FY2021 Financial Results

Company

HEALIOS K.K. (TSE 4593)

Date

February 14, 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

Update

Healios

Management Team

Since July 2019

Jun Narimatsu	Richard Kincaid	David Smith	Michael Alfant	Gregory Bonfiglio	Yoshinari Matsuda	Seigo Kashii
Accountant Supporting various venture companies in the field of IT/ Healthcare	**Executive Officer CFO** Experienced at Nezu Asia Capital Management (hedge fund)	Served at Lonza Extensive experience in cell manufacturing	Group Chairman & CEO, Fusion Systems, Co., Ltd. Presidents Emeriti, ACCJ	Founder & Managing Partner of Proteus, LLC. (Investment in RM ventures)	Attorney-at-Law, Senior Management Partner of Uruma Law Offices Legal Professional Corporation	Ex-corporate auditor of Astellas Pharma

Junichi Kotera	Masanori Sawada	Hardy TS Kagimoto	Kouichi Tamura	Michihisa Nishiyama	Koji Abe
Executive officer Manufacturing field Over 30 years experience in manufacturing	Executive Vice President, CMO (Chief Medical Officer) MD, PhD, MBA	Chairman and CEO MD, Founder	Executive officer Research field Ex-Astellas US Director of Laboratories Expertise in Immunosuppressant Research	Executive Officer Development field Constructed network for Tacrolimus approval and sales at Astellas in the US and Europe	Executive Officer HR & GA field Over 30 years experience in HR

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 Dainippon Pharma

Clinical Development Capabilities

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

Program Overview

New Healios

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
Near term revenue & Commercial capabilities	**Innovative best in class programs**	

[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 data key-open: Q2 2022 SAKIGAKE designation
	HLCM051	ARDS	MultiStem®	Japan			Phase 2	Preparing for NDA filing 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 Dainippon Pharma (DSP); Pending trial initiation by DSP
	–	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.

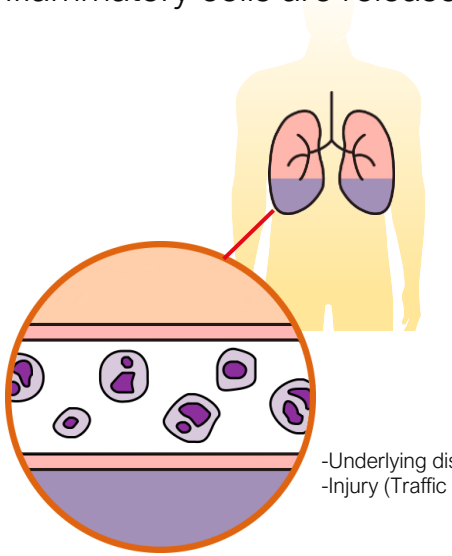
(source)
＊1 The number of ARDS patients in Japan is estimated by Healios based on the incidence rate of epidemiological data and the total demographical population in Japan.
＊2 ARDS treatment guideline 2016

HLCM051 ARDS: Mechanism of Action

Expected effects of HLCM051, 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

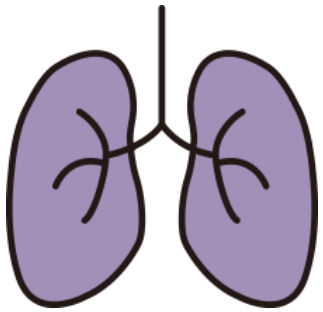
Inflammatory cells are released



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

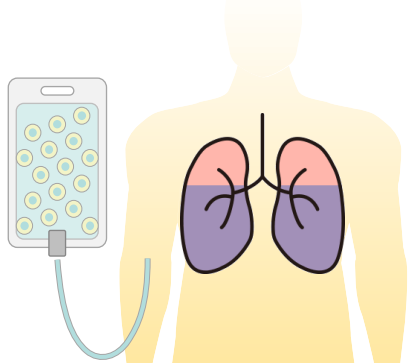
When the tissue is damaged, inflammatory cells are released in large quantities.

Inflammatory cells attack the lungs



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

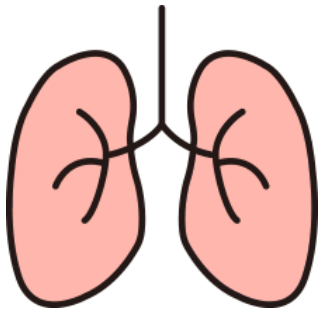
HLCM051 administered



- 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

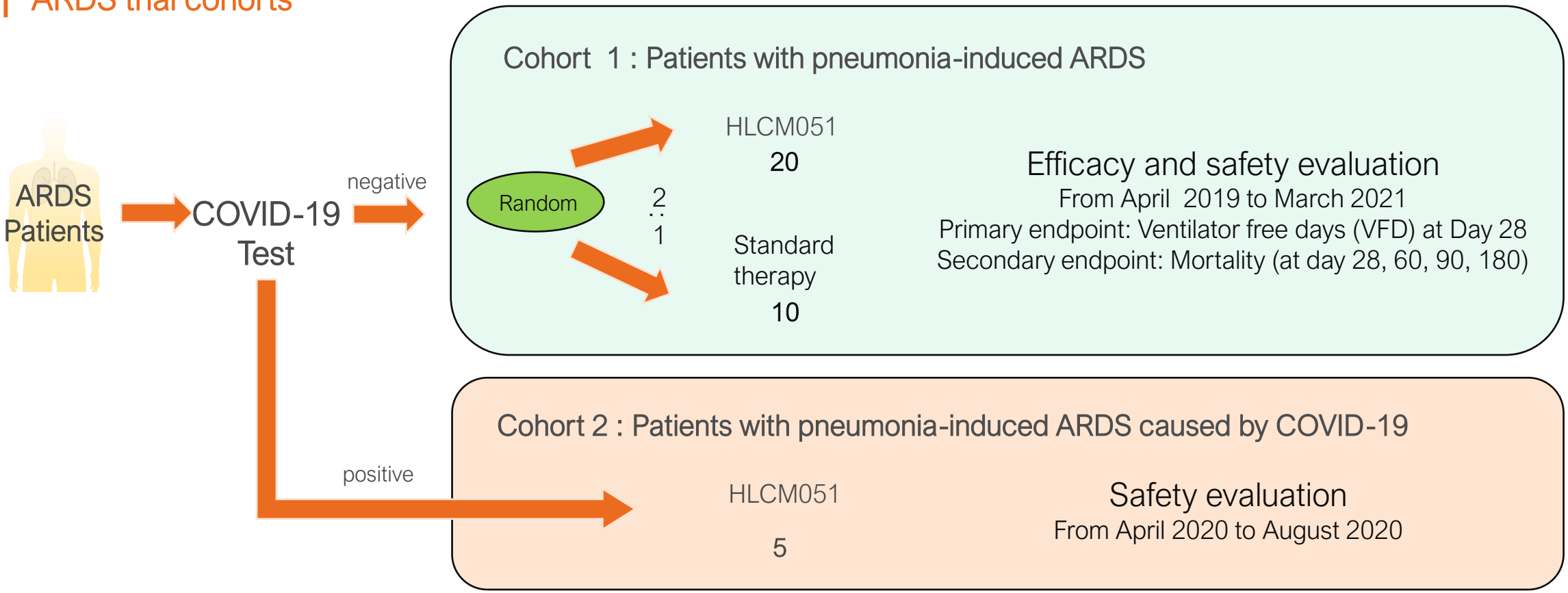


We can anticipate earlier ventilator removal and a lower mortality rate.

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%**

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

Update

Healios

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）

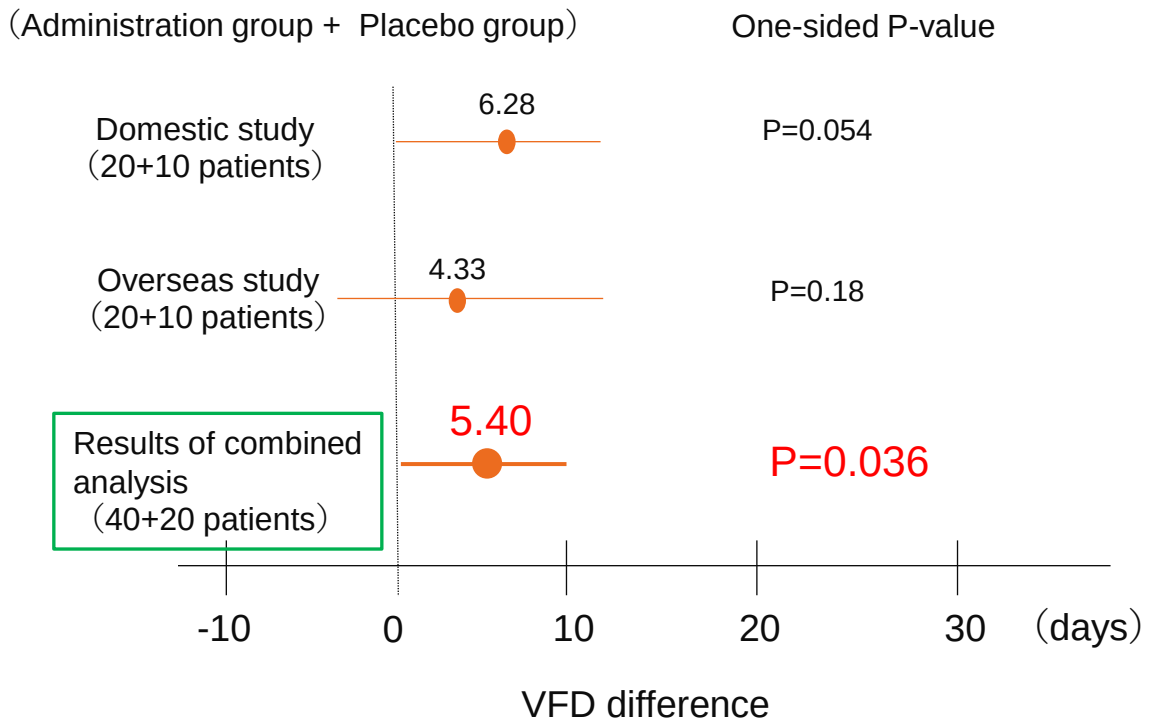
Report of Placebo-Controlled Clinical Trial Evaluating MultiStem Cell Therapy for ARDS Published in Intensive Care Medicine（Link to Athersys' Website November 30, 2021）

（Source）Athersys

Reference: Combined Analysis of Domestic and Overseas ARDS Studies

Combined analysis of VFD data in the domestic study (ONE-BRIDGE study, cohort 1) and the overseas study (Athersys' MUST-ARDS study) reinforces the tendency of HLCM051 to improve VFD.*

Combined analysis results



Summary

After adjusting for baseline age and PF ratio as continuous risk factors, the average improvement in 28-day VFD for the two trials on a combined basis was 5.40 days with a one-sided p-value of 0.036.

