COMPANY RESEARCH AND ANALYSIS REPORT

Kubota Pharmaceutical Holdings Co., Ltd.

4596

Tokyo Stock Exchange Growth Market

27-Apr.-2023

FISCO Ltd. Analyst
Yuzuru Sato

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

Kubota Pharmaceutical Holdings Co., Ltd.
4596 Tokyo Stock Exchange Growth Market
27-Apr.-2023
https://www.kubotaholdings.co.jp/en/ir/index.html

Index

Summary

Focused on strengthening marketing and making product improvement, etc. for Kubota Glass

Kubota Pharmaceutical Holdings Co., Ltd. <4596> (hereinafter "the Company") develops innovative medical devices and therapeutic drugs to preserve and restore vision, in keeping with its Corporate Philosophy, "World Without Blindness." The Company has three main projects in its development pipeline: Kubota Glass, which is a wearable myopia control device that aims to treat and control the progression of myopia; Patient Based Ophthalmology Suite (PBOS), which is a remote retinal monitoring device for patients with retinal diseases such as age-related macular degeneration (AMD); and emixustat hydrochloride (HCl), which is a drug candidate indicated for Stargardt disease.

1. Trends of wearable myopia control device

It is said that a majority of myopia cases are axial myopia in which vision is impaired due to elongation of the eye's axial length*1 preventing light from falling into focus on the retina. Kubota Glass technology shortens the axial length in such cases by using augmented reality (AR) technology to project, via micro LEDs, images that are brought into focus in front of the peripheral retina, a process called myopic defocus. Clinical studies have produced data showing better rates of axial elongation control and myopia progression control than competitor products, and safety is also assured through ISO certification. The device is worn for a short time, one to two hours per day, and the technology, which can efficiently control the progression of myopia, has been well received by ophthalmologists and others involved in myopia research. Kubota Glass, which uses this technology, was registered as a medical device with the U.S. Food and Drug Administration (FDA) in June 2022, and sales were commenced. In Japan, where it is marketed as an AR device that recreates outdoor activities, sales were launched in August 2022 at ophthalmologist clinics and at various retail stores and online sites (priced at ¥770,000 with tax). It is still at the soft launch*2 stage, and in FY12/23, the Company intends to enhance the supply chain and make product improvements as it expands the scope of distributors handling the product in Japan. It will also continue to build evidence through clinical studies. Ultimately, the Company intends to acquire approval for Kubota Glass to be sold as a device that controls the progression of myopia with the aim of selling it around the world. The global market for lenses for myopia control is expected to increase from US$24.4bn in 2021 to US$27.0bn in 2025 as the myopic population increases, so the potential market for the product is sizable. The product's effectiveness in controlling myopia appears to be the highest among devices being developed by companies, and there are reports of customers coming to Japan from overseas in order to purchase it, so there seems to be strong interest in it. Going forward, the keys to its growth will be acquiring approval for its sale as a myopia control device and lowering the cost.

*1 The length from the cornea to the retina. The eye's axial length for adults is around 24 mm on average. An elongation of even 1-2 mm can cause parallel rays of light to be brought to focus before the retina, resulting in blurred sight at a distance. (This condition is known as myopia.)
*2 Test sales undertaken for the purpose of troubleshooting and validating market fit in the process from manufacturing to sales, delivery, and aftercare.

2. Trends of development of other major pipeline projects

The Company announced in August 2022 that topline data from a phase 3 clinical study of emixustat HCl, which is being developed as a treatment for Stargardt disease, a genetically inherited retinal disease, showed no significant difference from the placebo group in the progression rate of macular atrophy, which was the study's primary endpoint. However, further analysis of the data showed a significant difference for the patient group in the early stages of the disease, so the Company will search for a co-development partner based on this data, and if it can find a partner, it intends to try again. Regarding PBOS, the Company began a clinical trial for diabetic retinopathy patients at Joslin Diabetes Center in the U.S. in January 2023. Based on the results of the study, it will hold discussions with partner candidates and explore the potential for co-development and commercialization in the U.S.

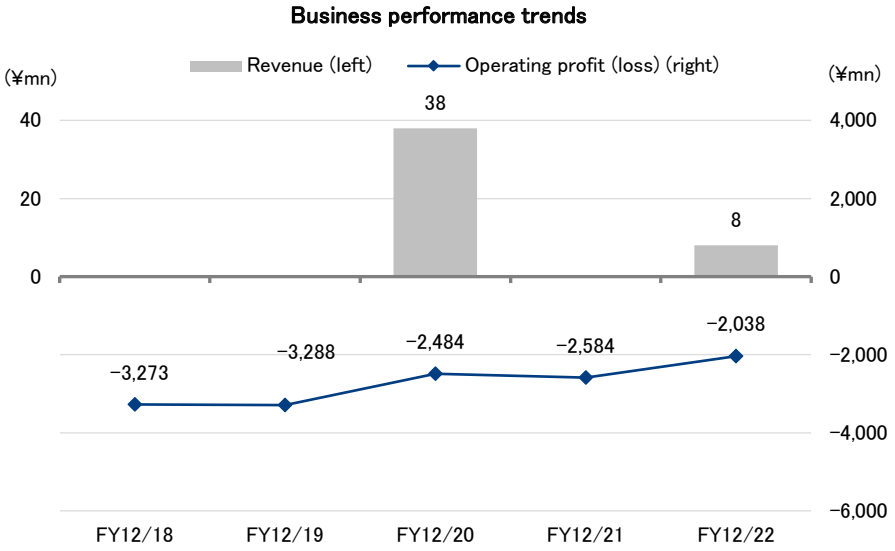
3. Business performance trends

Looking at consolidated results for FY12/22, the Company posted revenue of ¥8mn (up ¥8mn year on year (YoY)) and an operating loss of ¥2,038mn (contracted by ¥546mn). The revenue was from sales of Kubota Glass in Japan and the U.S. Regarding expenses, research and development (R&D) expenses, which were primarily for development of emixustat HCl and the wearable myopia control device, declined by ¥527mn, which was a factor in the smaller operating loss. The Company has not disclosed performance forecasts for FY12/23 because it has been determined that they would be difficult to calculate rationally as of the present because it is difficult to project sales trends for Kubota Glass and because the situation with R&D expenses, which are currently declining, could change, depending on circumstances. Cash on hand stood at ¥4,048mn as of the end of FY12/22. Although the Company has secured around two years' worth of funds for operating activities, the Company is still in a development stage, so it will review its fund procurement situation as necessary.

