

Healios

“To be the change in an ever evolving world
through enrichment of living”

FY2016 2Q Financial Results

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1. Financial Highlights

Statement of income

(Million yen)

	FY 2015 2Q	FY 2016 2Q		
			YoY change	Reasons for increase/decrease
Sales	59	41	▲18	
Operating income	▲513	▲2,602	▲2,089	Research & Development Cost ▲2,030
Ordinary income	▲418	▲2,647	▲2,229	-
Net income	▲417	▲2,650	▲2,233	-
R&D	292	2,322	+2,030	Multistem License-in +1,809
Amortization of goodwill	50	50	–	-
Number of employees	42	52	+10	-

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Balance sheet

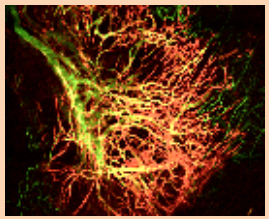
(Million yen / %)

	December 31,2015	June 30, 2016		
			Change	Main reasons for increase/decrease
Current assets	9,325 (88.9%)	9,271 (89.2%)	▲54	
Non-current assets	1,162 (11.1%)	1,123 (10.8%)	▲38	
Total assets	10,487 (100.0%)	10,395 (100.0%)	▲92	
Current liabilities	1,080 (10.3%)	1,130 (10.9%)	+50	
Non-current liabilities	29 (0.3%)	2,532 (24.4%)	+2,503	Long-term debt +2,500
Total liabilities	1,110 (10.6%)	3,663 (35.2%)	+2,552	
Total equity	9,377 (89.4%)	6,731 (64.8%)	▲2,645	Earned surplus ▲2,650
Total assets	10,487 (100.0%)	10,395 (100.0%)	▲92	

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2. FY2016 2Q Updates

Highlights：FY2016 2Q Updates

Somatic stem cell regenerative medicine	MultiStem®		- Advancement of preparation toward the start of a clinical study from the second half of this fiscal year after consulting with PMDA - Consideration of construction of the sales system with alliance
iPSC Regenerative medicine	RPEs in Japan		- Optimization for manufacturing process with Sumitomo Dainippon Pharma - Start of Clinical studies originally scheduled in 2017 may be delayed due to changes in pre-clinical study plans. - A new clinical research will be started by RIKEN in the near future that includes “Allogeneic×Suspension” RPE cells. - Joint R&D related to pre-transplant immune reaction testing method
	RPEs overseas		- Optimization of process development is underway at the contract manufacturer
	3D organs (Liver)		- Promotion of collaborative research with Yokohama City University. - Consideration of reagents that comply with Japanese Standards for Biological Ingredients in a case of manufacturing a liver bud
Compounds	BBG		- Advancement towards GMP production at the contract manufacturers of the drug substance/product - Results of a Phase III investigator initiated trial were published in an academic journal

2

Collaborative research agreement with Universal Cells

Research for “next-generation iPS cell” that causes no immunorejection will start

1

3

(Note) RPE: retinal pigment epithelium

(Sources) MultiStem images = Created by Healios from the images provided by Athersys
“3D organs” image = Takebe,T., et al. Nature Protocols, 9, 396–409 (2014)

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Collaborative research agreement with Universal Cells, Inc. in June 2016

1

iPSC Regenerative medicine

- RPEs in Japan
- RPEs Overseas
- 3D organs (Liver)

Healios entered a collaborative research and exclusive option agreement with Universal Cells, Inc. regarding application of their genome editing technology to process iPS cells. With this technology, expression of HLA (cell surface molecules that identify self and nonself) can be controlled, and pluripotent cells can be manufactured to avoid transplant rejection.

The exclusive option for various indications
The cell line developed under this agreement will be proprietary to Healios

About Universal Cells

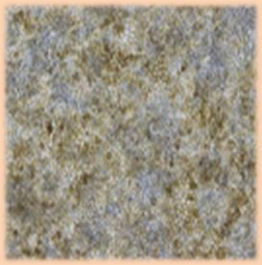
Universal Cells is a private biotechnology company developing proprietary nuclease-free genome editing technologies that allow efficient and accurate editing of any gene without cutting the genome.
For more information: http://www.universalcells.com

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Announcement of a new clinical research by RIKEN in June, 2016

iPSC Regenerative medicine

RPEs in Japan



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

2

Outline of the research plan

In the previous clinical research started from 2013, retinal pigment epithelial (RPE) sheets differentiated from a patient derived (autologous) iPS cells were used for transplantation.
In the new clinical research, not only limited to the method with autologous cells/ RPE sheets, but use of allogeneic cells or transplantation with RPE suspension are also planned.

		Sheet	Suspension
		High-risk surgery	Low-risk surgery
Autologous cells	High manufacturing cost	A few cases are planned to be operated.	A few cases are planned to be operated.
Allogeneic cells	Low manufacturing cost	A few cases are planned to be operated.	A few cases are planned to be operated.

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

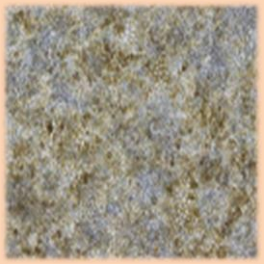
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Joint R&D Related to Pre-Transplant Immune Reaction Testing Method in June 2016

2

iPSC Regenerative medicine

RPEs in Japan



-Joint R&D to develop a new testing method to confirm prior to transplantation whether cells are suitable for transplant, including the possibility to cause immunorejection.

sysmex × Healios × Sumitomo Dainippon Pharma

Details of Joint R&D

Healios and Sumitomo Dainippon Pharma will provide Sysmex with RPE cells they have produced from allogeneic iPS cells, and Sysmex will use its proprietary imaging flow cytometers and protein analysis technology to develop a pre-transplant immune reaction testing method. It is anticipated that testing results can be reflected in optimal immunosuppressive therapy such as optimizing immunosuppressive agent administration frequency and dosages for patients following allogeneic cell transplantation.

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Results of a Phase III investigator initiated trial were published in an academic journal in June, 2016

3

Compounds | BBG



Preparation for marketing approval in Japan
Advances towards GMP production at the contract manufacturers of the drug substance/product

Journal of Japanese Ophthalmological Society Vol. 120, No. 6
- Efficacy was demonstrated by data for the results of a Phase III investigator initiated trial.
- Especially the results confirmed effectiveness across all cases.

Item	Sample size	Percentage (%)	95% confidence interval (Wilson score interval)
Analysis object	30	-	-
Effective*	30	(100.0)	(88.6~100.0)
Ineffective**	0	(0.0)	(0.0~11.4)

*: Effectiveness indicates 2 and more by 5-level scale.
**: Ineffectiveness indicates under 2 by 5-level scale.
(Sources) Created by Healios from Journal of Japanese Ophthalmological Society Vol. 120, No. 6

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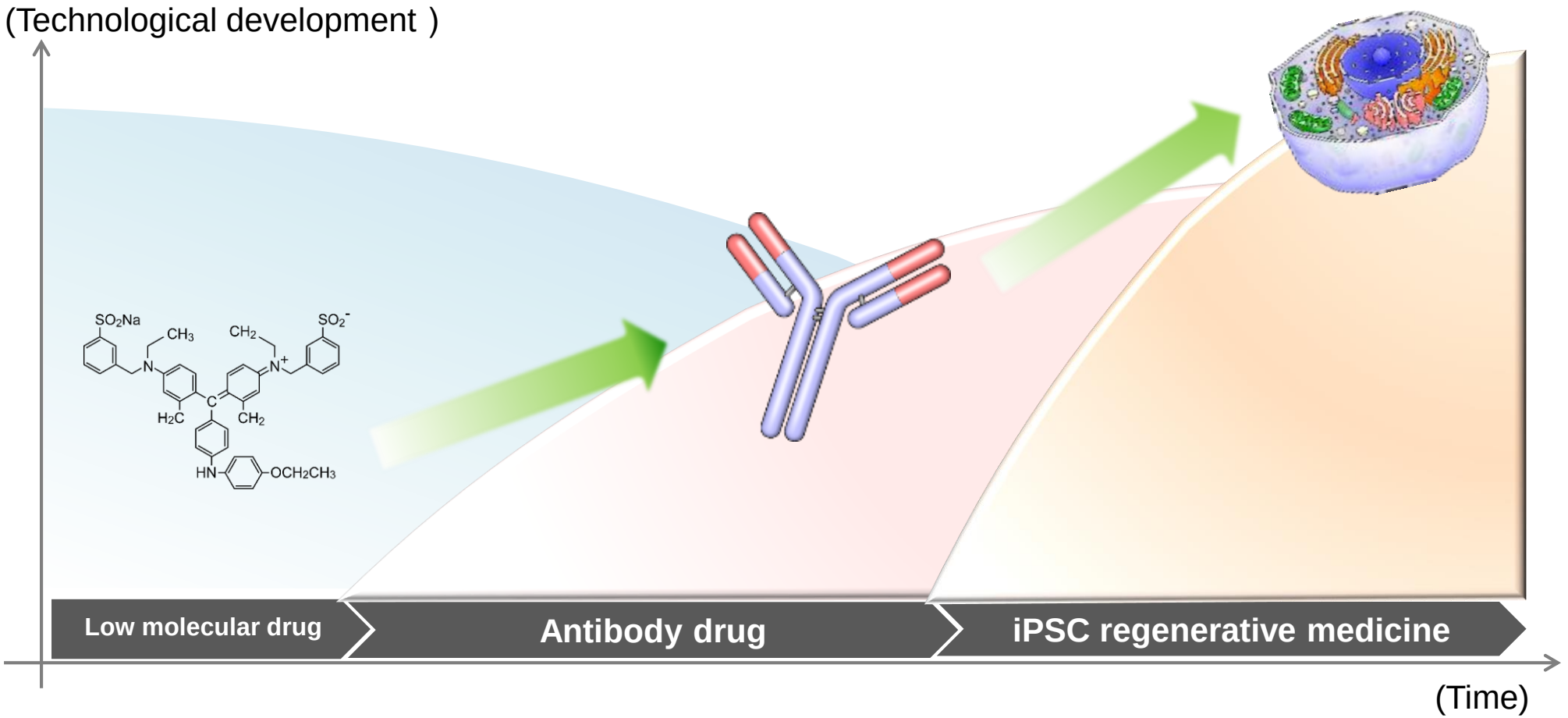
Pipeline

Filed	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	→	→					Planning to start Clinical Trial in the second half of FY2016
iPSC Regenerative Medicine	HLCR011	Wet AMD	Japan	→						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
Compound drug	HLM0021	Vitreous surgery	Japan	→	→	→	→			Under development at WAKAMOTO Co., Ltd.
	HLM0021	Cataract surgery	Japan	→	→	→				Development will be advanced immediately after licensee is determined.
	HLM0022	ILM Peeling	EU	→	→	→	→	→	→	Launched
	HLM0023	ILM Peeling	US	→	→	→	→			Under development at D.O.R.C.

