GENE TECHNO SCIENCE

Unlimited drug discovery from the beginning

MOthers
Ticker symbol:
4584

Gene Techno Science Co., Ltd.

Financial results for the second quarter of the fiscal year ending March 2018

November 16, 2017

Mount Tokachi

GENE TECHNO SCIENCE

Corporate overview and business highlights

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Corporate overview

Chief Executive		Masaharu Tani, President
Founded		March 2001
Listed on the stock exchange		November 2012 (Tokyo Stock Exchange Mothers Index)
Capital		100 million yen (as of August 1, 2017)
Locations	Head office	Kita 2-Nishi 9-1, Chuo-ku, Sapporo
	Tokyo office	2-10-8 Nihonbashi, Chuo-ku, Tokyo
	Laboratory	Kita 21-Nishi 11, Sapporo Inside the Center of Promotion for Platform for Research on Biofunctional Molecules, Hokkaido University Creative Research Institution

Time		Event
2001	March	GTS founded to translate findings from research conducted at the Institute for Genetic Medicine at Hokkaido University into diagnostic reagents and drugs
2007	June	Out-licensed anti-α9 integrin antibody to Kaken Pharmaceutical Co., Ltd.
	October	Signed joint development agreement for filgrastim (G-CSF) biosimilar with Fuji Pharma, Co., Ltd.
2012	November	Listed on the Tokyo Stock Exchange Mothers Index and obtained marketing approval for filgrastim biosimilar
2013	May	Filgrastim biosimilar listed in NHI price list and brought to market
	August	Formed capital and business alliance for biosimilars with ITOCHU CHEMICAL FRONTIER Corporation
2014	January	Signed joint development agreement for darbepoetin alfa biosimilar with Sanwa Kagaku Kenkyusho Co., Ltd. (started phase III clinical trial in Sep 2016)
2016	April	Joined Noritsu Koki Group through common stock takeover bid and formed capital and business alliance
	May	Signed collaboration agreement with Senju Pharmaceutical Co., Ltd. for biosimilars in the field of ophthalmology Signed agreement with Changchun Changsheng Life Sciences Ltd. to expand our biosimilar business to the Chinese market
	October	Formed capital and business alliance with Japan Regenerative Medicine Co., Ltd. (JRM) to develop business in regenerative medicine using cardiac stem cells
	December	Signed collaboration agreement with Mochida Pharmaceutical Co., Ltd. for biosimilars in the field of oncology
2017	February	Signed joint research agreement with Juntendo University for immune tolerance induction technology
	March	Formed capital and business alliance for developing new biosimilars with ITOCHU CHEMICAL FRONTIER Corporation

Business model

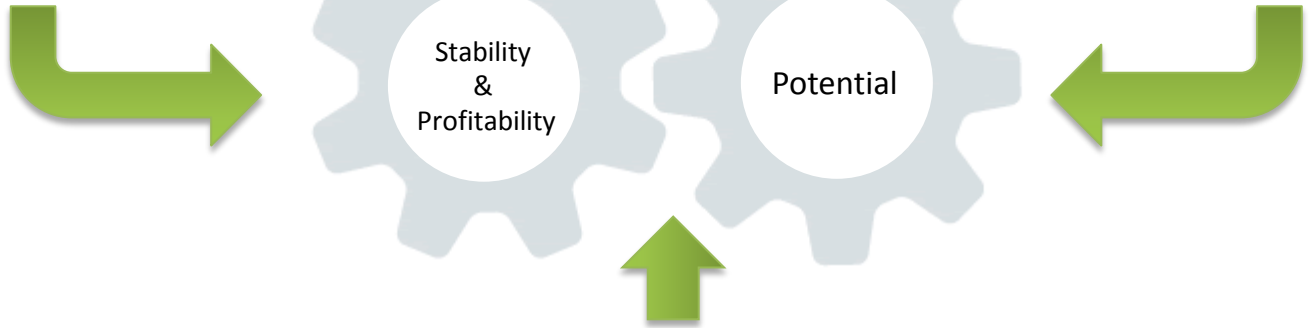
A hybrid business structure consisting of biosimilars and new biologics with the addition of a regenerative medicine business

Biosimilar business

- Development and provision of drug substances
- Alliances with pharmaceutical companies

New biologics business

- R&D centered on therapeutic antibodies
- Laboratory at Hokkaido University Creative Research Institution

