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FISCO Ltd. Analyst Yuzuru Sato

Succeeded in generating antibodies for the Ebola virus and is accelerating development in the field of "pandemic contagious diseases"

Chiome Bioscience Inc. <4583> (subsequently, "the company") is a biotechnology company that discovers antibodies for medical applications using a proprietary technology discovered by RIKEN. It also supports the research and development of such antibodies by other entities. This technology, called the ADLib® (Autonomously Diversifying Library) system, has three distinct features: 1) it can generate antibodies for a wider range of antigens than most conventional methods, 2) it generates antibodies faster than other methods, and 3) it can be applied to tough antigens for which it is tough to generate antibodies by other methods.

The company had been aiming for the practical use of its fully human ADLib[®] system to generate antibodies for pandemic contagious diseases by 2018, but recently has decided to accelerate this development. The background to this decision is the increased interest in this technology, particularly in the United States, based on the spread of the Ebola virus contagion and the greater threat posed by bioterrorism. In October 2014 the company announced that it had actually used the ADLib[®] system to generate antibodies for multiple influenza viruses in a short time period, and followed this with an announcement in December that it had succeeded in generating antibodies for the Ebola virus.

In order to accelerate development in the field of "pandemic contagious diseases," the company announced on November 20 that it would raise funds through equity financing. This current round of financing will raise approximately ¥2,000 million, which it plans to allocate to various costs in the period up to 2017, including for R&D costs for "pandemic contagious diseases" and the costs to acquire peripheral technologies and to strengthen personnel.

On October 30, 2014, the company announced that it had revised its FY12/14 consolidated results. It now forecasts sales ¥65 million less than the initial forecast, of ¥277 million, and an operating loss reduced by ¥135 million, to ¥907 million. The main reasons for the revisions are that it has reviewed the order of priorities for its R&D activities and now plans to concentrate its management resources following the progress made in the joint research project between its subsidiary LivTech, Inc., and Yakult Honsha Co., Ltd. <2267>.

The status of the fully human ADLib[®] system is that the company is currently at the stage of receiving inquiries from other companies, including from major pharmaceutical companies in Japan and overseas. Going forward, while continuing to further improve its technologies for acquiring antibodies, it is aiming to construct the ultimate system for generating human antibodies. The plan is to conclude technology licenses in FY12/16 and primarily for this reason, for its consolidated results in FY12/16 it is targeting sales of \pm 3,452 million and operating income of \pm 651 million, bringing operations out of the red for the first time.

Check Point

- Raised funds of ¥2,000 million, which it is allocating as a priority to R&D
- Due to the change of fiscal year, the current fiscal period is 9 months and the extent of the loss will be less than initially forecast
- It is aiming for sales of $\pm 3,452$ million and operating income of ± 651 million in FY12/16, the final year of the medium-term plan



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*Reflecting a change of fiscal year, FY12/14 contains nine months

Accelerating developments for pandemic contagious diseases

Raised funds of $\pm 2,000$ million, which is being allocated as a priority to R&D

The company's medium-term management vision has been to develop antibodies for pandemic contagious diseases by 2018. But upon reaching its current point, it has decided to push forward this schedule and strengthening its efforts in this area.

The background to this includes the rapid increase in social anxiety in Europe and the United States due to the spread of the Ebola virus contagion and also the rising threat posed by bioterrorism, which has caused interest in the company's ADLib® system to grow, particularly in the United States. This is because the features of the ADLib® system, which are that it can generate antibodies for a wider range of antigens than most conventional methods, it generates antibodies faster than other methods, and it can be applied to tough antigens for which it is tough to generate antibodies by conventional methods, are being highly evaluated.

In conjunction with these market trends, in October 2014 the company announced that it had used its original ADLib[®] system to generate in a short period of time antibodies that showed responsiveness to the antigens of multiple influenza viruses (the weakly virulent type and the strongly virulent type). Then in December, it announced that it had succeeded in a short period in generating antibodies for the Ebola virus. It intends to positively press ahead with R&D for therapeutic antibodies for a treatment for the Ebola virus, and in the future plans to continue with further R&D on physical properties, functionality, and efficacy, including by generating a variety of antibodies.

