October 16, 2025

Company name: SanBio Co., Ltd.
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Notice Regarding the Subcommittee Review Results on Partial Change Approval for "AKUUGO® Suspension for Intracranial Implantation" (INN: Vandefitemcel)

SanBio Co., Ltd. (head office: Tokyo, representative director & CEO: Keita Mori) hereby announces that today at the Subcommittee on Regenerative Medical Products and Biological Technologies of the Pharmaceutical Affairs and Food Sanitation Council, Ministry of Health, Labour and Welfare (MHLW), the proposal titled *"Partial change to the marketing authorization and revision of the approval conditions for the regenerative medical product AKUUGO® suspension for intracranial implantation"* was reviewed, and it was concluded that the approval of the proposal would be acceptable.

Based on this review result, approval regarding partial change by the MHLW is expected to follow. After the NHI price listing, the company plans to launch "AKUUGO® suspension for intracranial implantation" (INN: vandefitemcel; hereafter, "AKUUGO®"). AKUUGO® is the world's first regenerative therapy for the brain. It was granted conditional and time-limited approval in Japan in July 2024 — the first such approval in the world — as a treatment for chronic motor paralysis associated with traumatic brain injury.

【Explanation of Approval Conditions】

AKUUGO® received conditional and time-limited marketing authorization on July 31, 2024, with the following four conditions attached. At today's Subcommittee meeting, the application materials submitted by SanBio were deemed to have satisfied Condition ① below, and it was determined that the restriction on product shipment imposed under this condition may be lifted. Please note that AKUUGO® remains approved under the conditional and time-limited framework, and the Company continues to plan to obtain full approval within the seven-year period following the initial approval granted last year.

[Approval Conditions Attached as of July 31, 2024]

① Considering the limited manufacturing record for the Product, the Company shall promptly collect information on the Product's quality based on a pre-determined plan, and evaluate and report on the equivalence/homogeneity, in terms of quality, of the investigational product (clinical trials product) and the Product intended for commercial distribution. Based on the evaluation results, the Company shall apply for a partial change of approved matters. It shall not ship the Product until the partial change application has been approved.

② The Company must ensure that the Product is used in medical facilities fully equipped to handle emergencies, by physicians who possess sufficient knowledge and experience in the diagnosis and treatment of traumatic brain injury and stereotactic brain surgery techniques. The physicians must also have sufficient knowledge of the clinical trial results and adverse events of the Product.

③ Until the Company re-applies for marketing approval for the Product prior to the expiration of the conditional and time-limited approval, the Company must conduct post-marketing evaluation of all cases where the Product is used.

④ Until the Company re-applies for marketing approval for the Product prior to the expiration of the conditional and time-limited approval, the Company must collect information on the biological characteristics reflecting the mechanisms of action of the Product and take necessary measures, such as improving its quality control strategy.

Future Outlook

Going forward, in line with our medium- to long-term growth strategy, we will advance business activities targeting traumatic brain injury in the U.S. market. Regarding our traumatic brain injury program, we have already reached agreement with the U.S. Food and Drug Administration (FDA) on the Phase 3 clinical trial design, and preparations for the clinical trial are scheduled to begin in the next fiscal year. In Japan, we also plan to initiate discussions with the Pharmaceuticals and Medical Devices Agency (PMDA) regarding clinical trials for our stroke program in the next fiscal year. The Company aims to become a global leader in the field of regenerative medicine and will continue to strive to maximize corporate value.

We recognize that the impact of this matter on the current fiscal year's business results is minimal.

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Keita Mori CEO of SanBio commented as follows.

“"The adult brain does not regenerate." This discovery by Dr. Santiago Ramón y Cajal of Spain, who won the Nobel Prize, has been considered common knowledge for over a century. Since our founding, however, we have challenged this conventional wisdom and have pursued research and development for 25 years with the aim of turning humanity’s dream of brain regeneration into reality. As a result, we have accomplished creating AKUUGO®, the world’s first therapy to regenerate the brain.