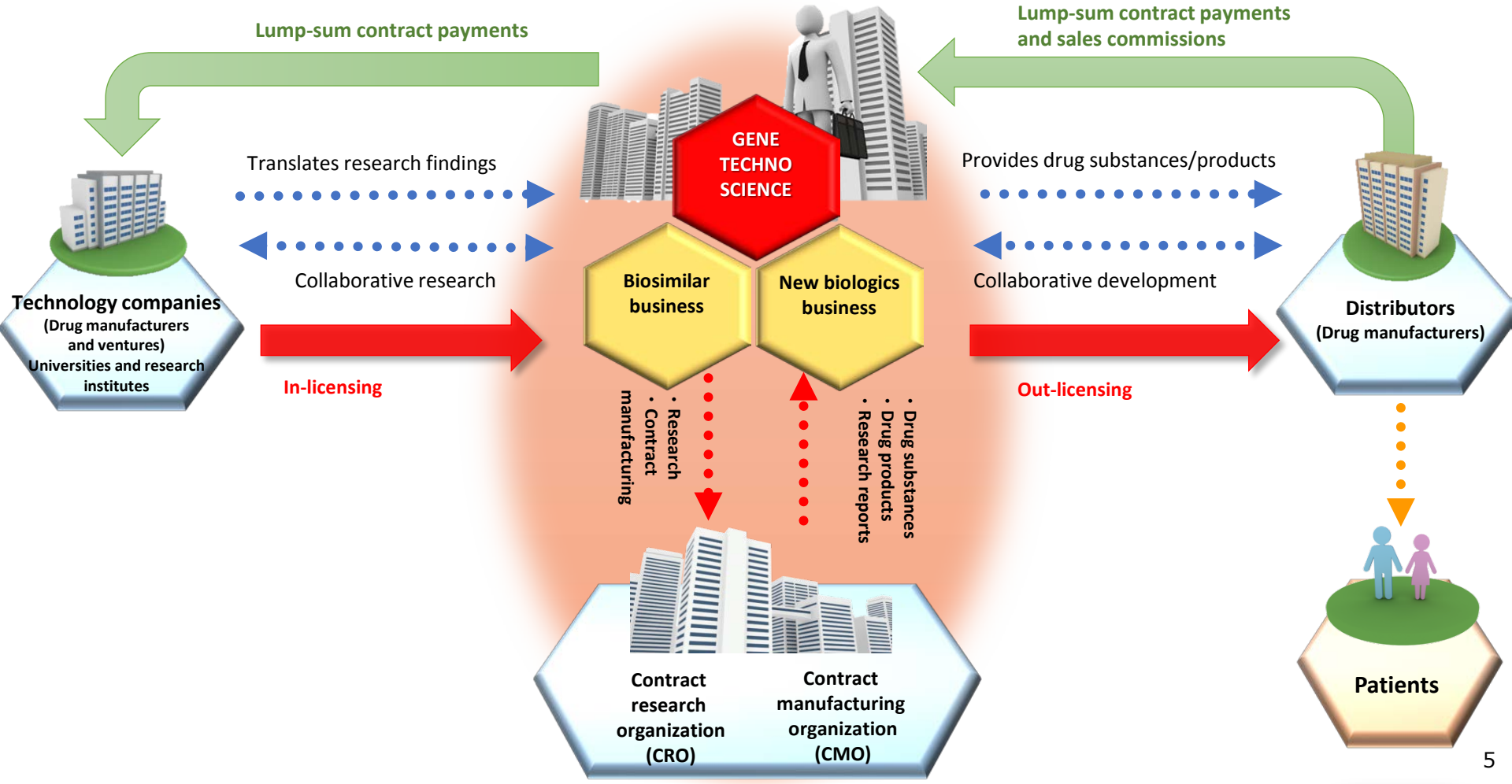


Regenerative medicine business

Business development system

Advantages of a fabless business model

1) **Flexibility: Can structure the optimal collaborative system for each project**
2) **Speed: Can start projects quickly and change plans quickly**
3) **Investment risk: Avoid large capital investments in items such as manufacturing equipment**



Financial results from the second quarter of the fiscal year 2018 (April–September)

◆ Financial results from the second quarter (April–September)

	Sales (in millions of yen)	Operating profit (in millions of yen)	Ordinary profit (in millions of yen)	Net profit for the quarters (in millions of yen)	* Per share Net profit for the quarters (in yen)
Results from April–September of fiscal year 2017 (A)	490	△731	△757	△803	△92.85
Results from April–September of fiscal year 2018 (B)	446	△431	△427	△428	△44.77
Change (B-A)	△44	300	330	375	

* The company split each share into 2 shares on October 1, 2016. Per-share net profit for the quarter was calculated based on the assumption that the split was conducted at the beginning of fiscal year 2017.

Financial forecasts for fiscal year 2018

*Unaltered initial forecasts

◆ Sales and profit forecasts

	Sales (in millions of yen)	Operating profit (in millions of yen)	Ordinary profit (in millions of yen)	Net profit for the quarters (in millions of yen)	Per share net profit for the quarters (in yen)*
Results from fiscal year 2017 (A)	1,089	△1,184	△1,176	△1,224	△137.01
Forecasts for fiscal year 2018 (B)	1,166	△977	△992	△994	△103.96
Change (B-A)	77	207	184	230	

- ✓ We predict that sales of filgrastim will remain steady
- ✓ We expect to receive income from contracts for GTS-developed products with partner companies and achievement of development milestones
- ✓ We are actively pursuing an increase in upside through alliance-making efforts

- ✓ Sales of filgrastim alone are predicted to fully cover fixed expenses
- ✓ We will appropriate any retained earnings exceeding fixed expenses to R&D expenses, and predict that this will reduce losses while also accelerating R&D progress

◆ R&D expense forecasts

	R&D expenses (in millions of yen)
Results from fiscal year 2017 (A)	1,433
Forecasts for fiscal year 2018 (B)	1,197
Change (B-A)	△236

- ✓ We will pass peak R&D spending
- ✓ We will accelerate R&D efforts to ensure sound progress with product launches

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Business highlights from fiscal year 2017

Regenerative medicine

Established Minerva Medica and started joint research with Sapporo Medical University

- We established the Hokkaido-based regenerative medicine venture company Minerva Medica and signed a joint research agreement with Sapporo Medical University **(announced June 7)**
- Four companies and financial institutions with offices in Hokkaido, including GTS, provided the investment to launch the venture
- Findings will be applied to create the world's first treatment for diabetic nephropathy using mesenchymal stem cells

New biologics

Submitted patent application related to new antibody drug candidate

- We discovered a new antibody drug candidate that inhibits neovascularization through a novel mechanism **(announced September 13)**
- Applied for patent in September 2017
- We aim to use this antibody to discover new drugs in the fields of ophthalmology and oncology

Regenerative medicine

Subcontracted work to develop an immune tolerance induction business to MEDINET Co., Ltd.

- Subcontracted work to MEDINET, a company specialized in cell processing **(announced September 27)**
- We aim to establish a cell therapy platform to apply the technology for induction of immune tolerance that we are jointly researching with Juntendo University
- They will develop manufacturing processes, shipping methods, and safe storage methods for the product, then proceed to clinical studies

Biosimilars

Officially launched collaboration with Changsheng Bio on adalimumab biosimilar

- Finished transferring our drug substance manufacturing technology to Changsheng Bio **(announced September 28)**
- Adalimumab, the drug being developed, is a blockbuster drug that generates over 1 trillion yen in sales globally
- After this, we will accelerate development with the aim of getting approval in China. Will receive milestones according to the development stage

Biosimilars

Started phase III study for ophthalmology biosimilar being jointly developed with Senju Pharmaceutical

- We started a phase III clinical study for an ophthalmology biosimilar jointly developed with Senju Pharmaceutical in November **(announced November 9)**
- We aim to bring this drug to the Japanese market in 2020 or later
- We are also looking to market overseas in the near future, and are planning a wide range of business development efforts

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Biologics market

- New biologics and biosimilars -

Top 10 Best-Selling Drugs in the World (2016)

Biologics continue to dominate the top 10 sellers!

