FY2024 Q2 Financial Results

Company

HEALIOS K.K.

Date

August 13, 2024

Important Note on Future Events, etc

This material has been prepared solely for the purpose of disclosing relevant information regarding HEALIOS K.K. (“HEALIOS”). This document does not constitute an offer to sell or the solicitation of an offer to buy any security in the United States, Japan or any other jurisdiction.

This presentation contains statements that constitute forward-looking statements, including estimations, forecasts, targets and plans, and such forward-looking statements do not represent any guarantee by management of future performance. [In many cases, but not all, HEALIOS uses such words as “aim,” “anticipate,” “believe,” “continue,” “endeavor,” “estimate,” “expect,” “initiative,” “intend,” “may,” “plan,” “potential,” “probability,” “project,” “risk,” “seek,” “should,” “strive,” “target,” “will” and similar expressions to identify forward-looking statements.] You can also identify forward-looking statements by discussions of strategy, plans or intentions. Any forward-looking statements in this document are based on the current assumptions and beliefs of HEALIOS in light of the information currently available to it, and involve known and unknown risks, uncertainties and other factors. Such risks, uncertainties and other factors may cause HEALIOS’s actual results, performance, achievements or financial position to be materially different from any future results, performance, achievements or financial position expressed or implied by such forward-looking statements.

This presentation is based on the economic, regulatory, market and other conditions as in effect on the date hereof, and HEALIOS does not guarantee that the information contained in this presentation is accurate or complete. It should be understood that subsequent developments may affect the information contained in this presentation, which HEALIOS is not under an obligation, or does not plan, to update, revise or affirm. The information in this presentation is subject to change without prior notice and such information may change materially. Neither this presentation nor any of its contents may be disclosed to or used by any other party for any purpose without the prior written consent of HEALIOS.

The information in connection with or prepared by companies or parties other than HEALIOS is based on publicly available and other information as cited, and HEALIOS does not have independently verified the accuracy and appropriateness of, nor makes any warranties with respect to, such information.

The information about regenerative medicine products (including products currently in development) which is included in this material is not intended to constitute an advertisement or medical advice.

© HEALIOS K.K. All rights reserved.

Business Overview

© HEALIOS K.K. All rights reserved.

Acquisition of Substantially All of the Assets of Athersys

Link

On April 3, 2024, completed the acquisition of MultiStem® and other assets of Athersys.

- No longer subject to milestones and royalty payments to Athersys regarding the license for MultiStem
- Now the owner of global rights to MultiStem and an intellectual property portfolio that currently includes over 400 patents

Acquired Assets

- MultiStem assets including 3 INDs* and clinical data for ischemic stroke, ARDS, and trauma
  The phase 3 MASTERS-2 study in ischemic stroke conducted mainly in the U.S.
  The phase 2 MUST-ARDS study in ARDS in the U.S. and Europe
  The phase 2 MATRICS study in trauma conducted in the U.S.
  * Investigational New Drug Application
- MultiStem biological materials including 3D clinical product
  Hundreds of doses of MultiStem and 3D bioreactor manufactured clinical product.
- License agreement in the animal field
  Out-licensing of MultiStem for use in non-human mammals with a focus on dogs, cats, and horses in the U.S. domestic market
- SIFU technology
  Advanced frozen cell product storage device called SIFU™ (“Secure Integrated Freezer Unit”) for extremely low temperature storage and logistics

© HEALIOS K.K. All rights reserved.

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

New

Healios

September Consultation with FDA to Initiate the Global Phase 3 Trial

Link

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 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.

- Availability of development funding

(Focus on subsidiary financing, specific options include royalty investment, third-party allotment of subsidiary shares, etc.)

-Healios NA or a new subsidiary in the U.S. to be funded

Continued consultation with regulatory authorities in Japan regarding application for conditional and time-limited approval

- The global trial to be agreed upon with the FDA to act as a confirmatory study to be completed after conditional and time-limited approval in Japan.
- Proceed with further consultation with the regulatory authorities regarding the conditional and time-limited approval, based on the positive results of the completed Phase 2 trial (ONE-BRIDGE study) and the initiation of a global Phase 3 confirmatory trial.

© HEALIOS K.K. All rights reserved.

Business Alliances and License Agreements

New Healios

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

Nobelpharma Co., Ltd. (announced on June 28) 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 September.