These achievements signify that the ADLib[®] system can generate in a short period of time antibodies that possess efficacy against a variety of viruses. The company does not disclose specific data on its patent strategy, but going forward, as it plans to report its research results through overseas biotechnology conferences and academic societies, it seems likely that interest in the business potential for its ADLib[®] system for developing antibodies for contagious diseases will rapidly increase.



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Based on this sort of situation, the company has decided to further strengthen and accelerate its R&D for contagious diseases compared to that anticipated in its previous medium-term plan, and it announced that it would be newly raising funds (November 20, 2014). Specifically, in addition to the issue of 1.44 million new shares through a public offering at the beginning of December 2014, it sold 216,000 shares as an over-allotment (share dilution rate of approximately 8.1%). It expects to raise around ¥2,000 million through the current round of financing. The table below shows for what specific purposes it will use these funds and over what time periods.

Uses of financing (December 2014)

	Basic use	Amount (¥million)	Scheduled time period for spending
Investment capital and various costs to acquire technologies in the area of therapeutic antibodies			Until December 2015
Funds for capital investment for the management of its domestic research facilities and for research			Until December 2015
Technologies to establish an antibodies drug-discovery platform, costs to acquire licenses from targets, etc.			Until December 2017
	Research costs, such as for screening, in order to acquire new antibody candidates for contagious diseases	361	Until December 2017
R&D costs	Physical property and drug efficacy tests for lead antibody candidates	457	Until December 2017
	Costs for joint research with overseas research facilities	250	Until December 2017
	Development of next-generation technologies	135	Until December 2017
	Total	2,004	

So in terms of how the funds will be used, the fully human ADLib® system will provide the technological foundation and the funds are expected to be used for the costs of acquiring the peripheral technologies that are needed to advance the development of therapeutic antibodies for contagious diseases, for the costs of acquiring licenses from targets and others, to pay for capital investment for new facilities at domestic research facilities, and to increase the number of researchers. It is also thought that M&As are one option available to the company as a means of acquiring technologies.

The plan is to spend around ¥1,200 million over three years until December 2017 on R&D costs for contagious diseases. The subsidiary LivTech will carry out the animal tests for the physical-properties tests and drug-efficacy tests for its lead antibody candidates. The company also plans to use external resources. In terms of its joint research with overseas research facilities, the company has already concluded a joint research partnership agreement with the U.S. nonprofit organization the Clayton Medical Research Foundation (subsequently, Clayton; Q1 FY12/14). Clayton provides planning for R&D projects in the biotechnology field and plays the role of the coordinator connecting universities with biotechnology companies for each project. The company has already started a joint research project with Clayton as the coordinator. It is not known whether this project is in the area of contagious diseases, but in the future it seems highly likely that it will use Clayton to advance joint research with universities in the area of contagious diseases.



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Business trends

2Q was roughly in line with company forecasts

(1) 1H FY12/14 Results

On November 14, 2014, the company announced its consolidated results for 1H FY12/14 (April to September) reporting sales of ¥158 million, an operating loss of ¥581 million, an ordinary loss of ¥582 million, and a net loss of ¥557 million. Sales were roughly unchanged year-on-year (y-o-y) with the increase in R&D costs corresponding to the rise in the operating loss, and the results were roughly in line with company forecasts.





Trends according to business segment were as follows.



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- *1 LIV-2008 is a humanized monoclonal antibody that binds to specific antigens (target molecules) expressed on the cell surface of solid tumors, including breast, lung, pancreatic, and colorectal cancers, thereby inhibiting proliferation of the cancer cells.
- *2 Vascularization is the formation of a new blood vessel when an existing blood vessel bifurcates for some reason.