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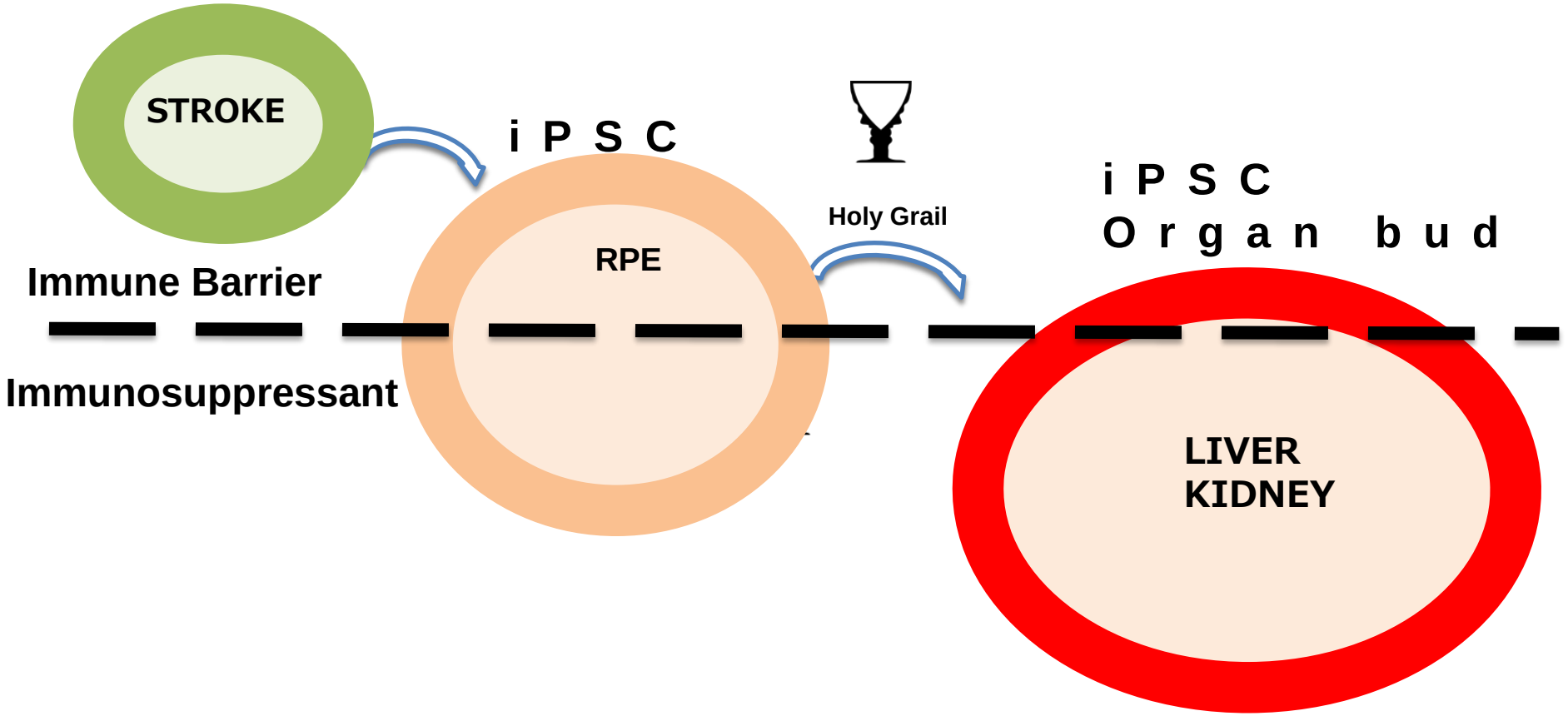
Transition to iPSC Regenerative Medicine

Technological development from low molecular drug to antibody drug to iPSC regenerative medicine, etc.



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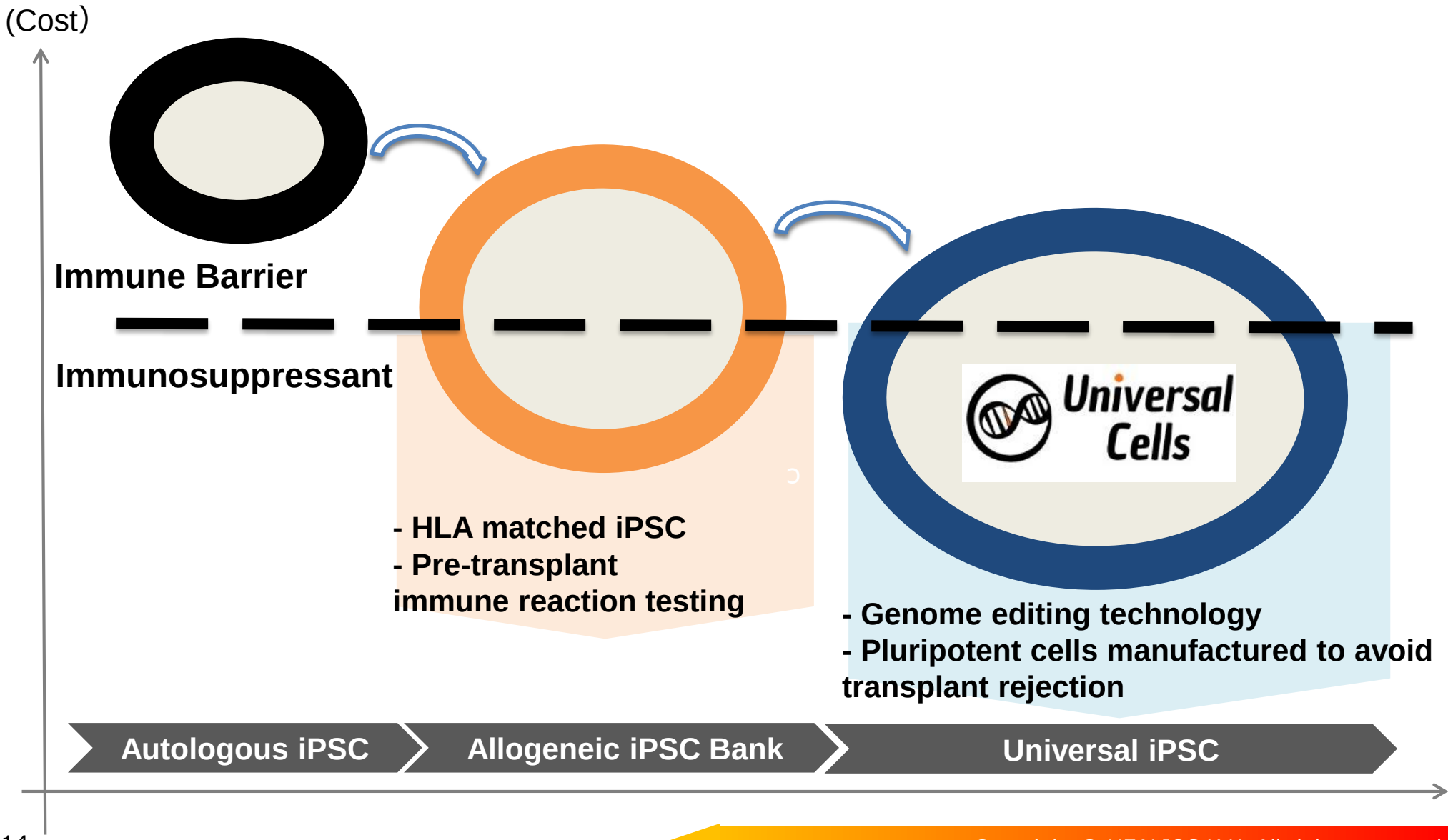
Image of Development of Regenerative medicine



Somatic stem cell → iPS Cell(Mono) → iPS Cell(3D)

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Healios' approach for Technology for Immune Reaction



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3. Details of Somatic Stem Cell Regenerative Medicine

Licensing Contract Concluded between Athersys and Healios

Healios and Athersys, Inc. (“Athersys”) entered into a license agreement over products for regenerative medicine marketed in Japan, making use of the stem cell product MultiStem® and related technology, whose patent right and patent licensing authority are held by Athersys.

① An exclusive license for the development and distribution of MultiStem cell therapy for ischemic stroke in Japan and

② An exclusive license for the research and development of MultiStem as a material for manufacturing products for regenerative medicine (targeting metabolic liver diseases) now under joint research and development by Healios and the Public University Corporation Yokohama City University.

About Athersys, Inc

Company name	Athersys, Inc. （NASDAQ:ATHX）
Representative	Gil Van Bokkelen, Ph.D. Chairman and CEO
Head Office	3201 Carnegie Avenue, Cleveland, Ohio
Paid in Capital	$323 million (As of end of December 2015）
Number of Employees	60 (As of end of December 2015）
Research Institution	Cleveland, Ohio (U.S.A.) and Leuven, Belgium (E.U.)
Major Share Holders	Pappas Ventures, Sabby Management, The Vanguard Group, M&G IM

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Outline of Ischemic Stroke in Japan

Ischemic stroke

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

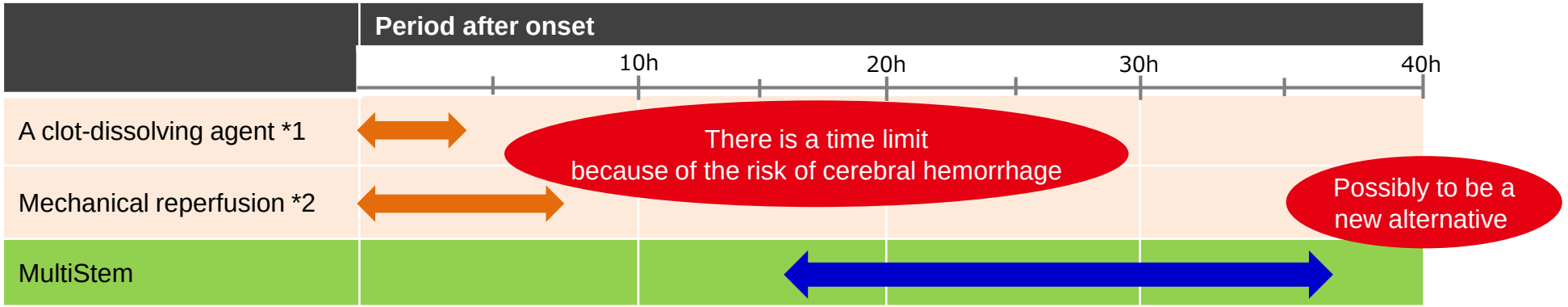
It is estimated that 37.9% of bedridden patients and 21.7% of persons who were in need of care were affected by ischemic stroke



（Source） Athersys

Treatment in accordance with the period after onset

■ Expected development of a new therapy that can be used during a longer period after 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 recovering 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.

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Annual number of new patients with ischemic stroke in Japan

Target population

	Japan	Note
Number of patients (year)	**230,000 – 330,000**	Annual medical costs for ischemic stroke estimated at 1070.7 billion yen（2009）
Severe patients（atherothrombotic and cardiogenic cerebral infection)	**130,000**	
patients within 36 h after onset	**62,000**	

Distribution system to be established for the target (with the help of alliance partners, etc.)

(Source) Healios estimated the annual number of new patients with ischemic stroke in Japan according to the 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 estimate 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 result of its market research.

