | 2,570 | -242 | 5,453 |
| Operating income | -2,385 | -2,570 | +185 | -5,453 |
| Net income | -2,048 | -3,207 | -1,158 | -5,544 |
| Yen/US$ exchange rate | 109.93 | 107.48 | - | 110.00 |

# Consolidated Balance Sheet

**Although cash and deposits decreased by JP¥2,738 million, maintained a stable financial base with progress as planned.**

| Unit: Million yen | As of January 31, 2020 (A) | As of July 31, 2020 (B) | (B)-(A) | Factors of Difference |
|---|---|---|---|---|
| Cash & cash equivalents | 13,646 | 10,907 | ▲2,738 | |
| Supplies | 469 | 448 | ▲20 | |
| Current assets | 14,626 | 11,728 | ▲2,897 | |
| Non-current assets | 979 | 2,068 | +1,089 | Increase mainly due to valuation gain on investment securities |
| Total assets | 15,605 | 13,796 | ▲1,808 | |
| Current liabilities | 1,175 | 2,619 | +1,444 | Mainly increase in long-term loans payable |
| Non-current liabilities | 3,500 | 2,157 | ▲1,342 | The decrease accompanying increase in long-term payable |
| Total liabilities | 4,675 | 4,776 | +101 | |
| Net assets | 10,930 | 9,019 | ▲1,910 | |
| Total liabilities and net assets | 15,605 | 13,796 | ▲1,808 | |

# 2. Product approval filings for TBI program in Japan

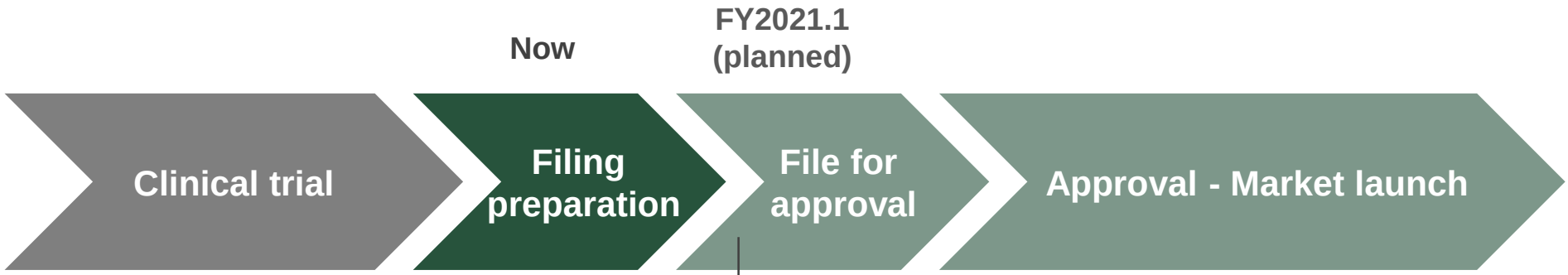
# Progress on three key issues

**Progressing as planned toward product approval filings in Japan.**

| Issues | Status |
|---|---|
| Technology transfer under new arragements | Mostly complete |
| Establishing the management system for commercial production | Progressing as planned |
| Establishing standard testing procedures | Progressing as planned |

# Timeline of product approval filings in Japan

## Aiming to file for approval in FY2021.1.




As the product received the Sakigake designation for accelerated review, the review period is expected to take six months instead of the usual one year.

# 3. Analysis results for US Phase 2 study for the Treatment of Patients with Chronic Stroke (STR-02)

September 14, 2020
SanBio Co., Ltd.

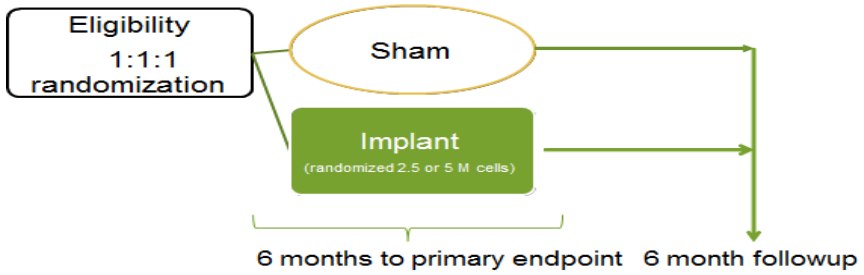
**Additional analytical results of the US-based Phase 2b clinical trial of regenerative cell medicine SB623 for the treatment of chronic motor deficit from ischemic stroke, and review of plans to initiate clinical trials for the ischemic stroke and hemorrhagic stroke programs in Japan based on these results**

SanBio Co., Ltd. (headquarters: Chuo-ku, Tokyo, Representative Director and President: Keita Mori, hereafter "SanBio") hereby announces that it has obtained new analytical results from the Phase 2b clinical trial (the "trial") of SB623 for the treatment of chronic motor deficit resulting from ischemic stroke the SanBio Group (SanBio Co., Ltd. and its subsidiary SanBio, Inc.) conducted in the US. It also announces that based on the newly obtained results, it has updated its development plans, including in regard to late-stage clinical trials for the ischemic stroke and hemorrhagic stroke programs of SB623 in Japan.

