FY2017 Financial Results

February 2018

HEALIOS K.K.
(TSE 4593)

Contents

1. Financial Highlights

Statement of income

(Million yen)

	FY 2016	FY 2017		
			YoY change	Main reasons for increase/decrease
Sales	77	**27**	▲49	Compound drug business transfer
Operating income	▲3,507	**▲2,348**	+1,159	Research & Development Cost decreased ＋1,229
Ordinary income	▲3,426	**▲2,414**	+1,011	-
Net income	▲3,433	**▲1,776**	+1,656	Gain on Business transfer +641
R&D	2,959	**1,730**	▲1,229	(Due to MultiStem License-in in FY2016 ▲1,809)
Amortization of goodwill	100	**33**	▲66	-
Number of employees	58	74	+16	-

Balance sheet

(Million yen / %)

		December 31, 2016	December 31, 2017		
				Change	Main reasons for increase/decrease
	Current assets	8,073 (88.0%)	**19,288** (97.9%)	+11,214	Cash and deposit ＋11,213 (Cash and deposit balance 19,040)
	Non-current assets	1,101 (12.0%)	**408** (2.1%)	▲692	Goodwill ▲691
Total assets		9,174 (100.0%)	**19,696** (100.0%)	+10,521	
	Current liabilities	772 (8.4%)	**1,300** (6.6%)	+528	
	Non-current liabilities	2,408 (26.2%)	**2,232** (11.3%)	▲176	
Total liabilities		3,180 (34.7%)	**3,532** (17.9%)	+352	
Total equity		5,994 (65.3%)	**16,163** (82.1%)	+10,169	Capital etc. ＋11,918 Earned surplus ▲1,776
Total assets		9,174 (100.0%)	**19,696** (100.0%)	+10,521	

2. FY2017 Business Overview

Fund raising in FY2017

①Business and Capital alliance with Nikon (March 2017)

Healios promotes the search for and development of new seeds in the regenerative medicine field.

Nikon supports these new seeds from the viewpoint of contract manufacturing of cells / cell quality evaluation with image analysis etc.

Number of new issued shares:
1,037,400 common shares
Total issue price：
About 2 billion Yen

②Issuance of share options (From March to December 2017)

In March 2017, 71,457 units of share options issued and allocated to Nomura securities.

→**Execution completed on December 6, 2017**

Number of exercised share:
7,145,700 common shares
Amount of fund raising:
9,873 million yen

①+②　New shares were issued for 20% of the number of outstanding shares
Raised 12 billion yen

End of April 2017, Compound drug business transferred.　→ 1.3 billion yen

Pipeline

Field	Development Code	Indication	Market	Pre-clinical test	Phase I Trial	Phase II Trial	Phase III Trial	Apply-approve	On the Market	Progress Status
Somatic stem cell Regenerative Medicine	HLCM051	Ischemic Stroke	Japan	→	→	→	→			Phase 2/3 Trial
iPSC Regenerative Medicine	HLCR011	Wet AMD	Japan	→	⇢ Transplantation conducted under Clinical research(*1)					Start of clinical studies originally scheduled in 2017 may be delayed
	HLCL041	Metabolic Liver Disease	Japan	→						Joint research with Yokohama City University
	HLCR012	Dry AMD	US	→						Technical transfer
	HLCR012	Dry AMD	EU	→						Global Trial Under Consideration based on US Phase III Trial

* 1 “Clinical research of transplantation of induced pluripotent stem cells – derived retinal pigment epithelium (RPE) cells for exudative age-related macular degeneration (AMD)” conducted by RIKEN etc.

Compound drug pipeline (HLM021, HLM022, HLM023): Business transfer completed on April 30, 2017

HLCM051: Clinical trial status

Somatic stem cell regenerative medicine

HLCM051
MultiStem®

"Placebo-Controlled, Double-Blind, Phase 2/3 Efficacy and Safety Trial of HLCM051 (MultiStem®) in Patients With Ischemic Stroke"
(**TREASURE study)**

▲Problems at the manufacturing contractor in the United States
▲Patient enrollment had been temporarily suspended due to the deviation of placebo

The first patient was enrolled on November 15, 2017.
Enrollment continues to make good progress.
It will take about 2 years for the inclusion of subjects as originally estimated.

Clinical trial
（Subjects　220）
（In total, over 35 clinical sites will be expected to conduct TREASURE study)

Prepa ration

Apply

Approval/ Sales

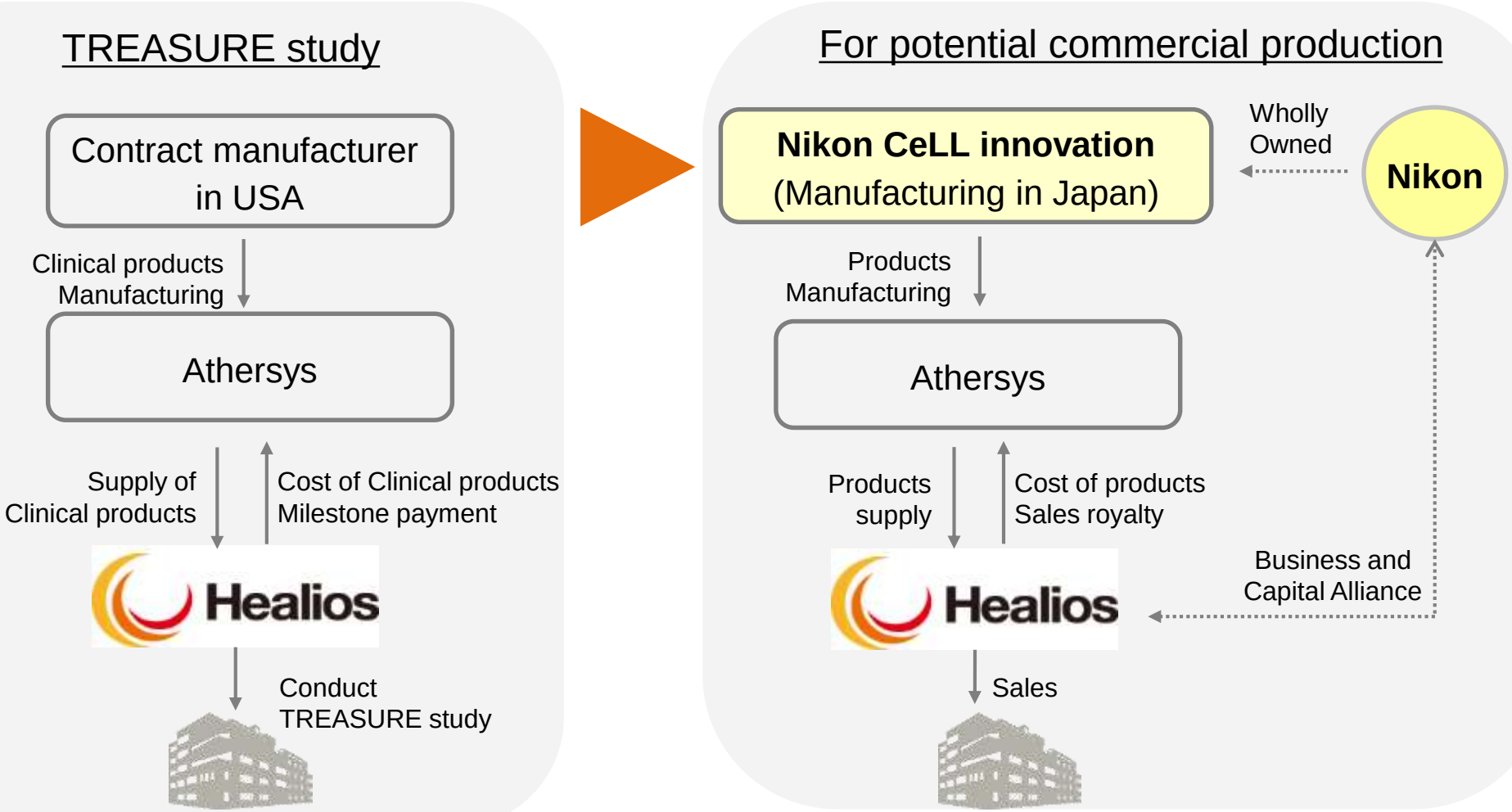
First Patients enrolled
Nov 2017

TREASURE study completion: within FY2020
Note: This includes 1 year follow up, but primary endpoint assessment will occur at 3 months after last subject enrolled