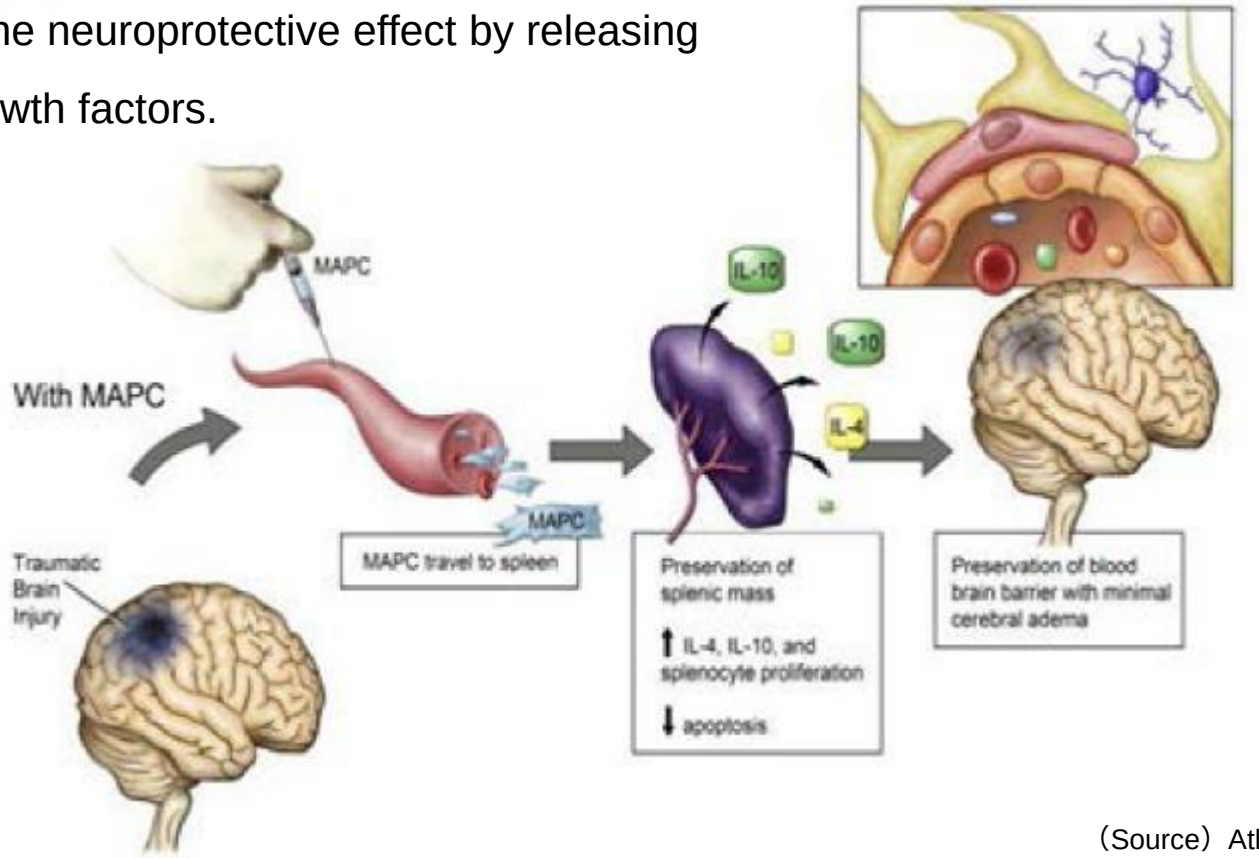
(Note)Calculated using 2013 and 2014 fiscal year-end exchange rates.

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Mechanism of treatment using MultiStem

Exhibits its therapeutic efficacy by suppressing inflammation and immune reactions and stimulating the formation of neuroprotective substances

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



（Source）Athersys

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MultiStem Product Profile



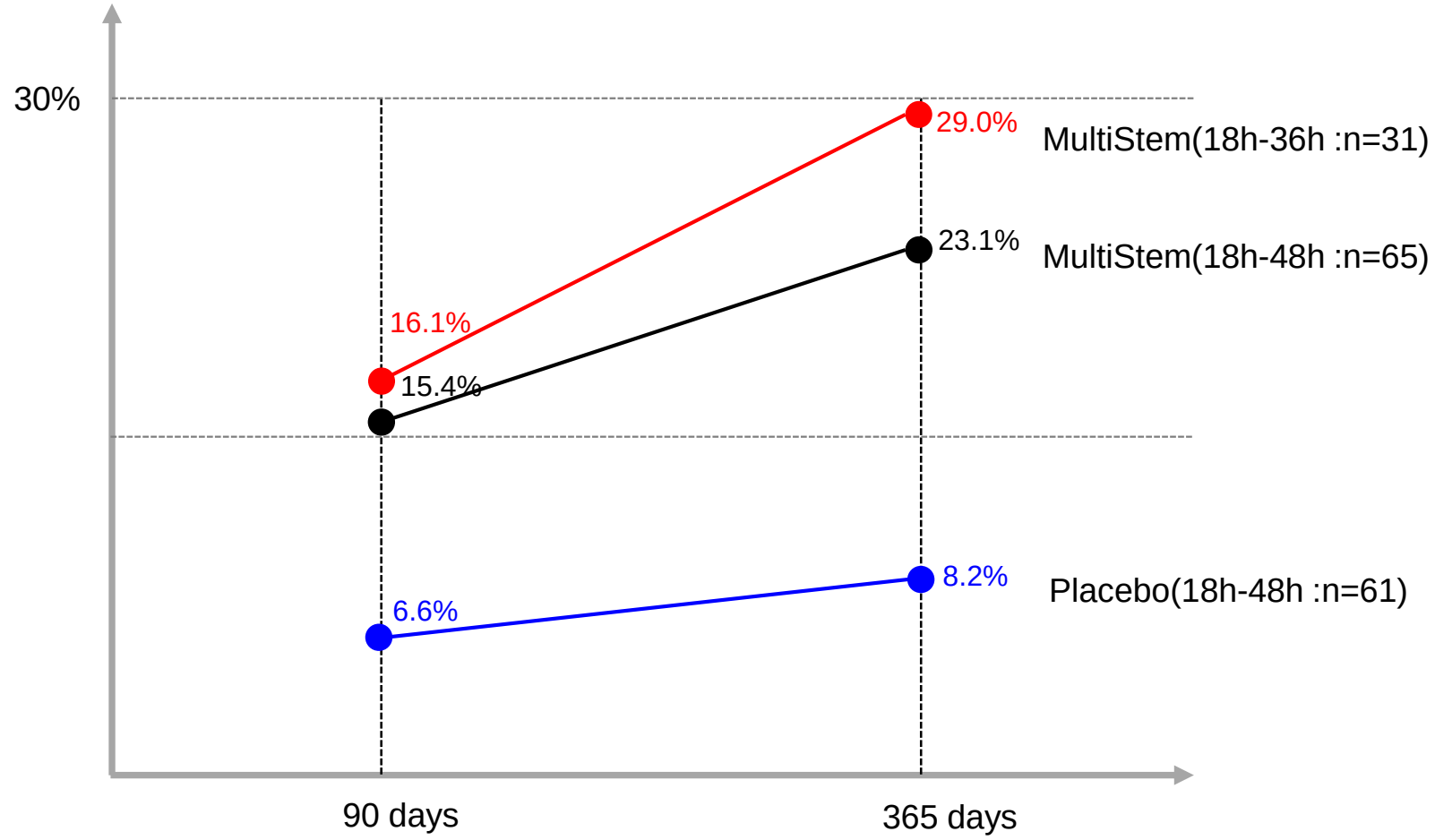
（Source）Athersys

- Cell therapy product based on patented technology
- Developing for “off-the-shelf” administration: no tissue matching needed
- Long shelf life: can be kept stably frozen 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

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Long-term (1 year) Results of Phase 2 clinical trial in the U.S. and U.K.

Percentage of Patients with Excellent Outcome



(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）

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Strategic Background of Introduction of the Stem Cell Product, MultiStem

Development in the field of stroke

- Cerebral infarction therapy with a new mechanism can be proposed and high market needs can be expected.
- Deliver it promptly to Japanese patients as a regenerative therapy product.

Technical synergistic effects with iPSC regenerative medicine field

- Dramatic improvement in production and development efficiency as materials for a regenerative therapy product (3D organs) are expected.
- Formation of alliance with companies that have GMP grade mass cell culture technologies.

Aim to generate profits at Healios promptly

- Phase II clinical studies have already been conducted in Europe and the U.S.
- In Japan, prompt launch of a clinical study is planned.

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4. Details of iPSC Regenerative Medicine

