FY2022 Q1 Financial Results

Company

HEALIOS K.K. (TSE 4593)

Date

May 10, 2022

Important Note on Future Events, etc

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Contents

Vision

To become a global biopharma company committed to transforming the lives of patients by creating, developing and commercializing cutting edge cell therapy technologies.

Corporate Highlights

Background:

- Incorporated in 2011; IPO in 2015 (Japan)
- Headquartered in Tokyo
- ~150 employees

Experienced Leadership:

- **Pioneers in cell therapy**: First in human iPSC technology in the world
- **Innovative R&D capabilities for engineered iPSC therapies**
- **Extensive manufacturing expertise**
- **Clinical development experience**: Largest cell therapy trial in Japan

Global Corporate Strategy

Building a commercial infrastructure to launch MultiStem® for ARDS & stroke in Japan

Near-term commercial revenue

Expanding capabilities for iPSC platform

Accelerating innovative iPSC platform development for immuno-oncology & cell replacement therapies

Focus on clinical development of **engineered-NK (eNK)** for solid tumors in Japan and US

Advancement of therapies derived from proprietary hypo-immune Universal Donor Cell (UDC) line

Continued investment in precision manufacturing capabilities and strengths in Japan to support future global supply

HEALIOS K.K. Leadership

Junichi Kotera	Michihisa Nishiyama	Richard Kincaid	Yoshinari Matsuda	Masanori Sawada	Kouichi Tamura	Koji Abe
Executive officer **Manufacturing field** Over 30 years experience in manufacturing	**Executive Officer** **Development field** Constructed network for Tacrolimus approval and sales at Astellas in the US and Europe	**Executive Officer** **CFO** **Director** Extensive finance experience at Goldman Sachs and Nezu Asia Capital Management	**Director** Attorney-at-Law, Senior Management Partner of Uruma Law Offices Legal Professional Corporation	**Executive Vice President, CMO (Chief Medical Officer)** MD, PhD, MBA	**Executive officer** **Research field** Ex-Astellas US Director of Laboratories Expertise in Immunosuppressant Research	**Executive Officer** **HR & GA field** Over 30 years experience in HR

Paul Bresge	Cam Gallagher	Ms. Yuko Yogo	Hardy TS Kagimoto	Dr. Toichi Takenaka	Seigo Kashii	Dr. Glenn Gormley	James Paradise
Outside Director Currently founder and CEO of Ray Therapeutics	**Outside Director** Co-founder and executive director of Zentalis.	**Outside Director** Previously a senior HR professional at JP Morgan and Fidelity.	**Chairman and CEO** **Director** MD, Founder	**Outside Director** Previously Chairman & CEO of Astellas. PhD	**Outside Director** Ex-corporate auditor of Astellas Pharma	**Outside Director** Previously Global Head of R&D at Daichi Sankyo, and CMO of Astra Zeneca. MD, PhD,	**Outside Director** Previously president of Goldman Sachs in Asia and member of Goldman Sachs' global management committee.

Healios Is Uniquely Positioned To Leverage Strong Japanese Proficiencies

Favorable External Environment In Japan

iPSCs Discovered in Japan

The Nobel Prize in Physiology or Medicine (2012) Shinya Yamanaka, M.D, Ph.D (Professor at Kyoto University)

Expedited Regulatory Framework

- Conditional and time limited authorization system
- SAKIGAKE (fast-track designation)

Precision Manufacturing in Cell Therapy

- Clinical and scale-up infrastructure for commercial purposes

Intrinsic Healios Strengths

Established Innovative R&D Expertise

- First in human iPSC technology in the world
- Proprietary hypo-immune universal donor iPSC platform technology
- Kobe Research Institute: ~100 people (incl > 30 Ph.D. holders)
- Numerous high-profile R&D partnerships & JVs

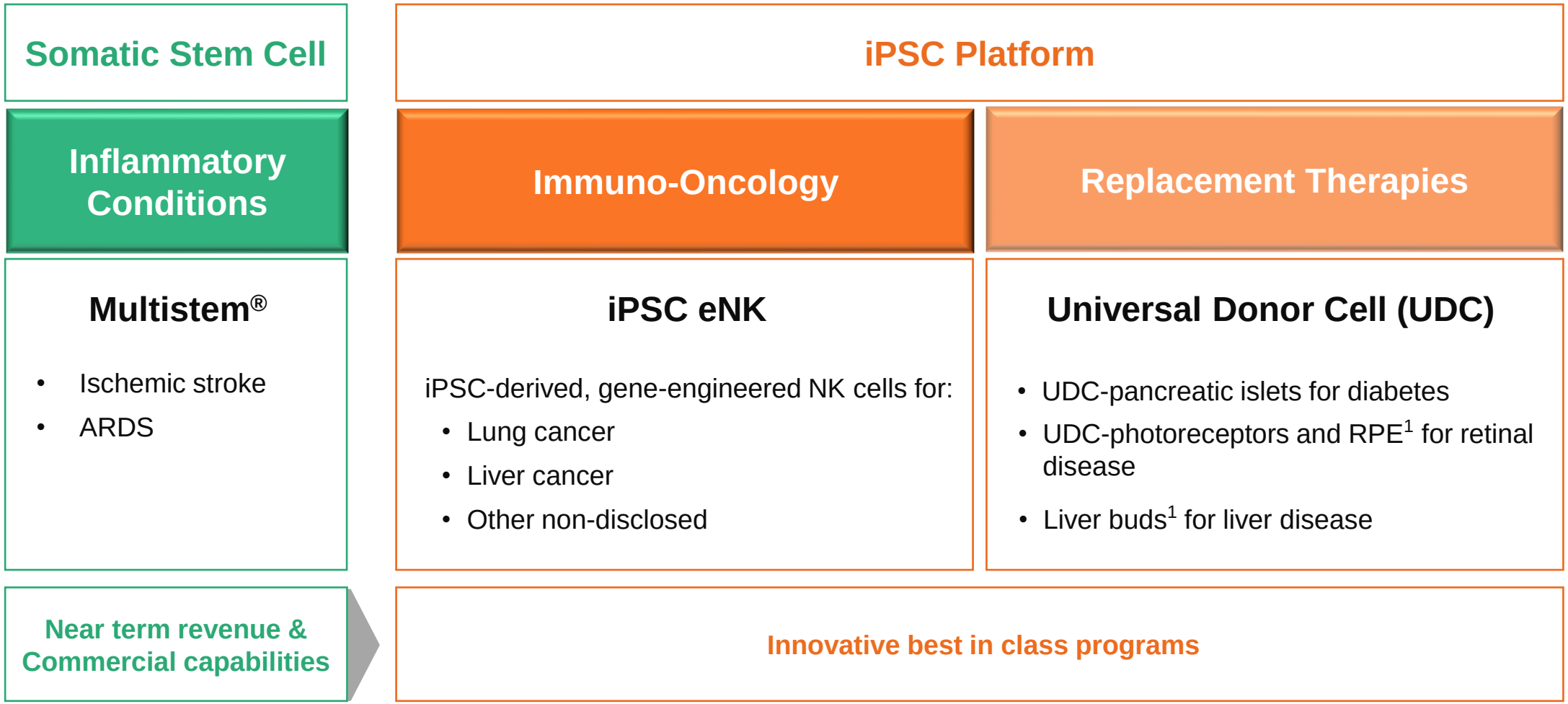
Robust CMC Expertise & Foundational Alliances with Global Players

- GCTP/GMP manufacturing facility; 31 FTEs
- Automated 3D bioreactor system for eNK
- Advanced 3D organ manufacturing
- Long-standing alliances with Nikon & Sumitomo Pharma Co., Ltd.

Clinical Development Capabilities

- Completed enrolment in two major trials in 2021 including the largest Japanese cell therapy trial in history

Program Overview



[1]Future migration to UDC platform

Pipeline

Update

Healios

	Development Code	Therapeutic Area	Therapy	Region	Discovery	Pre-Clinical	Clinical	Comments
Inflammatory Conditions	HLCM051	Ischemic stroke	MultiStem®	Japan			Phase 2/3	Stroke topline results: May 2022 SAKIGAKE designation
	HLCM051	ARDS	MultiStem®	Japan			Phase 2	Consultations with the regulator are ongoing Orphan designation
Immuno-Oncology	HLCN061	Solid tumors	eNK	Global				Pre-IND: 2022, IND: 2024 Joint research with National Cancer Center Japan & Hiroshima University
	–		CAR-eNK	Global				
Replacement Therapies	HLCR011	AMD	RPE	Japan				Co-development with Sumitomo Pharma Co., Ltd. Pending trial initiation
	–	Retinal disease	UDC-photoreceptors & RPE*	Global				
	HLCL041	Liver disease	Liver buds	Global				Joint research with Yokohama City University
	–	Diabetes	UDC-pancreatic islets	Global				Joint research with National Center for Global Health and Medicine

* Future migration to UDC platform

MultiStem®
Inflammatory Conditions

Somatic Stem Cell	iPSC Platform	
Inflammatory Conditions	**Immuno-Oncology**	**Replacement Therapies**
Multistem® • Ischemic stroke • ARDS	**iPSC eNK** iPSC-derived, gene-engineered NK cells for: • Lung cancer • Liver cancer • Other non-disclosed	**Universal Donor Cell (UDC)** • UDC-pancreatic islets for diabetes • UDC-photoreceptors and RPE[1] for retinal disease • Liver buds[1] for liver disease

HLCM051 ARDS: Target Disease

There is demand for new treatments for ARDS that will lead to improvements in patients' symptoms and prognosis

The number of ARDS patients in Japan is estimated at approximately 7,000 to 12,000 per year*1

About ARDS*2

Acute Respiratory Distress Syndrome (ARDS) is a general term for the symptoms of acute respiratory failure suddenly occurring in all seriously ill patients.

The mortality rate is approximately 30 to 58%*2.

Approximately 1/3 of ARDS cases are caused by pneumonia.

ARDS is a common cause of morbidity and mortality in severe COVID-19.

（Source）Athersys

Current Treatment

At present, there are no therapeutic drugs that can make a direct improvement to a patient's vital prognosis when ARDS develops.

The only symptomatic treatment for respiratory failure includes artificial respiration.

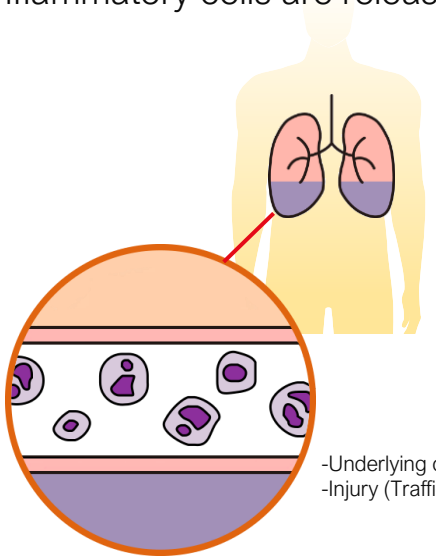
(source)
＊1 The number of ARDS patients in Japan is estimated by Healios based on the incidence rate of epidemiological data and the total demographical population in Japan.
＊2 ARDS treatment guideline 2016

HLCM051 ARDS: Mechanism of Action

Expected effects of HLCM051(MultiStem®) , bone marrow-derived somatic stem cells

- Relief of inflammation, regulation of immune function
- Promotion of angiogenesis
- Promote protection and repair of injured cells and tissues
- Improvement of lung tissue and respiratory function

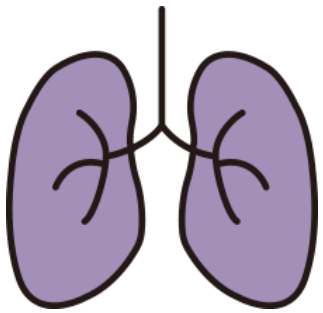
Inflammatory cells are released



-Underlying disease (pneumonia, etc.)
-Injury (Traffic accident, etc.)

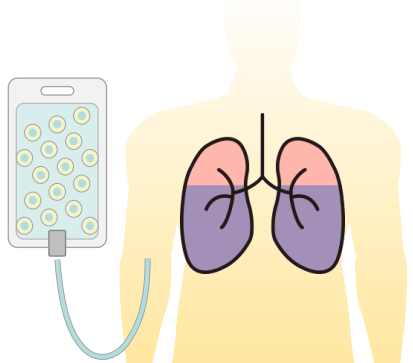
When the tissue is damaged, inflammatory cells are released in large quantities.

Inflammatory cells attack the lungs



The inflammatory cells attack the lungs. As a result, hypoxia develops and the patient falls into severe respiratory failure.

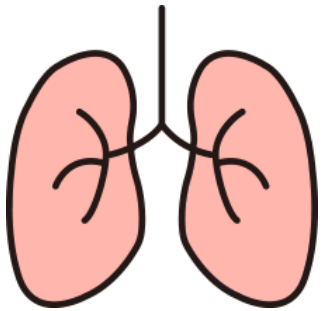
HLCM051 administered



- Suppresses excessive inflammation in the lungs.
- Protects damaged tissue and facilitates healing.

HLCM051 accumulates in the lungs as a result of intravenous administration.

