R&D Meeting 2022

Growth Strategies of Cell Therapy (Regenerative Medicine) Business

November 9, 2022

Kidswell Bio Corporation

Agenda

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1. Opening Remarks

- **Pipelines in Cell Therapy (Regenerative Medicine) Business**

Masaharu Tani
President & CEO

2. Our strategies of SHED Platform

- **Intellectual Property Strategies**

  Joint patent application on cell therapy for cerebral palsy utilizing SHED with Tokai National Higher Education and Research System (Nagoya University)

Masayuki Kawakami
COO

- **2nd Generation SHED**

  Collaborative research with Hamamatsu University School of Medicine
  - Potential application for brain cancer-

Yasuyuki Mitani
Director, Business Development Dept., Business Development Div., Regenerative Medicine Unit Leader

3. Market Potential of SHED

- **Potential Market size of Regenerative Medicine Products**
- **Market Potential of SHED**
  - Nervous System and Muscle/ Bone Diseases, Brain Cancer-

Masaharu Tani
President & CEO）

4. Concluding Remarks

- **Our Vision**

Masaharu Tani
President & CEO

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1. Opening Remarks

Pipelines in Cell Therapy (Regenerative Medicine)

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Development Product	Target disease	Symptom	Existing Treatment	Therapeutic target	Partners	Number of patients (Domestic) ※2	Number of patients (Global) ※2
1st generation SHED	Pediatric disease Cerebral palsy	Quadriplegia and Posture disorder	None	Nerve protection, activation and regeneration	Nagoya University, Tokyo Medical and Dental University	2,000 patients per year, 30,000 patients in total	100,000 patients per year, 1.7 millions patients in total
	Pediatric disease Congenital Isolated Hypoganglionosis	Intestinal obstruction	Enterectomy, colostomy	Ganglion regeneration	Mochida Pharmaceutical	100 patients	–
	Including Pediatric disease Spinal cord injury	Loss of motor function and sensation	None	Nerve protection, activation and regeneration	Nagoya University	5,000 patients per year, 100,000 patients in total	25,000 patients per year, 500,000 patients in total (US, EU and Japan)
	Non-union fractures	Chronic pain, gait disturbance	Surgery	Bone regeneration	Hokkaido University and Spinal Injuries Center	100,000 patients per year	–
	Ophthalmologic disease	※1	※1	※1	Gifu Pharmaceutical University	※1	※1
	Peripheral nerve palsy	Motor function and sensation disorder	Nerve reconstruction (Autologous nerve transplantation)	Peripheral nerve regeneration	Oita University	8,000 surgeries per year	–
	Pediatric disease Cleft lip and palate	Eating and speech disorder	Lip arthroplasty + iliac bone graft	Maxilla bone regeneration	ORTHOREBIRTH	2,000 patients per year	15 out of 10,000 newborns
2nd generation SHED	Brain cancer	Poor life prognosis	Surgery, radiation therapy, chemotherapy	Anticancer, prevention of recurrence	**Hamamatsu University School of Medicine**	20,000 patients per year	830,000 patients in total
	※1	※1	※1	※1	NanoCarrier, BioMimetics Sympathies	※1	※1

※1 Details not disclosed, ※2 KWB research based on public and relevant information

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2. Our Strategies of SHED Platform

Intellectual Property Strategy

Strengthen Interictal Property Strategies

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Accelerate and maximize the growth by combining R&D, Business Development and Intellectual Property strategies

R&D

- Proceed R&D strategies based on analysis of information on the prior patents
- Proceed R&D and intellectual property strategies based on the present state of targeted disease and issues.

Management Strategies

Business Development

- Business collaboration, own patent license for licensing-out activities and mutual use of patent
- Joint patent applications with academias and development partners

Intellectual Property

Proceed intellectual property strategies effectively combined with R&D and business development strategies

- **Proceed strategic patent applications and life cycle management of the patents.**
- **Drive patent applications in USA, Europe and Asia as well as Japan**
  - ✓ **Apply for a substance (cell) patent for differentiating SHED from other cells.**
  - ✓ **Apply for a use patent for securing rights of treatment methods of targeted diseases.**
  - ✓ **Apply for patents of manufacturing and administration methods for extension of patent terms.**

Joint Patent Application

October 24, 2022

Announcement of a patent application on cell therapy for cerebral palsy utilizing SHED with Tokai National Higher Education and Research System
(Extracted from Japanese version)

Tokyo, October 24, 2022 – Kidswell Bio Corporation (KWB) is delighted to announce that the joint patent application agreement was executed with Nagoya University (Tokai National Higher Education and Research System is established in April 2020 including Nagoya University and Gifu University) and the patent on the cell therapy for cerebral palsy utilizing SHED (stem cells from human exfoliated deciduous teeth) was applied through the collaborative research with KWB and Nagoya University.

