FY2024 Q3 Financial Results

Company

HEALIOS K.K.

Date

November 13, 2024

Important Note on Future Events, etc

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Business Overview

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HLCM051 ARDS: Global Phase 3 Trial and Conditional and Time-limited Approval in Japan

Update

Healios

September 6, Agreement with the FDA on Pivotal, Global Phase 3 Trial

Link

Details of Agreement: REVIVE-ARDS Study

- Primary endpoint: VFD (Ventilator Free Days: the number of days a patient does not require mechanical ventilation out of 28 days post administration in REVIVE-ARDS study, which is consistent with that utilized in the ONE-BRIDGE study previously completed in Japan.)
- Number of patients: Interim analyses will be conducted at the 300 and 400 patient stages, and the REVIVE-ARDS study can be completed when statistical significance is confirmed. The maximum number of patients is 550.
- The framework was confirmed for utilizing 3D investigational product in this study.
- Development funding: Focus on subsidiary financing, specific options include royalty investment, third-party allotment of subsidiary shares, etc.

Global Phase 3 Trial Opportunity

- Large market size and larger number of target patients for ease of enrollment
- Fast Track and RMAT designation from the FDA

  -Systems that allow for expedited approval of drugs and cellular products that meet certain conditions for the development of new drugs for serious or life-threatening diseases or diseases for which no treatment is available.
- Availability of development funding

October 2, Decision to Apply for Conditional and Time-Limited Approval and Termination of Phase 3 Trial in Japan

Link

- Based on the positive results of the Phase 2 study (ONE-BRIDGE study) in Japan and the Phase 2 study (MUST-ARDS study) in the U.S. and the U.K., and on the premise that the above-described REVIVE-ARDS study will be conducted as a confirmatory study

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Update

Healios

Milestone Achieved Pursuant to Joint Research Agreement with AND medical and Projected Demand for Culture Supernatant

Link

Outline of the Agreement

- Healios will provide regenerative medicine technology and raw materials to AND medical for use in the development of a new therapy.
- Received upfront payment of JPY60M at signing and **1st milestone payment of JPY60M** in Q4 2024. Healios will receive **total 180 million yen** based on the progress of the research.
- Confirmed **positive component analysis results**
- After the manufacturing method and system for the raw materials have been established and the objectives of the Agreement have been achieved, Healios expects to enter into an **agreement to supply culture supernatant** to AND medical on an ongoing basis.

Projected Demand

Healios starts to provide **25 liters of culture supernatant per month** during fiscal year 2025 to meet demand specifically from AND medical, and will increase production based on an ongoing assessment of demand.

Price: Based on Healios' own market analysis, most culture supernatant products carry a unit price of approximately 10,000 yen to 30,000 yen per cubic centimeter (cc) when sold as a raw material. The final unit price per cc will be determined with AND medical after additional confirmation of the quality of Healios produced culture supernatant.

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Business Alliances and License Agreements

Update

Healios

Nobelpharma Co., Ltd. (announced on September 30)

Link

- Extended the expected deadline for the conclusion of an agreement between Healios and its Subsidiary ProcellCure, Inc. for the Development and Commercialization of MultiStem® in Japan for ARDS by the end of January, 2025.

  Reason: Since the development strategy including clinical trials in the U.S. and the application for conditional and time-limited approval in Japan will affect the development approval process in Japan with Nobelpharma, we are extending the period of time until the conclusion of this agreement

Alfresa Corporation (announced on June 5)

Link

- Basic Business Alliance Agreement concerning the distribution and sale of products owned by Healios
- The First and Second Series of Straight Bonds Purchase Agreement for total of 1.6 Billion of Yen

Astellas Pharma Inc. (announced on June 19)

Link

- License Agreement with AIRM, a subsidiary of Astellas Pharma Inc., granting AIRM a non-exclusive license to use patents for the method of production and purification of RPE (Retinal Pigment Epithelium) cells in all applicable countries, except Japan.
- Upfront payment of US$3 million in July and up to US$8 million in milestone payments expected from AIRM

