COMPANY RESEARCH AND ANALYSIS REPORT

Tsubota Laboratory, Inc.

4890

Tokyo Stock Exchange Growth Market

26-Aug.-2024

FISCO Ltd. Analyst
Yuzuru Sato

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

Tsubota Laboratory, Inc.
4890 Tokyo Stock Exchange Growth Market

26-Aug.-2024
https://tsubota-lab.com/en/ir/

Contents

Summary

Plans to announce trial results for a myopia progression curtailment device in around spring 2026

Tsubota Laboratory, Inc. <4890> (hereafter, also "the Company") is a bio-venture company launched from Keio University that develops medical devices and drugs that harness violet light with potential effects in curtailment of myopia progression and activation of the brain. It listed on the Tokyo Securities Exchange's (TSE) Growth Market in June 2022. With a mission of brightening the future with VISIONary INNOVATION, the Company aims to "deliver revolutionary innovations for myopia, dry eye, presbyopia, and brain diseases."

1. Development pipeline situation

As the development pipeline in the myopia field, the Company completed recruitment in October 2023 for a verification clinical trial of the TLG-001 myopia progression curtailment device covering after-school child centers that began in 2022. It plans to summarize and disclose trial results after two years of observations in around spring 2026. If the results are positive, the Company will apply for sales approval. JINS Holdings Inc. <3046>, which has received the sales license, will conduct sales, and the Company will receive royalty income. Furthermore, the phase-one clinical trial for TLM-003, which the Company is developing as a drug that curtails myopia progression, started in Japan in November 2023 at licensee Rohto Pharmaceutical Co., Ltd. <4527>. The Company has also concluded a license agreement contract related to a separate eyedrop drug in March 2024. Additionally, the Company began designated clinical research for TLM-007 in February 2024. It has concluded a joint research contract with Sumitomo Pharma Co., Ltd. <4506> in the brain disease field and finished designated clinical research for people with Parkinson's disease, depression, and mild dementia complications in spring 2024 (it is continuing observation for mild dementia complications). Since it found an effect for some symptoms related to Parkinson's disease and obtained results that show efficacy in depression treatment, the Company announced on July 9, 2024 that it intends to continue clinical research and process with business development. As new pipeline areas, its development work using violet light to treat retinitis pigmentosa (TLG-020) and irregular menstruation (TLG-021) has been selected for public-entity grant projects, and the Company is preparing for designated clinical research. It is also beginning a pilot trial aimed at improvement of cognitive function in elderly dogs (TLG-019). These efforts are seeking to broaden the pipeline.

2. Overview of FY3/24 results

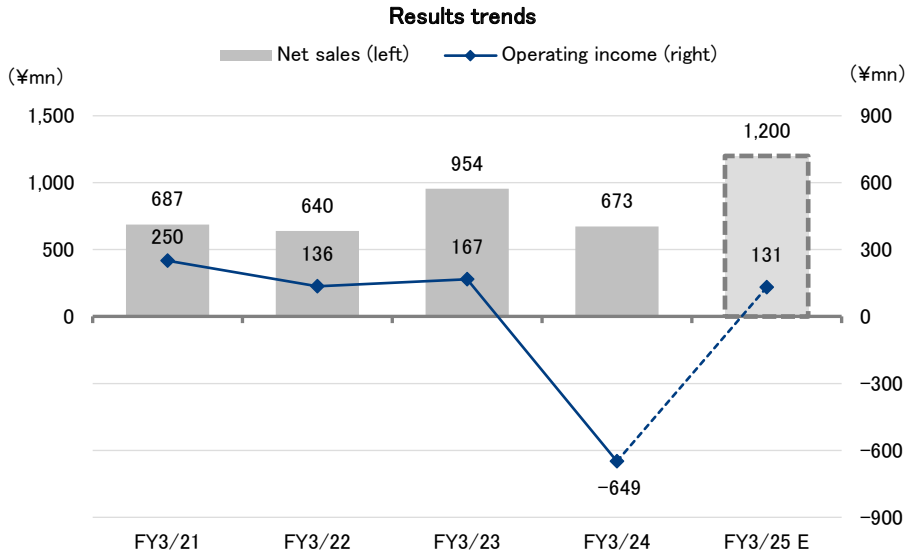
In the FY3/24 results, the Company reported ¥673mn in net sales (down 29.5% YoY) and operating loss of ¥649mn (vs. an income of ¥167mn in the previous fiscal year). Net sales mainly came from one-time contract payments and milestone income. The Company had lower milestone income in FY3/24 than in the previous year. On the other hand, profits are decreased due to lower sales and recording of ¥328mn of provision for loss on contracts caused by cost overruns resulting from the extension of the TLG-001 clinical trial for roughly one year longer than planned.