7 of 10 in 2016!!!

Drugs in red are biologics

Ranking	Brand name	Generic name	Indication	Manufacturer	Sales (millions of USD)
1	Humira	Adalimumab	Rheumatism/Psoriasis	AbbVie/Eisai	16,515
2	Enbrel	Etanercept	Rheumatism/Psoriasis	Amgen/Pfizer/Takeda	9,248
3	Harvoni	Ledipasvir + sofosbuvir	Hepatitis C	Gilead Sciences	9,081
4	Remicade	Infliximab	Rheumatism/Crohn's disease	J&J/Merck/Tanabe Mitsubishi	8,070
5	Lantas	Insulin glargine	Diabetes	Sanofi	8,027
6	Rixutan	Rituximab	Cancer/Lymphoma	Biogen/Roche/Chugai	7,482
7	Revlimid	Lenalidomide	Multiple myeloma	Celgene	6,974
8	Avastin	Bevacizumab	Cancer/Colon and breast cancer	Genentech/Roche/Chugai	6,885
9	Herceptin	Trastuzumab	Cancer/Breast cancer	Genentech/Roche/Chugai	6,884
10	Januvia	Sitagliptin	Diabetes	Merck	6,440

Source: Our own analysis referencing Evaluate Pharma 2017

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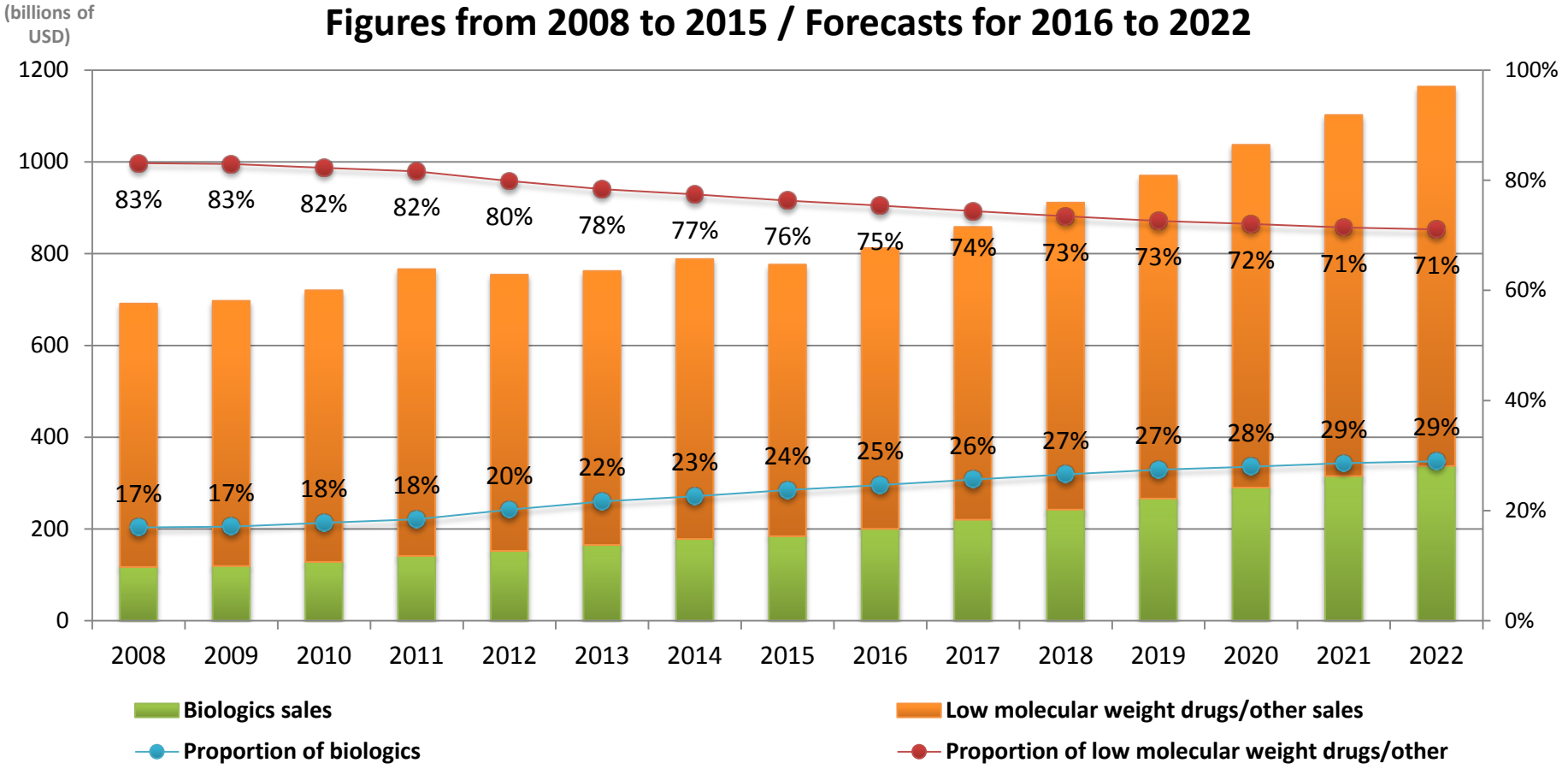
Expansion of the biologics market