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Pipeline

Update

Healios

	Development Code	Therapeutic Area	Therapy	Region	Discovery	Pre-Clinical	Clinical P1	Clinical P2	Clinical P3	Comments
Inflammatory Conditions	HLCM051	ARDS	MultiStem®	Japan			Preparing for approval			Preparing to apply for Conditional and Time-Limited Approval Orphan designation
				Global (USA)			Preparing for Phase 3			Agreed with FDA on Global Phase 3 trial design in the U.S. Fast Track and RMAT designation (USA)*1
	HLCM051	Ischemic Stroke	MultiStem®	Japan			Phase 2/3			Consulting with regulatory authorities on application policy in Japan based on clinical trial data from the U.S. and Japan. SAKIGAKE designation (Japan) Fast Track and RMAT designation (USA)
				Global (USA)			Phase 3			
	HLCM051	Trauma	MultiStem®	Global (USA)			Phase 2			Funded by MTEC (United States Department of Defense) and the Memorial Hermann Foundation

*1 Fast Track and RMAT designations relate to a system that allows for expedited approval of drugs (RMAT is for cellular processed products) that meet certain conditions for the development of new drugs for serious or life-threatening diseases or diseases for which no treatment is available.

	Development Code	Therapeutic Area	Therapy	Region	Discovery	Pre-Clinical	Clinical P1	Clinical P2	Clinical P3	Comments
Replacement Therapies	HLCR011	RPE tear AMD	RPE*2	Japan			Phase 1/2			Joint research with Sumitomo Pharma Co., Ltd. Scheduled to be launched in FY2028 First subject enrollment initiated

*2 Retinal Pigment Epithelium

Immuno-Oncology	HLCN061	Solid Tumors*3	eNK	Global						Pre-IND started IND: 2025 planned
	–	Solid Tumors	CAR-eNK	Global						

*3 Gastric cancer, Mesothelioma, Lung cancer and Hepatocellular carcinoma

Note: Excludes pipeline assets scheduled to be carved out

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Update Healios

Three pillars to monetization

Accelerate development in the U.S. market as a growth driver while monetizing other assets

Medical Materials

HLCM051 Culture Supernatant

Universal Donor Cell

iPS cell lines, etc.

SIFU™

Culture Supernatant:
FY2024: Promote joint research
Received milestone from AND medical group
Preparing for mass production (Positive component analysis results obtained)
FY2025: Commencement of sales

SIFU technology:
In discussions with Japanese and U.S. potential partners

Bone marrow-derived cells

ARDS

Global Phase 3 trial under preparation

Preparing to apply for Conditional and Time-limited Approval in Japan

Ischemic Stroke

Consulting with regulatory authorities on application policy in Japan

Trauma

Phase 2 trial with U.S. DoD budget

iPS cells

Replacement Therapies
RPE
First subject enrollment initiated in July 2024

Immuno-Oncology
Gene-engineered NK cells

Business scale expansion by securing global rights

Steady progress toward the start of Phase 3 trial for ARDS in the U.S., the world's largest market.

Proceed with a combination of partnering, carve-outs, and grants

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HLCM051 ARDS: Development Status

