

# **SHED Master Cell Bank Completed**

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**Kidswell Bio Corporation**



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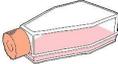
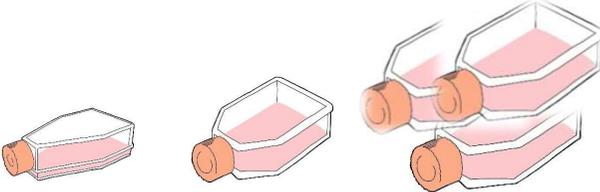
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This material includes information on pharmaceutical products and regenerative medicine (or related products), etc., which is being developed or launched. However, this is not intended to promote our products or provide medical advices.

# **SHED Master Cell Bank**

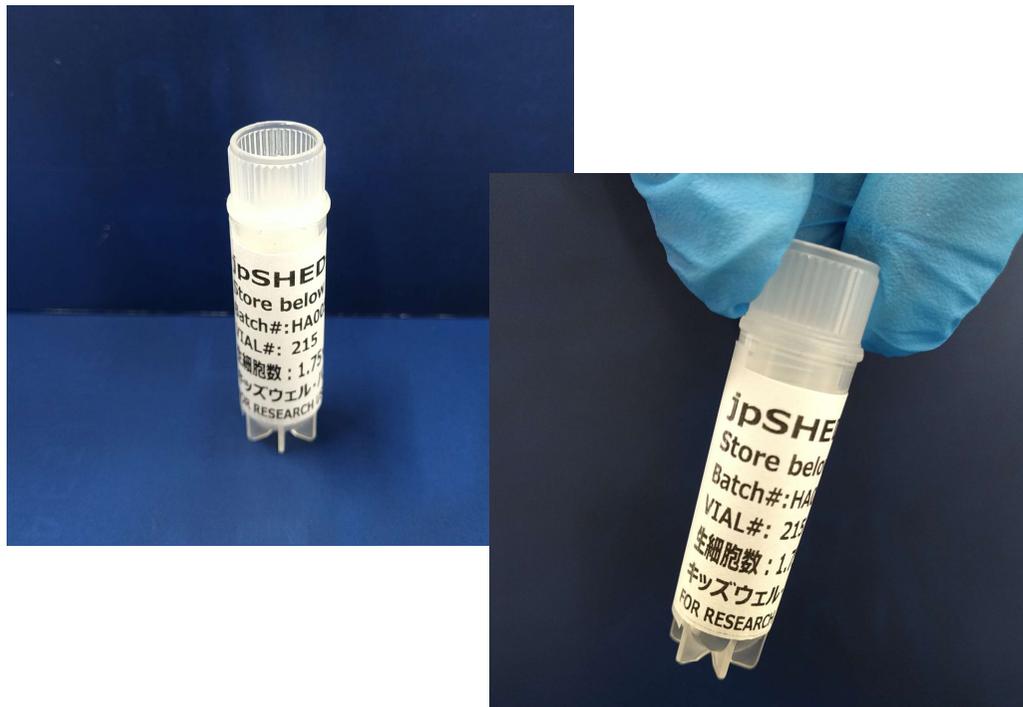
## First in the world!

