COMPANY RESEARCH AND ANALYSIS REPORT

NanoCarrier Co., Ltd.

4571

Tokyo Stock Exchange Mothers market

8-Sept.-2021

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Summary

Conducted a business integration with AccuRna Inc., and is leveraging business synergies through the complementarity and combination of excellent management capabilities and cutting-edge nucleic acid drug discovery capabilities

NanoCarrier Co., Ltd.<4571> (hereafter, also "the Company") is a bio-venture company established in 1996 by the two inventors of micellar nanoparticles. The Company's name is a portmanteau of nanoparticle technology (micellar nanoparticle technology) and carrier (the carrier of the drug). It is one of only a few companies in Japan conducting drug discovery using its own platform technology (DDS*), which encapsulates anti-cancer drugs (approved, discontinued, and new) in its own micellar nanoparticles technology that carries them directly to the target site, which makes possible the effective use of drugs. It has few side effects and increases drug efficacy, so it is contributing to expanding the scope of drug discovery.

* DDS: Drug Delivery System refers to a technology that aims to maximize the effects and minimize the side effects of a drug by controlling its distribution within the body.

AccuRna Inc., is a nucleic acid drug discovery venture company that has the same technological backbone as the Company (application development of DDS, etc., based on the micellar nanoparticles technology). The Company was a "brother company" to AccuRna and its investor at the time it was founded in 2015. AccuRna was granted a partial license to the Company's patented technology. It then conducted an absorption merger of AccuRna in September 2020. AccuRna has an abundance of findings and technologies in the nucleic acid drug discovery area, while the Company specializes in clinical development, pharmaceutical affairs, and manufacturing of drugs (including GMP management). With the business integration, the Company established an integrated system for a new modality from R&D and clinical research and clinical trials through to manufacturing and quality control. Also, there are great expectations for the Company's two-person management structure, of President & CEO Tetsuhito Matsuyama, who is demonstrating outstanding management skills, and CSO Shiro Akinaga, who is one of the leading experts in Japan in the anti-cancer drug development and nucleic acid drug discovery areas.

1. Concentrating activities on three late-stage clinical development drugs

The Company's pipeline has completely changed compared to a few years ago. It is focusing on in three products in the late stages of their clinical development: VB-111 (ovarian cancer) and ENT103 (otitis media), which are in phase III clinical trials, and NC-6004 (head and neck cancer), which is in a phase II clinical trial. A feature for each is that the Company is developing them jointly with partner. In other words, it is not being restricted to its own technologies and development and is actively working on joint development and on licensing-in external technologies, so it can be said to be broadly steering a course to development that prioritizes speed. For these three late-stage clinical development drugs, the Company is aiming to generate profits by FY3/24 by accelerating licensing-out and approval applications.

2. Expanding the pipeline in the nucleic acid drug area by incorporating a new modality

It seems that the number of inquiries and consultations that the Company is receiving about nucleic acid drugs is rapidly increasing. The nucleic acid drug area (its global market scale is forecast to be ¥2.1tn by 2030) is said to be the third modality of drug discovery following small molecular weight drugs and antibody drugs, and it has the potential for developing drugs indicated for diseases that are difficult to treat using existing drugs, so they are attracting attention as drugs that can open up the next generation of medical treatment. Also, there are hardly any companies in Japan researching mRNA drugs, which are attracting attention as a vaccine, and the fact that the Company is a pioneer in nucleic acid drug development is considered to be the reason why it has a particularly large volume of findings and information in comparison to the R&D of other drug discovery manufacturers and academia in Japan. In the nucleic acid drug pipeline, it has a lineup of three products–NC-6100 siRNA (breast cancer), RUNX1 mRNA (osteoarthritis), and TUG1 ASO (glioblastoma)–and there are expectations for their development as promising products that will become major nucleic acid drugs in 5 to 10 years' time. In the short term, the Company is focusing on and specializing in the three late-stage clinical development drugs in the existing pipeline, but in the medium- to long-term, it can be said to be implementing a growth strategy by both rebuilding the business portfolio through shifting R&D resources to nucleic acid drugs, and becoming profitable at an early stage and developing the next generation of products (nucleic acid drugs).