Update

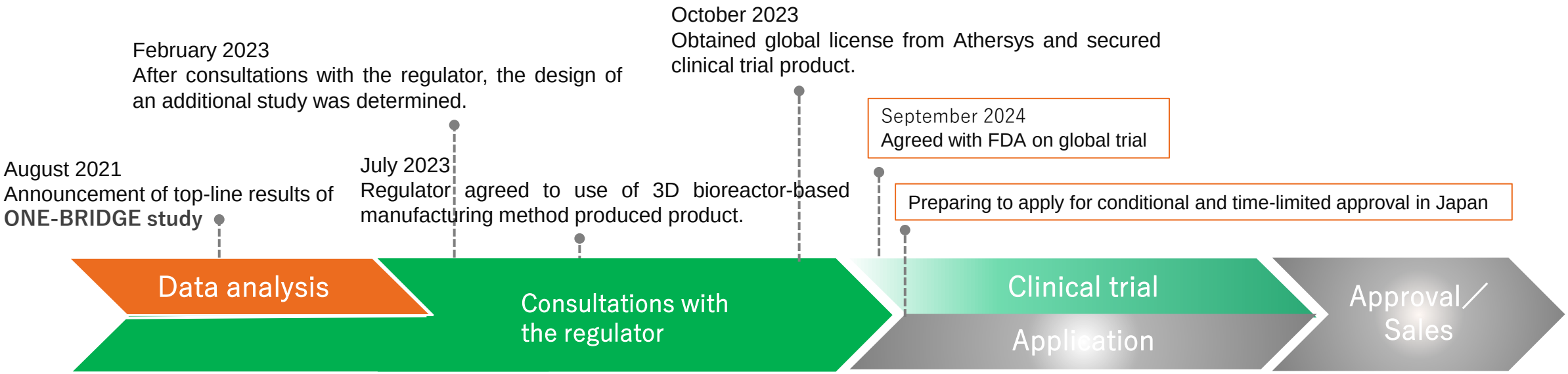
Healios

Inflammatory Conditions

Global Phase 3 clinical trial (REVIVE-ARDS Study) under preparation

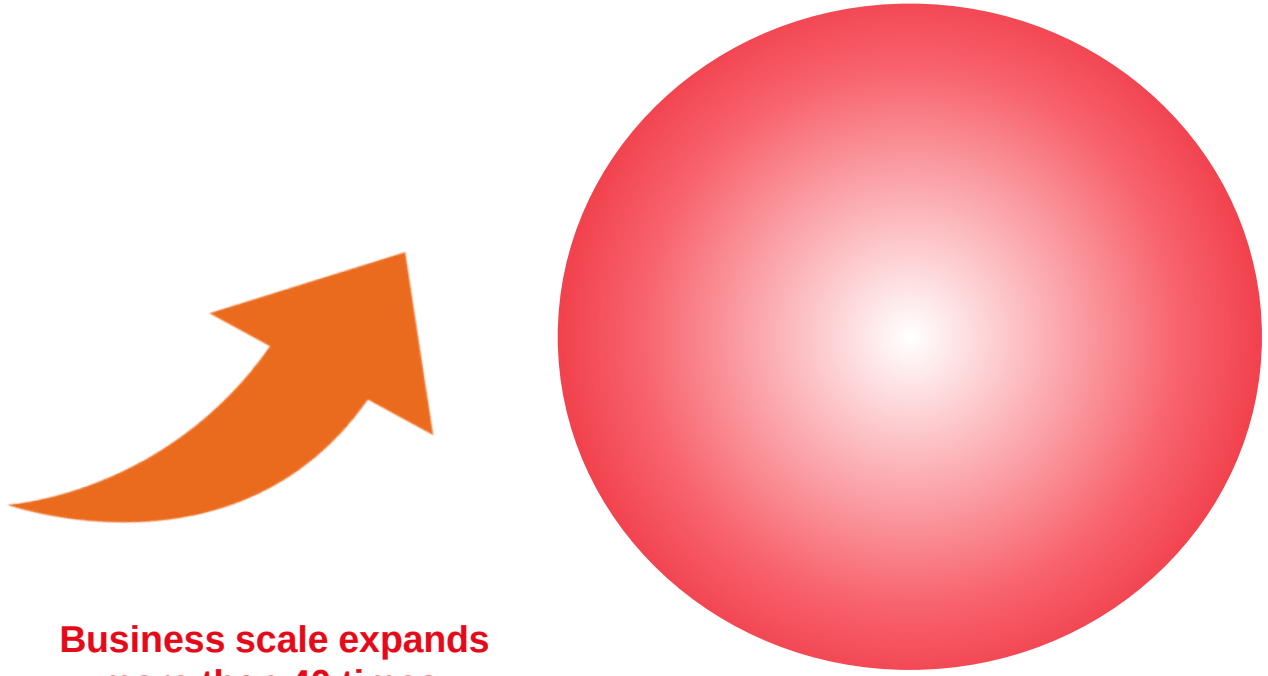
ARDS

- **Preparing for Global Phase 3 trial in the U.S. (agreed with the FDA on September 6)**
- **Decided to apply for Conditional and Time-limited Approval in Japan based on the positive results of the Phase 2 study (ONE-BRIDGE study) and on the premise that the REVIVE-ARDS study will be conducted as a confirmatory study**



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HLCM051 ARDS: Global Market (Expansion)



Japan 28,000

Business scale expands more than 40 times.