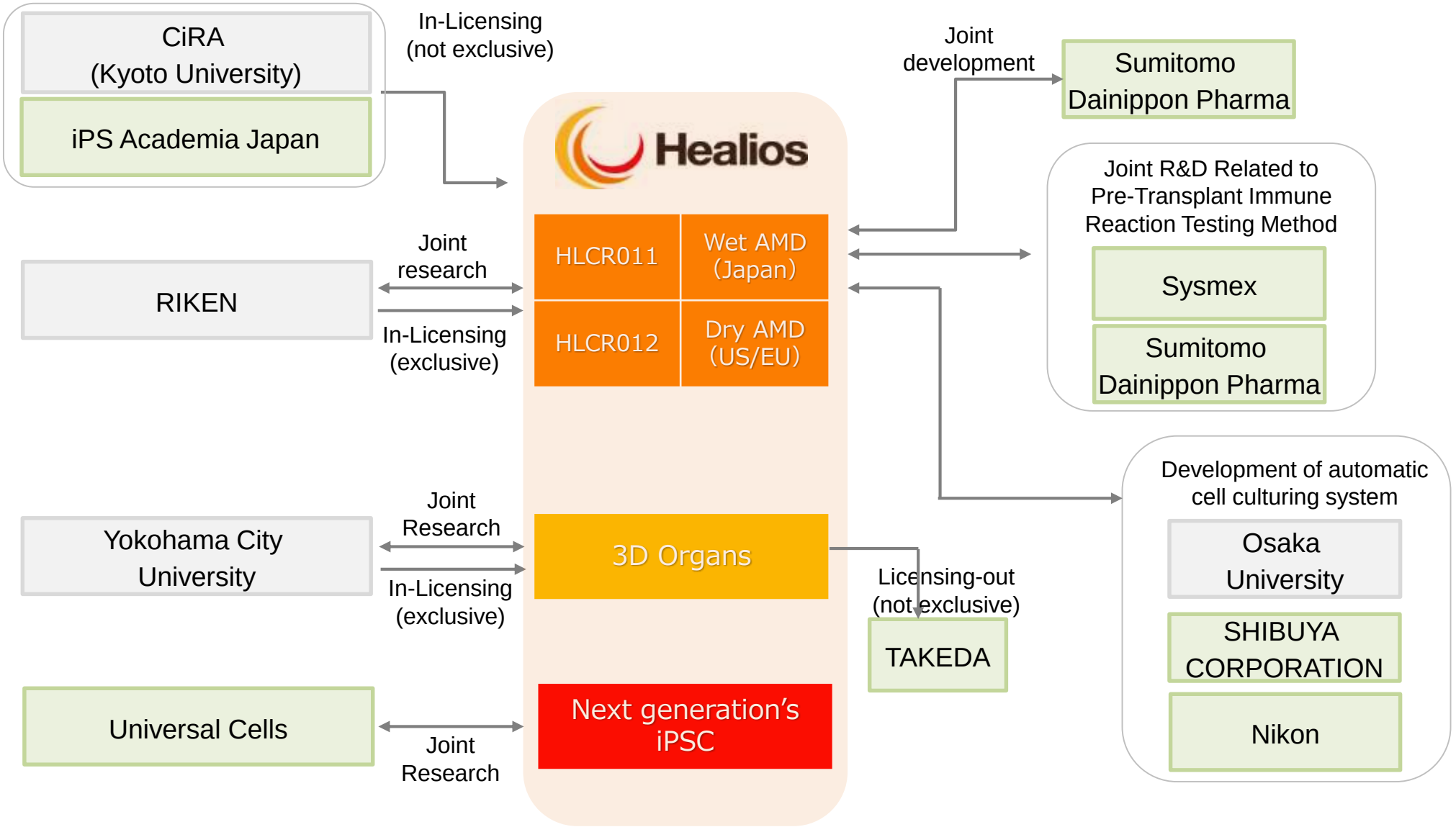
The approval period may be shortened from 12 months to 6 months by the SAKIGAKE Designation System

HLCM051: Business Partners

In October 2017, Nikon CeLL innovation executed a manufacturing service agreement with Athersys in preparation for the commercialization of HLCM051



iPSC Regenerative Medicine field: Business Partners



Status of clinical research by RIKEN etc.

iPSC Regenerative medicine

RPEs in Japan

"Clinical research of transplantation of allogeneic induced pluripotent stem cells – derived retinal pigment epithelium (RPE) cells for exudative age-related macular degeneration (AMD)"

March 2017:
Operation on first subject in clinical research using Allogeneic iPSC-derived RPE cell suspension.
November 2017:
Operations using Allogeneic iPSC-derived RPE cell suspension completed on 5 subjects. Continuing follow-up observation for one year.

January 2018:
In one case an epiretinal membrane, deemed to be one of causes of retinal edema, was removed to improve symptoms during the clinical research.

Dr. Takahashi from RIKEN explained that "The adverse effect was not imminent or urgent in nature. This event will not have any impact to our clinical studies in the future."

	Sheet	Suspension
Autologous cells	Operation on 1 subject (in 2014)	To be determined.
Allogeneic cells	To be determined	Operations on 5 subjects (in 2017)

(Sources) Created by Healios
from the data at a press conference by RIKEN

Published in Cell Reports

iPSC Regenerative medicine

Organ bud

Results on the method of producing ultra-large amounts of human mini-liver from iPS cells, which Dr. Takebe and Dr. Taniguchi from Yokohama City University succeeded to develop under the industry-academia collaboration system (Healios also in cooperation), were published in *Cell Reports*.

Cell Reports (2017)
https://doi.org/10.1016/j.celrep.2017.11.005

“Massive and Reproducible Production of Liver Buds Entirely from Human Pluripotent Stem Cells”

▶Succeeded in producing all three kinds of cells necessary for mini-liver production from HLA homo donor iPS cells (for research).
▶ With the development of a special culture plate, it became possible to produce miniaturized high-quality mini-livers.
▶ Scale up to 100 times or more became possible.

(Source）https://www.yokohama-cu.ac.jp/amedrc/news/20171204Takebe.html

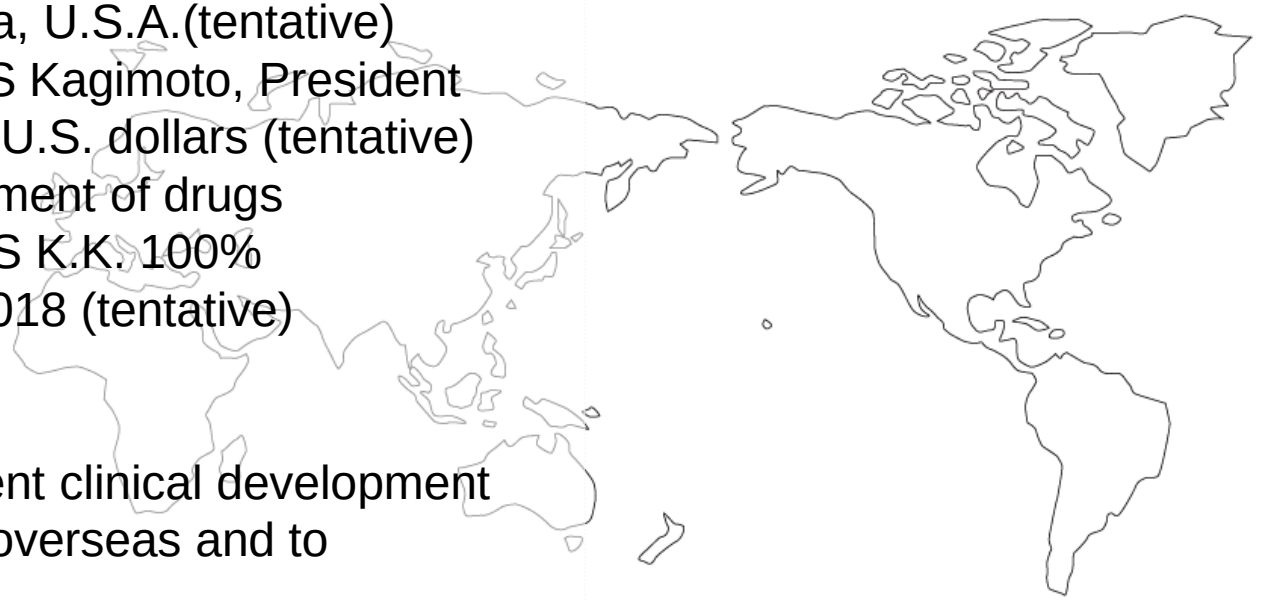
Photo (source) Takebe,T., et al. Nature Protocols, 9, 396–409 (2014)

3. New Steps for Further Business Development

Establishment of New Subsidiary in the US

On February 13, 2018, Healios decided to establish a subsidiary in the US.

