COMPANY RESEARCH AND ANALYSIS REPORT

Carna Biosciences, Inc.

4572

TSE JASDAQ Growth

11-May.-2017

FISCO Ltd. Analyst
Yuzuru Sato

FISCO Ltd.
http://www.fisco.co.jp

Carna Biosciences, Inc.
4572 TSE JASDAQ Growth

11-May.-2017
http://www.carnabio.com/english/

Index

Summary

In FY12/17, sales are set to increase in both the Drug Discovery Support business and the Drug Discovery and Development business and a profit to be recorded for the first time in two fiscal periods

Carna Biosciences, Inc. <4572> (hereafter, also "the Company") is a bio-venture company that conducts drug discovery and drug discovery support businesses focused on the functions of kinase, which are intracellular signaling substances. In its Drug Discovery and Development business, it is developing kinase inhibitors for cancers and for diseases with high unmet medical needs. In May 2016, it licensed-out the CDC7 kinase inhibitor, a cancer drug candidate, to ProNAi Therapeutics, Inc. (currently, Sierra Oncology, Inc.; hereafter, Sierra) and concluded a global licensing agreement with it.

1. Licensed-out the CDC7 kinase inhibitor to Sierra in FY12/16

In the FY12/16 consolidated results, net sales declined 48.3% year on year (YoY) to ¥811mn and the operating loss was ¥423mn (compared to operating income of ¥472mn in the previous fiscal year). In the Drug Discovery and Development business, upfront licensing agreement payments fell ¥515mn YoY, while sales also declined in the Drug Discovery Support business. The increase in R&D expenses and other factors contributed to the deterioration in earnings. The CDC7 kinase inhibitor, which has been licensed-out to Sierra, is expected to be effective against many cancers. That said, it is highly possible research is progressing as a treatment for intractable cancers like pancreatic cancer and triple negative breast cancer, with the aim of designating it as a breakthrough therapy*, which will enable it to be approved at an early stage. The total milestone payments until the market launch will be US$270mn. Also, it is considered that the royalty rate after the market launch will be a high single-digit percentage of sales.

> * This is a system in which the Food and Drug Administration (FDA) in the United States designates a drug as representing a breakthrough as it is far more therapeutically effective than other therapies already on the market. For such a drug, the time taken from clinical trials to acquiring approval can be shortened from the normal time of five to six years to around three years, and it may also be approved on examining the results of the phase II clinical trial. Introduced in 2012, Opdivo from Ono Pharmaceutical <4528> has been recognized as such a drug.

2. The outlook for FY12/17 is for sales to increase in both the Drug Discovery Support business and Drug Discovery and Development business and a return to profitability.

The forecasts for the FY12/17 results are for net sales to increase 77.4% YoY to ¥1,440mn and operating income of ¥39mn (compared to a loss of ¥423mn in the previous fiscal year). In the Drug Discovery and Development business, milestone income of ¥440mn from Sierra is scheduled, while in the Drug Discovery Support business also, sales are forecast to increase, mainly from the acquisition of orders for large-scale assay kits for lipid kinase inhibitors. In the other drug discovery pipeline, an investigation is underway toward investigator-initiated clinical trials for the TNIK inhibitor (NCB-0846), which is a colorectal cancer drug candidate, and they are expected to start in 2018 at the earliest. The Company's policy is to proceed with licensing-out activities based on the data on a drug's efficacy and safety in humans in the clinical trials.

Summary

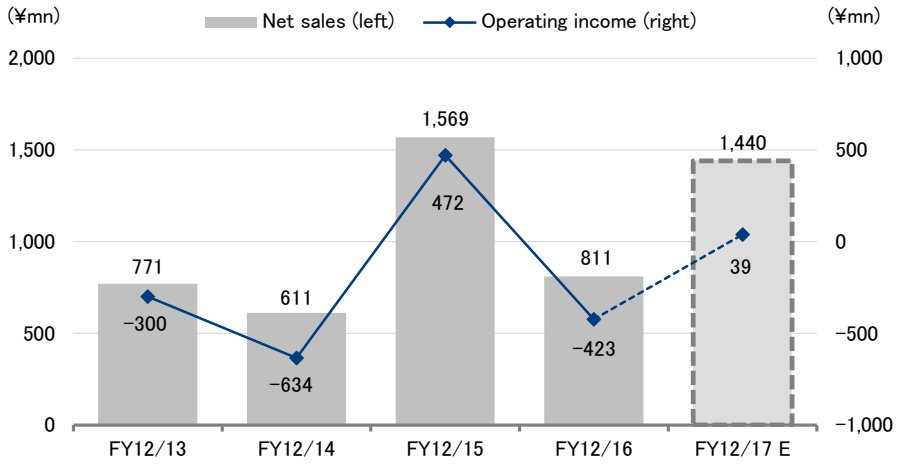
3. Announced the Mid-Term Business Plan basic policies

The Company has announced the basic policies in the Mid-Term Business Plan up to FY2019. The policies are to implement measures to turn the consolidated operating loss to a profit in FY12/17, to license-out multiple drugs in the drug discovery pipeline, to initiate in-house clinical studies with the aim of maximizing the value obtained from the pipeline, and to secure stable earnings in the Drug Discovery Support business. With regard to clinical studies, the Company will conduct clinical trials up to early Phase II (hereafter, PII a) in-house and then conduct licensing-out activities. Therefore, in the Drug Discovery and Development business, R&D expenses are forecast to increase from 2018 onwards, so in the results, there is a risk it will once again record on operating loss, depending on whether it has milestone income and licensing agreements. In terms of its new measures, in January 2017 it concluded a joint-research agreement with U.S. bio-venture EpiBiome, Inc. The two companies will conduct joint research for drug discovery in the bacterial diseases field by combining the Company's drug discovery technologies for small molecule compounds with EpiBiome's advanced profiling technologies in the microbiome (bacterial flora) field. While this agreement will not affect results for the time being, we will be paying attention to developments in the future.