Lung function improves

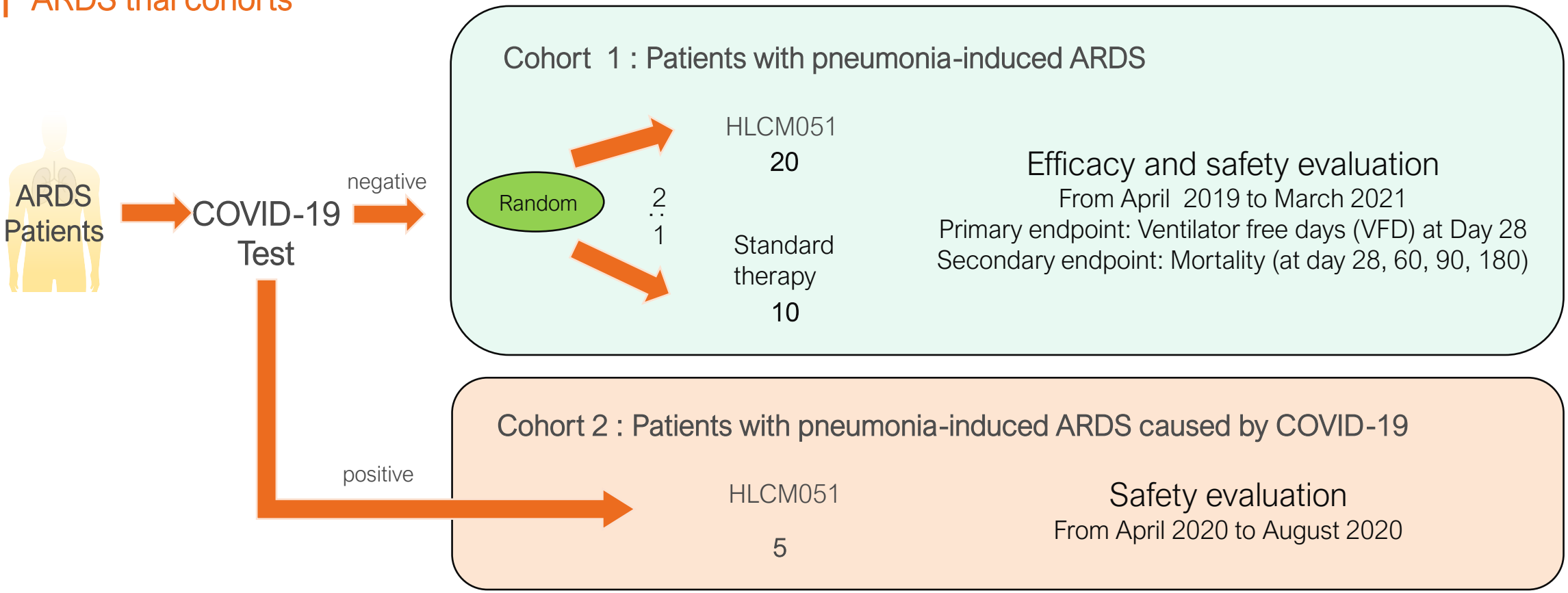


We can anticipate earlier ventilator removal and a lower mortality rate.

HLCM051 ARDS: ONE-BRIDGE Study

Phase II study investigating the efficacy and safety of HLCM051 in pneumonia induced ARDS patients

ARDS trial cohorts



Patient enrollment of COVID-19 pneumonia-derived cases (Cohort 2) was performed separately from the conventional clinical trial administration group (Cohort 1).

HLCM051 ARDS: ONE-BRIDGE Study Results at 180 Days Post Administration

Cohort 1

No safety concerns.

The HLCM051 treated group demonstrated a 9-day higher median VFD than the standard therapy group.

The treated group saw a 39% reduction in mortality as compared to patients treated with standard therapy.

Cohort 2

No deaths, no safety concerns.

The ventilator was withdrawn within 28 days for all five patients and in three days or less for three of these patients.

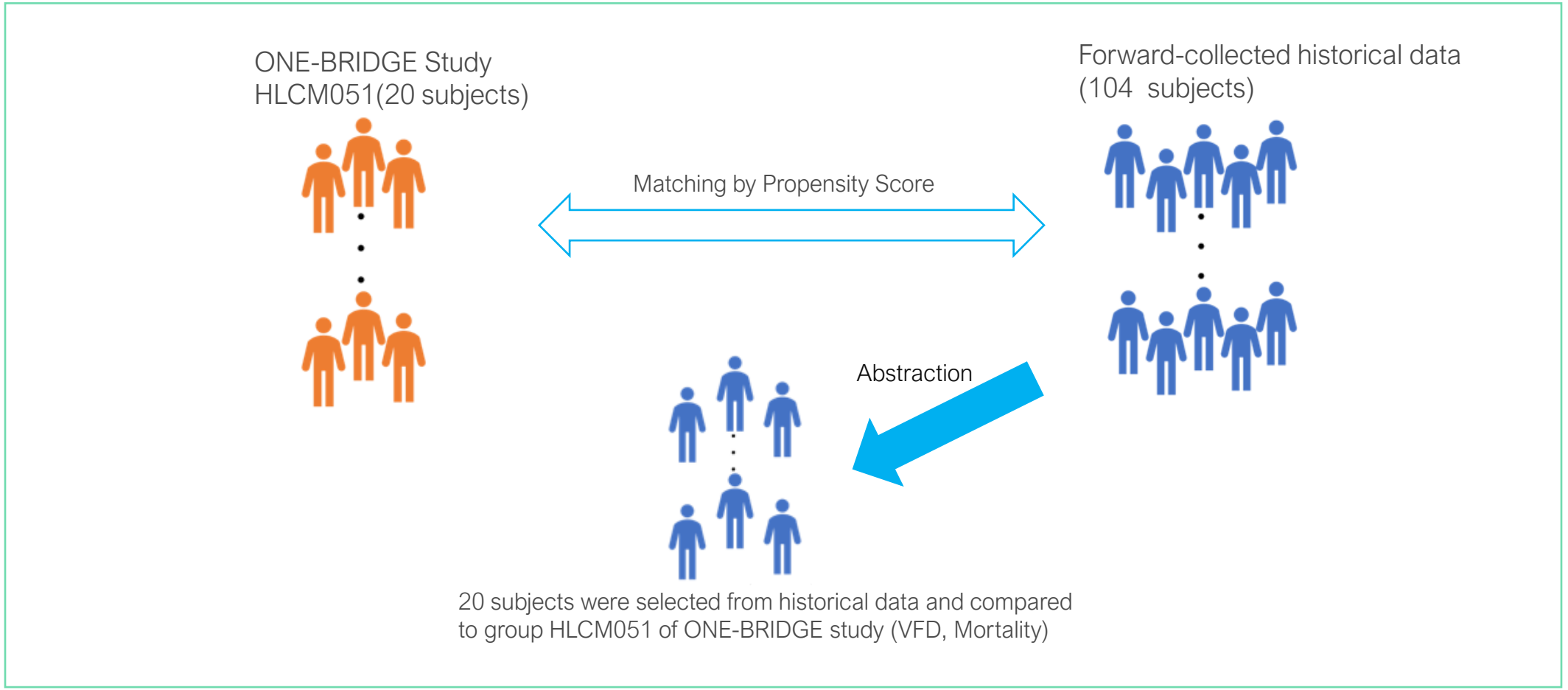
	Cohort 1	
	HLCM051	Standard therapy
Primary Endpoint		
VFD (the number of days out of 28 during which a ventilator was not used for the patient)	**20 days**	**11 days**
Secondary Endpoint		
Mortality (180 days after administration)	**26.3%**	**42.9%**

	Cohort 2
	HLCM051
Primary Endpoint	
Safety	**No safety issues**
Secondary Endpoint	
VFD	**25 days**
Mortality (180 days after administration)	**0%**

HLCM051 ARDS: Comparison with Historical Data

New Healios

Comparison with historical data was a secondary efficacy endpoint of the study protocol



- Matching comparison was performed with historical data from the paper on which the study design is based.
- Historical data source reported in Scientific Reports (Sci Rep. 2021; 11: 20051.) in October 2021

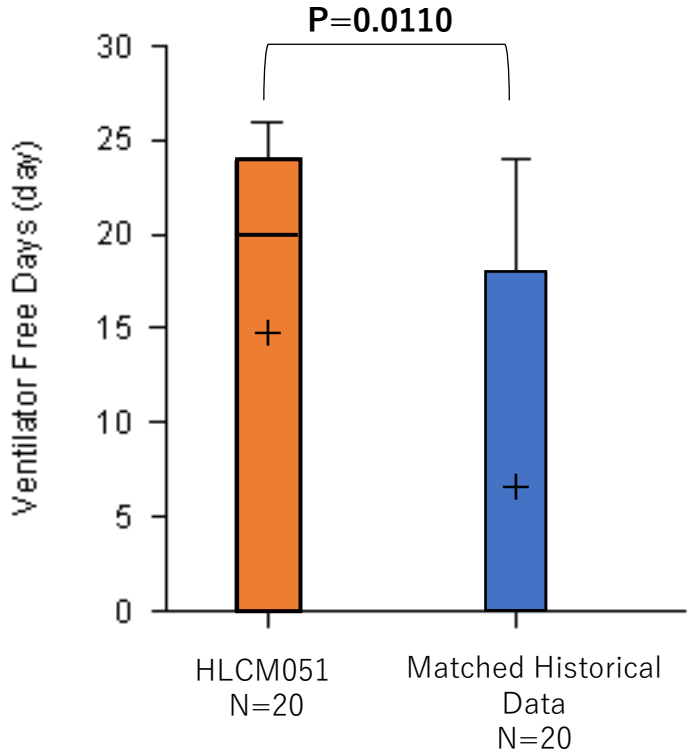
HLCM051 ARDS: Comparison with Historical Data

New Healios

Consistent with the ONE-BRIDGE study, VFD was prolonged and mortality improved.

In the matched historical data comparison, the VFD was prolonged by 8.1 days (mean), and the mortality rate was 33.7% lower (reflecting a 56% decline in mortality as compared to the historical data group).

	Compared with historical data	
	HLCM051	Matched historical data
Primary Endpoint	**P=0.0110**	
VFD (the number of days out of 28 during which a ventilator was not used for the patient)	**14.8days**	**6.7日 days**
Secondary Endpoint	**P=0.0536**	
Mortality (180 days after administration)	**26.3%**	**60.0%**



(Source) in-house data

Results of Double-blind Study Conducted by Athersys <ARDS>

Based on one-year follow-up summary results, an evaluation of quality-of-life suggests further potential benefits from MultiStem treatment including faster rehabilitation.

No serious adverse events were observed.

Analysis of the Double-blind study conducted by Athersys

	MultiStem	Placebo
Mortality	25%	40%
Ventilator- free (VF) days	12.9 days	9.2 days
Intensive Care Unit (ICU) free days	10.3 days	8.1 days

Post-hoc Analysis of patients in severe condition and pneumonia-induced ARDS

	MultiStem	Placebo
Mortality	20%	50%
Ventilator- free (VF) days	14.8 days	7.5 days
Intensive Care Unit (ICU) free days	12.0 days	5.0 days

In the above analysis based on data obtained 90 days after administration, the mortality rate and the number of ventilator-free days (VFD) within a 28-day post-administration period et al. tended to improve in the MultiStem group compared with the placebo group. The results of the 1-year follow-up after administration showed a similar trend.

Overview of the Analysis

Clinical trial	Exploratory clinical trial (Phase 1/2) conducted by Athersys in US and UK （MUST-ARDS study)
Subjects	ARDS patients administered MultiStem or Placebo intravenously (In Phase 2 trial, MultiStem 20, Placebo 10)
Endpoints	- Mortality - Ventilator Free days (The number of the days out of 28 in which a ventilator was not used for the patient) - ICU Free Days The number of the days out of 28 in which the patient was out of Intensive Care Unit

【Reference】

Research contents on MultiStem's mechanism of modulating the inflammatory response in critical care indications Published in Scientific Reports （Link to Athersys' Website June 30, 2021）

Report of Placebo-Controlled Clinical Trial Evaluating MultiStem Cell Therapy for ARDS Published in Intensive Care Medicine（Link to Athersys' Website November 30, 2021）

（Source）Athersys

HLCM051 ARDS: ONE-BRIDGE Study

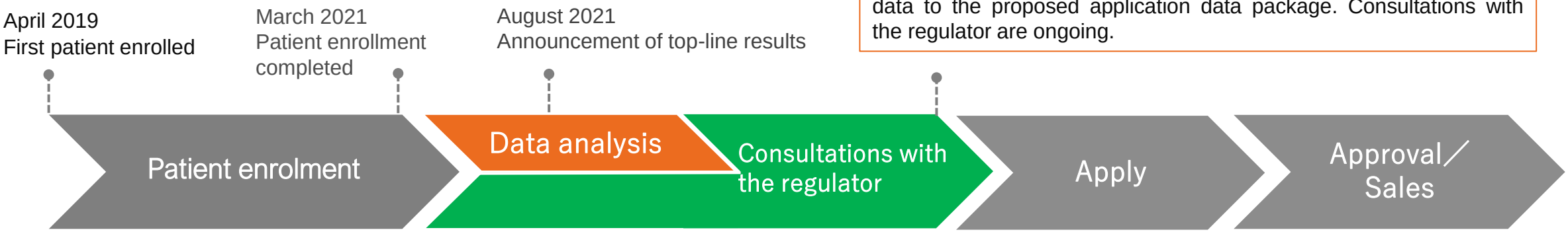
Update

Healios

Development plan

Regenerative medicine product pre-application consultation with the PMDA was conducted in March 2022.

Healios was advised that when making a future application for approval for the ARDS indication, it needs to add certain supporting data to the proposed application data package. Consultations with the regulator are ongoing.



HLCM051 has been designated as an **orphan regenerative medicine product** for use in the treatment of ARDS by the Ministry of Health, Labor and Welfare. (It has received SAKIGAKE status for ischemic stroke.)

HLCM051 can be the first available therapeutic medicine for ARDS

- Currently only artificial respiration and ECMO (Extracorporeal Membrane Oxygenation) are available as coping therapies.
- ECMO has a limited number of installations at medical institutions, requires multiple medical staff with special skills, and has a high cost of management.