Key Points

- The Company began sales of Kubota Glass in 2022 and will continue to develop it going forward through product improvements and building evidence in clinical studies
- For PBOS, an investigator-initiated clinical trial for diabetic retinopathy was started in the U.S. in 2023
- For emixustat HCl, efficacy for patients in the early stages of Stargardt disease was suggested in a phase 3 clinical trial, and the Company will begin looking for a co-development partner
- R&D expenses will decline in FY12/23, but the Company intends to make expenditures to expand sales of Kubota Glass

Summary



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

Company profile

A U.S.-born venture company that seeks to develop innovative pharmaceuticals and medical devices focused on the ophthalmology field

1. Company history

In 2002, Dr. Ryo Kubota, a researcher and ophthalmologist, founded the former Acucela Inc. in Seattle, Washington, U.S.A., for the purpose of developing pharmaceuticals and medical devices focused on the ophthalmology field. In February 2014, shares of the former Acucela Inc. were listed as foreign shares on the Tokyo Stock Exchange Mothers Board. Subsequently, in December 2016, Acucela Japan KK, a Japanese subsidiary, was turned into a holding company named Kubota Pharmaceutical Holdings Co. Ltd. through a triangular merger, and Kubota Pharmaceutical Holdings Co., Ltd. was relisted on the Tokyo Stock Exchange Mothers Board as a domestic stock. (The former Acucela Inc. was delisted at the end of November 2016.) It is currently listed on the Tokyo Stock Exchange Growth Market.

Since its founding, the Company has conducted business activities in keeping with its management philosophy of "Contributing to society by creating innovative drugs and medical technologies to preserve and restore vision for millions of people worldwide." In 2006, the Company initiated development of emixustat hydrochloride (HCl), a drug candidate using Visual Cycle Modulation (VCM) technology.* In 2008, the Company concluded a co-development and commercialization agreement with Otsuka Pharmaceutical Co., Ltd. (a group company of Otsuka Holdings Co., Ltd. <4578>) for emixustat HCl for geographic atrophy secondary to dry age-related macular degeneration. However, the agreement was terminated following the announcement in May 2016 of the results of a phase 2b/3 clinical trial of emixustat HCl for geographic atrophy secondary to dry age-related macular degeneration. In addition, the Company carried out a phase 3 clinical study of emixustat HCl for Stargardt disease, which is a genetically inherited retinal disease, but it announced in August 2022 that no significant difference had been found with respect to the primary endpoint. However, further data analysis confirmed a significant difference for the patient group in the early stages of the disease, so the Company will make preparations and try again.

* Visual Cycle Modulation technology: A therapeutic technology that is expected to have the effect of reducing toxic by-products that accumulate in the retina, alleviating retinal disorders caused by oxidative stress, and protecting the retina from light damage, through the visual cycle (the mechanism that converts photons to electrical signals within the retina in the posterior of the eye). The results of clinical studies have confirmed that emixustat HCl has the effect of selectively inhibiting an enzyme called RPE65 that performs a key function in the visual cycle.

Looking at medical devices development pipeline projects besides Kubota Glass, a wearable myopia control device aiming to treat and control the progression of myopia, the Company is pursuing Patient Based Ophthalmology Suite (PBOS), which is a remote retinal monitoring device for retinal diseases such as age-related macular degeneration (AMD). PBOS allows patients to self-measure the condition of their retina at home. With respect to Kubota Glass, the product was soft launched in the U.S. in June 2022 and in Japan in August 2022. In addition, in March 2019 the Company concluded a development agreement with TRISH,* which is a consortium affiliated with NASA, to develop a miniature OCT (Optical Coherence Tomography) device together with NASA. The miniature OCT device will allow monitoring of the health of astronauts' retinas during spaceflight. Phase 1 of development was completed in February 2020 and a development report submitted to NASA and TRISH in April 2020.

* TRISH (Translational Research Institute for Space Health): Partnering with NASA through a cooperative agreement, TRISH is a consortium that funds transformative technologies to protect and preserve astronaut physical and mental health during NASA's Deep Space missions.

Utilizing advanced technology to take on the challenge of developing innovative medical devices and therapeutic drugs guided by a vision of "World Without Blindness"

2. Growth strategy

Guided by its vision of "World Without Blindness," the Company works to develop medical devices using the latest digital technologies as well as therapeutic drugs for eye disorders that lack effective treatments. In its development strategy, the Company is focused on drug development and also for the past few years on the field of medical devices, which has relatively shorter development periods. By building a business portfolio with different risk-return profiles, the Company is working to increase corporate value while reducing business risk.

In addition, drugs require a long development period. The Company aims to out-license drugs to partner companies so that it can maximize corporate value. In the process, the Company considers a comprehensive range of key factors, such as a product's risks, development costs and period, and management resources. Basically, the Company's strategy is to conduct in-house development until it reaches the stage of completing Proof of Concept (POC)* in humans. Thereafter, the Company will proceed with development by concluding co-development and sales license agreements with pharmaceutical companies. The Company will aim to capture milestone payments, which depend on progress with development, and royalty payments on product sales after products are launched. For medical devices as well, when large-scale clinical trials are required, the Company will proceed by concluding co-development and sales license agreements.

* POC (Proof of Concept): POC refers to the process of proving the anticipated effects of a drug, as determined by basic research, through an actual administration trial of the drug in human subjects.

In other areas, the Company is implementing an intellectual property (IP) strategy. This IP strategy is crucial to maintaining corporate competitiveness. In medical device inventions, the Company has 31 granted patents and 125 pending patents, and in drug inventions, it has 53 granted patents and 39 pending patents (as of February 2023). As of the end of December 2022, the Company had seven employees on a consolidated basis. They consist primarily of administrative staff. Regarding development, the Company has brought onboard famous university professors, doctors and others in the ophthalmology field as advisors and receives their advice while collaborating with external partners for development on a project by project basis. This asset-light management structure is a feature of the Company.

Outline of major development pipeline projects and status of progress

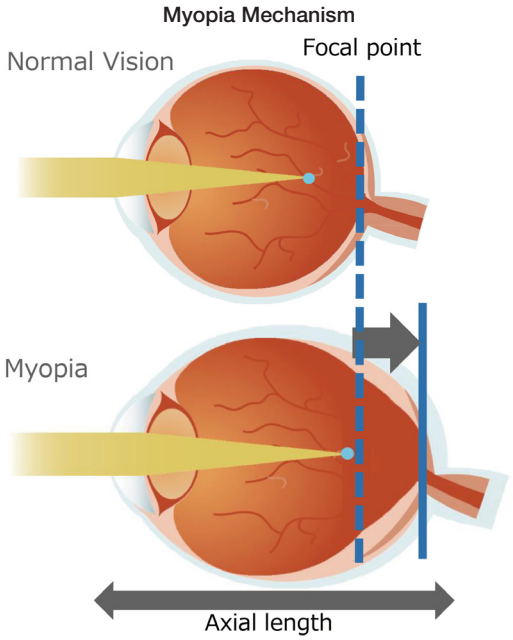
The Company began sales of Kubota Glass in 2022 and will to continue to develop it going forward through product improvements and building evidence in clinical studies

1. Wearable myopia control device Kubota Glass

(1) Market trends related to myopia

The Company is focused on the development of Kubota Glass, a wearable myopia control device aiming to treat and control the progression of myopia. Myopia is classified into refractive myopia, axial myopia, pseudo myopia, nuclear myopia and certain other types. Many myopia cases are classified as axial myopia. Looking at how axial myopia works, an increase in the eye's axial length causes the retina to move behind the focal point, which results in blurry vision at a distance. It follows that if the axial length could be reduced, axial myopia could be corrected. Currently, there is no way to treat the underlying cause of axial myopia. Refractive correction, including the use of eyeglasses, contact lenses, and refractive surgery, is used to bend light rays so they focus on the retina, thereby correcting vision.