3. FY3/25 results outlook and future initiatives

In the FY3/25 results forecast, the Company projects ¥1,200mn in net sales, an increase of 72.8% YoY and ¥131mn in operating income (vs. an income of ¥649mn in the previous fiscal year). It expects to conclude multiple licensing contracts in overseas markets and sales are expected to increase with increase in one-time payments for licensing contracts. In earnings, it expects to return to the black on the boost from higher sales and non-recurrence of provision for loss on contracts booked in the previous fiscal year. However, since the timing for conclusion of licensing contracts remains fluid, it is necessary to be aware of lingering uncertainty in the earnings outlook. The Company sees steady advances in pipeline development and publishing academic papers and acquiring patents to enhance pipeline value as the way to boost enterprise value, rather than focus on single fiscal-year results, and intends to reinforce the pipeline at a pace of 1-2 additions annually. Over the medium term, FISCO expects a shift in the income structure from the existing structure dominated by one-time contract payments and milestone income to a more stable foundation with steady rise in the royalty income percentage from 2028 when royalty income is likely to expand on the start of TLG-001 sales.

Key Points

- Bio-venture company originating from a university founded to pursue R&D and commercialization of products in myopia, dry eye, and presbyopia areas
- Plans to announce results from a clinical trial for its myopia progression curtailment device in spring 2026
- Expects higher sales and profits in FY3/25 on increase in one-time contract payments from multiple licensing deals



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

Company profile

Bio-venture company originating from a university founded to pursue R&D and commercialization of products in myopia, dry eye, and presbyopia areas

1. History

The Company's predecessor is Dry Eye KT, Inc. established by Representative Director Kazuo Tsubota, who was a professor at in the Department of Ophthalmology at Keio University School of Medicine, in 2012 (it changed the company name to the current one in February 2015). Inspired by a desire to work on something that contributes to the world before his retirement, Mr. Tsubota decided to launch this business with the aim of commercializing science from the ophthalmology field where he personally conducted research for many years in order to resolve the issue of excess imports in the field amid advances in excess importing of medical devices and drugs. Additionally, since only a few domestic universities were delivering innovations that actually contribute to society with the results of their research activities at the time, he founded the business and implemented business activities with a goal of clarifying the path to a successful university-launched bio-venture ahead of others.

He came up with the idea of a myopia progression curtailment device using violet light, the Company's main development pipeline item at this point, in around 2014. It began with theorization that the difference in patients with diminished eyesight and those that maintained their eyesight level after intraocular lens (IOL) surgery stemmed from the intraocular lens itself (lenses that transmit violet light versus those that block it). He initially conducted research on chicks and then proceeded to research using myopia model mice. These activities obtained results that adhered to the theory and discovered the mechanism of action for curtailing myopia progression. Specifically, he found that irradiation with 360-400nm violet light stimulates the OPN5 non-visual light reception protein in the inner layer of the retina and resulting improvement in blood flow maintains choroid thickness. This mechanism curtails myopia progression (blood flow shortage thins to choroid and this leads to myopia progression). Since sunlight contains violet light, shortage of exposure to violet light caused by decline in outdoor activities is a contributing factor to the steep rise in myopia prevalence in recent years.

Mr. Tsubota announced the research results in an academic journal submission and strengthened the intellectual property strategy by applying for patents in Japan and other countries. He also predicted that if OPN5 stimulation improved blood flow to the eye, it could also improve blood flow to the brain. The Company hence conducted research on depression, Parkinson's disease, and dementia too. Based on results from animal tests, it concluded a joint research contract related to depression and dementia using violet light with Sumitomo Dainippon Pharma Co., Ltd. (now, FrontoAct) in March 2019 (TLG-005). It also concluded a license agreement with JINS Holdings for the myopia progression curtailment device (TLG-001) in May 2019 and is implementing joint research. It subsequently concluded a licensee agreement for myopia curtailment eyedrops (TLM-003) with Rohto Pharmaceutical in October 2020 and initiated joint research. The Company concluded a license agreement for a therapeutic agent that treats Meibomian gland dysfunction (TLM-001) with Maruho Co., Ltd. in April 2021 for Japan, the United States, France, the United Kingdom, Germany, and other countries. As an overseas corporate partner, it concluded an exclusive license agreement for TLM-003 in the United States and Europe with France-based Laboratoires Théa in December 2022. The Company has been actively arranging licensing deals.

The Company listed on the TSE Growth Market in June 2022. It had seven employees (four R&D personnel, two business development personnel, and one management department personnel) at the end of March 2024, a decline of three people versus the end of the previous fiscal year. After hiring new employees, it has about 10 people as of June 2024. The Company outsources the majority of R&D work and has 38 researchers, including external consignments, as of April 2024.