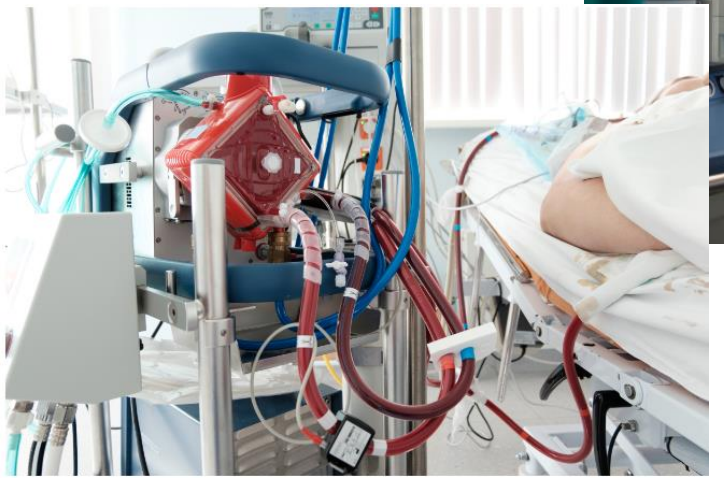
Contribution to patients ⇒ Providing new treatment
Improvement of mortality and QOL

- Improving patient lifesaving rate and QOL
- Shortening the treatment period (ICU use, length of hospital stay, etc.)

Contribution to medical ⇒ Reducing the burden on medical staff and hospitals

- Improving effective use of artificial respiration including ECMO
- Curbing medical resources per patient

ECMO

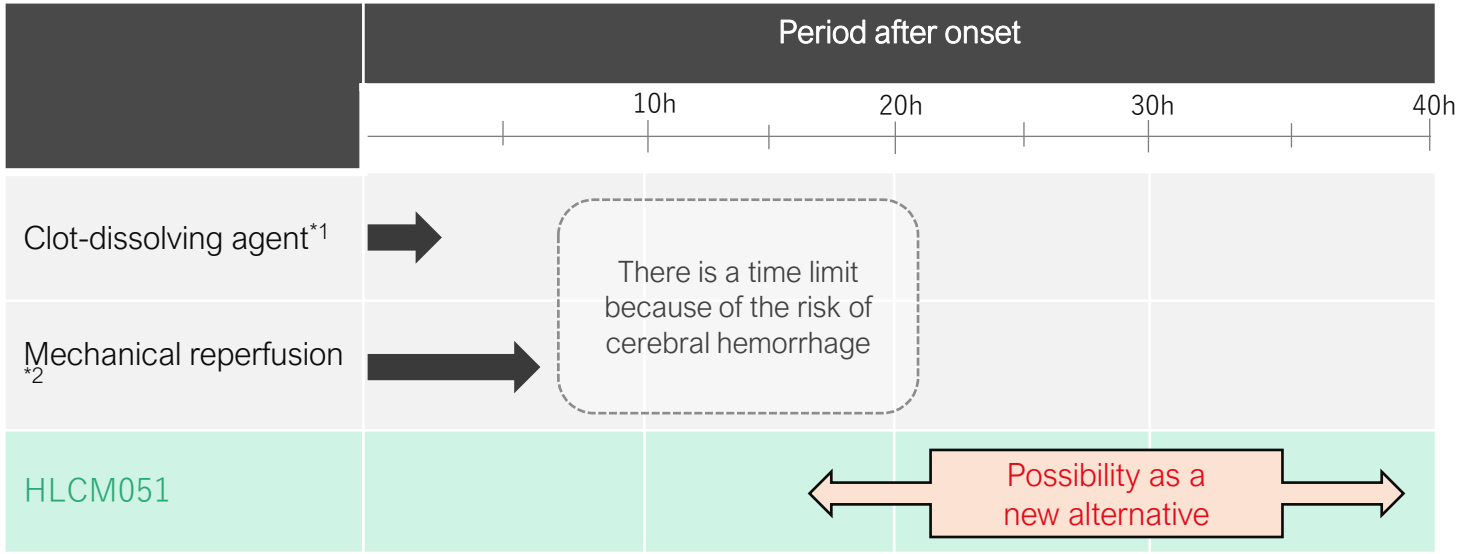


Artificial Respiration

HLCM051 Stroke: Outline of Ischemic Stroke in Japan

Expected development of a new therapy that can be applied in a longer treatment window period following the onset of ischemic stroke (ability to help more patients)

Treatment in Accordance with the Period After Onset



※1 Dissolves blood clots in the brain vessels
※2 Insertion of the catheter into a blood vessel and recovery of the thrombus directly with a wire.

(Note) This material was prepared to explicitly describe the major therapeutic options for ischemic stroke and their treatment window periods after onset. Appropriate treatments are conducted according to patients' conditions and classification of their symptoms. Experimental or investigational treatments not included in the above are also performed.

Ischemic Stroke

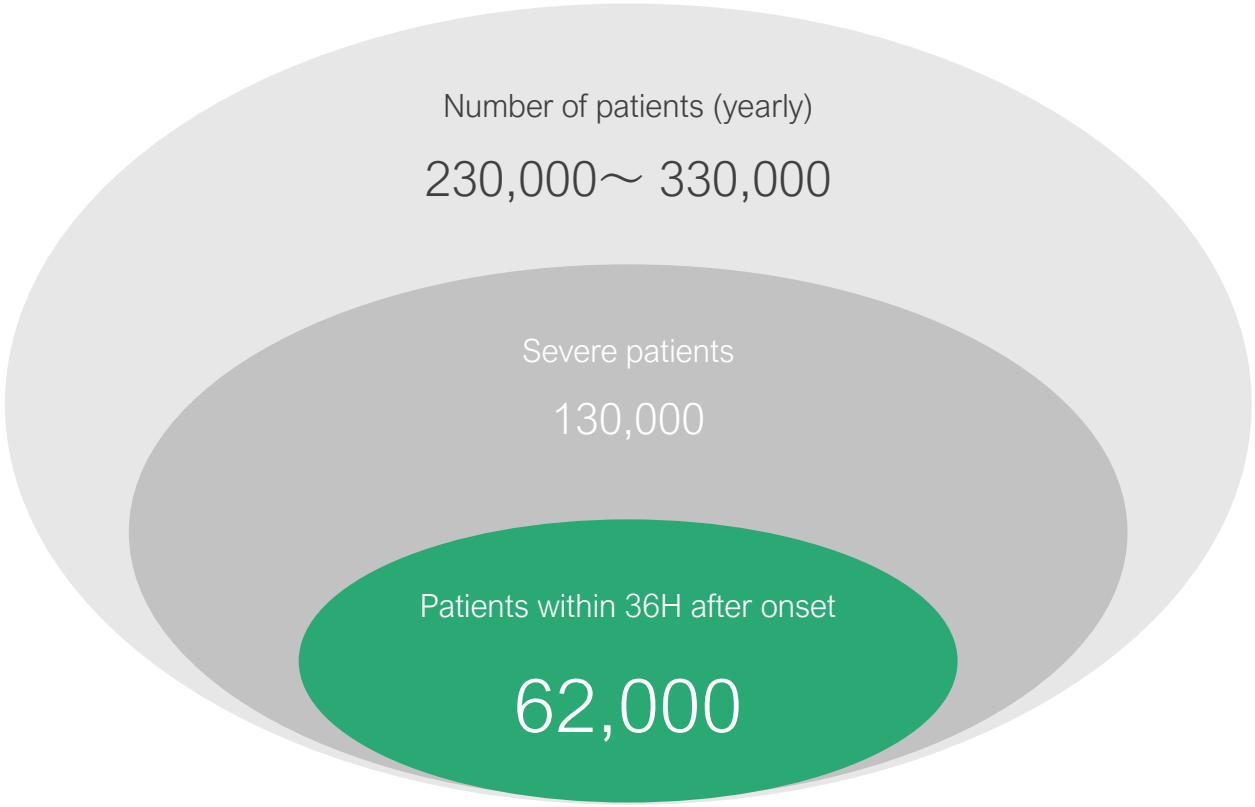
Ischemic stroke, which represents the most common form of stroke (70 - 75% of cases in Japan), is caused by a blockage of blood flow in the brain that cuts off the supply of oxygen and nutrients, resulting in tissue loss.

(Source) Athersys

It is estimated that 37.9% of bedridden patients and 21.7% of persons who were in need of care were affected by ischemic stroke.

HLCM051 Stroke: Annual number of New Patients with Ischemic Stroke in Japan

The number of patients in Japan targeted for HLCM051 is estimated to be 62,000 a year



Number of patients with ischemic stroke in Japan (yearly)

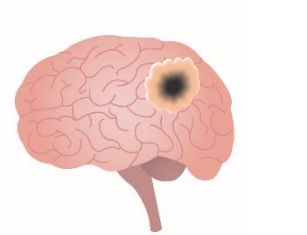
Severe patients （atherothrombotic and cardiogenic cerebral infarction)

Patients within 36 hour after onset

(Source) Healios estimated the annual number of new patients with ischemic stroke in Japan according to materials issued by the Fire and Disaster Management Agency, the Ministry of Internal Affairs and Communication, and the Ministry of Health, Labour and Welfare – DATAMONITOR epidemiological estimates also shown as upper end of range.
(Source) Healios estimated the percentage of patients who reach the hospital within 36 hours after onset at 47% according to the results of its market research.

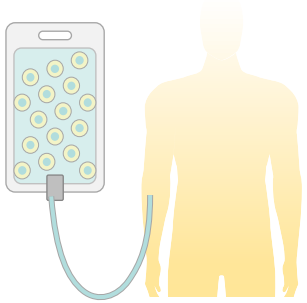
HLCM051 Stroke: Mechanism of Action

Stroke-induced neuronal damage

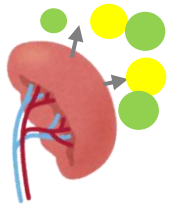


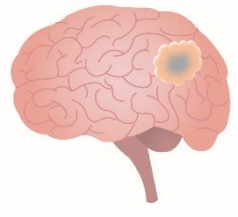
Primary Damage

With HLCM051



HLCM051
-suppress the mobilization/ release of inflammatory cells (lymphocytes, cytokines)
-activate the mobilization/ release of anti-inflammatory cells



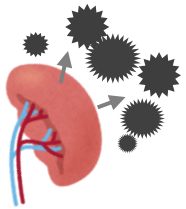


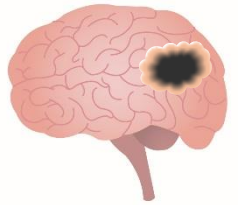
Attenuate neuronal damage in the acute phase of stroke caused by inflammatory cells

Secondary Damage mitigation

Without HLCM051

Activate mobilization / release of inflammatory cells (lymphocytes, cytokines) in the spleen





Neuronal damage exacerbated by inflammatory chemokines/cytokines
Inflammatory cells are released from the spleen and exacerbate the neuronal damage of the ischemic site.

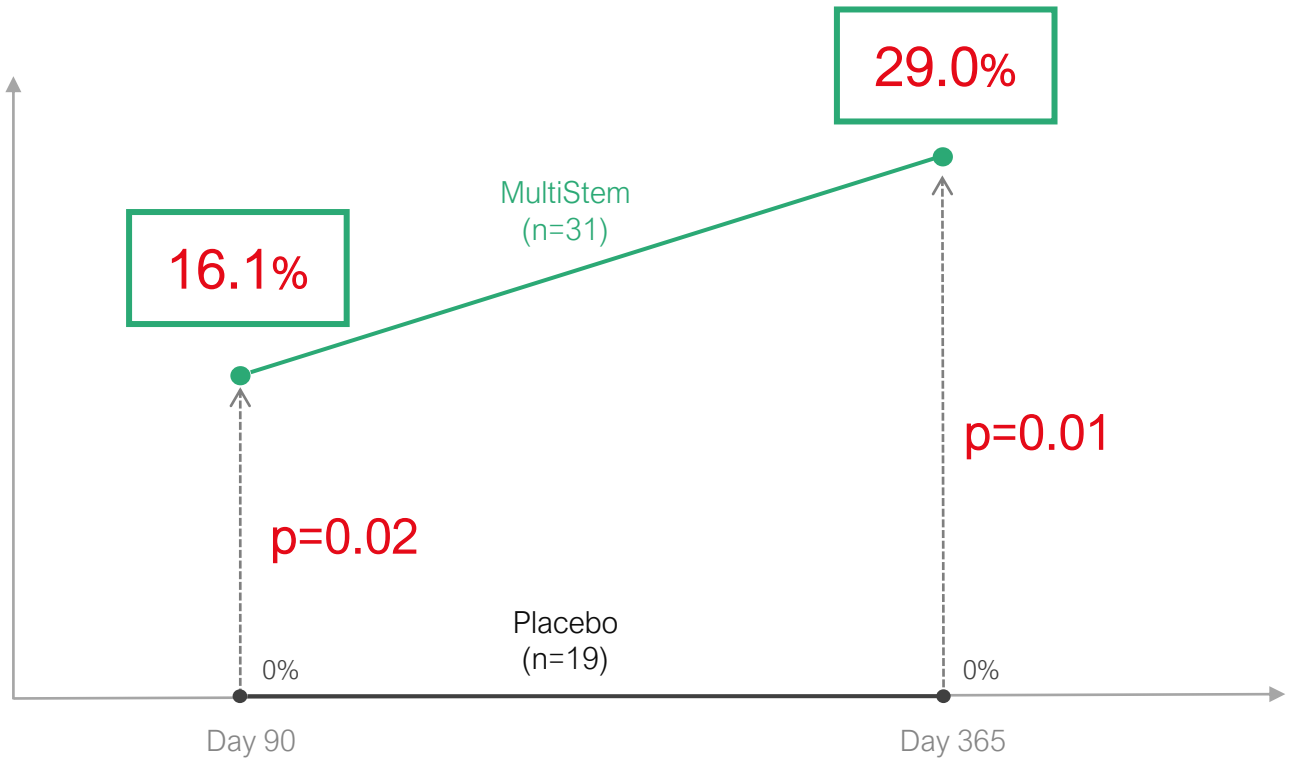
Secondary Damage

（Source） This figure was based on Stroke. 2018 May;49(5):1058-1065.Fig.2

Results of Double-blind Study Conducted by Athersys <Stroke>

The proportion of patients who achieved Excellent Outcome was statistically significant in the group of patients who received MultiStem within 36 hours of the onset of cerebral infarction

Analysis of the Double-blind study conducted by Athersys



(Source) This material was based on *Lancet Neurol*. 2017 May;16(5):360-368; 16 360–68 Supplementary appendix Table 5

Overview of the Analysis

Trial	The placebo-controlled double-blind Phase 2 study conducted by Athersys in the US and the UK（MASTERS study)
Subjects	Administered MultiStem or Placebo within 36 hours of the onset of stroke
Endpoint	Proportion of subjects with an Excellent Outcome* on Day 90 and Day 365

*<Excellent Outcome> is defined as mRS score of ≤1 (scale, 0 to 6), NIHSS score of ≤1 (scale, 0 to 42), and BI score of ≥95 (scale, 0 to 100).