### Essential component for high-quality cell therapy

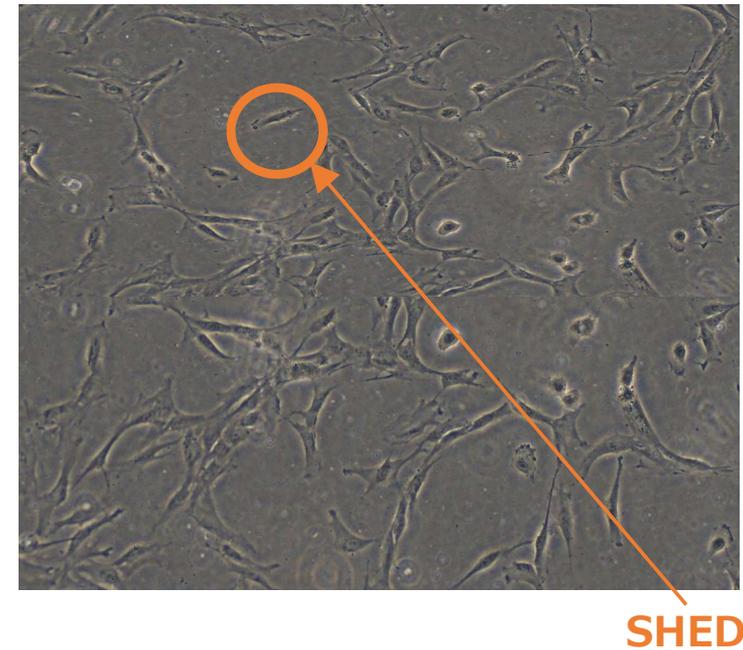
<p>Process</p>	 <p><b>Extract SHED<sup>※</sup></b></p>  <p><b>Isolation culture Selectively increase SHED</b></p>	 <p><b>Cell expansion</b></p>	 <p><b>SHED Master Cell Bank<sup>※</sup></b></p>
<p>Challenges</p>	<p><b>Isolation culture of SHED</b></p> <ul style="list-style-type: none"> <li>• Formulated criteria for extraction of deciduous teeth</li> <li>• Improved appropriate culture condition</li> <li>• Improved whole process from SEHD extraction to isolation culture</li> </ul>	<p><b>Cell (SHED) expansion</b></p> <ul style="list-style-type: none"> <li>• Improved conditions during culture days and culture methods (cell density, etc.)</li> <li>• Improved whole manufacturing process of cell expansion</li> </ul>	<p><b>SHED Master Cell Bank<sup>※</sup></b></p> <p>※ For the purpose of pharmaceutical manufacturing, specific cells are cultured and frozen in storage tube</p>