Outline of major development pipeline projects and status of progress



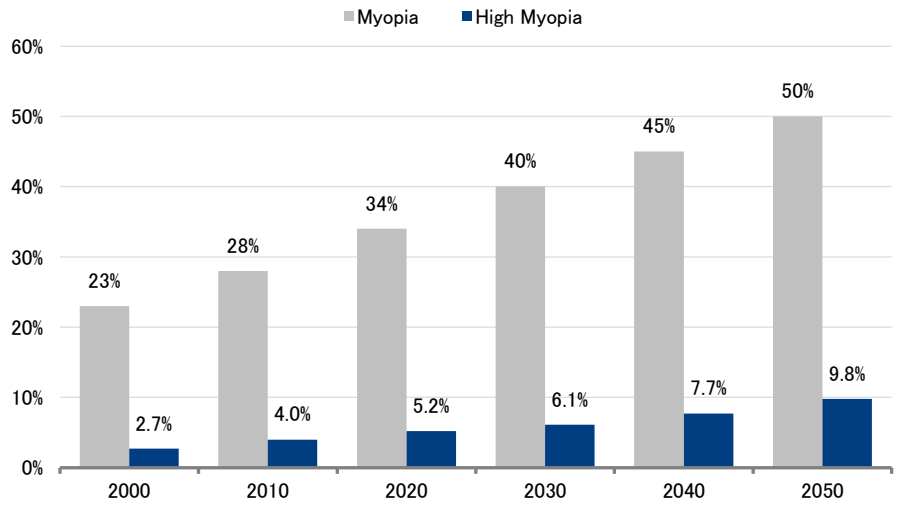
Source: Published from the Company's results briefing materials

The myopic population has continued to increase as a trend globally, due partly to changes in lifestyle patterns. Myopia is now said to be one of the world's most familiar diseases. According to Company materials, the prevalence of myopia in the global population stood at around 28% in 2010 but is projected to rise to approximately 50% by 2050 (affecting around 4.7bn people). Since 2020, the World Health Organization (WHO) has sounded the alarm about the increasing prevalence of myopia worldwide, which has been due in part to more time spent at home because of the COVID-19 pandemic and the widespread use of smartphones and other such devices.

Notably, the myopic population has apparently been increasing sharply in Asian countries. There is an increasing number of countries where the prevalence of myopia in young people (20 years old or under) is over 80%, and by 2050, the cost of correcting myopia in Asian people is projected to reach ¥450tn. If myopia progresses, the risk of sight-threatening diseases such as glaucoma and cataracts is said to increase to a level 2-5 times higher than the risk faced by those with normal vision (emmetropia). Therefore, myopia is a disease for which a fundamental treatment is eagerly awaited.

Outline of major development pipeline projects and status of progress

Prevalence of myopia in the world population

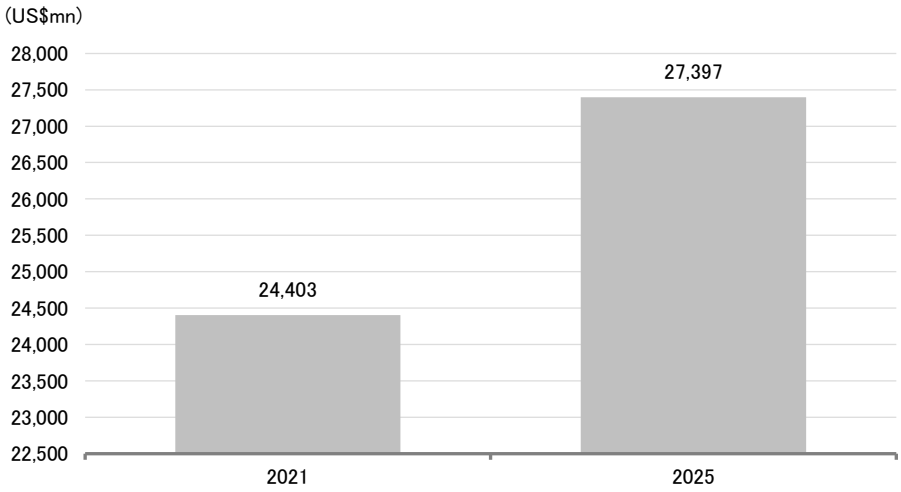


Note: The Impact of Myopia and High Myopia. Report of the Joint World Health Organization-Brien Holden Vision Institute Global Scientific Meeting on Myopia. March 2016.
Source: Prepared by FISCO from the Company's financial results briefing materials

The global market for lenses for myopia control is predicted to grow more than 10% in the next 5 years, from US$24.4bn in 2021 to US$27.3bn in 2025. If the Company successfully commercializes Kubota Glass, it estimates that potential demand for this product could reach up to ¥1,300bn* by 2030.

* An amount calculated by multiplying the Company-estimated adoption rate within the myopic population and the device price.

Forecast of global market for lenses for myopia control



Note: Research by Azoth Analytics
Source: Prepared by FISCO from the Company's financial results briefing materials

(2) How Kubota Glass works

Kubota Glass technology is an active stimulation technology developed by the Company in-house that aims to control and treat the progression of myopia. It uses AR technology to actively stimulate the retina with artificial light. Images are projected using micro-LEDs and mirror lenses so that they are brought into focus in front of the peripheral retina, a process called myopic defocus. This serves to shorten the eye's axial length, or control its elongation, in order to control the progression of myopia. A POC clinical study has already been performed in humans and has confirmed that the technology is effective in controlling elongation of the axial length.* In addition, Scientific Reports, an international academic journal published by Springer Nature, reported on a four-month clinical study with seven test subjects (adults) who wore the device 3-5 days a week, 1.5 hours a day, and it was confirmed that elongation of the axial length was controlled in the subjects' eyes. (This was announced by the Company in July 2022.) Data from clinical trials in children exists for competitor products, but Kubota Glass is the first device in which a trial was conducted in adults and the effects confirmed.

* A specialized ophthalmology research institute in the U.S. investigated the effect of an electronic tabletop optical projection device, which was a prototype based on Kubota Glass technology, on axial length in 12 subjects aged 21 to 32 years old with myopic tendencies. In May 2020, the Company announced that the results of the study confirmed that axial length decreases in the test eye compared to the control eye. In August 2020, the Company announced that it had confirmed the same effect with a wearable myopia control device prototype.