Name	Healios N.A. Inc.,
Location	California, U.S.A.(tentative)
Representative	Hardy TS Kagimoto, President
Capital	150,000 U.S. dollars (tentative)
Business	Development of drugs
Ownership	HEALIOS K.K. 100%
Establishment	March 2018 (tentative)



Healios intends to implement clinical development not only in Japan but also overseas and to strengthen alliances.

Strategic Investment in GAIA BioMedicine

On February 13, 2018, Healios decided to make a strategic investment in GAIA BioMedicine

GAIA BioMedicine, Inc.

A company engaged in the development of immune cell therapies for cancers and other regenerative medicine with its technologies that enable highly pure and efficient expansive cultivation of natural killer (NK) cells* having strong antitumor activity, based on the study results of Professor Yoshikazu Yonemitsu, MD, PhD, FAHA, of Pharmaceutical Sciences, Kyushu University, who is the founder of GAIA BioMedicine.

※Natural killer (NK) cells
Natural killer (NK) cells are a subset of lymphocytes (a type of white blood cell). NK cells play a central role in a cell mediated defense system that human bodies naturally have, and attack cancer cells and virus-infected cells. The expected efficacy of treatments using NK cells includes life-extending effectiveness, relief of symptoms, improvement of the quality of life, and the promotion of healing.

Healios seeks to promote a strategic partnership

4. Details of Somatic Stem Cell Regenerative Medicine

Introduced new pipeline: HLCM051 in January 2016

Athersys inc.

（Source）Athersys

- Cell therapy product based on patented technology
- Developing for “off-the-shelf” administration: no tissue matching needed
- Long shelf life: can be kept frozen in a stable condition for years
- Consistent safety profile
- Promotes healing and tissue repair through multiple mechanisms of action
- Not a permanent transplant: cells cleared from the body over time

Outline of ischemic stroke in Japan

Ischemic stroke

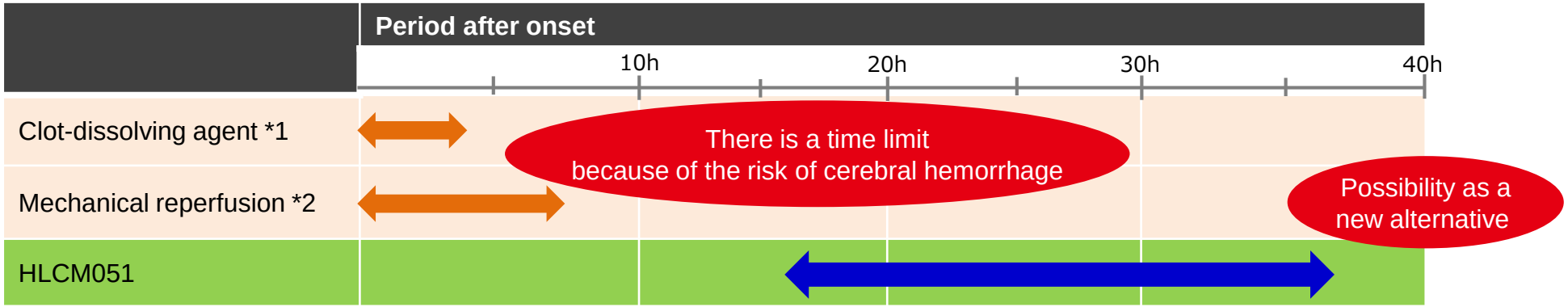
Ischemic stroke, which represents the most common form of stroke (70–75% of cases in Japan), is caused by a blockage of blood flow in the brain that cuts off the supply of oxygen and nutrients, resulting in tissue loss.

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.

（Source）Athersys

Treatment in accordance with the period after onset

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



*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.

Annual number of new patients with ischemic stroke in Japan

Target population

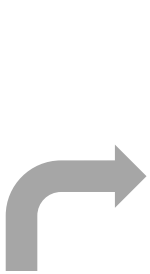
	Japan	Note
Number of patients (yearly)	**230,000 – 330,000**	Annual medical costs for ischemic stroke estimated at 1,070.7 billion yen（2009）
Severe patients（atherothrombotic and cardiogenic cerebral infarction)	**130,000**	
patients within 36 h after onset	**62,000**	

(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.

(Note) Calculated using 2013 and 2014 fiscal year-end exchange rates.

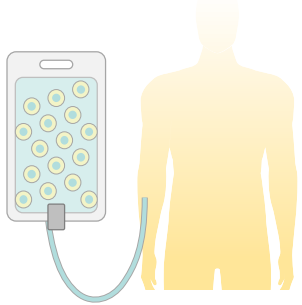
Mechanism of HLCM051 treatment

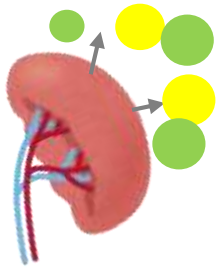
- Following intravenous administration after acute neurological injury, HLCM051 distributes to spleen, downregulating hyperinflammatory response.
- HLCM051 promotes the neuroprotective effect by releasing various cytokines and growth factors.



Stroke-induced neuronal damage (Primary)

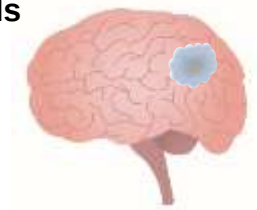
With HLCM051



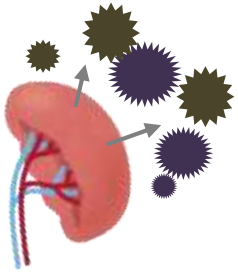


HLCM051
- **Suppress the mobilization/ release of inflammatory cells (lymphocytes, cytokines)**
- **Activate the mobilization/ release of anti-inflammatory cells**

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



Without HLCM051



Mobilization / release of inflammatory cells (lymphocytes, cytokines) in the spleen is activated

Exacerbate neuronal damage caused by inflammatory chemokines/ cytokines (Secondary)

Inflammatory cells are released from the spleen and exacerbate the neuronal damage of the ischemic site.

HLCM051 Clinical trial

Somatic stem cell regenerative medicine

HLCM051
MultiStem®

“Placebo-Controlled, Double-Blind, Phase 2/3 Efficacy and Safety Trial of HLCM051 (MultiStem®) in Patients With Ischemic Stroke”

Study Design

Subjects: Patients with onset of ischemic stroke within 18 to 36 hours prior to the start of the administration of the investigational product.

Enrollment: 220 (HLCM051 group [n=110], or placebo group [n=110], randomized)

Number of Clinical trial sites: Plan to conduct at over 35 sites.

Primary Endpoint: Proportion of subjects with an excellent outcome defined by the functional assessments on Day 90.

*Excellent Outcome

“Excellent Outcome” is defined as achieving mRs ≤1, NIHSS ≤1, and BI ≥95 in mRS, NIHSS, and BI, the three major indices of functional assessments for stroke patients.