The trial evaluated efficacy and safety of SB623 in 163 patients suffering from chronic motor dysfunction from ischemic stroke. On January 29, 2019, SanBio announced that the trial did not meet its primary endpoint, as it failed to demonstrate statistical significance in the difference in the proportion of patients whose Fugl-Meyer Motor Scale (FMMS) score improved by 10 or more points from the baseline (primary endpoint) between the treatment group that received SB623 and the control group. Since then, the SanBio Group had continued to work on additional analysis of the trial data, and results of the additional analysis are as follows.

# SB623 Study (STR02) –*Previously Announced*

## A Double-Blind, Controlled Phase 2b Study of the Safety and Efficacy of Modified Stem Cells in Patients with Chronic Motor Deficit from Ischemic Stroke




| | Screening | Baseline | Sham or Cell Administration | | Follow-Up Period | | |
|---|---|---|---|---|---|---|---|
| Time | -28 to -6 days | -5 to -2 days | Pre-op day -1 | Post-op day 1 | Post-op day 2 | Week 1 | Month s 1, 3, 6, 9, 12 |
| Site | Assessme nt | Assessme nt | Surgery | | | | Assessme nt |

- The Fugl-Meyer Motor Scale (FMMS) is widely recognized as a clinically relevant measure of body function impairment
- The FMMS includes items measuring movement, upper extremity subscale (scored 0-66) and lower extremity subscale (scored 0-34)

**FMMS Responders at Month 6 – primary endpoint (mITT)**

| | Sham Surgery (N=52) | SB623 2.5 Million (N=55) | SB623 5.0 Million (N=56) | Combined SB623 (N=111) |
|---|---|---|---|---|
| Responders | 7/45 ( 15.6) | 7/53 ( 13.2) | 9/54 ( 16.7) | 16/107 ( 15.0) |
| GLMM Odds Ratio (95% CI) | | 1.12 (0.23, 5.32) | 1.58 (0.35, 7.11) | 1.33 (0.35, 5.09) |
| GLMM P-value | | 0.888 | 0.551 | 0.674 |
| Logistic Odds Ratio (95% CI) | | 1.16 (0.38, 3.61) | 1.65 (0.53, 5.11) | 1.35 (0.50, 3.67) |
| Logistic P-value | | 0.836 | 0.373 | 0.554 |

FMMS Responder: >= 10 points improvement from baseline in FMMS motor total score.

9/15/2020

# Background of Composite FMMS settings

## Minimally Clinically Important Difference (MCID)

- A statistically significant mean difference does not necessarily represent a difference that is perceived as meaningful by patients[3]
- Regulatory agencies require an outcome to be BOTH statistically significant AND clinically meaningful
- Minimally Clinically Important Difference (MCID) is defined as the smallest change on a measure that is reliably associated with a meaningful change in a patient's clinical status, function, or quality of life[1,2]
- We determined MCID by performing all three methods: Delphi Expert panel, Anchoring on the GRPC form TBI trial and Distribution methods
- The expert panel recommended to assess the MCID separately for the upper and lower extremity, as it would be clinically more relevant
- Composite endpoint is a modified version of the Fugl-Meyer Motor Scale: FMMS Total, FMMS Upper Extremity, and FMMS Lower Extremity subscales
- Composite endpoint requires attaining MCID threshold in at least one of the following at 24 weeks:
  - FMMS Total ≥9 points improvement from baseline
  - FMMS UE ≥6 points improvement from baseline
  - FMMS LE ≥4 points improvement from baseline

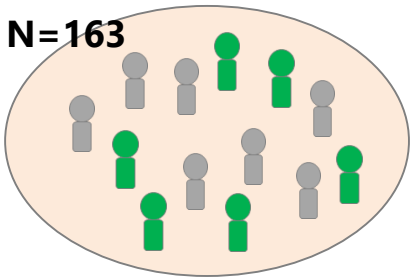
*1:Revicki D, Hays RD, Cella D, Sloan J. Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. Journal of Clinical Epidemiology. 2008;61:102-109.