History

Date	History
May 2012	Founded the Company's predecessor Dry Eye KT, Inc. for the purpose of developing and producing a new dry eye drug and dry eye care goods
June 2014	Submitted a patent application for myopia prevention goods and a myopia prevention set (TLG-001)
February 2015	Merged Dry Eye KT with Myopia Research Institute, Inc. and Presbyopia Research Institute, Inc. to become Tsubota Laboratory, Inc.
December 2015	Submitted a patent application for an irradiation device worn on the body that can prevent myopia or delay myopia progression (TLG-001)
March 2017	Submitted a patent application for a myopia prevention or curtailment drug, a method for creating a myopic mice guidance model, and a screening method for a myopia prevention or curtailment drug
May 2017	Submitted a patent application for a myopia prevention composite or functional food (TLM-005)
March 2019	Concluded a contract for joint research on depression and dementia using violet light (TLG-005) with Sumitomo Dainippon Pharma Co., Ltd. (now, Sumitomo Pharma Co., Ltd.)
April 2019	Started an exploratory clinical study using medical device TLG-001 aimed at curtailing myopia progression
May 2019	Concluded a license agreement for TLG-001 with JINS Holdings Inc.
November 2019	Selected as a business for the New Energy and Industrial Technology Development Organization's (NEDO) FY2019 "Research and Development Startup Support Project/Seed-stage technology-based Startups" (TLG-005)
October 2020	Concluded a license agreement for intellectual property and R&D results related to the Company's myopia curtailment eyedrops with Rohto Pharmaceutical Co., Ltd. (TLM-003) Concluded a joint R&D contract for the myopia curtailment mechanism, rebound, and other basic research with Rohto Pharmaceutical Co., Ltd. (TLM-003)
March 2021	Concluded a joint research contract for depression, mild dementia complications, and Parkinson's disease using brain-stimulation violet light glasses (TLG-005) with Sumitomo Pharma
April 2021	Concluded a license agreement with Maruho Co., Ltd. for a therapeutic agent that treats Meibomian gland dysfunction (TLM-001) covering Japan, the United States, France, the United Kingdom, Germany, and other countries
June 2021	Concluded a memorandum that added Taiwan, Vietnam, and Indonesia to countries covered by the license agreement contract completed with Rohto Pharmaceutical Co., Ltd. in October 2020
June 2022	Listed its shares on the TSE Growth Market
November 2022	Concluded an exclusive license agreement contract for North America and South America for TLG-001 with US-based Twenty Twenty Therapeutics (TTT) (likely to be dissolved because of TTT's planned liquidation)
December 2022	Concluded an exclusive license contract for the United States and Europe for TLM-003 with France-based Laboratoires Théa
September 2023	Selection of "R&D for a cognitive function improvement device that addresses decline in the cognitive function of aging dogs" as a R&D Support Program for Growth-oriented Technology SMEs (Go-Tech Program)
March 2024	Selection of "development of an innovative medical device for retinitis pigmentosa" as a grant project for the TOKYO Strategic Innovation Promotion Program Selection of "development of device for treatment of irregular menstruation using light irradiation" as a grant project for the femtech development support and promotion program Concluded an intellectual property license agreement for intellectual property and R&D related to the Company's eyedrops (TLM-018) with Rohto Pharmaceutical Co., Ltd.

Source: Prepared by FISCO from the Company's securities report

R&D-type bio-venture company with strength in science and commercialization

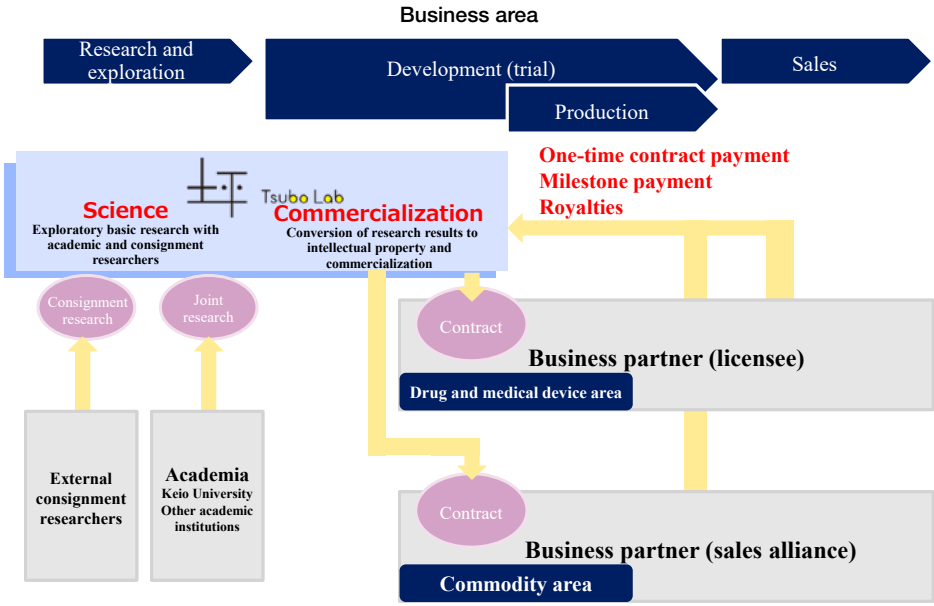
2. Business model and strengths

With a mission of brightening the future with VISIONary INNOVATION*, the Company aims to “deliver revolutionary innovations for myopia, dry eye, presbyopia, and brain diseases” and is steadily promoting business activities. It seeks to increase enterprise value by solving societal issues, such as the steep rise in myopia globally, decline in quality of life (QOL) due to dry eye, and strong needs for presbyopia preventive treatment.