3. Actively progressing M&A and partnerships

NK-105 (Nippon Kayaku Co., Ltd. <4272>), which the Company licensed-out at the initial stage, did not in the end acquire approval in the phase III clinical trial, damaging the expectations of stakeholders. The reason was because stakeholders thought the Company's pipeline only consisted of one, high risk development project (commonly seen in bio-ventures) without much of a backup plan for if the project fails. However, several years ago the Company changed to a growth strategy that aims to avoid concentrated risk and has reformed to a "concentrated and diversified" pipeline that is composed of multiple promising development drugs. Therefore, it is actively progressing the licensing-in of external technologies and M&A (to save time). Also, some listed bio-ventures that have been unable to move pipeline drugs to the next stage have hidden excellent technologies and human resources. CEO Matsuyama thinks that listed bio-ventures, even if small individually, can form a technological group able to compete with major and medium-sized pharmaceutical companies if they are complementary and can combine, and that they have the potential to create new value and to grow and develop. This would seem to be the part of the "Bio-venture Union" concept.

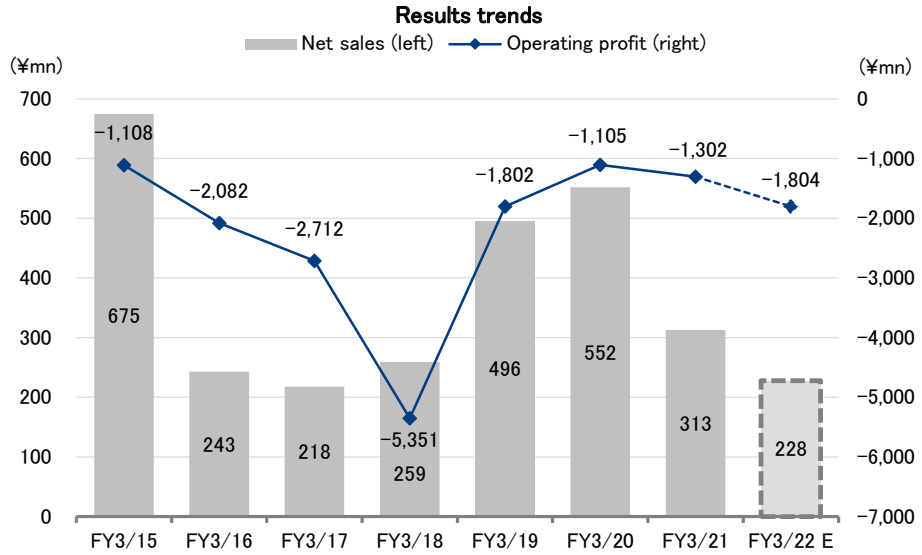
4. Company-wide initiatives for SDGs and contribution to a sustainable society

The Company has changed its previous message of "We will provide new pharmaceuticals through nanotechnology" to its new message of "We will contribute ourselves to the health and wellbeing of people by creating new value." Currently, the entire Company is working together on corporate activities for Sustainable Development Goals (SDGs) and on social contribution. For the 17 SDGs, it is arranging and defining them from the viewpoints of "social contribution," "human resources development," and "environmental conservation," and raising awareness of them within the Company. In fact, the Company's lineup of development drugs includes ovarian cancer treatment (VB-111), breast cancer treatment (NC-6100), and intractable infertility treatment (PRP therapy), so its business activities have socially significance because it will provide new treatments to patients looking for breakthrough treatments.

Summary

Key Points

- Concentrating activities on three late-stage clinical development drugs
- Expanding the pipeline in the nucleic acid drug discovery area
- Rebuilding the business portfolio with a growth strategy to become profitable early and develop next generation products (nucleic acid drugs)
- Actively progressing M&A and partnerships
- Conducting Company-wide initiatives for SDGs and contributing to a sustainable society



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

Company profile

Steadily evolving and growing as a drug discovery bio-venture

1. History

The Company is a venture company established in 1996 by The University of Tokyo Professor Emeritus Kazunori Kataoka and Tokyo Women's Medical University Emeritus Professor Teruo Okano to apply the micellar nanoparticles they invented to DDS drug formulation and to start a business. DDS was actively studied in the U.S. state of Utah, where Professor Kataoka and Professor Okano had conducted research. To disseminate the micellar nanoparticles technology they had invented from Japan to the world, they newly established the Company. The Company established a research institute in 2000 and began full-scale research activities.