Global over 1.1 million

Business Policy

1) In-house clinical trials in the U.S. and Japanese markets with the highest investment efficiency

   Focus on subsidiary financing

   Specific options include royalty financing, third-party allotment of subsidiary shares, etc.

2) Outside of the U.S. market (Japan, Korea, Taiwan, and China), conclude licensing agreements and aim for early monetization.

Estimated number of ARDS patients worldwide

China 670k、US 262k、Europe 133k、Japan 28k

(Source)
Japan: Estimated by Healios based on the incidence rate of epidemiological data and the total demographical population in Japan.
USA: Diamond M et al. 2023 Feb 6. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–.PMID: 28613773
Europe: Community Research and Development Information Service (CORDIS) 2020 7-9
China: song-et-al-2014-acute-respiratory-distress-syndrome-emerging-research-in-china

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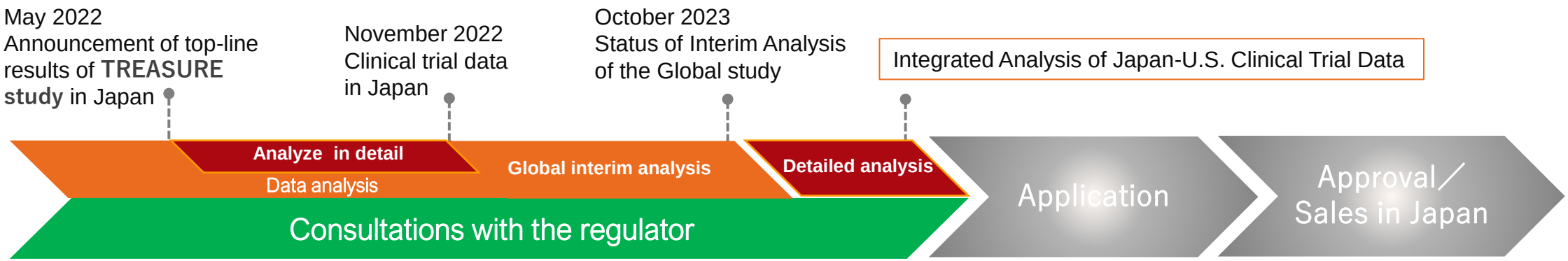
HLCM051 Ischemic Stroke: Development Status