Business trends

ODrug discovery alliance business

In 1H FY12/14 (April to September), sales were ¥72 million (compared to ¥70 million in the previous fiscal half year) and segment income was ¥45 million (42 ¥million). Sales to the Chugai Pharmaceutical Group $\langle 4519 \rangle$ declined y-o-y, but R&D activities are going ahead steadily and the progress being made is in line with the plan. Also, the subsidiary LivTech carried out part of the development for the generation of antibodies and pre-clinical trials for LIV-2008*1, which is an antibody medicine indicated for cancer that it is jointly researching with Yakult Honsha. In October, it was announced that LivTech had succeeded in reaching the development milestone for LIV-2008 and so expected to record milestone income as sales in the October–December 2014 fiscal period (the amount is negligible so undisclosed). The progress made in the development of this antibody indicated for cancer is thought to mainly be in confirming efficacy above a certain numerical value in animal trials.

OLead antibody licensing business

The lead antibody licensing business does not currently record sales as it is at the stage of progressing research into various antibodies in the development pipeline. Among them, anti-semaphorin 3A is the company's first lead antibody candidate and it is advancing joint research with Professor Goshima's laboratory in Yokohama City University. They have started drug efficacy tests using an animal model for human diseases toward an inflammatory diseases model (sepsis and DIC model) and indications in the area of oncology. Also, in the R&D project to develop an antibody indicated for cancer research with Biotecnol, which is a technology alliance partner, during 1H FY12/14 (April to September) it was advanced by one stage, from generating antibodies to verifying functions.

In addition, during Q2 FY12/14 the company started joint research toward generating new antibodies with the laboratory of Professor Uemura in Nagoya City University and the laboratory of Professor Takei in Yokohama City University. The laboratory of Professor Uemura in Nagoya City University specializes in ophthalmology and because neurophilin, which is a receptor for the anti-semaphorin 3A antibodies, functions to suppress vascularization*², they are thought to be pursuing research toward its indication for conditions like age-related macular degeneration and diabetic retinopathy. On the other hand, the laboratory of Professor Takei in Yokohama City University specializes in the central nervous system and so their joint research is expected to be in this area. It is hoped that both projects will produce development pipeline drugs in the future.

OLicensing out platform technology business

In 1H FY12/14 (April to September), sales were ¥7 million and segment income was ¥7 million, which is roughly the same as in the previous fiscal half year. In December 2013, the European subsidiary of Fujirebio Inc., which is the company's original ADLib® system licensee, launched a diagnostic kit that included an antibody from the ADLib® system for measuring vitamin D (used for diagnosing rachitic patients), and the company is recording royalty income based on its sales and also the annual license fees for the ADLib® system. In addition, it is conducting technology assessment tests and negotiating technology license schemes with companies from Japan and overseas that have expressed an interest in licensing its technology.



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Business trends

OR&D Conditions

The fully human ADLib[®] system is now at a level where it can be practically used. But the company intends to focus on further finalizing this technology toward licensing it to pharmaceutical companies, and so currently it is continuing to improve its level of diversification and expanding its library. Also, since the announcement in March 2014 that the fully human ADLib[®] system had reached the level where it could be practically used for generating antibodies, the company has received a number of inquiries from pharmaceutical companies, including so-called 'mega pharmas' within Japan and overseas. In addition, since September it has been giving presentation overseas and so it seems likely that an increasing number of companies are expressing an interest in it. Going forward, the company is expected to conclude trial contracts with a number of companies, which should result in technology licenses (licensing-out platform technology sales) in FY12/16.

Due to the change of fiscal year, the current fiscal period is 9 months and the extent of the loss will be less than initially forecast

(2) Results forecasts for FY12/14

On October 20, the company announced that it had revised its forecasts for its consolidated results for FY12/14 (9 months). As shown in the table, it downwardly revised its sales forecast slightly to \pm 277 million, but conversely it is now anticipating a reduced operating loss of \pm 907 million. The main reason for the revisions was that it reviewed its order of priorities for its R&D activities and is now aiming to concentrate its allocation of management resources after it subsidiary LivTech achieving the development milestone for "LIV-2008".