Key Points

- Conducts the Drug Discovery and Development business and the Drug Discovery Support business focused on the functions of kinase
- The Drug Discovery Support business will reach net sales of ¥1bn for the first time in 2017 from the fully fledged contribution to earnings of lipid kinase-related products
- Is aiming to maximize pipeline value from licensing-out multiple drugs and initiating of in-house clinical studies

Results trends



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

Company profile

Conducts the Drug Discovery and Development business and the Drug Discovery Support business focused on the function of kinase

1. Company history

The Company was established in Kobe, Hyogo Prefecture, in April 2003, by way of spin-off of the pharmaceutical research facility of Dutch pharmaceutical major Organon's Japanese entity Nippon Organon K.K., and it aimed to develop a drug discovery support business and a drug discovery and development business specializing in kinase.

It established its corporate headquarters and laboratory in April 2003 in the Kobe International. Business Center (KIBC) in Kobe City. In 2004, it set up a laboratory for animal testing in the Kobe Business Support Center for Biomedical Research Activities and commenced animal testing. In March 2008, it listed its shares on the JASDAQ NEO (currently JASDAQ Growth) exchange, and the following month, it established a sales subsidiary, CarnaBio USA, Inc., as its first overseas base. Since 2010, it has focused in earnest on drug-discovery research, and in June 2015, in a first for the Company, it concluded a licensing agreement for a pipeline compound with Janssen Biotech, one of US-based Johnson & Johnson's pharmaceutical divisions, but in August 2016, this agreement was ended for strategic reasons at Janssen Biotech. Also, in February 2016, within the incubation laboratory of J&J Innovation in south San Francisco, the United States, it opened the research facility CarnaBio C-Lab. This facility is located within a cluster of biotech research facilities and therefore offers several advantages, including for constructing a network of many bio-venture researchers and obtaining the latest technologies and information.

History

Date	Major event
April 2003	Established in Kobe, Hyogo Prefecture, with the spin-off of Nippon Organon K.K., aimed at developing a drug discovery support business and a drug discovery and development business specializing in kinase
October 2003	Commenced operations in the Kobe International Business Center
August 2004	Established a new facility at the Kobe Business Support Center for Biomedical Research Activities and commenced animal testing
October 2007	Established a new chemical testing facility at the Kobe Healthcare Industry Development Center
March 2008	Listed on the JASDAQ NEO exchange (currently JASDAQ Growth)
April 2008	Established CarnaBio USA, Inc., in the US
December 2008	Integrated its headquarters and research facility, shifting to the Kobe Business Support Center for Biomedical Research Activities
October 2013	Made ProbeX K.K. a fully-owned subsidiary by way of simplified share swap
June 2015	Concluded an exclusive global licensing agreement with Janssen Biotech of the US for BTK inhibitors created by the Company (Agreement ended in August 2016)
February 2016	Opened CarnaBio C-Lab as its U.S. research facility
May 2016	Concluded a global, exclusive licensing agreement with U.S. ProNAi Therapeutics, Inc. for its CDC7 kinase inhibitor

Source: Prepared by FISCO from Company materials

2. The characteristics of kinase inhibitors

While on the one hand anti-cancer and other medications in use up to the present time are effective treatments, on the other hand they have serious side effects that place a considerable mental and physical burden on the patient. In contrast, molecular targeted drugs*, of which kinase inhibitors are a leading example, selectively inhibit the functions of the specific molecules that are functioning abnormally within the body, so they have the advantage that compared to conventional treatments, their therapeutic effects are high but they have few side effects. The first time a kinase inhibitor was approved for manufacturing and marketing was in 2001, when the FDA in the United States approved Gleevec as a treatment for chronic myelogenous leukemia, and since then a succession of kinase inhibitors have been released onto the market. Currently, pharmaceutical companies and research facilities around the world are conducting R&D into kinase inhibitors as one of the leading types of molecular targeted drugs.

* Drugs with therapeutic effects from inhibiting the functions of specific molecules that cause a disease.

In the field of molecular targeted drugs, other than into kinase inhibitors (small molecule compounds) R&D is also being actively conducted into antibody drugs (high molecule compounds). But on examining the differences between kinase inhibitors and antibody drugs, we find that antibody drugs are biopharmaceuticals and require large-scale cell culturing facilities for their production, so their medication costs are extremely high and moreover they must be administered at a hospital by injection, so arguably they place a considerable burden on the patient. In contrast, kinase inhibitor drugs are small molecule compounds, and apart from being able to keep medication costs low by allowing mass production through chemosynthesis, their characteristics include that because they are oral medicines, they may be prescribed for home use, so the patient does not have to visit the hospital and the physical burden placed on them is light.

3. The drug discovery research process

In the drug discovery research process for kinase inhibitors, first, the specific target kinase for the disease in question on which drug discovery research will be undertaken is determined. Then there is selection from a screening process for hit compounds that function to inhibit this specific kinase function. Then several types of compounds that are likely drug candidates are selected from amongst the hit compounds and, based on this, similar compounds are further synthesized to optimize the molecular structure to realize enhanced selectivity and reduced side effects. For example, if the target kinase A is functioning abnormally, a compound that inhibits only A is important to develop a drug with few side effects. This is because if a different kind of kinase is inhibited, other normal functions will not work and these changes in the body will be manifested as side effects. The testing to determine which kinase functions that a developed compound inhibits and which it does not is called “profiling.” After this sort of research process is completed, drug candidate compounds to proceed to the preclinical trials are identified from the compounds that have been optimized.

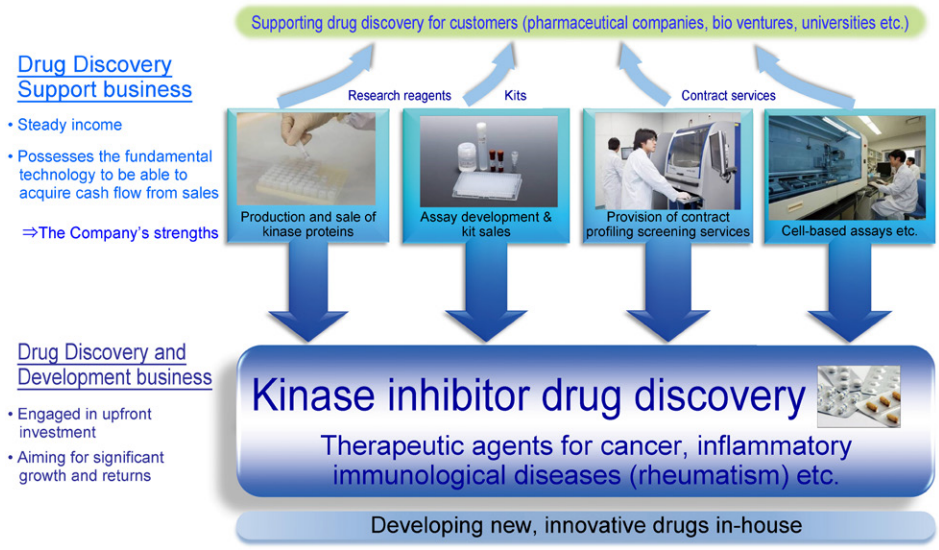
In the research process for a series of kinase inhibitor drugs, what is important is the evaluation system for drugs used in screening and profiling (called “assays”). This is because if the quality of the kinase used in the assays, the precision of the measuring system, or the ability to duplicate results are not high, it will be difficult to select a drug candidate compound, and also the research efficiency will be lowered. The Company’s strengths are its expertise in screening, profiling, and also its production technologies for high quality kinase.