Update

Healios

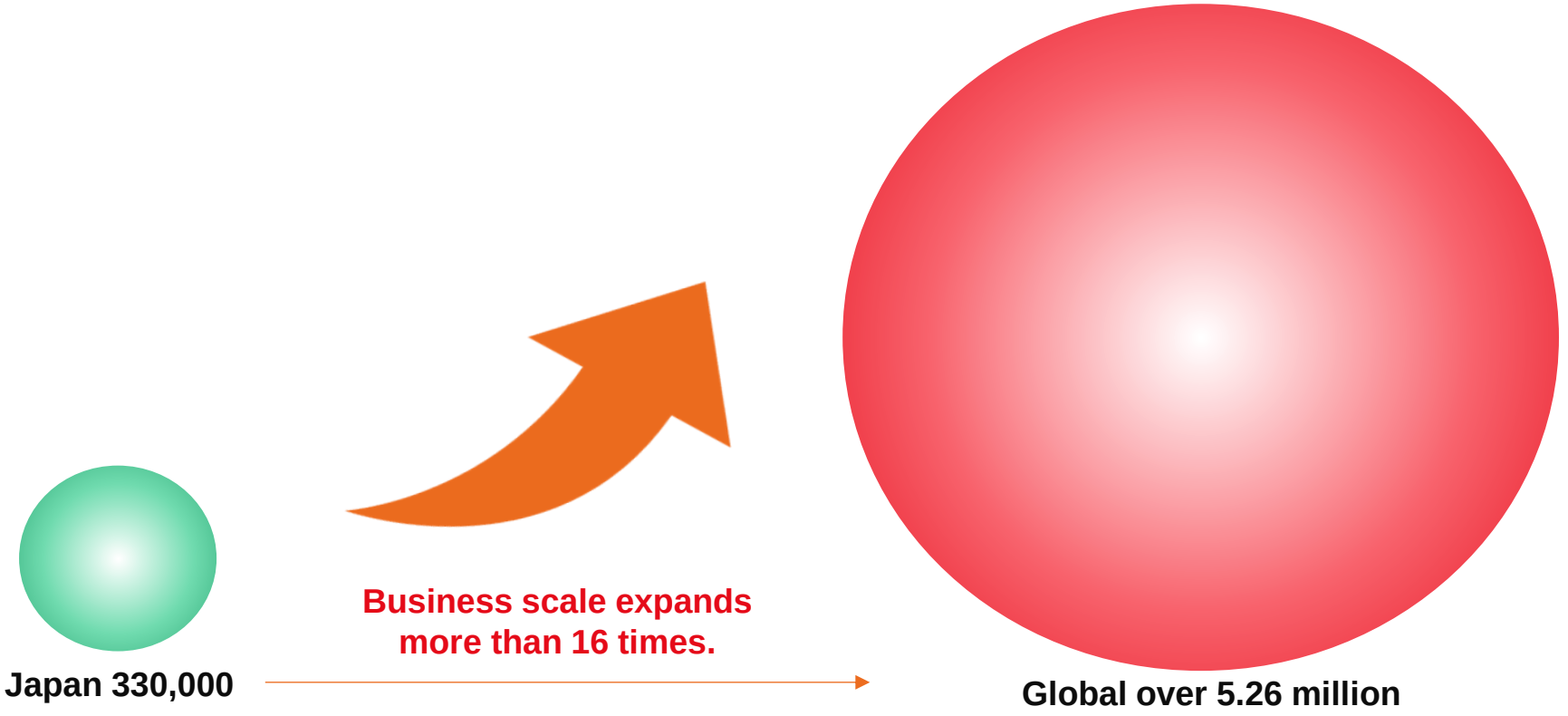
Inflammatory Conditions

Ischemic stroke	**Consulting with regulatory authorities on application policy in Japan based on clinical trial data from the U.S. and Japan.**



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HLCM051 Ischemic Stroke: Global Market (Expansion)



Business Policy

1) In-house clinical trials in the U.S. market with the highest investment efficiency

   Focus on subsidiary financing

   Specific options include royalty investment, third-party allotment of subsidiary shares, etc.

2) Outside of the U.S. market (Japan, Korea, Taiwan, and China), conclude licensing agreements and aim for early monetization.

Estimated number of Stroke patients worldwide

China 3.4mn、Europe 840k, US 690k, Japan 330k

（Source）
Japan： Estimated the annual number of new patients according to materials issued by the Ministry of Health, Labour and Welfare.
USA： "Stroke Facts" by CDC
Europe：Burden of Stroke in Europe: An Analysis of the Global Burden of Disease Study Findings From 2010 to 2019
China: Estimated Burden of Stroke in China in 2020

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HLCM051 Trauma: Development Status

MATRICS-1 study（USA）

Inflammatory Conditions

Trauma

Took control of a 156 patient, Phase 2 clinical trial in trauma

Funded almost entirely by MTEC (United States Department of Defense) and the Memorial Hermann Foundation

Conducted at University of Texas Health Science Center at Houston (UTH) and Memorial Hermann Texas Medical Center, the busiest level 1 trauma center in the U.S.

- The trauma being treated in this study is that which results from car accidents, industrial accidents, gun shot wounds, etc.
- The leading cause of death for people under the age of 45, third leading cause of all deaths in the U.S. and the leading cause of quality-of-life years lost*
- The use of MultiStem® in the treatment of trauma also has meaningful potential US military applicability

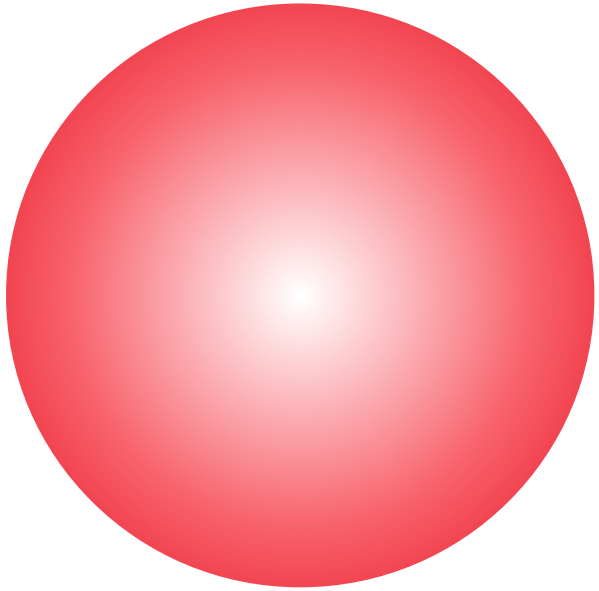
* Source: the Centers for Disease Control (CDC)