⇒ Solved various issues and improved processes by accumulated KWB's know-how

※ SHED : Stem cells from Human Exfoliated Deciduous teeth 4



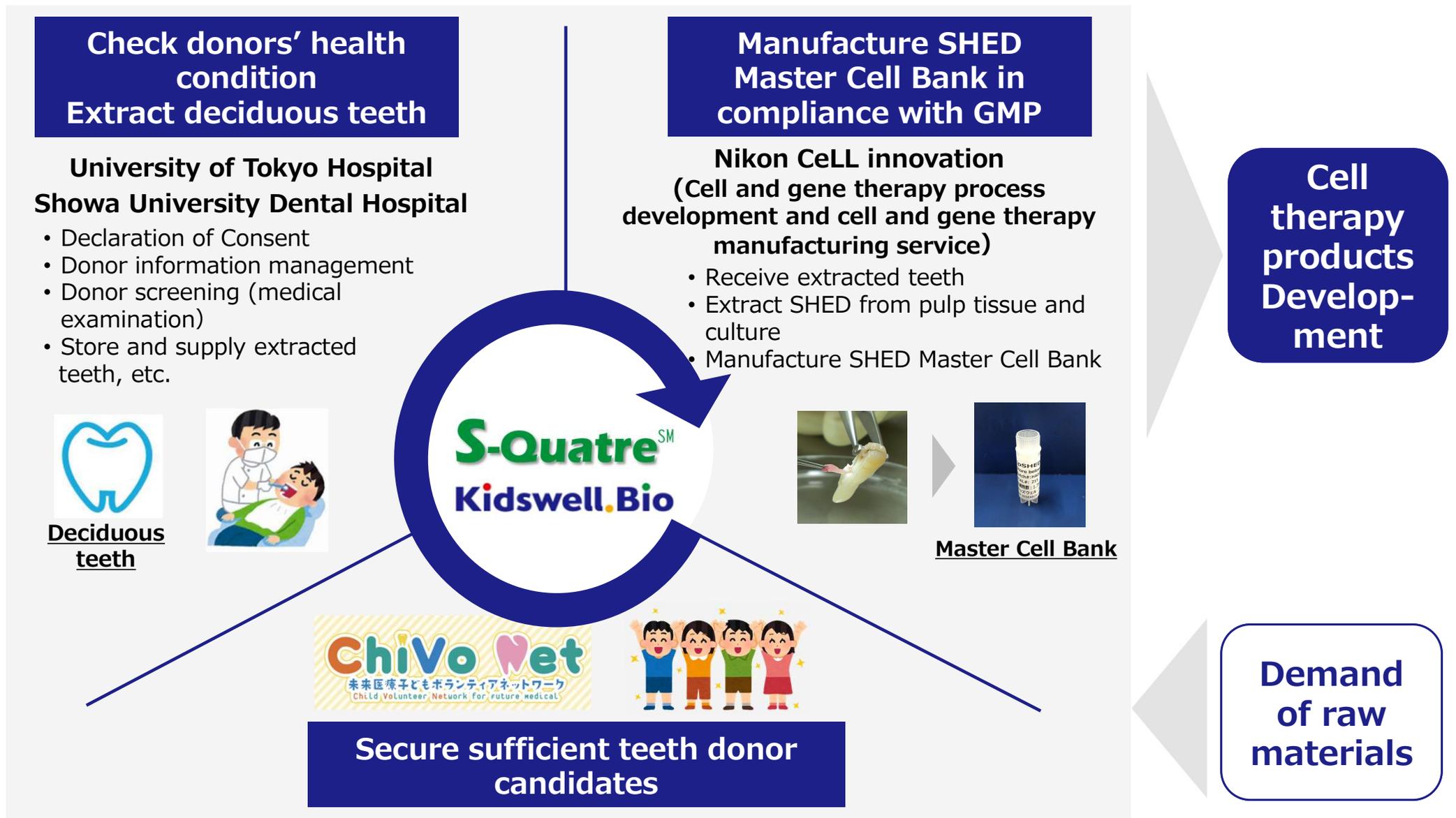
Frozen SHED MCB in a storage tube\*



Microscope image of SHEDs\*

\*Sample

## From teeth donation to SHED Master Cell Bank



## Launch the world's first SHED cell & gene therapy

### SHED: 1<sup>st</sup> generation

Strive to establish SHED business

**Target diseases: Diseases related to nervous, muscular and bone system**

**Market potential: Expect to grow 700 to 800 billion yen market size by 2040<sup>※1</sup> (Global)**

### SHED: 2<sup>nd</sup> generation

Designer cells

**Target diseases: Genetic disease, neurodegenerative disease and cancer**

**Market potential: Expect to grow over 1 trillion yen market size by 2028<sup>※2</sup> (e.g. CAR-T cell therapy: over 13.5 billion dollars in the world)**

### SHED Supply Business

For other modalities

- **Products utilizing SHED-derived cell organs and extracellular vesicles (exosome and mitochondria, etc.)**
- **Drug Delivery System utilizing SHED**

**Market potential: Expect hundreds of billions yen market size<sup>※3</sup>**

## SHED Master Cell Bank



## For improvement of corporate value



**KIDS WELL, ALL WELL**

**SHED Master Cell Bank Completed**

**Accelerating cell therapy products development**

**Focusing on SHED development**

- Accelerating development in overseas. in addition to domestic development
- Active investment in human resources and capital
- Accelerating R&D by fund-raising from overseas investors

**Launching cellular medicine /cell therapy products**

**Aiming to launch the world's first SHED medicine/ therapy by FY2030**

- Steady development progress in Japan and overseas
- Establishment of SHED platform
- Strengthening SHED business activities
- Diverse personnel structure, including experts of cell medicine development and human resources with knowledge of new modalities

**Establishment of revenue base**

**Establishment of biosimilar development technology**

- Strong sales of GBS-007
- Progress of the development of the 4<sup>th</sup> BS

**SHED + Human Resource Development**

**Maintaining stable revenue from biosimilar business**

Founded (2001) to FY 2021

FY 2022

FY 2025  
(3 billion yen of sales and 1 billion yen of operating profit)

FY 2030 onward

# KIDS WELL, ALL WELL



# Appendix

- Apply to various products utilizing SHED Master Cell Bank
- Established stable manufacturing and supply system for regenerative medicine products

## SHED Master Cell Bank

### SHED: 1<sup>st</sup> Generation

#### Strive to establish SHED business

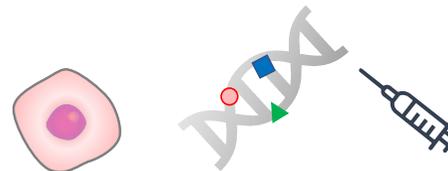
- Research collaboration with academia
- Drive activities for starting clinical research and trials