Some research results in the filed patent will be announced at Japan Society for Neonatal Health and Development (Nov. 24 to 26, 2022)

Strengthen Interictal Property Strategies

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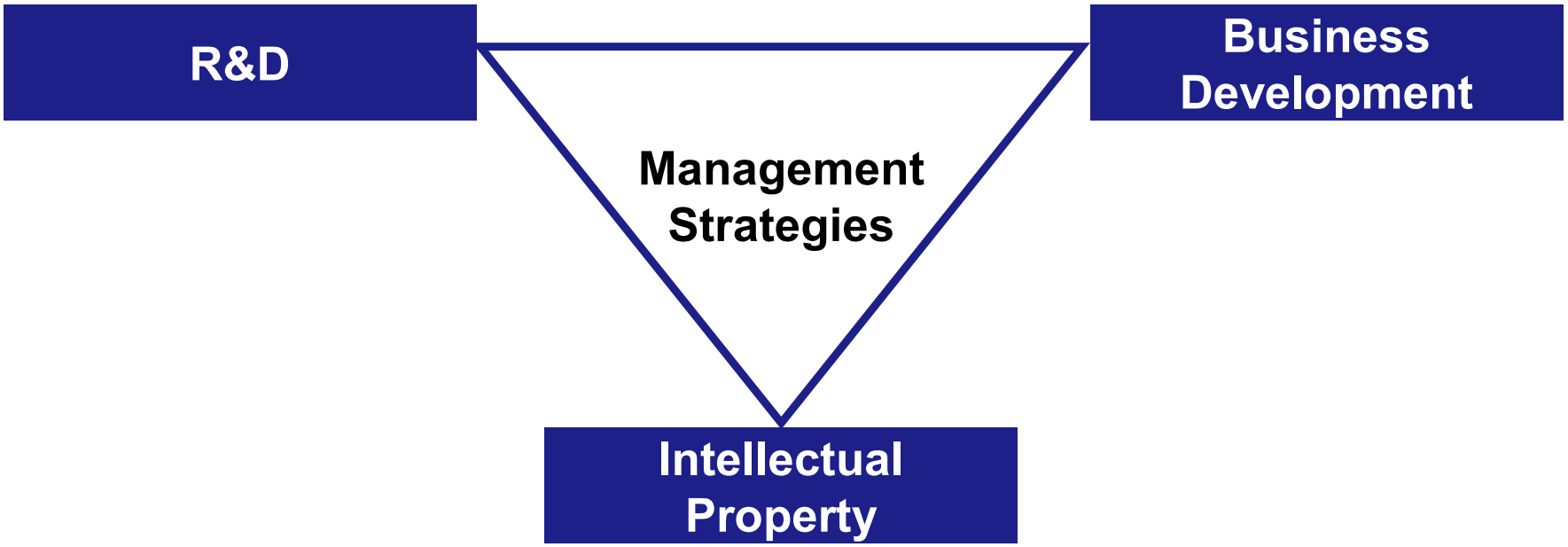
Combined effects of R&D, Business Development and Intellectual Property



Proceed intellectual property strategies effectively combined with R&D and business development strategies

2nd Generation SHED

2nd Generation SHED Development

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Launched development of designer cells as reinforced SHEDs to achieve high medical treatment goals

Development of new gene transfer methods
(Ex: NanoCarrier)

Development of new culture methods
(Ex: BioMimetics Sympathies Inc.)

Verification of the effects of various types of transgenes
(Ex: Hamamatsu University School of Medicine, Nagoya Univ.,)

Reinforced SHED

Target diseases of development※

- Cancer, etc.
- Genetic diseases
- Degenerative (Nerve)

※ in addition to nervous and muscle/bone diseases in the list of target diseases of 1st generation SHED

Aim to develop reinforced SHED with enhanced therapeutic efficacy

	Infection	Lifestyle related	Degenerative (Nerve・Organ)	Autoimmunity	Cancer	Genetic diseases
	Pediatric diseases					
Permanent Cure Treatment	Vaccine (Prevention・Treatment)	1st Generation Cell Therapy Non-Recombinant Type of Stem Cells etc.	2nd Generation "Designer Cells" Recombinant Cell Therapy (Stem Cell-Based) Add/Enhance Functions by Genetic Engineering			
Symptomatic Treatment	Small, Mid Molecule Drug	DTx	Antibody Drug			Nucleic Acid Medicine

* Created by Kidswell Bio Corporation referring from Strategic Proposal of Designer Cell by Japan Science and Technology Agency.