Total global drug sales and share of biologics

Figures from 2008 to 2015 / Forecasts for 2016 to 2022

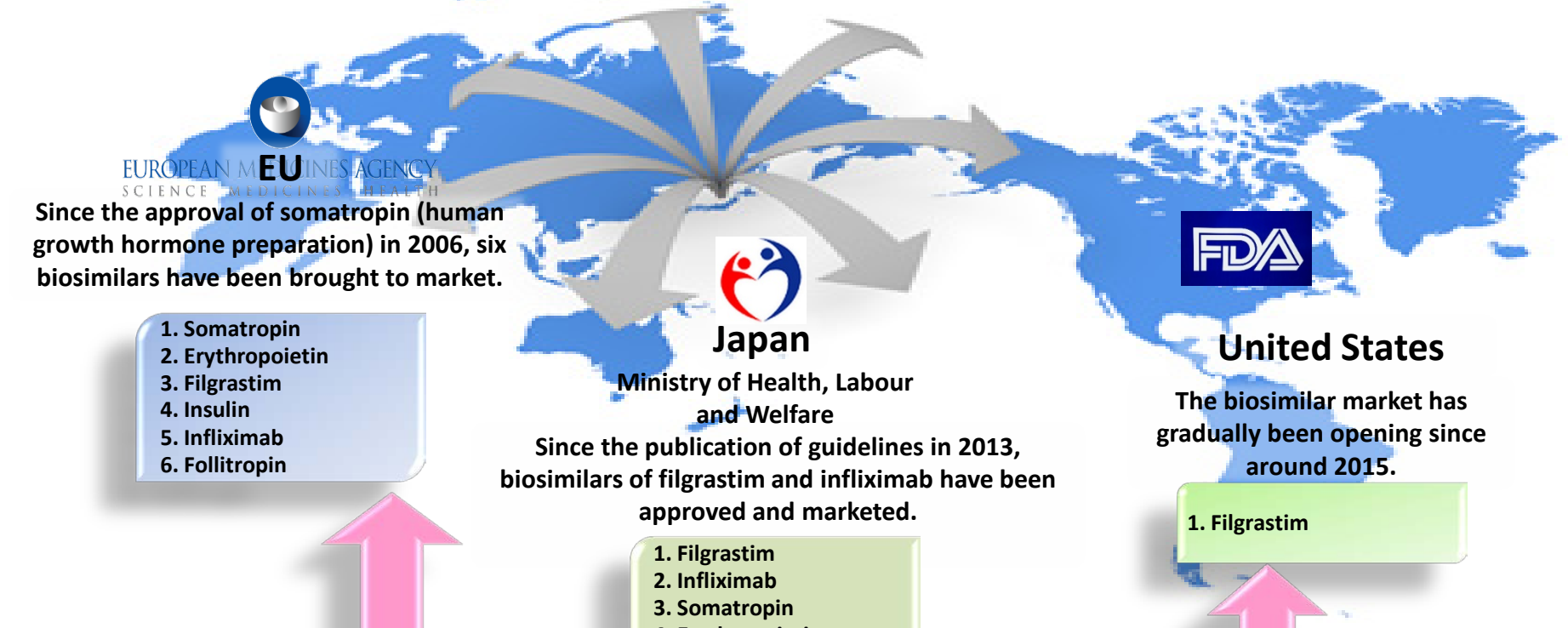


Source: Modified from Evaluate Pharma materials

In the year 2022, the global market share of biologics in terms of sales...
is predicted to increase to 29% and 337 billion dollars.
= The biologics market is expanding!

Biosimilar market: Products brought to market

Biosimilar development is steadily progressing in every country and region of the world.



EU

Since the approval of somatropin (human growth hormone preparation) in 2006, six biosimilars have been brought to market.

1. Somatropin
2. Erythropoietin
3. Filgrastim
4. Insulin
5. Infliximab
6. Follitropin

New marketing approvals obtained

January 2016: Etanercept biosimilar (Samsung Bioepis)
January 2017: Teriparatide biosimilar (STADA, Gideon Richter)
February 2017: Rituximab biosimilar (Celltrion)
March 2017: Adalimumab biosimilar (Amgen)

Japan

Ministry of Health, Labour and Welfare

Since the publication of guidelines in 2013, biosimilars of filgrastim and infliximab have been approved and marketed.

1. Filgrastim
2. Infliximab
3. Somatropin
4. Erythropoietin
5. Insulin

United States

The biosimilar market has gradually been opening since around 2015.

1. Filgrastim

New marketing approvals obtained

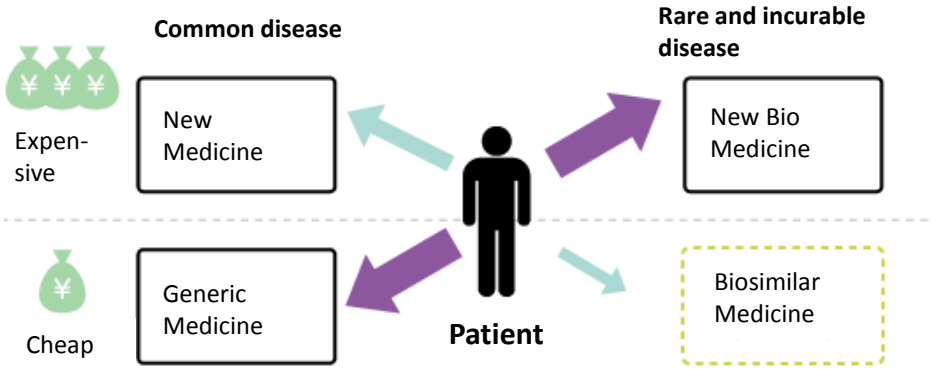
April 2016: Infliximab biosimilar (Pfizer/Celltrion)
August 2016: Etanercept biosimilar (Sandoz)
September 2016: Adalimumab biosimilar (Amgen)
April 2017: Infliximab biosimilar (Samsung Bioepis)

The societal need for biosimilars

Question: Why are medical costs not decreasing despite steady adoption of generics?

Reason: The use of expensive biologics is canceling out the effect of switching to generics.