Based on the micellar nanoparticles basic patent licensing agreement with TODAI TLO, Ltd., the Company has concluded a polymer supply agreement with NOF CORPORATION <4403> and a Paclitaxel Micelle joint development and licensing agreement with Nippon Kayaku Co., Ltd. It has also been progressing clinical development and creating pipeline drugs in-house. In March 2008, the Company's shares were listed on the Tokyo Stock Exchange (TSE) Mothers market, but due to the global financial crisis in September of the same year, there was a period in which investment cooled-down significantly in all venture companies in Japan, and it became difficult to raise the funds necessary for R&D. The funds raised by the Company at the time of the listing were only around ¥600mn, which is an extremely low level, and it became difficult to move the development of NC-6004, which had been conducted in Europe up to that time, to the next stage, and it was forced to change its strategy. Immediately, the Company aimed for development in Asia, the Company has entered into a licensing agreement for NC-6004 (joint development, fund raising through investment etc.) in the Asia region with Orient Europharma Co., Ltd. (hereafter, OEP), which is a Taiwanese pharmaceutical company, and it has been steadily progressing its development through this agreement.

Bio-ventures have concerns, including having to postpone or suspend development due to a lack of funds. But in 2012, the Company raised funds from Whiz Partners Inc., and conducted a capital increase through a third-party allocation with Shin-Etsu Chemical Co., Ltd.<4063> and also concluded a joint research agreement for a materials-production technology with it. Then in 2013, Global Finder (principal company, JP Morgan <JPM>) became an arranger, and it raised funds of approximately ¥9bn from institutional investors in Europe, the United States and Asia, and it succeeded in making dramatic progress for in-house pipeline development. At that time, it can be said that broadening the scope of the pipeline development strategy and drug discovery increased the Company's appeal to overseas institutional investors as one of only a few Japanese companies conducting drug discovery through a US-type in-house platform technology. Also, the Company has benefited from the boom in bio-ventures that reignited following Professor Shinya Yamanaka of Kyoto University being awarded the Nobel Prize in 2012 for his research on iPS cells.

Since around that time, it has become possible to recruit mid-career hires, of human resources with experience in the research and clinical development of cancer therapeutic agents, and the Company started clinical development in Europe and the United States as in-house development. Also, in 2015 President Matsuyama joined the Company as the CFO, from which time it strengthened its policy of advancing both M&A and partnerships and made progress including by licensing-in pipeline drugs that could be called cutting-edge even globally. The gene therapy agent licensed-in from Vascular Biogenics Ltd. (hereafter, VBL) of Israel in November 2017 is at the stage of the international phase III clinical trial (for platinum-resistant ovarian cancer). Japan will be able to participate in the trial that 75% of patient registrations have been already completed in the United States and other countries overseas. This will shorten the development period considerably (shorten the usual period of at least 10 years to a few years), as well as enabling development costs to be reduced (from the usual billions of yen to hundreds of millions of yen), and it is being licensed-in as a drug that will contribute to the Company becoming profitable early. It is also licensing-in a product in the infertility treatment and a drug in the ear, nose and throat areas, and while focusing on the practical use of micellar nanoparticles, it is licensing-in innovative drugs to stabilize the earnings foundation early.

2. Business description

The Company has worked on expanding its pipeline, centering on developments of anti-cancer drugs and, with the business integration with AccuRna, complementarity and combinations of technologies and pipelines have greatly strengthened its product development capabilities and broadened its business area to the nucleic acid drug area, which will be the core area of next generation pharmaceuticals.

(1) Will become profitable early by acquiring approval for drugs and accelerating licensing-out

The Company is concentrating activities on three pipeline drugs in their late stages of clinical development (VB-111/ovarian cancer, ENT103/otitis media, and NC-6004/head and neck cancer). The VB-111 gene therapy drug developed overseas is indicated for platinum-resistant ovarian cancer, and it is a therapeutic agent with high social significance by providing a new treatment option for patients for who there is currently no effective treatment. There are expectations for ENT103, which is indicated for otitis media, as a new therapeutic agent in the ear, nose and throat area as the first fledgedly developed within Japan in this therapeutic area in a quarter of a century. As for NC -6004, the Company is progressing the development in combination with immune checkpoint inhibitors (ICIs), which have become a focus of cancer treatment. Drugs used in combination with ICI is an area that pharmaceutical companies are highly interested in, so it will license it out as soon as receiving the results of the trial. The Company is aiming to generate profits from acquiring approval for and launching into the market VB-111 and ENT103, and licensing-out NC-6004 by FY3/24.

(2) Expanding the pipeline through a new modality

In the medium- to long-term and centered on its own technologies, the Company will create therapeutic agents that will be cutting-edge even when viewed globally, including next-generation modalities like nucleic acid drugs, and develop them to be a new pillar of earnings. As one part of this, in 2020 it conducted an absorption merger of AccuRna, which handles nucleic acid drugs including messenger RNA (mRNA) drugs. mRNA drugs are a new drug discovery technology that have attracted a lot of attention globally as COVID-19 vaccines. The merger has combined AccuRna's nucleic acid drug discovery capabilities and excellent human resources specializing in RNA with the Company's drug development capabilities, and based on these complementary strengths, it will develop nucleic acid drugs to be its second business pillar.