2nd Generation SHED – Potential application for brain cancer –

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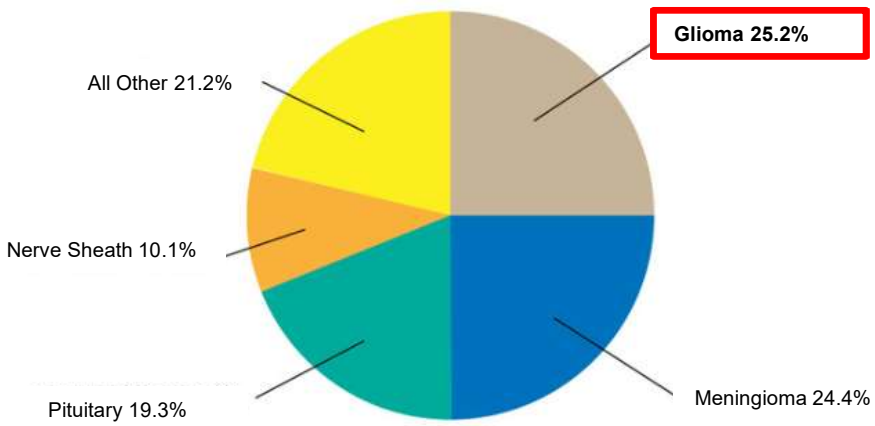
Brain Cancer

- There are primary or metastatic brain cancer. Most common brain cancer is primary gliomas.
- Low survival rate: Less than 10% of 5-year survival rate for primary gliomas.
- Metastatic brain cancer is about 15% of all type of brain cancer, half of which is lung cancer brain metastases.
- Low survival rate: Less than 10 to 30% of 5-year survival rate for metastatic brain cancer.

Primary Brain Cancer（WHO Grade I-IV）



Brain tumor registry in Japan 2001-2004

5-year survival rate by type of brain cancer

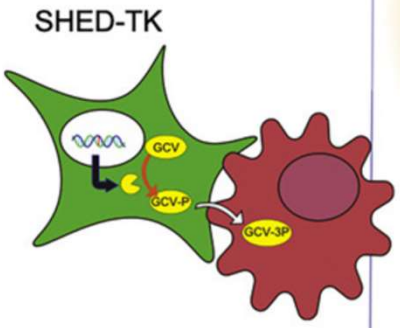
	Histology/Year	1969–1975	1976–1980	1981–1985	1985–1990	1991–1996	1997–2000	2001–2004
Primary	Diffuse astrocytoma	50.9	63.2	61.6	62.8	66.5	68.3	75.0
	Oligodendroglioma	54.5	75.1	80.4	78.3	82.0	87.8	90.0
	Anaplastic astrocytoma	21.7	25.3	27.1	20.7	23.4	33.9	41.1
	Anaplastic oligodendroglioma	31.2	68.5	66.8		68.2	63.0	68.2
	Glioblastoma	11.9	12.0	9.8	7.6	7.0	6.9	10.1
	Ependymoma	42.4	55.8	68.9	65.2	72.9	75.1	86.3
	Anaplastic ependymoma	22.9	50.9	22.9	37.6	23.5	60.1	58.1
	Primary CNS lymphoma						23.4	42.3
	Medulloblastoma	22.2	32.1	36.3	41.8	60.1	58.0	68.7
	Germinoma	63.3	74.6	89.0	88.8	91.0	94.6	97.1
	Meningioma	99.6	100.0	100.0	91.8	93.7	95.9	97.4
	Neurinoma	91.9	100.0	100.0	95.1	96.9	98.0	98.8
	Pituitary adenoma	100.0	100.0	100.0	95.5	96.2	97.4	98.7
Metastatic	Brain metastases	11.0	8.5	9.2	9.4	13.6	15.0	26.3