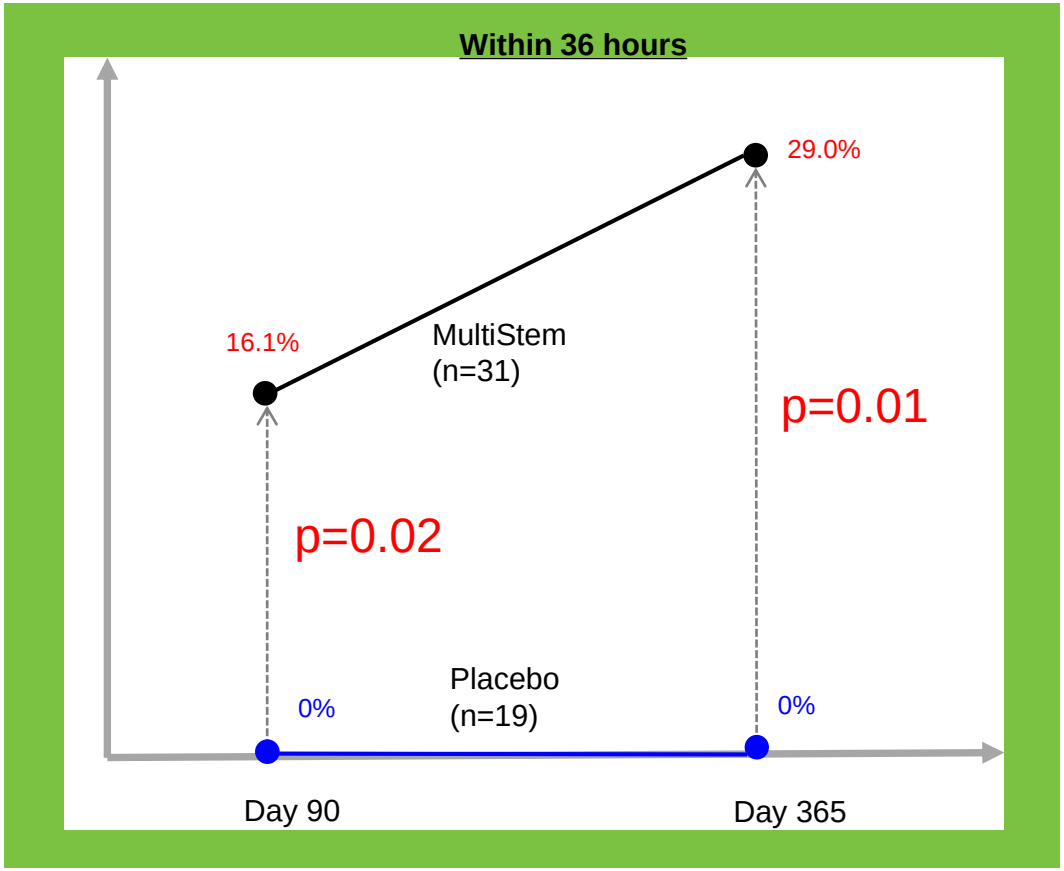
(Source) Image: prepared by Healios based on the materials provided by Athersys

Study Design Based on the Result of the Phase II Study by Athersys in Europe and America

Somatic stem cell regenerative medicine

HLCM051
MultiStem®

The proportion of patients who achieved Excellent Outcome was statistically significant (compared with the placebo group) both at Day 90 and Day 365 in the group of patients who received MultiStem within 36 hours of the onset of cerebral infarction.



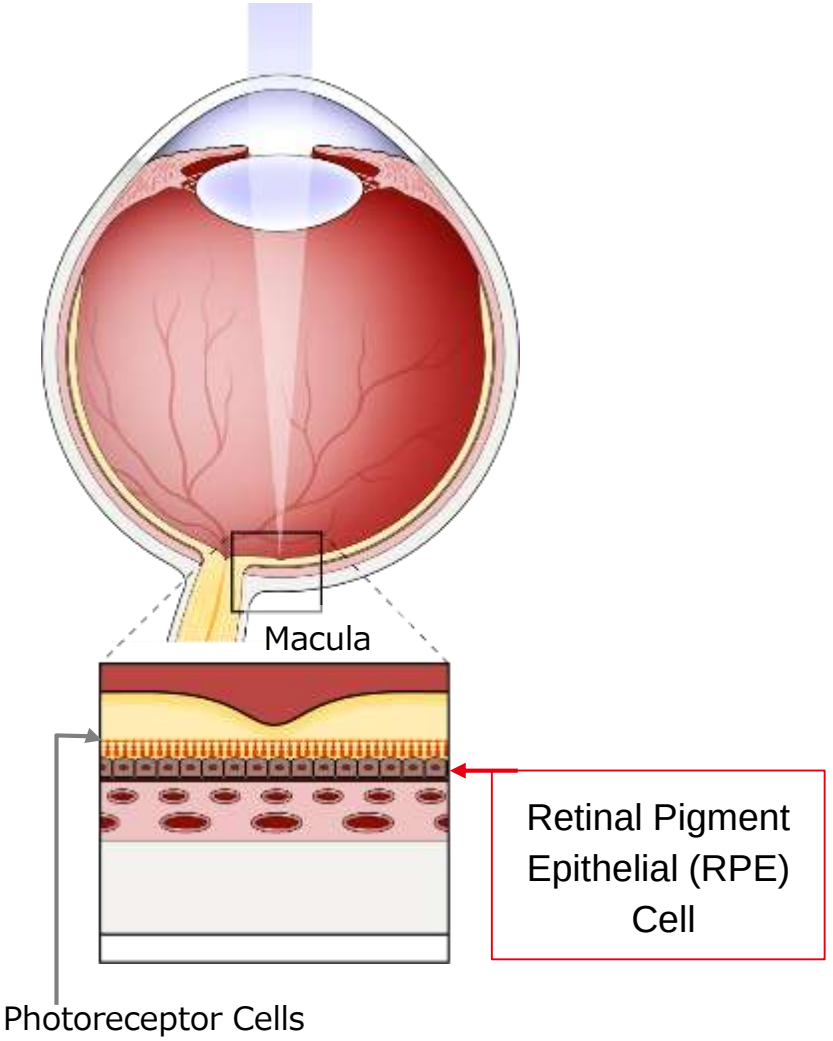
(Source) Prepared by Healios based on the data provided by Athersys.

(Note) Excellent outcome = All of the following: mRS ≤ 1, NIHSS ≤ 1, and BI ≥ 95)

5. Details of iPSC Regenerative Medicine

Explanation of AMD pathological condition

AMD causes RPE Cells to degenerate, which damages function.