*2:Malec JF, Kean J, Monahan PO. The Minimal clinically important difference for the Mayo-Portland adaptability inventory. Journal of Head Trauma Rehabilitation. 2017;32:E47-E54.

*3:Malec JF, Ketchum JM. A standard method for determining the minimal clinically important difference for rehabilitation measures.
Archived of Physical Medicine and Rehabilitation. 2020;101:1090-1094.

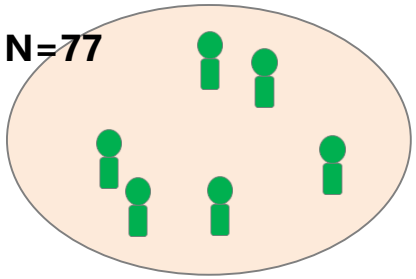
# Results of Additional Analysis:
# FMMS Composite Endpoint at Month 6

**In patients with infarct size less than a certain amount, there was a 30% difference in "Composite Response %" between SB623 group (49%) and control group (19%).**




**Condition 1.**

Select patients with infarct size less than a certain amount




**Condition 2.**

Composite endpoint requires attaining in at least one of the following:

1. FMMS Total ≥9 points improvement from baseline
2. FMMS UE ≥6 points improvement from baseline
3. FMMS LE ≥4 points improvement from baseline

**Overall Population: Of the 163 enrolled patients, 158 were evaluable at 6 months**

| | Count | Composite Responders | Avg. Baseline FMMS | Composite Response (%) |
|---|---|---|---|---|
| Treatment | 107 | 42 | 44.87 | 39% |
| Control | 51 | 16 | 47.35 | 31% |
| p-value | | 0.42 | 0.33 | 0.42 |

**Population with infarct size less than a certain amount (77patients: 48.7%)**

| | Count | Composite Responders | Avg. Baseline FMMS | Composite Response % |
|---|---|---|---|---|
| Treatment | 51 | 25 | 48.55 | 49% |
| Control | 26 | 5 | 49.42 | 19% |
| p-value | | 0.02 | 0.8 | 0.02 |

# Significance of volume of stroke's in clinical and preclinical (animal behavioral) outcomes and biology of stroke brain tissue

## Is there any clinical relationship Vol Stroke & functional outcomes?

### In Human

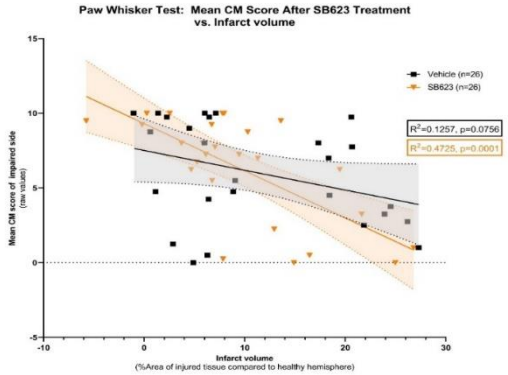
***Baseline FMMS vs Volume of Stroke***

**Association of follow-up infarct volume with functional outcome in acute ischemic stroke: a pooled analysis of seven randomized trials**

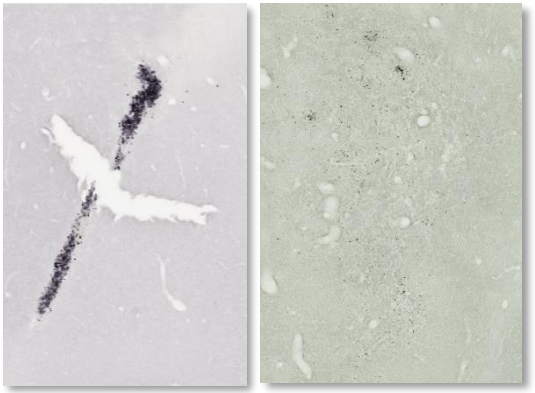
[April 7, 2018]. *J Neurointerv Surg*. Doi:10.1136/neurintsurg **Anna M M Boers**

**1665 included patients, 83% were imaged with CT. Median Follow-up infarct volume (FIV) was 41 mL (IQR 14–120). A large FIV was associated with worse functional outcome with OR=0.88(95% CI 0.87 to 0.89) per 10 mL in adjusted analysis.**