Jpn J Neurosurg (Tokyo) 24: 699-704, 2015

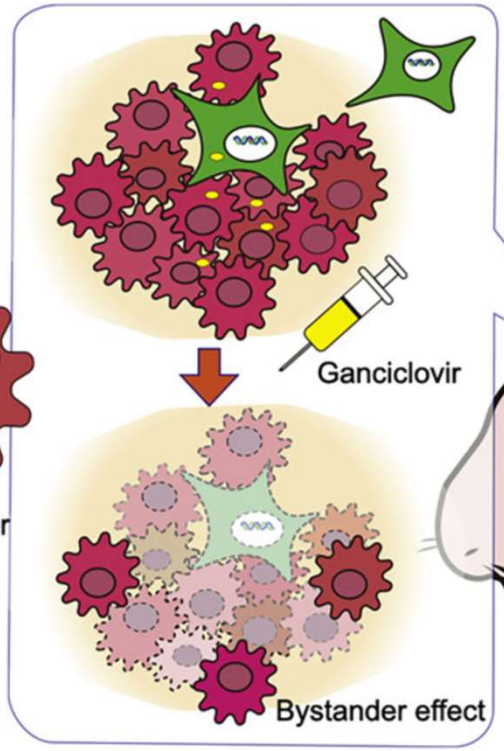
Concept of the potential therapeutic application of the next generation SHED for brain cancer

Oishi et al., *Mol Ther Methods Clin Dev*. 2022

①Administration of the SHED engineered to express an enzyme, thymidine kinase (TK) to brain



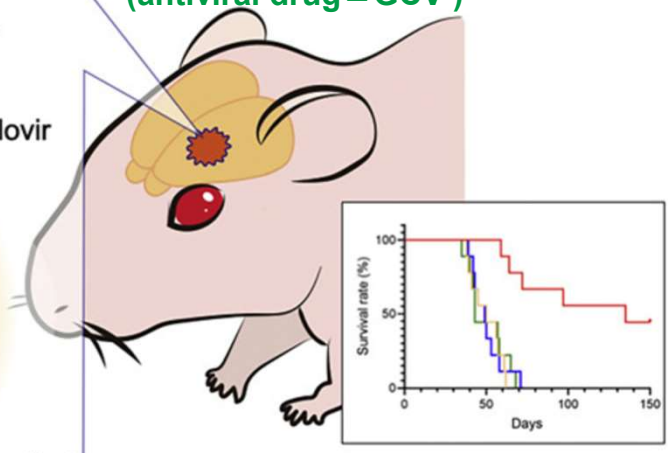
④GCV converted into a toxicant by TK, and permeated cancer cells adjacent to SHEDs



Migration

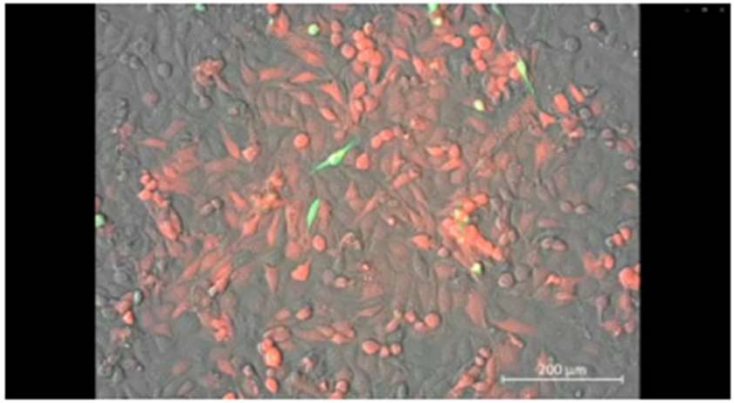
②Confirmed the migratory ability of SHED for glioma cells.

③Systemic administration of ganciclovir (antiviral drug＝GCV)

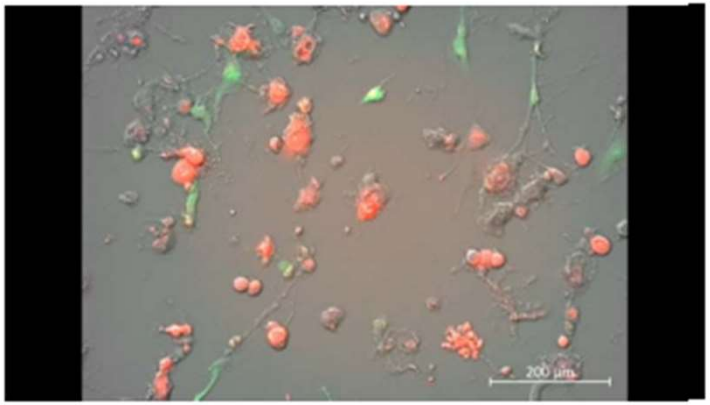


⑤ Toxicants were permeated cancer cells and cancer cells disappeared one after another (＝bystander effect)