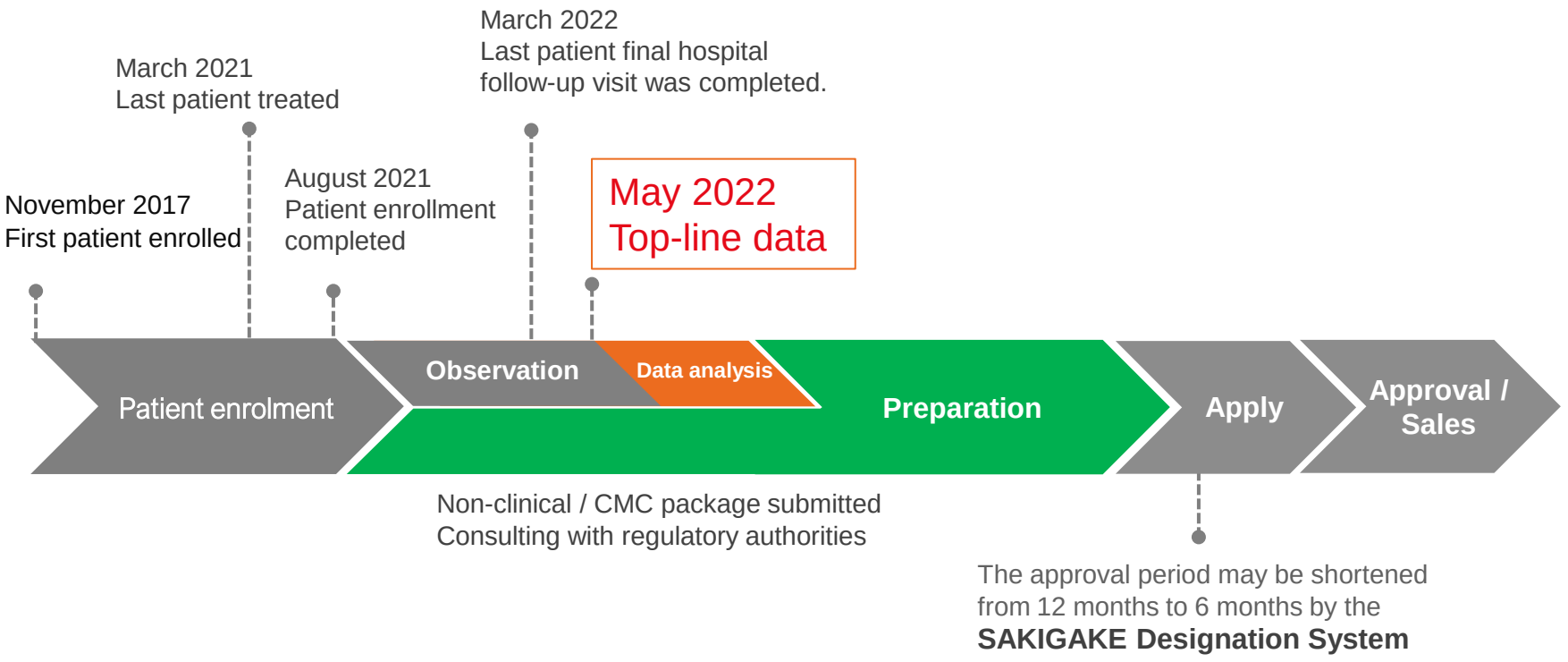
HLCM051 Stroke: TREASURE Study

Update

Healios

90 and 365-day top-line results of the TREASURE study planned for May 2022.

Development Plan

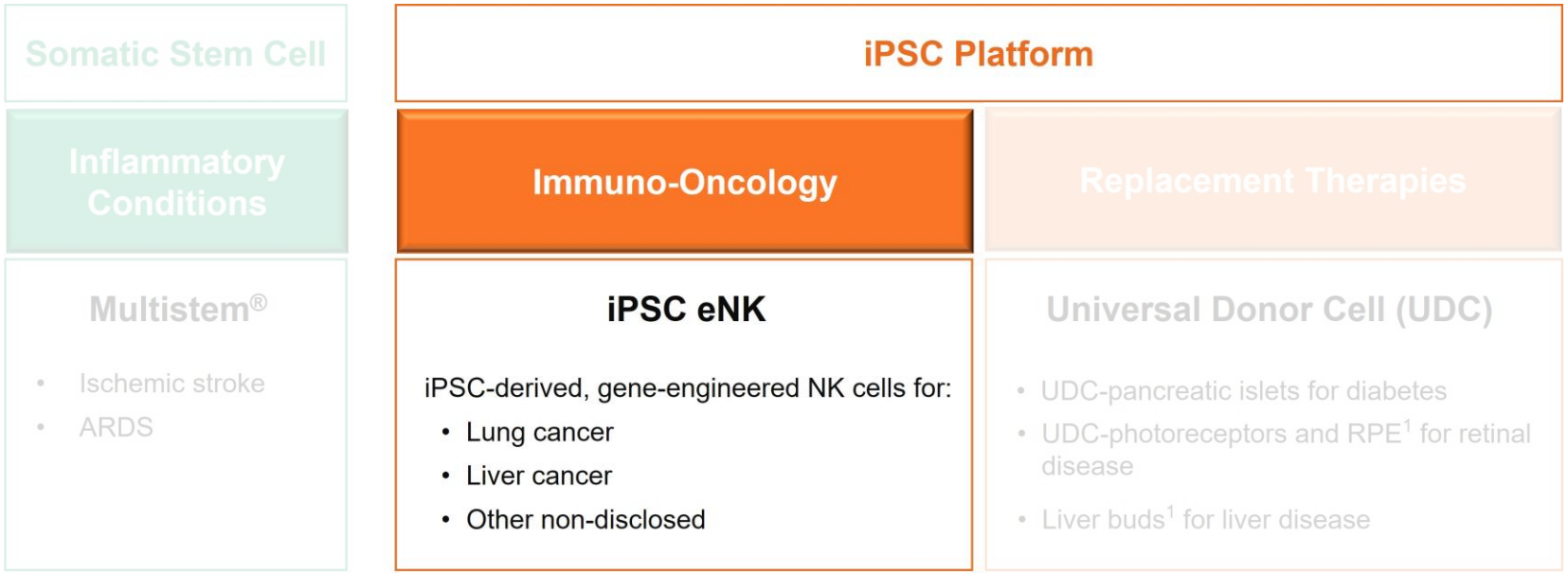


Overview

Trial	Placebo-Controlled, Double-Blind, Phase 2/3 Efficacy and Safety Trial of HLCM051 in Patients With Ischemic Stroke（TREASURE study）
Subjects	Ischemic stroke within 18 to 36 hours
Conditions	Placebo-Controlled, Double-Blind
Enrollment	220 (HLCM051 [n=110], placebo [n=110], randomized)
Primary Endpoint	Proportion of subjects with an Excellent Outcome* defined by functional assessments [Day 90]
Secondary Endpoints (examples)	Proportion of subjects with an Excellent Outcome defined by functional assessments [Day 365] Proportion of subjects exhibiting functional outcome throughout the range of mRS scores by shift analysis [Days 90 and 365]

*"Excellent Outcome" is defined as achieving mRS ≤1, NIHSS ≤1, and BI ≥95. mRS, NIHSS, and BI are the three major indices of functional assessment for stroke patients.

iPSC eNK
Immuno-Oncology



The Promise of NK Cells as a Treatment for Solid Tumors

Key Facts about Cancer and the Unmet Need

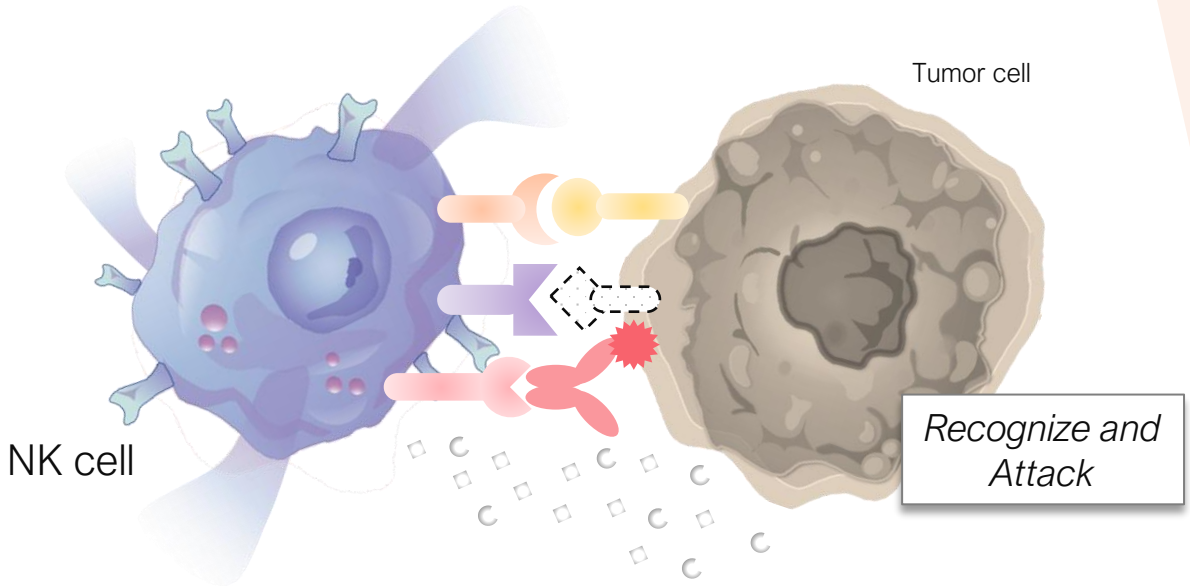
- Solid tumors are the number one cause of death in Japan (~90% of cancer deaths)
- Cancer is the leading cause of death worldwide, accounting for nearly 10 million deaths in 2020[1]
- The economic impact of cancer is significant and increasing: The total annual economic cost of cancer in 2010 was estimated at US$ 1.16 trillion[1]

The Potential for Natural Killer (NK) Cells

- Offer tremendous promise as a new therapeutic approach to treating solid tumors.
- Innate, central role in a cell mediated defense system in humans, and attack cancer cells and virus-infected cells.
- Reported advantages over T cell-based therapies:
  - Broad mechanism to recognize tumor cells
  - Fewer adverse effects (e.g. CRS & GVHD)
  - Less exhaustion

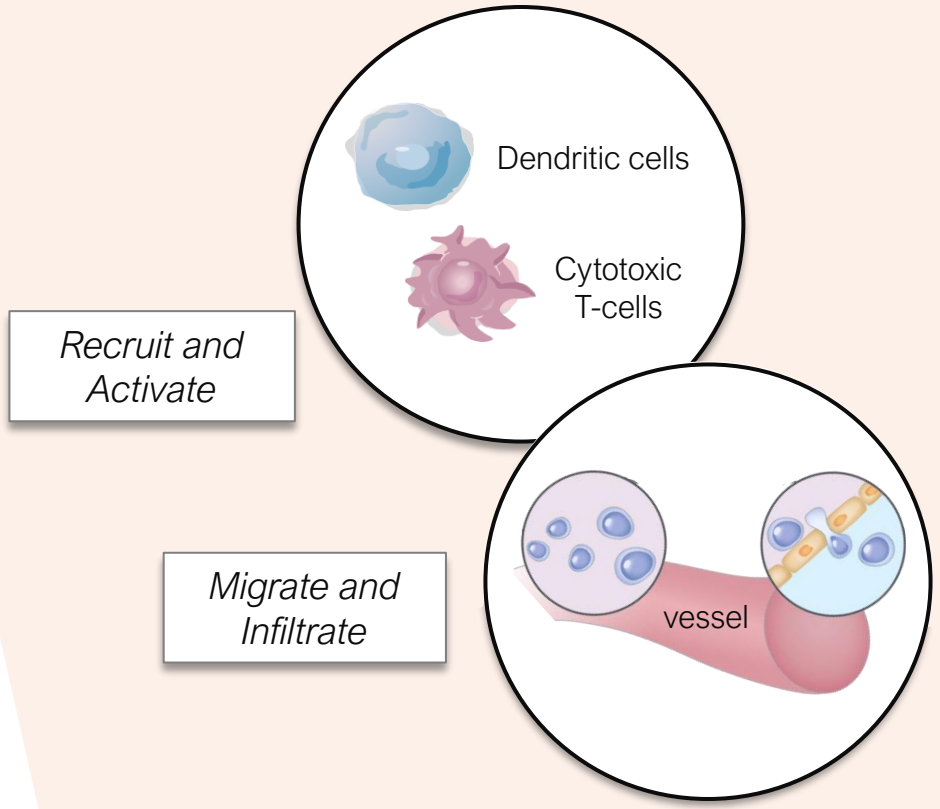
[1]https://www.who.int/news-room/fact-sheets/detail/cancer

Healios' Three-Pronged NK Cell Therapy Approach



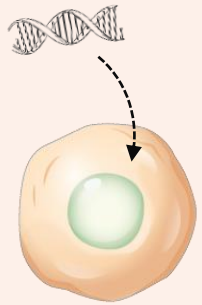
Natural killer (NK) cells, a type of white blood cell, play a central role in a cell mediated defense system that human bodies naturally have, and attack cancer cells and virus -infected cells.