As of the end of December 2016, the Company possessed 357 varieties of kinase and 433 products, making it a world leader in terms of number of kinases produced. By way of reference, it is said that 518 varieties of kinase exist in human cells and thus the Company covers approximately 70% of them. The functions that most of the remaining 30% perform in the body are not clear, so the product lineup of kinase that has drug candidates is already substantial. Competitors that undertake kinase production and screening services include Thermo Fisher Scientific Inc. of the United States and Merck Millipore of Germany.

4. Business description

As well as the parent company, the Group is comprised of two consolidated subsidiaries (CarnaBio USA, Inc. and ProbeX K.K.) and has two business segments, the Drug Discovery Support business and the Drug Discovery and Development business. The Company's fundamental technologies consist of its assays kinase expertise, including on kinase production technologies, profiling, screening and other technologies required in kinase inhibitor research, and its ability to construct a library of original compounds with kinase inhibitory activity. The Company obtains stable income from the Drug Discovery Support business utilizing its fundamental drug discovery technologies, while conducts the Drug Discovery and Development business with the funds gained. Its business model aims to achieve high growth and returns by licensing out the drugs which are discovered in the Drug Discovery and Development business.

The Company's business model



Source: From the Company's results briefing materials

(1) Drug Discovery Support business

This business involves the sale and provision of products and services to pharmaceutical companies, universities and other research facilities to support the drug discovery research they are engaged in. The products it sells are kinase proteins used in kinase inhibitor drug discovery research and assay kits*1, while its services include carrying out screening and profiling of the compounds that form the foundation of drugs produced by pharmaceutical companies and other organizations, developing assay kits from specific requests by customers, and cell-based assay services developed by the Company or the companies it collaborates with. Amidst the advances in kinase inhibitor research, cell-based assay services meet customer needs for lower costs and faster evaluation of compounds at a cellular level. Further, its subsidiary ProbeX, undertakes R&D and provides stable cell lines based on complementary split luciferase assay technology*2. Most of the sales in this business segment are from kinase proteins and screening and profiling services. The main customers for these services are Ono Pharmaceutical in Japan and Gilead Sciences in the United States. Recently, there have been increases in customer orders for kinase proteins and profiling and screening services, and the Company is aiming to improve customer satisfaction and expand sales through sales to academia.

*1 Assay is the generic term for measurement testing and refers to checking how much a test compound inhibits or doesn't inhibit a target kinase function (measurement of kinase activity), with the kinase required for testing, the buffering solution, and the other necessary elements being sold as a kit.

*2 Complementary split luciferase assay technology refers to a technique of utilizing a phenomenon whereby the luciferase (an enzyme present in the body of light-emitting organisms, such as fireflies) DNA sequence is divided into two at an appropriate juncture, and each of these pieces is introduced into a cell to produce luciferase protein fragments within the cell that do not exist in the natural world. When these protein fragments become physically close within the cell, even though they are divided, light emission is restored.

(2) Drug Discovery and Development business

This business is based on the Company's fundamental drug discovery technologies relating to kinase inhibitors. It can search efficiently for drug candidate compounds by utilizing its technologies for manufacturing high quality kinase and its advanced profiling and screening technologies. In addition, it has a fully-fledged chemical synthesis laboratory in-house and can optimize compounds at any time, which is a factor differentiating it from its competitors. All the drugs in the Company's drug discovery pipeline have been created either independently by the Company or through joint-research with academia or other organizations, and they are highly original. It not only possesses a library of unique compounds with kinase inhibitory activity that it has created up to the present time, it also has the human resources and facilities in place to evaluate in-vitro and in-vivo and has completed the main investment to construct the research system.

In terms of the business model, the Company conducts R&D in-house up to clinical trials PII a, licenses-out drug candidate compounds that are considered promising, receives upfront payments and milestone income in return for the licensing out, and obtains royalty income after the market launch. Up to the present time, it has licensed-out compounds in the preclinical trial stage to pharmaceutical companies and other organizations, but going forward it is aiming to maximize the value of licensing-out in the development pipeline by conducting development in-house up to the clinical trials stage to confirm the compound's efficacy and safety in humans, and then licensing it out.

The Company has selected unmet medical needs (where innovative treatment methods haven't been established) as the core of its drug discovery research themes, undertaking research into cancer and inflammatory immunological diseases as key disorder areas. Drugs with sales on a scale of over ¥100bn are referred to as blockbusters, with R&D being undertaken in its drug discovery pipeline towards the goal of producing drugs that can become blockbusters for the Company.

Results trends

Sales and profits fell in FY12/16, despite licensing-out the CDC7 kinase inhibitor

1. Overview of the FY12/16 results

In the FY12/16 consolidated results, net sales decreased 48.3% YoY to ¥811mn, the operating loss was ¥423mn (compared to operating income of ¥472mn in the previous fiscal year), the ordinary loss was ¥440mn (ordinary income of ¥492mn), and the net loss attributable to the owners of the parent was ¥289mn (net income of ¥456mn).

In the Drug Discovery and Development business, the Company licensed-out the CDC7 kinase inhibitor to Sierra in June 2016 and recorded income of ¥98mn from the upfront licensing agreement payment, but net sales still declined YoY to ¥515mn. In the Drug Discovery Support business also, sales fell in Japan and overseas and gross profit declined ¥742mn. In addition, SG&A expenses, which are mainly R&D expenses, increased ¥154mn, and alongside this, profits declined ¥896mn on an operating income basis. As extraordinary income, the Company and CrystalGenomics (South Korea), with which it had a capital and business-tie up, each sold their holdings of the other's shares, and as a result it recorded a gain on sales of investment securities of ¥177mn in this fiscal period.