Cancer cells + SHED-TK



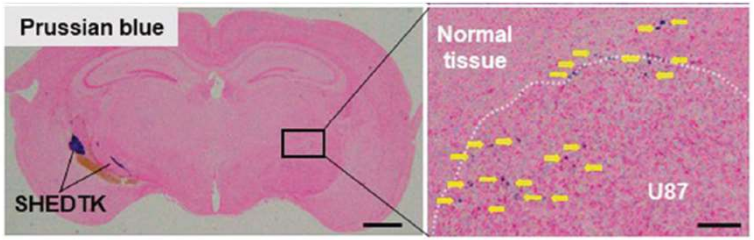
Cancer cells + SHED-TK + GCV



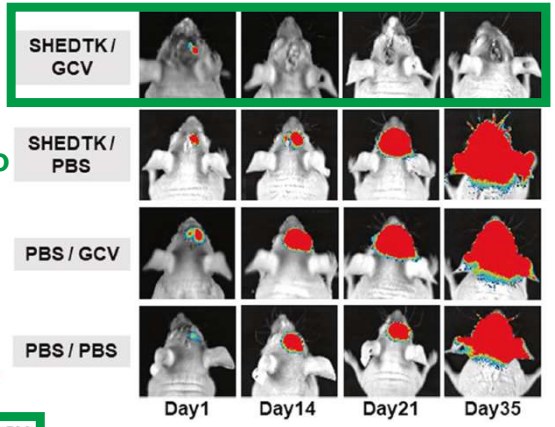
SHED-TK effect in a mouse model of brain cancer

Potent bystander effect and tumor tropism in suicide gene therapy using stem cells from human exfoliated deciduous teeth

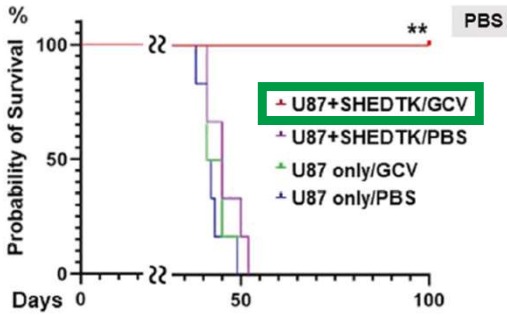
Makoto Horikawa[1], Shinichiro Koizumi[1], Tomoya Oishi[1], Taisuke Yamamoto[1], Masashi Ikeno[2], Masahiko Ito[3], Tomohiro Yamasaki[1], Shinji Amano[4], Tetsuro Sameshima[1], Yasuyuki Mitani[5], Yoshihiro Otani[6], Yuanqing Yan[7], Tetsuro Suzuki[3], Hiroki Namba[8] and Kazuhiko Kurozumi[1]



Administered SHED-TK to the opposite side of the brain, where the glioma implanted, and SHED-TK migrated and accumulated toward the glioma.



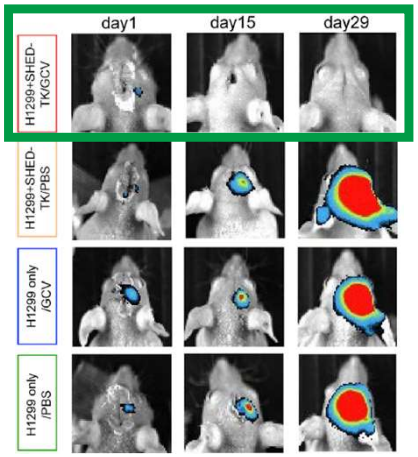
No mice were dead in the SHED-TK/GCV group due to extinction of glioma cells.