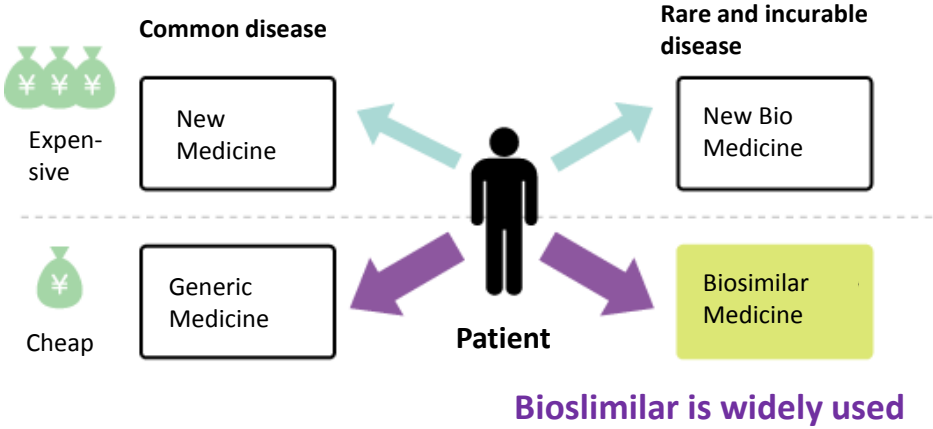
Current situation



△

- **Use of biologics produces high medical costs.**
- **Even as generics are adopted, the use of expensive biologics also increases, and society as a whole does not see a large reduction in medical costs.**

Ideal situation



Bioslimilar is widely used

○

- **Lower medical costs!**
- **Lower medical costs mean that more patients can receive advanced care.**
- **Reduces the strain of healthcare financing on the Japanese government**

Biosimilars hold the key to reducing medical costs!

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New biologics business

Discovered a new antibody that inhibits neovascularization through a novel mechanism

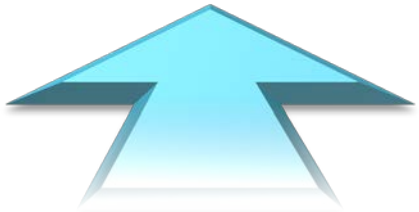
Target market: Scale of 1.5 to 2.0 trillion yen

(1) Take market share from existing anti-VEGF drugs
(2) Create a new market by providing a new treatment option for patients who do not respond to existing anti-VEGF drugs

Refer to: Rough estimate of the scale of anti-VEGF drug market

2016	Ophthalmology (Eylea/Lucentis)	Oncology (Avastin)
(in Japan)	¥65 billion	¥92 billion
(outside Japan)	¥950 billion	¥700 billion

Calculated from Evaluate Pharma materials and financial materials available from drug manufacturers.



We successfully discovered a new antibody and will accelerate research and development of new biologics!

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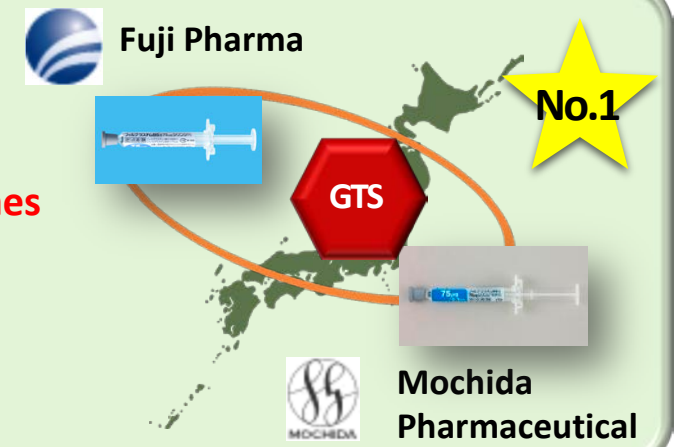
Biosimilar business

Successes in developing our biosimilar business

◆ Filgrastim biosimilar brought to market in Japan

First Japanese biosimilar following the biosimilar guidelines

Nov 2012	Obtained marketing approval
May 2013	Started sales in Japan through Fuji Pharma and Mochida Pharmaceutical



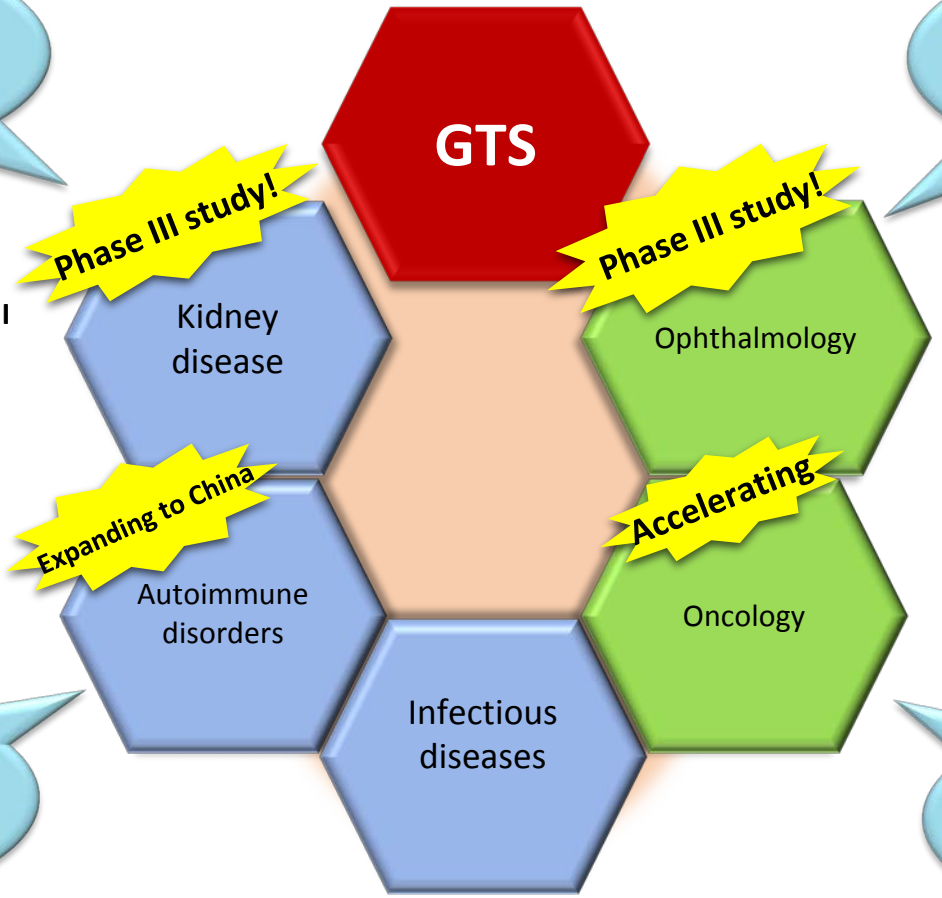
◆ Gene Techno Science
Drug substance development