* Development of Vision (eye disease) and Visionary (having foresight) innovative medical and healthcare products

(1) Business model

As the business model, the Company pursues conversion to intellectual property and finds joint development partners for development candidates created from exploratory basic research with Keio University, other academic institutions, and external consignment researchers, obtains one-time contract payments and milestone income by concluding development and sales contracts, and acquires royalty income based on sales volume after the start of development candidate sales. The Company’s development candidates include drugs and medical devices that require production and sales approval from regulatory authorities based on clinical trial results and also commodity products that do not need these approvals. Since one-time contract payments and milestone income are currently the primary income source, sales fluctuate depending on progress with these efforts. Once sales ramp up for development candidate products and expand, royalty income should increase in sales composition and thereby enhance income stability. For example, in a case with a contract that projects roughly ¥200.0bn total sales of the product by the contract partner and income of ¥20.0bn for the company as a 10% share, the Company will negotiate the one-time contract payment, milestone income, and the royalty rate (percentage of total income for each of these sources will differ depending on the contract).



Source: From “Business Plan and Items Related to Growth Possibilities”

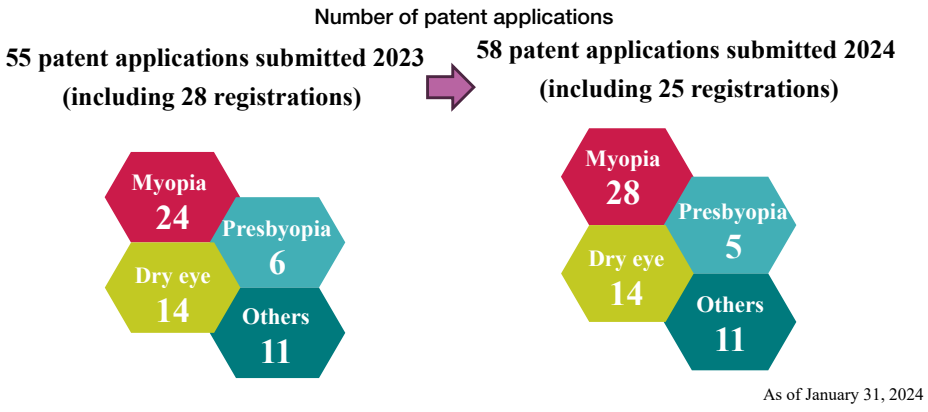
The Company currently does not have any development candidates approved as drugs or medical devices and only receives royalty income from commodity products. The FY3/24 result was just ¥7mn. Commodity product commercialization examples are Rohto Pharmaceutical supplement “Rohto Clear Vision Junior,” JINS’ violet-light transmission glasses “Violet+” and eyeglass frame that enhances moisturizing effect around the eye “JINS PROTECT MOIST,” and NEC Corporation’s <6701> notebook PC (violet light irradiation) “LAVIE Limited-Edition Model” (released in 2023). The Company is currently promoting the development of various products based on violet-light technology.

(2) Company strengths

An important strength is the Company’s established regulatory science operation. Regulatory science refers to the science of appropriately and promptly forecasting, assessing, and determining the quality, efficacy, and safety for commercialization of R&D results in the medical field based on scientific knowledge. It reflects the ability to develop scientific policies and testing methods for R&D activities and prepare and evaluate data. These are key factors in intellectual property strategy, such as formulating academic papers and acquiring patents, and licensing.

On the intellectual property front, the Company had 58 patent application submissions (including 25 registrations) as of the end of January 2024 with a breakdown of 28 in the myopia field, 14 in the dry eye field, 5 in the presbyopia field, and 11 in brain disease and other areas. Furthermore, the total impact factor*, an indicator that assesses the level of impact of published academic papers (31 papers), improved from 168.3 in 2023 to 187.8 in 2024 and 5.2 to 6.1 per paper, and this trend confirms rising assessment of the Company’s academic papers.

* This factor shows the average number of citations of an academic paper carried in a scientific journal in all academic papers published in the subject fiscal year.



Source: From “Business Plan and Items Related to Growth Possibilities”

In research operations, the Company is currently working with two research teams at Keio University (School of Medicine, School of Science and Engineering) and implementing joint research. It is also securing researchers with necessary skills as necessary via outsourcing arrangements. These resources provide the operations to carry out research work. While the Company itself has 4 full-time R&D employees, overall scale including outsourced members is 38 people. It has enhanced development capacity by utilizing these research resources and is making efforts to strengthen the pipeline as well. Use of an outsourcing format has the benefit of improving the fluidity of R&D costs.

Another strength is commercialization. In this case, commercialization refers to early arrangement of contracts (development contracts and joint research) for development candidates. The Company has concluded development contracts with 6 companies* since 2019 and conducts and joint research and other contracts (including contract research, consignment research, and outsourcing) with more than 20 companies and organizations. It was also selected for three grant projects by public entities in FY3/24 (violet light treatment for retinitis pigmentosa, irregular menstruation, and aging dog cognitive functions). We think it has achieved these results by effectively preparing evidence, including mechanism of action, with an intellectual property strategy that leads to early contracts and publishing academic papers based on non-clinical data and clinical research data. By leveraging this strength, the Company will continue advancing developments with early licensing, acquiring royalty income via sales of medical devices and drugs, and enhancing enterprise value.