(3) Actively progressing M&A and partnerships and is opening-up the pharmaceutical market through a new concept to generate profits

In the future also, the Company's policy is to actively progress M&A and partnerships in order to expand its pipeline and technological foundation. It has drugs in their late stages of clinical development like VB-111, and it is discovering and incorporating into its pipeline cutting-edge technological products whose market scales are insufficient for major pharmaceutical companies, despite being revolutionary. It is also promoting and expanding the drug discovery business by utilizing partnerships, such as with a company with innovative technologies under the umbrella of Axcelead, Inc., which is a partner promoting tissue regeneration, and also Axcelead's expansive network, and by working on various innovative technologies through open innovation, including joint R&D with major pharmaceutical companies.

3. Features and strengths

(1) Features and strengths

The Company is one of only a few bio-venture companies in Japan targeting drug discovery and development based on its own platform technology. By encapsulating anti-cancer drugs in micellar nanoparticles and delivering them directly to the target tissue, it is contributing to expanding the scope of drug discovery through increasing the efficacy of drugs with few side effects. This technology also helps to stabilizing unstable substances, and the Company is contributing to the development of new modalities, including nucleic acid.

Up to the present time, the Company has worked on many clinical trials and is conducting developments of multiple late-clinical-stage drugs. As a result, it has an abundance of experience and findings relating to clinical development, including drug manufacturing that it strictly managed, such as for quality control in large-scale production, and it is accumulating technological assets over a wide range of areas, from the oncology area to other therapeutic areas awaiting next-generation pharmaceuticals (antibodies and nucleic acid).

The anti-cancer drug market continues to expand globally, including in recent years from the market launches of revolutionary new drugs such as KEYTRUDA, an immune checkpoint inhibitor with global sales of approximately UD$14.4bn in 2020. The Company has flexibly revised its development strategy so it is in line with current global cancer treatment trends, and its strengths include that it is promoting development with a long view of the anti-cancer drug market. For instance, among the products it has developed, it is adding pharmaceutical value with the combination drug KEYTRUDA, which has become the focus of cancer treatment, as a combination drug. Also, the Company is bringing together experts in development in the anti-cancer drug area, and as with VB-111, its strength is that it can evaluate the licensing-in of overseas products, such as their market potential and innovativeness.

Also, a market is being opened-up for nucleic acid drugs that has not existed before, and in terms of market potential, it is forecast to be on a scale of ¥2.1tn by 2030. By merging with AccuRna, which is the leading specialized company in nucleic acid drug discovery in Japan, it is considered that the Company will be able to utilize accumulated research results in the nucleic acid area, including on mRNA, up to now, and this will become its strength in the future.

(2) Business model

The Company conducts clinical development of drugs discovered and manufactured in-house and drugs licensed-in from the outside. It is expected to secure income from sales of them by the Company itself, and also to secure agreement lump sum income, milestone income, and royalty income through licensing-out to other companies at the stage when a drug is being developed.

a) Licensing-in

The Company licenses-in other companies' promising pharmaceutical candidates and books sales income through developing and selling them. However, the Company pays to the license holder agreement lump sum payment, milestone payments, and royalties depending on sales, and also the costs for providing the drug formulation. Licensing-in incurs a certain level of costs through introducing the promising pharmaceutical candidate at a later stage of its development, but it can be expected to be market launched in a short period compared to if it had been developed from the initial stage.

b) Licensing-out

The Company licenses-out pharmaceutical candidates for which it has conducted R&D in-house, from which it expects to obtain agreement lump sum income, milestone income that is paid when certain development milestones are reached, and royalty income depending on sales after the drug is market launched. After a licensing-out agreement, the R&D costs and other costs are borne by the partner, which reduces development costs and development risk for the Company.