MATRICS-1 study

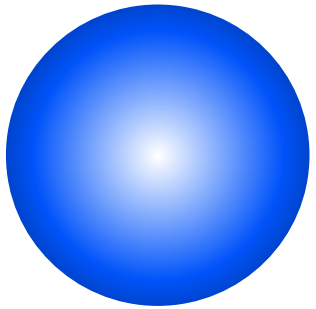
Overview: MultiStem® for Treatment of Trauma Induced Multiple Organ Failure/Systemic Inflammatory Response Syndrome (SIRS).
Single center, prospective, randomized, double-blind, pragmatic phase 2 clinical study.
Primary endpoint: Kidney injury stage (Day 30)
Secondary endpoint: Mortality etc.
Participant: Severely injured trauma patients within hours of hospitalization who have survived initial resuscitation

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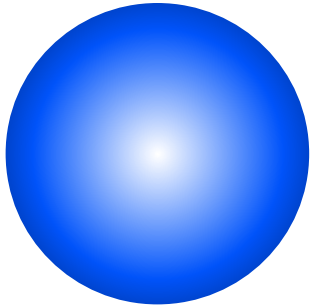
HLCM051 Trauma: US Market (New Pipeline)



Yearly 220,000 (deaths)



45% About 100,000
Trauma or acute poisoning under the influence of drugs



55% About 120,000
General trauma

Market Characteristics

1) 3rd cause of death: 220,000 per year.

   1st cause of death under age 45: 87,000 per year

2) Wartime Injury

   Afghanistan: Casualties 2,354 / Injured and sick 20,149

   Iraq War: Casualties 4,431 / Injured and sick 31,994

(Source)
DOD: Department of Defense (U.S.)
https://www.defense.gov/casualty.pdf

CDC: Centers for Disease Control and Prevention
https://wisqars.cdc.gov/lcd/?o=LCD&y1=2022&y2=2022&ct=10&cc=ALL&g=00&s=0&r=0&ry=0&e=0&ar=lcd1age&at=groups&ag=lcd1age&a1=0&a2=199

NIH: National Institutes of Health (U.S.)
https://www.ncbi.nlm.nih.gov/books/NBK547669/

Pathological conditions leading from trauma to death

Systemic inflammatory response syndrome (SIRS) resulting from trauma is an excessive self-protective response to external stresses, including trauma (e.g., car accidents, gunshot wounds), drugs, and infection, which first results in autonomic, endocrine, hematologic, and immunologic changes.

These changes, initially intended to protect the body, become an unregulated cytokine storm, leading to a massive inflammatory cascade, organ damage, and death.