A gene-engineered iPSC-NK cell platform designed not only with enhanced cytotoxicity but also with recruitment and trafficking properties



Core eNK Platform Technologies & Competencies

Engineered iPSC Lines



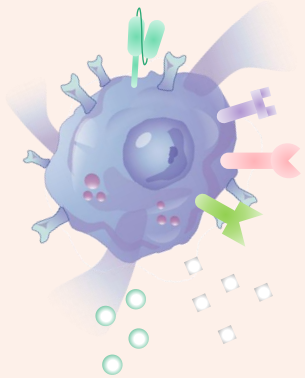
NK differentiation

Proprietary iPSC lines

Cell engineering

Master cell banks established for NK cell production

Differentiation of NK Cells With Enhanced Functionality



eNK

- Optimized ADCC
- Enhanced NK function, proliferation & persistence
- Increased trafficking & homing
- Holistic immune system recruitment

Process Optimization, Scale Up & Manufacturing

GCTP/GMP Manufacturing
@ HEALIOS Facility
in Kobe, Japan

Validated CARs for Multiple Products

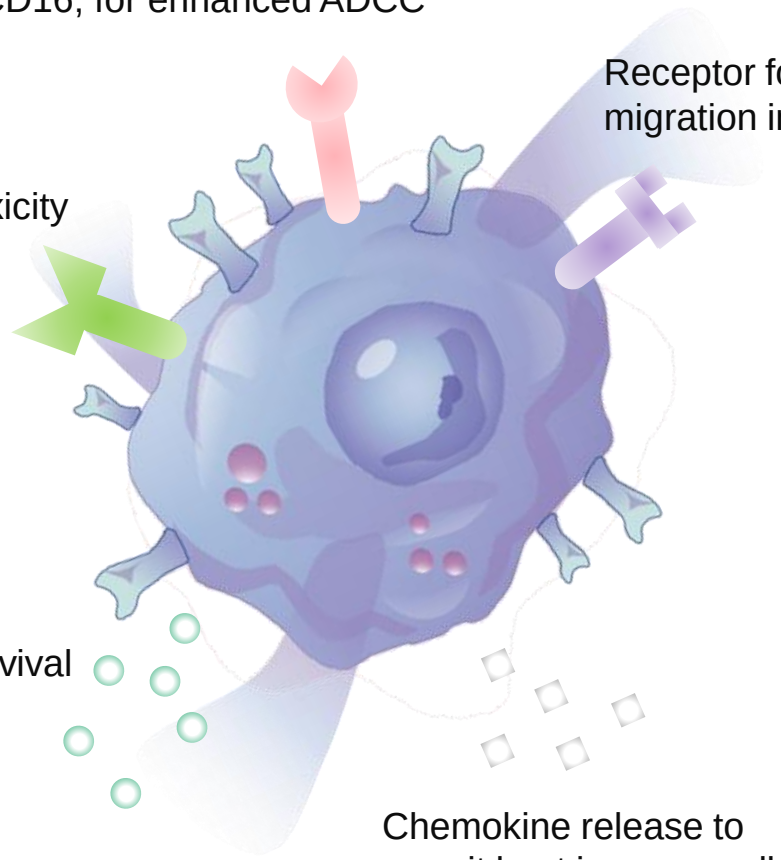
Product 1 Product 2 ... Product n

Key Characteristics of the Healios iPSC eNK Cell Platform

CD16; for enhanced ADCC

Receptor for improved migration into solid tumors

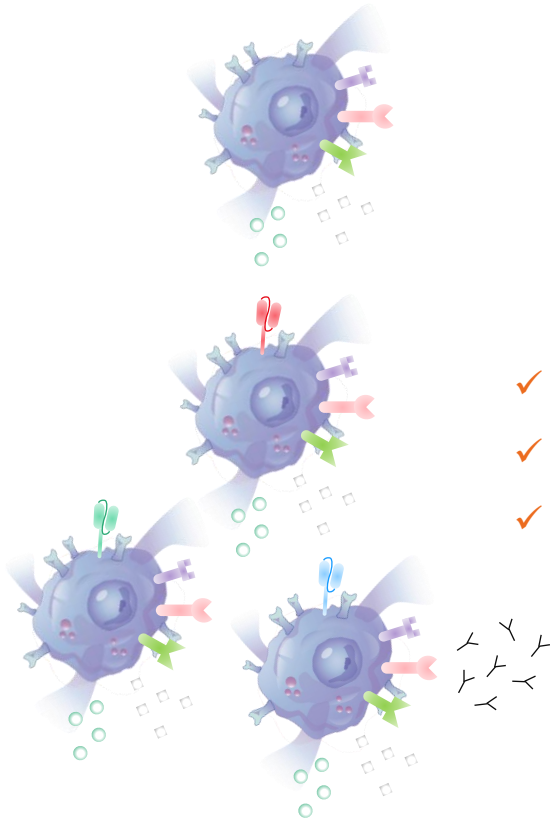
Receptor for enhanced recognition and cytotoxicity



IL-15; for improved persistence and survival

Chemokine release to recruit host immune cells

Multiple Product Candidates



Stand-alone eNK product

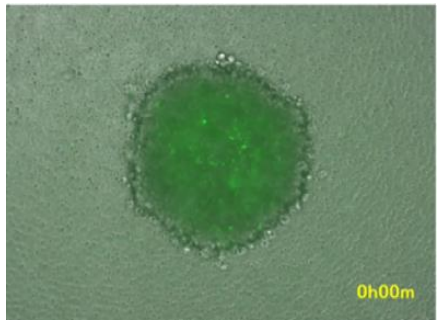
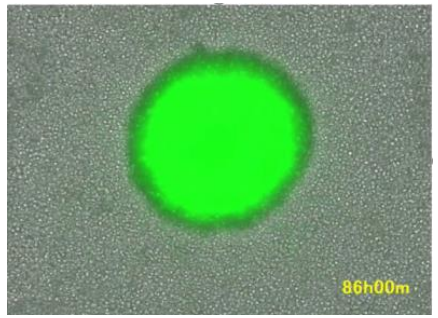
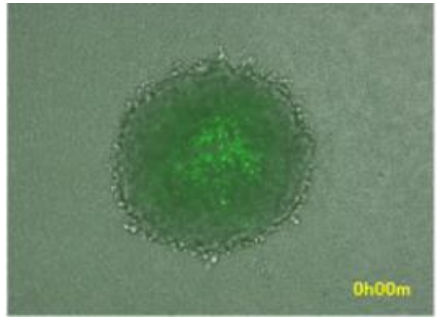
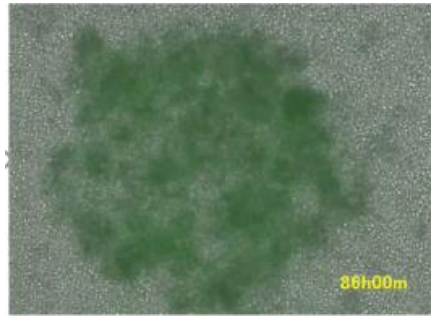
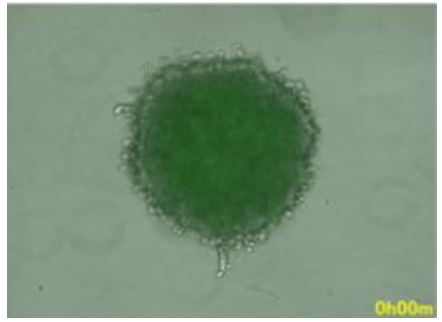
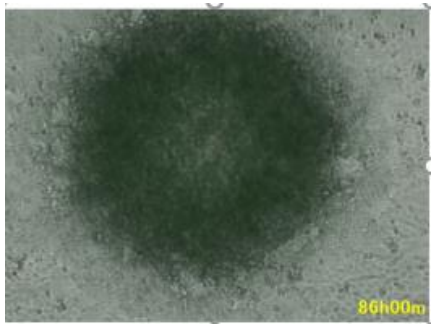
CAR-eNK products against specific targets

- ✓ **CAR eNK**
- ✓ **Dual CAR eNK**
- ✓ **Bispecific CAR eNK**

In combination with antibody therapies

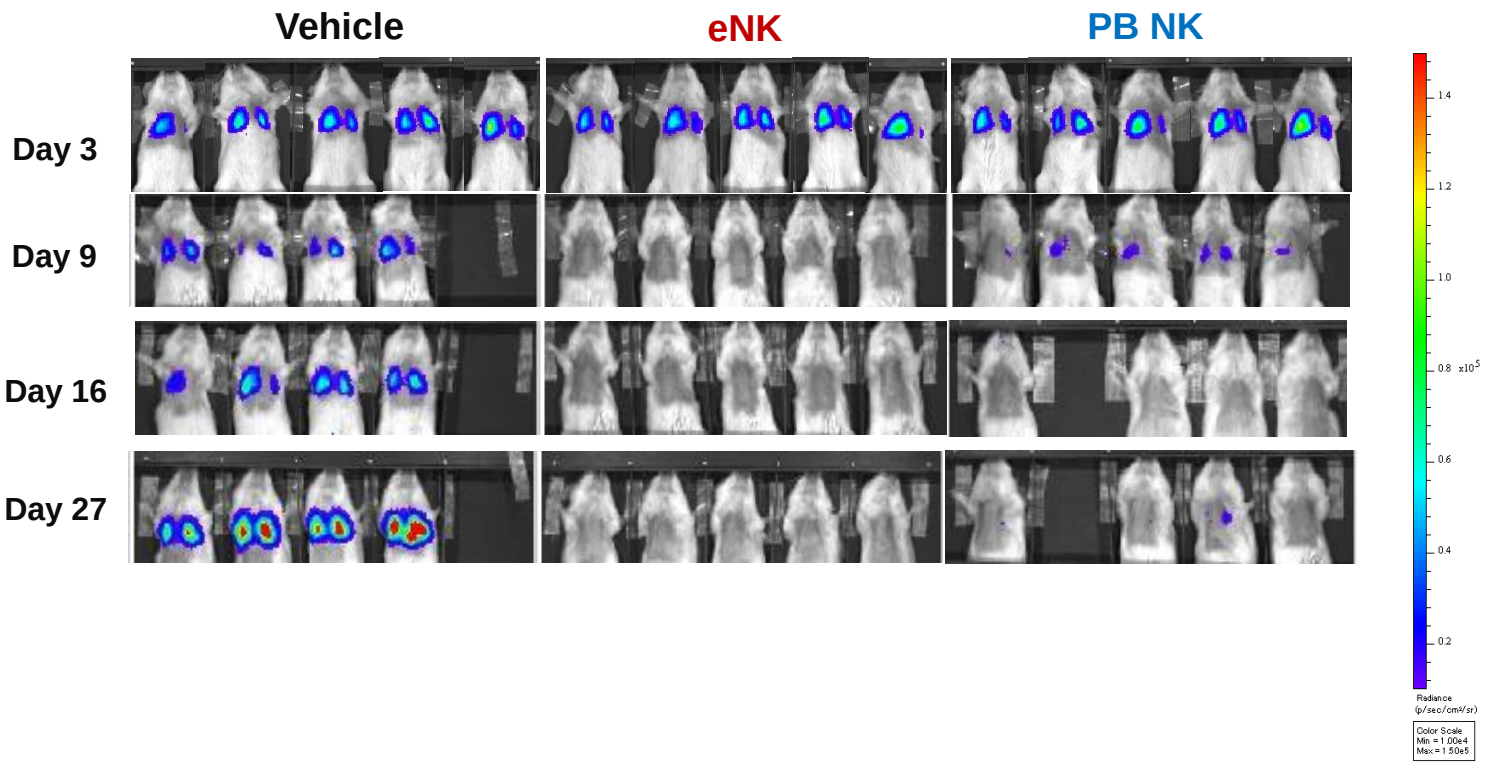
In Vitro Evidence of Anti-tumor Effect as Mono- and Combination Therapy (Lung, A549)

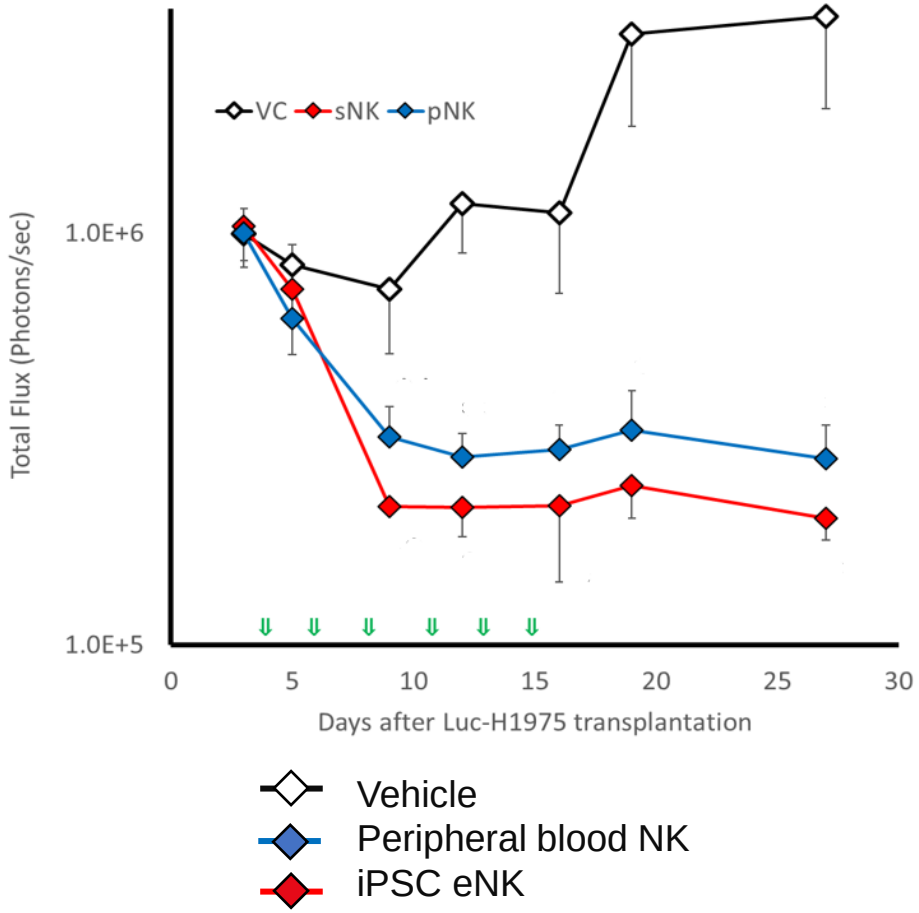
Bright green: apoptotic cells

	0h	86h (3.5 days)	
eNK only			eNK cells have killed the cancer cells
eNK with anti-EGFR antibody			The lung cancer cells were efficiently killed and the lung cancer cell spheroid was destroyed.
Anti-EGFR antibody only			The cancer cells survived and the cancer cell spheroid expanded for 86 hours.