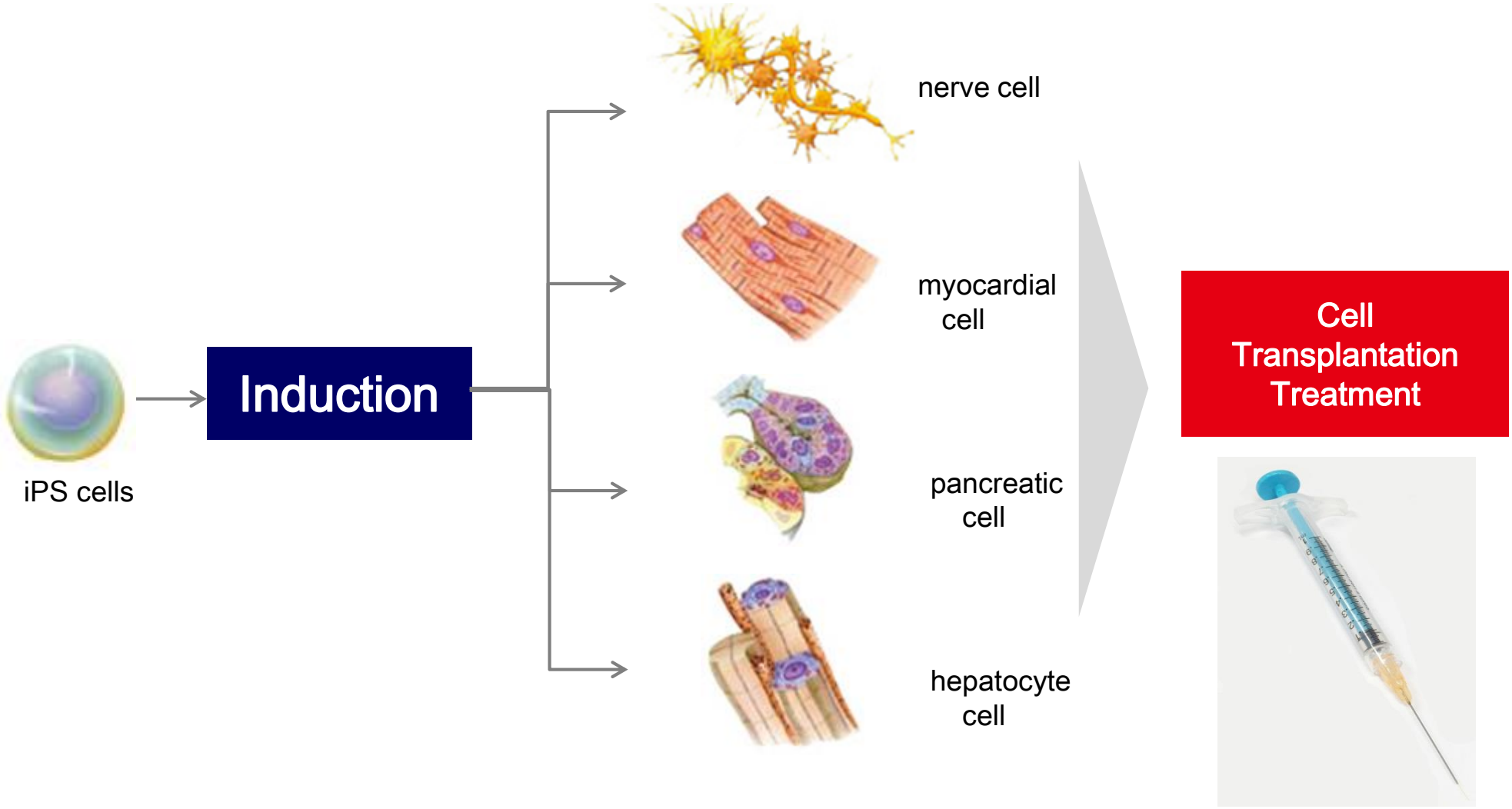
Step 1 Treat diseases with iPS Cells

Step 2 About AMD and Profitability

Step 3 Strategy for Placing RPE Cell Medicine on the Market

Concept of iPSC Regenerative Medicine

Make “Regular Cells” from iPS Cells



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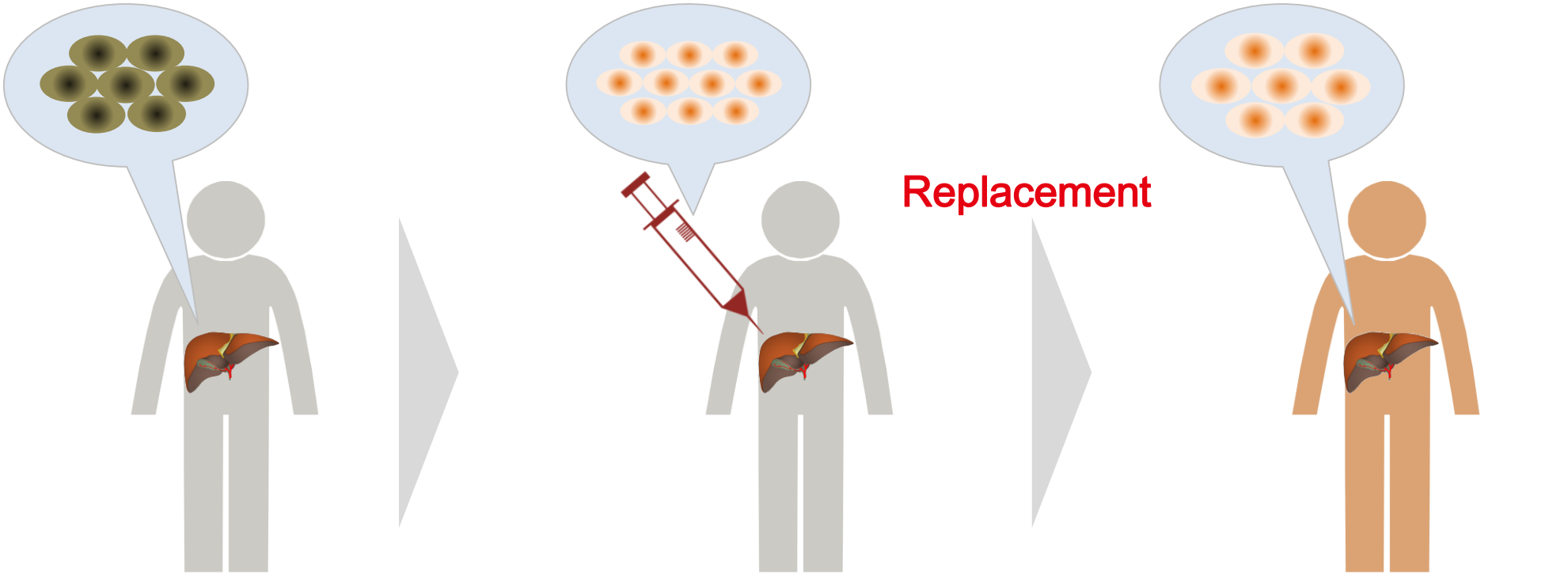
Mechanism of iPS Regenerative Medicine

Replace damaged cells with regular cells

Tissue (cells) Damaged by Aging, Disease or Accident

iPSC Regenerative Medicine
Target Cells made from iPS cells

Replace Damaged Tissue (cells) with regular cells



Patient

Recovery of Organ Function

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4. Details of iPSC Regenerative Medicine

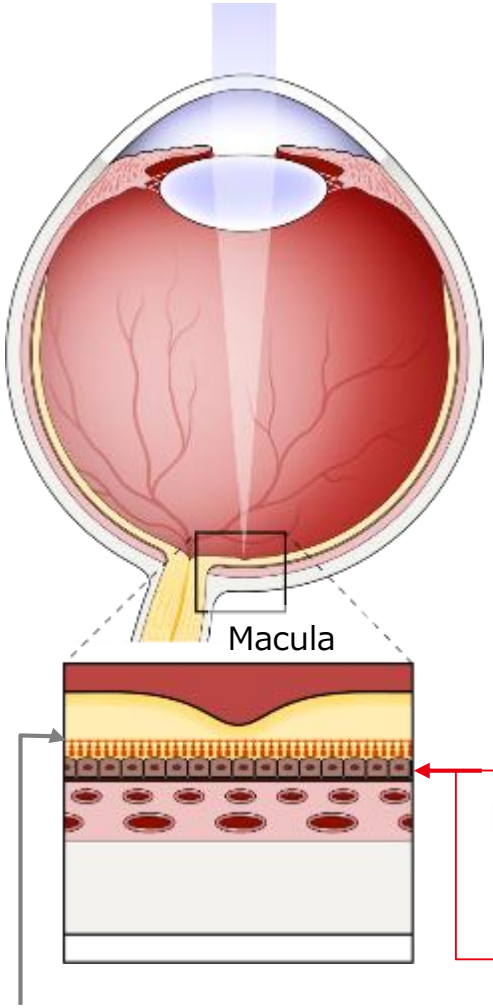
Step 1 Treat diseases with iPS Cells

Step 2 About AMD and Profitability

Step 3 Strategy for Placing RPE Cell Medicine on the Market

Explanation of AMD Pathological Condition

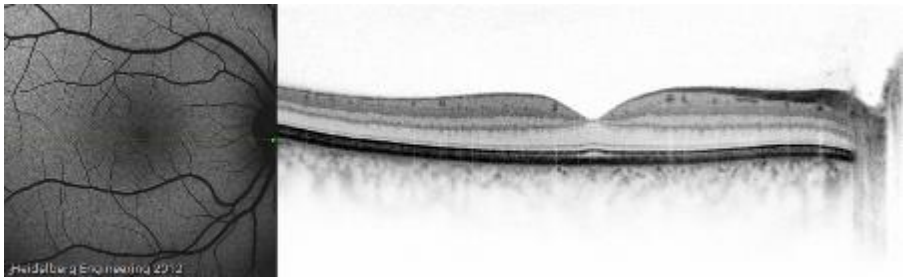
AMD causes RPE Cells to degenerate, which will damage functions



Retinal Pigment Epithelial Cell (RPE)

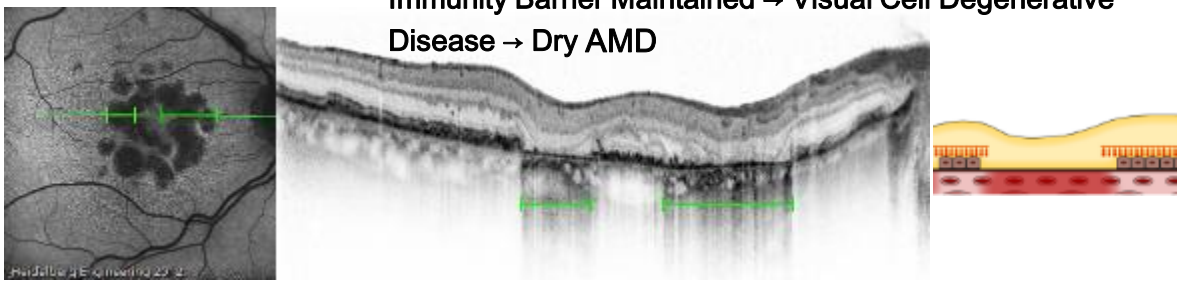
Photoreceptor Cells

Regular Macular Part



Developed Dry AMD

Immunity Barrier Maintained → Visual Cell Degenerative Disease → Dry AMD



Wet AMD

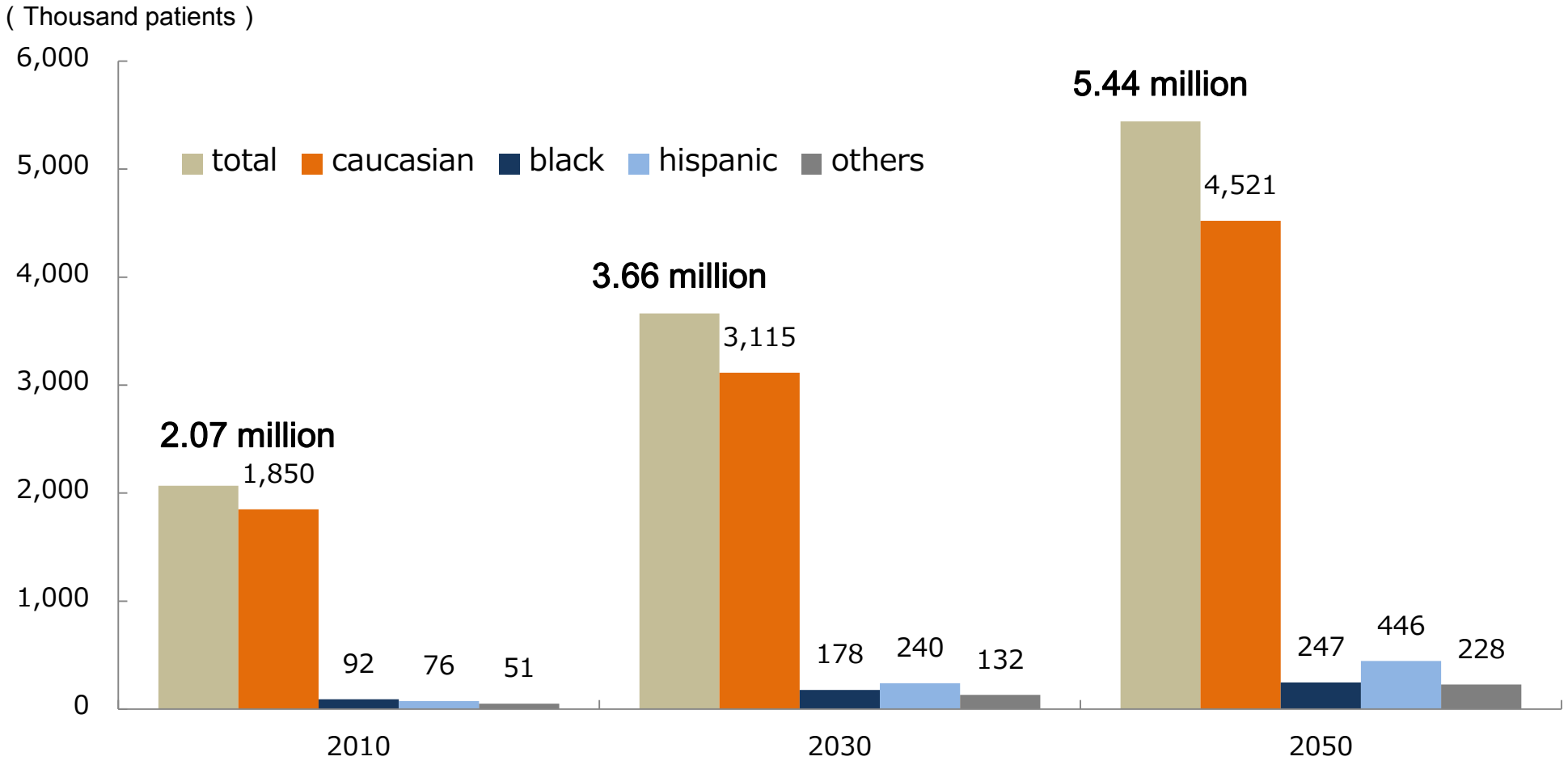
Destruction of Immunity Barrier → Invasion of Immunity Cells → Inflammation → Wet AMD



