COMPANY RESEARCH AND ANALYSIS REPORT

Gene Techno Science Co.,Ltd.

4584

TSE Mothers

30-Aug.-2018

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Summary

Has in sight the market launches of multiple pipeline development drugs and has started measures toward further business expansion

Gene Techno Science Co.,Ltd. <4584> (hereafter, also "the Company") is a drug discovery bioventure originating from Hokkaido University. It specializes in biologics and biosimilars, and it was the first company in Japan to market launch a filgrastim biosimilar from among all the biosimilars launched in accordance with the Japanese biosimilar guidelines. In 2016, it became a group company of Noritsu Koki Co., Ltd. <7744>, and it is also entering the field of regenerative medicine as a new biotech business, following its biosimilar and new biologic businesses. It is aiming to be an engineering company that creates value in the bio field.

1. Overview of the FY3/18 results

In the FY3/18 results, net sales decreased 2.7% year-on-year (YoY) to ¥1,059mn and the operating loss was ¥913mn (compared to a loss of ¥1,184mn in the previous fiscal year). Net sales were basically as forecast, with sales of the filgrastim BS (biosimilar) increasing 3.6% to ¥852mn, and in addition, revenue from intellectual property rights, etc., rising 41.1% to ¥121mn. In terms of costs, R&D costs declined, down 22.7% to ¥1,107mn, which was the main reason for the reduction in the operating loss. For the progress made in the development pipeline, the biosimilar in the ophthalmology field (an age-related macular degeneration therapeutic agent) that the Company is jointly developing with Senju Pharmaceutical Co., Ltd., started phase 3 clinical trials in November 2017. Also, for the new biotech business, it established Minerva Medica Co., Ltd. (in May 2017), and it has started joint research through the Company for a treatment for diabetic nephropathy using autologous bone marrow mesenchymal stem cells, which is being researched by Sapporo Medical University.

2. Movements in the development pipeline

Looking at the main movements in the development pipeline in the biosimilar business, the phase 3 clinical trials of darbepoetin alfa BS (a renal anemia therapeutic agent) are being progressed by its joint-development partner Sanwa Kagaku Kenkyusho Co., Ltd. They are expected to be completed during 2018, with the aim of applying for manufacturing and sales approval during FY3/19 and then a domestic market launch in the first half of 2020. Also, the phase 3 clinical trials of the biosimilar in the ophthalmology field will be completed around 2020 and the goal is to market launch it during 2021. Overseas also, the Company intends to conclude various agreements during FY3/19, while it is also aiming to acquire manufacturing and sales approval for the PEG-filgrastim BS in the 2020s.

3. The business strategy for the future

In the biosimilar business from 2020 onwards, the Company has in sight the market launches of multiple pipeline biosimilars, while it has indicated that its policy is to achieve further growth by working to develop the new biologics business and a new biotech business that will be centered on the regenerative medicine field. It also intends to expand the fields it targets to pediatric diseases, in addition to the previously targeted fields of intractable and rare diseases. For new biologics, the Company is conducting licensing-out activities for GND-004 targeting the ophthalmic diseases and cancer fields, while it also progressing joint development with academia for multiple development candidate drugs. In addition, in the regenerative medicine field, its joint-research partner, Japan Regenerative Medicine Co., Ltd., is conducting clinical trials on cell therapy for childhood congenital heart disease using intra-cardiac stem cells, toward a market launch in Japan during the 2020s at the earliest, while it also plans to progress its development for the markets in Europe and the United States.

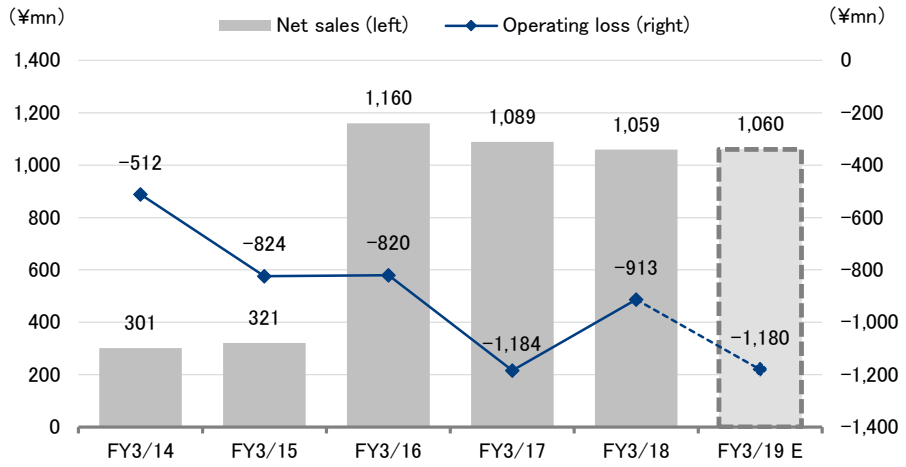
4. Results outlook

The forecasts for FY3/19 are for net sales to be around the same level YoY, at ¥1,060mn, and an operating loss of ¥1,180mn. Sales of filgrastim BS are expected to be the same as in the previous fiscal year, while the higher R&D costs will cause the operating loss to increase. So the operating loss is expected to continue for the time being due to the upfront investment in R&D costs, but the Company will enter a sales-growth phase from around 2021 onwards, which is when the ophthalmology-field biosimilar is scheduled to be market launched. So it has in sight becoming profitable in the near future.

Key Points

- A bioventure originating from Hokkaido University that is a pioneer in biosimilar development in Japan
- Following on from the biosimilar and new biologics businesses, is starting measures for a new biotech business (regenerative medicine field) as its third business
- Expected to achieve operating profit during the 2020s following the scheduled market launches of multiple biosimilars

Results trends



Source: Prepared by FISCO from the Company's financial results

Company profile

A bioventure originating from Hokkaido University that is a pioneer in biosimilar development in Japan

1. History

The Company is a bioventure company that was established within Hokkaido University in 2001 with the objective of developing diagnostic and therapeutic agents based on the research of the University's Division of Molecular Interaction in the Institute for Genetic Medicine. In terms of research and development of new biologics, it licensed-out the anti-integrin alpha 9 antibody to Kaken Pharmaceutical Co., Ltd. <4521> in June 2007, and currently also it continues to advance its R&D. The Company also began developing biosimilars in order to build a stable earnings foundation. In 2007, it entered into a joint-development agreement with Fuji Pharma Co., Ltd. <4554> for a filgrastim* biosimilar, and in November 2012, it was the first company to obtain approval for manufacturing and sales for a biosimilar under Japan's biosimilar guidelines. This product has been marketed by Fuji Pharma and Mochida Pharmaceutical Co., Ltd. <4534> since May 2013. The Company was listed on the Tokyo Stock Exchange (TSE) Mothers market in November 2012.

* Filgrastim: a granulocyte growth factor drug product (G-CSF). Following chemotherapy (dosages of anti-cancer agents), white blood cells decrease and immunity is weakened (called neutropenia), causing various symptoms, and filgrastim is used to treat this. The innovator drug is Gran by Kyowa Hakko Kirin Co., Ltd. <4151>.