(3) Comparisons with competitor products

Myopic control devices are being developed by various companies, and one product has already been approved in the U.S. as a medical device and is currently on the market.*1 There are a number of competitor products that use myopic defocus, including MiSight, but they all employ passive stimulation with natural light and sharply differ from devices like the Company's that apply AR technology to actively and effectively stimulate the retina with artificial light. For this reason, Kubota Glass only needs to be worn 1-2 hours a day, whereas competitor products must be worn for 12-15 hours, nearly all day. One of the strong points of Kubota Glass is that it can effectively control myopia when used for a short period of time. Moreover, when comparing clinical trial data from other companies, Kubota Glass is top-class in the data on rates of myopia progression control and axial elongation control, so its effectiveness has also been found to be superior to competitor products. There are other treatment methods, eye drops and orthokeratology*2, but they have not become widespread due to side effects and higher risk.

*1 MiSight 1 day, a contact lens from CooperVision of the U.S. became the first product approved for sale in 2019.
*2 A method for correcting myopia in which a specially designed contact lens with high oxygen permeability (differs from a regular contact lens) is worn at night to correct the shape of the cornea and allows the person to go without corrective lenses during the day. It was approved in Japan in 2009.

The safety of Kubota Glass is assured. It meets the safety requirements for classification as a Group 1 instrument under ISO 15004, which regulates the safety of light emissions from ophthalmic instruments. Group 1 is the class of instruments in which "no potential light hazard exists." It has also been certified as a medical device for children under ISO 13485, which requires an even higher level of safety. Kubota Glass technology has earned a certain level of praise from ophthalmologists and scholars involved in myopia research, who say the approach makes good sense, and research continues to take place. The technology is characterized by a low level of invasiveness, a high level of safety assurance, good usability such that the device can be put on and taken off by children as young as six years old, a high level of effectiveness, and amenability to being used together with other myopia treatments. FISCO believes that there is adequate room for Kubota Glass to develop a market in the future as a myopia control device.

Outline of major development pipeline projects and status of progress

Features and Effectiveness of Kubota Glass and Competitor Products

Devices for myopia treatments	Kubota Glass	MiYOSMART <HOYA>	Stellest <Essilor>	MiSight <CooperVision>	DOT Lens <SightGlass Vision>	Violet light-transmitting lens <Tsubota Laboratory>	Low-level red-light therapy	Low-concentration atropine eyedrops (0.05%)	Orthokeratology
Mechanism of action	Active stimulation: Peripheral myopic defocus	Passive stimulation: Peripheral myopic defocus	Passive stimulation: Peripheral myopic defocus	Passive stimulation: Peripheral myopic defocus	Passive stimulation: Peripheral contrast reduction	Passive stimulation: Transmittance of violet light	Active simulation: Exposure to bright red light	Unknown	Passive stimulation: Peripheral myopic defocus
Specification	Spectacles lens	Spectacles lens	Spectacles lens	Soft contact lens	Spectacles lens	Spectacles lens	Tabletop device	Eye drops	Hard contact lens
Wear time	1.5–2 hours/day, 6 days/week	15 hours/day, 7 days/week	12 hours/day, 7 days/week	12–13 hours/day, 6 days/week	12 hours/day, 7 days/week	Constant wear	3 minutes, 2 times/day (4 hours between times), 5 days/week	N/A	When sleeping
Average age of test subject	13.6 years old	10.4 years old	10.7 years old	10.1 years old	8.1 years old	9.4 years old	9.4 years old	8.5 years old	9.2 years old
Spherical equivalent refraction (SER) reduction	0.46D	0.38D	0.53D	0.40D	0.40D	0.22D	0.59D	0.54D	N/A
Rate of myopia progression control	148%	69%	65%	69%	74%	27%	75%	67%	N/A
Axial length (AL) reduction	0.20mm	0.21mm	0.23mm	0.15mm	0.15mm	0.07mm	0.26mm	0.21mm	0.17mm
Rate of axial elongation control	91%	66%	64%	63%	50%	14%	66%	51%	45%

Note: The data on the effectiveness of competitor products is taken from the results of clinical trials for one year. The data on the effectiveness of Kubota Glass is estimated based on the results of a six-month clinical trial in children.
Source: Prepared by FISCO from the Company's financial results briefing materials

(4) Business plan

The Company began selling Kubota Glass via a soft launch in the U.S. in June 2022 upon completing its registration as a medical device in Taiwan and the U.S. by 2022.*1 It also began selling the product in Japan in August 2022 as an AR device that recreates outdoor activities. In Taiwan, the Company apparently intends to conduct clinical trials through its distributor*2, and as of now it is still to be determined when sales will commence. The device is priced at ¥770,000 (with tax) in Japan, and revenue in FY12/22 was ¥8mn, so it appears that about a dozen units have been sold.

*1 Sales were commenced (priced at US$5,200) through Manhattan Vision Associates (MVA), which manages ophthalmology labs and clinics, but Japan currently has supply priority, so new purchases have been temporarily halted in the U.S.
*2 The Company concluded a distributor agreement with EverLight Instrument Company, a major seller of ophthalmologic instruments, in July 2022.

Kubota Glass

Source: Published in Kubota Glass official SNS

There are currently three types of purchasers: parents/guardians who buy the device for their children engaged in studying for school, businesspeople in the prime of their working life who are mainly involved in office work, and foreigners who come to Japan from other countries to purchase the device. One-fifth of purchasers are people from overseas, and some customers had been waiting for sales of the product to begin after Kubota Glass had been introduced on TV in 2021 and became a topic of conversation. It is drawing interest from people in a wide range of regions, including China, Singapore, Malaysia, South Korea, France and the United Arab Emirates. The Company also reports that inquiries have come in from people in English speaking countries who learned about the results of clinical trials from the academic literature and other sources.

So, this product is drawing a high level of interest, but there are still some issues. The first is the lead time. Production is in extremely small lots, so the order is only placed with the contracted manufacturer after the order is received from the customer. The lenses, light source and other precision parts are made in Europe, the device is assembled in Southeast Asia, and after adjustments it is shipped to Japan, which means it takes two to three months from order to delivery. The Company will work to shorten the lead time by reviewing its supply chain and establishing a system for mass production. The Company believes it will be able to achieve same-day delivery by having non-prescription glasses and parts kept at stores as inventory and then conducting assembly and final adjustments. Lowering the cost is also an important issue. If mass production becomes possible, parts costs will go down of their own accord, but in addition to this the process of adjusting the placement of the micro-LED, which is the light source, and the lenses requires fine adjustments depending on the size and other details, which is a factor in the high cost. It is thought that costs will go down by automating this process to a certain extent.