（Source）in-house data

One Example of the Promising Effect of eNK Cells in Tumor Bearing Mice (Lung, H1975)





(Source) in-house data

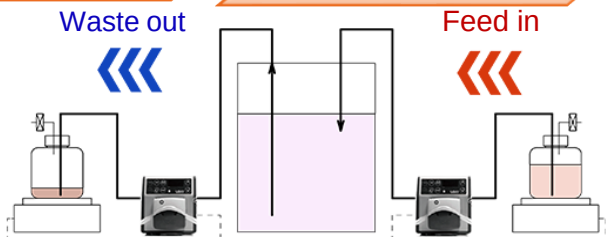
eNK Cell Production Method: Upstream Process and Downstream Process

New Healios

① Upstream Process （All processes are feeder cell free）

iPSC Sphere Formation → HPC Differentiation Induction → eNK cell Differentiation Induction → eNK cell Expansion

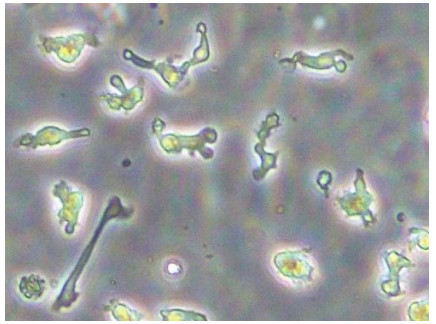
500mL Single Use Bioreactor



Perfusion Bioreactor System
Fully Closed & Automated Medium Exchange

＊Illustration of Perfusion System: adopted from homepage of SATAKE MultiMix

3L Single Use Bioreactor



100 billion NK cells per production run

②Downstream Process

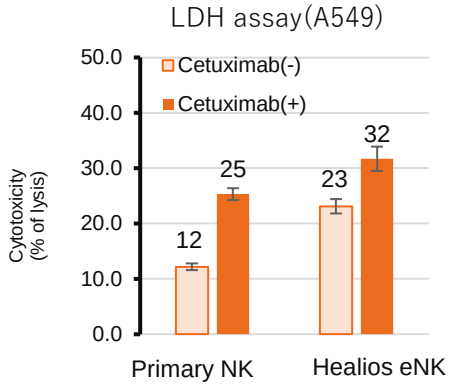
Cell Harvest: Concentrate・Wash Cryoprotectant Mixing → Aseptic Filling and Finish → Cryopreservation → Storage Cold chain

Cryoprotectant Design (Healios KK Original)

Automatic Filling and Finish Machine (Healios KK Original)

Controlled Rate Freezer

Storage: Liquid Nitrogen Tank



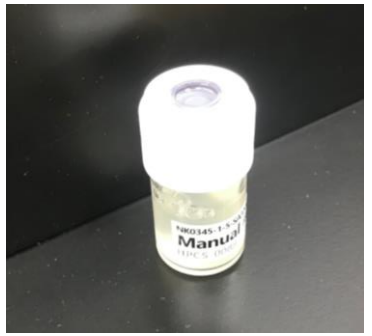
In this process, cryopreserved samples show high cytotoxicity

（Source）in-house data

iPSC-Derived Product Manufacturing: A New and Dedicated GMP Facility

To control the schedule and quality of clinical trial product manufacturing, Healios established a new facility for cell processing and manufacturing (CPC) in Kobe, Japan, which will be fully operational by mid-2022.

Proprietary, automated 3D perfusion bioreactor system for eNK production



3D manufactured eNK finished product

Summary: iPSC eNK Immuno-Oncology

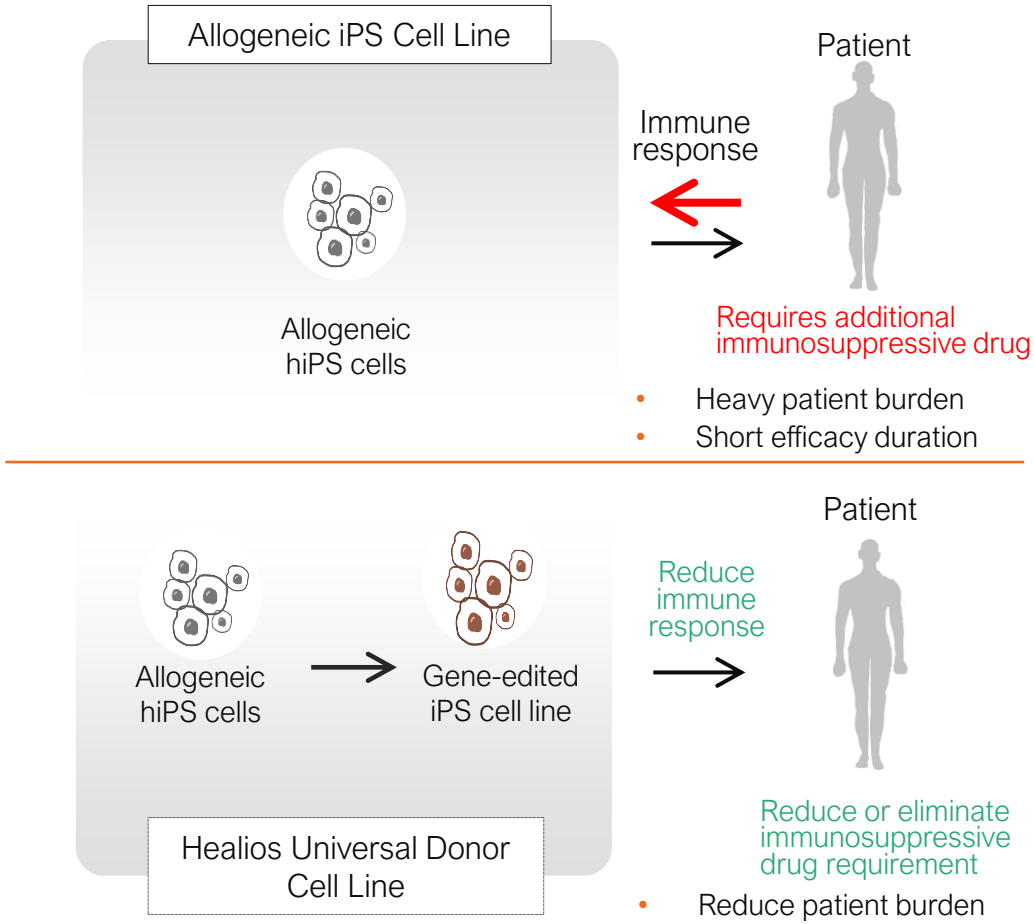
- **Unique Approach**: A gene engineered iPSC-NK cell platform designed not only with enhanced cytotoxicity but also with recruitment and trafficking properties
- **Initial Target Indications**: Lung cancer, liver cancer, other non-disclosed
- Promising *in vitro* and *in vivo* evidence
- Robust and advanced manufacturing processes and infrastructure in place
- Multiple strong collaborations
- Near-term regulatory milestones: Pre-IND: 2022, IND: 2024

Universal Donor Cell (UDC) Replacement Therapies

Somatic Stem Cell	iPSC Platform	
Inflammatory Conditions	**Immuno-Oncology**	**Replacement Therapies**
Multistem® • Ischemic stroke • ARDS	**iPSC eNK** iPSC-derived, gene-engineered NK cells for: • Lung cancer • Liver cancer • Other non-disclosed	**Universal Donor Cell (UDC)** • UDC-pancreatic islets for diabetes • UDC-photoreceptors and RPE[1] for retinal disease • Liver buds[1] for liver disease

Hypo-immune Universal Donor Cell (UDC) Platform

World-leading engineered “universal” iPSC platform: “UDC”

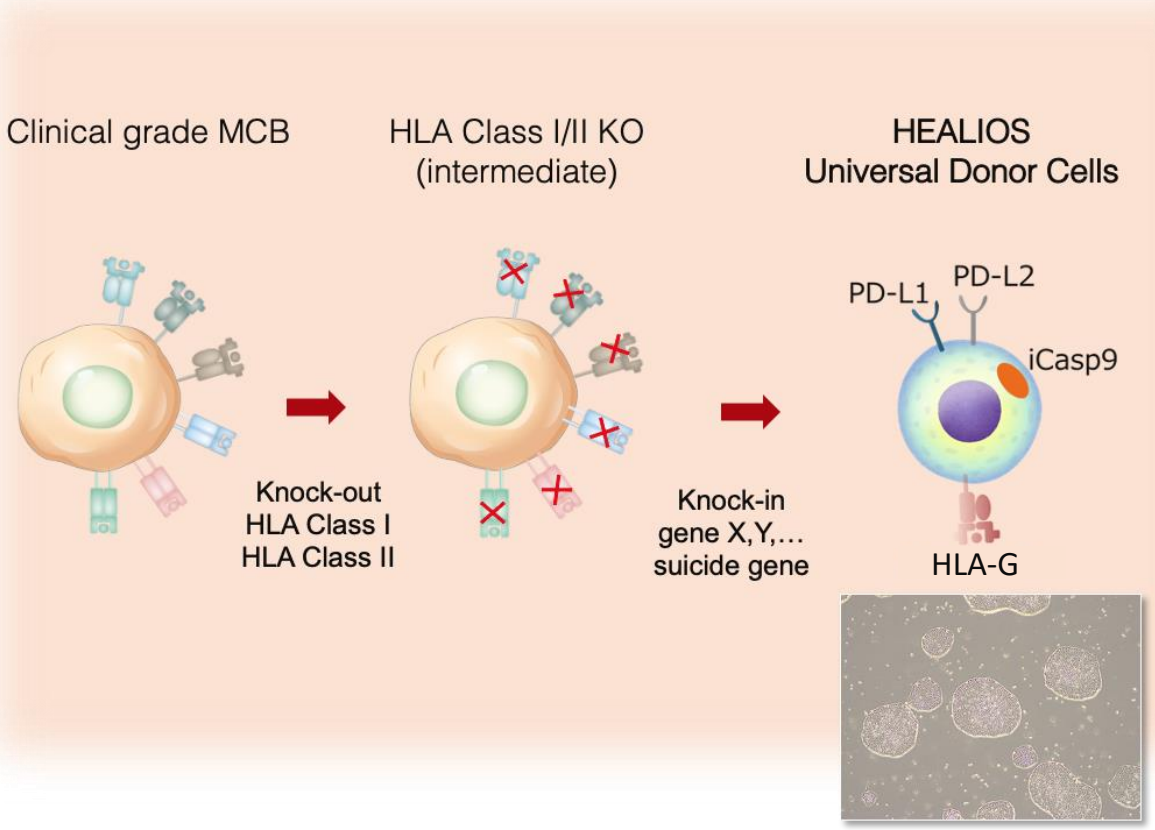


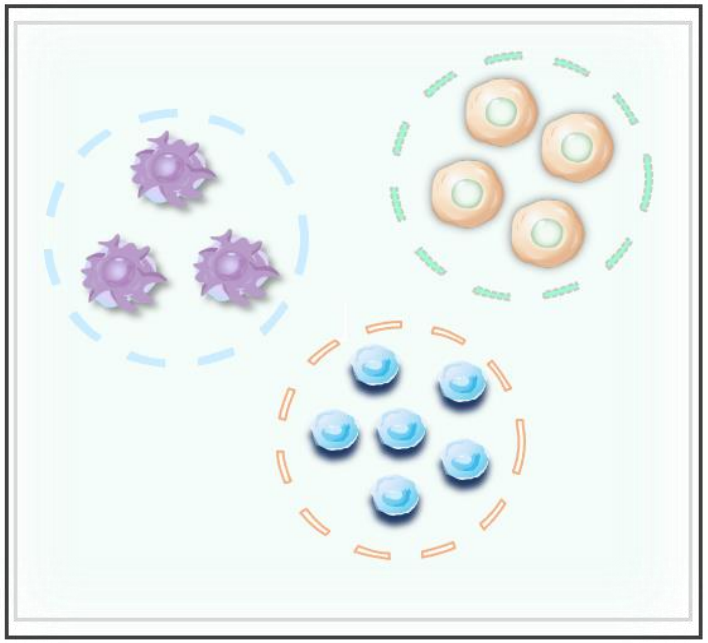
Targeted cell programming through gene-editing

- In October 2020, Healios established a clinical grade universal donor IPS cell line that can be clinically applied to humans in each of Japan, the United States and Europe.
- Master Cell Bank established in 2021
- Healios has led the development of high-quality, universal donor iPS cells in accordance with global standards.
- Consultations with the FDA and PMDA led to no concerns in relation to clinical use of UDC derived therapeutics.
- The UDC line differentiates readily into various in-house made cells (e.g. NK cells, liver progenitor cells, vascular endothelial cells, etc.).
- Active discussions with several companies and academic institutions in relation to use with various therapeutic candidates.