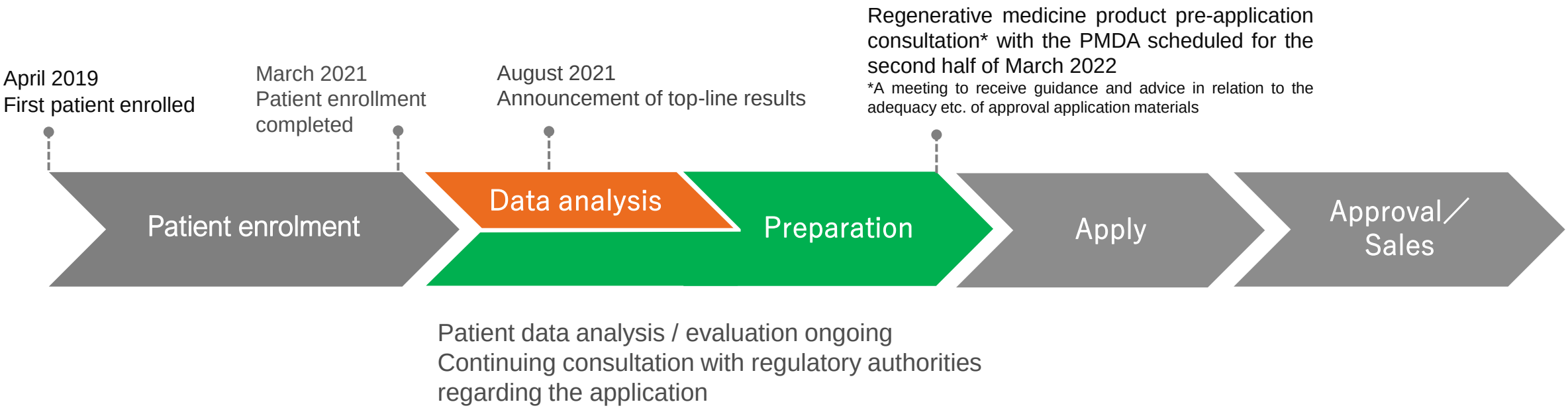
*Note: In the VFD analysis of each study, analysis of covariance was performed with the treatment method, P / F ratio (PaO2 / FIO2 ratio, gas exchange index in the lungs), and age as independent variables. In the combined analysis, covariance analysis was performed in the same manner, and adjustments were made based on the P / F ratio, age, test, interaction between P / F ratio and test, and interaction between age and test. The results of the combined analysis suggest that the 90% confidence interval exceeds 0 (90% CI: 0.48 to 10.32, one-sided P-value 0.036, which is suggestive of the above conclusion).

HLCM051 ARDS: ONE-BRIDGE Study

Update

Healios

Development plan



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.)

We are continuing to consult with the regulatory authorities in preparation to file for regulatory approval as soon as possible.

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.

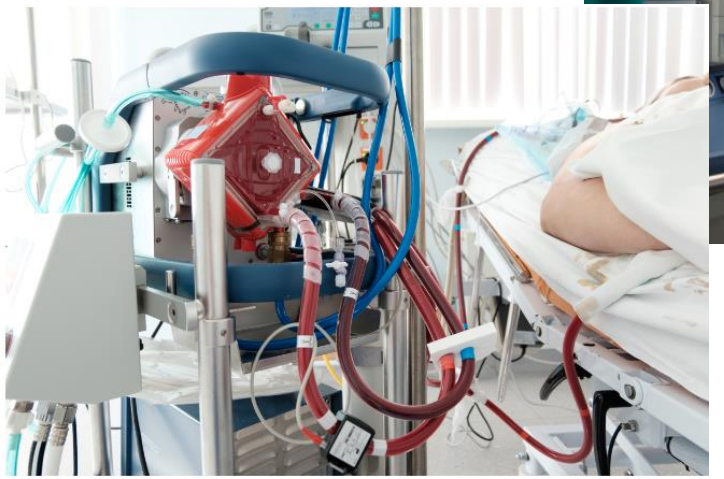
Contribution to patients ⇒ Providing new treatment
Improvement of mortality and QOL

- 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

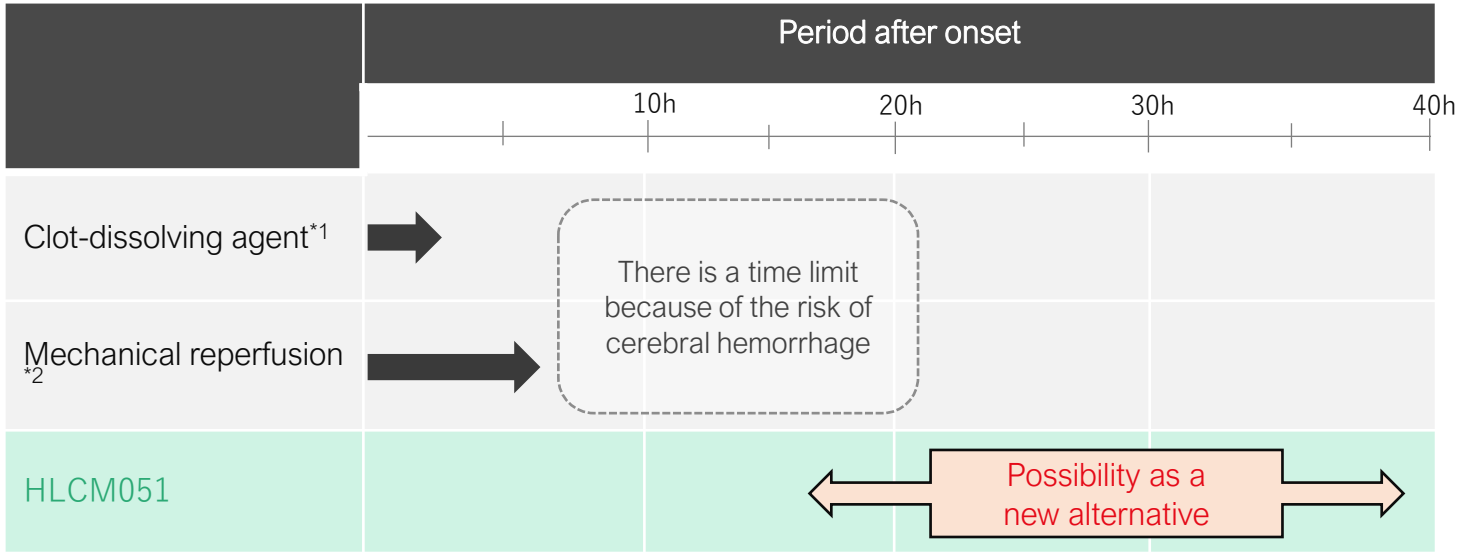


Artificial Respiration

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

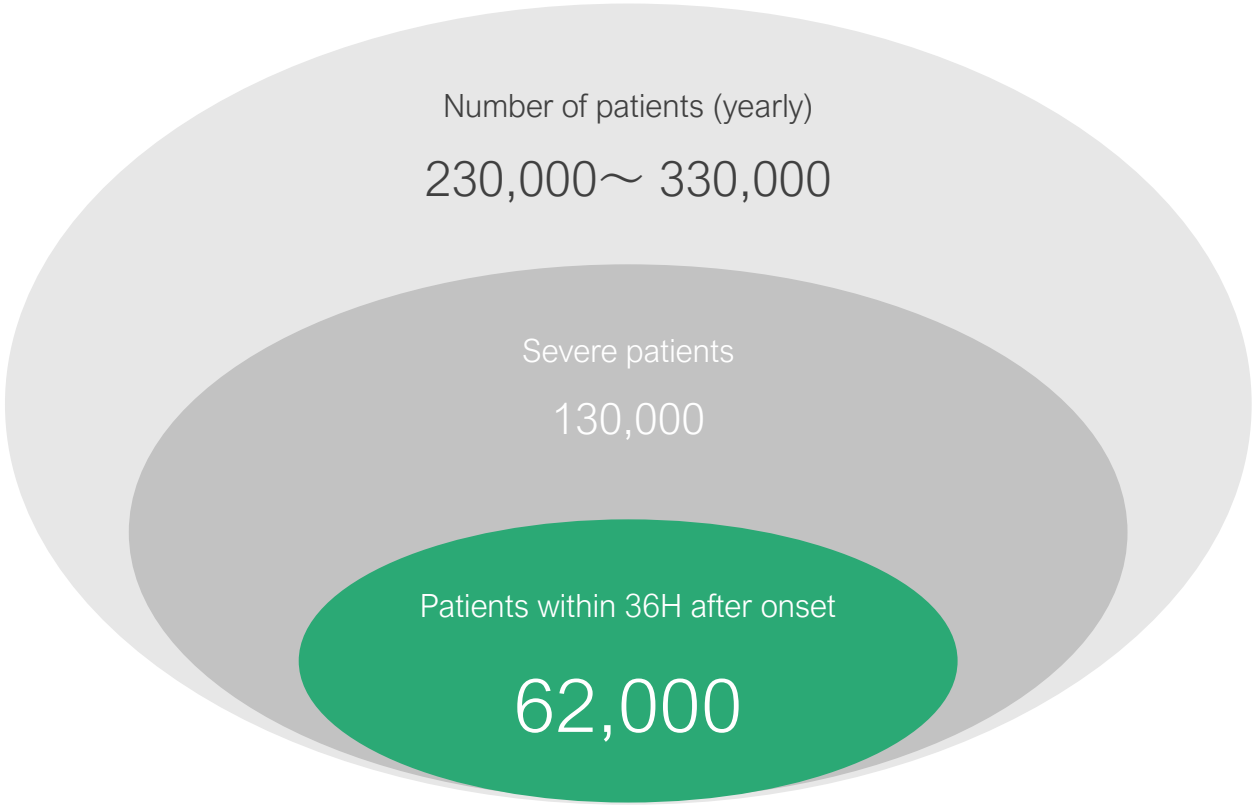
Ischemic stroke, which represents the most common form of stroke (70 - 75% of cases in Japan), is caused by a blockage of blood flow in the brain that cuts off the supply of oxygen and nutrients, resulting in tissue loss.

(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)

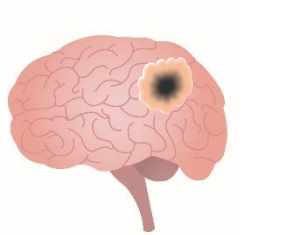
Severe patients （atherothrombotic and cardiogenic cerebral infarction)

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.