Regarding the Company's sales plans for 2023 and subsequent years, in Japan, it plans to expand the scope of clinics and stores that handle the product, train staff to increase sales efficiency, and create video content and other materials to explain the product in a straightforward manner in order to continue to grow sales of the product as an AR device. It also intends to provide useful information for customers, such as feedback from actual users.

Regarding the clinics and stores that handle Kubota Glass, orders are currently taken at ophthalmology clinics and optical stores (two in Hyogo Prefecture and one in Kanagawa Prefecture). The Company also opened a directly managed store (in Shinjuku, Tokyo) in December 2022. Most recently, in February 2023, the Company concluded a distribution agreement with EYETOPIA Co., Ltd., which operates a network of 169 Megane Stores primarily in the Kanto region, and some of these stores are slated to begin handling Kubota Glass from the spring of 2023 onward. The Company otherwise intends to expand its sales network at optical stores, ophthalmology clinics and other locations. It will also accommodate demand from countries where Kubota Glass is not sold via online sales.

At the same time, in the U.S. and Taiwan, where the product can be sold as a medical device, the Company will expand sales as soon as the situation is in order. In other countries, the Company is considering the same model that it is selling in Japan (as an AR device) because it would be easier to launch quickly given the regulations and other hurdles in these countries. Regionally, it plans to prioritize the Asian region because of the size of the potential market.

On the development front, the Company plans to continue to make product improvements while simultaneously building evidence by conducting clinical studies, including long-term trials. Regarding clinical trial evidence, the results of a long-term clinical trial in children conducted in the U.S. were announced in September 2022. The test subjects were between 10 and 17 years old. They wore Kubota Glass under the projecting conditions of approximately 1.5 hours per day, five days a week. As a result, it was found that myopia progression and axial length elongation were controlled compared to the historical control group. When using this data to estimate the effects had the trial had been conducted over 12 months, myopia progression would have been reduced by 0.42D (131% control) and axial length elongation by 0.21 mm (96% control).

At the same time, in Japan, the Company announced the start of a prospective intervention study on Kubota Glass at Kagoshima Sonoda Eye Clinic & Plastic Surgery in February 2023. The study is intended to evaluate the usability of Kubota Glass in children age seven and up. The evaluation trial in children conducted in the U.S. is also being carried out in Japan to verify whether the product can be used on a continuing basis by Japanese people. The Company aims to sell Kubota Glass as a medical device in Japan and will continue to build evidence for this.

With regard to product improvements, the Company is considering making the device more amenable to consumers such as by listening to their feedback and increasing the sizes available, which are currently limited to a few types, or adding a function that allows the size to be adjusted. There is also room to lower costs by reviewing the design and individual components, and if the cost can be brought down, it is possible that sales will immediately increase because potential demand is substantial. The Company is also considering commercializing a contact lens product and has acquired related patents as part of its IP strategy.*

* The Company announced in August 2022 that it had acquired patents in the U.S. related to two inventions: "Electro-switchable spectacles for myopia treatment" and "Supporting pillars for encapsulating a flexible PCB within a soft hydrogel contact lens."

For PBOS, an investigator-initiated clinical trial for diabetic retinopathy was started in the U.S. in 2023

2. Remote retinal monitoring device PBOS: Patient Based Ophthalmology Suite

(1) PBOS features and competition

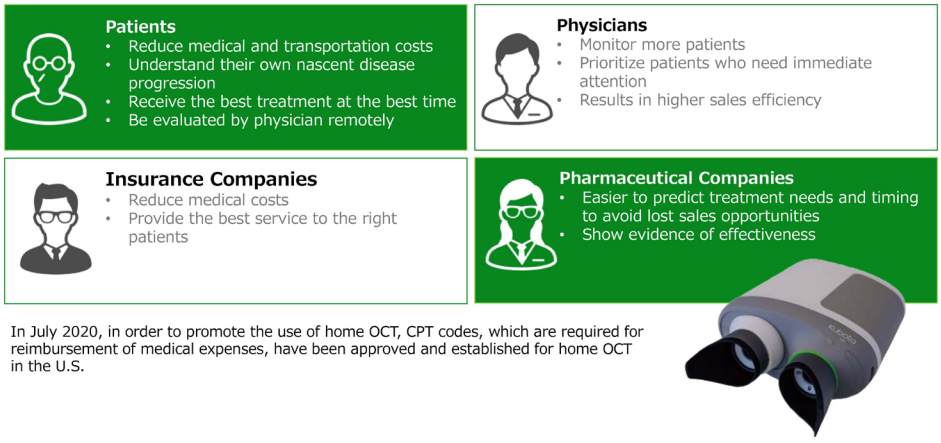
PBOS is a remote retinal monitoring device for patients with wet age-related macular degeneration (wet AMD), diabetic macular edema (DME) and other retinal diseases. Patients use the device to measure and take images of the thickness of their own retina, and their attending physician reviews the data over the Internet and determines whether treatment (administering a drug) is necessary.

Previously, these patients regularly visited hospitals to undergo OCT* tests and receive treatment (intraocular injections) as necessary. PBOS enables such tests to be easily conducted at home. Doing so provides advantages such as eliminating the need to regularly visit hospitals for tests, allowing patients to be treated at the right time, and reducing the risk of a deterioration in symptoms. Many patients experience worsening symptoms when they are unable to regularly visit hospitals due to long distances or financial problems. For this reason, it appears that there is a large unmet need for a device that can be used to conduct tests easily at home. For hospitals, it is more beneficial from a management perspective to increase time spent on treatment rather than on testing. Pharmaceutical companies could also benefit from a higher sales volume than before as drugs are administered more appropriately. In these ways, one feature of this home-based ophthalmic care framework is that all related parties can benefit from it.

* OCT (Optical Coherence Tomography): A testing device that uses infrared rays to take precise cross-sectional pictures of the retina. OCT is used as diagnostic tool for patients with retinal diseases such as glaucoma and age-related macular degeneration (AMD).

Outline of major development pipeline projects and status of progress

Potential advantages of remote retinal monitoring in the U.S.



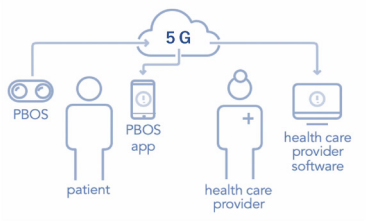
Source: Published from the Company's results briefing materials

Notably, the need for home OCT has been increasing since the COVID-19 pandemic, due partly to measures to prevent the spread of the disease. Therefore, in order to promote the use of home OCT, the American Medical Association (AMA) published guidelines on procedures needed to apply insurance to home OCT on July 1, 2020. Accordingly, it can be said that the conditions needed for the widespread use of home OCT are already in place.