Hypo-immune UDC: Engineered Genetic Profile

Gene Editing Procedure for Healios UDC





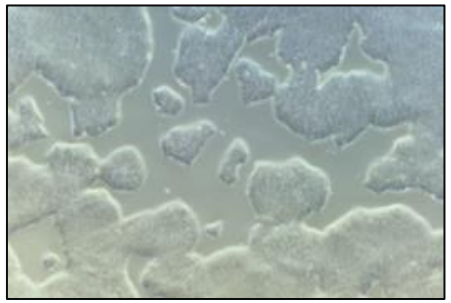
- Off-the-shelf, scalable and cost-efficient
- Address broadest population with single product
- Enhanced level and duration of efficacy

Clinical grade line and Master Cell Bank established in 2020/2021

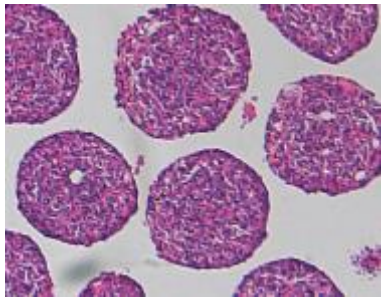
（Source）in-house data

Hypo-immune UDC: Examples Of Cell Therapies

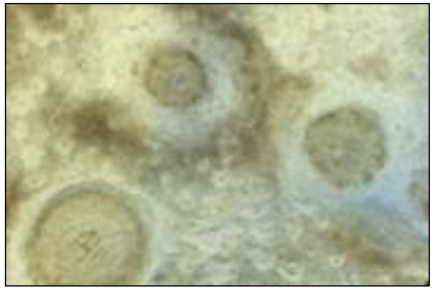
Universal Donor Cells (UDC)



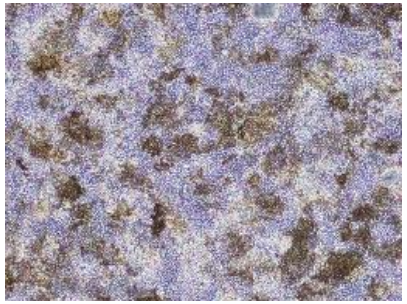
Pancreatic β cells



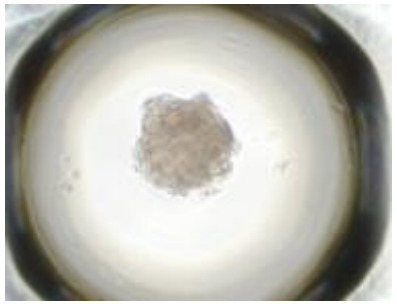
Photoreceptor cells



RPE cells



Liver buds



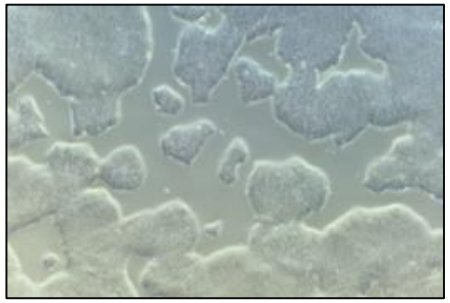
Successfully differentiated from UDCs

Future migration to UDC platform

（Source）in-house data and Joint research data

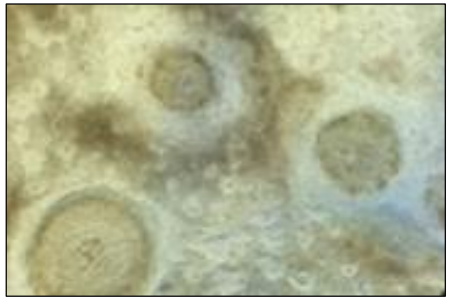
Hypo-immune UDC: Differentiation and Induction of Photoreceptor Cells

Photoreceptor cells



UDC

Differentiation and induction

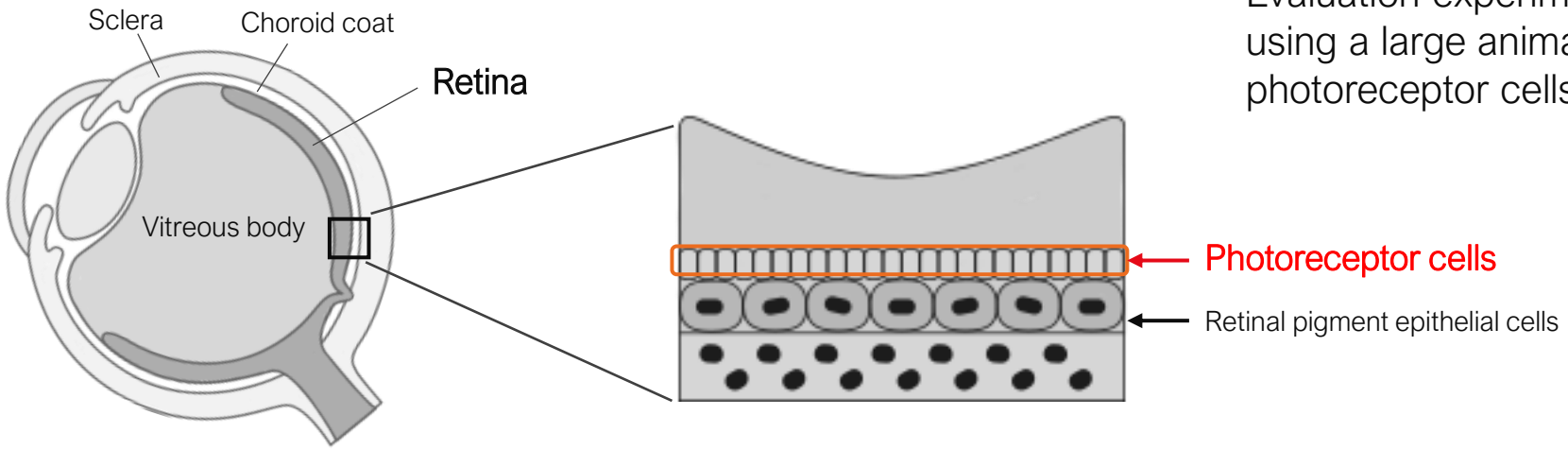


Photoreceptor cells From UDC

Photoreceptor cells are one of the cells that compose the retina and are particularly responsive to light.

Through our joint research, we have succeeded in the culturing of photoreceptor cells from iPS cells. We have also successfully differentiated and induced photoreceptors from UDCs.

Evaluation experiments are currently underway using a large animal disease model in which photoreceptor cells are damaged.

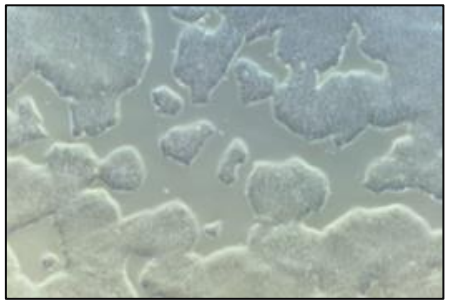


(Source) Joint research data

Hypo-immune UDC: Differentiation and Induction of Pancreatic β-cells

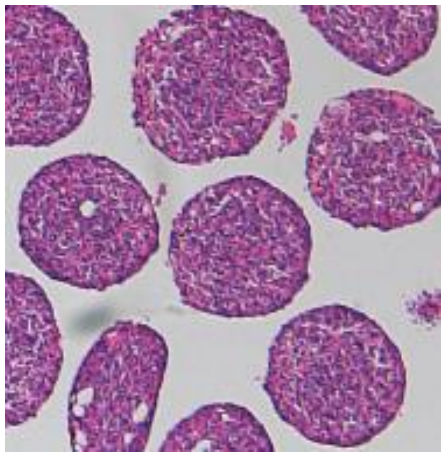
Joint research with the Department of Regenerative Medicine at the National Center for Global Health and Medicine in Tokyo

Pancreatic β-cells



UDC

Differentiation and induction



UDC-derived pancreatic β cells (HE staining)

(Photo provided by the National Center for Global Health and Medicine)

Pancreatic β-cells are a type of cell present in the islets of Langerhans within the pancreas. They produce and secrete insulin in response to blood glucose levels and serve to regulate the amount of glucose in the bloodstream.

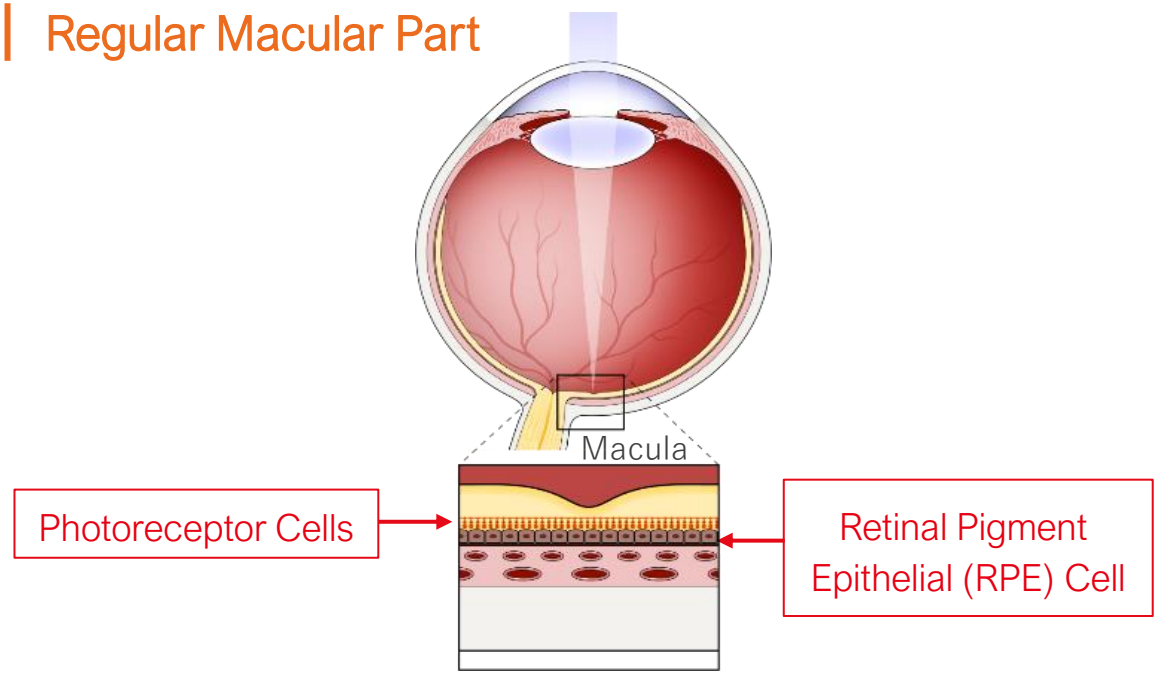
In our joint research with the Department of Regenerative Medicine at the National Center for Global Health and Medicine in Tokyo, we have been aiming to establish a method for inducing differentiation of human iPS cells into pancreatic β-cells for use in clinical applications such as the treatment of diabetes, and we are pleased to announce that **we have successfully confirmed the differentiation of UDCs into pancreatic β-cells.**

Moving forward, our joint research will work on optimizing the process and verifying the efficacy and safety of these cells in animal models of diabetes. Through this achievement, we hope to develop a new more effective therapeutic approach for diabetes and further expand the value and impact of our company's iPSC platform

(Source) Joint research data

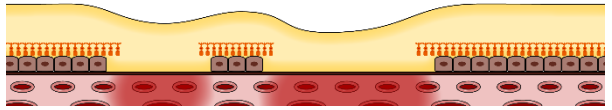
Age-related Macular Degeneration (AMD) causes Retinal Pigment Epithelial (RPE) cells to degenerate, which damages function

Regular Macular Part



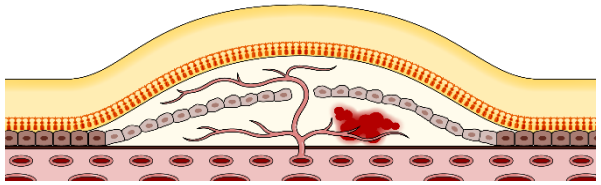
Developed Dry-AMD

Immunity barrier maintained
→ Degeneration of photoreceptor→ Dry AMD



Wet AMD

Destruction of immunity barrier → Invasion of immune cells
→ Inflammation → Wet AMD



Joint Development

In Japan, HEALIOS and Sumitomo Pharma Co., Ltd. are jointly developing a treatment using iPS cell-derived RPE cells.