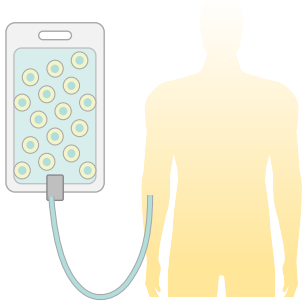
HLCM051 Stroke: Mechanism of Action

Stroke-induced neuronal damage

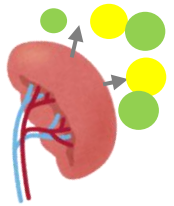


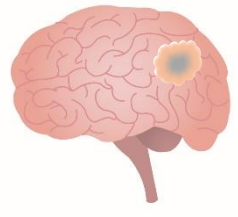
Primary Damage

With HLCM051



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



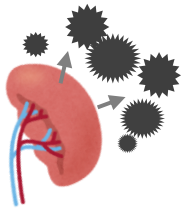


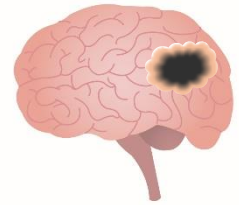
Attenuate neuronal damage in the acute phase of stroke caused by inflammatory cells

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

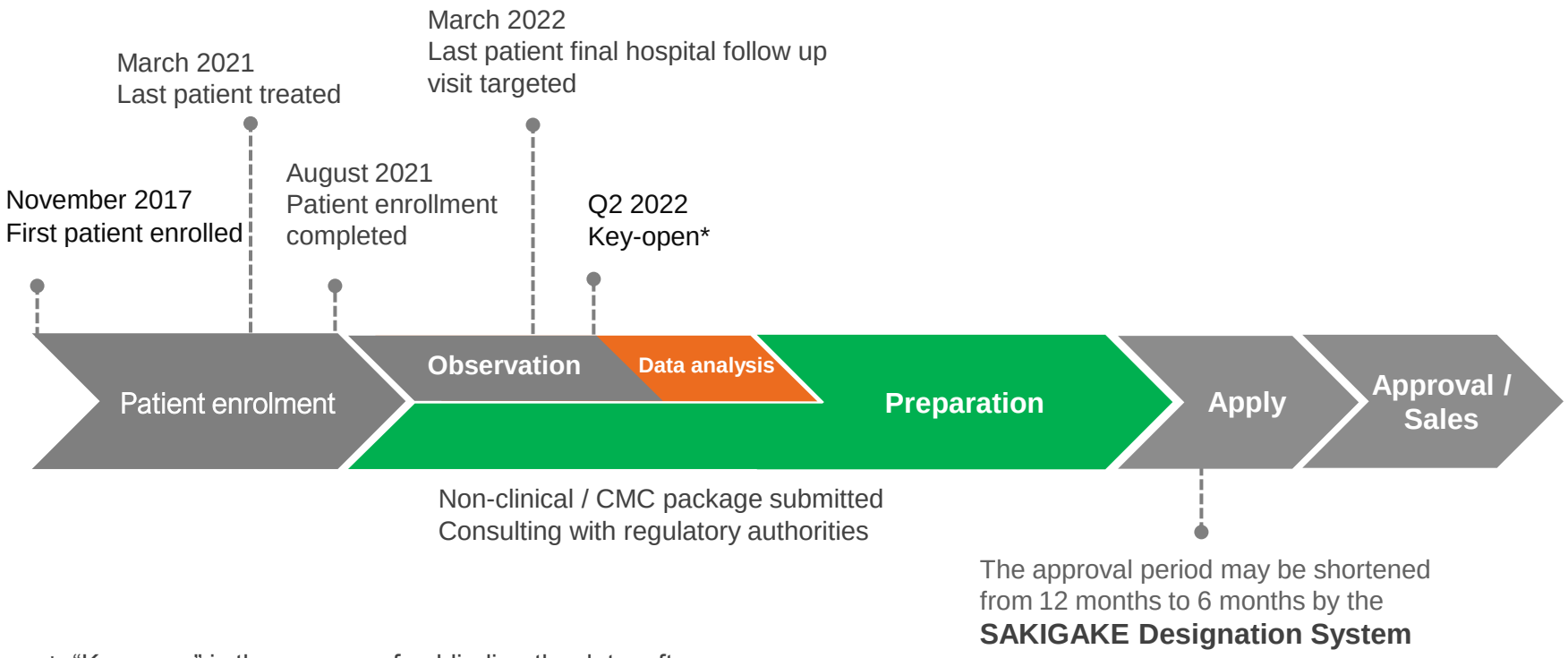
HLCM051 Stroke: TREASURE Study

Update

Healios

The 90 and 365-day results of the TREASURE study will be unblinded in Q2 2022.

Development Plan



＊ “Key-open” is the process of unblinding the data, after which analysis can be completed. Results will be released promptly post key-open and completion of analysis.

Overview

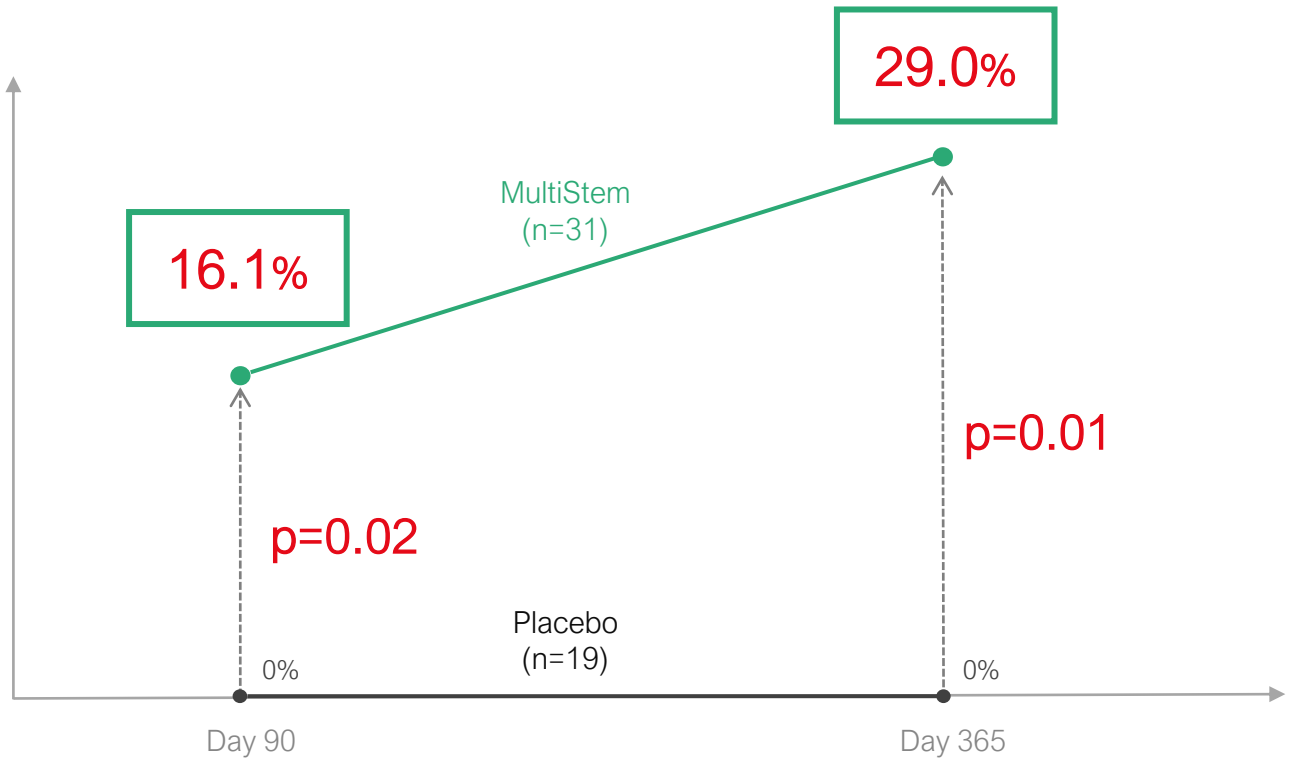
Trial	Placebo-Controlled, Double-Blind, Phase 2/3 Efficacy and Safety Trial of HLCM051 (MultiStem®) in Patients With Ischemic Stroke （TREASURE study）
Subjects	Ischemic stroke within 18 to 36 hours
Conditions	Placebo-Controlled, Double-Blind
Enrollment	220 (HLCM051 [n=110], placebo [n=110], randomized)
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.

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

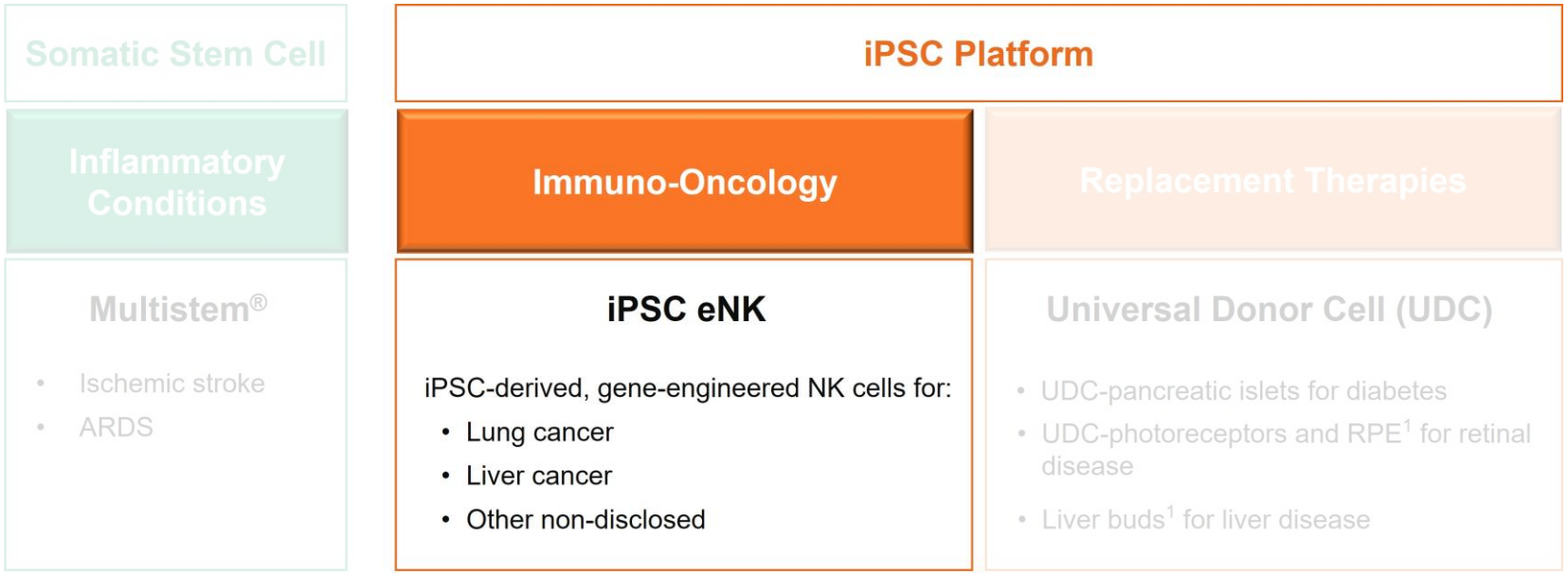
*<Excellent Outcome> is defined as mRS score of ≤1 (scale, 0 to 6), NIHSS score of ≤1 (scale, 0 to 42), and BI score of ≥95 (scale, 0 to 100).