* 6 companies: JINS Holdings, Sumitomo Pharma, Rohto Pharmaceutical, Maruho, Laboratoires Théa (France), and Twenty Twenty Therapeutics (US)

Pipeline trends

Planning to announce results of a clinical trial for the myopia progression curtailment device in spring 2026

1. Medical devices and drugs

The Company's medical device and drug pipeline is currently moving forward with 11 developments (7 medical devices, 4 drugs), mainly in myopia, dry eye, and brain disease fields.

Pipeline trends

Medical device and drug pipeline (requires pharmaceutical approval or certification)

Code	Indication	Related patents*1		Partner	Development stage
TLG-001	Myopia progression curtailment	Registered	Japan and Europe*2	JINS Holdings (Japan)	Completed subject registration for verification clinical research in October 2023, currently in a two-year observation period and plans to announce results in around spring 2026
		Applied	China		
TLG-003	Keratoconus progression curtailment	Registered	Japan	Undecided	Completed designated clinical research, reviewing the future development policy
		Applied	US, India, Brazil		
TLG-005M	Mild dementia complications	Registered	Japan	Sumitomo Pharma	Completed subject registration for designated clinical research in March 2024, currently under observation
		Applied	US, Europe, China, Israel, Brazil, Korea		
TLG-005D	Depression	Registered	Japan	Sumitomo Pharma	Completed designated clinical research in May 2024, preparing an academic paper
		Applied	US, Europe, China, Israel, Brazil, Korea		
TLG-005P	Parkinson's disease	Applied	International (PCT) (including Japan)	Undecided	Completed designated clinical research in March 2024, preparing an academic paper
TLG-020	Retinitis pigmentosa	Applied	International (PCT) (including Japan)	Undecided	Preparing designated clinical research
TLG-021	Irregular menstruation	Preparing an application		Undecided	Preparing for designated clinical research
TLM-003	Myopia progression curtailment (curtailing sclera thinning)	Registered	Japan, Korea	Rohto Pharmaceutical (Japan, three Asian countries*3)	Rohto Pharmaceutical started a phase-1 clinical trial in Japan in November 2023 Laboratoires Théa preparing clinical trial in Europe
		Applied	US, Europe, China, Asia	Laboratoires Théa (US, Europe)	
TLM-007	Myopia progression curtailment (increase in eye blood flow)	Registered	Japan	Undecided	Started small-sale designated clinical research in Japan in February 2024
		Applied	US, Europe, China, Canada, Australia, Taiwan, Korea, Asia		
TLM-001	MGD*4 treatment drug	Registered	Japan, US, UK, Germany, France	Maruho (global)	Maruho preparing a domestic clinical trial
TLM-018	Undisclosed	Applied	Japan	Rohto Pharmaceutical	Non-clinical trial

*1 Violet light-related products (TLG-001, TLG-003) are covered by basic patents. The Company has registered the basic patents in Japan, the US, China, Taiwan, and Korea and is applying in Europe, Korea, and Singapore
*2 UK, France, Germany, Italy
*3 Taiwan, Vietnam, Indonesia
*4 Meibomian Gland Dysfunction
Source: Prepared by FISCO from "Business Plan and Items Related to Growth Possibilities"

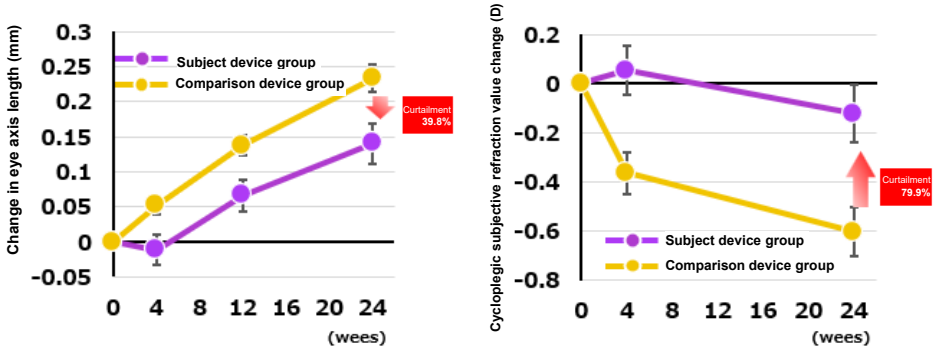
(1) TLG-001

The myopia progression curtailment device (TLG-001) is attracting the most attention in the development pipeline. It attaches a violet light source to eyeglasses and actively irradiates the eye with violet light for roughly three hours a day. This stimulates OPN5 non-visual light reception protein in the inner layer of the retina and resulting improvement in blood flow maintains choroid thickness and curtails myopia progression.