Trends in the development pipeline

Trends in the development pipeline

Drug	Indicated disease	Development stage				Development area	Partner
		Non-clinical	ph1	ph2	ph3		
VB-111	Ovarian cancer					Japan, the United States, Europe Israel	Joint development (licensed-in) VBL
	*Combination treatment with Paclitaxel (gene treatment drug)						
ENT103	Otitis media					Japan	Joint development Ceolia Pharma
	*Antimicrobial drug (ears, nose, and throat area)						
NC-6004 Cisplatin micelle	Head and neck cancer					Europe Taiwan	Joint development (licensed-out) OEP
	*Combination treatment with Pembrolizumab (KEYTRUDA)						
NC-6300 Epirubicin micelle	Soft tissue sarcoma					USA	
	*Narrowed down indications to angiosarcoma and is current conducting the phase I part expansion cohort (additional case studies trial)						
NC-6100 PRDM14 (siRNA)	Breast cancer					Japan	Investigator-initiated trial The Cancer Institute Hospital of JFCR
	*Drug discovered by former AccuRna Co., Ltd.						
TUG1 (ASO)	Glioblastoma					Japan	Joint development Nagoya University
	*Drug discovered by former AccuRna Co., Ltd.						
RUNX1 (mRNA)	Osteoarthritis					Japan	PrimRNA Axcelead
	*Drug discovered by former AccuRna Co., Ltd.						

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

1. Rebuilding the pipeline

Through M&A and partnerships, the Company has licensed-in products and integrated its business with AccuRna, so its pipeline has changed compared to a few years ago. It is aiming to become profitable early by concentrating on three products that are in the late stages of their clinical development: VB-111 (ovarian cancer) and ENT103 (otitis media), which are in phase III clinical trials, and NC-6004 (head and neck cancer), which is in a phase II clinical trial. It also has three pipeline drugs in the nucleic acid drug area, which are expected to be innovative therapeutic agents: NC-6100 siRNA (breast cancer), RUNX1 mRNA (osteoarthritis), and TUG1 ASO (glioblastoma).

2. The three late-stage clinical development drugs

(1) Status of and progress made in developing the gene therapeutic agent (VB-111/ovarian cancer)

This is a gene therapeutic agent for which the license was obtained from VBL (Israel). The Company's micellar nanoparticle drug formulation is intended to be a therapeutic agent that targets tumor cells. In contrast, VB-111 targets tumor vessels in order to starve the cancer, and it is also expected to have the effect of causing tumor immunity. It is in the pipeline as a therapeutic agent with a different mechanism to that of micellar nanoparticles, and it will contribute to broadening the Company's choices and to strengthening its business foundation in the cancer area.

Generally speaking, a clinical trial normally requires from billions of yen to tens of billions yen, depending on its scale. But if the drug is in the phase III clinical trial stage, it is considered sufficiently worthy of investment on considering factors such as the probability of success and the subsequent development costs. The Company has already procured not only the development funds, but also the funds to strength its management foundation, such as to enter-into business partnerships. Therefore, in November 2017 it acquired the development and marketing rights for Japan from VBL. This business is in the gene therapy agent field, and while it is a gene therapy using viral vector, its business characteristics are similar in terms of delivering the drug to tumors. So the Company, which has experts in clinical development, has been able to undertake its development in-house in Japan. Also, the gene therapy agent VB-111 meets needs in the cancer treatment environment, such as having the effect of eliciting an immune response. Moreover, as a systemic administration-type drug, it is expected that its applications will be expanded, including to various types of solid tumors, and VBL is conducting a trial in the United States indicated for colon cancer and glioblastoma.

VBL, which is developing VB-111, announced in June 2021 at a meeting of the American Society of Clinical Oncology (ASCO) that its “application for approval may be one year ahead of schedule.” From this, it is estimated that the clinical trial will make major progress.

Also, in the development being undertaken by the Company in Japan, 12 leading medical facilities for cancer treatment (National Cancer Center Japan, the Cancer Institute Hospital of JFCR, etc.) have started to recruit patients for the phase III clinical trial and administered the drug to the first patients in June 2021.

VB-111 is indicated for platinum-resistance ovarian cancer, and it is a therapeutic agent that has social significance in that it can be provided as a new treatment option to patents for who the platinum therapy, which is the first-line treatment, is no longer effective and so for who it is said that there is no effective treatment. At the current time, with no competitive therapeutic agents, cancer treatment doctors are saying that “it fills a highly unmet medical need.” Overseas, trials took place first in the United States and Israel, to which was added Europe, and Japan’s participation also became possible during the phase III clinical trial. Globally, from among the 400 planned subjects, approximately 300 subjects have already been enrolled, and of these, the plan is to enroll 30 subjects in Japan. The enrollment is scheduled to be completed by the end of March 2022, and after that, following the completion of the observation period, including of the final subjects, data on all the subjects will be collected. If the trial progresses smoothly, Progression-free Survival (PFS) data can be expected in around one year. If the results are good, it will then proceed to applying for approval, with a market launch expected after two or three years (around 2024).