FY12/16 consolidated results

(¥mn)

	FY12/15		FY12/16			
	Actual results	% of sales	Company target	Actual results	% of sales	YoY change
Net sales	1,569	-	804	811	-	-757
Gross profit	1,299	82.8%	-	557	68.7%	-742
SG&A expenses	826	52.7%	-	981	120.9%	+154
(R&D expenses)	417	26.6%	-	513	63.2%	+96
Operating income	472	30.1%	-432	-423	-52.2%	-896
Ordinary income	492	31.4%	-449	-440	-54.3%	-932
Extraordinary income	-6	-	-	151	-	+157
Profit attributable to owners of parent	456	29.1%	-299	-289	-35.7%	-746

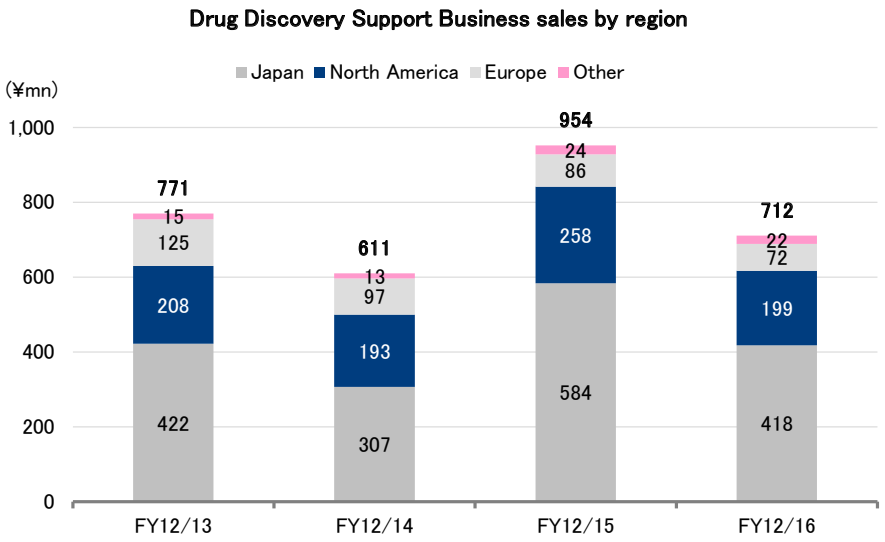
Source: Prepared by FISCO from the Company's financial results
Note: Company targets are the values announced in December 2016

2. Trends by business segment

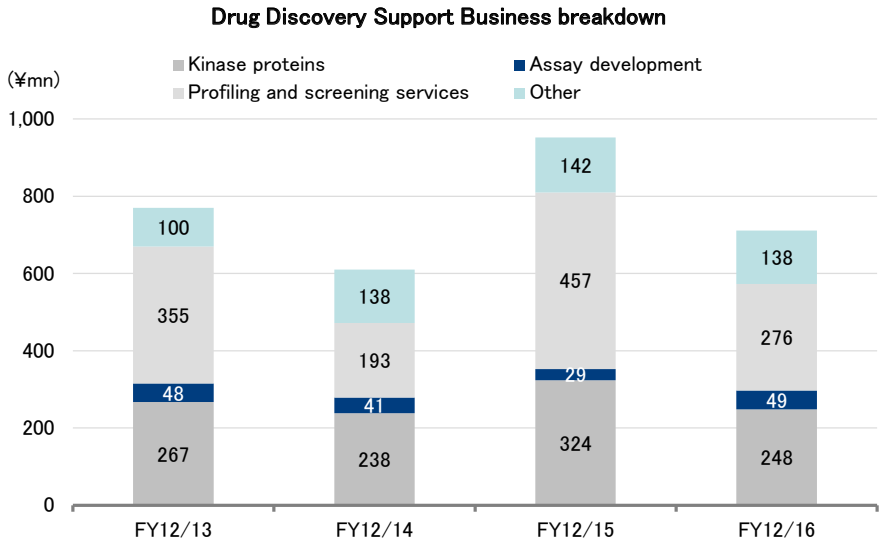
(1) Drug Discovery Support business

In this business, net sales declined 25.3% YoY to ¥712mn and operating income fell 53.5% to ¥192mn. Looking at the sales breakdown, net sales were down 28.4% to ¥418mn for Japan, down 22.8% to ¥199mn for North America, down 16.3% to ¥72mn for Europe, and down 10.1% to ¥22mn for other regions. Within Japan, the biggest factor was the decline in net sales from the large-scale contract with Ono Pharmaceutical, its main customer, which fell 38.7% to ¥194mn. Overseas, net sales declined due to the appreciation of the yen by around 10% compared to the previous fiscal year from ¥121.11 to 108.81 against US$, and in addition, because of the fall in sales in North America of kinase proteins and profiling and screening services. Although the North America region is a major market, it requires strategic sales activities because it is broad geographically, and the Company's results were impacted by the fact its sales system does not necessarily function effectively to this extent.

Results trends



Source: Prepared by FISCO from the Company materials



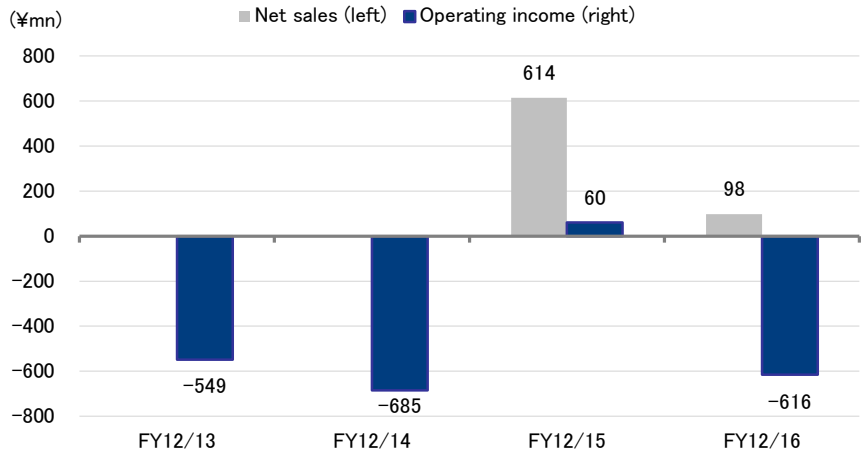
Source: Prepared by FISCO from the Company materials