### In Animal



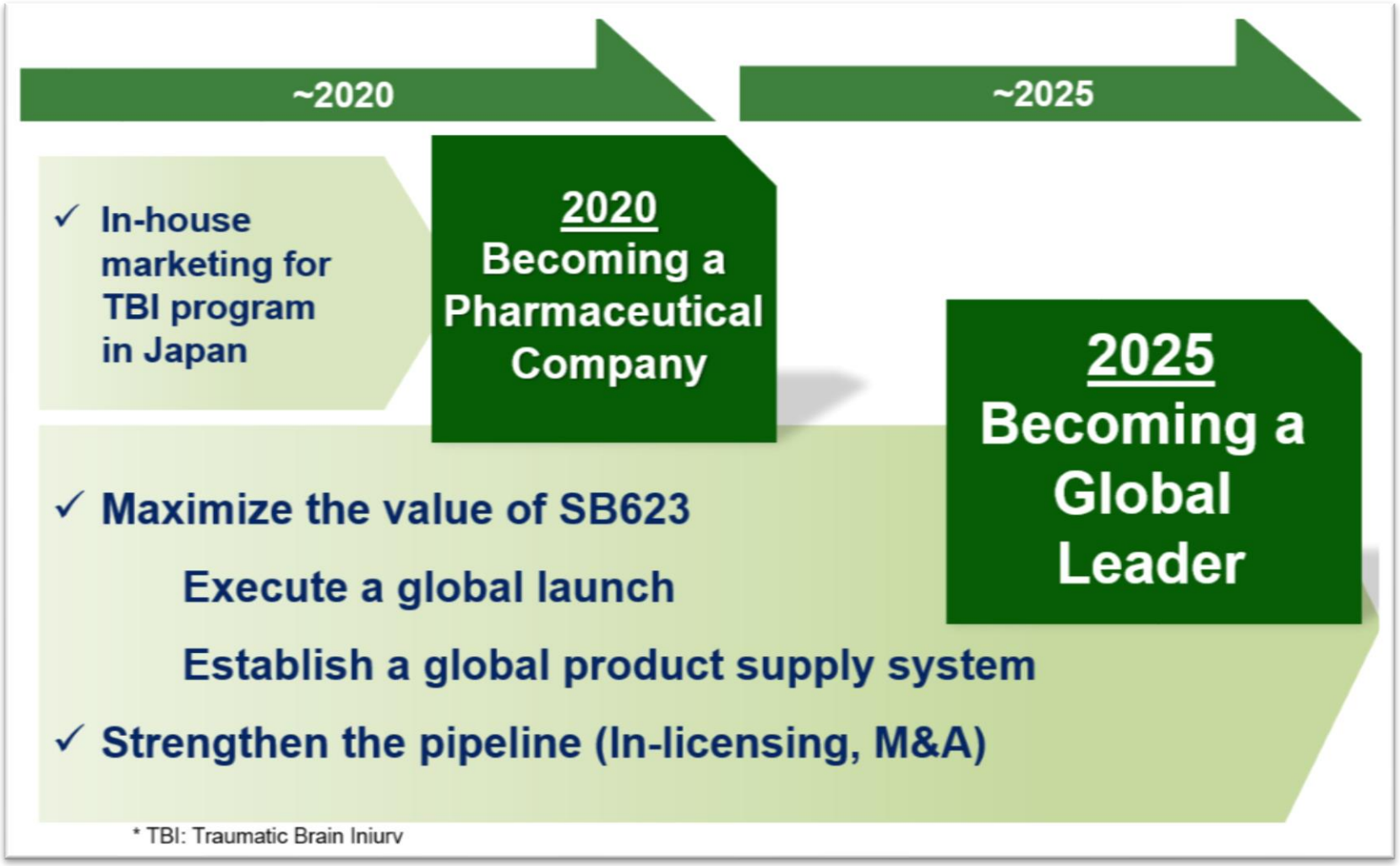

### In Biology, Is there any explanation at the tissue level



SB623 cells were noticeably scattered in the penumbral regions (tissue which is still viable, but not functional, located between normal tissue and stroke core and relevant to the impairment). persistence of these cells in this condition are better than in severe stroke environments.

# 4. Going forward

**Although the timeline is behind the target, the direction remains unchanged, aiming to become a pharmaceutical company and become a global leader.**



# New management for global leadership

## Senior Managing Director and Corporate Officer Akihiro Tsujimura becomes Executive Vice President, Corporate Officer, and COO.