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Estimated Number of AMD Future Patients in Serious Cases in US

Expected to Increase over Medium to Long Term as Society Ages



(source) National Eye Institute

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Number of AMD Patients

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

(Thousand patients)

	America	Japan	Others
The Number of AMD Patients	10,000	9,230	13,000
The 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 Institute reports, includes the total number of age-related macular degeneration patients in light 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

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Market Scale of AMD

Annual Sales of Medicinal Treatments of Wet AMD: 831.6 billion yen. No Medicine for Dry AMD.

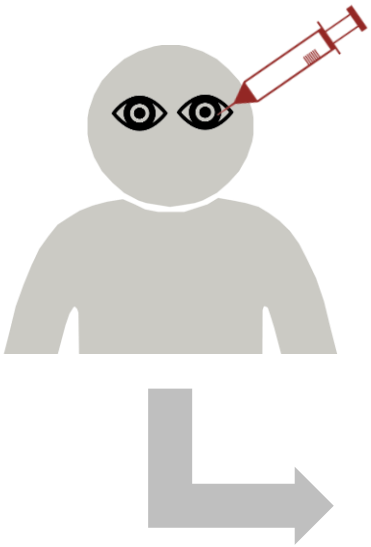
Condition	Medicine/Effect	Year	America	Japan	Others	Total
Wet	Anti-VEGF Medicine/ Restraint of New Blood Vessels	2013	363.6 billion yen	38.0 billion yen	294.7 billion yen	696.3 billion yen
		2014	414.1 billion yen	55.7 billion yen	361.8 billion yen	831.6 billion yen
Dry	No Medicine					

(source)Market scale was calculated using official materials from drug companies (Roche Diagnostic, Novartis, Regeneron,Bayer HealthCare, Santen Pharmaceutical Co., Ltd). Calculated using 2013 and 2014 fiscal year-end exchange rates.

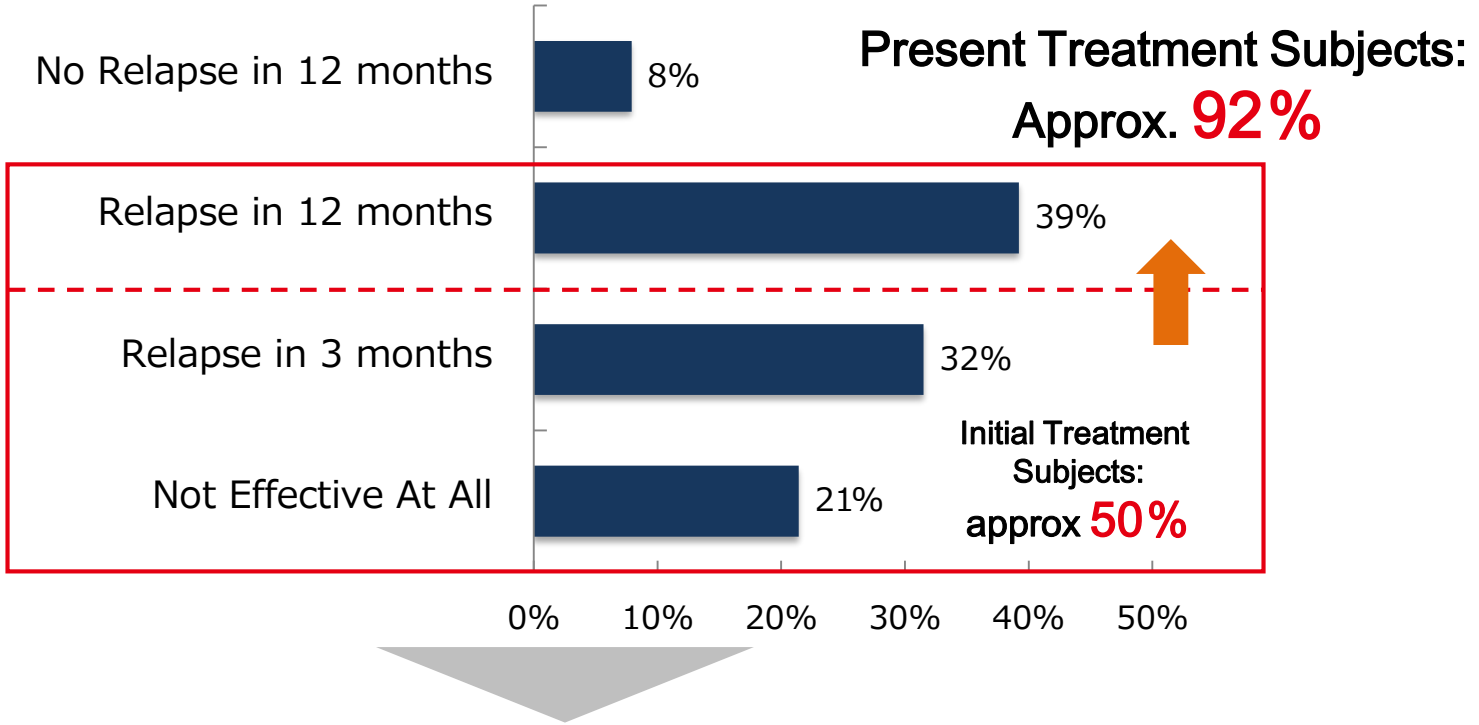
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Treatment Subjects for Wet AMD

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



Recurrence frequency after receiving anti-VEGF medication



Present Treatment Subjects: Approx. 92%

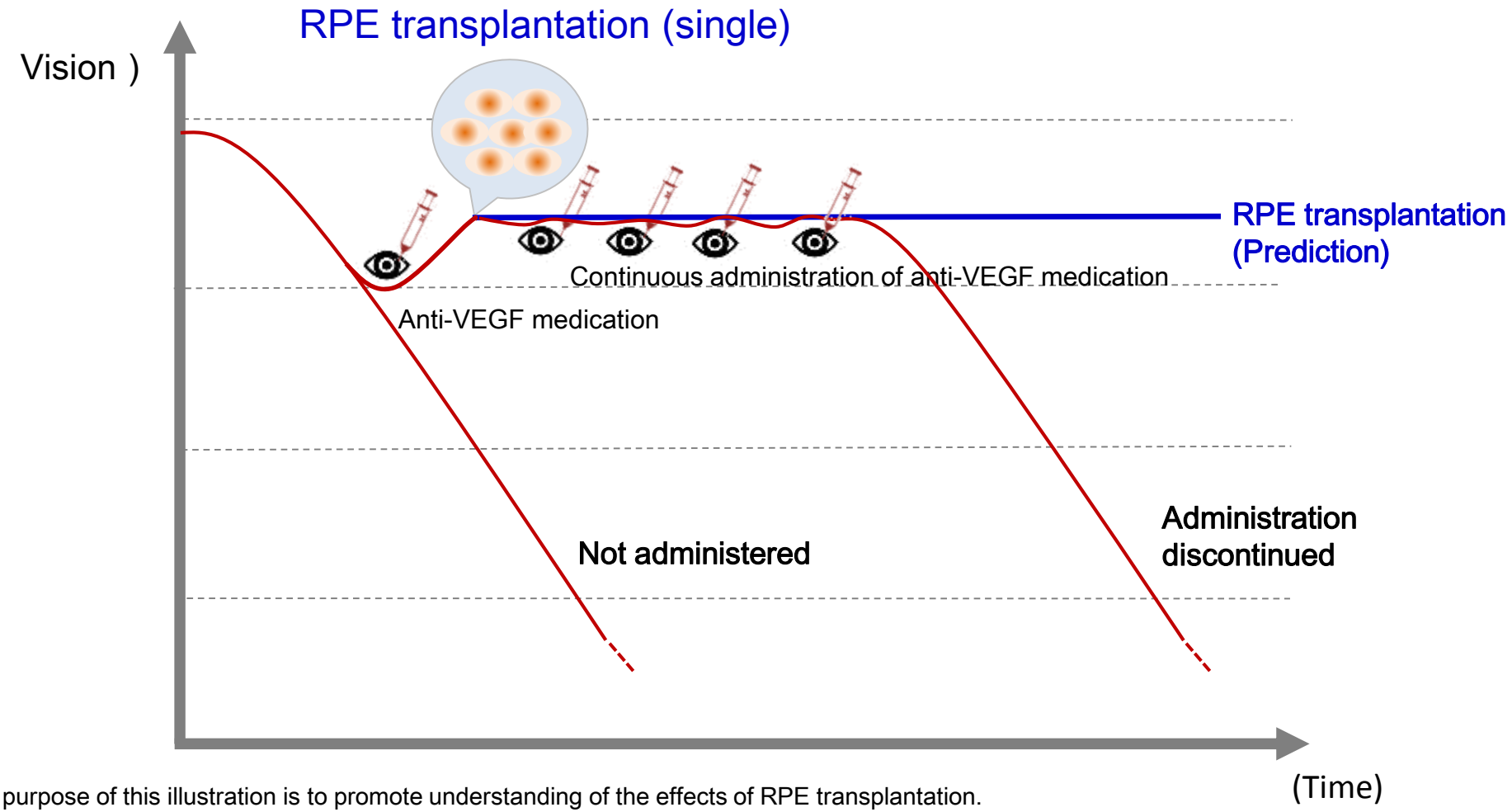
Initial Treatment Subjects: approx 50%

QOL of Continuously Medicated Patients is not High.

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

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Good vision can be maintained with early treatment



* The purpose of this illustration is to promote understanding of the effects of RPE transplantation.
Changes in vision with the administration of anti-VEGF medication are not the same as the above according to patient symptoms and administration frequency.