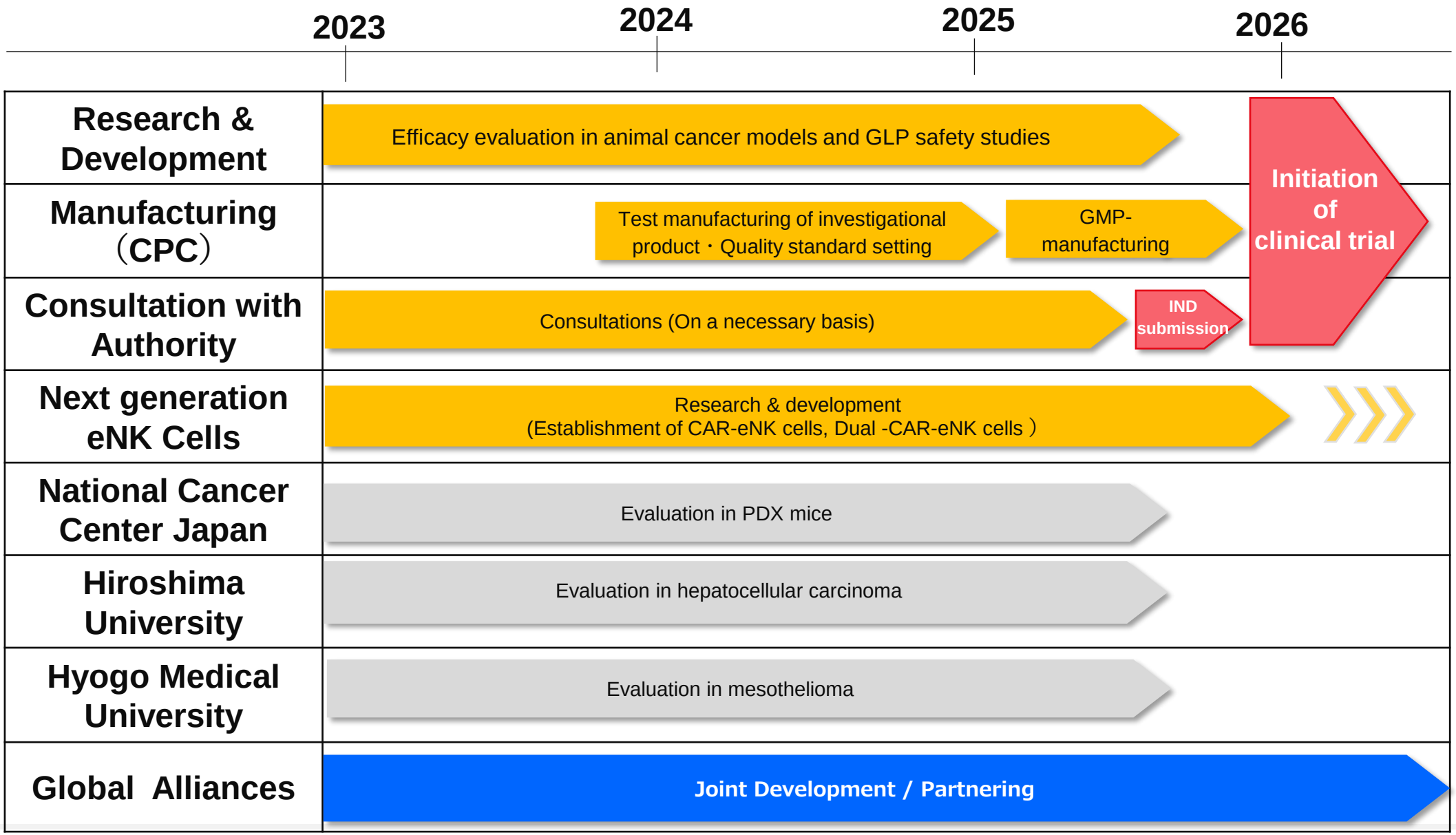
Currently, there is no effective treatment for patients who have reached this point, and only coping therapies are available for each symptom.

Expected effects of MultiStem®

As shown in ARDS and other clinical trials, the ability to suppress inflammation in the acute phase is expected to suppress cytokine storms and have an effect on patient prognosis. In clinical trials for trauma, we are conducting clinical trials with renal function as the primary endpoint to facilitate evaluation of efficacy.

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R&D Roadmap of eNK Cells (HLCN061)



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Conference Presentations and Articles (FY2024)

Link from underlined parts

Conference	Date／Venue	Title	Author／Department
AACR Annual Meeting 2024	April 8 / San Diego, U.S.A.	Verification of the effect of human allogeneic iPS cell-derived gene-engineered NK cells (eNK cells HLCN061) on mesothelioma	Dr. Seiji Matsumoto, MD Hyogo Medical University
Stem Cell Research and Therapy	July 2 / Academic paper	Hypoimmunogenic human iPSCs expressing HLA-G, PD-L1, and PD-L2 evade innate and adaptive immunity	Norihiro Tsuneyoshi, et al. Kobe Research Institute, Healios K.K.

Note: The above shows only overseas presentations. In Japan, researchers from the joint research institutions and Healios' Kobe Research Institute have presented their research at numerous academic conferences.