Summary: MultiStem® Program

- Stroke data key-open* Q2 2022
- Preparing for NDA submission for ARDS (orphan designated product)
- Building a commercial infrastructure
  - Near-term revenue
  - Establish operational proficiency & distribution capabilities in Japan
  - Gain key insights for further iPSC platform development

* “Key-open”: process of unblinding the data, after which analysis can be completed.
Results will be released promptly post key-open and completion of analysis.

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

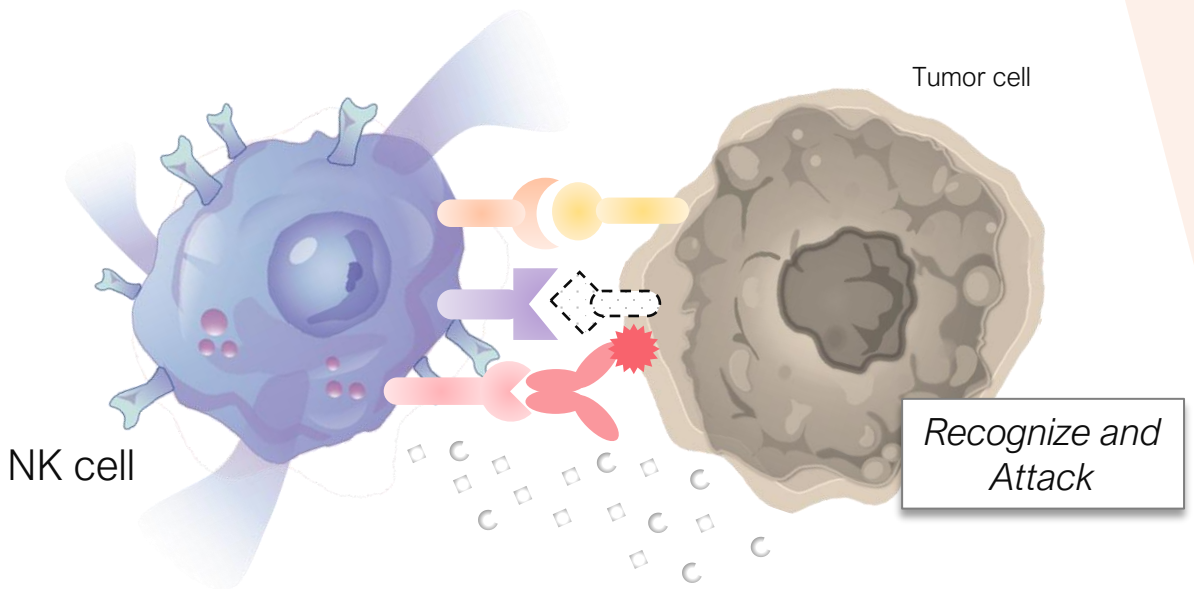
[1]https://www.who.int/news-room/fact-sheets/detail/cancer

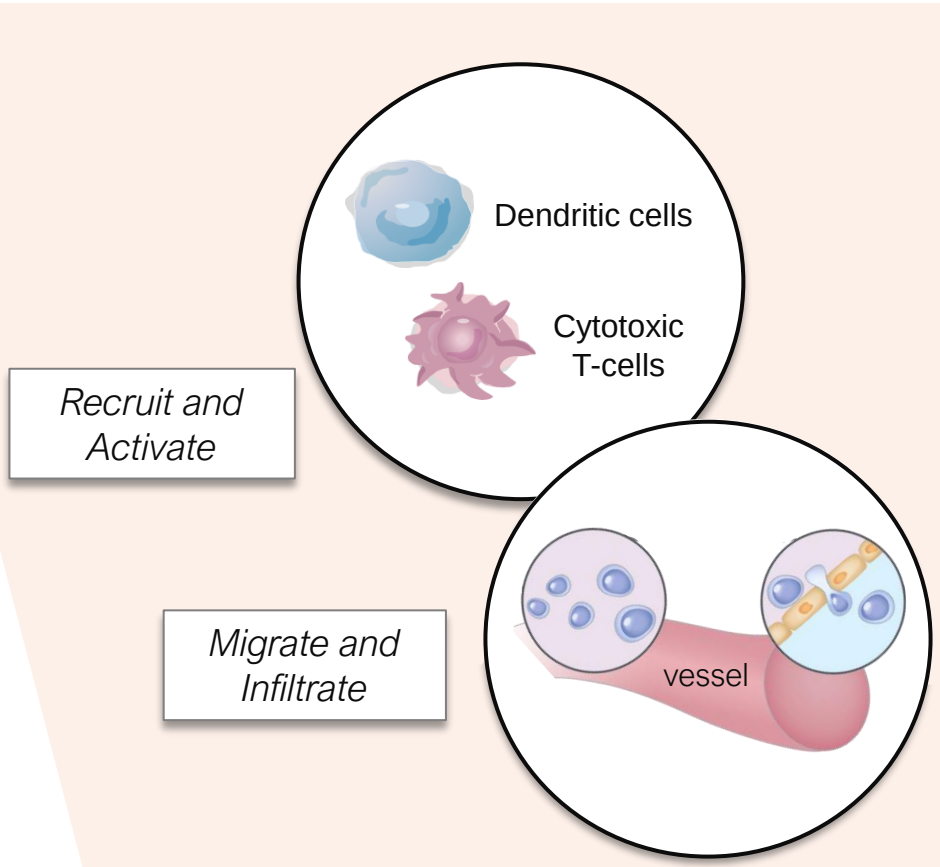
Healios' Three-Pronged NK Cell Therapy Approach

New

Healios

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

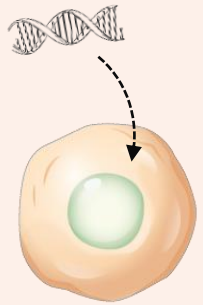




Core eNK Platform Technologies & Competencies

New Healios

Engineered iPSC Lines



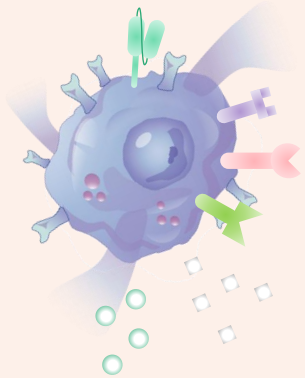
NK differentiation

Proprietary iPSC lines

Cell engineering

Master cell banks established for NK cell production

Differentiation of NK Cells With Enhanced Functionality



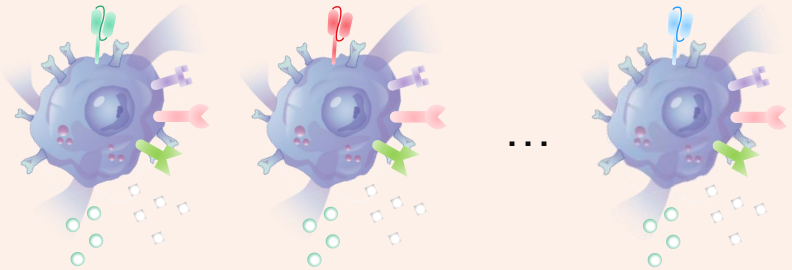
eNK

- 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

New Healios

CD16; for enhanced ADCC

Receptor for improved migration into solid tumors

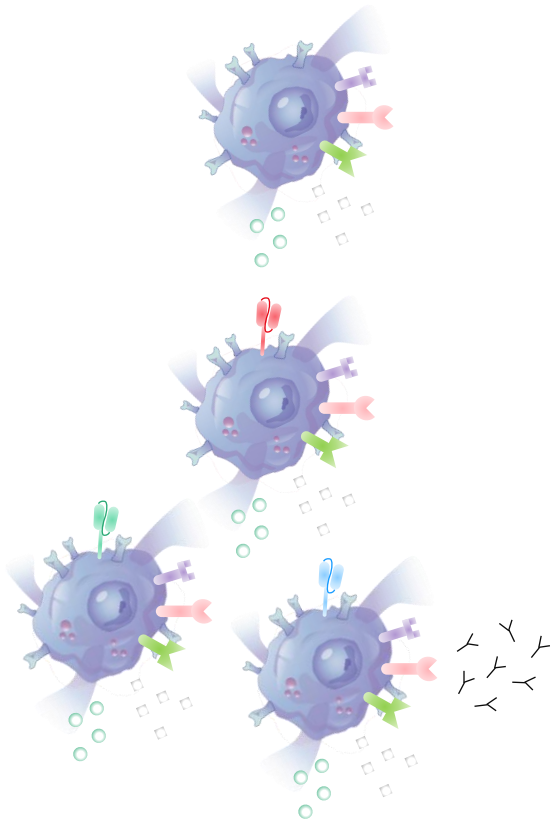
Receptor for enhanced recognition and cytotoxicity