Even though the agreement for the BTK kinase inhibitor licensed-out in 2015 has ended, it is continuing development in-house and aiming to license it out again

(2) Drug Discovery and Development business

In this business, net sales fell 83.9% YoY to ¥98mn and the operating loss was ¥616mn (compared to operating income of ¥60mn in the previous fiscal year). Net sales were comprised of income from the upfront payment from Sierra of the United States following the conclusion of a global licensing agreement for the CDC7 kinase inhibitor. In the previous fiscal year, the Company recorded income of ¥614mn from an upfront licensing agreement payment from Janssen Biotech for the BTK kinase inhibitor, and as a result, net sales declined YoY. In terms of profits, the continuing upfront investment, including for development pipeline R&D, was a factor behind the recording of a loss.

Drug Discovery and Development business results trends



Source: Prepared by FISCO from the Company materials

The licensing agreement concluded with Janssen Biotech of the United States in June 2015 was ended in August 2016 due to strategic reasons at the other party. Janssen Biotech had been advancing pre-clinical trials to develop a rheumatism therapeutic agent, but the compound developed by the Company has the problem that it is difficult to dissolve. It was considered that it would require about one year to solve this problem and during this time, its competitor, Merck of Germany, had started Phase I clinical trials around the start of 2016 for a candidate therapeutic agent targeting BTK kinase. In contrast, Janssen Biotech would not be able to start Phase I clinical trials until around 2019, which means it is possible that its pharmaceutical would not be launched until several years after that of its competitor. Mainly for this reason, it was forced to change its strategy.

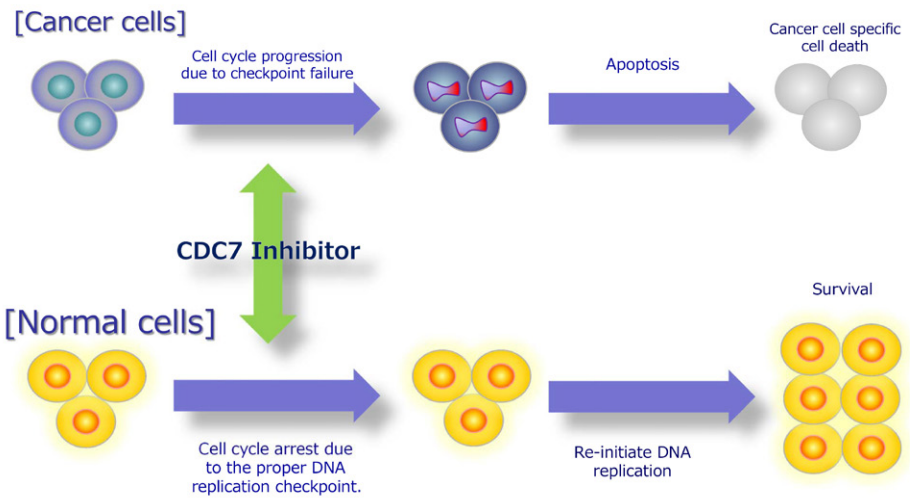
But going forward, the Company plans to conduct in-house the remaining pre-clinical trials for the returned compound and to pursue activities to license it out to another pharmaceutical company. While the above-described dissolving problem seems to have been resolved, based on the pharmaceutical standards, it will still take about half a year to synthesize the large volume of the compound necessary to start the pre-clinical trials, so it is anticipated that these trials will start in 2018 or after. While other companies have drug candidate compounds at more advanced stages of development than the Company, the market for rheumatism therapeutic agents is huge, with a market scale of around ¥2 trillion for antibody pharmaceuticals (4 to 5 products). So it is considered that if an oral medicine can be developed with the same level of efficacy as other therapeutic agents, the market size is sufficient to accept even late-developed products. There is also the possibility that the Company's compound may precede other compounds due to changes in development policy for the products that are currently at a more advanced stage of development.

On the other hand, the Company conducted the pre-clinical trials for the CDC7 kinase inhibitor, and after licensing it out, Sierra is currently progressing its development. CDC7 kinase inhibitor is a drug that acts on the cell cycle and therefore seems to have a therapeutic effect for many cancers, but it is not known for which cancers Sierra is progressing its development. However, there are research reports indicating that it is effective for intractable cancers, such as pancreatic cancer and triple negative breast cancer, and if it is designated as a breakthrough therapy in the intractable cancer area, a market launch could be realized as early as in around three years from the start of clinical trials, at the soonest. Therefore, at FISCO we think it is highly possible that the development is being progressed in this area. After licensing-in the Company's CDC7 inhibitor, Sierra licensed-in a CHK1 kinase inhibitor from another company and is conducting Phase I clinical trials, and it is considered that synergies can be expected from the two drugs as they both target the DDR (DNA Damage Response) region.

In the current agreement, it seems that the Company will receive total milestone income of US$270mn alongside the progress made in the CDC7 inhibitor program, and after the market launch, it will receive a high single-digit percentage of the sales as the royalty rate. Sierra has announced plans to start Phase I clinical trials in the United States in 2017, from which the Company is expected to receive milestone income of ¥440mn. Takeda Pharmaceutical <4502> has started Phase I clinical trials for a CDC7 kinase inhibitor indicated for solid cancers and it seems to be at a more advanced stage of development.

The mechanism of the CDC7 kinase inhibitor is that in the chromosome cycle, such as DNA replication, which is important in cell division, by inhibiting the CDC7 kinase that is deeply involved in its regulation, it destabilizes the genome in cancer cells and kills these cells. Since normally functioning cells are not affected, the risk of side effects is thought to be low. Sierra is aiming to develop a drug that will inhibit the kinase involved in DDR, and it is considered that by combining a CHK1 kinase inhibitor with a CDC7 kinase inhibitor, the therapeutic effects as an anti-cancer drug will be further increased.