  Reason: Since the development strategy including clinical trials in the U.S. will affect the development approval process in Japan, we are extending the period of time until the conclusion of this agreement in order to consider and establish the development strategy in Japan based on the details of the agreement with the FDA scheduled in September

© HEALIOS K.K. All rights reserved.

HLCR011 RPE Tear: Phase 1/2 Trial

First patient has been enrolled

Link

Healios and Sumitomo Pharma Co., Ltd. are co-developing a treatment using retinal pigment epithelial (RPE) cells derived from allogeneic iPS cells (development code: HLCR011) and has initiated the first patient enrollment in a Phase 1/2 trial for patients with an RPE tear.

Outline of the clinical study

Test product	HLCR011: iPS cell-derived retinal pigment epithelial (RPE) cells suspension
Development stage	Phase 1/2
Subjects	Patients with retinal pigment epithelium tear
Design for the clinical study (target number of cases)	Part 1: Unmasked, uncontrolled (one HLA-mismatched subject) Part 2: Unmasked, randomized (treatment/observation groups, 10 subjects/group, total 20 subjects)
Primary endpoint	Safety of subretinal administration of HLCR011 in patients with retinal pigment epithelium tear (number and ratio of subjects with observed adverse events)
Secondary endpoint (efficacy)	Visual function evaluation

© HEALIOS K.K. All rights reserved.

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			Phase 3			Started clinical trial in Japan Orphan designation
			MultiStem®	Global (USA)			Phase 2/3			Consultation with FDA is scheduled to initiate Global Phase 3 trial Fast Track and RMAT designation (USA)*1
	HLCM051	Ischemic Stroke	MultiStem®	Global (USA / Japan)			Phase 3			Global Phase 3 trial under consideration with integrated data analysis of Phase 3 trial (MASTERS-2 study) in the U.S. and Phase 2/3 trial (TREASURE study) in Japan. SAKIGAKE designation (Japan) Fast Track and RMAT designation (USA)
	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

Excludes pipeline assets scheduled to be carved out

© HEALIOS K.K. All rights reserved.

Update Healios

Three pillars to monetization

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

Medical Materials	Bone marrow-derived cells	iPS cells
HLCM051 Culture Supernatant **Universal Donor Cell** **iPS cell lines, etc.** **SIFU™**	**ARDS** **Global Phase 3 trial under preparation** **Conditional and Time-limited Approval in Japan** **Ischemic Stroke** **Global Phase 3 trial under consideration** **Trauma** **Phase 2 trial with U.S. DoD budget**	**Replacement Therapies** **RPE** **First subject enrollment initiated in July 2024** **Immuno-Oncology** **Gene-engineered NK cells**

Culture Supernatant:
FY2024: Promote joint research AND medical group
FY2025: Commencement of sales

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

Business scale expansion by securing global rights

Steady progress toward the start of two Phase 3 trials in the U.S., the world's largest market, in ischemic stroke, ARDS and trauma

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

© HEALIOS K.K. All rights reserved.