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Financial Highlights

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Consolidated Statement of Income

Update

Healios

(Units: millions of yen)

	FY2023 Q3(YTD)	FY2024 Q3 (YTD)		
			YoY variance	Main reasons for increase/decrease
Revenue	114	542	428	Increase mainly due to revenues related to license agreements for RPE cell production method.
Operating profit	-2,298	-1,976	323	Increase in SG&A expenses ＋133 Decrease in R&D expenses -57
Profit	-2,076	-4,475	-2,399	Increase in finance income +51 Increase in finance costs -2,844 (Primarily non-cash activity; please refer to the next page for details)
R&D expenses	1,531	1,474	-57	
Number of employees	63	**58**	-5	

(Note)
* For details of the financial figures, please refer to the summary of the financial results announced today.

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Supplemental Explanation of Finance Income and Finance Costs

Update

Healios

Details of finance income and finance costs

In the nine months ended September 30, 2024, we recorded finance income of ¥431 million and finance costs of ¥2,957 million.

Finance income was mainly due to the recording of ¥391 million in profit or loss transferred to equity interests held by external investors in the Saisei Fund[*1] and ¥39 million in interest income.

Finance costs were mainly due to the recording of ¥2,592 million in loss on remeasurement of derivatives[*2] ,¥181 million in loss on remeasurement of investment securities, ¥73 million in interest expenses on bonds[*3], ¥ 55 million in share acquisition rights issuance costs and ¥51 million in foreign exchange losses.

*1. Profit or loss transferred to equity interests held by external investors in the Saisei Fund

Profit or loss transferred to equity interests held by external investors in the Saisei Fund is the transfer amount of profits and losses of Saisei Bioventures, L.P., the consolidated subsidiary of our company, to limited partners other than our company. Saisei Bioventures, L.P. is a limited partnership established by Saisei Capital Ltd., the general partner and consolidated subsidiary of our company.

*2. Loss on remeasurement of derivatives

This is mainly a non-cash gain/loss item recorded in accordance with the International Financial Reporting Standards (IFRS), which represents the loss on remeasurement of the 21st and 22nd stock acquisition rights issued by the Company at fair value as of the end of the 3rd quarter of the fiscal year ended December 2024.

Under Japanese GAAP (JGAAP), the amount to be paid in for stock acquisition rights is recorded as equity. Under IFRS, the amount to be paid in for stock acquisition rights is recorded as a liability, and the fair value is measured at the end of each period and the gain or loss on remeasurement is recorded in financial income or financial costs.

*3. Interest expenses on bonds

Of the total interest on bonds of 73 million yen posted for the nine months ended September 30, 2024, 42 million yen was charged to income using the amortized cost method. This is a non-cash expense recorded in accordance with IFRS.

Under JGAAP, amount of bonds issued were accounted for as liabilities and issue fees were accounted for as expenses. Under IFRS, however, proceeds, after deducting issue fees from amount of bonds issued, based on a certain standard. As a result, the difference between the face value of bonds and the amount recorded as liabilities is amortized (expensed) over the period.

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Consolidated Statement of Financial Position

Update

Healios

(Units: millions of yen)

		December 31, 2023	September 30, 2024		
				Variance	Main reasons for increase/decrease
	Current assets	7,683 (50.7%)	5,077 (39.8%)	▲2,606	Decrease in cash and cash equivalents -2,190 (Cash and cash equivalent balance at 9/30/24 was 4,533)
	Non-current assets	7,471 (49.3%)	7,668 (60.2%)	196	Increase in intangible assets +288
Total assets		15,155 (100.0%)	12,745 (100.0%)	▲2,410	
	Current liabilities	5,169 (34.1%)	3,972 (31.2%)	▲1,198	Decrease in bonds and borrowings -3,958 Increase in other financial liabilities +2,870
	Non-current liabilities	6,118 (40.4%)	7,035 (55.2%)	916	Increase in bonds and borrowings +1,599 Decrease in equity interests held by external investors in Saisei Fund -348
Total liabilities		11,287 (74.5%)	11,006 (86.4%)	▲281	
Total equity		3,867 (25.5%)	1,739 (13.6%)	▲2,129	Recording of loss -4,475 Issuance of new shares +2,181
Total liabilities and equity		15,155 (100.0%)	12,745 (100.0%)	▲2,410	

(Note) * For details of the financial figures, please refer to the summary of the financial results announced today.

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Healios

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