Pipeline trends

After confirming safeness in an exploratory clinical trial with myopic children in the past (six-month period) and obtaining favorable results for efficacy at the six-month inspection with 39.8% curtailment of advancement in eye axis lengthening versus the comparison group and 79.9% curtailment of cycloplegic objective and subjective refraction change, the Company started a verification clinical trial in June 2022. The trial method evenly allocates 160 children aged 6-12 with mild myopia (-1.5D to -3.0D) into the subject device group and comparison device group and has them wear the device daily for 12 months. For the next 12 months, it observes the situation without wearing the device. Nine tests are conducted over two years. The main endpoint is measurement of change in the cycloplegic objective refraction value for the period from the start of wearing the trial device until the 12-month timing and comparison with the other device group. Secondary endpoints are change in eye axis length and choroid thickness at the 1-month, 3-month, 6-month, 9-month, and 12-month points after starting use of the trial device. Since the Company confirmed in the exploratory clinical trial that there is a statistically meaningful difference in a short period (six months) and that myopia tends to progress over time, it anticipates obtaining results that are even more positive in this clinical trial.

Data from exploratory clinical research



Source: From “Business Plan and Items Related to Growth Possibilities”

The Company completed the recruitment of trial participants in October 2023, and the observation period ends in October 2025. If the trial proceeds smoothly, the Company should be able to announce clinical trial results in as early as spring 2026. JINS Holdings, the development partner, plans to apply for production and sales approval if the results are positive, and this might facilitate the start of sales in Japan as soon as 2027. Since rise in the percentage of children with myopia has become a societal issue and statistical data indicate heightened risk of eye disease in the future in cases of severe progression of myopia, this device is likely to make inroads in Japan and other countries once it is available if it successfully curtails myopia progression. Some forecasts project increase in the percentage of the population with myopia increasing to 50% globally in 2050 (vs. 28% in 2010). This business has substantial social significance.

Meanwhile, Twenty Twenty Therapeutics, which concluded an exclusive licensing contract for the Americas with the Company in November 2022, is currently undergoing a dissolution procedure, and business development rights for the mainland US will return the Company after the dissolution. A change in strategy at Santen Pharmaceutical Co., Ltd. <4536>, which entered into a basic agreement for conclusion of an exclusive sales and licensing contract that covered major Asian countries, including China, Korea, Thailand, and the Philippines, in September 2021, ended its agreement with the Company in February 2024. The Company hence intends to actively promote overseas licensing negotiations for TLG-001. In particular, R&D is ramping up in China, which has a high level of myopia prevalence on par with Japan and Korea, in response to the government’s goal to curtail the myopic population. Many Chinese companies have expressed interest in the Company’s technology, and President Tsubota gave a presentation to the Chinese Ophthalmological Society as an invited speaker. He visited China four times in FY3/24 and built a human network that lays the foundation for future business initiatives.

China offers very large growth potential, and the Company opened an office in Eye Valley* in Wenzhou (Zhejiang), the main city for the ophthalmology business in China, in July 2024. This is a first for a Japanese company. The office, which serves as a business travel destination from Japan and does not have permanent local employees for the time being, will gather local information and is likely to move forward with initiatives aimed at building contacts for research and clinical operations with local companies. Additionally, the Company announced that Mr. Tsubota has taken a position as a visiting professor in the ophthalmology department of Wenzhou Medical University, a top-level academic institution in China's ophthalmology field, based on an invitation from the department. By integrating respective knowledge, this activity could contribute to further advances in myopia research.

* This is a world-first multi-function facility for eye health science, technology, human resources, and industry that opened in June 2020. It promotes comprehensive progress in the eye health industry by attracting global advanced resources and is building a world-class hub for technology R&D, industry cultivation, academic exchange, high-end medical services, and innovative human resources. Just under 200 companies currently have a presence, including 32 research institutes.

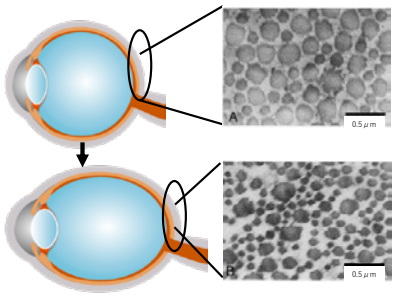
(2) TLM-003, TLM-007

The Company is developing two drugs that address myopia curtailment. TLM-003, which is one of these drugs, is an eyedrop drug that prevents myopia progression by administering eyedrops 1-2 times per day. Sclera*1 endoplasmic reticulum stress*2 is viewed as a source of myopia occurrence and the progression mechanism. Stimulation caused by endoplasmic reticulum stress results in thinning of the sclera and are thereby makes the eye axis more prone to lengthening and myopia progression. It is thought that administering eyedrops containing 4-PBA (4-phenylbutyric acid), which has the effect of curtailing endoplasmic reticulum stress stimulation can restrict myopia progression. An experiment on myopic model mice already verified the curtailment effect on myopia progression. The Company concluded a joint research contract with Rohto Pharmaceutical in October 2020, and the companies have implemented basic research since then. Rohto Pharmaceutical started a phase-1 clinical trial in November 2023 and plans to finish it in November 2024. It will proceed to a phase-2 clinical trial if safeness is confirmed. 4-PBA is currently used as an oral drug to treat pediatric kidney disease. This is the first development of 4-PBA as an eyedrop, and the Company has already obtained a usage patent.