### SHED: 2<sup>nd</sup> Generation

#### Designer cells

- Introduce the next generation technologies (in vivo/ex vivo, virus, artificial chromosome, etc.)
- Combine SHED with other devices with synergistic effects



### SHED Supply Business

#### For other modalities

- Products utilizing SHED-derived cell organs and extracellular vesicles (exosome and mitochondria, etc.)
- Drug Delivery System utilizing SHED



**Accelerate to launch new cell & gene therapy**

**Strengthen SHED Supply Business**

## Strive to launch the world's first cell therapy fully utilizing the characteristics of SHED

### 1<sup>st</sup> generation

Pulp stem cells from neural crests are expected to be particularly applicable to **diseases of the nervous and muscle/bone systems**.

Features of SHED	Application for regenerative medicine
High proliferative ability <sup>※1,2</sup>	Sufficient cells in a short period of time
Expression of <b>neurogenesis</b> -related genes <sup>※1,3</sup> , high secretion of <b>nervous</b> system growth factor <sup>※1,4</sup> and high nerve <b>regenerative</b> ability <sup>※1,5</sup>	Diseases related to nerve regeneration (Ex. Spinal cord injury, brain infarction, cerebral palsy, etc.)
High <b>bone</b> regenerative ability <sup>※1,6</sup>	Diseases required bone regeneration (Ex. Non-union fracture, osteonecrosis of the femoral head, etc.)

※1: Data from KWB & Research collaboration, ※2: Miura et al. PNAS. 2003, ※3: Terunuma et al. J Stem Cell Regen Med. 2019, ※4: Mead et al. PLoS One. 2014, ※5: Sakai et al. J Clin Invest. 2012, ※6: Nakajima et al. BBRC. 2018

### Companies of cell medicine development (Japan)

Tissue type	Product name	Target disease	Company
<b>Deciduous teeth-derived</b>	(Non-clinical studies)	<b>Nervous and muscle/bone diseases</b>	<b>KWB</b>
Bone marrow-derived (Allogenic)	Temcell (Launched)	Acute GVHD	JCR Pharmaceuticals
Bone marrow-derived (Autologous)	Stemirac (Launched)	Spinal cord injury	Nipro Corporation
Adipose-derived (Allogenic)	Alofisel (Launched)	Perianal fistula	Takeda Pharmaceuticals

**Expect to launch an epoch-making cell (SHED) therapy for severe diseases**

### 2<sup>nd</sup> generation

**Focus on develop reinforced SHED with enhanced therapeutic efficacy**

#### Design Technology

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: Nagoya Univ., Hamamatsu University School of Medicine, etc )

#### Target diseases of development<sup>※</sup>

Genetic diseases  
Degenerative (Nerve)  
Cancer, etc.