◆ Fuji Pharma/Mochida Pharmaceutical
Clinical development and sales

Filgrastim biosimilar injection ○○ μg syringe "F"/"Mochida"

We are also seeing steady growth in sales for fiscal year 2018!

Advances in our biosimilar business



Business alliance with Sanwa Kagaku Kenkyusho

January 2014–

Nesp biosimilar

- **September 2016:Started phase III clinical study**

Capital and business alliance with Senju Pharmaceutical

November 2015–

- **May 12, 2016: Signed collaboration agreement**
- **November 2017: Started phase III clinical study**

Collaboration with Changsheng Bio (China)

May 2016–

Humira biosimilar

- **September 28, 2017: Completed transfer of drug substance manufacturing technology**
- **We aim to bring this drug to the Chinese market**

Business alliance with Mochida Pharmaceutical

August 2015–

- **December 5, 2016: Signed collaboration agreement**

Progress in our biosimilar pipeline

Development code	R&D	Phase I clinical study	Phase III clinical study	Application submitted/ reviewed Approved/ marketed	Rough estimate of the scale of the biosimilar market* Japan	Global (excluding Japan)
GBS-001 (cancer) Filgrastim					¥8 billion	¥40 billion
GBS-010 (cancer) PEG-filgrastim					¥8 billion**	¥208 billion
GBS-011 (kidney disease) Darbepoetin alfa					¥22 billion	¥92 billion
GBS-005 (autoimmune disorders) Adalimumab					¥14 billion	¥520 billion
GBS-007 (eye diseases)			Progressing!		¥25 billion***	¥307 billion***
GBS-008 (infectious diseases) Palivizumab					¥15 billion	¥59 billion
GBS-004 (cancer) Bevacizumab					¥38 billion	¥250 billion
				Total	¥130 billion	¥1476 billion

* It is estimated that the biosimilar market will be about 40% of the brand name drug market in terms of sales. (Biosimilar penetration rate of 60% × Cost is 70% that of brand name drugs = 42%)

** Because brand name sales started in 2014, the drug price calculation is for a new drug. Peak sales were used as reference values (Central Social Insurance Medical Council; November 26, 2014).

*** To avoid disclosing the name of the drug, the scale of the ophthalmology biologics market was used as a reference value.

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New biologics business

- Projects in regenerative medicine (cell therapy) -

Capital and Business Alliance with Japan Regenerative Medicine Co., Ltd. (JRM)

Reasons

- **Stepping into the field of regenerative medicine!**
- **Starting a new pipeline using cardiac stem cells that JRM is developing.**

Establishing treatments using cardiac stem cells!

- **JRM-001 is a cell therapy product that JRM has been developing since the technology was transferred from Dr. Hidemasa Oh of Okayama University Hospital.**
- **It is a cell suspension of cardiac stem cells produced by isolating and culturing autologous heart tissue collected during heart surgery.**
- **Transplantation of JRM-001 into the coronary artery of the heart using a catheter about 1 to 1.5 months after surgery could potentially regenerate heart tissue and improve heart function.**

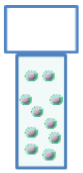
The first application will be for treatment of congenital heart disease in children!

Hospital → JRM → Hospital

1. Operational repair to treat single ventricle disease

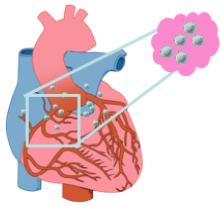
CPC center

3. Receive material

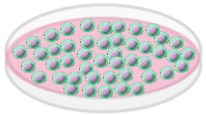


5. Dispatch JRM-001

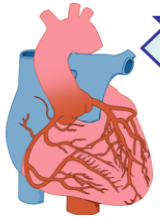
Expected improvement in heart activity



2. Obtain autologous tissue from heart during operation



4. Culturing the separated heart stem cell



6. Transplant into the heart

Source: Prepared from JRM materials

Cardiac stem cells hold hidden potential for new treatments for serious heart disease in Japan, where heart transplants are still difficult to get.