The results for Q4 (October to December 2014), obtained by subtracting the results up to Q2 from the full-year results were sales of ¥118 million (compared to ¥79 million in the previous quarter) and an operating loss of ¥325 million (¥296 million). The primary factor behind the increase in sales is thought to be the recording of LivTech's milestone income as sales. Conversely, the rise in R&D costs accompanying the expansion of the development pipeline seems to be the reason for the higher operating loss. The plan is for LivTech to continue to develop "LIV-2008" toward its licensing-out to Yakult Honsha.

Results forecasts for FY12/14

					(¥million, ¥)
	Sales	Operating income	Ordinary income	Net income	EPS
Initial company forecast	342	-1,043	-1,041	-1,043	-54.56
Current company forecast	277	-907	-907	-891	-44.04
Absolute change	-65	136	134	152	10.52



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Medium-term plan

Aiming for sales of $\frac{43,452}{16}$ million and operating income of $\frac{4651}{16}$ million in FY12/16, the plan's final year

(1) Outline of the medium-term plan

In May 2014, the company announced its three-year plan ending in FY12/16 with targets calling for a dramatic improvement in performance bringing operations out of the red for the first time in FY12/16, as is shown in the graph. As it has decided to strengthen its development for contagious diseases, R&D costs may rise above the amount initially assumed from FY12/15, but there has been no change to its fundamental strategy or direction.

Consolidated results targets in the medium-term plan

						(¥ million)
	FY12/14	(9 months)	FY1	2/15	FY1	2/16
	Target	% of sales	Target	% of sales	Target	% of sales
Sales	277	-	732	-	3,452	-
Drug discovery alliance	247	89.2%	366	50.0%	614	17.8%
Lead antibody licensing	0	0.0%	300	41.0%	460	13.3%
Licensing-out platform technology	30	10.8%	66	9.0%	2,378	68.9%
SG&A costs	1,184	-	2,275	-	2,801	81.1%
R&D costs	636	-	1,224	-	1,490	43.2%
Other	548	-	1,051	-	1,311	38.0%
Operating income	-907	-	-1,543	-	651	18.9%
Ordinary income	-907	-	-1,541	-	655	19.0%
Net income	-891	-	-1,503	-	670	19.4%
No. of employees (people)	81	-	87	-	90	-

Note: FY12/14 values are the revised values

For FY12/15, the company projects that its consolidated sales for the full year will be ¥732 million. In the drug discovery alliance business, it expects an increase in trial contracts for using the fully human ADLib[®] system to contribute to sales, while in the lead antibody licensing business, it plans to license its anti-semaphorin 3A antibody. In addition, in the licensing out platform technology business, it anticipates an increase in royalty income from Fujirebio Inc.

In FY12/16, the company anticipates a surge in sales to $\frac{43,452}{100}$ million, which will be driven by the licensing out platform technology business. It expects a massive jump in sales from licensing out its platform technology to a number of Japanese and overseas companies, reflecting the higher maturity of the fully human ADLib® system. It is thought that the company will limit the number of companies it concludes licensing agreements with. This is because the company itself is aiming to primarily be a drug discovery company that targets the development of lead antibodies. Currently, it is mainly advancing development projects in the field of oncology, but as was explained above, going forward it also intends to strengthen its development in the area of pandemic contagious diseases.

In the future, the company is aiming to establish its fully human ADLib[®] system as a drug discovery platform that will enable the discovery of high value-added lead antibodies, and thereby realize is vision of providing the "ultimate made to-order medicine" (targeting by 2023).



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Strengthened financial structure through equity financing and there are no funding concerns

(2) Financial condition

The balance of total assets at the end of September 2014 was down ¥480 million compared to the end of the previous fiscal year, to ¥4,532 million. The main reason was a decline of cash and deposits of ¥1,769 million due to a rise in operating expenses. Liabilities declined ¥32 million compared to the end of the previous fiscal year, to ¥420million, primarily because the interest-bearing debt balance had become zero. Net assets declined ¥447 million, to ¥4,111 million, mainly due to a fall in retained earnings. As of the end of September, the company's total cumulative loss was ¥2,742 million.