*1 White membrane portion on the outside of the eyeball
*2 An endoplasmic reticulum is an organelle with a bag-shaped structure inside cells that handles the role of transporting substances within the cell. Endoplasmic reticulum stress refers to the state of excess accumulation of protein not correctly folded into the endoplasmic reticulum and protein that is not properly modified.

TLM-003 (myopia progression curtailment eyedrop drug): Started a domestic clinical trial

Curtails extension of the sclera through restriction of sclera thinning and thereby limits myopia



The sclera consists of Type-I collagen fiber and other extracellular matrix. In myopia, there is evidence of remodeling of the scleral tissue's collagen fiber, and it is not possible to curtail extension of eye axis length.

Source: The Company's results briefing materials

Additionally, in overseas markets, the Company and Laboratoires Théa*1 concluded an exclusive licensing contract*2 for intellectual property rights in mainly the US and Europe in December 2022 and preparations for a clinical trial in Europe are advancing. There is strong interest from Chinese companies as well, and the Company intends to continue proceeding with overseas licensing activity.

*1 This is a major European independent drug group in the ophthalmology field. It has over 1,600 employees and sells products in 75 countries worldwide.
*2 EUR41.5mn in one-time contract payment and milestone payments + royalties

TLM-007 is an expanded indication of glaucoma eyedrop drug "Bunazosin 0.01%" that has an effect of increasing blood flow. The Company started designated clinical research in February 2024. This research aims to confirm the myopia progression curtailment effect and safeness via a study of 21 myopic participants aged 6-15 placed in three groups for use of Bunazosin 0.01%, Atropine 0.025%, and combined Atropine 0.025% and Bunazosin 0.01% (eyedrops administrated twice per day). It has already recruited the participants and will conduct observations and inspections for intervals of 4 weeks, 8 weeks, 12 weeks, and 24 weeks after beginning administration. The study should finish in December 2024, and results are likely to be known in the first half of 2025. Santen Pharmaceutical developed Bunazosin and Atropine and submitted an application for sales approval of Atropine as a myopia progression curtailment eyedrop drug in February 2024. While the Company is likely to proceed with a verification clinical trial if either standalone Bunazosin or the combination of Bunazosin and Atropine delivers a better medicinal effect than standalone Atropine, it should pursue a partner contract at that time. It has already obtained a usage patent.

(3) TLG-005

The Company concluded a joint research contract with Sumitomo Pharma on the theme of "developing a therapeutic method using violet light" for brain diseases (depression, mild dementia, Parkinson's disease) in 2021 and implemented designated clinical research on each of these diseases. On July 9, 2024, it announced preliminary results related to two clinical research efforts, excluding mild dementia that remains under ongoing observation. For Parkinson's disease, it conducted the research with 20 patients and found no problems with safety, the main endpoint, and regarding efficacy, the secondary endpoint, it obtained results showing an improvement effect in some symptoms in the evaluation test for Parkinson's disease symptoms* for prior to irradiation and 12 weeks later. Sumitomo Pharma concluded that it was difficult to calculate business value based on the latest research results and announced the dissolution of its existing license in May 2024. The Company, meanwhile, clarified a policy of continuing research and business development efforts.

* This test determines whether someone sees illusions, such as a person's face or an animal, in a landscape image and is used as substitute test for hallucinations. The frequency of hallucinations is known to increase in Parkinson's disease patients, and the test can help in ascertaining and managing symptoms.

The clinical research on depression, meanwhile, conducted a double blind comparative study for 70 patients diagnosed with major depressive disorder with the subject device (violet light irradiation) and comparative device for all cases. The Company announced results that confirmed a meaningful improvement effect for the subject device versus the comparative device for the MADRS score*, which was the main endpoint, from prior to starting device use to after irradiation and also did not find any safety issues. Based on these results, the Company intends to continue research and business development efforts.

* This is a general measure used to assess depression symptoms. It is widely used in clinical trials and clinical treatment to evaluate depression severity and treatment effect.

(4) TLM-001

For TLM-100, which the Company is developed as a dry eye therapeutic drug, it concluded a global licensing contract with Maruho in April 2021, and Maruho is currently preparing the clinical trial. Dry eye is a disease that destabilizes the tear film (oily layer, watery layer, and mucin layer and causes chronic pain. It is an eye disease with rapid increase in patient volume in modern society with high stress. Trouble with any of the three layers destabilizes the tear film. Reports indicate that dry eye linked to oily layer impact has risen recently. Oil constituent that comprises the oily layer is secreted from a sebaceous gland on the edge of the eyelid known as the Meibomian gland. It is thought that decline in gland function due to aging or inflammation leads to dry eye. The Company proved in animal experiments and clinical research that a vitamin D-related substance revives the function. It is currently developing an eye ointment primarily based on the vitamin D-related substance. As the development stage advances at Maruho, the Company receives milestone income. If the product is sold, there will be royalty income.

(5) New pipeline

In FY3/24, the Company added new pipeline items with TLG-020 that treats retinitis pigmentosa*, TLG-021 for irregular menstruation, and TLM-018 as an eye disease therapeutic drug.