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Guide to Medicine Price – Approach from Medical Expense of Existing Health Care

Healios

Anti-VEGF Medicine mostly Continues From the Beginning of the Treatment to 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

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4. Details of iPSC Regenerative Medicine

Step 1 Treat diseases with iPS Cells

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Step 3 Strategy for Placing RPE Cell Medicine on the Market

Autologous and Allogeneic Transplantation

We Handle Cross-Regenerative Medical Treatment , with High Profit Margins

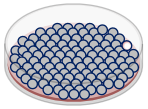
iPSC Regenerative Medicine
(Autologous)

Patient A

Cell Extraction

Cultivation Induction Formulation

Patient A



Transplant One's Own Cells

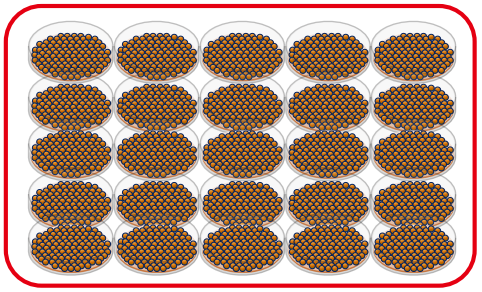
iPSC Regenerative Medicine
(Allogeneic)

Donor

Cell Extraction

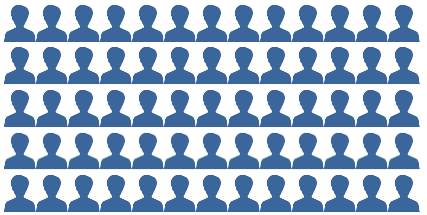
Cultivation Induction Formulation

Patient



Mass Production

High Profit



Transplant Other Cells

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Project System

Arranged Domestic Value Chain by Cooperation with Sumitomo Dainippon Pharma Co., Ltd

Development → Production → Marketing → Sales

Can Build Up Developing, Sales and Manufacturing in Japan

Development	Production	Marketing	Sales	
Healios 6.8 billion yen by Collaborative Development with Sumitomo Dainippon Pharma Co., Ltd	**SighRegen** (※) Secured Personnel Structure for Pharmaceutical Manufacturing	**SighRegen** Approved Sales Promotion	**Healios** Sales	Medical Institution

(※) Joint Venture with Sumitomo Dainippon Pharma Co., Ltd

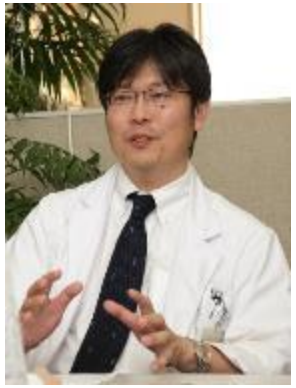
Flexibly Examine Collaborative Development, Prioritizing Self-Manufactured Sales

Development	Production	Marketing	Sales	
Healios Initial POC in Japan	**Healios** Contract Manufacturing to Lonza	**Under Consideration** (Under Consideration)	**Under Consideration** (Under Consideration)	Medical Institution

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5. Expansion to 3D Organs（Liver）

Leading authority of organ regeneration



Department of Regenerative Medicine, Yokohama City University Graduate School of Medicine
Prof. Hideki Taniguchi

1995 MD, PhD, University of Tsukuba Graduate School of Medical Sciences
University of Tsukuba Hospital
2002 Professor, Yokohama City University School of Medicine

2003-2008 Research Unit Leader (Concurrent post)
RIKEN Center for Developmental Biology

2003- Professor, Department of Regenerative Medicine, Yokohama City University Graduate School of Medicine (Main post)

Prominent researcher of human organ construction



Department of Regenerative Medicine, Yokohama City University Graduate School of Medicine
Associate Prof. Takanori Takebe

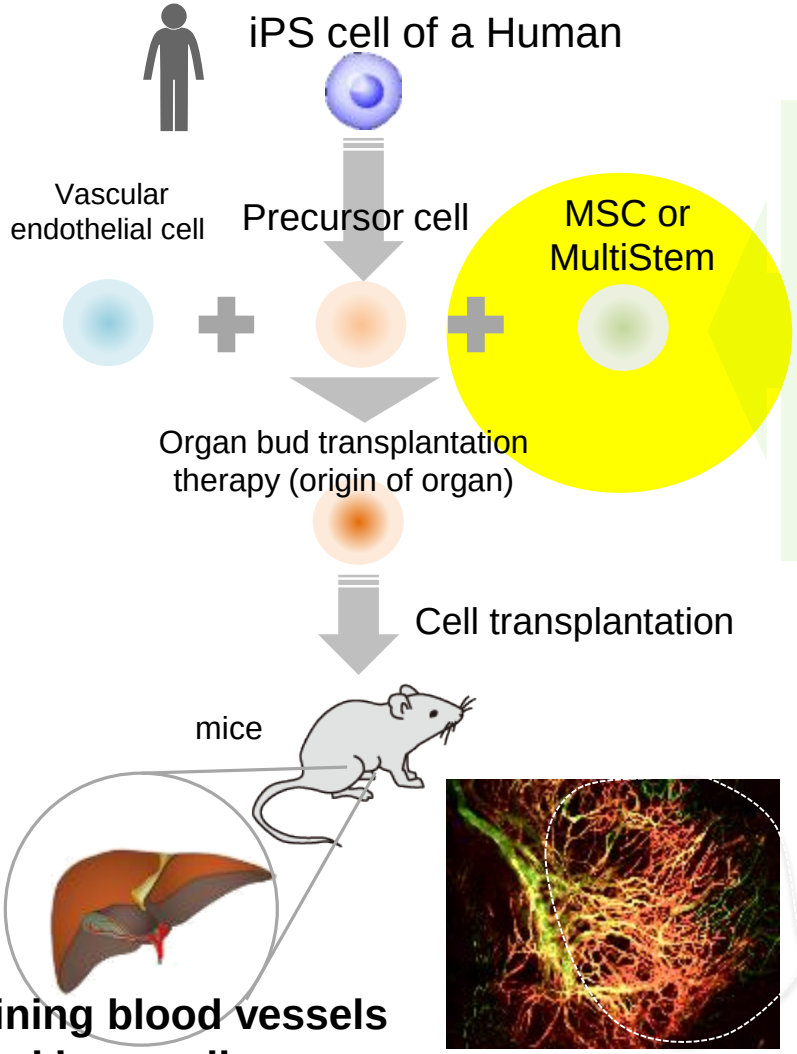
2009 Researcher, Scripps Research Institute (Chemical Department)
2011 MD, Medical Course, Yokohama City University School of Medicine
Assistant at the university at Department of Regenerative Medicine
2013-Present Associate Professor of Department of Regenerative Medicine, Yokohama City University School of Medicine (Main post)
2015 Associate Professor (Concurrent post)
Cincinnati Pediatric Hospital
Pediatric Digestive Organ Department

- July 2013 *Nature* article: World's First Case of Successfully Creating Functional Human Organ with Vascular Structure from iPS Cells
- December 2013 *Science* article: Chosen as "Science Breakthrough Of The Year" (Top 10 News in the World)
- Received 2014 Baelz Prize: Organ Regenerative Medicine: Paper by Prof. Taniguchi and Associate Prof. Takebe selected.
  * Traditional medical prize established in 1964 by Boehringer-Ingelheim with the purpose of deepening medical interchanges between Japan and Germany.

(Source) Compiled by Healios based on the "Department of Regenerative Medicine, Yokohama City University Graduate School of Medicine" website http://www-user.yokohama-cu.ac.jp/~saisei/index.html

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Consideration as a candidate for the one of the 3 types of cells that are necessary to create liver organ bud



Containing blood vessels and human liver

Consideration of the availability of MultiStem

Consideration of the large supply of MultiStem

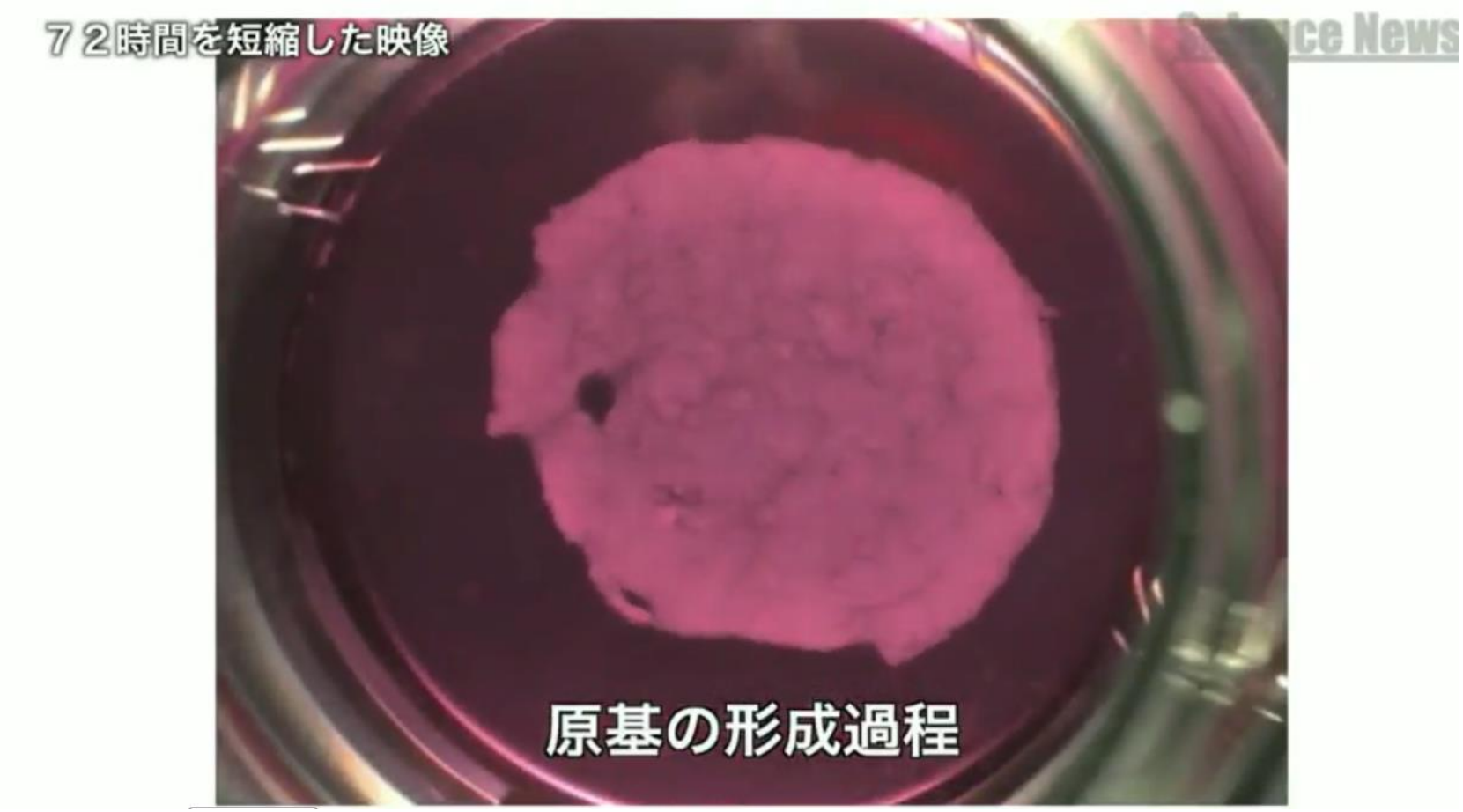


(Source) Athersys

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

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Formation process of 3D Organ