(2) Status of and progress made in the development of the otology antibiotic (ENT103/otitis media)

The Company is jointly developing this drug with Ceolia Pharma. It is a new antibiotic drug in the otology (ear) area, and is the first fully-fledged trial conducted in Japan in a quarter of a century. It is expected to have high efficacy, of antibiotic activity of around 10 times that of conventional drugs, so the aim is for it to replace existing drugs. In Japan, a phase III clinical trial for otitis media is being conducted, and the enrollment was completed in May 2021. The goal is to apply for approval in FY2021 toward its market launch around 2023. Patients with severe otitis media include both men and women and the old and young, and moreover there are comparatively many such patients, so it is expected to generate profits early.

(3) Status of and progress made in developing cisplatin micelle (NC-6004/head and neck cancer)

In the anti-cancer drug development market, immune checkpoint inhibitors, such as OPDIVO, have started to appear, and the anti-cancer drug development environment has changed drastically. The Company is conducting a phase II clinical trial for NC-6004 in Europe and the United States for head and neck cancer, as a new combination therapy with KEYTRUDA, and it plans to license it out to pharmaceutical companies when the trial is finished. Many reports have confirmed that cisplatin, which is encapsulated in NC-6004, has synergistic effects for cancer treatment when used in combination with an immune checkpoint inhibitor, and it is expected to be developed as a therapeutic agent that utilizes the strengths of NC-6004 to reduce the strong side effects of cisplatin. In the phase IIa trial, it has been confirmed that it improved both the frequency of occurrence and the severity of the side effects of cisplatin, which include physical symptoms such as fatigue, nausea and vomiting, and difficulty breathing. Also, it was reported that no cases of hearing impairment, which is a clinical problem with cisplatin, were observed, and the incidence rate of peripheral neuropathy was low and its severity was mild. For the phase IIb trial, the enrollment is scheduled to be completed during FY2021 and more than half of the 124 subjects have already been enrolled. Development is taking place mainly in Europe, and the plan is to license it out based on the phase IIb clinical trial's results, which are expected in FY2022.

3. Nucleic acid drugs

Nucleic acid drugs are able to select new targets, such as transcription factors within cells, that cannot be targets of the anti-cancer drugs and antibody drugs used up to the present time. So they have the potential to be provided as a new treatment option. On the other hand, nucleic acid is very unstable after administration into a body so the use of a DDS is essential, and therefore it is an area in which the Company's technologies can be expected to be utilized.

NC-6100 (siRNA drug /breast cancer) is an siRNA drug that suppresses the functions of PRDM14, which is a transcription factor overexpressed in breast cancer cells, and it suppresses the growth of cancer stem cells. Therefore, there are expectations for it as a new therapeutic agent for breast cancer for which existing anti-cancer drugs and antibody drugs are not effective. The investigator-initiated phase I clinical trial began in September 2020 at the Cancer Institute Hospital of JFCR.

TUG1 ASO drug (glioblastoma) is an ASO drug that suppresses the functions of TUG1, which highly expressed in glioblastoma, a malignant brain tumor. There is no effective drug for glioblastoma except temozolomide, so it is an area in which the new therapeutic agents is required. In a joint research project with the Tokai National Higher Education and Research System, Nagoya University, it was selected for the Innovative Cancer Medical Treatment Practical Application Research Project of the Japan Agency for Medical Research and Development (AMED) and received development funds (upper limit of ¥77mn a year per project). The plan is to establish a manufacturing process for the study drug and to complete the non-clinical studies in three years from April 2020, which will then lead to the clinical trial.

mRNA drugs are a technology that are attracting a lot of attention globally primarily as infectious disease vaccines, but also in the areas of cancer vaccines, local regenerative medicine, rare genetic diseases (an alternative to gene therapy), and gene editing. Among these, the Company is applying its micellar nanoparticle technology, which is one of its strengths, to the development of Polyplex Micelles toward securing a competitive advantage in mRNA drug development. The name awareness of mRNA drugs has changed in the pandemic environment, but the situation can still be said to be that up to the present time, hardly any companies in Japan have progressed the development of mRNA drugs.

The Company is progressing development of an mRNA drug. The RUNX1 mRNA drug (knee cartilage regeneration) is a new type of therapeutic agent for knee osteoarthritis, in which mRNA translated RUNX1 protein, a cartilage inducing transcription factor, is administered directly into the joint cavity, promoting regeneration of the cartilage in the damaged area. It has acquired the development funds up to the completion of the investigator-initiated phase I clinical trial from AMED. For the development of this drug with Axcelead, the companies established the joint venture PrimRNA Co., Ltd. in April 2021. They aim to complete the phase I clinical trial in around four years' time. The partnership with Axcelead includes partnerships with a company under its umbrella that has a track record globally for non-clinical studies and a contract manufacturing organization, so it will be the major driving force behind the development of this drug.