HLCM051 ARDS: Development Status

Update

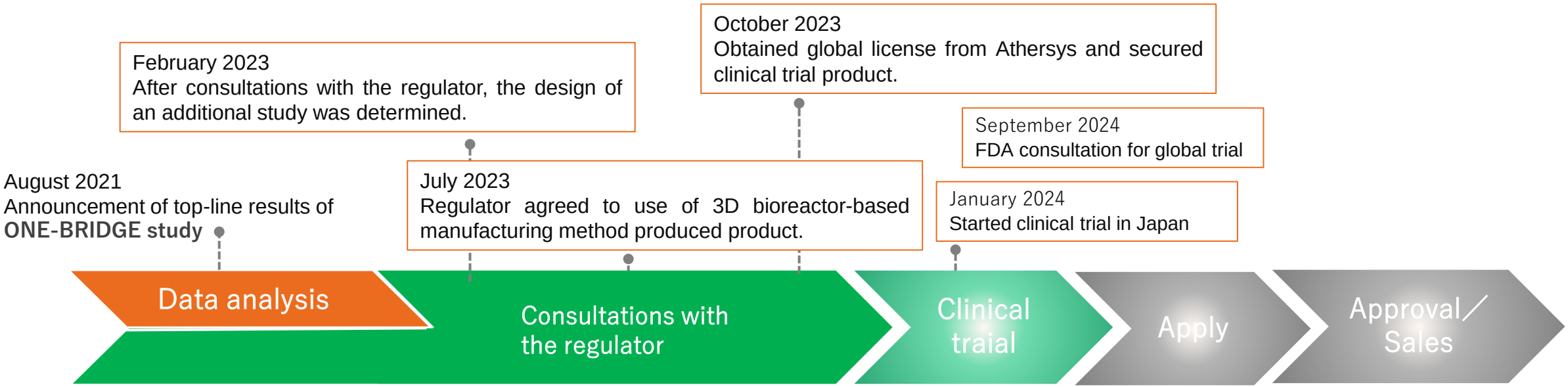
Healios

Inflammatory Conditions

Global Phase 3 clinical trial under preparation

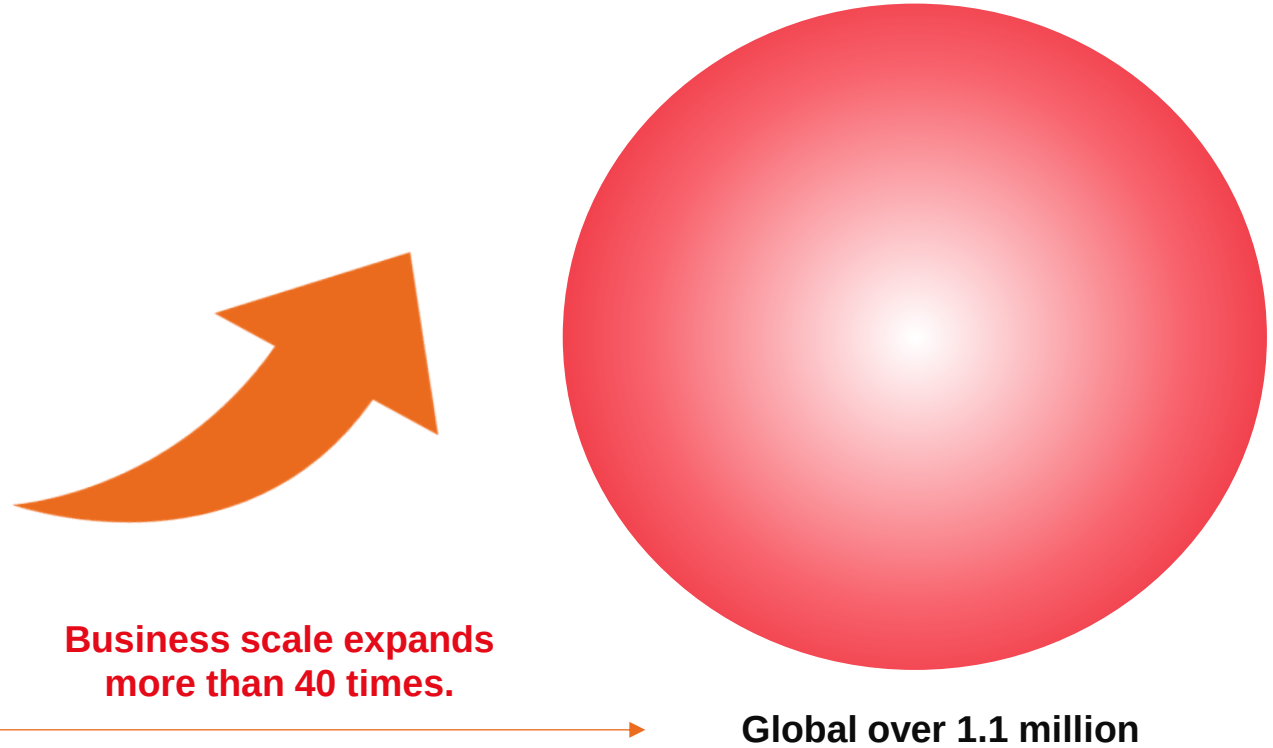
ARDS

- **Preparing for global Phase 3 trial in the U.S. (FDA interview scheduled on September 6 after completion of Phase 2 trial)**
- **Discussing with regulators regarding the application for conditional and time-limited approval in Japan, based on the positive results of the completed Phase 2 trial (ONE-BRIDGE study) and the initiation of a global Phase 3 trial**



© HEALIOS K.K. All rights reserved.