- Preparations for clinical trial ongoing

HLCL041: Liver Organ Bud Platform

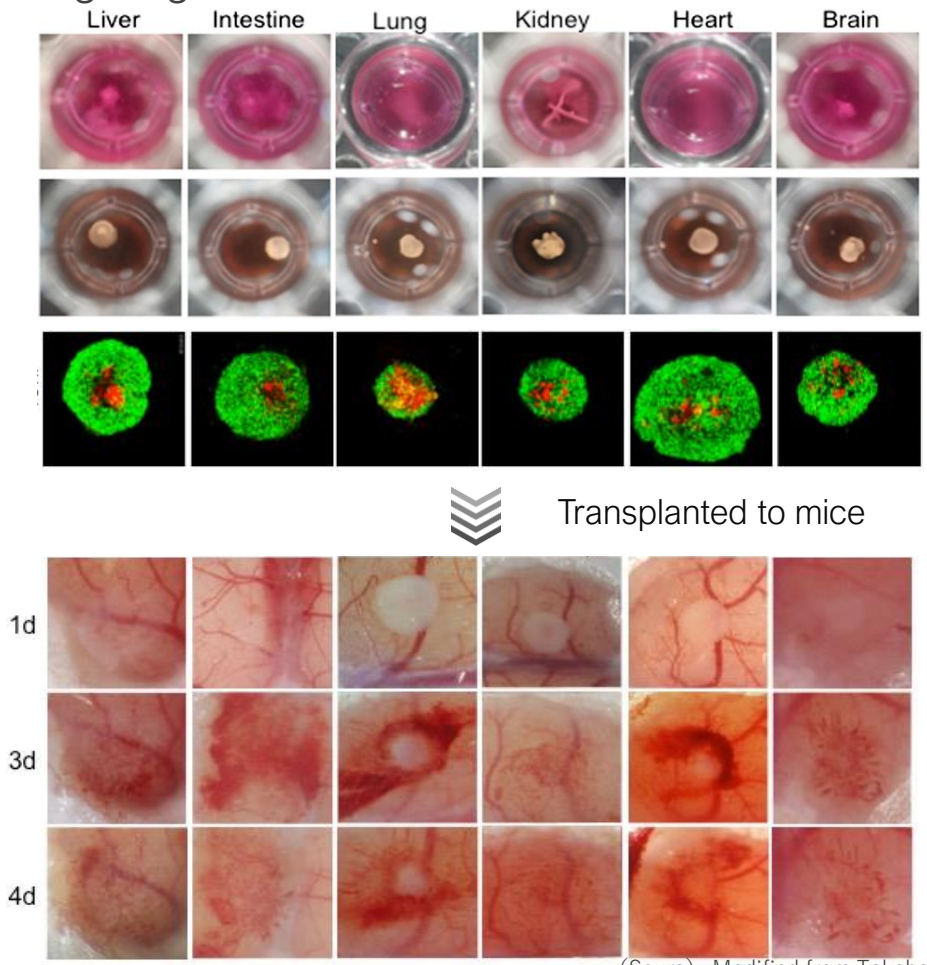
By creating an "Organ Bud" of each organ with iPS cells, we have laid the groundwork for paradigm shifting therapies to emerge for various severe diseases.

UDCs allow for the realization of organ replacement using organ buds.

*movie

The vascularization was confirmed in vivo by transplantation to mice.

（Sours） Japan Science and Technology Agency　Science News “Diverse Approaches in Regenerative Medicine from Cell to Tissue/Organ” (Distributed October 3, 2013)
https://sciencechannel.jst.go.jp/M130001/detail/M130001005.html



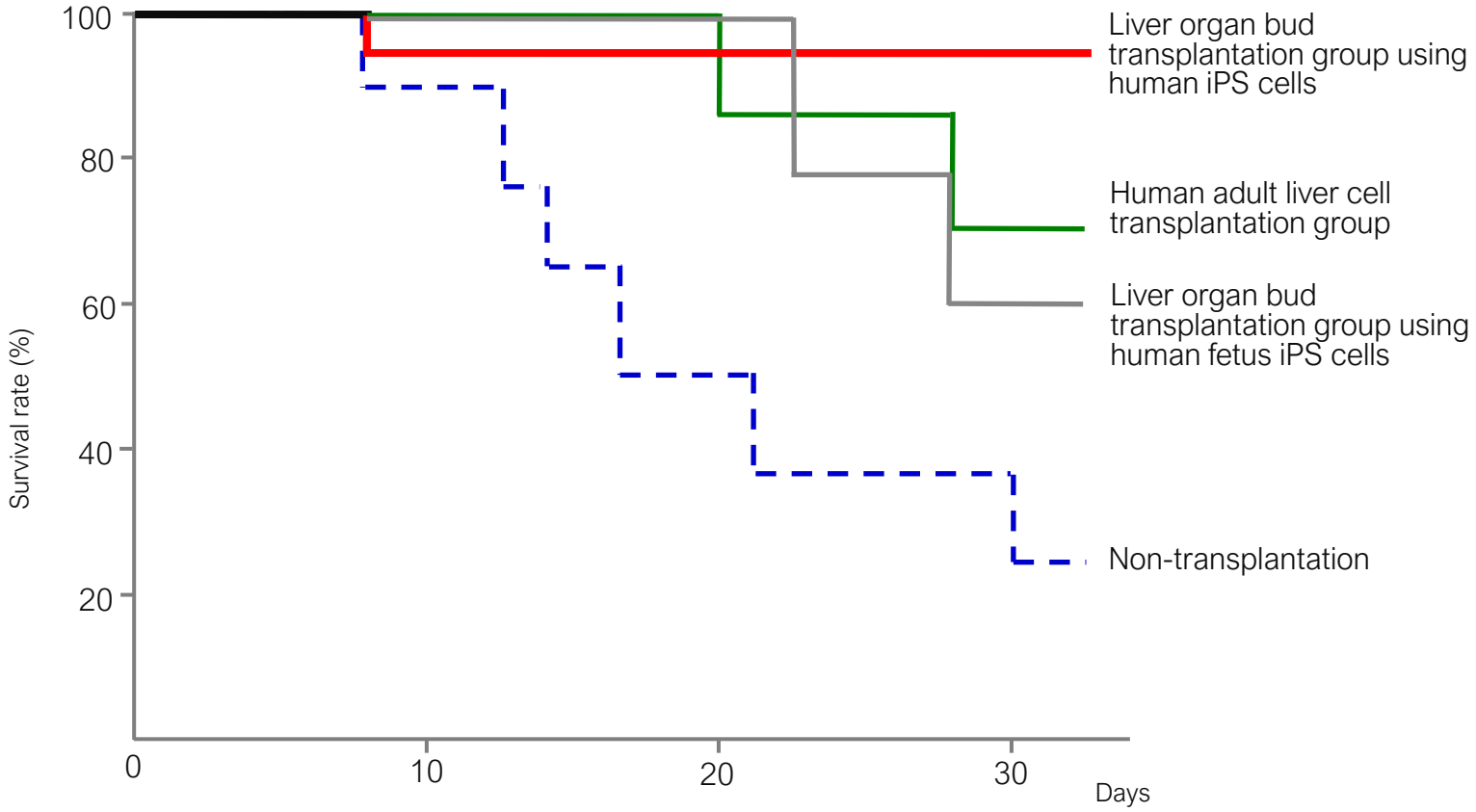
Green：Cells of each organ
Red：Vascular endothelial cell
Black：MSC

（Sours） Modified from Takebe T. et al., Cell Stem Cell, 2015

HLCL041: Liver Organ Bud Platform: Survival Rate of Liver Failure in Mouse Model

Survival rate improves significantly in transplantation experiments

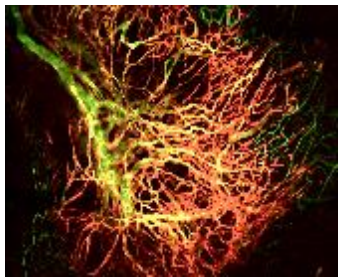
Treatment effects of liver bud transplantation to mouse using hiPSC

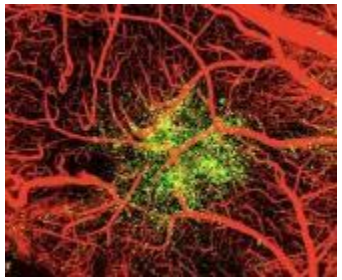


（Source） Adapted by Healios from Takebe. T, et al. Nature, 499 (7459),（2013）

Process

Process by which organ forms from organ bud links mouse‘s vascular network autonomously





（Source）Takebe,T., et al.
Nature Protocols, 9, 396–409 (2014)

HLCL041 Initiated Joint Research on Liver Buds Using UDCs

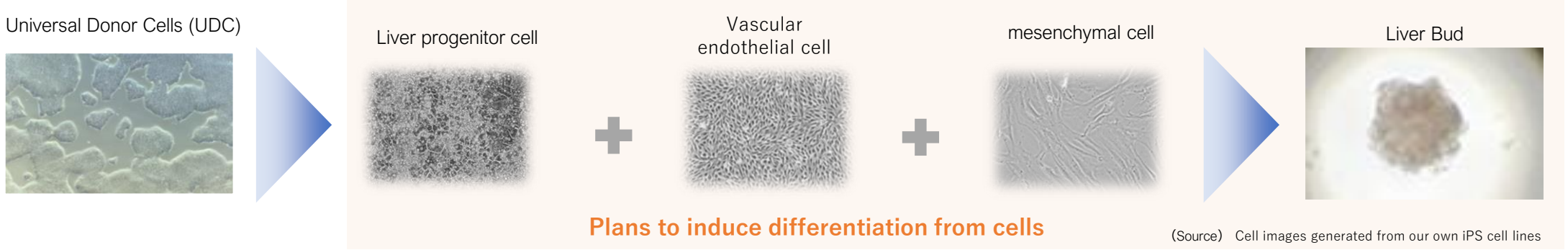
New Healios

Entered into a joint research agreement with the Division of Regenerative Medicine (Prof. Hideki Taniguchi) of the Institute of Medical Science at the University of Tokyo, to advance HLCL041 utilizing UDCs

Division of Regenerative Medicine of the Institute of Medical Science at the University of Tokyo × Healios

Utilizing the knowledge accumulated through our research to date to:

- Establish a new method for inducing differentiation of liver buds using UDCs
- Develop a highly efficient and scalable cell culturing and mass manufacturing system



(Source) Cell images generated from our own iPS cell lines

Organ buds are a platform technology with potential as an alternative to organ transplantation.
We are aiming to create functional, 3D human organs as new regenerative medicine products.

Financial Highlights

Consolidated Statement of Income

Update

Healios

(Units: one million US dollars)

	FY2021 Q1(YTD)	FY2022 Q1(YTD)		
			YoY variance	Main reasons for increase/decrease
Revenue	0.09	0.09	0.00	
Operating profit	-13.24	-12.28	0.96	Mainly due to decrease in SG&A expenses ＋$2.37mn and increase in R&D expenses −$1.42mn.
Profit	-9.70	-12.56	-2.85	Mainly due to increase in finance costs -$0.26mn and decrease in finance income -$3.17mn (Please refer to the next page for details)
R&D expenses	7.93	9.34	1.42	
Number of employees	111	**115**	4	

(Note) * For details of the financial figures, please refer to the summary of the financial results announced today.
* Adopt average exchange rate (JPY/USD) over respective 3-month periods for P&L; FY2021 106.08 yen per dollar and FY2022 116.33 yen per dollar.

Supplemental Explanation of Finance Income and Finance Costs

Update

Healios

Details of finance income and finance costs

In the first quarter, we recorded finance income of ¥193 million and finance costs of ¥184 million. Finance income was mainly due to the recording of ¥166 million in gain on remeasurement of derivatives*1 and ¥ 27 million in profit or loss transferred to equity interests held by external investors in Saisei Fund *2.
Finance costs were mainly due to the recording of ¥140 million in interest expenses on bonds*3, ¥ 18 million in loss on remeasurement of warrants, ¥ 14 million in loss on remeasurement of investment securities and ¥12 million in interest expenses.

*1. Gain on remeasurement of derivatives

Gain on remeasurement of derivatives is the net unrealized gain on the convertible bond-type bonds with subscription rights to shares, which our company issued to overseas investors in July 2019, at fair value as of the end of the first quarter. These are non-cash items booked in accordance with the International Financial Reporting Standards (IFRS), which was introduced by in the first quarter of the fiscal year ended December 2020.

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

Profit or loss transferred to equity interests held by external investors in 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.

Supplemental Explanation of Finance Income and Finance Costs

Update

Healios

*3. Interest expenses on bonds

Of the total interest expenses on bonds of ¥140 million, ¥131 million was charged to interest expenses using the amortized cost method. As in *1 above, this is a non-cash expense recorded in accordance with the International Financial Reporting Standards (IFRS), which was introduced in the first quarter of the fiscal year ended December 2020.

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

Consolidated Statement of Financial Position

Update

Healios

(Units: one million US dollar)

	December 31, 2021	March 31, 2022		
			Variance	Main reasons for increase/decrease
Current assets	142.83 (68.5%)	122.08 (66.4%)	-20.76	Due to decrease in cash equivalents, including due to fx translation (see note below),$21.20mn. (cash equivalent balance at 3/31/22 was $110.30mn).
Non-current assets	65.58 (31.5%)	61.74 (33.6%)	-3.84	
Total assets	208.41 (100.0%)	183.82 (100.0%)	-24.59	
Current liabilities	52.53 (25.2%)	48.31 (26.3%)	-4.22	Mainly due to decrease in bonds and borrowings -$1.55mn and decrease in other financial liabilities -$1.45mn.
Non-current liabilities	80.72 (38.7%)	80.04 (43.5%)	-0.68	
Total liabilities	133.25 (63.9%)	128.36 (69.8%)	-4.89	
Total equity	75.16 (36.1%)	55.46 (30.2%)	-19.70	Mainly due to net loss -$12.56mn and decrease in other components of equity -$2.94mn.
Total liabilities and equity	208.41 (100.0%)	183.82 (100.0%)	-24.59	

(Note) * For details of the financial figures, please refer to the summary of the financial results announced today.
* Adopt spot rate (JPY/USD) at end of fiscal period for B/S ; FY2021 Q4 115.02 yen per dollar and FY2022 Q1 122.39 yen per dollar.

Conclusion

- Continued pioneering in cell therapy
- Uniquely positioned to leverage strong Japanese proficiencies
- Substantial infrastructure to support multiple programs across development stages
- Global strategy
  - Building a commercial organization to launch MultiStem® for ARDS & stroke in Japan
  - Accelerating innovative iPSC platform development for immuno-oncology & cell replacement therapies
    - Focus on clinical development of engineered-NK (eNK) cells for solid tumors in Japan and US
    - Advancement of therapies derived from proprietary hypo-immune Universal Donor Cell (UDC) line
  - Continued investment in precision manufacturing capabilities and strengths in Japan to support future global supply

Committed to transforming the lives of patients by

creating, developing and commercializing cutting edge cell therapy technologies

Healios

＜Contact information＞
Corporate Communications
HEALIOS K.K.

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