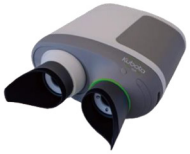
No companies have commercialized home OCT yet. Only a few companies have developed home OCT products, including the Company, Notal Vision, Inc. and certain others. The Company's product offers a user-friendly design that reflects the needs of elderly patients. For example, the product has large buttons and a function that helps users operate the device with voice guidance. The testing time is shorter than competitor Notal Vision's product and it is easier to use. At the same time, it only has the minimum functions necessary. Approval for Notal Vision's product that will be sold in the U.S. is currently pending, so the Company is a little behind, but it appears to still have the opportunity to catch up going forward.

Remote Retinal Monitoring Device PBOS – Home-based miniature OCT (Optical Coherence Tomography)

<Monitoring Model>



<The first fully-functional PBOS prototypes completed>



Source: Published from the Company's results briefing materials

(2) Status of development

Regarding the current status of PBOS's development, a prospective intervention study at a medical institution in Japan (Kagoshima Sonoda Eye Clinic & Plastic Surgery), which started in January 2022, was completed (41 cases conducted), and the device received high ratings for its usability. In addition, the Company announced the start of two investigator-initiated clinical trials—one to evaluate the device's utility as a screening device for diabetic retinopathy patients and one to compare the device with other OCT devices on the market, in January 2023 at the Joslin Diabetes Center, which is affiliated with Harvard University Medical School in the U.S. The Company previously conducted clinical studies for AMD and accumulated data and made software improvements to raise the precision of AI diagnostics, but this did not lead to a partnership agreement, so this time it has expanded the scope to DME patients. It is common to treat DME with direct injections of anti-VEGF drugs into the eyeball, the same as AMD. It is unclear how long the clinical study period will last, but the Company will try to negotiate a partnership agreement based on this trial data, and if an agreement is concluded, clinical trials will be conducted on joint basis in the U.S. Product development is over, so no new expenses will be incurred, but when a partnership agreement is decided, additional development costs could arise based on the needs of the partner. The Company is working to acquire patents for PBOS and in November 2022 announced that it had acquired two, including for the device's measurement method.

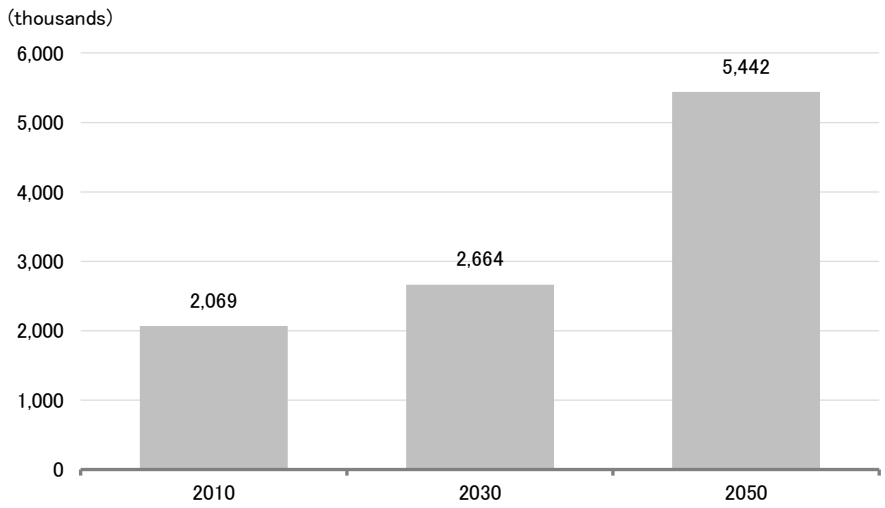
(3) Business model and market size

The Company's business model in the U.S. is likely to be based on a format where monthly usage fees are collected as a rental service, which will reduce the initial cost burden on patients. If insurance is applied, the burden on patients can be greatly reduced, so the adoption of PBOS can be expected to accelerate. Because no fundamental treatment exists for age-related macular degeneration (AMD) and other retinal diseases, patients are highly likely to continue using PBOS once they start using it, unless they become blind. As a recurring-revenue business, PBOS is likely to grow into a steady source of revenue in the future.

The potential market size in the US market covers patients with retinal diseases such as wet AMD and diabetic macular edema (DME). According to the Company's disclosure materials,*1 the number of AMD patients in the U.S. is predicted to increase from 2.06mn in 2010 to 2.66mn in 2030, and then 5.44mn in 2050, marking a 2.7-fold increase. About 10% of those AMD patients is expected to have wet AMD. Among patients with dry AMD, a similar number of patients as those with wet AMD is expected to experience geographic atrophy of the macular region and worsening of symptoms, and these patients will also be eligible for PBOS. For this reason, the number of eligible AMD patients is expected to reach around 1.10mn in 2050. Meanwhile, the number of diabetes patients in North America is expected to increase from 51.00mn in 2021 to 63.00mn in 2045.*2 The prevalence of diabetic retinopathy in diabetes patients in Japan is around 15–23%. Reports show that around 20% of those with diabetic retinopathy also concurrently experience DME.*3 Assuming similar percentages of prevalence as patients in the U.S., the number of DME patients in the U.S. is expected to be around 1.80mn to 2.30mn in 2045. Combined with the number of AMD patients eligible for PBOS, the number of potential users in the U.S. is estimated to increase from around 2.00mn at present to 3.00mn sometime around 2050.

*1 Source: Market Scope, The Global Retinal Pharmaceuticals & Biologic Market, 2015
*2 Source: International Diabetes Federation "IDF Diabetes Atlas," Tenth Edition, 2021
*3 Sakiko Nakano, The 114th Annual Meeting of the Japanese Ophthalmological Society 2010:135 (based on a report that DME occurs in 20% of diabetic retinopathy patients)

Projected Number of AMD Patients in the U.S.



Note: Research by the US National Eye Institute, 2019
Source: Prepared by FISCO from the Company's financial results briefing materials

Assuming a monthly usage fee of ¥1,000 and an adoption rate of 50% for PBOS in 2050, the market size will be ¥18.0bn in 2050. At that time, PBOS is highly likely to have been widely adopted in Europe and Japan as well, so the global market for PBOS is expected to be several times larger in size. Retinal diseases such as AMD are one leading cause of blindness, and the elderly population will only continue to increase moving forward. Considering these factors, we at FISCO believe that PBOS harbors massive latent growth potential.