Mechanism of CDC7 inhibitor



Source: Company's results briefing materials

Interest-bearing debt increased, but financial soundness is being maintained

3. Financial position and management indicators

Looking at the financial position in FY12/16, total assets at the end of the period were up ¥228mn compared to the end of the previous fiscal year to ¥2,566mn. The main reason for this was in current assets, with an increase in cash and deposits of ¥536mn and a decrease in accounts receivable of ¥68mn. Also, in non-current assets, investment securities fell ¥274mn.

Liabilities were up ¥359mn on the end of the previous fiscal year to ¥826mn. While income taxes payable and accrued consumption tax fell ¥33mn and ¥19mn respectively, interest-bearing debt increased ¥484mn. Net assets were down ¥131mn on the end of the previous fiscal year to ¥1,739mn. Capital stock and capital surplus increased ¥283mn following the issuance of shares resulting from exercise of subscription right to shares. Retained earnings declined ¥289mn due to the recording of a loss attributable to owners of parent, while the shares valuation difference fell ¥114mn following the sale of investment securities.

Looking at the financial indicators, in the indicators of stability, the shareholders' equity ratio fell from 79.7% in the previous fiscal year to 67.6%, while the interest-bearing debt ratio rose from 9.1% to 27.2%. The main factor was the increase in interest-bearing debt, but net cash flow (cash and deposits - interest-bearing debt) changed from ¥1,411mn in the previous fiscal year to ¥1,463mn, so trended at around the same level, and at the current stage it is judged that financial soundness is being maintained. However, going forward, in the Drug Discovery and Development business the Company will conduct in-house up to Phase IIa clinical trials of compounds, which will also appear in the pipeline, so due to the increase in development expenses, it will continue to record a loss and is expected to raise funds.

Results trends

Consolidated balance sheet

(¥mn)

	FY12/13	FY12/14	FY12/15	FY12/16	Change
Current assets	1,361	907	1,995	2,492	496
(cash and deposits)	1,067	626	1,624	2,161	536
Non-current assets	527	313	341	73	-268
Total assets	1,888	1,221	2,337	2,566	228
Total liabilities	291	391	467	826	359
(interest-bearing debt)	140	160	213	697	484
Total net assets	1,597	830	1,870	1,739	-131
(stability)					
Shareholders' equity ratio	84.1%	67.2%	79.7%	67.6%	
Interest-bearing debt ratio	7.4%	13.2%	9.1%	27.2%	
(profitability)					
ROA (return on assets)	-18.4%	-39.0%	27.7%	-18.0%	
ROE (return on equity)	-22.9%	-70.3%	34.0%	-16.1%	
Operating income margin	-39.0%	-103.8%	30.1%	-52.2%	

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

Business outlook

Is set to record a profit in FY12/17 for the first time in two fiscal years following the increase in sales

1. Outlook for the FY12/17 results

The Company disclosed its full-fiscal year consolidated results forecasts in its FY12/16 financial results summary. From the FY12/14 results forecasts, it had only disclosed sales targets for the Drug Discovery Support business because it is thought that the disclosure of forecasts of the Drug Discovery and Development business would act as impediments to maximizing value in the licensing-out activities in this business, and also that its results are greatly affected by the outcomes of agreement negotiations and developments at the pharmaceutical companies it enters into the agreements with. However, for FY12/17, it has disclosed consolidated results forecasts including for the Drug Discovery and Development business, because the timing of the recording of milestone income based on the licensing agreement with Sierra is on the start of Phase I clinical trials, and Sierra has announced they will start during 2017.

Specifically, the forecasts are for net sales to increase 77.4% YoY to ¥1,440mn, operating income of ¥39mn (compared to a loss of ¥423mn in the previous fiscal year), ordinary income of ¥35mn (a loss of ¥440mn), and profit attributable to owners of parent of ¥6mn (a loss of ¥289mn). In the Drug Discovery Support business, net sales are set to increase ¥287mn to ¥1,000mn, while in the Drug Discovery and Development business also, they will increase ¥341mn from the recording of milestone income of ¥440mn from Sierra. R&D expenses will continue to rise, increasing ¥74mn to ¥588mn, but this will be covered by the higher sales and the outlook is for operating income to be achieved for the first time in two fiscal years. The forecasts assume an exchange rate of ¥110/US$1.

Outlook for FY12/17 consolidated results

(¥mn)

	FY12/16		FY12/17		
	Actual results	% of total	Company target	% of total	YoY change
Net sales	811	-	1,440	-	+628
Drug Discovery Support business	712	87.8%	1,000	69.4%	+287
Drug Discovery and Development business	98	12.2%	440	30.6%	+341
Operating income	-423	-	39	2.7%	+462
Drug Discovery Support business	192	26.9%	443	44.3%	+250
Drug Discovery and Development business	-616	-	-403	-	+213
Ordinary income	-440	-	35	2.4%	+475
Profit attributable to owners of parent	-289	-	6	0.4%	+295

Source: Prepared by FISCO from the Company materials

The Drug Discovery Support business will reach net sales of ¥1bn for the first time in 2017 from the fully-fledged contribution to earnings of lipid kinase-related products

2. Outlook by business segment

(1) Drug Discovery Support business

In this business, the outlook is for net sales to increase ¥287mn YoY to ¥1,000mn and operating income to rise ¥250mn to ¥443mn. Looking at the sales breakdown, net sales will increase ¥213mn from assay development and ¥60mn from kinase proteins, and most of the higher sales will be from the increases in these two areas. The increase from assay development will be from the expected acquisition of orders for large-scale assay kits for the lipid kinase DGK (diacylglycerol kinase; the Company sells 10 types and is the only company in the world to sell them), for which it launched sales in July 2016. The increase from kinase proteins is because the Company is aiming to recover the sales for them that fell in the last fiscal period.

Since the presentation by Professor Thomas Gajewski of the University of Chicago at the American Cancer Society last year, DGK has been attracting attention in the field of small molecule cancer immunotherapy. This is because he clarified its involvement in the functions of the killer T cells that attack cancer cells. Specifically, it is understood that two types of kinase, called DGKα and DGKζ, play the role of transmitting a signal that puts the killer T cells to sleep. Therefore, if a drug inhibits the actions of DGKζ and DGKζ, the killer T cells would be activated and their ability to attack the cancer cells restored. In therapies using checkpoint inhibitors, such as Opdivo, therapeutic effects are only seen in around 30% of melanoma and other cancer patients, but it is estimated that this is because these are patients whose whole body immune system has declined or even if their immune system is functioning, their killer T cells are not fully active. It is known that killer T cells do not function sufficiently because of the actions of DGKζ and DGKζ, so it is expected that the therapeutic effects of cancer immunity checkpoint inhibitors will be further increased if a candidate compound that targets DGKζ and DGKζ is developed.