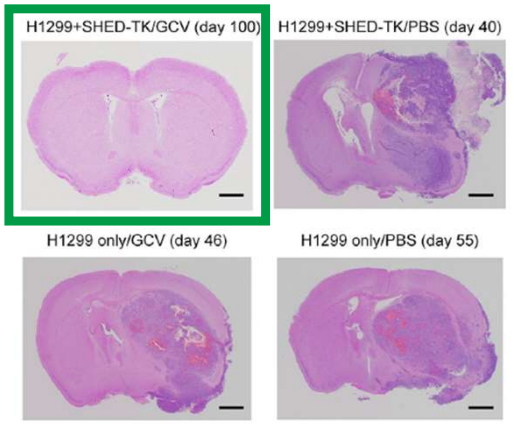


Cancer Gene Ther. 2022

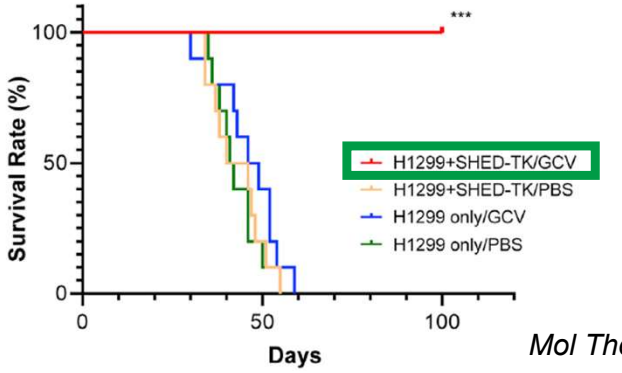
Efficacy of HSV-TK/GCV system suicide gene therapy using SHED expressing modified HSV-TK against lung cancer brain metastases

Tomoya Oishi,[1] Masahiko Ito,[2] Shinichiro Koizumi,[1] Makoto Horikawa,[1] Taisuke Yamamoto,[1] Satoru Yamagishi,[3,4] Tomohiro Yamasaki,[1] Tetsuro Sameshima,[1] Tetsuro Suzuki,[2] Haruhiko Sugimura,[5] Hiroki Namba,[6] and Kazuhiko Kurozumi[1]





No mice of lung cancer brain metastases were dead in the SHED-TK/GCV group due to extinction of glioma cells.



Mol Ther Methods Clin Dev. 2022

Drive further R&D for clinical applications

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3. Market Potential of SHED

Potential Market size in Regenerative Medicine Products

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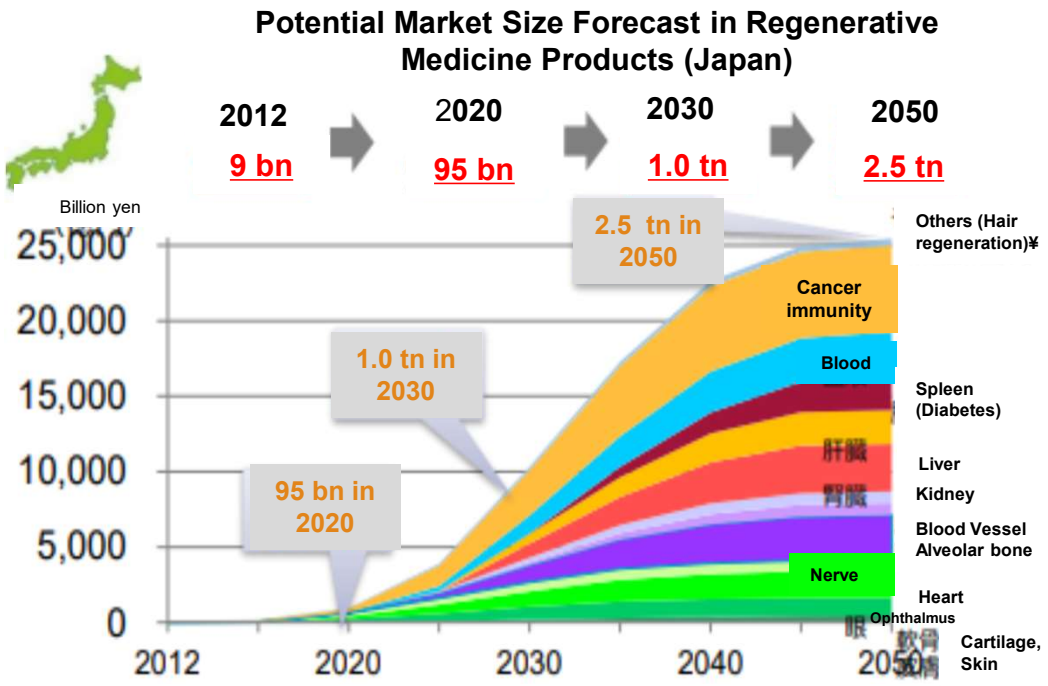
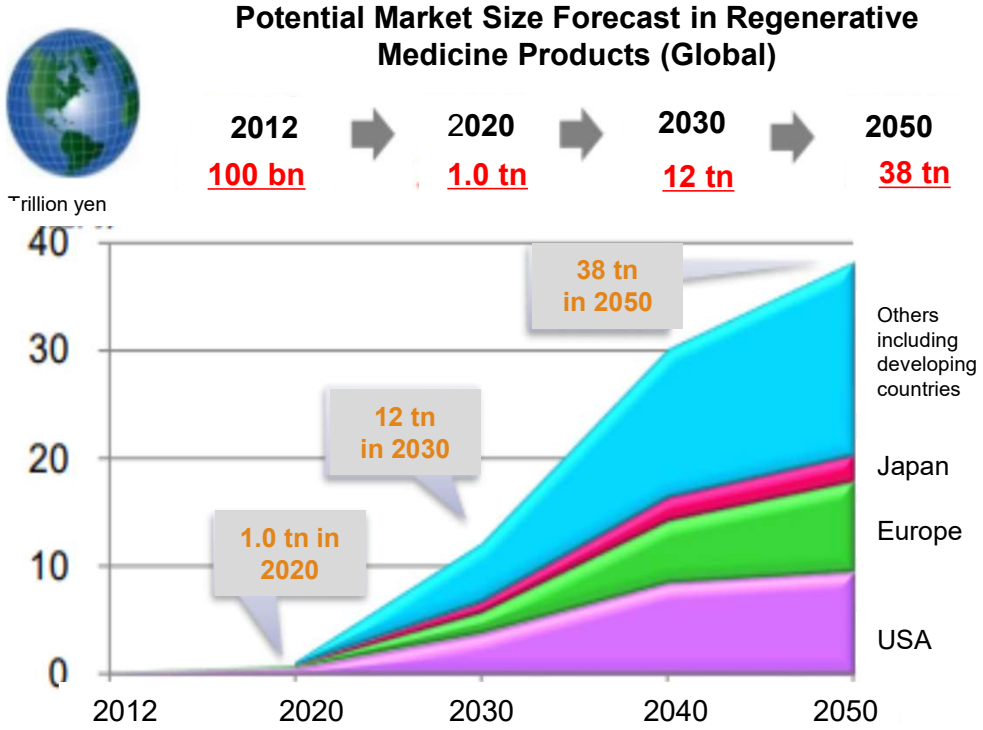
The Market Size of Regenerative Medicine Products in 2050