CAR

IL-15; for improved persistence and survival

Chemokine release to recruit host immune cells

Multiple Product Candidates



Stand-alone eNK product

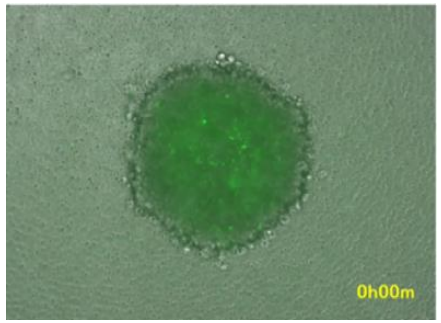
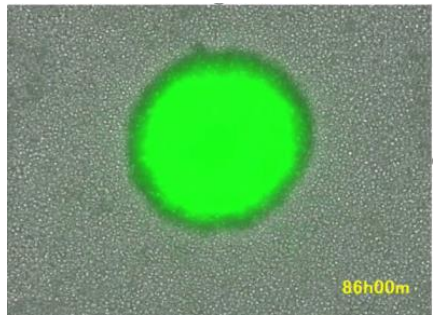
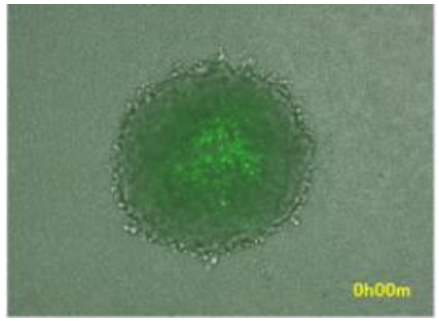
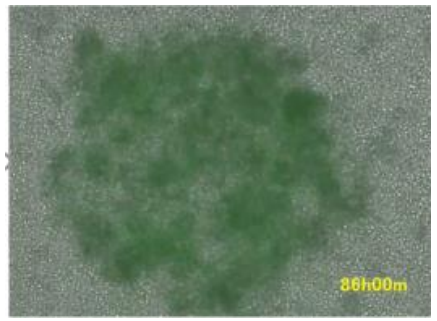
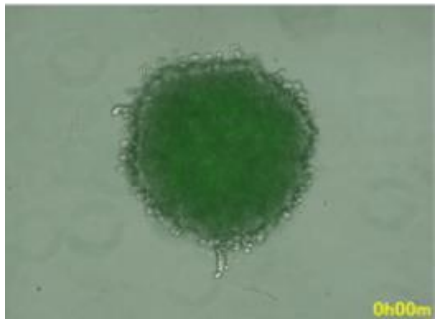
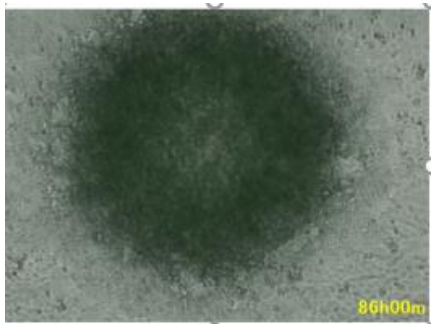
CAR-eNK products against specific targets

In combination with antibody therapies

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

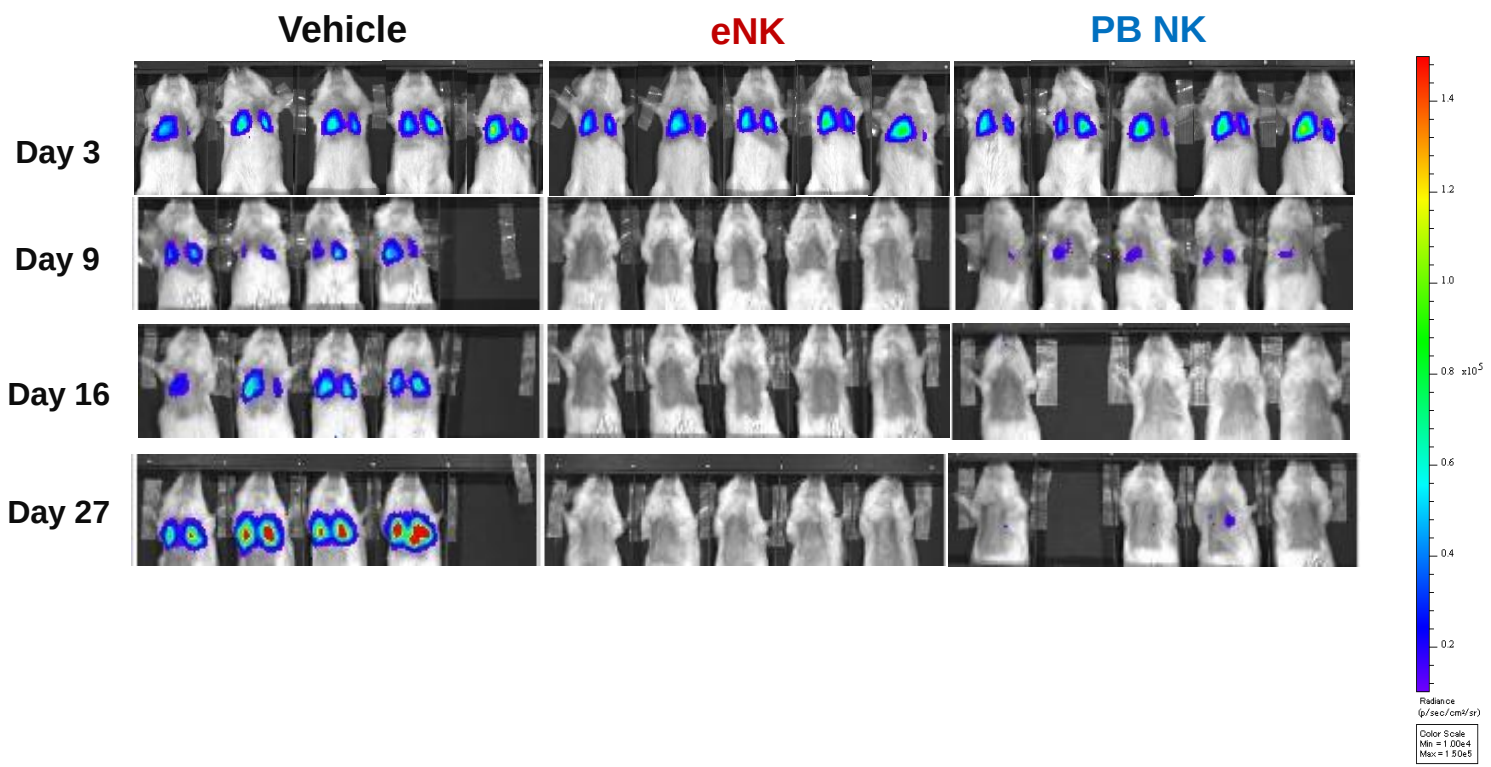
New Healios

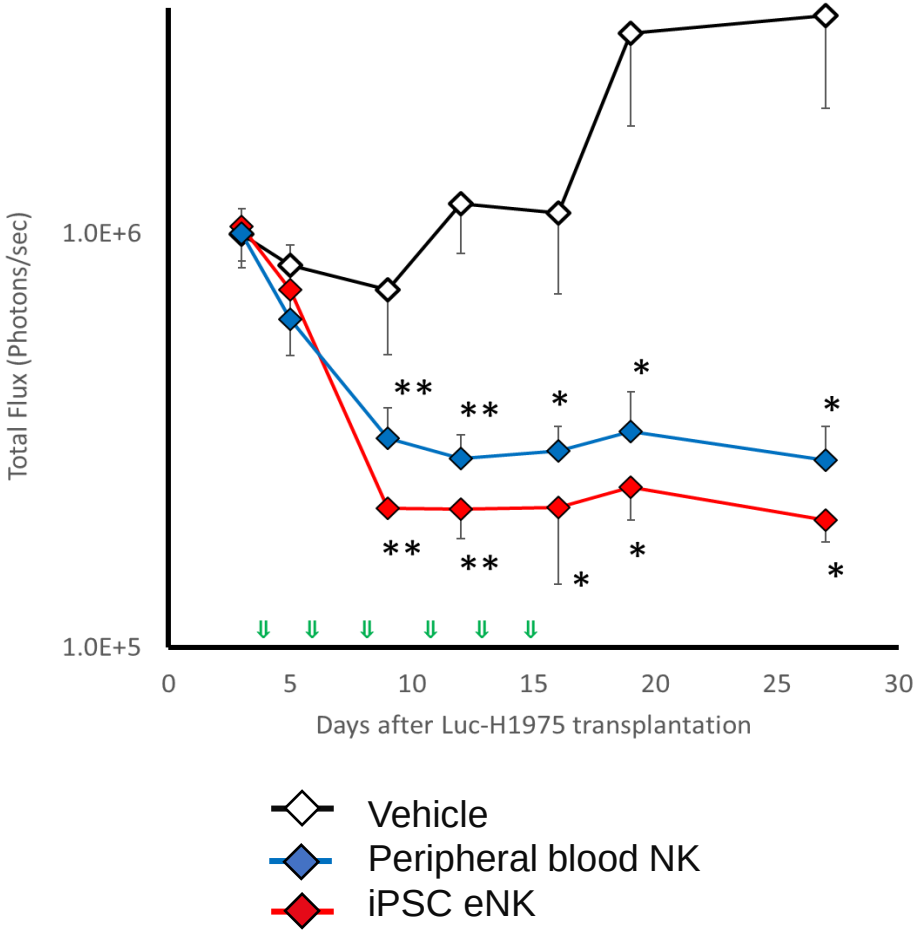
Bright green: apoptotic cells

	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

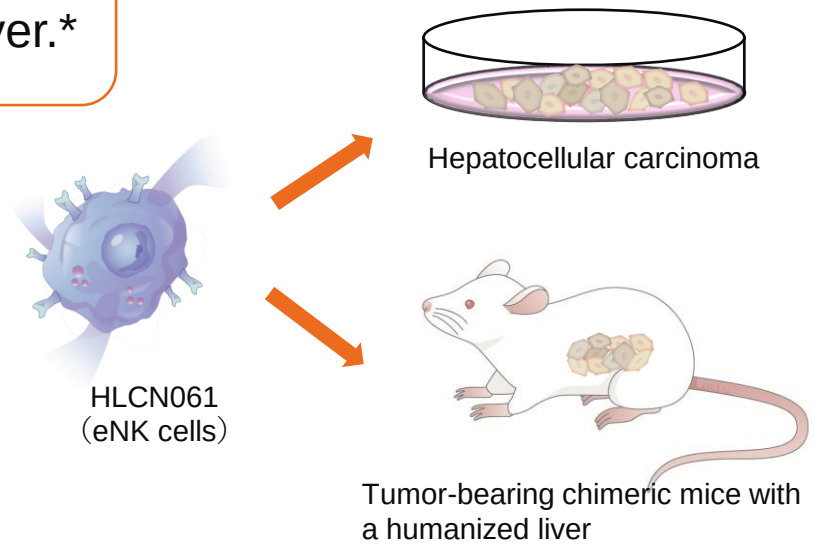
HLCN061 Joint Research with Hiroshima University

Healios has entered into a joint research agreement with the Department of Gastroenterological and Transplant Surgery, Graduate School of Biomedical and Health Sciences, Hiroshima University, to advance HLCN061 for hepatocellular carcinoma.