Leading causes of blindness

Japan		U.S.		Europe	
Glaucoma	21%	Age-related macular degeneration (AMD)	54%	Age-related macular degeneration (AMD)	26%
Diabetic retinopathy (DR)	16%	Cataracts	9%	Glaucoma	20%
Retinitis pigmentosa	12%	Glaucoma	6%	Retinitis pigmentosa	9%
Age-related macular degeneration (AMD)	10%	Diabetic retinopathy (DR)	5%	Others	45%
Retinochoroidal atrophy	8%	Others	25%		
Others	34%				

Note: Data for Japan is from the "FY2013 Survey and Research Concerning Retinochoroidal and Optic Atrophy" report by the Research Program for Overcoming Intractable Diseases of the Ministry of Health, Labour and Welfare. Data for the U.S. is from research by Nathan C. et al., Causes and Prevalence of Visual Impairment Among Adults in the United States. Arch Opthalmol. 122 (2004). Data for Europe is from research by Kocur I, Resinikoff S: Visual Impairment and blindness in Europe and their prevention. British Journal of Ophthalmology 86, 716-722 (2002)
Source: Published from the Company's results briefing materials

For emixustat HCl, efficacy for patients in the early stages of Stargardt disease was suggested in a phase 3 clinical trial, and the Company will begin looking for a co-development partner

3. Emixustat hydrochloride (HCl)

Stargardt disease (STGD) is a genetically inherited retinal disease. The main symptoms are a decrease in vision and color blindness presenting from childhood to young adulthood. It is also known as juvenile macular degeneration and is estimated to affect one in 8,000 to 10,000 people. It is reported that most patients' vision drops to below 0.1. No effective treatments have been established at this time, making STGD a disease with high unmet medical needs. Emixustat hydrochloride (HCl) (hereinafter "emixustat") is designated in the U.S. as an orphan drug. According to market research released by the Company, the STGD market will be approximately ¥160.0bn in 2027.*

* WISEGUY RESEARCH CONSULTANTS PVT LTD Global Juvenile Degeneration (Stargardt Disease) Market Research Report- Forecast to 2027

On August 12, 2022, the Company announced that topline data from a phase 3 clinical study for STDG (194 test subjects) did not show a significant statistical difference from the placebo group for the primary endpoint and secondary endpoints. Regarding the progression rate of the primary endpoint of macular atrophy, the group administered emixustat was 1.280 mm^2/year and the placebo group was 1.309 mm^2/year (p=0.8091). However, based on the results of further analysis, when limiting the data to the group of test subjects with a smaller atrophy area at the baseline (in the early stages of the disease), it was confirmed that the macular atrophy progression rate in the 24th month in the emixustat group was controlled substantially, at 40.8%, compared to the placebo group, which is a significant difference (P=0.0206, emixustat group n=34, placebo group n=21). The Company will therefore search for a co-development partner based on this trial data and has expressed its intention to conduct another clinical trial.

The Company estimates that over 80% of STDG patients are at an early stage of the disease, which would make them potential candidates for the treatment. In the phase 3 clinical trial, only around 30% of the test subjects were in this category, partly, it is thought, because the minimum age for test subjects was set at 16 years old. The trial has shown that if emixustat is administered from an early stage of the disease in childhood, it has the potential to significantly control its subsequent progression, so there is a sufficient likelihood that a co-development partner will emerge going forward.

Additionally, a phase 2 clinical study of emixustat was conducted for proliferative diabetic retinopathy (PDR) in the U.S. from April 2016 to November 2017. As a result, compared to the placebo group, in the group administered emixustat HCl, moderate improvement was found in the concentration of vascular endothelial growth factor (VEGF), a biomarker related to the onset and worsening of retinal diseases, but no significant difference was obtained with respect to other biomarkers. Phase 3 clinical studies incur a substantial cost, so the Company plans to move forward if a co-development partner can be found. For the time being, it is lowering its development priority.

NASA project currently suspended, but may be resumed if a budget is made available

4. SS-OCT, a miniature OCT device for astronauts

The Company signed a development agreement with NASA to develop a Swept Source-OCT (hereinafter, "SS-OCT"), a miniature OCT device, in order to conduct research into eye disorders that can occur in spaceflight. The project began in 2019 and phase 1 of the development mission was completed at the start of 2020. Phase 2 of development has been temporarily suspended due in part to NASA's development budget being cut as a result of control of the U.S. government passing to the Democratic Party in 2021 and federal budget priority being put on pandemic-control measures to address the COVID-19 pandemic.

A research report* has stated that approximately 69% of long-duration spaceflight crewmembers present with Spaceflight Associated Neuro-ocular Syndrome (SANS), which could lead to vision impairment and blindness. Based on this report, the purpose of this project is to research the effects of spaceflight on the ophthalmology field. The commercially available off-the-shelf (COTS) OCT devices currently deployed to the International Space Station (hereinafter, "ISS") are benchtop models and complicated to operate. In fact, astronauts staying in the ISS for several months were only able to conduct tests three times. The miniature SS-OCT to be developed will allow the astronauts themselves to take daily measurements and save the records. The impact of spaceflight on retinal disorders will be analyzed in greater detail and this will help in the mitigation and prevention of disease risk.

> * Eye disorder symptoms such as blurry vision, optic disc edema, posterior globe flattening, and cotton wool spots have been reported.

The development mission is divided into three phases. Phase 1 of the mission was to perform Proof of Concept (POC) testing of a device using durable and inexpensive lasers. The Company set out to develop a device that measures the shape of the optic disc with high resolution using multiple lasers. In January 2020, the Company conducted a demonstration of the device at NASA and received strong evaluations from the NASA project personnel.* The Company completed phase 1 of development in February 2020 and submitted a development report to NASA and TRISH in April 2020. The Company posted development service revenue of ¥37mn from the NASA project as revenue for FY12/20.

> * The Company received the following comments from NASA personnel: "Your device is quite impressive with its small size, ease of use and its speed in data acquisition. A device such as this could be quite helpful on the International Space Station aiding NASA in its quest for understanding how spaceflight affects some of our astronauts' eyes," and, "All Phase 1 goals were not only attained, but surpassed. Physically, it has the appearance of a polished product, and it rests lightly and comfortably in your hands. I am truly excited to see the Phase 2 deliverable."

Phase 2 will comprise the process of determining the operationally required specifications regarding what kinds of imaging and analysis techniques will be employed using this device to investigate eye disorders caused by spaceflight. In Phase 3, the final stage, the Company will develop a device that will be usable in the actual spaceflight environment. In particular, together with its partner companies, the Company will jointly develop the development of hardware that has the durability needed to withstand exposure to cosmic ray radiation and can be operated by the astronauts themselves in a zero-gravity environment.

The project is currently suspended but the Company meets regularly with NASA's project representative and has confirmed NASA's intention to continue with the project. For this reason, it is expected to resume as soon as a development budget is made available. At NASA, budgetary allocations are beginning to be made again, with a new moon-landing project getting started, for example, so FISCO believes that there is a sufficient likelihood the project will be resumed going forward.

Business performance and financial condition

R&D expenses will decline in FY12/23, but the Company intends to make expenditures to expand sales of Kubota Glass

1. Business performance trends

(1) FY12/22 results

In the consolidated results for FY12/22, the Company recorded revenue of ¥8mn (up ¥8mn YoY), an operating loss of ¥2,038mn (a contraction of ¥546mn), loss before tax of ¥2,015mn (a contraction of ¥600mn) and loss attributable to owners of parent of ¥2,015mn (a contraction of ¥600mn). Losses continued, but they were generally in line with the Company's initial forecasts.