Whilst strengthening its biosimilar development pipeline, the Company has been actively forming partnerships with other companies for joint developments. It entered into an agreement with Sanwa Kagaku Kenkyusho for the joint development of darbepoetin alfa BS in January 2014, then it concluded basic agreements for joint development and sales with Mochida Pharmaceutical in the oncology field in August 2015 and with Senju Pharmaceutical in the ophthalmology field in November of the same year, and they are progressing the joint development of each.

Also, in 2016, the Company conducted a capital participation in NK Relations Co., Ltd, which is a member of the Noritsu Koki Group (hereafter, also "the NK Group"), and it became a member company of this Group. It concluded a capital and business partnership agreement with Japan Regenerative Medicine, which is also a member of the NK Group, and it is advancing developments in the regenerative medicine field, which is building the footholds for a new biotech business. In addition, the Company concluded a capital and business partnership agreement with JSR Corporation <4185>, and in 2017, it entered into a capital and business partnership agreement with ITOCHU CHEMICAL FRONTIER Corporation for the joint development of a second biosimilar development drug (it received a capital investment for the first drug in 2013). Then in April 2018, it concluded a capital and business partnership agreement with NanoCarrier Co., Ltd.<4571>, and each partner company is a major shareholder of the Company.

History

Date	Major event
March 2001	Established in Sapporo with the objective of developing diagnostic and therapeutic agents based on the research of the Division of Molecular Interaction, Institute for Genetic Medicine, Hokkaido University
June 2002	As a bioventure certified by the National Institute of Advanced Industrial Science and Technology (AIST), it newly established research facilities within the Hokkaido Center of AIST and reinforced its research and development into new biologics
June 2007	Licensed-out the anti-integrin alpha 9 antibody to Kaken Pharmaceutical Co., Ltd.
October 2007	Entered into a joint-development agreement with Fuji Pharma Co., Ltd. for a filgrastim (G-CSF) biosimilar
January 2008	Licensed-in a filgrastim biosimilar cell line and basic production technology from Dong-A Pharmaceutical Co., Ltd.
November 2012	Fuji Pharma Co., Ltd. and Mochida Pharmaceutical Co., Ltd. domestically acquired manufacturing and sales approval for the filgrastim biosimilar (launch in May 2013)
November 2012	Listed on the Tokyo Stock Exchange (TSE) Mothers (market of the high-growth and emerging stocks)
August 2013	In the biosimilar business, entered into a capital and business partnership with ITOCHU CHEMICAL FRONTIER Corporation
January 2014	Entered into a joint-development agreement with Sanwa Kagaku Kenkyusho Co., Ltd., for a darbepoetin alfa biosimilar
June 2014	Entered into a nucleic-acids joint business agreement with Gene Design Inc. with the objective of commercializing a nucleic-acid pharmaceuticals platform
November 2014	Entered into a capital and business partnership with ORTHOREBIRTH Co., Ltd., which is conducting research and development on synthetic bones
August 2015	Entered into a basic agreement for a business partnership with Mochida Pharmaceutical Co., Ltd. toward the joint development and sales of a biosimilar in the anti-cancer field (concluded an agreement to launch a joint business in December 2016)
November 2015	Entered into a basic agreement for a capital and business partnership with Senju Pharmaceutical Co., Ltd. toward the joint development and sales of a biosimilar in the ophthalmology field (concluded an agreement to launch a joint business in May 2016)
March 2016	Entered into a capital and business partnership agreement with NK Relations, a group company of Noritsu Koki (became a Group subsidiary in June 2016)
October 2016	Entered into a capital and business partnership agreement with Japan Regenerative Medicine, a group company of Noritsu Koki
December 2016	Entered into a capital and business partnership agreement with JSR Corporation
February 2017	Entered into a joint R&D agreement with Juntendo University for immunological tolerance induction
March 2017	Entered into a capital and business partnership agreement with ITOCHU CHEMICAL FRONTIER Corporation for the joint development of a second biosimilar
May 2017	Together with AIN HOLDINGS Inc., and others, the Company established Minerva Medica with the aim of starting a stem cell therapy business (investment ratio, 25%)
April 2018	Entered into a capital and business partnership agreement with NanoCarrier

Source: Prepared by FISCO from the securities report and press releases

Developments in capital and business partnerships

Company name	Objective of the capital and business partnership
Japan Regenerative Medicine	Toward launching a business for the first time in the world of regenerative medical products that utilize intra-cardiac stem cells, which are being developed by Japan Regenerative Medicine, the companies will utilize the expertise in biologics development that the Company has accumulated and steadily work to launch a business for regenerative medical products at an early stage. In addition, synergies are expected with the new biotech business that the Company will develop.
JSR	By combining the management resources of both companies, the aim is to strengthen the Company's biologics business and JSR's life science business. Specifically, for the development of the drugs in the Company's development pipeline, KBI (a biologics development and manufacturing outsourcing company), which is a subsidiary of JSR in the United States, has been positioned as one manufacturing outsourcing candidate, and it will develop and construct the manufacturing process. Also, in the process of developing the manufacturing process, it will actively investigate the bio-process materials, including the refining agents and other products being developed by JSR, and it will cooperate in the development of the bio-process materials. The aim is that in the future, the Company's biologics will be utilized at the time of commercial production.
NanoCarrier	The goal is to make use of each company's respective strengths, of NanoCarrier's micellar nanoparticle technologies, the Company's biologics drug discovery technologies, and the NK Group's regenerative medicine business, to create new therapeutic products and also to advance excellent bio-technologies toward launching a global business.

Source: Prepared by FISCO from the Company press releases

Possesses the leading expertise within Japan for the development of biosimilars

2. Biologics and biosimilars

The biologics developed by the Company refer to pharmaceuticals that are manufactured utilizing the ability of microorganisms or cells to create specific proteins (such as hormones, enzymes, and antibodies) that are useful for pharmaceuticals. As it involves creating pharmaceuticals using the proteins that are originally present in the human body, a strength of biologics is that they are kind to the human body, and antibody pharmaceuticals, which are one type of biologics, have a lower risk of side effects as they act directly on the diseased or affected area. Well-known biologics include insulin (a diabetes therapeutic agent) and interferon (a hepatitis C therapeutic agent).

General pharmaceuticals (small molecule drugs) are mass-produced by chemosynthesis on a molecular level. But in contrast, biologics utilize gene recombination technologies and cell culture techniques to synthesize microorganisms and cells in large volume, and therefore major costs must be undertaken for their development and the manufacturing facilities for their mass production. They also tend to have shorter expiry periods than small molecule drugs, leading to higher product prices.