Evaluate the anti-tumor effect of HCLN061 in hepatocellular carcinoma

- *in vitro* : functional evaluation
- *in vivo* : evaluation in tumor-bearing chimeric mice with a humanized liver.*

Hiroshima University × Healios



The Department of Gastroenterological and Transplant Surgery,
Graduate School of Biomedical and Health Sciences, Hiroshima University:

- A wide range of research from basic to clinical studies on postsurgical adjuvant immunotherapy using hematopoietic stem cell-derived activated NK cells for viral hepatitis and hepatocellular carcinoma
- Clinical research involving the use of NK cells. In particular, vast knowledge and experience in the research of cancer immunotherapies for hepatocellular carcinoma.

＊ Mice in which at least 70% of the liver has been transplanted with human liver cells called hepatocytes.

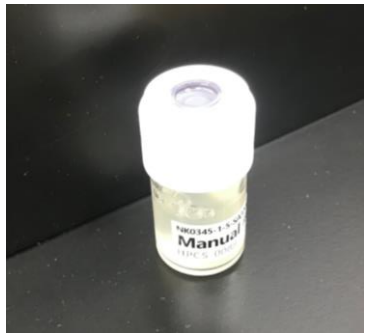
iPSC-Derived Product Manufacturing: A New and Dedicated GMP Facility

Update

Healios

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

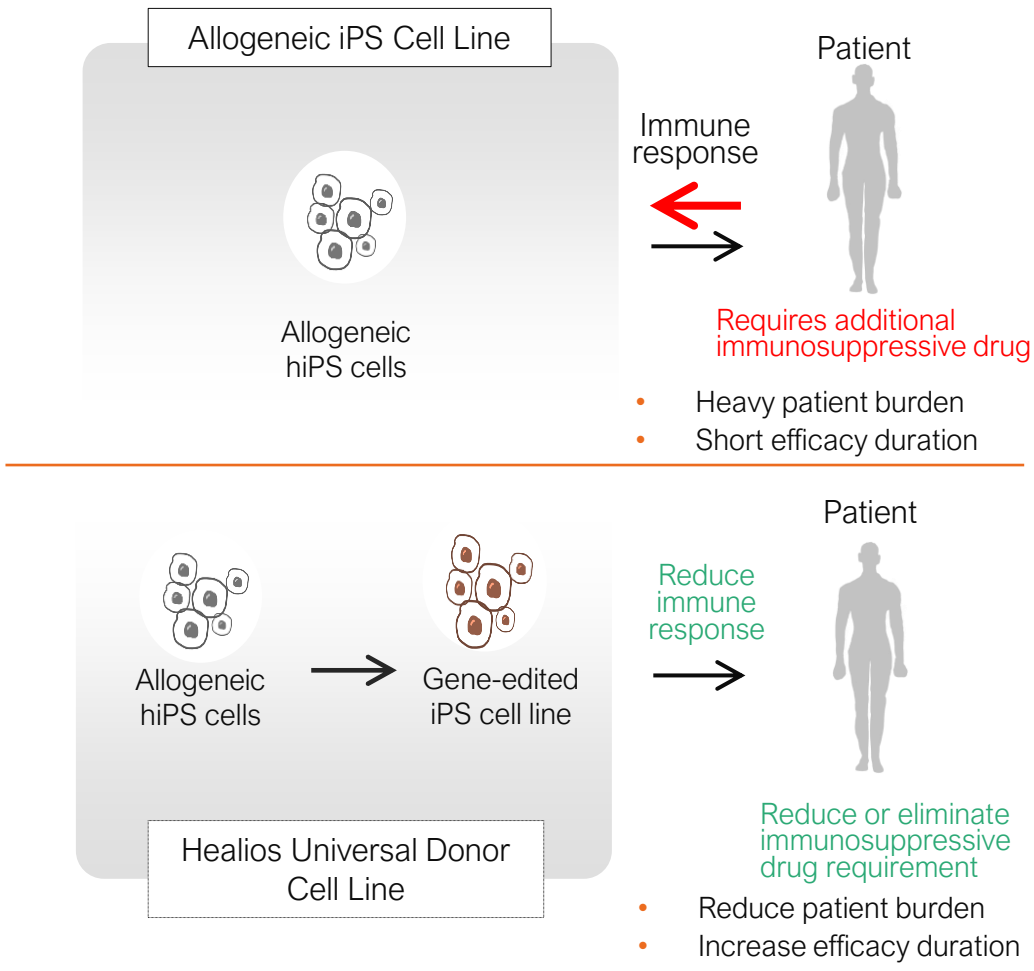
Somatic Stem Cell	iPSC Platform	
Inflammatory Conditions	**Immuno-Oncology**	**Replacement Therapies**
Multistem® • Ischemic stroke • ARDS	**iPSC eNK** iPSC-derived, gene-engineered NK cells for: • Lung cancer • Liver cancer • Other non-disclosed	**Universal Donor Cell (UDC)** • UDC-pancreatic islets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

Hypo-immune Universal Donor Cell (UDC) Platform

Update

Healios

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



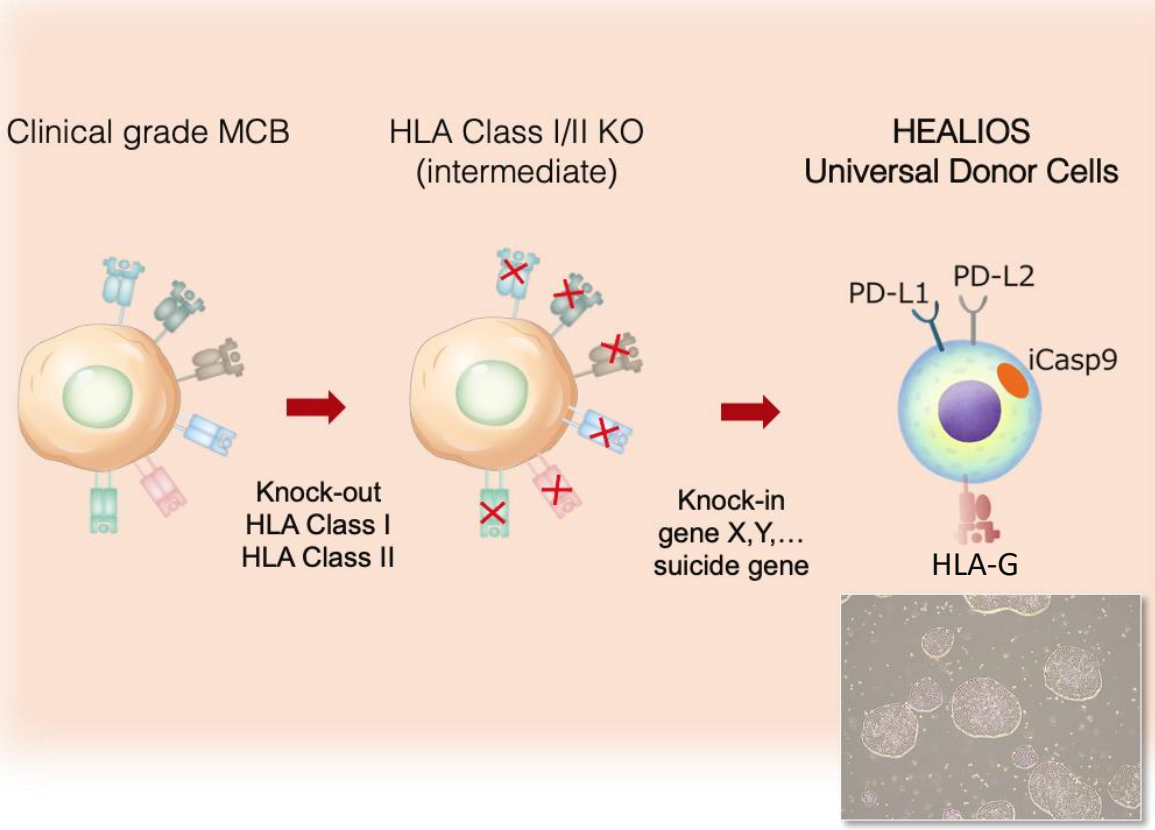
Targeted cell programming through gene-editing

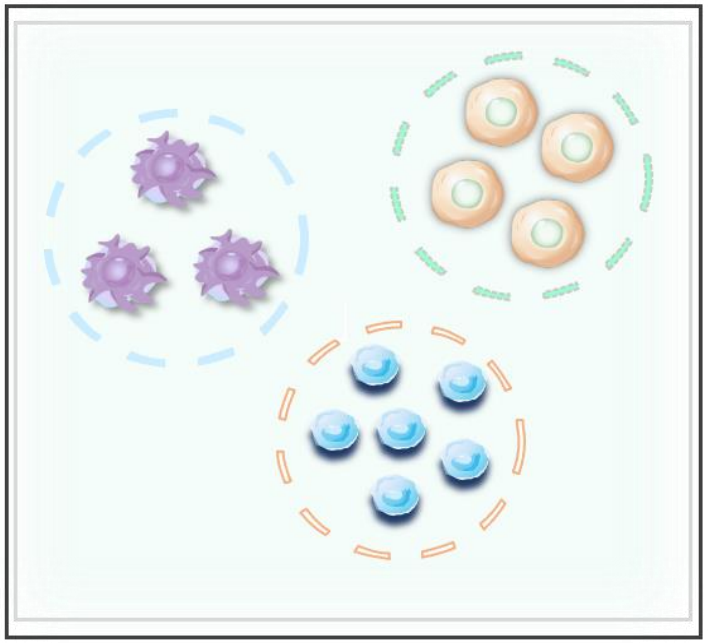
- In October 2020, Healios established a clinical grade universal donor IPS cell line that can be clinically applied to humans in each of Japan, the United States and Europe.
- Master Cell Bank established in 2021
- Healios has led the development of high-quality, universal donor iPS cells in accordance 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

Update

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

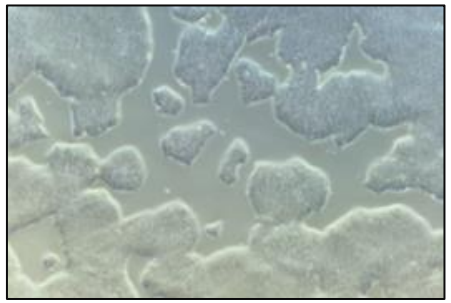
Clinical grade line and Master Cell Bank established in 2020/2021