HLCM051 ARDS: Global Market (Expansion)



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

© HEALIOS K.K. All rights reserved.

HLCM051 Ischemic Stroke: Development Status

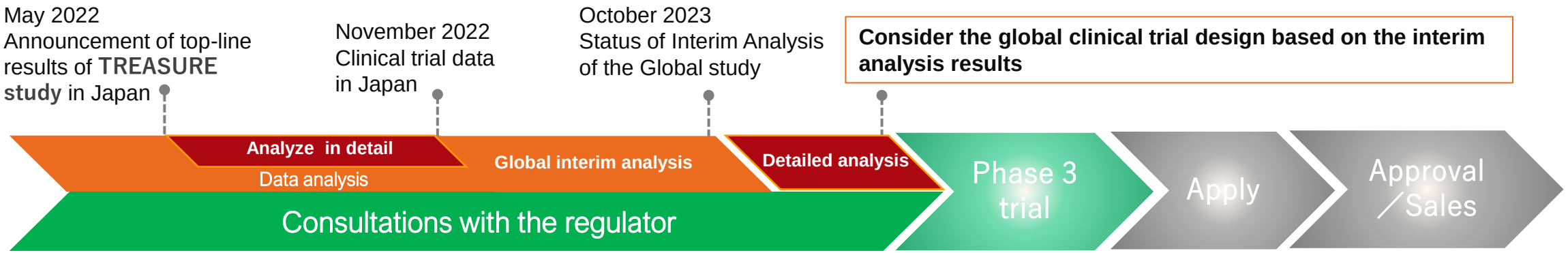
Inflammatory Conditions

Consider global Phase 3 clinical trial based on the results of interim analysis in the U.S.

Ischemic stroke

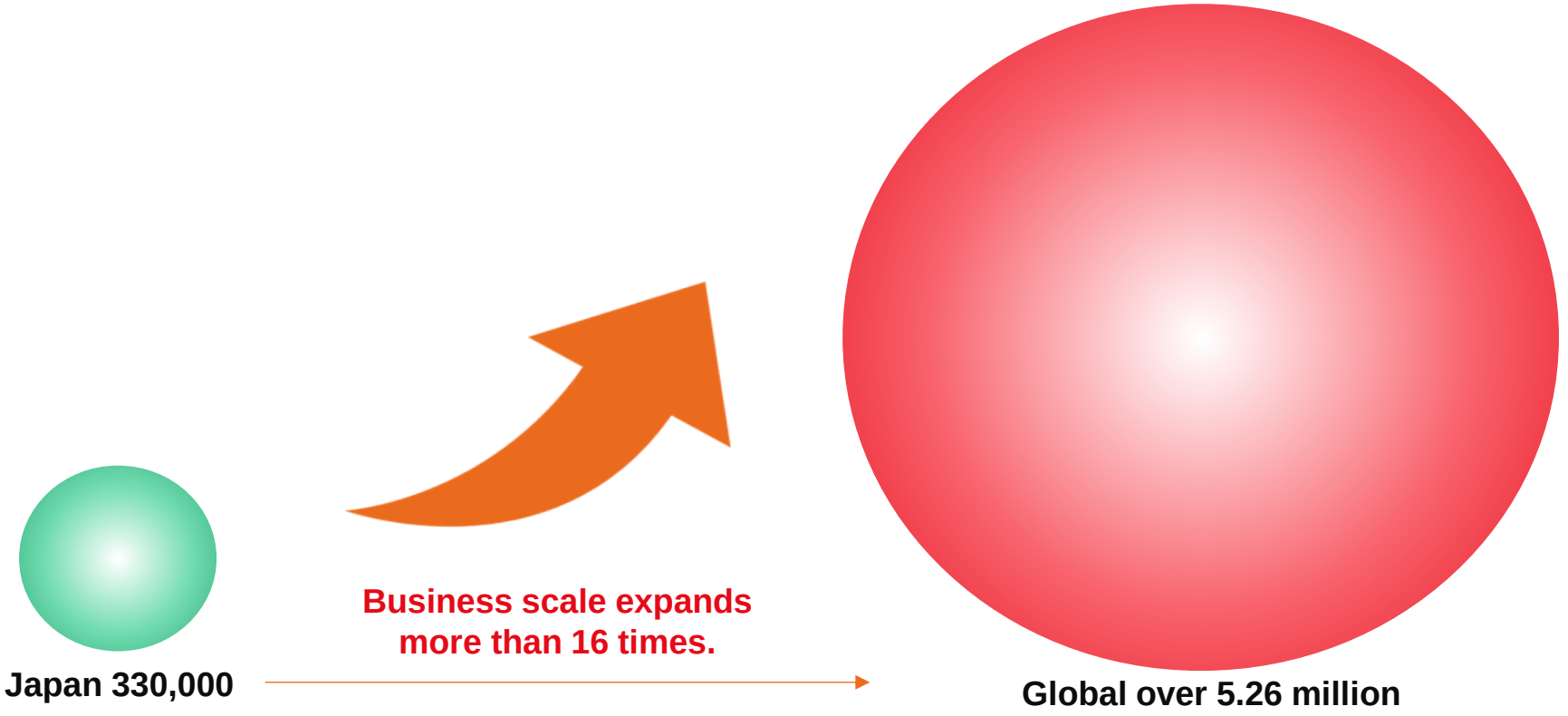
Based on the results of further data analysis from the interim analysis*1 of the global clinical trial*2, we will conduct an analysis of data from a total of approximately 400 people in Japan and the U.S. (about 200 people each in country) to determine a design and development policy that can obtain approval in Japan and the U.S. with a high probability of success.