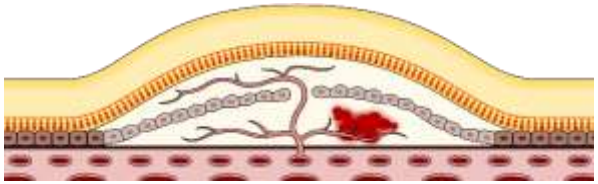
Regular Macular Part

Developed Dry AMD

Immunity Barrier Maintained
→ Degeneration of photoreceptor→ Dry AMD

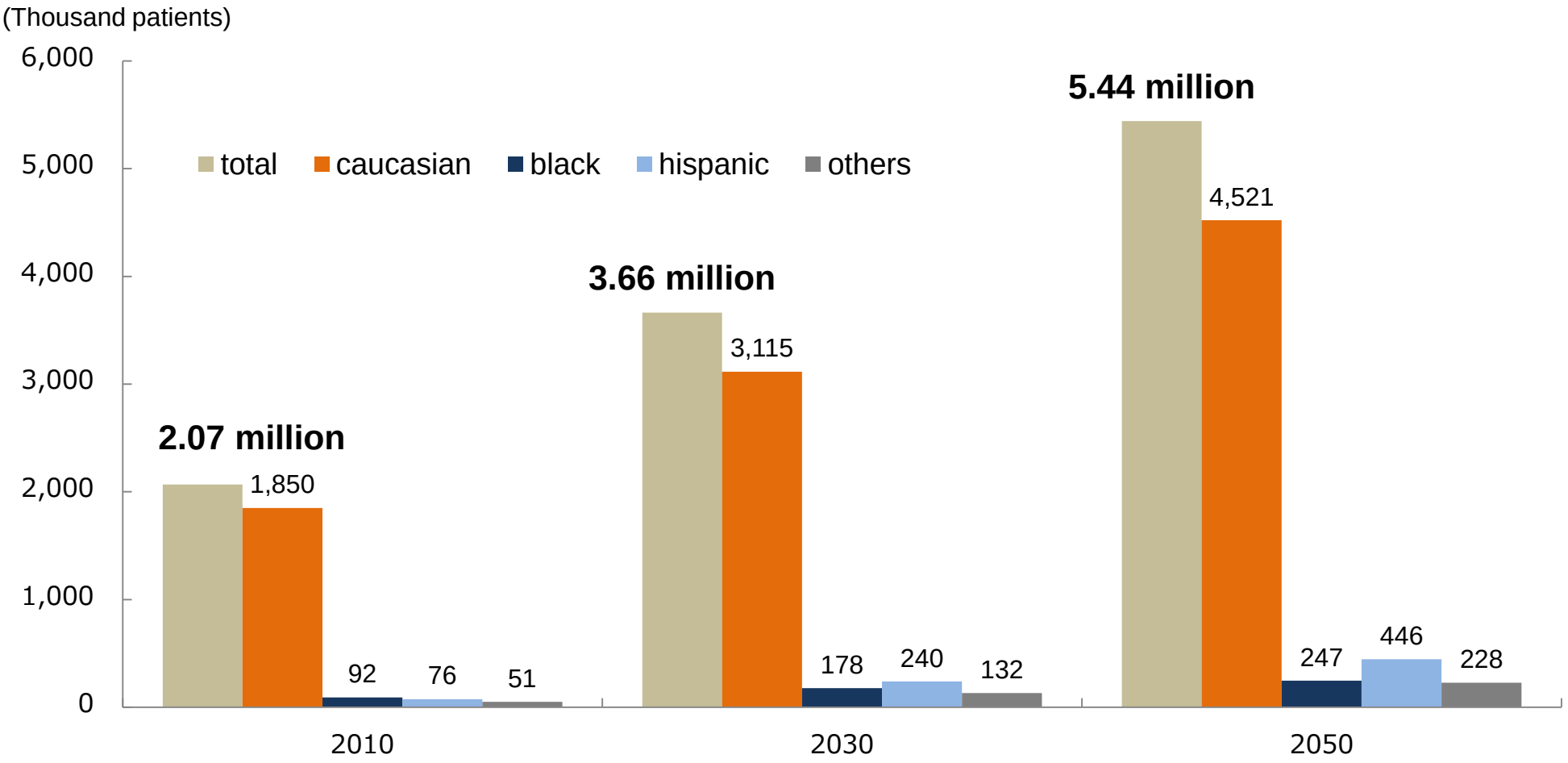
Wet AMD

Destruction of Immunity Barrier → Invasion of Immune Cells
→ Inflammation → Wet AMD



Estimated number of future serious case AMD patients in the US

Expected to increase over medium- to long-term as society ages



(source) National Eye Institute

Number of AMD patients

Number of both Wet and Dry patients (including mild cases)

（Thousand patients）

	America	Japan	Others
Number of AMD Patients	**10,000**	**9,230**	**13,000**
Number of AMD Patients in Serious Cases	**2,000**	**690**	**2,600-3,220**
Wet-patients in serious cases	**1,000-1,500**	**630**	**1,300-1,950**
Dry-patients in serious cases	**850-900**	**60**	**1,100-1,170**

※According to research by Hisayama Kyushu University Graduate School of Medicine in Fukuoka (based on a comprehensive study), the total number of patients in Japan is calculated, estimating the total number of first-stage age-related macular degeneration and latter stage of age-related macular degeneration based on population statistics (2007). Also, the Disease Information Center announced that the number of patients suffering serious cases is approximately 690,000. The total number of patients in the US, which the National Eye Institute reports, includes the total number of age-related macular degeneration patients in mild cases and patients with visual field defects. Also, our company calculated the total number of Dry/Wet patients based on the incidence rates presented by AMDF (2010). Our company calculated the total number of patients in Europe based on incidence rates in each grade of European population statistics （2010)

※source: Prevalence of age-related maculopathy in older Europeans: the European Eye Study (EUREYE).Source: Arch Ophthalmol. 2006 Apr;124(4):529-35

Market scale of AMD

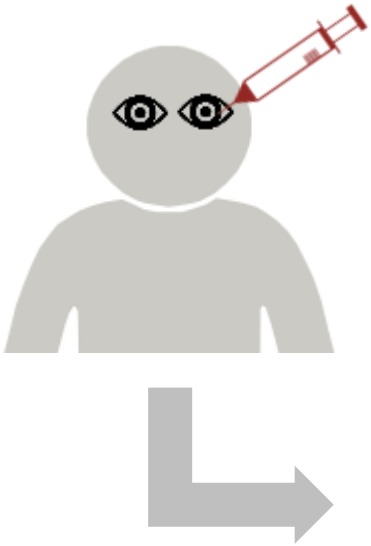
Annual sales of medicinal treatments of Wet AMD: 8.44 billion USD.
No medicine for Dry AMD.

Condition	Medicine / Effect	Year	America	Japan	Others	Total
Wet	Anti-VEGF Medicine/ Restraint of New Blood Vessels	2016	**4,729 million USD**	**580 million USD**	**3,127 million USD**	**8,436 million USD**
Dry			**No Medicine**			

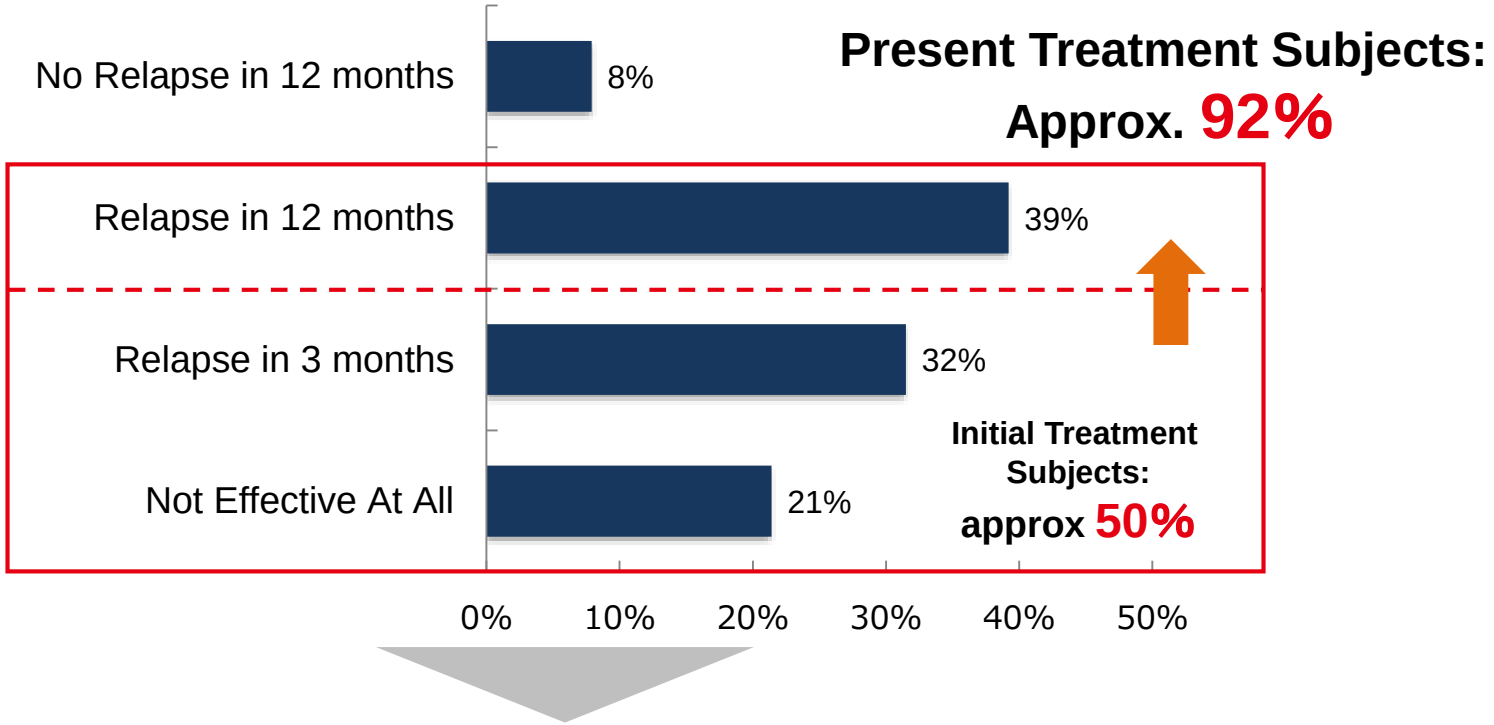
(source) Market scale was calculated using official materials from drug companies (Roche Diagnostic, Novartis, Regeneron, Bayer HealthCare, Santen Pharmaceutical Co., Ltd). Calculated using 2016 fiscal year-average exchange rates.

Treatment subjects for Wet AMD

Patients recurring within 1 year, which is the case for approx. 92% of Wet AMD Patients, are the candidates for treatment.