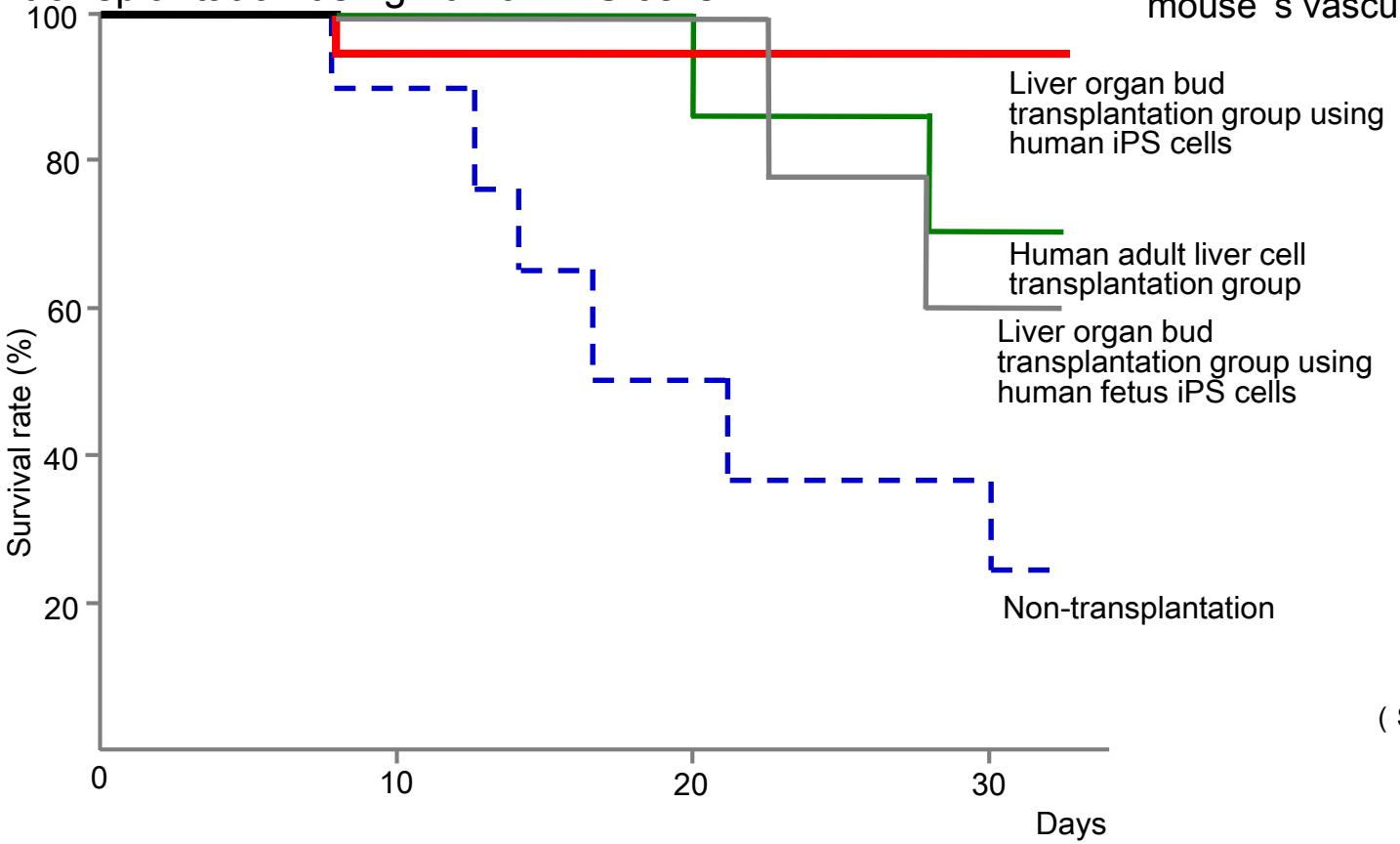
(Source) Japan Science and Technology Agency
Science News “Diverse Approaches in Regenerative Medicine from Cell to Tissue/Organ” (Distributed October 3, 2013)
https://sciencechannel.jst.go.jp/M130001/detail/M130001005.html

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Survival Rate of Liver Failure Model Mouse

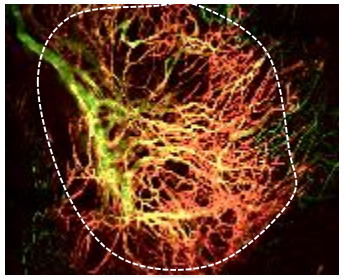
Survival rate improves significantly in transplantation experiments

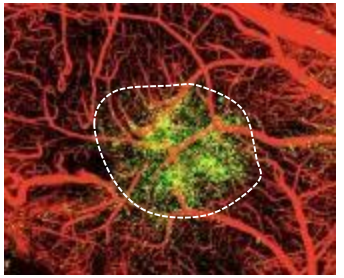
Treatment effects of liver organ bud transplantation using human iPS cells



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

Process in which organ formed from organ bud links mouse ‘s vascular network autonomously





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

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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 (year)	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, incidence rate.

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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

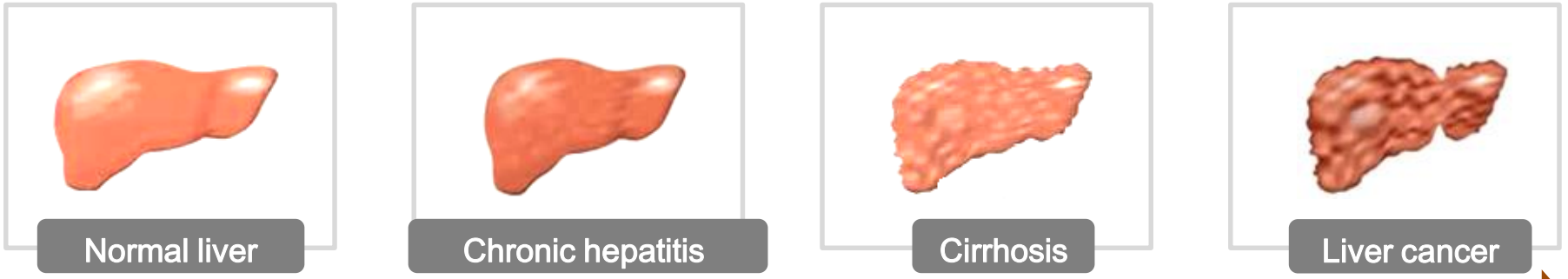
（Source）Compiled by Healios based on materials disclosed by Japanese Liver Transplantation Society, UNOS, Eurotransplant, UK Transplant, Agence de la biomédecine, and Scandia Transplant.

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

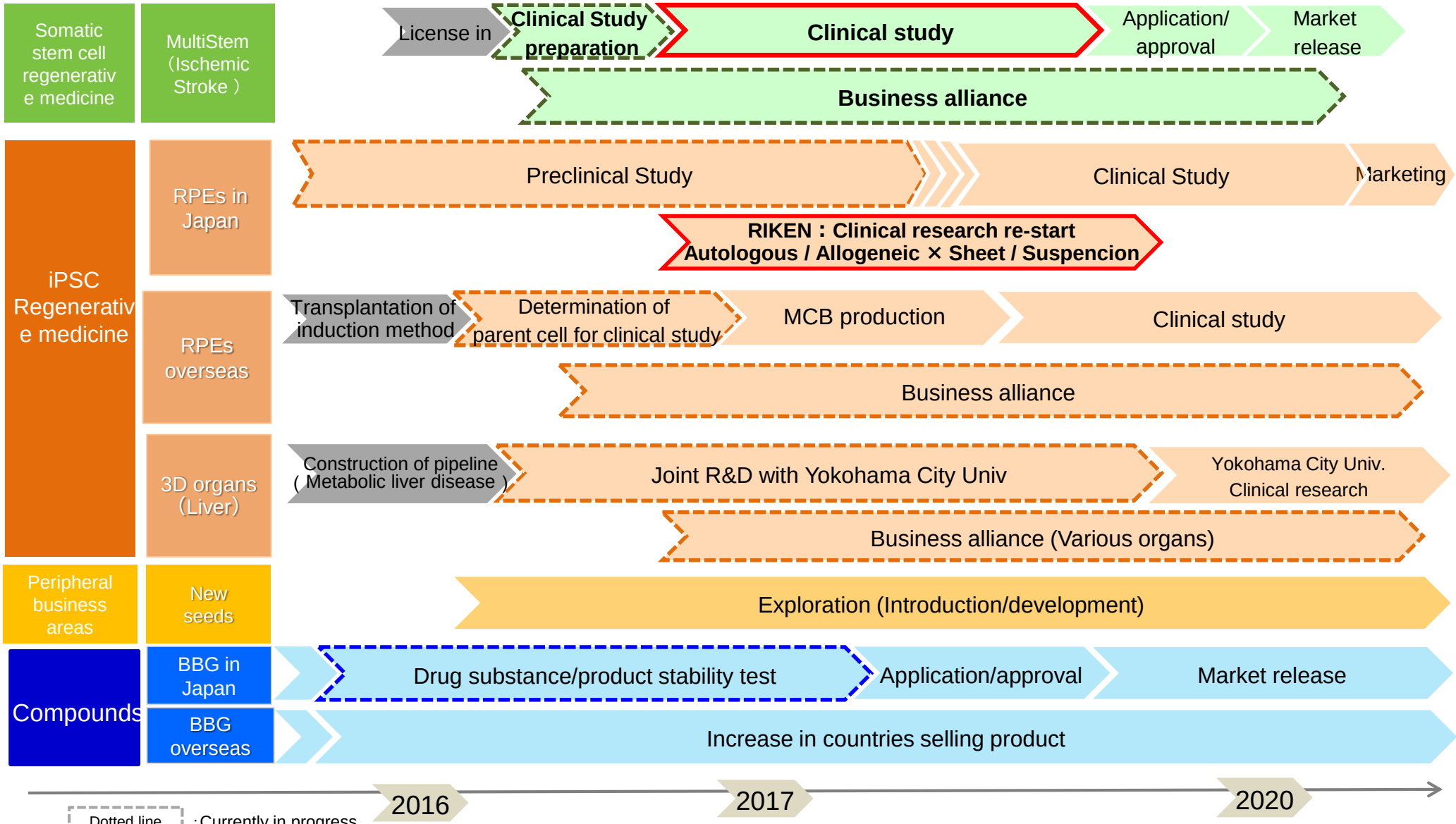
Progress of liver disease



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6. News Follow-Up

Summary of Main News Follow-Up



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7. Company Overview

About Us

Company Name	HEALIOS K.K. (TSE: 4593)
Representative	Hardy TS Kagimoto,MD　President and CEO
Head Office	World Trade Center Building 15F 2-4-1 Hamamatsucho Minato-ku, Tokyo Japan 105-6115
Paid in Capital	5380million yen(As of end of June, 2016)
Research Institution	Kobe and Yokohama
Number of Employees	52　(As of end of June, 2016)
Affiliated Company	SighRegen Co., Ltd. (Joint Venture with Sumitomo Dainippon Pharma Co., Ltd.)