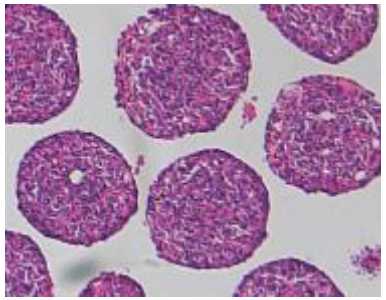
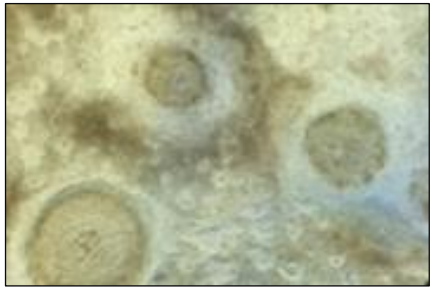
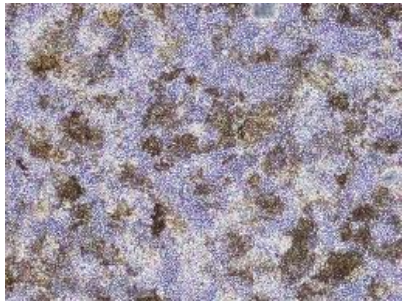
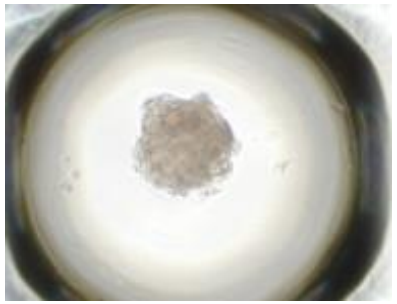
（Source）in-house data

Hypo-immune UDC: Examples Of Cell Therapies

New Healios

Universal Donor Cells (UDC)



Pancreatic β cells	Photoreceptor cells	RPE cells	Liver buds
			

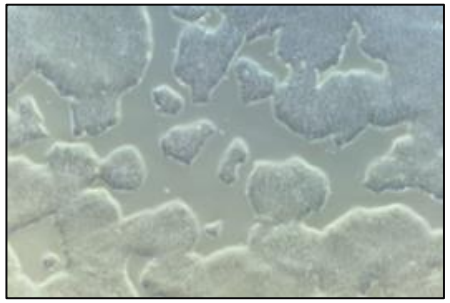
Successfully differentiated from UDCs

Future migration to UDC platform

（Source）in-house data and Joint research data

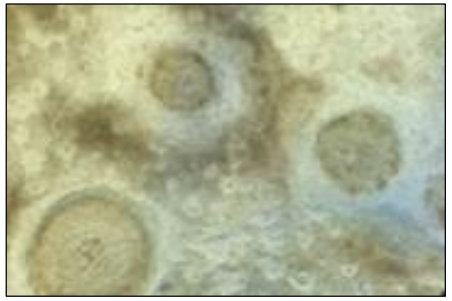
Hypo-immune UDC: Differentiation and Induction of Photoreceptor Cells

Photoreceptor cells



UDC

Differentiation and induction

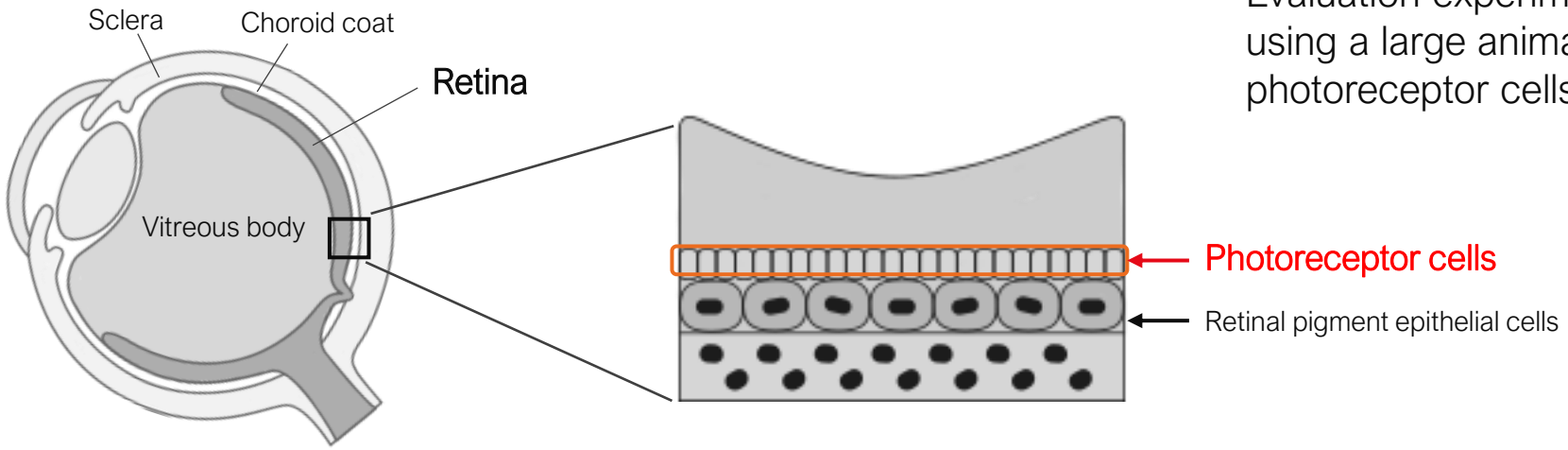


Photoreceptor cells From UDC

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.

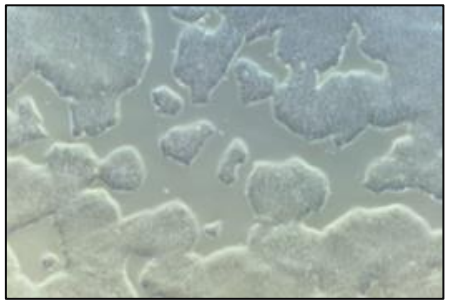


(Source) Joint research data

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

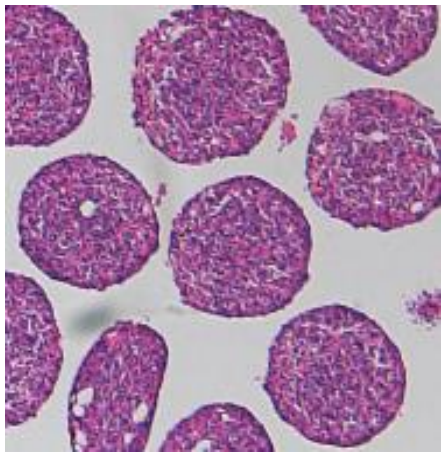
Joint research with the Department of Regenerative Medicine at the National Center for Global Health and Medicine in Tokyo

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.

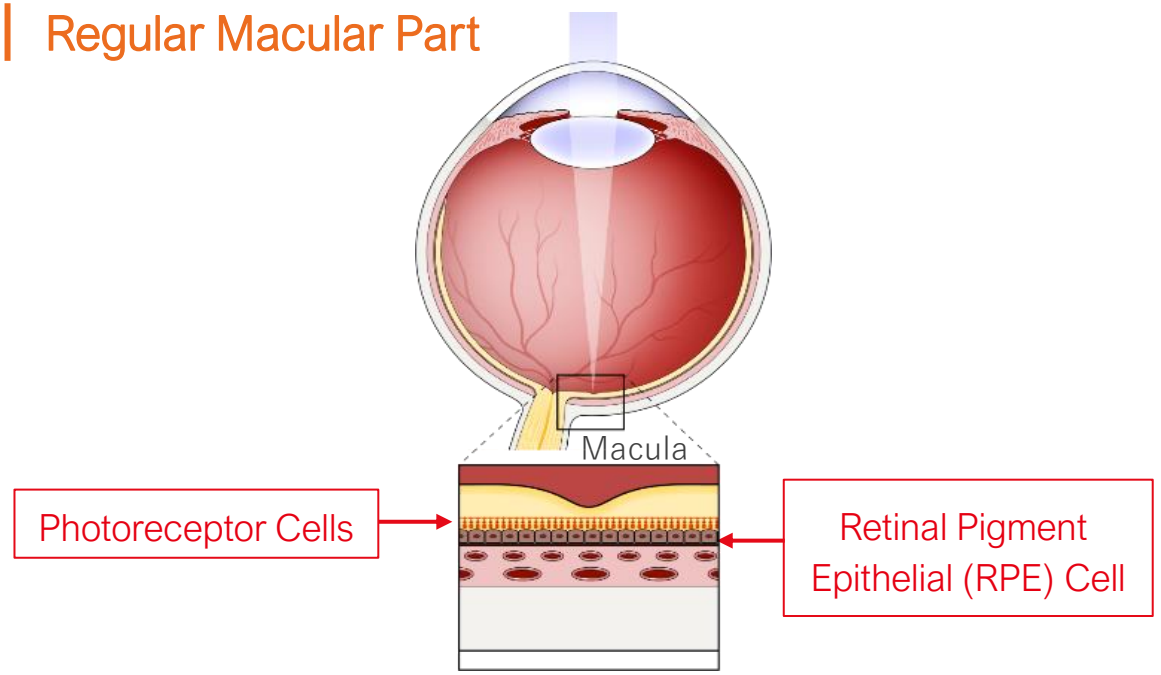
In our joint research with the Department of Regenerative Medicine at the National Center for Global Health and Medicine in Tokyo, we have been aiming to establish a method for inducing differentiation of human iPS cells into pancreatic β-cells for use in clinical applications such as the treatment of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

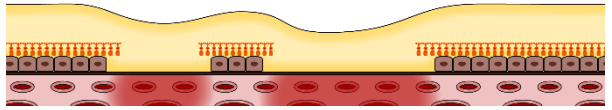
Age-related Macular Degeneration(AMD) causes Retinal Pigment Epithelial (RPE) cells to degenerate, which damages function

Regular Macular Part



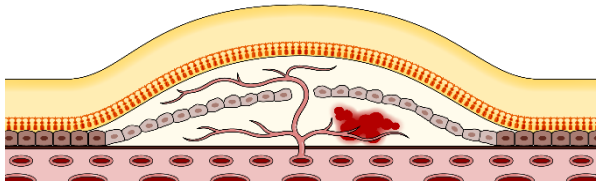
Developed Dry-AMD

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 Dainippon Pharma jointly develop a treatment using iPS cell-derived RPE cells.