In the same way that general pharmaceuticals have innovator drugs, which are the drugs that were developed first and then followed by generic pharmaceuticals that use the same molecules as these innovator drugs, biosimilars are the follow-on products of biologics. In the case of biosimilars, the drug efficacy and safety do not change compared to the innovator drug because the type of protein is the same as that in the innovator drug. However, the sugar chain attached to the protein is slightly different, so biosimilars are not identical to their innovator drugs. Therefore, in order to demonstrate the similarity between the innovator drug and the biosimilar, it is necessary to establish an independent manufacturing process and to accumulate physicochemical data to prove their similarity. It is also necessary to conduct clinical trials to prove the biosimilar's safety and efficacy. Approvals are given based on meeting these requirements, and therefore the R&D costs of biosimilars are much higher than those of generic pharmaceuticals.

As the drug price of biosimilars are set at around 70% of the prices of the innovator drugs, high productivity in the development and manufacturing process are important for the commercialization of biosimilars. In particular, there are not many companies in Japan that possess the expertise necessary to establish the required manufacturing process or to analyze the characteristics and the quality levels of the developed biosimilars. The Company specializes in biologics and biosimilars and has accumulated a track record in this field from conducting research and development for more than 10 years, establishing its position as the leading expert for the development of biologics and biosimilars in Japan.

When comparing new biologics and biosimilars, the period of time from the start of research to market launch is 16 to 17 years for a new biologic, but only 6 to 8 years for a biosimilar. In the case of a new biologic, it takes 2 to 3 years to search for the gene (functional analysis) and 2 to 4 years to screen the drug candidate compounds. It also takes a long time from the start of the non-clinical trials to the end of the clinical trials. Therefore, the scale of the R&D costs is ¥20bn to ¥30bn for a new biologic, but only ¥5bn to ¥10bn for a biosimilar. Moreover, the probability of success, from development through to market launch, is considerably higher for a biosimilar compared to a new biologic. So for a bioventure like the Company, it can be said that the biosimilar business is a field with high development efficiency.

Characteristics of biologics

- Biologics refers to the application of gene recombination, cell culture and other technologies and techniques, and the utilization of the ability of microorganisms or cells to create proteins for the mass production and commercialization of specific proteins (including hormones, enzymes, and antibodies) as pharmaceuticals.
- The main biologics include insulin (a diabetes therapeutic agent), interferon (a hepatitis C therapeutic agent), and adalimumab (a rheumatism and psoriasis therapeutic agent).

	Biologics	General pharmaceuticals
Size (molecular weight)	Approx. 10,000~	100~
Manufacturing method	Synthesized within microorganisms and cells	Chemosynthesis
Production	Unstable (the product can change depending on the conditions of the microorganisms and cells)	Stable

Explanation of biosimilars

Biosimilars are pharmaceutical products that have demonstrated the equivalent efficacy and safety compared to previously approved biologics through clinical trials.

Differences between biosimilars and other generic pharmaceuticals

	Biosimilars	Other generic pharmaceuticals
Molecular structure	Large and complex	Small and simple
Efficacy and safety	Substantially the same as innovator drug (Amino acid sequence is the same, but aspects such as the molecular structure and manufacture process differ)	Same as innovator drug (Same molecular array, same structure)
Development cost and manufacturing equipment cost	High (¥20–30 billion) * Innovator drug: ¥100 billion	Low (around ¥0.1 billion) * Innovator drug: ¥30–¥100 billion
Price difference against innovator drug	70% of innovator drug price * 60% for oral drugs when more than 10 biosimilars of a specific innovator drug are launched	60% of innovator drug price * 50% for oral drugs when more than 10 genericproducts of a specific innovator drug are launched

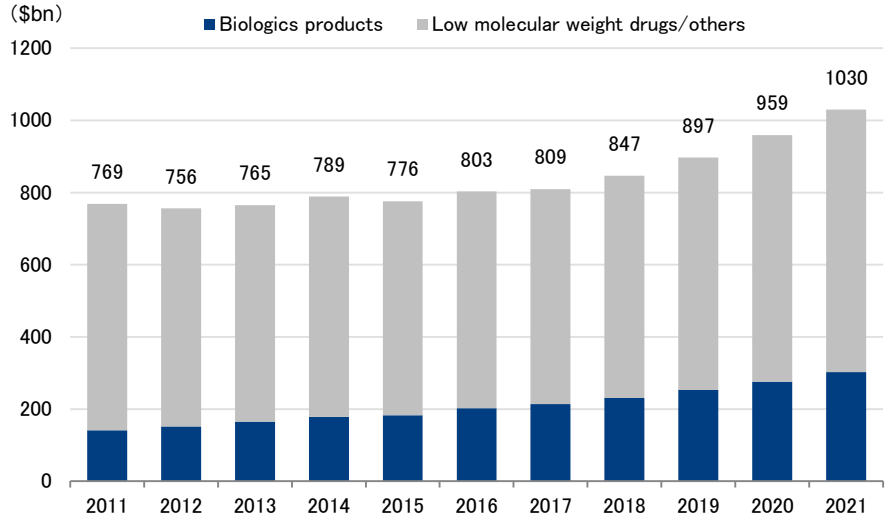
Source: extracted from “Current conditions of biosimilars” by the Ministry of Health, Labour and Welfare (July, 2014)

The scale of the biologics market is growing by 8% annually and is forecast to be worth US$300bn by 2021

3. The biologics market scale

The biologics market continues to grow year by year, and in 2016 it was worth around US$202bn, meaning it accounted for about 25% of the global pharmaceutical market that is worth approximately US$803bn. Going forward, the pharmaceutical market as a whole will continued to grow by 5% annually, but the biologics market is expected to achieve higher growth, of 8%. By 2021, it is evaluated that it will have grown in scale by 1.5 times compared to 2016, to be worth around US$302bn. Also, one of the features of biologics is that a high percentage of them are large-scale pharmaceuticals, and on looking at the sales ranking of pharmaceuticals in 2016, we see that 7 of the top 10 products were biologics.

Global pharmaceutical sales trends



Note: Figures from 2017 onwards are estimates and forecasts
Source: Prepared by FISCO from various materials

Large-scale pharmaceuticals' global net sales (2016)

Rank	Product name	Generic name	Medicinal effect	Manufacturer	Net sales (US$mn)	Patent expiry year
1	Humira	Adalimumab	Rheumatism / psoriasis	AbbVie / Eisai	16,515	United States (2016) Europe (2018)
2	Enbrel	Etanercept	Rheumatism / psoriasis	Amgen / Pfizer / Takeda	9,248	United States (2028) Europe (2015)
3	Harvoni	Sofosbuvir + Ledipasvir	Hepatitis C	Gilead Sciences	9,081	
4	Remicade	Infliximab	Rheumatism / Crohn's Disease	J&J / Merck / Mitsubishi Tanabe	8,070	United States (2018) Europe (2015)
5	Lantus	Insulin glargine	Diabetes	Sanofi	8,027	United States (2014) Europe (2014)
6	Rituxan	Rituximab	Anticancer agent / lymphoma	Biogen / Roche / Chugai	7,482	United States (2016) Europe (2013)
7	Revlimid	Lenalidomide	Multiple myeloma	Celgene	6,974	
8	Avastin	Bevacizumab	Anticancer agent / colon and breast	Genentech / Roche / Chugai	6,885	United States (2019) Europe (2022)
9	Herceptin	Trastuzumab	Anticancer agent / breast cancer	Genentech / Roche / Chugai	6,884	United States (2019) Europe (2014)
10	Januvia	Sitagliptin	Diabetes	Merck	6,440	