New position **Executive Vice President, Chief Operating Officer, SanBio, Inc. CEO Akihiro Tsujimura**

### Career

Mr. Tsujimura amassed wide ranging experience regarding overseas business administration with Nichimen Corporation (now Sojitz Corporation) and also served as the head of North America and Asia operations at Santen Pharmaceutical Co., Ltd., engaging in business development and M&A activities. Leveraging the accumulated experience and knowledge, he will lead SanBio operations in Japan and the US in pursuit of becoming a global leader.

### Key responsibility

**Provide sound management for the company's growing operations**

# SanBio taking on the challenge of change

**Launched a new management team spearheaded by leaders with proven experience and expertise in their respective fields, fully-equipped with the functions needed to fuel the company's growth.**

Executive directors

**Executive Chairman**
**Toru Kawanishi**

**CEO**
**SanBio, Inc. Chairman**
**Keita Mori**

**Executive Vice President, COO**
**SanBio, Inc. CEO**
**Akihiro Tsujimura**

Corporate officers

Manage pharmaceuticals, process and analytical development, supply chain, contract manufacturing, and product quality

**New post**

**CTOO (Chief Technical Operations Officer)**
**Chris Horan**

**CMO**
**(Chief Medical Officer)**
**Bijan Nejadnik**

**Business Head (Japan/Asia)**
**Hiroshi Yamamoto**

**Management Administration**
**Yoshihiro Kakutani**

# Summary of STR-02 additional analysis results

**We conducted additional analysis using a modified primary endpoint in a selected patient group. As a result, we now expect to obtain statistically superior results and clinically meaningful improvement in the next trial.**

| | Endpoint | Patients selected for analysis | Analysis results |
|---|---|---|---|
| **Analysis defined in the protocol (Jan. 29, 2019)** | Proportion of patients that achieved a total FMMS score improvement of 10 points or more from baseline at 24 weeks post-dose. | All patients enrolled in STR-02 trial | Primary endpoint not met<br>No statistical significance versus the control group |
| **Additional analysis (Today's announcement)** | Composite FMMS: Proportion of patients that achieved at least one of the following three FMMS improvement criteria (versus baseline) at 6-month post-dose<br>- FMMS for upper extremity: +6 points or more<br>- FMMS for lower extremity: +4 points or more<br>- FMMS total: +9 points or more | Among all patients enrolled in STR-02 trial, those with infarct size of less than a certain amount | Showed statistical significace versus the control group<br>Control group (19%: 5/26)<br>SB623 group (49%: 25/51) |

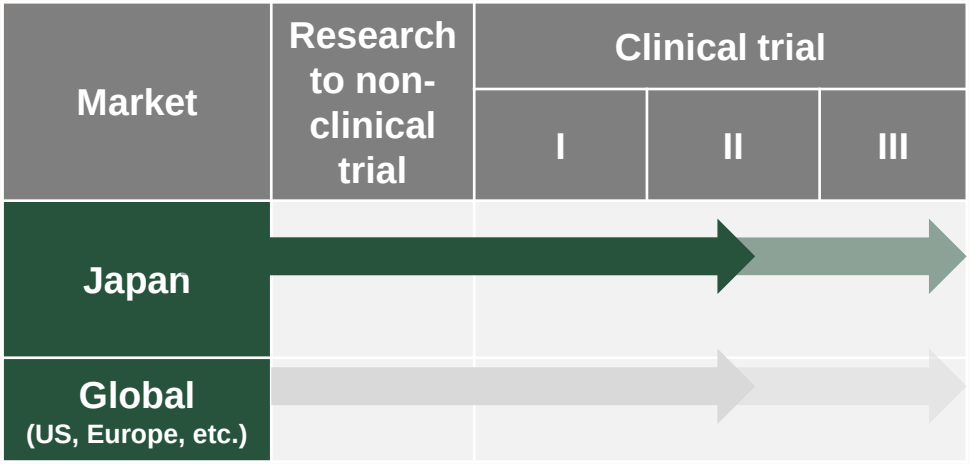
- For additional analysis, the primary endpoint was reviewed in light of the minimal clinically important difference (MCID: the smallest change that could be interpreted as a clinically beneficial change in patients) and the results of the Phase 2 trial for TBI program. Even when compared to the primary endpoint originally established, we believe the appeal of the clinical significance of the treatment responses stands.
- The group of patients selected for analysis represented approximately half of the total STR-02 trial subjects, and we believe this is a feasible patient group.