Recurrence frequency after receiving anti-VEGF medication



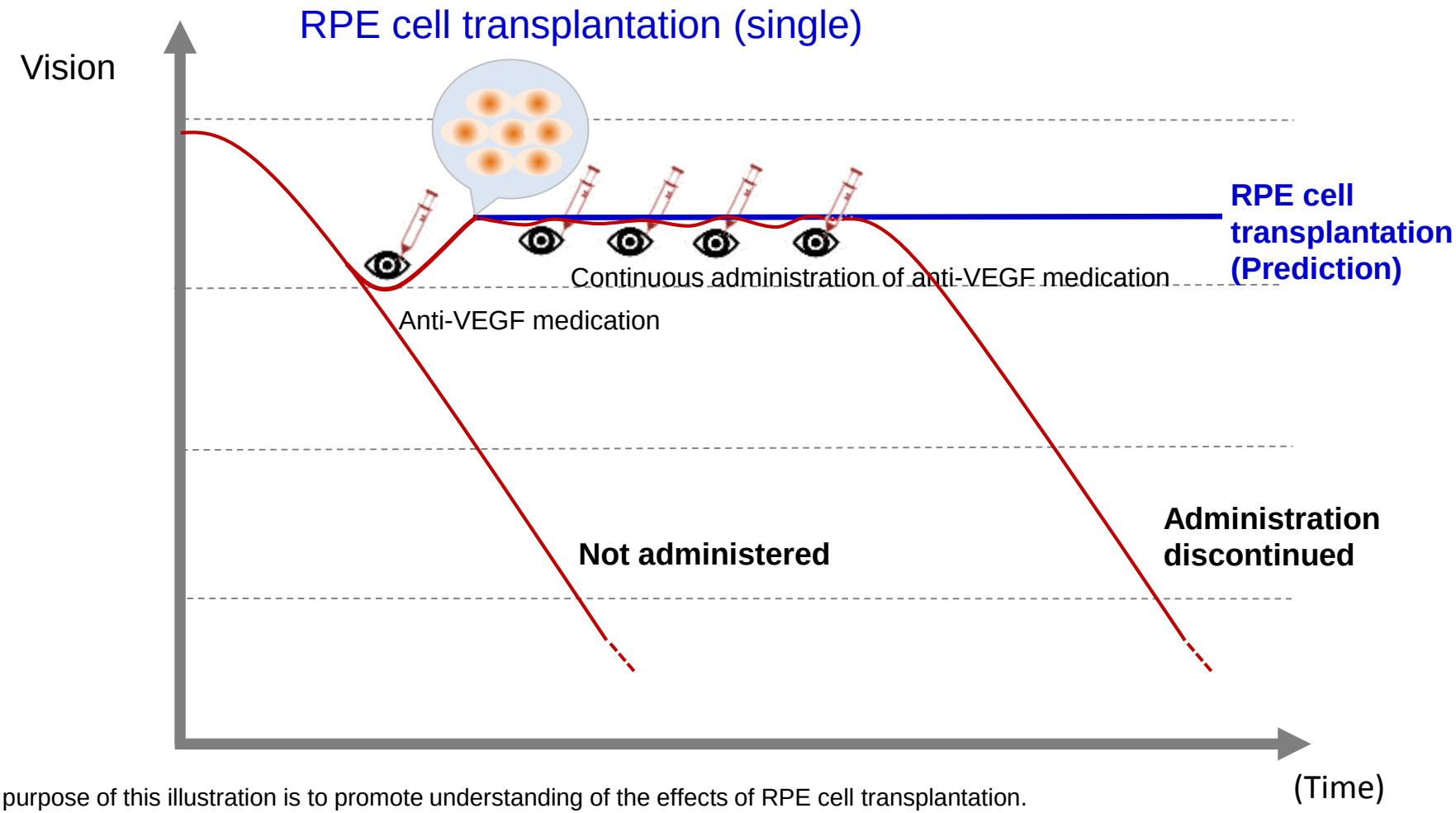
Present Treatment Subjects:
Approx. 92%

Initial Treatment Subjects:
approx 50%

QOL of continuously medicated patients is not high.

(source) 13th Annual Meeting of The Japanese Society for Regenerative Medicine March 19th 2014, Thurs, 12:00～12:50
Approach to Clinical Application of iPS cells Institute of Physical and Chemical Research, Mandai Michiko

Good vision can be maintained with early treatment



* The purpose of this illustration is to promote understanding of the effects of RPE cell transplantation.
Changes in vision with the administration of anti-VEGF medication vary according to patient symptoms and administration frequency.

Guide to medicine price – Approach based on the cost of existing treatment

Anti-VEGF medicine mostly continues from the beginning of treatment until death

Annual Medical Expense

Unit Price of Anti-VEGF **170,000 yen** ✖ Annual Recommended Medication Protocol **6 Times** = Annual Medical Expense **1,020,000 yen**

Estimate of Lifetime Medical Expense

On the Assumption of Average Life Span (Japan): 80years old (Male) / 86 years old (female)

			Estimate of Lifetime Medical Expense
Continuous Treatment for **50-year old Patient Onset** ＝approx. **30years**	✖ **1.02 million yen**	=	**Approx. 30 million yen**
60-year old Patient Onset＝approx. **20years**	✖ **1.02 million yen**	=	**Approx. 20 million yen**

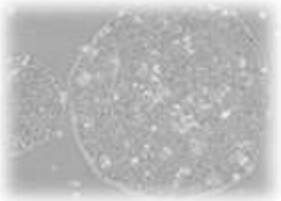
(source) Onset Data: National Eye Institute; Average Life Span: The Ministry of Health, Labor and Welfare; Annual Recommended Medication Protocol: Materials Presented by Institute of Physical and Chemical Research

6. Expansion to 3D Organs (Liver)

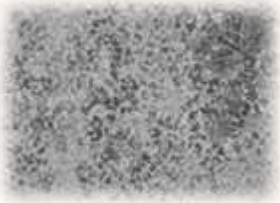
3D organ generation mechanism

Generating “Organ bud” by co-culturing 3 types of cells

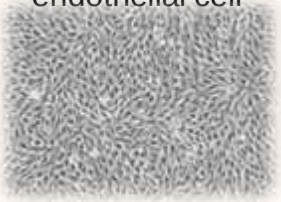
Human iPS cell



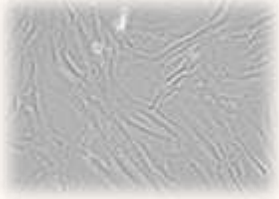
Precursor cell



Vascular endothelial cell



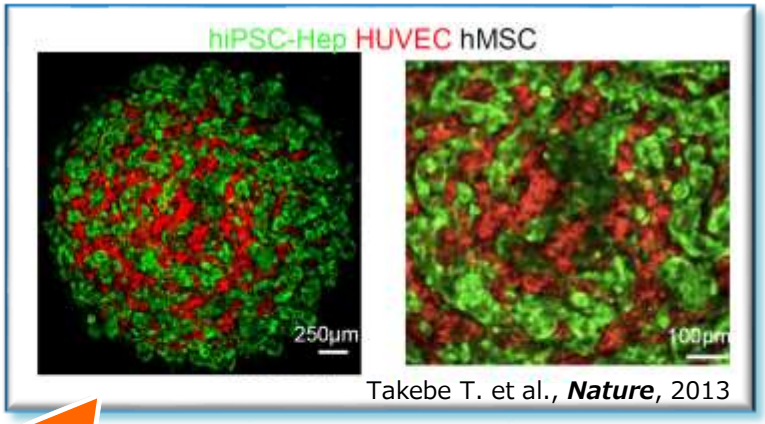
MSC



Organ bud*

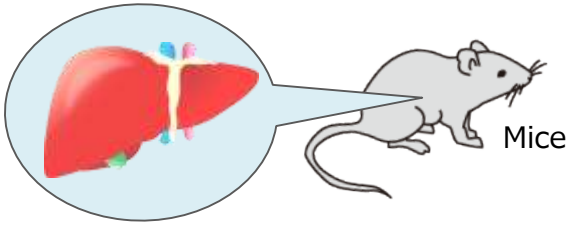
Organ bud=
Origin of organ

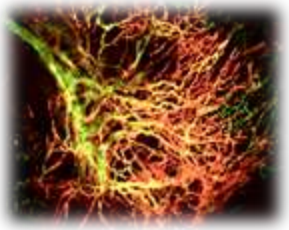
“Elplasia” from Kuraray Co., Ltd.
(http://www.elplasia.com/products/round_bottom/)