Note: Figures in red are biologics
Source: Prepared by FISCO from Evaluate Pharma2017

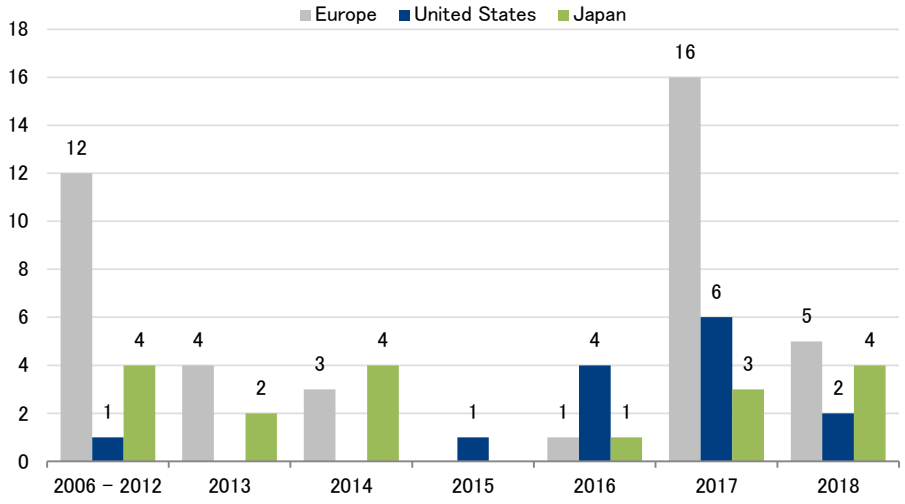
In this situation, the global market scale of biosimilars in 2016 was around US$1.6bn, and while the Japanese market is still small at approximately ¥18.4bn, it is forecast to grow rapidly in the future. This is because the patents of the biologics that currently rank top for sales will expire one after another up to 2020, so it will become possible to sell them as biosimilars. In the biosimilar market, since the launch of sales of a human growth hormone preparation in Europe in 2006, the EU has approved 41 products in 13 categories, while Japan has approved 18 products in 8 categories and the United States 14 products in 11 categories. In particular, the number of approved products has been increasing in the United States since 2016, following its publication of biosimilar guidelines in 2015. In regions outside of Japan, Europe, and the United States also, in many cases it is possible to obtain approval if the product has been approved by two of either Japan, the United States, or Europe.

Biosimilars approved in Japan, the US and Europe

Generic name	Disease indicated for	Number of approved products		
		Europe	United States	Japan
Insulin	Diabetes	3	1	2
Insulin lispro	Diabetes	1	1	-
Somatropin	Growth hormone preparation	1	1	1
Teriparatide	Osteoporosis	2	-	-
Epoetin	Renal anemia	5	1	1
Filgrastim	Neutropenia in cancer chemotherapy	8	1	5
PEG-filgrastim	Neutropenia in cancer chemotherapy	-	1	-
Follitropin alpha	Ovulation inducing agent	2	-	-
Infliximab	Rheumatism, Crohn's disease	4	3	5
Adalimumab	Rheumatism, psoriasis	4	2	-
Rituximab	Anticancer agent / lymphoma	6	-	1
Bevacizumab	Anticancer agent / colon and breast	1	1	-
Trastuzumab	Anticancer agent / breast cancer	3	1	2
Etanercept	Rheumatism, psoriasis	1	1	1
Total		41	14	18

Source: prepared by FISCO from materials from the National Institute of Health Sciences

Number of biosimilars approved by region



Note: Results for 2018 are up to June
Source: prepared by FISCO from materials from the National Institute of Health Sciences (June 2018 survey)

It is said that the spread in the use of biosimilars will become the trump card in keeping down medical expenses, which are increasing year by year. This is because while demand for biologics is growing every year due to their high medicinal efficacy, there is also the aspect of the pressure to keep down government medical expenditure due to their high drug prices. As the prices of biosimilars are about 70% of their innovator drugs, the spread in the use of biosimilars will have a major effect in keeping down medical expenses. However, although the Japanese government is advancing revisions to the dispensing fee system to raise-up the usage rate of generic drugs, it is not targeting biosimilars for these revisions, so the current situation in Japan is that the speed of their spread is low compared to in Europe. Therefore, in June 2017 the Japanese government announced a Cabinet resolution, that it would "supplement the policies to support biosimilar R&D with the aim of doubling the number of approved biosimilars by fiscal 2020," thereby setting out its policy of promoting the spread in the use of biosimilars within Japan. This policy can be expected to prove beneficial for the Company.

The Company has only a few domestic competitors for biosimilars that carry out cell line construction and drug manufacturing, including JCR Pharma Co., Ltd., <4552> and FUJIFILM KYOWA KIRIN BIOLOGICS Co., Ltd., which is a joint-venture company of Kyowa Hakko Kirin Co., Ltd., and Fujifilm Corporation.

Following on from the biosimilars and new biologics businesses, has started measures for a new biotech business (regenerative medicine field) as the third business

4. Business model

A feature of the Company's business model is the deployment on a virtual business structure of a biosimilar business that is highly stable and that can become profitable an early stage, and a new biologics business for which the aim is high growth. Also, since joining the NK Group in 2016, it has started measures for a new biotech business, including for the regenerative medicine field, as its third business.

Business model

Source: Company website

(1) Biosimilars business

The earnings model for the biosimilar business is comprised of sales from earnings at the R&D stage and the post-market-launch stage from supplying the drug substance that will be the main raw material for the drug product developed by the pharmaceutical company that is collaborating with the Company. Earnings are also comprised of agreement upfront payments and milestone payments that depend on the progress made in the non-clinical and clinical trials. The Company outsources all of the tasks that are the sources of earnings in the biosimilar business, of the manufacturing, analysis, and evaluation and other testing of the drug substance.

As an example, for the market-launched filgrastim biosimilar, the Company paid royalties to license-in the cell line from Dong-A Socio Holdings (formerly, Dong-A Pharmaceutical Co. Ltd.) of South Korea, it developed the drug substance and the manufacturing process for its commercial production, and it sells the developed drug substance to its partner, Fuji Pharma. Fuji Pharma manufactures and sells the drug product, and it also supplies the drug product to Mochida Pharmaceutical. The filgrastim biosimilar developed by the Company accounts for approximately 30% of the filgrastim sales in Japan since sales started in 2013, and this ratio is expected to rise even further in the future. Filgrastim biosimilars are sold by a number of pharmaceutical manufacturers other than Fuji Pharma and Mochida Pharmaceutical, including Nippon Kayaku Co., Ltd. <4272>, Takeda Teva Pharma Co., Ltd., Sawai Pharmaceutical Co., Ltd. <4555>, and Sandoz Co., Ltd. However, it seems that in Japan, the products of Fuji Pharma and Mochida Pharmaceutical, which hold the phase 3 clinical trial data, have the highest shares of the market.