In July of last year, AKUUGO® received conditional and time-limited approval. However, we faced a significant hurdle: further data accumulation and verification were required before it could be shipped. Over the past year, our entire team has diligently worked to build this track record. Today, we are truly pleased that our efforts have been recognized, and AKUUGO® can now be delivered to patients. We remain fully committed to providing new hope to patients suffering from traumatic brain injury and their families through AKUUGO®, and we will continue to dedicate ourselves wholeheartedly to this mission.”

Reference

Product Overview

Brand name	AKUUGO® Suspension for Intracranial Implantation
Generic name	Vandefitemcel
Indications and effects	Improvement of chronic motor paralysis associated with traumatic brain injury
Dosage and administration	For adults, implant 5 x10^6 live human (allogeneic) bone marrow-derived mesenchymal stem cells (300μL of cell suspension) to perilesional brain tissues via stereotactic brain surgery using the dedicated delivery device set. Implant the cells into the perilesional area through three trajectories via a burr hole made in the skull. To each trajectory, inject 100μL of the cell suspension, depositing 20μL of the solution each across a total of five sites placed at 5–6mm intervals from the deepest site. The rate of implantation should be approximately 10μL/min. Follow the steps below for implantation. 1. Before starting the procedure, attach the guide & stop and stylet-equipped inserter from the dedicated delivery device set to the head fixation device for invasive neurosurgery. 2. Thaw the cell suspension for intracranial implantation, wash it with the dedicated preparation solution, and adjust the concentration of the cell suspension to 1.67 x 10^6 cells/100μL using the dedicated preparation solution. Cleanse the micro-syringe fixed with the cannula from the dedicated delivery device set with the dedicated preparation solution before filling it with the prepared cell suspension.
Summary of Efficacy Evaluation	International Phase II Clinical Trial (TBI-01: U.S., Japan, Ukraine) Multi-center, randomized, double-blind, sham surgery-controlled

	study. Subjects were randomly assigned to the treatment or sham surgery groups at a 3:1 ratio. The treatment groups received AKUUGO® at doses of 2.5×10^6, 5.0×10^6, or 10.0×10^6 cells. Trial Results: Efficacy: The change from baseline in the Fugl-Meyer Motor Scale (FMMS) at Week 24, the primary endpoint, was 8.3 ± 10.6 in the pooled SB623 (AKUUGO®) groups (n=46) and 2.3 ± 4.7 in the sham surgery group (n=15), demonstrating a statistically significant difference (mean ± standard deviation, p=0.0401).
Date of marketing approval	July 31, 2024

Product image

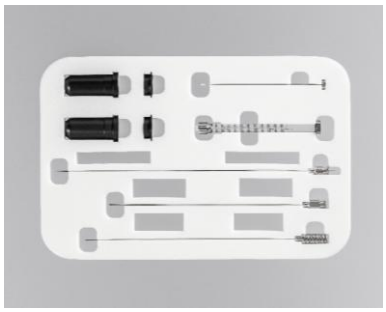
Vial containing cell suspension for intracranial implantation

Dry shipper

Hard case and dry shipper for transportation

Dedicated preparation solution

Outer package for dedicated preparation solution



Dedicated delivery device set

Outer package for dedicated delivery device set

About Traumatic Brain Injury

Traumatic brain injury (TBI) is one of the leading causes of death and disability worldwide. The estimated global incidence of acute TBI during 2016 was 27 million cases, and the estimated global prevalence of chronic impairment secondary to TBI was 55.5 million cases[1].Overall, TBI and long-term motor deficits secondary to TBI significantly impair a person's self-care, employability, and quality of life, and are major burdens on healthcare systems worldwide. In the United States, approximately 43% of surviving hospitalized persons with TBI experience long-term disabilities[2], and it is estimated that 3.17 million people are living with long-term disabilities secondary to TBI[3].