***1 An analysis performed by an independent statistician during the course of a clinical trial. The results can be used to redefine the number of patients required.**
***2 A Phase 3 study for ischemic stroke mainly in the U.S. (MASTERS-2 study)**



© HEALIOS K.K. All rights reserved.

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

© HEALIOS K.K. All rights reserved.

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

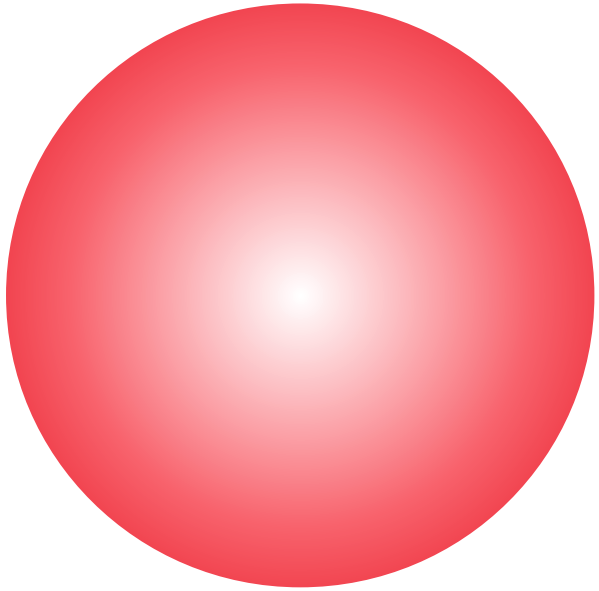
* Source: the Centers for Disease Control (CDC)

MATRICS-1 study

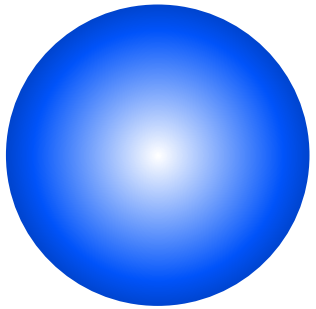
Overview: MultiStem® for Treatment of Trauma Induced Multiple Organ Failure/Systemic Inflammatory Response Syndrome (SIRS).
Single center, prospective, randomized, double-blind, pragmatic phase 2 clinical study.
Primary endpoint: Kidney injury stage (Day 30)
Secondary endpoint: Mortality etc.
Participant: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

© HEALIOS K.K. All rights reserved.

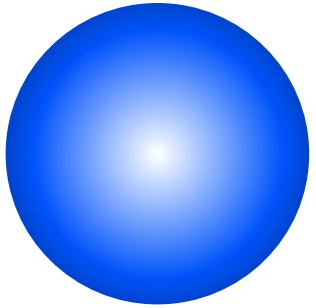
HLCM051 Trauma: US Market (New Pipeline)



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.

© HEALIOS K.K. All rights reserved.