# Development plans

**Resuming preparations for domestic clinical trials for ischemic stroke and hemorrhagic stroke programs based on latest analysis results and TBI program trial results. Expected to start from Phase 2b or Phase 3.**

## Ischemic stroke program


## Hemorrhage stroke program

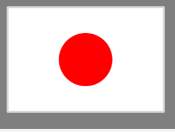



*** Clinical trials will begin from Phase 2b onward as safety has been confirmed in previous clinical trials for ischemic stroke and TBI programs.**

# Development plans

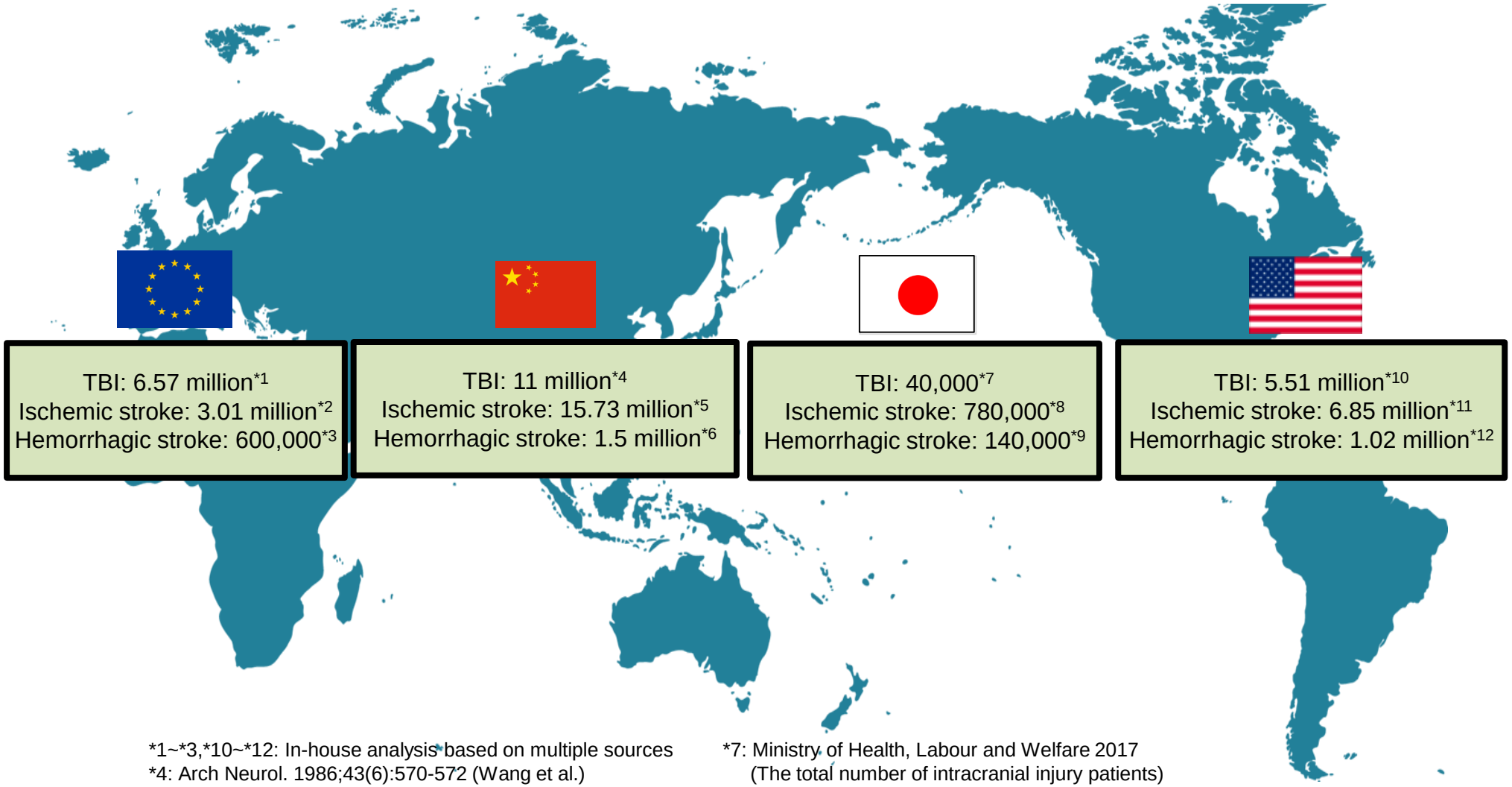
**Prioritizing domestic clinical trials for ischemic stroke and hemorrhagic stroke programs. Global Phase 3 trials for TBI program postponed to FY2022.1 onward.**