For these reasons, inquiries for the two types of DGK are particularly active from pharmaceutical companies and other organizations that are developing anti-cancer drugs. As DGK's substrate is a lipid, it does not dissolve in water, so it is very difficult to construct and to handle assays, and it seems highly likely that even if the customer simply purchases DGK proteins, it will still take a considerable amount of time before it is able to construct assays. Therefore, the Company is currently proposing that it sells the assay kits that it has already developed. If one customer orders two types of DGK assay kit, as one kit costs ¥100mn, the total sales would be ¥200mn, and the FY12/17 forecasts incorporate the acquisition of at least two orders from one customer. Looking at the number of megapharmas worldwide, it is conceivable that there could be around 10 customer companies.

For the remaining eight types of DGK also, as they are deeply related to brain functions and other functions, it is important that the compound does not affect the functions of these kinase to develop a drug candidate with few side effects. Therefore, a certain level of demand for profiling and related services is expected.

Looking by region, the targets are for sales to Japan to increase YoY ¥7mn to ¥426mn, to North America to rise ¥266mn to ¥466mn, to Europe to climb ¥11mn to ¥84mn, and to other regions to remain unchanged at ¥22mn. The Company expects to acquire orders for DGK assay development services for North America.

Drug Discovery Support business net sales

(¥mn)

	FY12/13	FY12/14	FY12/15	FY12/16	FY12/17 forecast	YoY change
Kinase proteins	267	238	324	248	309	+60
Assay development	48	41	29	49	262	+213
Contract screening and profiling	355	193	457	276	280	+3
Other	100	138	142	138	149	+10
Total net sales	771	611	954	712	1,000	+287
Operating income	249	50	412	192	443	+250

Source: Prepared by FISCO from the Company materials

(2) Drug Discovery and Development business

In this business, due to the previously mentioned milestone income from Sierra, net sales are forecast to be ¥440mn, but because of the increase in R&D expenses, an operating loss of ¥403mn is expected. The other main movements in the development pipeline are as follows.

a) Wnt-signal (TNIK)inhibitor

For the Wnt-signal inhibitor that targets cancer stem cells, the Company is conducting R&D into two types of compounds, NCB-0846 and NCB-0594, in collaboration with the National Research and Development Agency's National Cancer Center Japan.

In particular, in this drug discovery program, mutations in the Wnt-signal gene have been found in over 90% of cases of colorectal cancer, which is a cancer that the National Cancer Center Japan is focusing on. It is considered that the cancer stem cells are activated by the constant activation of the Wnt-signal transmission pathway, which causes the cancer to recur. TNIK kinase is a substance that is deeply involved in this activation of the Wnt-signal pathway, and the Company and the National Cancer Center Japan have jointly published a paper demonstrating that suppressing the functions of this kinase also suppresses the expression of colorectal cancer stem cells. This paper, which was published in the global academic journal Nature Communications in August 2016, demonstrated the use of the Company's compound NCB-0846 and was the first time in the world that these research results had been reported. Therefore, this compound will attract even more attention in the future as a therapeutic agent that could lead to a complete cure for colorectal cancer. NCB-0846 is currently being considered for investigator-initiated clinical trials at the National Cancer Center Hospital East. Going forward, preparations will be advanced, including conducting the pre-clinical trials based on the pharmaceutical standards and constructing the system for manufacturing the compound for the clinical trials. Even at the earliest, the clinical trials are not expected to start until 2018, and the Company plans to conduct licensing-out activities after increasing its added value by acquiring POC (proof of concept) in humans.

NCB-0846 and NCB-0594 are both the Company's compounds, but the difference between them is that while NCB-0846 has the effect of killing both cancer cells and cancer stem cells as it simultaneously inhibits multiple kinase, NCB-0594 kills cancer stem cells only as it selectively inhibits the Wnt signal. There are already many therapeutic agents that kill cancer cells on the market, and the need is increasing among overseas pharmaceutical companies to use NCB-0594 with existing therapeutic agents to increase therapeutic effects. This compound has the problem that it is difficult to dissolve, but a method of dissolving it has been found and the current stage is of accumulating animal model data.

b) TGFζ signaling inhibitor

The Company has been conducting joint research with Hiroshima University since 2015 on the TGF ß signing inhibitor targeting chronic myelogenous leukemia cancer stem cells. They are currently optimizing the compounds and plan to select the candidate compound during 2017 at the earliest, toward progressing to preclinical trials from 2018. Methods of treating leukemia include chemotherapy using anti-cancer drugs and hematopoietic stem cell transplants, but a problem with both is their severe side effects that place a considerable burden on the patient, which contrasts with molecular targeted drugs, including the kinase inhibitor imatinib (trade name Glivec®) and ibrutinib (trade name, Imbruvica®) that each have sales on a scale of hundreds of billions of yen. However, both are drugs for suppressing the proliferation of leukemia cells, so treat the symptoms and do not kill the leukemia stem cells. In contrast, the TGFζ signaling inhibitor being developed by the Company is intended to be a curative therapy that will kill the leukemic stem cells, and it is expected that its market value will grow if progress is made in the R&D. Therefore, the Company's R&D policy for this therapeutic agent would seem to be to proceed to the clinical trials stage and confirm its effectiveness and safety in patients in-house, and then license it out once its market value has been increased in this way.

c) Neurodegenerative disease therapeutic agents

For kinase inhibitors targeting neurodegenerative diseases, the Company is currently optimizing compounds as therapeutic agents for Alzheimer's disease and Parkinson's disease, and going forward, it plans to select the preclinical candidate compounds. It seems that the Company can form compounds that have strong inhibitory effects on the targeted kinase at the cellular level, so in the future, it will progress the selection of the compounds while confirming the compound has the same effects in-vivo (in the brain). However, as it takes time and costs to breed animals suitable for Alzheimer's research and to confirm effects, for the future it is considering schemes that will start with joint research with pharmaceutical companies and that will lead to licensing agreements.