Joint Research Agreement with AND medical group

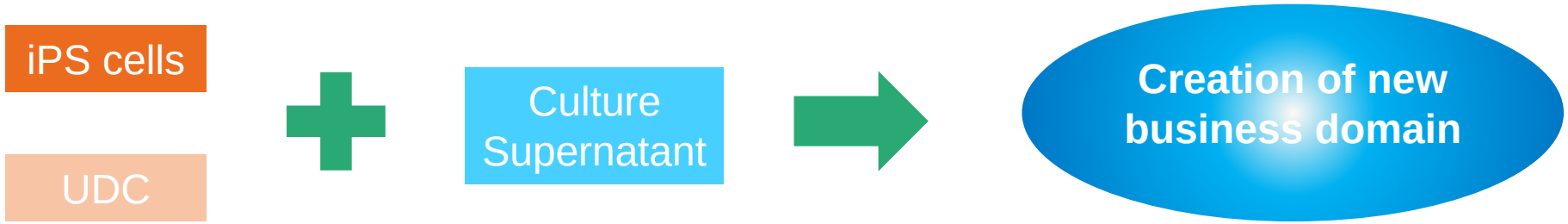
Link

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.
- Healios will receive 60 million yen as an upfront payment. Subsequently, the company will receive milestone payments based on the progress of the research, which together with the upfront payment will total 180 million yen.
- 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.

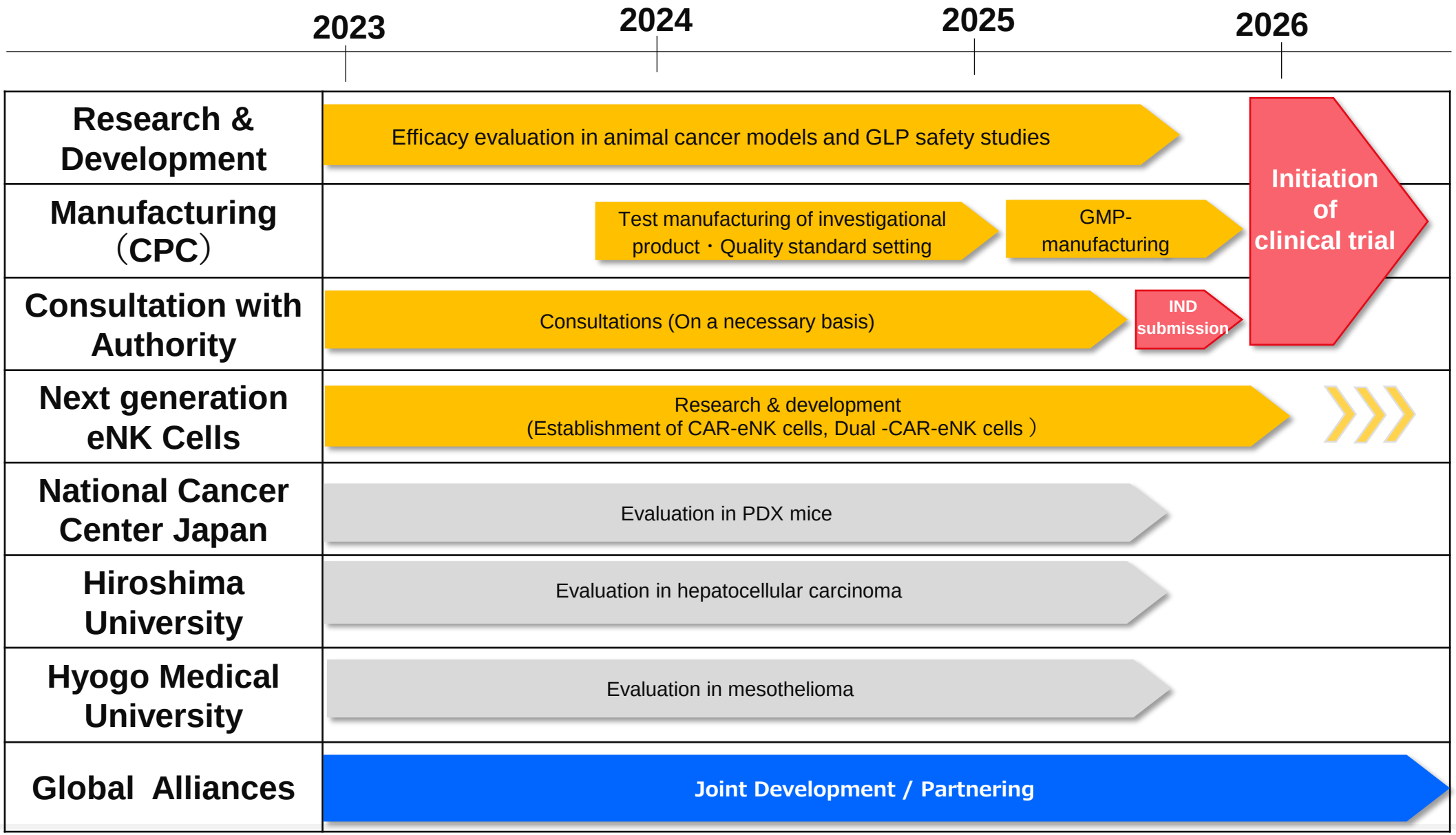
Utilization of medical materials generated during the production of regenerative medicine products