**Top priority**

| |  |   |
|---|---|---|
| **Traumatic brain injury (chronic phase)** | Approval filing planned for FY2021.1 | Clinical trials scheduled for FY2021.1 postponed to FY2022.1 onward*. |
| **Ischemic stroke** | Plan to discuss initiation of Phase 2b or 3 clinical trials with PMDA | Planning to start clinical trials from FY2022.1 onward*. |
| **Hemorrhagic stroke** | Plan to discuss initiation of Phase 2b or 3 clinical trials with PMDA | Planning to start clinical trials from FY2022.1 onward*. |

* Considering in-house development and partnership options

# Market size



| | | | |
|---|---|---|---|
| TBI: 6.57 million[*1]<br>Ischemic stroke: 3.01 million[*2]<br>Hemorrhagic stroke: 600,000[*3] | TBI: 11 million[*4]<br>Ischemic stroke: 15.73 million[*5]<br>Hemorrhagic stroke: 1.5 million[*6] | TBI: 40,000[*7]<br>Ischemic stroke: 780,000[*8]<br>Hemorrhagic stroke: 140,000[*9] | TBI: 5.51 million[*10]<br>Ischemic stroke: 6.85 million[*11]<br>Hemorrhagic stroke: 1.02 million[*12] |

*1~*3,*10~*12: In-house analysis based on multiple sources
*4: Arch Neurol. 1986;43(6):570-572 (Wang et al.)
*5: Circulation. 2017;135:759-771 (Wang et al., 2017).
*6: GHDx Healthdata IQVIA analysis 2020

*7: Ministry of Health, Labour and Welfare 2017
(The total number of intracranial injury patients)
*8: Ministry of Health, Labour and Welfare 2017
(The total number of cerebral infarction patients)
*9: Ministry of Health, Labour and Welfare 2017
(The total number of cerebral hemorrhage patients)

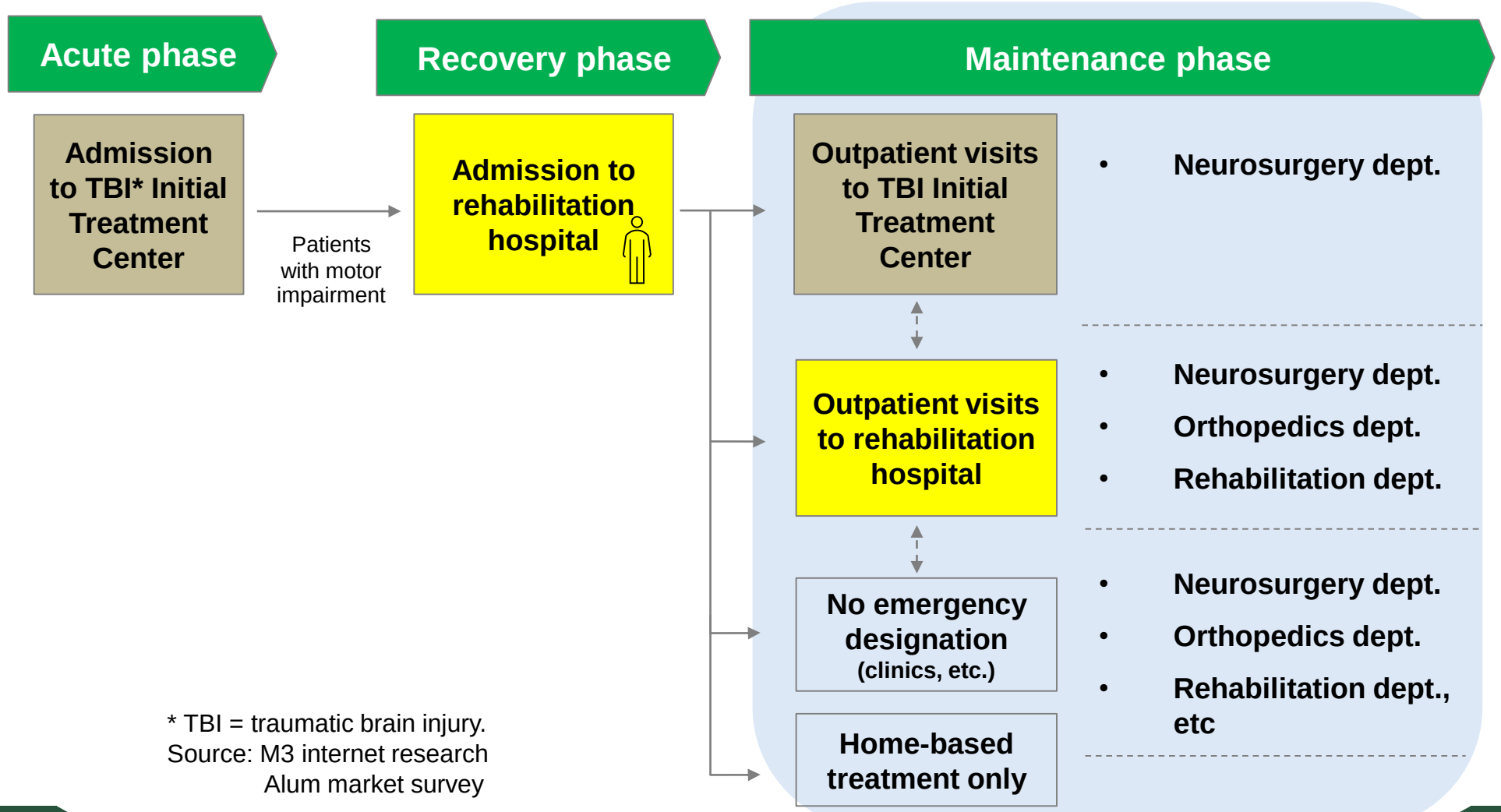
# Pre-launch medical activities for TBI, 80% completed