It is considered that many of the biochemical causes of Alzheimer's disease and Parkinson's disease remain unknown, but the current common treatment methods are to use multiple therapeutic agents to supplement dopamine, a neurotransmitter in the brain responsible for body movement, and to inhibit dopamine degradation. The kinase inhibitor for which the Company is progressing R&D is a drug which, based on the tau hypothesis, inhibits the accumulation of phosphorylated tau proteins and suppresses nerve necrosis.

Development pipeline status

Compound	Target kinase	Indication	Lead generation	Lead optimization	Candidate selection	Preclinical trials	Clinical trials	New drug application –launch
AS-141	CDC7	Cancer	Licensed-out to ProNAi Therapeutics, Inc. (currently, Sierra Oncology, Inc.) in May 2016					
NCB-0846	Wnt-signal (TNIK)							
NCB-0594								
Small molecule	TGFβ signaling	Leukemic stem cell Immuno-Oncology						
	Kinase	Autoimmune Diseases						
	N/A	Malaria						
	Kinase	Neurodegenerative disease						
		Anemia						

Source: Reprinted from parts of the financial briefing materials and an interview with the Company

Is aiming to maximize pipeline value from licensing-out multiple drugs and initiating of in-house clinical studies

3. The Mid-Term Business Plan basic strategy

The Company has announced the basic strategies for its Mid-Term Business Plan from 2017 to 2019, which are to implement measures for the following four points; first, to turn the consolidated operating loss to a profit in FY12/17; second, to license-out multiple drug discovery programs; third, to initiate in-house clinical studies with the aim of maximizing the value of pipeline; and finally, to secure stable earnings in the Drug Discovery Support business.

Within these policies, with regard to the licensing-out of multiple pipeline drugs, it is possible that it will realize the in-house implementation of clinical trials some time from the second half of 2018 to 2019. But on the other hand, it is expected that R&D expenses will also increase from 2018 onwards due to it conducting clinical trials in-house. Toward conducting the clinical trials in-house, it has already recruited one development researcher and it is thought that it intends to recruit a total of around three researchers. It is expected that around ¥500mn will be required to prepare the system to manufacture the compound to be used in the clinical trials in compliance with GMP, so it is possible that its demand for funds will temporarily increase in 2018. Therefore, if there are no upfront licensing agreement payments or milestone income in FY12/18, it may once again record a loss on an operating income basis. But in the Company's case, as its Drug Discovery Support business creates a stable earnings foundation, it is expected that even if it records a loss, to a certain extent it will be able to cover it. The Company is aiming to continue to achieve sales in the region of ¥1bn annually in the Drug Discovery Support business.

4. Joint research with EpiBiome

As a new initiative, in January 2017 the Company concluded a joint-research agreement (for two years) with EpiBiome of the United States. EpiBiome, which is a bio-venture company originating from Stanford University, has advanced profiling technologies for the analysis of microbiomes (bacterial flora). It has become well known as a company, as it has received several awards around the world for these technologies and has acquired excellent reputation.

Microbiomes refer to aggregations (ome) of microorganisms (microbes) that live within the body. Typical examples include intestinal flora, intestinal bacterial flora, and bacteria, and as many as 100 trillion of these microorganisms can live in the skin, oral cavities, and organs. Research in recent years has clarified that these microbiomes are deeply involved in people's health conditions and disease symptoms, and pharmaceutical companies in Japan and overseas have started to focus R&D investment into the microbiome field.

Within this situation, in the current joint-research agreement, the two companies will conduct joint research by sharing the Company's fundamental drug discovery technologies using small molecule compounds (including screening and profiling technologies) and its compound library, and EpiBiome's microbiome platform technologies and profiling technologies toward the discovery and development of new drugs in the bacterial diseases field, including for cholera, O-157, and dysentery. As they will start first by establishing and verifying hypotheses, it is considered that the agreement will have no effect on results in the immediate future. However, although the results of the joint research will be shared, the agreement will have a positive effect on the Company's profits if it leads to the discovery and development of promising drugs in the future, so we will be paying attention to developments.

In the background to the conclusion of this research agreement with EpiBiome is that in February 2016, the Company opened the CarnaBio C-Lab next to EpiBiome's research facility within an incubation facility in the United States, which provided the opportunity to deepen the ties between the researchers at both facilities. The fact that results are already starting to appear at such an early stage from the construction of a network of advanced companies in the biotech industry, which was one of the Company's aims in opening C-Lab, can be positively evaluated. Currently within C-Lab, R&D activities are being conducted by two researchers, one researcher who is permanently stationed locally and one who is stationed on a temporary basis, having been dispatched from Japan.

Shareholder returns policy

For the time being is allocating funds to R&D investment

The Company is a drug discovery venture currently in the R&D stage and it continues to have negative retained earnings carried forward, so it does not currently pay a dividend. Going forward, for the time being its policy is to allocate funds as a priority to drug discovery and to investment in R&D into fundamental drug discovery technologies, and thereby to work to strengthen its management foundations and enhance corporate value. In terms of returning profits to shareholders, it will consider paying a dividend at the stage when it becomes possible to do so in the future upon considering its business results and financial condition.

FISCO

Disclaimer

FISCO Ltd. (the terms “FISCO”, “we”, mean FISCO Ltd.) has legal agreements with the Tokyo Stock Exchange, the Osaka Exchange,and Nikkei Inc. as to the usage of stock price and index information. The trademark and value of the “JASDAQ INDEX” are the intellectual properties of the Tokyo Stock Exchange, and therefore all rights to them belong to the Tokyo Stock Exchange.

This report is based on information that we believe to be reliable, but we do not confirm or guarantee its accuracy, timeliness,or completeness, or the value of the securities issued by companies cited in this report. Regardless of purpose,investors should decide how to use this report and take full responsibility for such use. We shall not be liable for any result of its use. We provide this report solely for the purpose of information, not to induce investment or any other action.

This report was prepared at the request of its subject company using information provided by the company in interviews, but the entire content of the report, including suppositions and conclusions, is the result of our analysis. The content of this report is based on information that was current at the time the report was produced, but this information and the content of this report are subject to change without prior notice.

The final selection of investments and determination of appropriate prices for investment transactions are decisions for the recipients of this report.

FISCO Ltd.