The Company's revenue was from recording sales of Kubota Glass. In business expenses, research and development expenses declined by ¥527mn YoY to ¥1,512mn due to a decline in development expenses for emixustat HCl and the wearable myopia control device. Additionally, SG&A expenses decreased ¥2mn to ¥601mn. Marketing expenses were recorded in connection with the launch of Kubota Glass, but other general and administrative expenses were reined in through cost-cutting measures.

FY12/22 consolidated results

(Unit: ¥mn)

	FY12/21 Results	FY12/22		YoY		Difference from forecast
		Initial forecast	Results	Change	% change	
Revenue	-	-	8	8	-	8
Business expenses	2,644		2,119	-524	-19.8%	
Cost of sales	-		5	5	-	
Research and development expenses	2,040		1,512	-527	-25.9%	
SG&A expenses	603		601	-2	-0.4%	
Other operating income	59		73	13	23.1%	
Operating profit (loss)	-2,584	-2,000	-2,038	546	-	-38
Profit (loss) before tax	-2,616	-2,000	-2,015	600	-	-15
Profit (loss) attributable to owners of parent	-2,616	-2,000	-2,015	600	-	-15

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

(2) Outlook for FY12/23 results

The Company did not disclose consolidated results forecasts for FY12/23. Revenue is nearly entirely accounted for by revenue from sales of Kubota Glass, but results forecasts are difficult at the current time because of the difficulty in determining objective demand at the soft launch stage and, on the expenses side, the possibility that additional development expenses will be incurred while efforts are made to reduce manufacturing costs. The Company plans to disclose its outlook when it becomes possible to make rational calculations based on the progress of the business going forward.

Regarding the outlook for business expenses, the Company expects research and development expenses to decrease and expenses for expanding sales of Kubota Glass to increase. Expenses are projected to increase for promotional activities to increase recognition and for customer support. The Company also plans to hire personnel who will be needed for expanding sales in Japan and overseas. Overall, the Company's policy is to control costs while considering its financial condition.

Funds for operating activities secured for the immediate future, but the Company intends to consider fundraising in FY12/24 and beyond while carefully monitoring the situation

2. Financial condition

Total assets at the end of FY12/22 declined by ¥412mn compared to the end of FY12/21 to ¥4,419mn. In terms of the main factors behind this change, in current assets, cash and cash equivalents and other financial assets declined ¥366mn from the end of FY12/21 to ¥4,048mn in connection with expenditures on operating activities. In addition, related to Kubota Glass, trade receivables were ¥3mn and inventories were ¥7mn. In fixed assets, property, plant and equipment increased ¥11mn and other non-current assets increased ¥19mn.

Total liabilities were ¥470mn, a decrease of ¥209mn from the end of FY12/21. There were decreases of ¥128mn in accrued liabilities, ¥32mn in trade payables, and ¥51mn in current and non-current lease liabilities. Moreover, total equity amounted to ¥3,949mn, a decrease of ¥203mn from the end of FY12/21. Share capital and capital surplus increased by a combined ¥1,529mn due to the issuance of shares upon exercise of share acquisition rights. Also, other components of equity increased by ¥283mn in line with the yen's depreciation. Meanwhile, loss brought forward (accumulated deficit) increased due to the recording of loss attributable to owners of parent of ¥2,015mn.

Cash on hand at the end of FY12/22 was ¥4,048, continuing a downtrend, but the Company has secured around two years' worth of funds for operating activities. (The Company raised ¥38mn by issuing its 28th round of stock acquisition rights between January and February 2023; there are 63,414 stock acquisition rights that are unexercised (equivalent to 6,341,000 shares).) Until Kubota Glass is profitable, though, expenses will necessarily be incurred, including sales and marketing expenses, expenses for clinical trials to build evidence, development expenses for the next generation of the device, and other pipeline-related development costs. For this reason, it is expected that the Company will consider raising funds depending on the situation in FY12/24 and subsequent years. Sales and marketing expenses for Kubota Glass are expected to include promotional campaigns and the creation of sales tools for ophthalmologists and optical stores, training programs for sales representatives, and expenses for advertising in various media.

Consolidated balance sheet and business indicators

(Unit: ¥mn)

	End of FY12/19	End of FY12/20	End of FY12/21	End of FY12/22	Change
Current assets	8,177	6,417	4,625	4,181	-443
Cash and cash equivalents and other financial assets	7,970	6,317	4,415	4,048	-366
Non-current assets	563	274	207	237	30
Other financial assets	487	22	-	-	-
Total assets	8,740	6,691	4,832	4,419	-412
Current liabilities	538	506	542	360	-181
Non-current liabilities	158	192	137	109	-27
Total liabilities	696	698	679	470	-209
Total equity	8,043	5,993	4,152	3,949	-203
<business indicators>					
Ratio of equity attributable to owners of parent	92.4%	89.6%	85.9%	89.4%	3.5pt
Cash on hand*	8,458	6,339	4,415	4,048	-366

* Total of cash and cash equivalents and other financial assets
Source: Prepared by FISCO from the Company's financial results and financial results briefing materials

FISCO

Disclaimer

FISCO Ltd. (“FISCO”) offer stock price and index information for use under the approval of the Tokyo Stock Exchange, the Osaka Stock Exchange and Nikkei Inc.

This report is provided solely for the purpose of offering information, and is not a solicitation of investment nor any other act or action.

FISCO prepared and published this report based on information which it considered reliable; however, FISCO does not warrant the accuracy, completeness, fitness nor reliability of the contents of this report or the said information.

The issuers’ securities, currencies, commodities, securities and other financial instruments mentioned in this report may increase or decrease in value or lose their value due to influence from corporate activities, economic policies, world affairs and other factors. This report does not make any promises regarding any future outcomes. If you use this report or any information mentioned herein, regardless of the purpose therefor, such use shall be made based on your judgment and responsibility, and FISCO shall not be liable for any damage incurred by you as a result of such use, irrespective of the reason.

This report has been prepared at the request of the company subject hereto based on the provision of information by such company through telephone interviews and the like. However, the hypotheses, conclusions and all other contents contained herein are based on analysis by FISCO. The contents of this report are as of the time of the preparation hereof, and are subject to change without notice. FISCO is not obligated to update this report.

FISCO and its affiliated companies, as well as the directors, officers and employees thereof, may currently or in the future trade or hold the financial instruments or the securities of issuers that are mentioned in this report.

Please use the information in this report upon accepting the above points.

■ For inquiry, please contact: ■
FISCO Ltd.
5-13-3 Minami Aoyama, Minato-ku, Tokyo, Japan 107-0062
Phone: 03-5774-2443 (IR Consulting Business Division)
Email: support@fisco.co.jp