(2) New biologics business

The Company implements its new biologics business from the basic research for drug discovery. It conducts research not only in-house, but also jointly with universities and other research institutes. Manufacturing, quality testing, and non-clinical trials for the discovery of drug candidates are outsourced to CROs both domestically and overseas. As enormous costs will be subsequently incurred at the clinical trials stage, in principle its basic policy is to license-out the candidate to a pharmaceutical company at this stage.

Therefore, as its earnings model, the Company mainly enters into joint research and development agreements or license agreements and obtains earnings from agreement upfront payments, milestone payments depending on the progress made in the development, and then from royalties after the product is launched.

In terms of its licensing-out track record, in 2007 the Company provided the exclusive development, manufacture, and sales rights of an anti-integrin alpha 9 antibody (immune diseases and cancer diseases) to Kaken Pharmaceutical. Also, for the other drugs in its development pipeline, it is advancing joint research with academia and others in fields including cancer, immune diseases, and circulatory diseases, based on the keywords of intractable and rare diseases and pediatric diseases.

Status of the development pipeline

Has in sight the market launches of multiple pipeline biosimilars from 2020 onwards

1. Biosimilars business

Currently, within the biosimilar products that the Company has already launched or is currently developing, the potential markets for the main 7 products have been provisionally calculated to be ¥1.456 trillion globally and even ¥115bn for Japan alone (innovator sales × 60% as biosimilar volume penetration rate × 70% of the innovator drug price). Within these, for filgrastim BS, which it has already launched on the domestic market, the Company is achieving sales of around ¥90mn a year through sales of the drug substance, mainly to Fuji Pharma, and going forward also, these steady sales are expected to continue.

Other drugs within the development pipeline for which the Company has entered into a joint development agreement and that are currently being developed are the three products of GBS-011 (darbepoetin alfa), GBS-007 (biosimilar in the ophthalmological field), and GBS-005 (adalimumab). Also, although net yet announced, it seems that the Company has decided on the joint-development partner for GBS-010 (PEG-filgrastim). The current status of and future outlook for each pipeline drug is described below.

(1) GBS-011

GBS-011 is a biosimilar of darbepoetin alfa (product name: Nesp / Aranesp), which is a renal anemia therapeutic agent, and current its phase 3 clinical trials are being conducted by Sanwa Kagaku Kenkyusho, the Company's joint-development partner, with the aim of applying for manufacturing and sales approval in around 2018. As it takes more than a year from the time of application until the approval, if the approval review goes smoothly, it is expected to be market launched in around 2020. This product is manufactured by Dong-A ST of South Korea, while the Company is conducting joint development in the form of supporting the development by Sanwa Kagaku Kenkyusho. It will receive royalties after it is market launched, depending on the sales.

(2) GBS-007

GBS-007 is a biosimilar in the ophthalmology field for an age-related macular degeneration therapeutic agent, and currently Senju Pharmaceutical, the Company's joint-development partner, is conducting the phase 3 clinical trials. These trials are scheduled to finish around 2020, and the aim is to acquire manufacturing and sales approval and market launch it in around 2021. In terms of age-related macular degeneration therapeutic agents in Japan, two biologics, Ranibizumab (product name: Lucentis) and Aflibercept (product name: Eylea) are administered, and Ranibizumab's net sales are about ¥23bn, and Aflibercept's about ¥60bn. Therefore, the potential demand for a biosimilar of age-related macular degeneration therapeutic agents is provisionally calculated to be approximately ¥35bn for Japan.

In the global market, Ranibizumab's sales are approximately ¥350bn and Aflibercept's about ¥700bn, so if a biosimilar for both products can be sold domestically and overseas, the potential in terms of improving results is enormous. For the development of biosimilars in the ophthalmology field, overseas, Samsung Bioepis and one other company are conducting phase 3 clinical trials, but there is no other company in Japan doing so, so if the development is a success, the extent of its contribution to results is expected to be great.

(3) GBS-005

GBS-005 is a biosimilar of adalimumab (product name: Humira) which is the world's top selling drug (sales of ¥1.7 trillion in 2016) as a therapeutic agent for rheumatoid arthritis and psoriasis. As the size of the market for adalimumab is so large, the competition to develop biosimilars for it is also fierce, and already in the markets in Europe and the United States, 6 products have been approved since 2016. Therefore, the Company is searching for partners for GBS-005 for the Asian market, including in China.

(4) GBS-010

GBS-010 is a biosimilar of PEG-filgrastim (product name: G-Lasta / Neulasta) that reduces the frequency of drug administration and increases the sustainability of the drug's effects by modifying PEG (polyethylene glycol) with filgrastim. The non-clinical trials have already been completed, and in addition, although it has not been announced, the Company has decided on the joint development company and is aiming to start the phase 3 clinical trials by 2020. PEG-filgrastim BS is based on the raw material of filgrastim BS, which has already been marked launched, and this is considered to be an advantage for the Company in terms of progressing its development. The plan is to advance its development so that it can be launched without delay around the fall of 2022, which is the time of the expiration of the innovator drug's re-review period. Also, there are many interested companies in Asia, so it is possible that this will lead to a joint development agreement in the future.

(5) Others

In terms of the other pipeline biosimilars, GBS-004 (generic name: bevacizumab, product name: Avastin) and GBS-008 (generic name: palivizumab, product name: Synagis) are still at the research-and-development stage. Within them, the Company is searching for a Chinese company to be a partner for GBS-008, which is an infant infection therapeutic agent.

As its biosimilar pipeline, the Company plans to progress the development of another 1 or 2 products. The aim is to market launch these new pipeline biosimilars around 2025.

Status of the development pipeline

Main biosimilars in the pipeline

Pipeline (generic name)	Innovator drug and product name (indication)	Biosimilars' potential market scale		Progress	Partner
		Japan	The world		
GBS-001 (filgrastim)	Gran/Neupogen (biologics for neutropenia caused by chemotherapy)	¥8bn	¥40bn	Market launched domestically.	Fuji Pharma, Mochida Pharmaceutical
GBS-004 (Bevacizumab)	Avastin (anticancer drug)	¥37bn	¥250bn	Under development research	-
GBS-005 (adalimumab)	Humira (biologics for rheumatoid arthritis)	¥14bn	¥720bn	Under development research	Conducting licensing-out activities
GBS-007 (ophthalmic biologics)	Ophthalmic biologics age-related macular degeneration, etc.	¥10bn	¥87bn	Phase 3	Senju Pharmaceutical
GBS-008 (palivizumab)	Synagis (biologics for respiratory syncytial virus (RSV))	¥15bn	¥59bn	Under development research	
GBS-010 (PEG-filgrastim)	G-Lasta/Neulasta (biologics for neutropenia caused by chemotherapy)	¥8bn	¥208bn	Non-clinical trials have been completed.	1 company in Japan
GBS-011 (darbepoetin alfa)	Nesp/Aranesp (biologics for renal anemia)	¥23bn	¥92bn	Phase 3	Sanwa Kagaku Kenkyusho
Total		¥115bn	¥1,456bn		

In terms of the other candidates in the pipeline, the Company is currently developing drugs on a number of themes, including for cancer and immune disorders.