While the company continues to record a loss, it is strengthening its financial structure and in the last fiscal year carried out equity financing that increased its cash and deposits in excess of \pm 3,000 million. Further, it plans equity financing in December of more than \pm 2,000 million, further solidifying its financial foundation. Management indicators of financial stability, such as equity ratio and interest-bearing debt to asset ratio, are at acceptable levels, and there seems little cause for concern for its funding up to FY12/16.

Summary of balance sheet

					(¥ million)
	FY3/12	FY3/13	FY3/14	FY12/14 2Q	Absolute change
Current assets	1,096	1,084	4,514	4,015	-499
(cash and deposits)	1,013	988	4,349	2,508	-470
Property and equipment	169	211	498	517	19
Total assets	1,265	1,296	5,012	4,532	-480
Current liabilities	211	238	347	304	-42
Non-current liabilities	8	20	106	116	9
(interest-bearing debt)	84	132	20	0	-20
Total liabilities	220	258	453	420	-32
Total net assets	1,045	1,037	4,559	4,111	-447
(Ratios of financial stability)					
Current ratio (current assets ÷ current liabilities)	517.7%	455.8%	1,300.8%	1320.7%	
Equity ratio (equity capital \div total assets)	82.6%	76.3%	89.8%	90.2%	
Interest-bearing debt to asset ratio (interest-bearing debt \div total assets)	6.6%	10.2%	0.4%	0.0%	

Risks and Return to Shareholders

Will not pay a dividend in the near future

(1) Risks

We see the following three potential risks to the business of the company.

ORisk of delays in licensing agreement negotiations and R&D

Should there be a delay in licensing agreement negotiations with client candidates or should rupture of the agreement occur, there is the risk that these events could impact on the company's performance. Also, should the licensing of lead antibodies not progress as expected due to delays in R&D, or should the development be abandoned because of the results of assessments of drug efficacy or safety tests during the course of the drug development, which may arise at any time, there is the risk that these events could impact on the company's performance in the future.



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OSuperior technologies could be developed

If a technology far superior to the ADLib[®] system for producing antibodies or other new technologies are developed, this system may not be able to maintain its competitiveness in the market.

OHigh dependence on a single product is potentially dangerous

The Chugai Pharmaceutical group $\langle 4519 \rangle$ accounted for 88.9% of the company's total sales in FY3/14. If the business relationship with the group deteriorated for some reason, the company's performance would be severely threatened. On December 24, 2014, the company announced that its contracts with the Chugai Pharmaceutical Group for joint research and contract research using the ADLib[®] system had each been extended.

(2) Returns to shareholders

As the company still carries cumulative losses, it will not pay a dividend in the near future. However, after it establishes a basis for stable profits, its policy is that it will pay dividends that reflect its improved financial condition and business performance.

Company Description

The ADLib® system can generate broader antibody diversity than conventional antibody production systems.

(1) ADLib® System

The ADLib® system, the company's core technology, was developed by RIKEN as a method for antibody discovery in 2002. Today, the patent rights to it are shared equally by the company and RIKEN (50% each). Simply stated, the ADLib® system promotes DNA recombination (gene conversion) in the antibody locus of DT40 cells, a cultured cell line derived from chickens, to generate the antibody protein library. Then with magnetic beads the system collects only the cells that bind to the target antigen. Antigen–specific antibodies can be harvested by culturing those cells for about a week.





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Company Description

Most of the therapeutic monoclonal antibodies now on the market were discovered by one of two conventional methods; the mouse hybridoma method or the phage display method. The table below shows the differences between these existing technologies and the ADLib® system.