Takebe T. et al., ***Nature***, 2013

Cell Transplantation





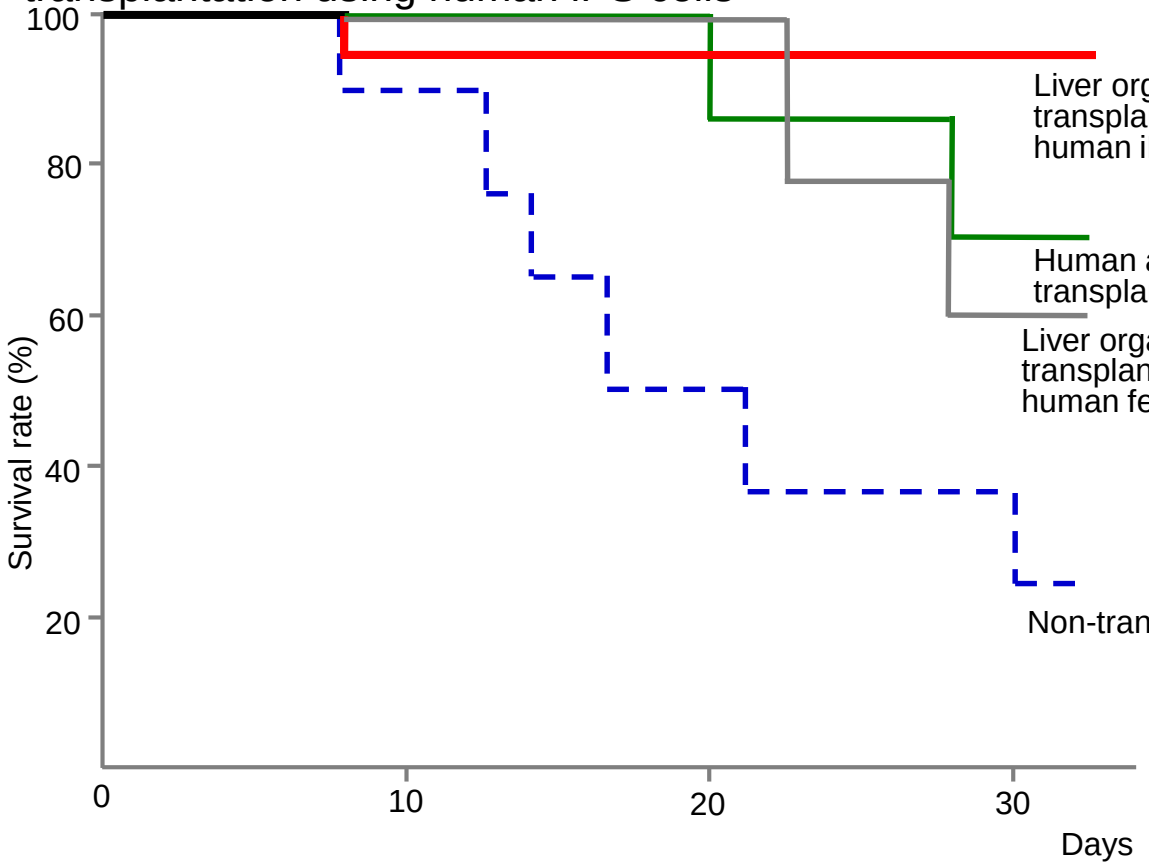
Containing blood vessels and human liver

Takebe T. et al., ***Nature Protocols***, 2014

Survival rate of liver failure model mouse

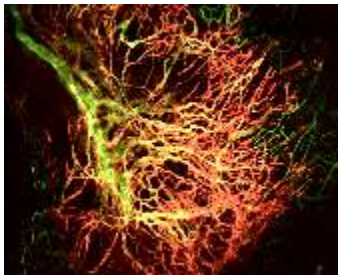
Survival rate improves significantly in transplantation experiments

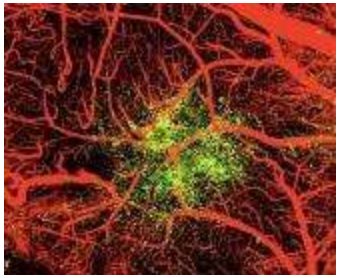
Treatment effects of liver organ bud transplantation using human iPS cells



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

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)

Yokohama City University planning to start clinical study in 2019

Urea cycle defect

Disease caused by congenital abnormality of enzyme functioning in metabolic pathway (urea cycle), which detoxifies ammonia in the liver and produces urea. Presently, the only definitive treatment available is liver transplantation.

* Even patients with minor conditions require treatment combining food treatment and medication to lower ammonia levels throughout their lives.

Estimated market size of metabolic liver disease in newborns

	US	Japan	Europe	Total
Number of patients (yearly)	**Approx. 160**	**Approx. 30**	**Approx. 230**	**Approx. 420**
Treatment costs (annual) Enzyme replacement therapy	**30 million yen – 50 million yen**			
Estimated annual market scale	**5 - 8 billion yen**	**1 - 1.5 billion yen**	**6 - 11.5 billion yen**	**12 - 21 billion yen**

∗ Number of patients and market size are estimated by Healios based on number of newborns and incidence rate.

Expansion of Marketability
(Alternative Treatment for Replacing Liver transplantation)

Prospecting R&D for alternative treatment for liver transplantation

	Liver transplantation			Total
	US	Japan	Europe	
Number of patients undergoing treatment (Annual)	**Approx. 6,000**	**Approx. 400**	**Approx. 4,000**	**Approx. 10,000**
Number of patients on waiting list (Annual)	**Approx. 15,000**	**Approx. 400**	**Approx. 4,000**	**Approx. 20,000**

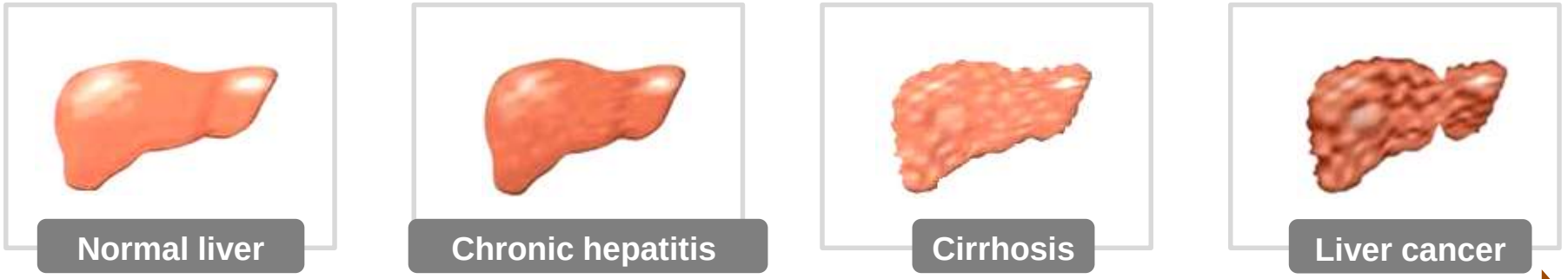
（Source） Compiled by Healios based on materials disclosed by Japanese Liver Transplantation Society, UNOS, Eurotransplan, UK Transplant, Agence de la biomédecine, and Scandia Transplant.

Liver disease drawing attention in future is cirrhosis

Estimated patients with cirrhosis in Japan: 400,000 to 500,000. About 56,000 receive treatment at medical facilities.
Annual deaths in Japan: 17,000 patients.