Note: the potential market scale is calculated as approximately 40% of that of the innovator drugs (innovator drugs net sales × biosimilar penetration volume rate 60% × 70% of the innovator drug price)
Source: Prepared by FISCO from the Company materials

2. New biologics business

For new biologics, the Company has licensed-out the anti-integrin alpha 9 antibody to Kaken Pharmaceutical, but little progress has been made for its development. In this situation, the Company is focusing on GND-004 as a novel antibody drug candidate for the ophthalmic diseases and cancer fields. This is because GND-004 is an angiogenesis inhibitor with a different mechanism of action to Ranibizumab and Aflibercept, so demand is expected from patients for who both drugs are not effective or for who bevacizumab is not effective. In September 2017, the Company filed for a patent for the antibody, and since the fall of 2018, it has been conducting full-scale licensing-out activities and aiming to conclude an agreement at an early stage. It appears to have already sounded-out major pharmaceutical manufacturing companies, and we shall be paying attention to developments in the future. In addition to these drugs, it is also progressing joint research with academia and other partners for several other development candidate drugs.

New biologics

Development code	Indication	Progress	Partner
GND-001 (anti-integrin alpha 9 antibody)	Immune diseases, cancers	Development research	Kaken Pharmaceutical
GND-004	Ophthalmic diseases, cancers	Development research	Conducting licensing-out activities
GND-007	Immune diseases	Basic research	-

Source: Prepared by FISCO from the Company website

3. New biotech business

Since joining the NK Group in 2016, the Company has started fully fledged measures for a new biotech business, which will be centered on the regenerative medicine field. In October 2016, Japan Regenerative Medicine, which is a member of the NK Group and with which the Company has a capital and business partnership, progressed the clinical trials it had been conducting, which are for a therapy that aimed to use intra-cardiac stem cells to improve cardiac function for the first time in the world, to the pioneering product review designation system*. If steady progress is made, this review will be completed in 2020 toward a market launch in 2021. The Company has been supporting Japan Regenerative Medicine, including in the non-clinical trials and the development of the manufacturing method. The current clinical trial is for autotransplantation, but going forward they would like to conduct further joint development including to investigate the possibility of allotransplantation and to expand its indications. Therefore, for the future, they have in sight its development for the European and United States markets.

* For innovative new drugs that meet certain requirements, such as the severity of the disease they are indicated for, the aim is to shorten the approval review period by designating these drugs as pioneering products from an early stage of their development, and treating them as a priority for the consultations and review relating to the regulatory approval. Through utilizing this system, it is possible to reduce the standard review period to 6 months, which is around half of the length of the usual time.

Also, in February 2017, the Company entered into a joint research agreement (for 3 years, up to February 2020) with Juntendo University for immunological tolerance* induction. The aim is to commercially launch a new immunosuppressive therapy method that utilizes immune tolerance, including the development of the antibodies required for this research. As this research is based on the existing research findings of Juntendo University's Atopy Research Center, clinical studies on renal transplantation and liver transplantation have already been conducted, and cases have been confirmed in which the amount of immunosuppressive drug to be taken was reduced or it was no longer necessary to take it. Related to this research, in September 2017 the Company concluded a development and manufacturing outsourcing agreement with Medinet Co., Ltd., <2370> for the processing technologies for the immune cells that will serve as the antibodies.

* It refers to a condition in which one's own cells that are responsible for the immune function do not recognize extraneous antigens as foreign substances and the immune reaction does not occur.

In addition to the above, with the aim of launching a business for a treatment for diabetic nephropathy using autologous bone marrow mesenchymal stem cells, which is being researched by Sapporo Medical University, in May 2017 the Company established Minerva Medica (investment ratio 25%), together with AIN HOLDINGS <9627> and North Pacific Bank, Ltd., <8524>. For this research, a certain level of effects has already been demonstrated in animal experiments, and going forward, the plan is to conduct clinical trials after establishing a stable cell production system and a safe and effective treatment method, toward its market launch at an early stage.

New biotech business (regenerative medicine field)

Development product	Indicated field	Progress	Joint development company, university, etc.
Intra-cardiac stem cells	Improving heart functions in children	Undergoing clinical trials using the pioneering product review designation system	Japan Regenerative Medicine
Immunological tolerance induction	Auto-immune diseases, organ transplantation, allergies	Basic research stage	Juntendo University
Bone marrow mesenchymal stem cells	Diabetic nephropathy	Basic research	Sapporo Medical University, Minerva Medica

Source: Prepared by FISCO from the Company website

Results trends

Aiming for a re-start under the new management system from FY3/19

1. Overview of FY3/18 results

In the FY3/18 results, net sales decreased 2.7% YoY to ¥1,059mn, the operating loss was ¥913mn (compared to a loss of ¥1,184mn), the ordinary loss was ¥903mn (a loss of ¥1,176mn), and the net loss was ¥904mn (a loss of ¥1,224mn).

Net sales of filgrastim BS increased 3.6% YoY to ¥852mn, while revenue from intellectual property rights, etc., rose 41.1% to ¥121mn, and in addition, revenue from services of ¥29mn was recorded. In costs, R&D costs, centered on the biosimilar business, were ¥1,107mn, down ¥325mn YoY, while development itself is progressing steadily. Also, other SG&A expenses remained at basically the same level as in the previous fiscal year. As a result, the operating loss contracted ¥270mn YoY, which was mainly due to the reduction in R&D costs, while it was also ¥63mn less than the Company forecast.

FY3/18 results

(¥mn)

	FY3/17	FY3/18				
	Result	Company target	Result	vs. sales	YoY change	vs. target change
Net sales	1,089	1,166	1,059	-	-29	-106
(filgrastim net sales)	822	-	852	80.5%	+30	-
(other revenue)	267	-	207	19.5%	-60	-
Gross profit	692	-	637	60.1%	-54	-
SG&A expenses	1,876	-	1,550	146.3%	-325	-
(R&D expenses)	1,433	1,197	1,107	104.5%	-325	-89
Operating loss	-1,184	-977	-913	-86.2%	270	63
Ordinary loss	-1,176	-992	-903	-85.2%	273	88
Net loss	-1,224	-994	-904	-85.4%	319	89

Source: Prepared by FISCO from the Company's financial results

2. FY3/19 outlook

The forecasts for FY3/19 are for net sales to be basically unchanged YoY at ¥1,060mn, an operating loss and ordinary loss of ¥1,180mn, and a net loss of ¥1,182mn. The outlook is for filgrastim BS net sales to remain at around the same level as in the previous fiscal year, as although they will be impacted by the revisions to drug prices, the increase in quantity will also have an effect. However, the plan is to increase R&D costs by ¥192mn YoY to ¥1,300mn, mainly for GBS-007, so the operating loss will grow slightly compared to in the previous fiscal year. In terms of the level of R&D costs, as the Company will incur development costs for biosimilars and new biologics and costs to enhance the new biotech business, it is forecast that going forward, they will be around ¥1,300mn a year for the foreseeable future.