4. Other pipeline drugs

For epirubicin micelle (NC-6300), which is in the clinical development stage, a phase I/II clinical trial is being conducted for soft tissue sarcoma, and among these conditions, the target has been narrowed down to angiosarcoma, for which the phase I part of the trial is currently being expanded. The enrollment of 10 subjects for the expanded trial against angiosarcoma has been completed. Moreover, NC-6300 is granted Orphan Drug designation for soft tissue sarcoma by the US Food and Drug Administration (FDA), and Fast Track designation for angiosarcoma. Based on the trial results, including of the expanded trial, the Company is aiming to acquire approval at an early stage of clinical development while cooperating with the FDA, and for the future, it has started to investigate licensing it out.

NC-6300 is designed to release the drug only within cells by adding pH responsiveness functionality, and it is expected to further reduce side effects and strengthen efficacy. In the NC-6300 phase I clinical trials conduced in Japan and the United States up to the present time, it was reported that tolerability was confirmed even for high dosages that greatly exceeded the clinical dose of epirubicin, the drug it encapsulates, and that moreover, it suppresses the occurrence of cardiac toxicity that is a feature of epirubicin, making possible long-term administration.

5. Products

In order to spread the use of regenerative medicine for infertility treatment in Japan, in April 2019, the Company acquired the sales right within Japan for Acti-PRP (a blood cell separating device) from Aeon International (Taiwan). Platelet-rich plasma (PRP) includes an abundance of growth factors that encourage cells to grow, and injecting it locally encourages tissue repair and other effects. Treatments using PRP are carried out in areas such as orthopedics, but the Company has licensed it in to be applied to the gynecology area to improve the endometrium environment. PRP therapy for infertility treatment is recommend by Dr. Tsutsumi Osamu, the Director of Sanno Hospital (Minato Ward, Tokyo), and awareness of it is widening, such as through infertility treatment seminars. In the clinical research, which so far has mainly been conducted at Sanno Hospital, embryo implantation has been confirmed in 15% of intractable infertility patients who did not became pregnant even after repeating three or more infertility treatments.

The Company supports Acti-PRP's clinical research and sells it to the nationwide member facilities of the Gynecology PRP Study Group. Based on the Company's philosophy of improving patients' QOL, it is entering into the regenerative medicine field and starting a new business in this area for the first time in Japan. It has completed its support, including for applications from membership facilities' regenerative medicine committees, and this business is now progressing while using practically no resources, and the Company is currently securing sales from its position as a sales agency.

The Company is advancing applications of its own technologies to cosmetics. Starting with products such as luxury cosmetics manufacturer Albion's Eclafutur, a cosmetics solution, and Depth, a hair care product, it is proving cosmetics materials and recording sales.

Through the above, the Company has achieved annual sales of more than ¥100mn, which is the requirement to remain listed on the TSE Mothers market, and it is building an environment that enables it to concentrate on its main business of pharmaceutical development.

Recent developments in partnerships

In April 2021, the Company established PrimRNA as a startup company. The aim of this new startup is to "develop the mRNA drugs which provides innovative treatment to maintain functions impaired by osteoarthritis." It is a joint venture with Axcelead, which is a wholly owned subsidiary of Whiz Partners (which undertakes growth investment for medium- to small-sized listed ventures that are strong in the healthcare field). This drug, which is the result of AccuRna's research in the nucleic acid drug area, has been selected for AMED's Medical R&D Innovative Foundation Creation Project, and has received funds for the development. The Company is collaborating with Professor Keiji Itaka of the Institute of Biomaterials and Bioengineering, the Tokyo Medical and Dental University, and with Professor Sakae Tanaka of the Department of Orthopaedic Surgery, Faculty of Medicine, the University of Tokyo, and the plan is to advance up to the investigator-initiated phase I clinical trial. It seems that there have already been inquiries from pharmaceutical companies showing an interest in it.

The Company is also progressing its partnership with Axcelead. Axcelead acquired part of the drug discovery research platform business of Takeda Pharmaceutical Company Limited <4502>, and it has built and is expanding a value chain that ranges from the R&D to the manufacturing of pharmaceuticals and medical devices. It is a comprehensive drug discovery solutions provider with multiple companies under its umbrella. For the mRNA drug for osteoarthritis, the Company can be expected to partner at an early stage with ALCARIS Co., Ltd. (Axcelead's subsidiary), which is a pharmaceutical contract development and manufacturing organization (CDMO) specializing in mRNA. It is also considering other partnerships in various forms, such as combinations with new modality technologies.