Japan: 2.5 trillion yen、Worldwide：38 trillion yen



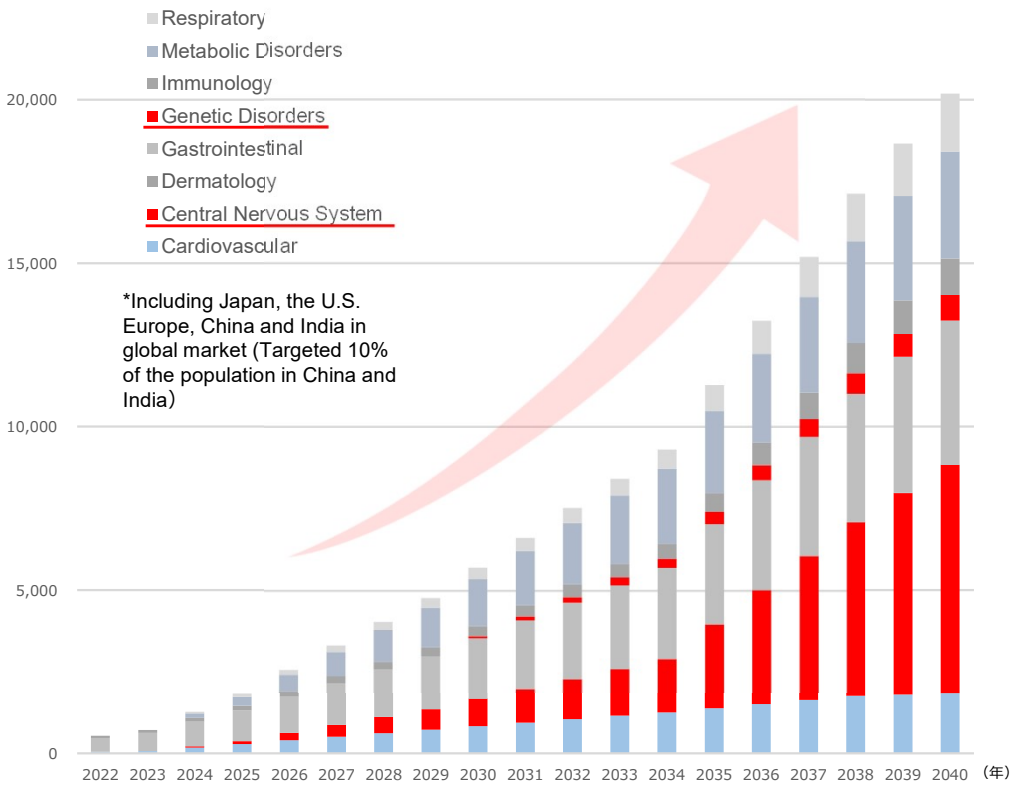


Source：*METI*「第１回 再生医療・遺伝子治療の産業化に向けた基盤技術開発事業複数課題 プログラム 中間（終了時）評価検討会」資料⑥

Market Potential

Nervous System and Muscle/ Bone Diseases: 1st Generation SHED

Grow from 700 billion to 800-billion-yen market by 2040.