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How it was founded

- Started business to establish treatments for age-related macular degeneration and determined to build up a pharmaceutical company which can provide treatments for intractable diseases.
- Founded Aqumen Biopharmaceuticals K.K. (later transferred business to Healios), succeeded in developing BBG250, entered into a contract with DORC, and started selling across Europe.
- Appraised by Institute of Physical and Chemical Research, including Dr. Masayo Takahashi, targeted the very first iPSC regenerative medicine based on iPS cells, which have the potential to be a complete cure for age-related macular degeneration, and we are responsible for putting retinal pigment epithelial cells to practical use.

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Our Experienced Team for Development

Lineup to Develop in Japan, US, and Europe

Ophthalmology Expert



President and CEO

Hardy TS Kagimoto, MD

- Succeeded in Developing BBG and Realized Sales in Europe

Expert in Age-related Macular Degeneration



Director Overseas Development

Al Reaves, Ph.D

- Responsible for innovative clinical programs for wet & dry AMD - Lucentis (X-US); Visudyne (global)

Experts in Immunosuppressant Development



Director of Laboratories in Kobe , Research and Manufacturing

Kouichi Tamura, Ph.D

- Astellas US Director of Laboratories
- Well-acquainted with Immunosuppressant Research



Director Domestic Development

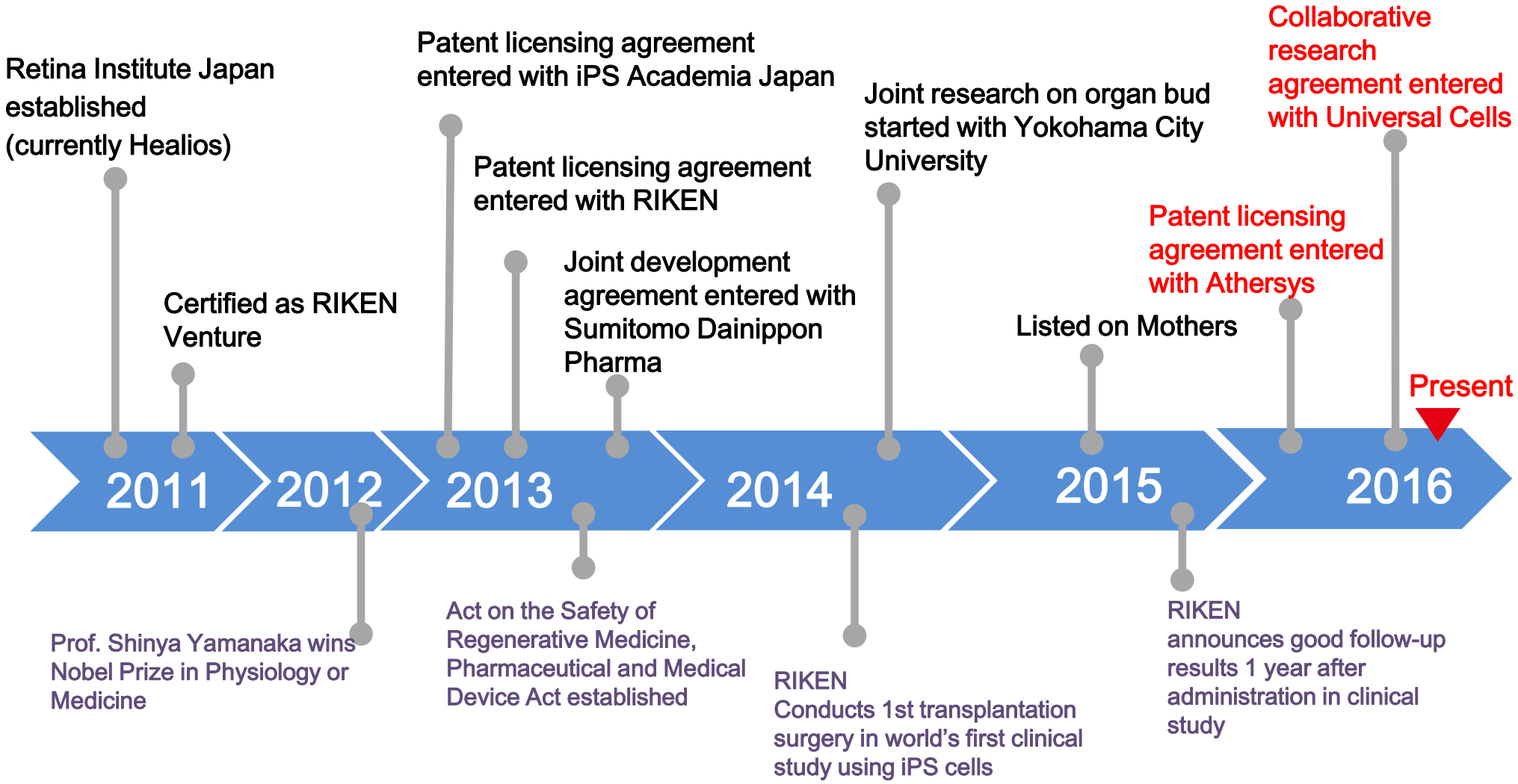
Michihisa Nishiyama

- Constructed Network for Tacrolimus Approval and Sales at Astellas in the US and Europe

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Company History and Social Trends

Pioneer of iPSC regenerative medicine development



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8. Appendix

Summary of safety results for all patients

- Safety results observed for MultiStem-treated vs placebo-treated patients

Parameter, at day 90	MultiStem (n=65)	Placebo (n=61)	Diff.
Baseline NIHSS(>24 hours)	13.4	13.3	n/a
Mortality	6.2%	14.8%	8.6%
Life threatening AEs and death	10.8%	24.6%	13.8%**
Secondary Infections	36.9%	47.5%	10.6%
Urinary Tract Infections	18.5%	27.9%	9.4%
Hospitalization days	7.9	9.8	1.9

NIHSS： National Institute of Health Stroke Scale
**： $p \leq 0.05$

（Source）Athersys

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Phase 2 clinical trial in the U.S. and U.K. [Efficacy]

Summary of efficacy results for the subset of patients

- It showed significantly favorable recovery compared to placebo at 90 days according to the second analysis of patients administered MultiStem within 36 h after onset

Parameter, at day 90	MultiStem (n=27)	Placebo (n=52)	Diff.
Baseline NIHSS(>24 hours)	12.9	13.4	n/a
Excellent Outcome(subjects achieving each of mRS ≤ 1,and NIHSS ≤ 1 ,and BI ≥ 95)	18.5%	3.8%	14.7%**
Global Recovery (subjects achieving each of mRS ≤ 2,and NIHSS Δ ≥ 75% ,and BI ≥ 95)	44.4%	17.3%	27.1%***
mRS ≤ 2	48.1%	30.8%	17.3%
NIHSS Δ > 75%	51.9%	30.8%	21.1%*
Barthel Index ≥ 95	55.6%	38.5%	17.1%

mRS: modified Rankin Scale　NIHSS: National Institute of Health Stroke Scale
BI: Barthel Index
* : p≤ 0.10　　** : p≤ 0.05　　*** : p≤ 0.01

（Source）Athersys

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Between-group Differences in Excellent Outcome at 90 and 365 Days

Subjects	90days	365days
MultiStem (n=65) within 48 hours of stroke	15.4%	23.1%
Placebo (n=61) within 48 hours of stroke	6.6%	8.2%
Between-group difference	8.8%	14.9%*
MultiStem (n=31) within 36 hours of stroke	16.1%	29.0%
Between-group difference	9.5%	20.8%**

*One had an excellent outcome if all of the following were met: mRS ≤ 1, NIHSS ≤ 1, and BI ≥ 95 (indices used to evaluate improvement in stroke outcome)
*: p=0.02 **: p< 0.01

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

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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

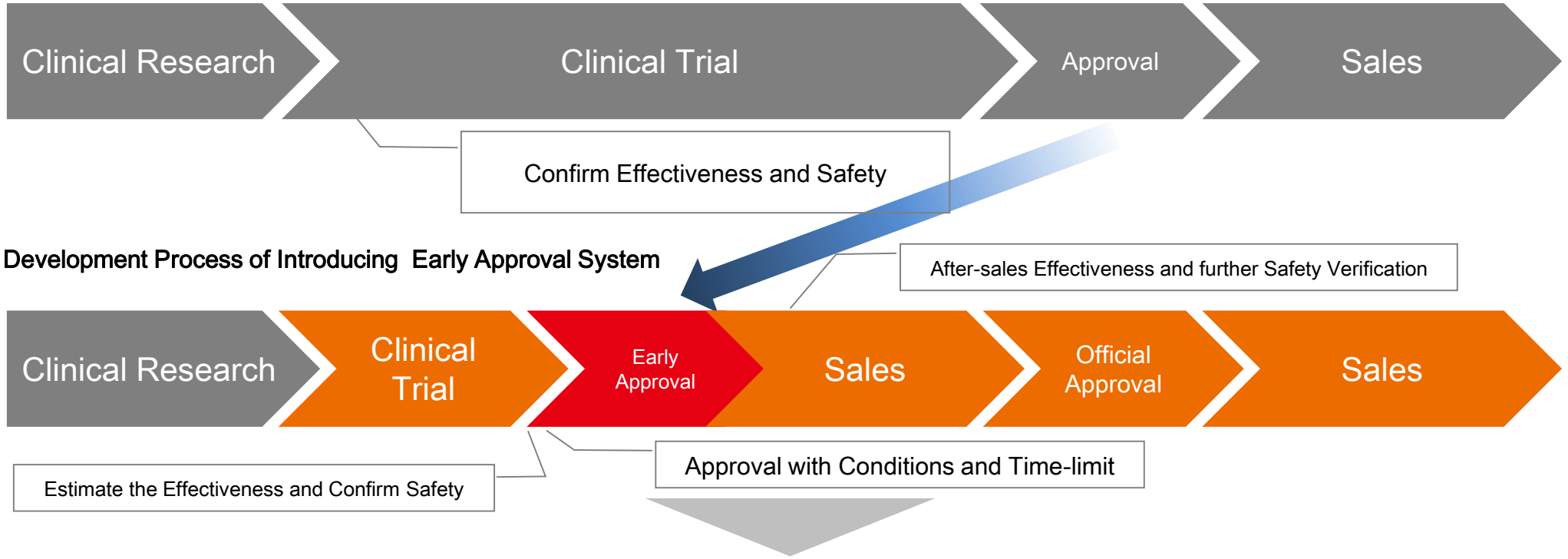
* The price of new drugs is basically calculated according to the prices of official articles with similar efficacy (price determination by comparable drug). However, if there are no appropriate similar official articles, required costs are added in the calculation of prices (cost accounting system).

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Historical Alleviation of Regulations

Japanese Government Revises Regulations to Put Japan at the Forefront

Process of the Development So Far



- Drastic reduction in the treatment period and number of patients (several dozen) with 'Early Approval System' .
- Insurance is listed at 'Early Approval' stage

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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.

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