In June 2018, the Company elected two new directors (one is an outside director) at the General Meeting of Shareholders and started a new management structure. In addition, it introduced a business headquarters system and is aiming to strengthen the business department structure. The newly appointed director, Mr. Ryo Noguchi, is a representative director of the NK Group companies of Japan Regenerative Medicine, and GeneTech Co., Ltd., and the aim is to strengthen cooperation with NK Group companies in the future. Also, Mr. Norikazu Eiki, who is the outside director, was the Chairman and Representative Director of the former Bayer Yakuhin Ltd., and he has a wide network of connections with overseas pharmaceutical companies. He also has a wide network elsewhere, including as a member of the Ministry of Health, Labor and Welfare's Project Committee on Biosimilars, and he is expected to contribute to developing the Company's business.

* From April 2018, the Company established a four headquarter structure; the business development headquarters, the R&D headquarters, the pharmaceutical headquarters, and the business administration headquarters.

FY3/19 outlook

(¥mn)

	FY3/18	FY3/19	
	Result	Company target	YoY change
Net sales	1,059	1,060	0
(R&D expenses)	1,107	1,300	192
Operating loss	-913	-1,180	-266
Ordinary loss	-903	-1,180	-276
Net loss	-904	-1,182	-277

Source: Prepared by FISCO from the Company's financial results

Will raise funds by issuing share subscription rights to promote its business in the future

3. Financial position and fund raising

Looking at the Company's financial position at the end of FY3/18, total assets were down ¥681mn on the end of the previous fiscal year to ¥3,025mn. The main change factors were that in current assets, cash and deposits decreased ¥488mn, while accounts receivable declined ¥182mn. Also, in non-current assets, shares of subsidiaries and affiliates (including Minerva Medica) increased ¥50mn.

Total liabilities were up ¥215mn on the end of the previous fiscal year to ¥421mn. Looking at the main change factors, there were increases in arrears of ¥179mn and accounts payable of ¥60mn, while income taxes payable decreased ¥25mn. Total net assets were down ¥896mn to ¥2,604mn, mainly due to the recording of a net loss of ¥904mn.

In FY3/17, the Company raised funds of ¥3,931mn through a capital increase from a third-party allocation and the execution of share subscription rights, thereby supplementing its funds. But to pay for upfront business investment in the future, mainly for R&D costs, in July 2018 it newly issued share subscription rights through a third-party allocation. The maximum number of shares to be issued is 3 million shares (share dilution rate, 15.68%), and when provisionally calculated based on the initial execution price of ¥1020.5, the amount of funds raised will be approximately ¥3bn. Since the lower limit exercise price has been set at ¥714.5, it will raise at least approximately ¥2bn if all the rights are exercised (the closing price on July 13 was ¥757).

For the uses of the funds raised, it is anticipated that ¥1,350mn will be used for preparatory costs up to the time of manufacturing and sales approval for the products whose development the Company is progressing within the existing biosimilars pipeline, ¥650mn will be used for the development costs of 1 or 2 new products in the new biosimilar pipeline, and ¥1,059mn will be used to develop existing new biologics and to license-in new biologics, and also for the costs to enhance the new biotech business.

Balance sheet

(¥mn)

	FY3/15	FY3/16	FY3/17	FY3/18	Change
Current assets	1,092	1,520	3,421	2,692	-729
(cash and deposits)	599	817	2,379	1,891	-488
Non-current assets	54	173	284	332	48
Total assets	1,146	1,694	3,706	3,025	-681
Total liabilities	876	1,290	205	421	215
(Interest bearing debt)	775	810	-	-	-
Net assets	270	403	3,500	2,604	-896
Management indicators					
Shareholders' equity ratio	21.7%	22.6%	93.8%	85.0%	-8.8pt

Source: Prepared by FISCO from the Company's financial results

Outline of the 6th share subscription rights

Maximum number of issued shares	3 million shares (share dilution rate, 15.68%)
Initial exercise price	¥1020.5
Lower limit exercise price	¥714.5
Exercise price adjustment	Fixed at 92% of the closing price on the trading day immediately before the effective date of each exercise request
Estimated amount of funds to be raised	¥3,059mn (assuming the initial exercise price)
Exercise period	July 2, 2018, to July 1, 2020
Purpose of fund raising	· Toward advancing the businesses in the future, to secure the funds necessary to further enhance corporate value by targeting the fields of rare and intractable diseases, especially in the pediatric field · To improve liquidity by expanding the investor groups
Uses of funds raised	· Within the existing BS pipeline, for the costs to finalize the manufacturing method for 3 products, to prepare for their supply as commercial products, and to prepare for the applications toward acquiring manufacturing and sales approval (¥1,350mn) · For the costs to develop the manufacturing process for 1 or 2 products in the new BS pipeline, and the costs relating to quality tests and non-clinical trials (¥650mn) · For the R&D costs of existing new biologics and to license-in new biologics, and the costs to enhance the new biotech business (¥1,059mn)

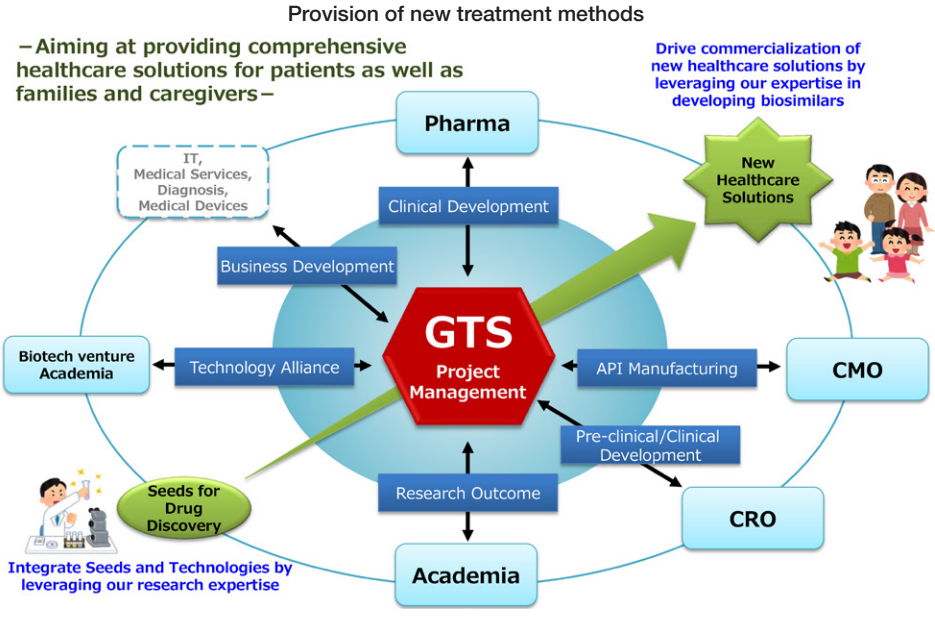
Source: Prepared by FISCO from the Company's results briefing materials