Joint research with Juntendo University

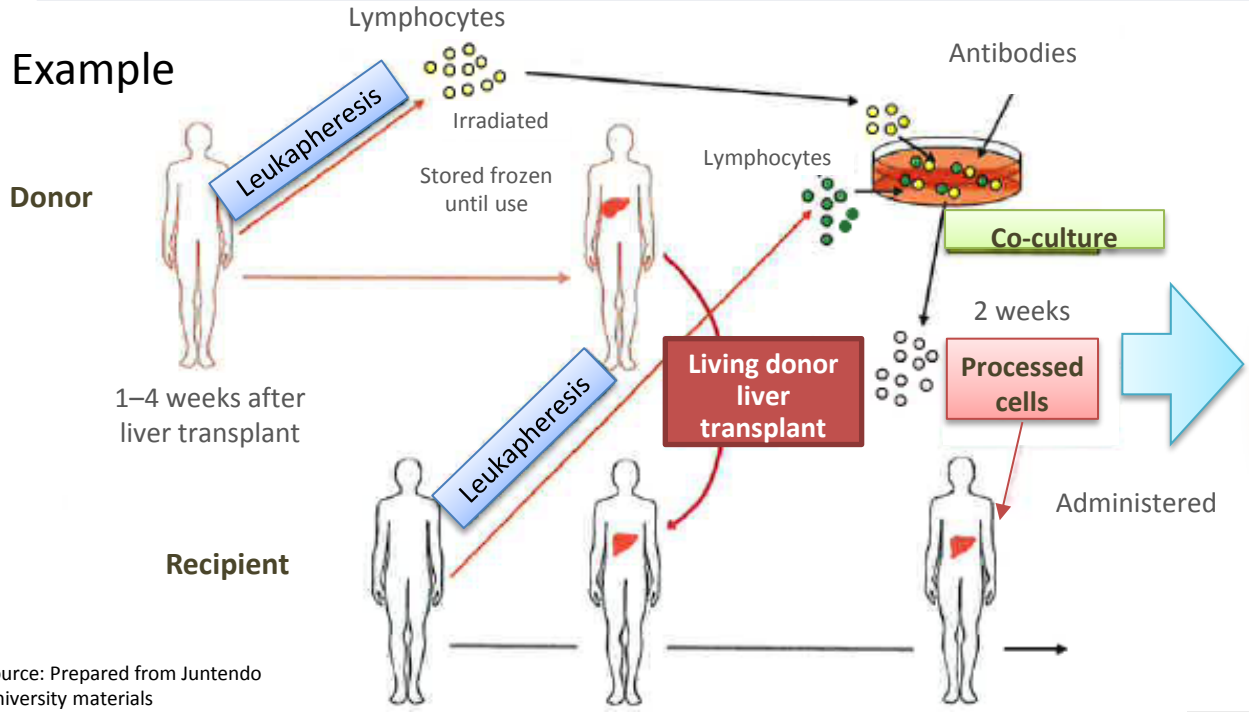
Reasons

- **Taking our next steps in the field of regenerative medicine!**
- **Expanding our immune tolerance induction technology to applications such as preventing transplant rejection and treating allergies.**

To establish the world's first technology for induction of immune tolerance!

- **We are conducting research on therapies involving control of immune function.**
- **Using organ transplantation as an example, white blood cells collected from the body are processed with donor immune cells in a culture machine to induce immune tolerance. Transplantation of these processed cells into the organ recipient (i.e., cell therapy) could potentially suppress rejection of the transplanted organ.**

Example



Source: Prepared from Juntendo University materials

Progressing!

September 2017
Signed contracting agreement with MEDINET Co., Ltd.

- ✓ We are conducting joint development with MEDINET, a company specialized in cell processing
- ✓ After establishing manufacturing processes, shipping methods, and safe storage methods for regenerative medicine products that utilize this technology, we will conduct clinical studies and bring products to market in the near future

We foresee applications in the treatment of autoimmune disorders, complications of organ transplants, and allergies (allergic rhinitis).

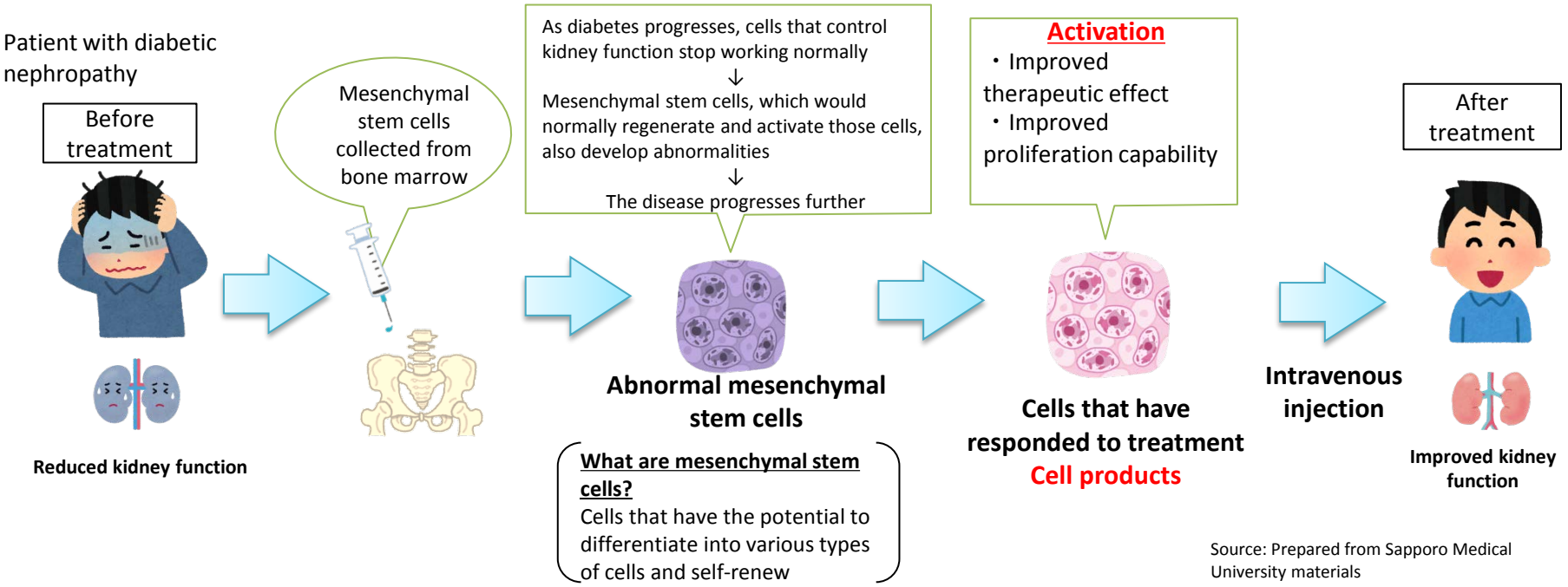
Established Minerva Medica and started joint research with Sapporo Medical University

Reasons

- **Taking even further steps in the field of regenerative medicine!**
- **Applying research findings to create the world's first treatment for diabetic nephropathy using mesenchymal stem cells**

Striving to overcome diabetic nephropathy for 9 million patients with diabetes!