（Source） Patient Survey 2011 Liver Cancer White Paper 2015

Progress of liver disease



7. Company Overview

Healios Overview

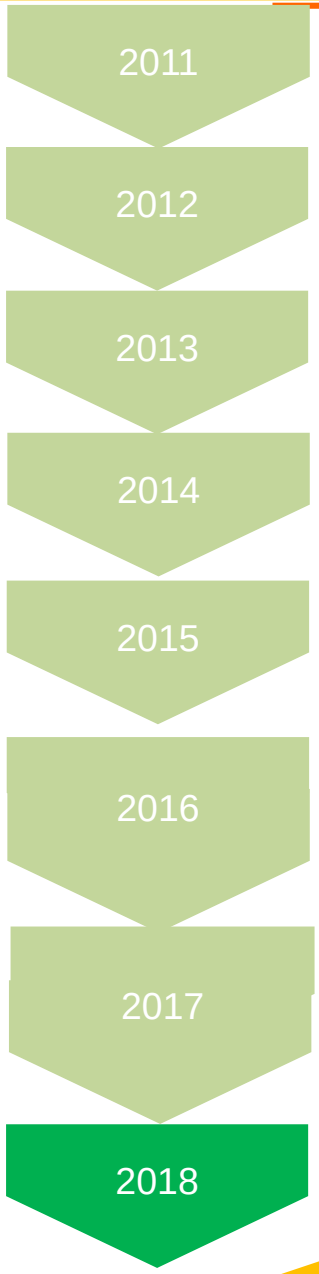
About Us

Company Name	HEALIOS K.K.（TSE: 4593）
Representative	 Hardy TS Kagimoto, MD President and CEO ■ Succeeded in Developing BBG250 and Realized Sales in Europe
Head Office	World Trade Center Building 15F 2-4-1 Hamamatsucho Minato-ku, Tokyo Japan 105-6115
Paid in Capital	11,353 million yen (As of end of December, 2017)
Number of Employees	74 (As of end of December, 2017)
Research Institution	Kobe and Yokohama
Affiliated Company	SighRegen Co., Ltd. (Joint Venture with Sumitomo Dainippon Pharma Co., Ltd.)

Our Experienced Team

Senior Managing Director CMO	Masanori Sawada, MD, PhD, MBA	■ Osaka University Invited Associate Professor
Managing Director	Yoshinari Matsuda	■ Attorney-at-Law ■ Led the alliance negotiations
Director of overseas development	Al Reaves, PhD	■ Responsible for innovative clinical programs for wet & dry AMD - Lucentis (X-US); Visudyne (global)
Director of Laboratories in Kobe, Research and Manufacturing	Kouichi Tamura, PhD	■ Astellas US Director of Laboratories ■ Well-acquainted with Immunosuppressant Research
Director of Domestic Development	Michihisa Nishiyama	■ Constructed network for Tacrolimus approval and sales at Astellas in the US and Europe
Director of Administrative field	Ken Ishikawa	■ Striving to strengthen organizational capabilities

Company History and Societal Trends



2011

Retina Institute Japan established (currently Healios)

◆ **Certified as RIKEN Venture**

2012

Prof. Shinya Yamanaka wins Nobel Prize in Physiology or Medicine

2013

Act on the Safety of Regenerative Medicine, Pharmaceutical and Medical Device Act established

◆ **Patent licensing agreement with RIKEN**

◆ **Joint development agreement with Sumitomo Dainippon Pharma**

2014

RIKEN Conducts 1st transplantation surgery in world's first clinical study using iPS cells

■ **Joint research on organ bud with Yokohama City University**

2015

RIKEN announces good follow-up results 1 year after administration in clinical study

✓ **Listed on MOTHERS**

2016

● **HLCM051 Patent licensing agreement with Athersys**

■ **Collaborative research agreement with Universal Cells**

2017

RIKEN Conducts 1st transplantation surgery in world's first clinical study using allogeneic iPS cells

✓ **Business and capital alliance agreement with Nikon**

✓ **BBG business transfer**

● **HLCM051 First patient In**

2018

✓ **Healios N.A**

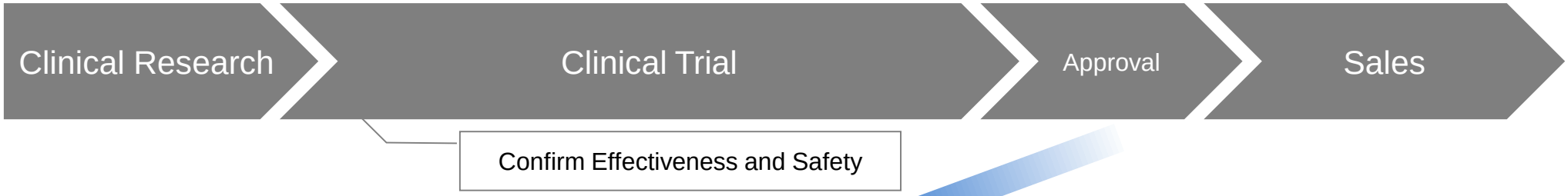
■ **Strategic investment in GAIA BioMedicine**

8. Circumstances of Regenerative Medicine

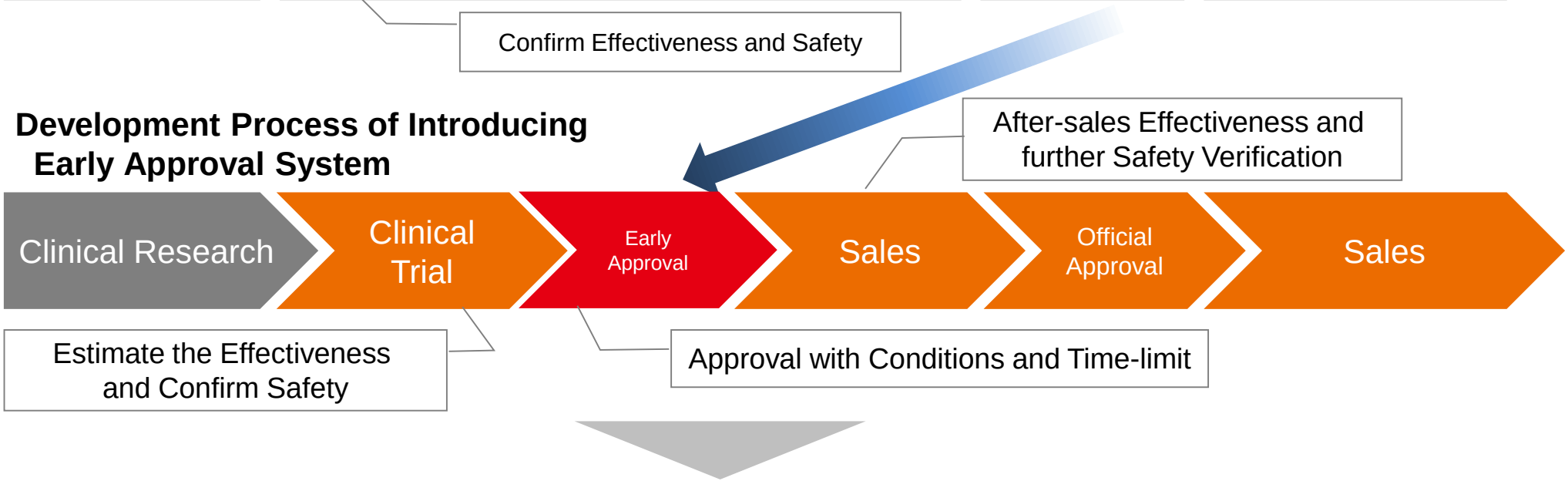
Historical Alleviation of Regulations

Japanese Government Revises Regulations to Put Japan at the Forefront

Process of the Development So Far



Development Process of Introducing Early Approval System



- Drastic reduction in the treatment period and number of patients with ‘Early Approval System’ .
- Insurance is listed at ‘Early Approval’ stage.

Rapid impact of modified regulations

Approval of regenerative medicine products, September 2015

Product Name	Temcell® HS Injection	Heart Sheet
Company	JCR Pharmaceuticals	Terumo
Indications	Acute GVHD after hematopoietic stem cell transplantation	Severe heart failure due to ischemic heart disease
Price	13.9 million yen	14.76 million yen
Important Point	First allogeneic cell-based regenerative product	First conditional approval

(note) Calculated using 2013 and 2014 fiscal year-end exchange rates.

Price calculation method prospects

Cost accounting system

* The price of new drugs is basically calculated according to the prices of official articles with similar efficacy (price determination by comparable drug). However, if there are no appropriate similar official articles, required costs are added in the calculation of prices (cost accounting system).

Descriptions of future events, etc. in this document include Healios' assumptions, prospects, etc. based on information which could be acquired at the time this document was presented. For this reason, actual performance, development progress, etc. may differ from those described in this document according to the outcome of R&D in the future, the actions of regulatory authorities, etc. in the future, and uncertain/pending factors as of this point.

Also, this document contains information on regenerative medicine and medical equipment that are currently under development or already on the market. Such information is not intended for promoting advertising or providing medical advice.

Healios

＜Contact information＞
Corporate Communication Group
Personnel and Administration Department
HEALIOS K.K.

Phone: +81-(0)3-5777-8308
Press contact: pr@healios.jp
Investor contact: ir@healios.jp