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

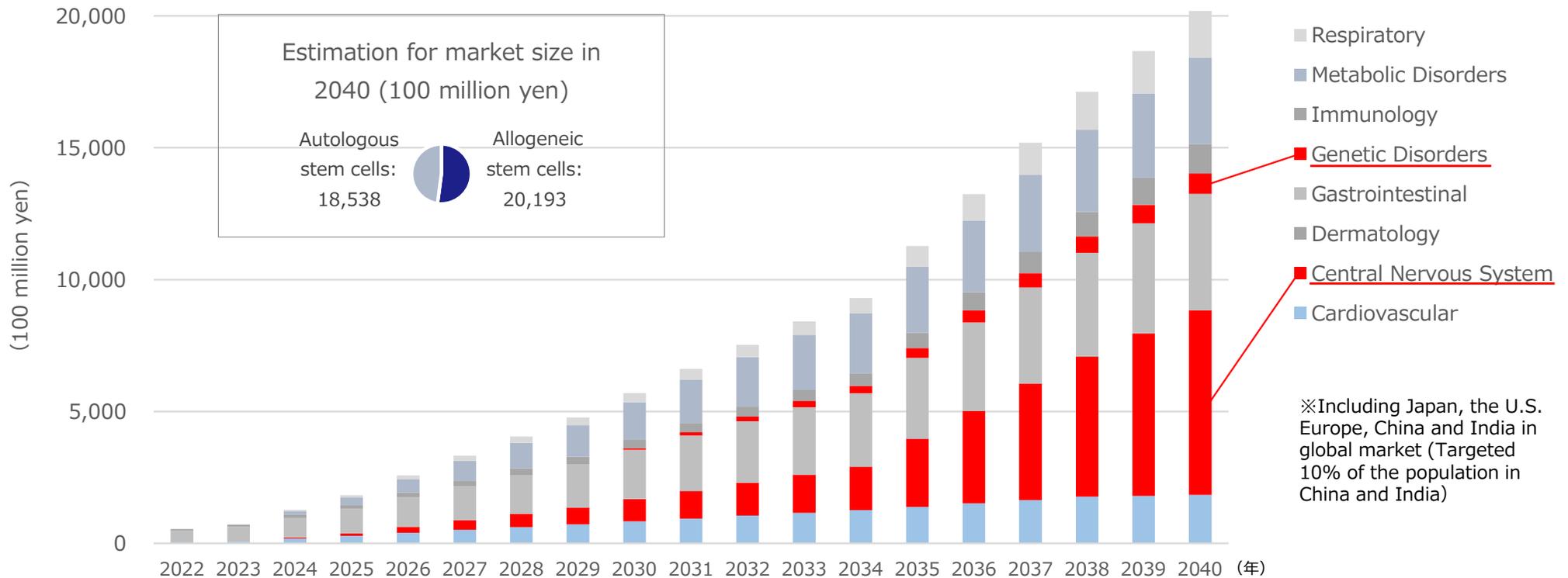
#### Cost-effective cell therapy (Evaluation results of NICE<sup>※</sup>)

Tissue type	Product name	Target disease	Company
Modified immune cells	Kymriah (Launched)	<ul style="list-style-type: none"> <li>Diffuse large B-cell lymphoma</li> <li>Follicular lymphomas</li> </ul>	Novartis

**KWB focuses on the development of a cost-effective cell (SHED) therapy.**

※National Institute for Health and Care Excellence

**Estimation: Nervous system and muscle/ bone diseases targeted by SHED will grow from 700 billion to 800 billion yen market by 2040.**



**Estimation for global market size of allogeneic stem cells**

**Accelerate SHED research & development as KWB's growth driver, expecting high profitability in growing global cell medicine market**

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

Term	Explanation
<b>Cell therapy (Regenerative Medicine)</b>	Cell therapy is the transplantation of human or animal cells to replace or repair damaged tissue. It includes utilizing immune cells in the blood, adipose-derived and born-derived mesenchymal stem cells.
<b>Designer cells</b>	Designer cells can enhance therapeutic efficacy and cell directionality for disease sites. They are of interest in the field of diseases without radical cure as a medical treatment of next generation.
<b>Exosome</b>	A tiny vesicle created and released from the plasma membrane of various types of cells, especially immune cells, and capable of inducing antigen-specific immune responses. Exosomes are of special interest in the field of medicine with their special ability.
<b>GMP</b>	<b>Good Manufacturing Practice (GMP)</b> is minimum required guidelines that a manufacturer must meet to assure that their products are consistently high in quality and work for their intended use. GMP is a part of a quality system covering the manufacture and testing of pharmaceutical ingredients, foods, pharmaceutical products, diagnostics, and medical devices.
<b>Master Cell Bank (MCB)</b>	Master Cell Bank (MCB) is cells for medical treatments that are expanded under the constant culture condition and divided into several vials for long frozen storage. Frozen MCB can be expanded again after thawing and utilized for regenerative medicine products as a raw material.
<b>SHED</b>	SHED : <b>S</b> tem cells from <b>H</b> uman <b>E</b> xfoliated <b>D</b> eciduous teeth SHED is a mesenchymal stem cell (MSC) extracted from a dental pulp cavity inside exfoliated deciduous teeth and is easy to differentiate into bone and nerve cells. Especially SHEDs from young donors have shown higher proliferative activity and secretory capacity of various growth factors (particularly neurotrophic factors) compared to stem cells from other tissues.