The business strategy for the future

Expects to achieve operating profit from 2022 to 2023, when multiple biosimilars are scheduled to be market launched

As the business direction it is aiming for in the future, the Company is advocating being an “Biotech Engineering Company, striving for value creation,” and in addition to the fields of rare and intractable diseases, it is expanding the fields it targets for developments, such as to pediatric diseases (including juvenile diseases) and diseases in Asia. Based on the expertise in developing biologics it has accumulated since its foundation and also its experience and expertise in developing highly efficient manufacturing processes for biosimilars, it policy is to work to create value not only through advancing the development of new drugs by combining various drug-discovery seeds, but also by leveraging synergies with the NK Group to develop new treatment methods and medical services (such as early diagnosis and genetic testing services).

As the differentiation technologies that it will strengthen in the future, the Company cites technologies for enhancing the effectiveness of the medicinal effect, technologies that enable the expansion of the treatment site (technologies to transport the drug to the target site), improvements in medication compliance (improving the sustainability of the medicinal effect), and the reduction of side effects (identifying molecules for which there is a risk of side effects). By combining these technologies, it will develop high value-added biologics. For technologies that make it possible to expand the treatment site, in April 2018 the Company entered into a capital and business partnership agreement with NanoCarrier, and it is expected to utilize this company’s technologies, including its micellar nanoparticle (polymer micelle) technologies, for this purpose.



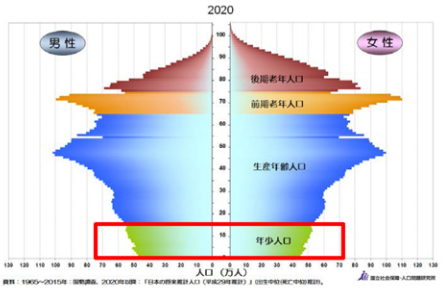
Source: reprinted from Explanatory Materials on the Business Direction being aimed for by GTS

Also, the recent addition of the field of pediatric diseases as a new target for developments is because the development of new drugs in this field is insufficient and competition is not intense, also that there is currently a boom in developments for rare and intractable diseases with high drug prices. Further, in the future, alongside the decline in the birthrate, it is considered that the spotlight will be placed on developments in the field of pediatric diseases. Pharmacy dispensing medical expenses related to pediatric diseases in Japan were approximately ¥500bn in 2015, accounting for only about 6.25% of the total, but there are many intractable pediatric diseases and the growth potential for this field is considered to be large. One pediatric disease is being targeted by the treatment method to improve cardiac functions using intra-cardiac stem cells that is currently being researched by Japan Regenerative Medicine, so we will be paying attention to development efforts in the future, including for regenerative medicine.

Pediatric diseases' potential

–Importance of improving the quality of comprehensive healthcare services for child and juvenile

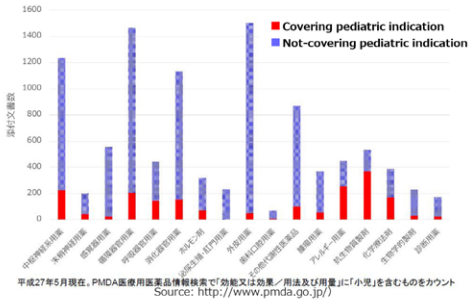
Age Pyramid of Japan



Source: http://www.ipss.go.jp/

- The population of many countries including Japan shows "inverse" pyramid style
- The portion of child/juvenile population (less than 15 years old) in Japan is approx. 12.5% of total population and tremendously getting lower.
- The decrease of child/juvenile population who would be a key for Japanese and global economic growth in the future should endanger maintenance of a solid and sustainable society.

The number of package inserts obtaining marketing authorization for pediatric indication



Source: http://www.pmda.go.jp/)

- The number of drugs which have pediatric indication and dosage is limited although they are available for adult.
- Healthcare cost dispensed at pharmacy for pediatric disease (less than 15 years old) is approx. 500 billion yen in 2015, approx. 6.25% of total healthcare cost at pharmacy in Japan (approx. 8 trillion yen).
- Considering the number of package inserts including pediatric indication, we estimate there should be a considerable number of patients who do not receive sufficient healthcare service and, therefore, a market potential should be larger.

Source: reprinted from Explanatory Materials on the Business Direction being aimed for by GTS

In terms of the image for results in the medium term, sales are increasing from the progress made in the development and the market launches of the existing pipeline biosimilars (GBS001 to GBS011). In addition, the Company's strategy is to aim to accumulate sales from the new pipeline drugs (1 or 2 products) from 2025 onwards. As products with upside potential, they are expected to contribute to sales from being licensed-out overseas. If steady progress is made in the development of the existing pipeline drugs, then 2 to 3 products are scheduled to be sequentially market launched from 2020 onwards. So at FISCO, we think it is possible that the Company will become profitable at the operating income stage from around 2022 to 2023.

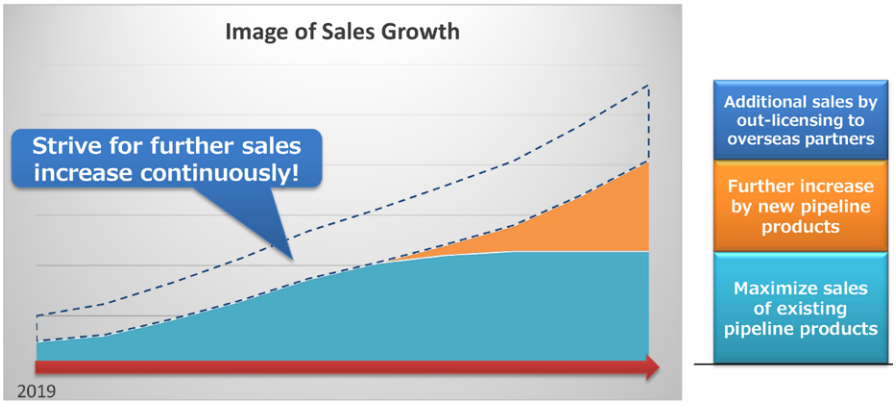
The business strategy for the future

Strategy

Strengthen mid, long-term business foundation

Action Plans

- Maximize sales of Filgrastim and launch 3 products from existing pipeline for achieving sales target
- Launch 1- 2 products from new pipeline for strengthening our business foundation further
- Pursue out-licensing opportunities to overseas partners



Source: reprinted from Explanatory Materials on the Business Direction being aimed for by GTS

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