| Purpose | Issues for launch |
|---|---|
| Build sales structure | Understand the current status of maintenance phase patient treatment and conduct strategic planning based on clinical department, insurance system, and physician's perspective in each treatment phase |
| | Carry out activities such as sound community collaboration efforts and post-surgery follow-ups |
| | Build appropriate cooperation system with patient groups while ensuring compliance |
| Build logistics system | Establish patient registration system including regenerative medicine product traceability |
| | Carry out activities to build logistics scheme in various communities |
| Create promotional materials | Prepare promotional materials and video content based on product marketing strategy |
| | Prepare website content based on product marketing strategy |
| Pricing | Prepare documents to calculate appropriate drug prices |

| Purpose | Issues for launch |
|---|---|
| Build system for appropriate use | Collect and deliver further medical information to ensure appropriate use |
| | Establish qualification assessment system that leverages ICT |
| | Establish medical structure for appropriate use after launch |
| Review medical fees | Clarify necessary requirements and regulatory compliance |
| Present evidence | Ensure to publicize results and achievements |

# Launching in Japan ahead of the rest of the world

**Identify maintenance phase contact points between head trauma patients with motor impairment and physicians, and establish an appropriate information delivery scheme.**




* TBI = traumatic brain injury.
Source: M3 internet research
Alum market survey

**Plans in place to carry out effective information delivery activities at launch while considering latent patient segments.**

## Maintenance (Chronic) phase TBI: Latent patient percentage by segment

Maintenance phase survey

| | Health Insurance/Nursing Care Insurance | | | | Home-based treatment (including out-of-pocket rehabilitation) |
|---|---|---|---|---|---|
| | Tertiary emergency care facility | Secondary emergency care facility | Primary emergency care facility | No emergency designation | |
| Neurosurgery | 1.2% | 11.7% | 2.5% | 4.0% | 51.7% |
| Orthopedics | 0.6% | 5.6% | 1.2% | 2.9% | |
| Rehabilitation | 0.2% | 1.7% | 0.2% | 1.8% | |
| Neurology | 0.2% | 1.7% | 0.3% | 1.5% | |
| Internal medicine | 0.3% | 3.0% | 1.0% | 7.0% | |

Source : Kumamoto head injury data bank
M3 internet research / Ministry of Health, Labour and Welfare data
SanBio external survey

# Becoming global leader in regenerative medicine


**Deliver novel therapeutics to patients as rapidly as possible to maximize corporate value**

# Disclaimer

This presentation material, including any comments made during or following the presentation, is provided solely for the purpose of reference to those investors who make their own evaluation of the company at their own risk. This material contains estimates, such as plans, strategies and judgments, that are forward-looking statements which are made based on management's assumptions and beliefs in light of the information currently available to it and may contain risks and uncertainty. Therefore you should not place undue reliance on them in making investment decisions.

SanBio cautions you that actual results may differ substantially from those discussed in this material due to various factors. We do not guarantee the accuracy or completeness of the information herein. Unless otherwise stated, estimates or forecasts are solely those of our company and subject to change without notice. We accept no liability whatsoever for any direct or consequential loss arising from any use of this report.

SanBio Company Limited

Management Administration

Contact: info@sanbio.jp


SanBio
Pioneering Regenerative Medicine