- Sumitomo Dainippon Pharma takes the lead in preparing for clinical trials

HLCL041: Liver Organ Bud Platform

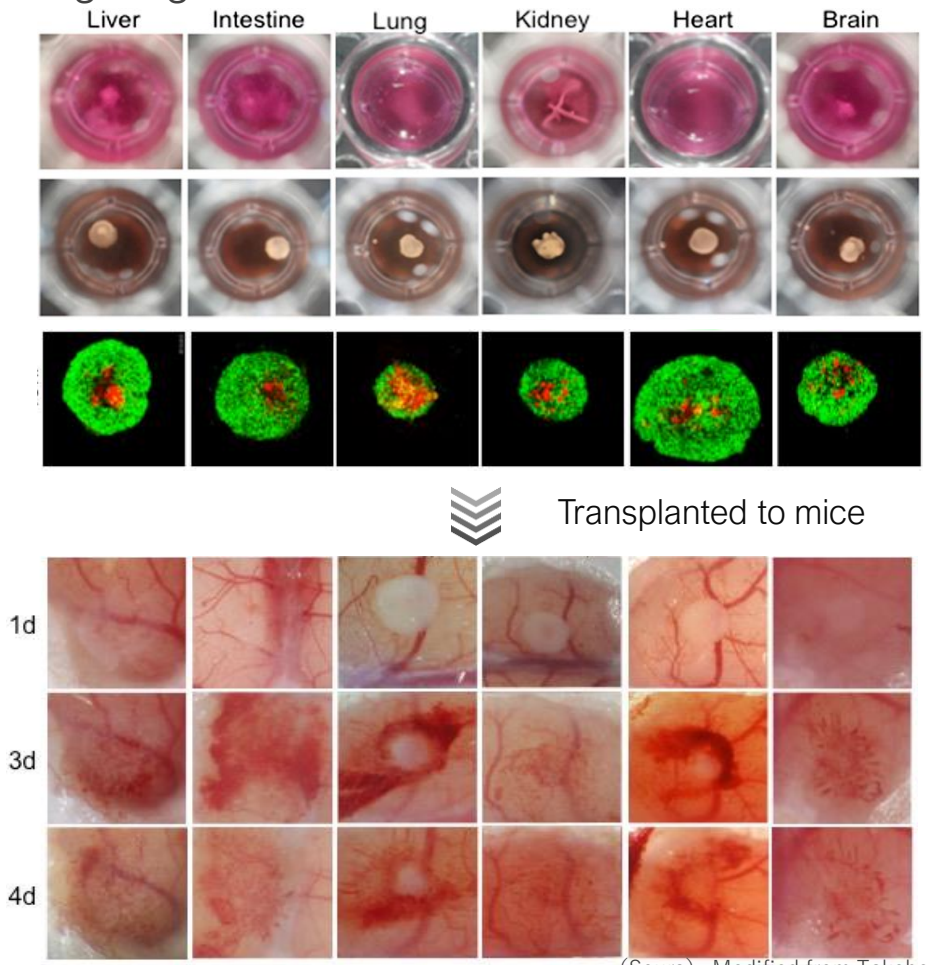
By creating an "Organ Bud" of each organ with iPS cells, we have laid the groundwork for paradigm shifting therapies to emerge for various severe diseases.

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



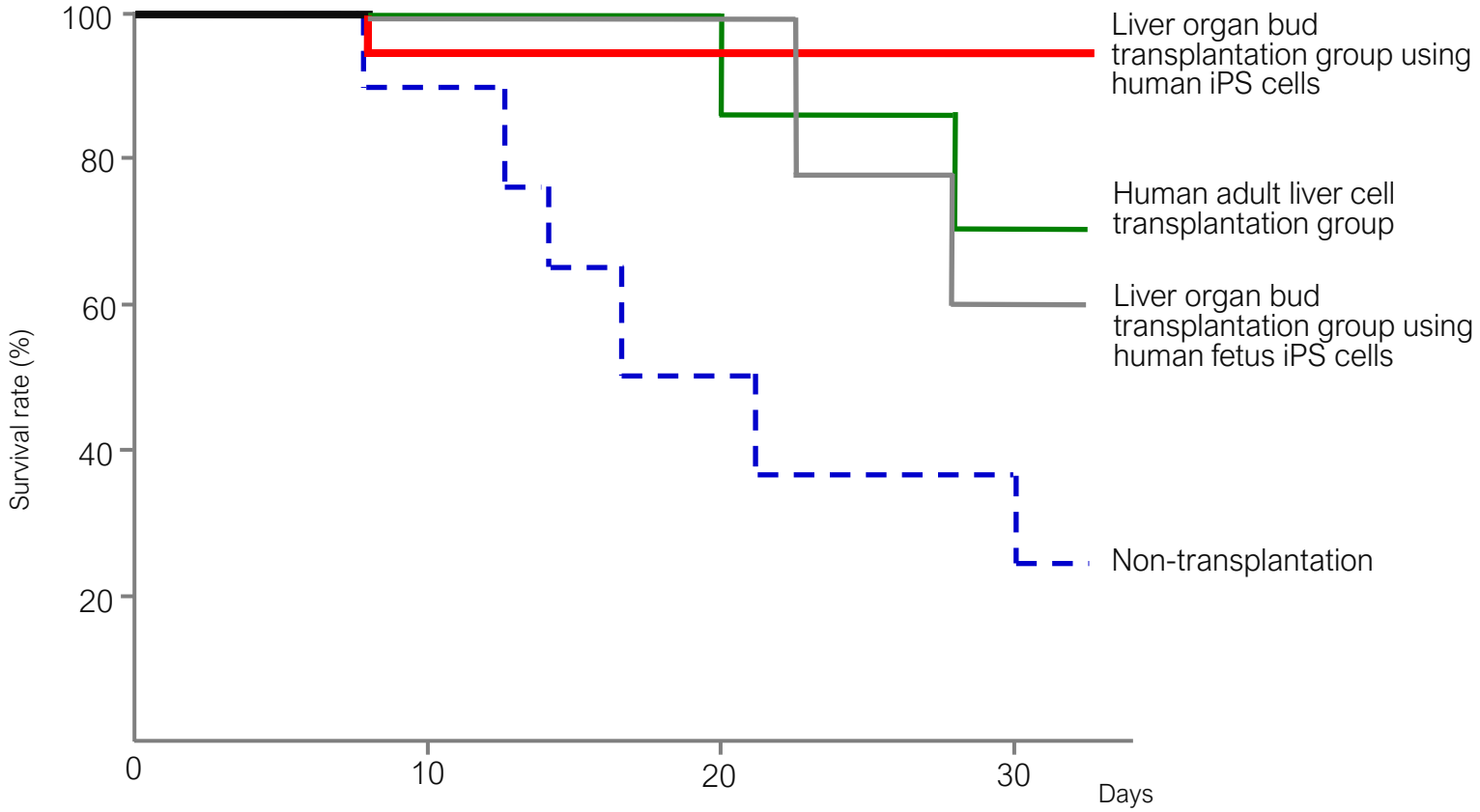
Green：Cells of each organ
Red：Vascular endothelial cell
Black：MSC

（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

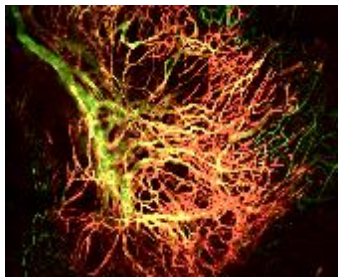
Treatment effects of liver bud transplantation to mouse using hiPSC

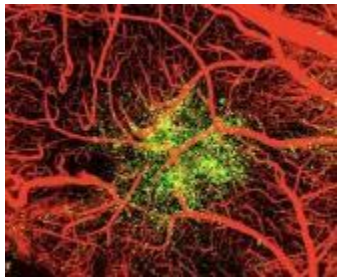


（Source） Adapted by Healios from Takebe. T, et al. Nature, 499 (7459),（2013）

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)

Financial Highlights

Consolidated Statement of Income

Update

Healios

(Units: one million US dollars)

	FY2020	FY2021		
			YoY variance	Main reasons for increase/decrease
Revenue	0.26	0.37	0.12	
Operating profit	-39.18	-48.99	-9.81	Mainly due to increase in SG&A expenses −$4.13mn and increase in R&D expenses −$5.71mn.
Profit	-51.64	-44.69	6.95	Mainly due to decrease in financial expenses +$3.77mn and increase in financial income +$15.72mn (Please refer to the next page for details)
R&D expenses	27.97	33.67	5.71	
Number of employees	113	116	3	

(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 12-month periods for P&L; FY2020 106.76 yen per dollar and FY2021 109.90 yen per dollar.

Supplemental Explanation of Financial Income and Financial Expenses

Update

Healios

Details of financial income and financial expenses

In the fiscal year ending December 2021, we recorded financial income of ¥1,728 million and financial expenses of ¥802 million. Financial income was mainly due to the recording of ¥1,620 million in gain on valuation of derivatives*1 and 96 million in amount reclassified to third-party interests *2.
Financial expenses was mainly due to the recording of ¥542 million in interest on bonds*3, the recording of ¥209 million in loss on valuation of warrants and ¥40 million in interest expenses.

*1. Gain or loss on valuation of derivatives

Gain or loss on valuation of derivatives are the net unrealized gains/losses 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 third 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 ending December 2020.

*2. Amount reclassified to third-party interests

Amount reclassified to third-party interests is the transfer of profits and losses of Saisei Bioventures, L.P., a 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 Financial Income and Financial Expenses

Update

Healios

*3. Interest on bonds

Of the total interest on bonds of ¥542 million, ¥502 million was charged to income 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 ending 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, 2020	December 31, 2021	Variance	Main reasons for increase/decrease
	Current assets	144.99 (64.8%)	142.83 (68.5%)	-2.16	Mainly due to decrease in cash equivalents $3.02mn. (cash equivalent balance at 12/31/21 was $131.51mn). New share issuance during the period raised $58.71mn of new cash.
	Non-current assets	78.89 (35.2%)	65.58 (31.5%)	-13.31	
Total assets		223.88 (100.0%)	208.41 (100.0%)	-15.47	
	Current liabilities	25.95 (11.6%)	52.53 (25.2%)	26.58	Increase in bonds and loans (primarily convertible bonds) payable +$41.17mn and decrease in other financial liabilities -$15.82mn, mainly due to the maturity of already existing convertible bonds now falling within a one-year time frame.
	Non-current liabilities	122.07 (54.5%)	80.72 (38.7%)	-41.35	Decrease in bonds and loans payable (primarily convertible bonds) -$47.49mn, mainly due to the maturity of already existing convertible bonds now falling within a one-year time frame.
Total liabilities		148.02 (66.1%)	133.25 (63.9%)	-14.77	
Total equity		75.86 (33.9%)	75.16 (36.1%)	-0.70	Mainly due to net loss -$44.69mn, issuance of new shares +$58.71mn and decrease in other components of equity -$10.66mn as a result of a decline in the price of Athersys shares.
Total liabilities and equity		223.88 (100.0%)	208.41 (100.0%)	-15.47	

(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 ; FY2020 Q4 103.50 yen per dollar and FY2021 Q4 115.02 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

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