- **Utilizing our own mesenchymal stem cells to treat kidney failure caused by diabetes**
- **It is not a symptomatic treatment for diabetes like diet therapy or dialysis, but rather enables radical treatment of kidney function by promoting treatment of the cells themselves**



Source: Prepared from Sapporo Medical University materials

We aim to utilize this technology to establish radical treatments for patients suffering from kidney failure and patients who currently have no other option but dialysis

Starting up a new biologics business focused on regenerative medicine

Research and develop treatments for refractory diseases and rare diseases using cutting-edge technology.

↓

- Ensure high growth potential and distribute development risk -

JRM

Juntendo University

Minerva Medica (Sapporo Medical University)

Develop cell and gene therapy products that use cardiac stem cells

- These have potential for treating and curing **serious heart diseases (e.g., diseases that require organ transplantation)** in Japan, where organ transplantation is rare and subject to many restrictions.

Develop new immunosuppressive therapies that use immune tolerance technology

- These have potential for treating or curing **common diseases and symptoms** such as allergic rhinitis and food allergies.
- Controlling immune function and suppressing transplant rejection could help ensure effective treatment of diseases that require organ transplantation.

Apply research findings to create treatments for diabetic nephropathy using mesenchymal stem cells

- Utilizing our own mesenchymal stem cells to treat kidney failure caused by diabetes
- It is not a symptomatic treatment for diabetes like diet therapy or dialysis, but rather has the potential to enable radical treatment of kidney function by promoting treatment of the cells themselves

Boost growth!

- Future revenue sources
- Distribute development risk

The role of GTS

Support development of the above three businesses by utilizing our experience and expertise in areas such as drug R&D and marketing approval applications cultivated through our biosimilar business!

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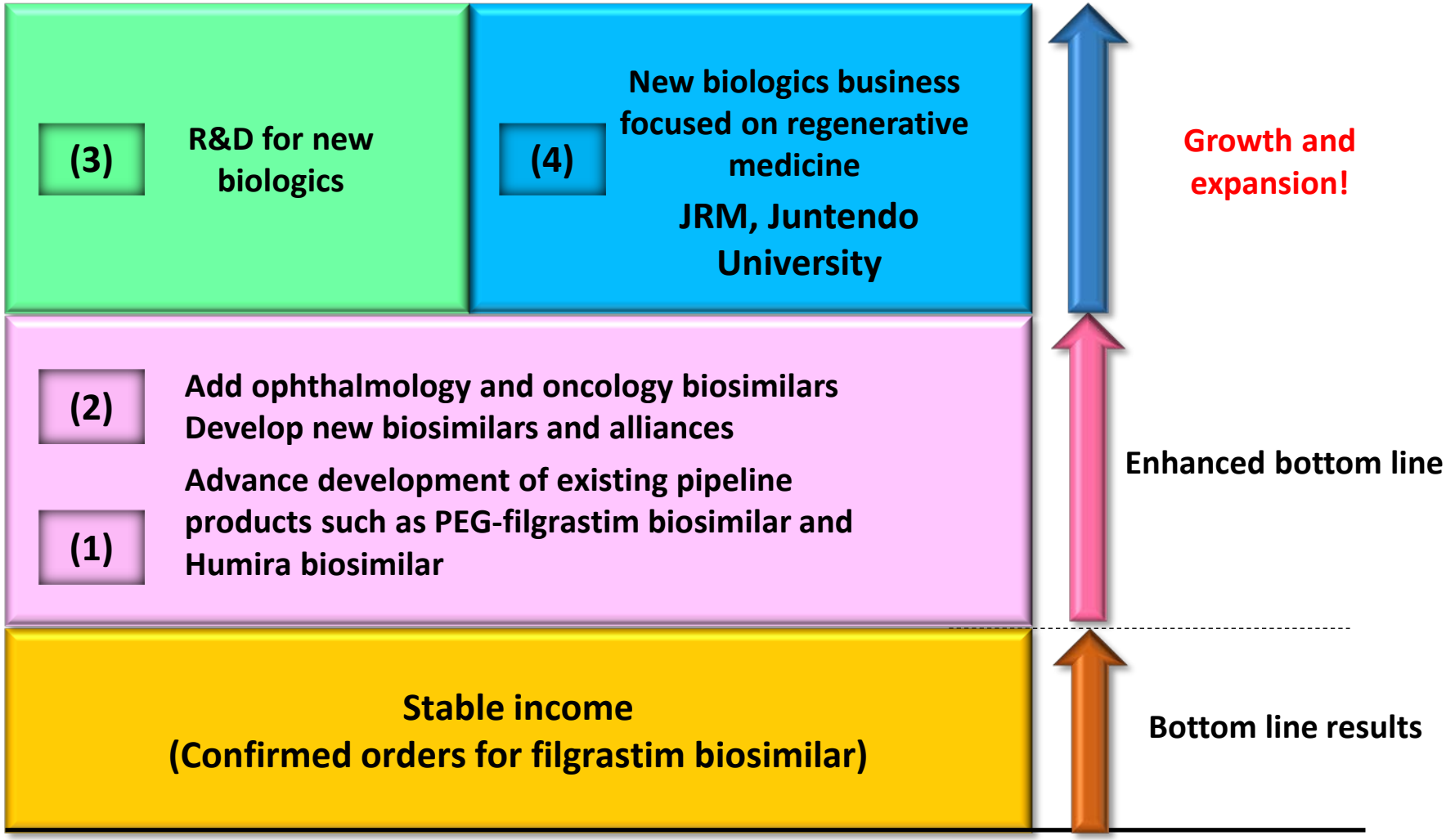
Medium-term vision

Medium-term income vision

We are expanding into new biologics and regenerative medicine using biosimilars as a stepping stone!



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We are becoming a profitable and growing bio-venture!

Keep an eye on our progress!

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Thank you for coming today.

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Unlimited drug discovery from the beginning