About "AKUUGO® suspension for intracranial implantation"

AKUUGO® suspension for intracranial implantation(INN: vandefitemcel) is an allogeneic, human bone marrow–derived mesenchymal stem cell product manufactured by culturing and processing mesenchymal stromal cells derived from the bone marrow fluid of healthy adult donors. When transplanted into damaged neural tissue in the brain, it releases fibroblast growth factor-2 (FGF-2), a type of protein that is expected to stimulate the brain's inherent regenerative capacity by promoting the proliferation and differentiation of neural cells. Vandefitemcel (SB623) has been designated by Japan's Ministry of Health, Labour and Welfare (MHLW) as a regenerative medical product under the Sakigake Designation System.

In the United States, it has been granted Regenerative Medicine Advanced Therapy (RMAT) designation by the U.S. Food and Drug Administration (FDA), and in Europe, it has been designated as an Advanced Therapy Medicinal Product (ATMP) by the European Medicines Agency (EMA).

Overview of AKUUGO® Efficacy Evaluation

The efficacy of AKUUGO® was primarily evaluated in the STEMTRA trial. The STEMTRA trial was a Phase II, multi-center, randomized, double-blind, sham surgery-controlled study designed to assess the efficacy and safety of the investigational product Bandefitem Cell (SB623) in patients with chronic motor dysfunction resulting from traumatic brain injury (TBI).
A total of 63 eligible patients were randomized in a 1:1:1:1 ratio to receive either low-dose SB623 (2.5×10^6 cells), medium-dose SB623 (5.0×10^6 cells), high-dose SB623 (10.0×10^6 cells), or sham surgery. Of these, 46 patients received SB623, and 15 patients were assigned to the control group and underwent sham surgery. The primary endpoint of the trial was the change from baseline in the Fugl-Meyer Motor Scale (FMMS) at Week 24. The results showed a statistically significant improvement in the SB623-treated groups compared with the sham surgery group (SB623: 8.3 [SD 1.4] vs. sham: 2.3 [SD 2.5], $p = 0.04$). At Week 48, the overall SB623-treated group did not demonstrate a statistically significant difference from the sham surgery group in FMMS change from baseline. However, the medium-dose group (5.0×10^6 cells) showed a significant improvement compared with sham (SB623 medium-dose: 10.5 [SD 1.8] vs. sham: 4.1 [SD 1.8], $p = 0.02$). Furthermore, patients treated with SB623 showed improvements from baseline at Week 48 in the Action Research Arm Test (ARAT), walking speed, and Neuro-QoL assessments of upper and lower limb function, indicating enhancements in both motor function and activities of daily living. SB623 continued to demonstrate good tolerability, consistent with previous results, and no new safety concerns were identified.

About SanBio Group (SanBio Co., Ltd. and SanBio, Inc.)

SanBio is engaged in the regenerative cell business—we research, develop, manufacture, and sell regenerative cell medicines. In July 2024, under the Sakigake Designation Program, we obtained conditional and time-limited approval for our mainstay product AKUUGO® for the indication of improving chronic motor deficit resulting from traumatic brain injury. Going forward, we will continue focusing our R&D efforts on central nervous system disorders with significant unmet medical needs that cannot be addressed by existing medicine or drugs. The Company is headquartered in Tokyo, Japan and Oakland, California, and additional information about SanBio Group is available at https://sanbio.com/en/

<References>

[1] James SL, et al. “Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990- 2016: a systematic analysis for the Global Burden of Disease Study 2016.” Lancet Neurol 2019;18:56-87.
[2] Selassie AW, et al. “Incidence of long-term disability following traumatic brain injury hospitalization, U.S.”, 2003. J Head Trauma Rehabil 2008;23:123-31
[3] Zaloshnja E, Miller T, Langlois JA, Selassie AW. Prevalence of long-term disability from traumatic brain injury in the civilian population of the United States, 2005. J Head Trauma Rehabil. 2008 Nov-Dec;23(6):394-400.

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