Results trends

Recorded an impairment loss of ¥1,553mn on goodwill generated through the AccuRna absorption merger

1. Outline of results for FY3/21

In FY3/21, the Company's net sales were ¥313mn (down 43.3% year-on-year (YoY)), mainly from development milestone income, cosmetics-related sales, and sales of medical devices relating to the PRP business. The operating loss was ¥1,302mn (a loss of ¥1,105mn in the previous period) and the ordinary loss was ¥1,278mn (a loss of ¥1,144mn). It also recorded an impairment loss of ¥1,553mn on goodwill generated by the absorption merger of AccuRna, and therefore the net loss was ¥2,835mn (a loss of ¥2,009mn).

2. Outlook for FY3/22

For FY3/22, the Company is forecasting net sales of ¥228mn (down 27.2% YoY), mainly from development milestone income, income from the provision of cosmetics materials, cosmetics sales, and sales of medical devices relating to the PRP business. It is also forecasting an operating loss of ¥1,804mn (a loss of ¥1,302mn in the previous period), an ordinary loss of ¥1,751mn (a loss of ¥1,278mn), and a net loss of ¥1,734mn (a loss of ¥2,835mn).

3. Financial condition, issue of share acquisition rights, etc.

Looking at the Company's financial condition in FY3/21, total assets decreased ¥1,123mn on the end of the previous fiscal year to ¥7,820mn, while total liabilities increased ¥145mn to ¥320mn. Net assets decreased ¥1,268mn to ¥7,499mn, mainly due to the recording of a net loss. At the 24th General Meeting of Shareholders held on June 26, 2020, the resolutions to reduce the amount of capital and to dispose of the surplus were approved, which became effective on August 1, 2020. Therefore the share capital decreased ¥3,818mn and retained earnings brought forward increased ¥3,818mn.

Also, through a third party allocation to be allocated to unlimited liability partner THE KENKO FUTURE Limited Partnership, for which Whiz Partner serves as the managing partner, the Company recruited for the 5th unsecured convertible bond-type share acquisition rights worth ¥1,150mn and the 19th share acquisition rights worth ¥2,992mn, and it carried out the allocations on May 10, 2021. As a result, it has funds of approximately ¥10,200mn, as the total of the funds newly acquired through these issues of ¥4,200mn (to be used freely) and its current holding of funds of ¥6,000mn. Going forward, they will be the source of funds for R&D in the nucleic acid drug area, and also for M&A measures and to acquire next-generation technologies.

Initiatives for the Future

1. Actively progressing M&A and partnerships

The Company is changing its pipeline from a one, high risk concentrated type project to a "concentrated and diversified" approach composed of multiple drugs in their later stages of clinical development. Therefore, it is actively licensing-in external technologies and progressing M&A (saveing time for clinical development). Also, some listed bio-ventures that have been unable to move major pipeline drugs to the next stage have hidden excellent technologies and human resources. CEO Matsuyama thinks that listed bio-ventures, even if small individually, can form a technological group able to compete with major and medium-sized pharmaceutical companies if they are complementary and can combine, and that they have the potential to create new value and to grow and develop, which would seem to be the part of the Bio-Venture Union concept.

2. Company-wide initiatives for SDGs and contribution to a sustainable society

The Company has changed its previous message of "We will provide new pharmaceuticals through nanotech" to its new message of "We will contribute ourselves to the health and wellbeing of people by creating new value." Currently, the entire Company is working together on corporate activities for Sustainable Development Goals (SDGs) and on social contribution. For the 17 SDGs, it is arranging and defining them from the viewpoints of "social contribution," "human resources development," and "environmental conservation," and communicating CSR information to employees and raising their awareness of SDGs. In fact, the Company's lineup of development drugs includes ovarian cancer treatment (VB-111), breast cancer treatment (NC-6100), and intractable infertility treatment (PRP therapy), so its business activities have social significance because it will provide new treatments to patients looking for breakthrough treatments.

The Company's management team is also highly interested in SDGs, and its policy is to progress measures for them in the medium- to long-term. It is communicating information to the media as a SDGs company, and moreover, it also holding SGDs study groups attended by all company employees and aiming to increase their awareness of and share information on topics such as SDGs, ESG investment, and the activities of women within the Company. Up to the present time, it has been rare for a bio-venture company to actively conduct corporate activities for SDGs, so the Company can be said to be adopting a strategy with a long-term perspective.

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