Aiming to strengthen our financial position as well as effective use of resources by increasing sales as soon as possible.



© HEALIOS K.K. All rights reserved.

R&D Roadmap of eNK Cells (HLCN061)



© HEALIOS K.K. All rights reserved.

Conference Presentations and Articles （FY2024）

Update

Healios

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.

© HEALIOS K.K. All rights reserved.

Financial Highlights

© HEALIOS K.K. All rights reserved.

Consolidated Statement of Income

Update

Healios

(Units: millions of yen)

	FY2023 Q2(YTD)	FY2024 Q2(YTD)		
			YoY variance	Main reasons for increase/decrease
Revenue	108	508	401	Increase mainly due to revenues related to license agreements for RPE cell production method.
Operating profit	-1,555	-1,331	224	Increase in SG&A expenses ＋87 Increase in R&D expenses +72
Profit	-1,384	-2,951	-1,567	Increase in finance income +155 Increase in finance costs -2,025 (Primarily non-cash activity; please refer to the next page for details)
R&D expenses	1,047	1,119	72	
Number of employees	63	**59**	-4	

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

© HEALIOS K.K. All rights reserved.

Supplemental Explanation of Finance Income and Finance Costs

Update

Healios

Details of finance income and finance costs

In the six months ended June 30, 2024, we recorded finance income of ¥463 million and finance costs of ¥2,100 million.

Finance income was mainly due to the recording of ¥431 million in profit or loss transferred to equity interests held by external investors in the Saisei Fund*1 and ¥29 million in interest income.

Finance costs were mainly due to the recording of ¥1,692 million in loss on remeasurement of derivatives*2 ,¥293 million in loss on remeasurement of investment securities, ¥56 million in interest expenses on bonds*3 and ¥ 55 million in share acquisition rights issuance costs.

*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 2nd quarter of the fiscal year ending 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 56 million yen posted for the six months ended June 30, 2024, 36 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.

© HEALIOS K.K. All rights reserved.

Consolidated Statement of Financial Position

Update

Healios

(Units: millions of yen)

		December 31, 2023	June 30, 2024		
				Variance	Main reasons for increase/decrease
	Current assets	7,683 (50.7%)	9,860 (55.4%)	2,177	Increase in cash and cash equivalents +2,172 (Cash and cash equivalent balance at 6/30/24 was 8,894)
	Non-current assets	7,471 (49.3%)	7,951 (44.6%)	480	Increase in other financial assets +325
Total assets		15,155 (100.0%)	17,811 (100.0%)	2,656	
	Current liabilities	5,169 (34.1%)	7,112 (39.9%)	1,943	Increase in other financial liabilities +1,969
	Non-current liabilities	6,118 (40.4%)	7,433 (41.7%)	1,315	Increase in bonds and borrowings +1,599
Total liabilities		11,287 (74.5%)	14,546 (81.6%)	3,258	
Total equity		3,867 (25.5%)	3,266 (18.4%)	-602	Recording of loss -2,951 Issuance of new shares +2,181
Total liabilities and equity		15,155 (100.0%)	17,811 (100.0%)	2,656	

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

© HEALIOS K.K. All rights reserved.



Healios

＜Contact information＞
IR & Finance and accounting Div.
HEALIOS K.K.

Press contact: pr@healios.jp
Investor contact: ir@healios.jp
https://www.healios.co.jp/contact/