Comparison of the ADLib® System with the Mouse Hybridoma Method and the Phage Display Method

Built a strong	competitive advantage through the establishment of the
fully human A	

	ADLib [®] system	Hybridoma	Phage display
Tough antigens*	Applicable	Applicable to some	Applicable to some
Antibody generation time	About 10 days	About 6 months	2.5 to 3.5 months
Amount of antigen required	10µg~100µg	~mg	~500µg
Automation	Yes	No	Yes
Fully human antibody	Practical ⇒ Fully workable	Fully workable	Fully workable

: a competitive advantage to other methods

* Tough antigen: an antigen for which antibodies are difficult to obtain

Source: from the company's briefing materials

As for above "Application to tough antigens", the aim is to use the ADLib® system to generate antibodies for those for which access by conventional antibody production methods is tough such as pathogenic toxins or proteins that are conserved across species by evolutionary mechanisms. Among those tough antigens, GPCR or G protein-coupled receptors is now the main focus of antibody development. It is a group of antigens with complicated structure for which it was tough to generate antibodies. However, several small-molecule medicines against diseases caused by these molecular group are now on the market (among these are Gaster to treat peptic ulcers and the antihistamine Claritin). There are several hundred such antigens for which it is tough to generate an antibody. The production of therapeutic antibodies for them would expand the market for antibody drugs substantially. The ADLib® system has the greatest advantages for this production, compared to conventional methods.

In addition, by utilizing the intrinsic gene diversification mechanism in DT40 cells or introducing the artificial arrangement of genes, the ADLib[®] system can generate broader antibody diversity than conventional antibody production systems, and indeed is theoretically capable of limitless diversity.

A short development time before a pharmaceutical is brought to market not only provides patients with a new drug faster, it will also contribute more to sales. Because patents expire after 20 years, a shorter period to generate the antibody makes it possible to reduce the time from discovery to market launch, which is another benefit of the ADLib[®] system.

The generation of fully human antibodies has been a big challenge in the past. However, on March 2014, the company announced that it had completed its technology for producing fully human antibodies and that opened the way for full-scale commercialized use of human ADLib® system. The fully human ADLib® system is able to generate human antibodies as drug candidates by humanizing chicken antibodies by replacing antibody genes in a DT40 cell line established from chicken lymphocyte with artificial human genes. As it only lags behind compared to existing methods in terms of its practical use for generating fully human antibodies, it seems that this achievement is extremely significant toward the company developing its business in the future.



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Structure of the Fully Human ADLib® System (outline)



Source: from the company's briefing materials

The drug discovery alliance business currently accounts for the majority of the company's revenues

2) Overview of Business Structure

With the ADLib $^{\scriptscriptstyle (\! 8\!)}$ system as its core technology, the company manages three types of business.



Source: from the company's briefing materials



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Company Description

The drug discovery alliance business generates new antibodies using the ADLib[®] system, mainly for therapeutic drugs, in collaboration with pharmaceutical companies around the world. This business currently accounts for a majority of the company's revenue, which consists of upfront income when a joint R&D contract is concluded, milestone income reflecting R&D expenses (including personnel expenses) and progress, and royalty income after a drug is marketed. In this business, in principle the company retains at least a 50% share of the right to a developed antibody, so it provides greater added value than conventional consigned or commissioned drug development. The standard time frame for antibody drug development is 6.5–10 years. This could be broken down into about 1 year of basic research and discovery, 1–2 years for non-clinical development, \rightarrow 3.5–5 years for clinical trials \rightarrow 1–2 years for review \rightarrow approval and marketing.

The Chugai Pharmaceutical Group is the main collaborative research partner for this segment (business with this group accounted for 88.9% of the company's total sales in FY3/14).

The licensing out platform technology business is the second pillar, in which the company licenses the ADLib[®] system to other companies, which use this technology to generate antibodies. From this business, it obtains upfront income when a licensing contract is concluded, annual license fees, milestone income reflecting the progress in the development of antibodies discovered using the ADLib[®] system, and royalty income after a drug is marketed. This business is highly profitable since the only costs, apart from the royalties paid to RIKEN are for technology transfer work (for about one month).