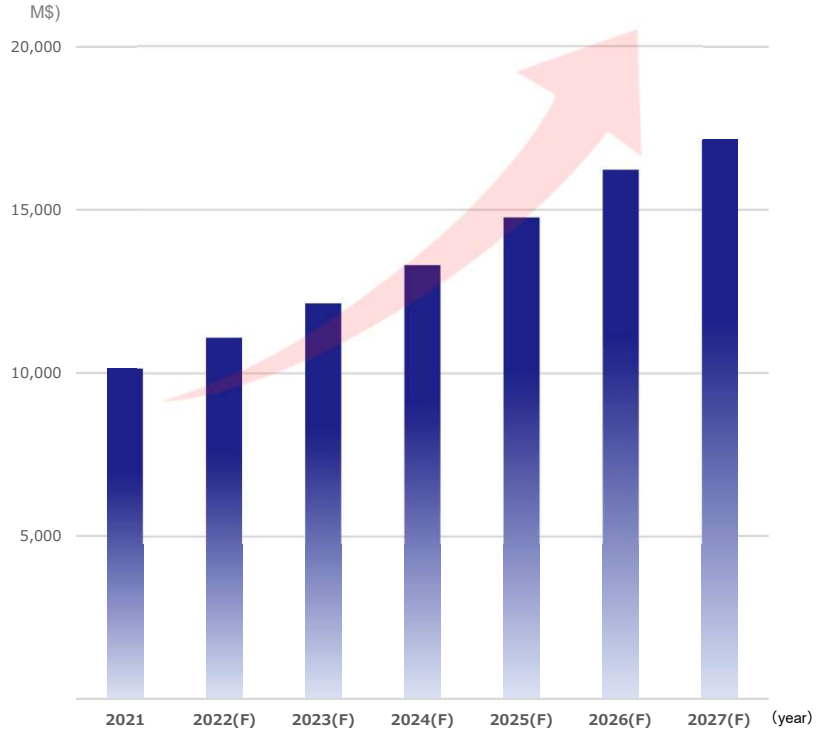


Estimation for market size of allogeneic stem cells[*1]

*1 KWB's research based on Regenerative medicine and gene therapy market research in 2019 Final report from the website of Japan Agency for Medical Research and Development, Global Data from epidemiological literature and websites from rare diseases (Orphanet, NORD, Japan Intractable Diseases Information Center, Clinical Development Success Rates 2006-2015, BIO Industry Analysis」and related documents from general meeting of Central Social Insurance Medical Council

Brain Cancer : 2nd Generation SHED

- Grow more than 2-trillion-yen market by 2027[*3]
- Genetically modified cell medicine (designer cells) is expected additional 350-billion-yen market[*4]



Sales forecast on potential applicable products for brain cancer [*2]

(Including all modalities, worldwide total, sales except from brain cancer)

**2: Global Data LLC（ Figures for 2022 and beyond are forecasts (F)）*

**3: 1USD=145円*

**4: Proportion of brain cancer among new cancer patients 1.4%（CA Cancer J Clin 2015;65:5–29), Assumingly calculated a 10% share of the cell medicine modality （KWB's forecast）*

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4. Concluding Remarks

Our Vision

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All for Kids, Kids for All

KIDS WELL, ALL WELL

～ For Comprehensive Healthcare System for Children as well as Families, and Society ～

Focus Area

Pediatric diseases including juvenile diseases, intractable & rare disease

Business Direction

Targeting diseases which has less accessibility for sufficient medical treatment

All for Kids, Kids for All

- Under the declining birthrate and aging population, reducing the burden on children is a major social issue.
- Provide new pharmaceuticals and therapeutics to patients suffering from diseases and contribute to the realization of a society where children and adults who support children live happily and brightly.

All for Kids, Kids for All

KIDS WELL, ALL WELL

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Cautionary Statement

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This material includes information on pharmaceutical products and regenerative medicine (or related products), etc., which is being developed or launched. However, this is not intended to promote our products or provide medical advices.