Currently, Fujirebio Inc. is the only licensee of the ADLib® system for the discovery of antibodies for in-vitro diagnostic agents. In December 2013, Fujirebio commenced sales in Europe of an in-vitro diagnostic kit that includes an antibody generated by the ADLib® system. This was the first commercialization of an antibody made with this system.

The third pillar, the lead antibody licensing business, is the licensing of antibodies that have been developed by the company in the discovery or pre-clinical stage. These antibodies are generated using the ADLib[®] system for target antigens obtained through joint R&D or business agreements with universities, public medical institutes and companies with proprietary technology, such as Biotecnol, Inc.* In the future, this business model will generate upfront income from licensing agreements, milestone income reflecting progress in antibody development, and royalty income after a drug is marketed, supplementing the company's revenue from the other two businesses. In this business, the company is collaborating with several organizations, including Yokohama City University, The University of Tokyo, National Cancer Center, and Biotecnol, although at the current stage it does not record sales in it.

The ADLib® system is patented in Japan, the U.S., Europe, and China. The patent rights are shared equally by the company and RIKEN and it pays royalties to RIKEN. This patent will expire in Japan, Europe and China in 2023, and in the U.S. in 2025. But the company has been applying for relevant patents, including the patenting of the fully human ADLib® system. Thus it should retain competitive advantage for the ADLib® system even after the existing patent expires.

* The company and Biotecnol concluded a joint research agreement in February 2013 and they are conducting R&D into the development and production of high value–added antibody medicines using Biotecnol's Tribody[™] technology and the ADLib® System. Their target medicines could not be generated using other current technologies.

The table below shows the main partners in each business and the purposes of the agreements.

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Chiome Bioscience Inc. 4583 TSE Mothers

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Company Description	Company	Description
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Partner	Agreement term	Purpose of agreement		
O Drug discovery a	lliance business			
Chugai Pharmaceutical Co., Ltd.	11/2008 - 12/2015	Joint R&D using the ADLib [®] system to generate antibodies.		
Chugai Pharmaceutical Co., Ltd.	7/2011 - 12/2016	Service agreement to support R&D using the ADLib® system to generate antibodies.		
Chugai Pharmabody Research Pte. Ltd.	8/2012 - undisclosed	Service agreement on the procurement of research materials necessary for efficient antibody drug development.		
O Licensing out pla	tform technology bu	siness		
Fujirebio Inc.	For life of patent	Generate and sell in−vitro diagnostic agents, including antibody generated using the ADLib [®] system to measure vitamin D.		
Fujirebio Inc.	For life of patent	Joint R&D and the non-exclusive right to use the ADLib® system.		
O Lead antibody lic	ensing business			
Yokohama City University	10/2008 - 3/2015	Develop a specific antibody to recognize the semaphorin molecule.		
Biotecnol, Inc.	2/2013 -	Research and develop novel and high value-added therapeutic antibodies that cannot be generated from conventional technologies.		

Main Partners of Each Business

Source: Company materials and Japanese Securities Report

Utilizing LivTech's animal research facility

(3) Subsidiary LivTech, Inc.

In December 2013, the company invested about ¥90 million for a 52.9% stake in LivTech, Inc., making the company a subsidiary. LivTech has been developing antibodies for cancer stem cell antigens and has two development pipelines. For one pipeline, it licensed one of these lead antibodies, LIV-2008, to Yakult Honsha Co., Ltd. in 2011 for joint R&D toward the production of a cancer medicine. For another, LIV-1205, LivTech is now seeking a pharmaceutical company as a partner for the development of a medicine based on its other lead antibody. It owns a facility for animal research and is particularly strong in developing antibodies up to the clinical trial stage. LivTech generates annual sales of about ¥100 million but suffers an annual operating loss of several tens of millions of yen.

The company acquired LivTech to obtain its expertise in the pre-clinical stage development of antibodies and in actual licensing record of antibodies, and it also gained access to LivTech's animal facility. By combining LivTech's expertise with its ADLib® system, the company will be able to accelerate its development of antibodies to counter the antigens causing cancer autoimmune diseases, and contagious diseases.

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