> * This is a rare genetic progressive disease that causes abnormality in the retina that covers the inside of the eyeball, and it poses risk of blindness at an advanced stage. There is currently not an effective treatment method, and Japan has designated it as an intractable disease.

TLG-020 offers the possibility of a new treatment method for retinitis pigmentosa with violet light that is being jointly development with Keio University School of Medicine. It was selected in March 24 as a grant project as “development of an innovative medical device for retinitis pigmentosa” for the FY2023 TOKYO Strategic Innovation Promotion Program by the Tokyo Metropolitan Small and Medium Enterprise Support Center (¥80mn grant for a three-year project period). The Company plans to utilize the grant funds to verify efficacy and safeness in non-clinical research and then proceed to designated clinical research in humans based on the results. It is likely to secure licensing contracts in Japan and other countries if it can be proven that violet light is meaningfully better in curtailing progression of the disease than existing symptomatic treatments.

TLG-021 was selected in March 2024 as a grant project as “development of device for treatment of irregular menstruation using light irradiation” in the FY2023 femtech development support and promotion program for women conducted by the Tokyo Metropolitan Small and Medium Enterprise Support Center (¥20mn grant for a project period through November 30, 2025). The Company plans to utilize the grant funds to conduct designated clinical research on a new treatment method aimed at confirming efficacy and safety in treating human irregular menstruation. It will also work on development of a medical device with an easy-to-use design for women in daily life. The violet light effect should improve circadian rhythm* via the brain center and eliminate irregular menstruation via the same effect.

> * The roughly body’s 24-hour cycle (body clock) is known as the circadian cycle.

TLM-018 is an eyedrop drug candidate for which Rohto Pharmaceutical concluded a licensing contract in March 2024. The Company has not yet disclosed the disease that it addresses. This should be clarified after further progress in development activity.

Jointly developing eyeglasses, supplements, and other commodity products with partner companies

2. Commodity products

The Company is steadily development commodity products that do not need pharmaceutical approval and certification with a wide range from supplements to eyeglasses, information terminals, and lighting devices. Some products are already being sold, including JINS Holdings' violet-light transmission glasses "Violet+" and eyeglass frame that provides a moisturizing effect around the eye (for prevention of dry eye) "JINS PROTECT MOIST," and Rohto Pharmaceutical supplement "Rohto Clear Vision Junior." NEC Personal Computer installed a violet-light LED in notebook PC "LAVIE Limited-Edition Model" released as a 40th anniversary model.

As another new pipeline item (TLG-019), the Company started a joint pilot trial in May 2023 with Azabu University School of Veterinary Medicine, Japell Co., Ltd., and others for the purpose of preventing cognitive decline in aging dogs utilizing violet light and supporting early intervention. This trial will observe individual changes using activity volume and cognitive function assessment sheets and confirm eye safeness in elderly dogs showing signs of functional decline who stay at the "Animal Care House" for aging dogs and cats operated by Japell. This research was selected in September 2023 in the Small and Medium Enterprise Agency's second-round recruitment for the FY2023 R&D Support Program for Growth-oriented Technology SMEs (Go-Tech Program) for a project period of three years and a grant value (maximum amount) of ¥45mn or less in a single fiscal year. The Company intends to utilize the grant funds to develop a new violet-light irradiation device aimed at improving cognitive function and conduct animal tests. It will pursue enhancements of the prototype too.

Pipeline besides drugs and medical devices
(not required to obtain pharmaceutical approval and certification)

Code	Product name	Product category	Features, ingredient	Related patents	Partner	Foundation	Clinical research	Sales start
TLM-005	Rohto Clear Vision Junior, etc.	Supplement	Crocetin	Registered: Japan, US, Europe (*7) Taiwan, Indonesia Applied: China, Vietnam	Rohto Pharmaceutical			
TLM-008	Violet+	Eyeglass lenses	Violet light transmission	Registered: Japan, US, Europe (*8), China, Singapore, Korea, Malaysia, Philippines, Thailand	JINS Holdings			
TLM-010	LAVIE Limited Model	Personal computer	Violet light irradiation	Registered: Japan, US, China, Taiwan, Korea, Vietnam, Indonesia Applied: Europe, Philippines, Thailand	NEC			
TLM-019	Undecided	Cognitive function improvement in aging dogs	Violet light irradiation	Applied: International (PCT) (including Japan)	Undecided			new

Note: PCT = International patent application based on the Patent Cooperation Treaty

*1 Basic patents cover violet light-related products (TLG-001, TLG-003). Basic patents been registered in Japan, the US, China, Taiwan, and Korea, and applications have been submitted in Europe, Korea, and Singapore.
*2 United Kingdom, France, Germany, Italy
*3 TTT = Twenty/Twenty Therapeutics
*4 Taiwan, Vietnam, Indonesia
*5 Thea = Laboratoires Thea
*6 MGD = Meibomian gland disorder
*7 United Kingdom, France, Germany, Austria, Poland, Turkey
*8 United Kingdom, France, Germany, Italy, Spain

These products are already available.

Source: From "Business Plan and Items Related to Growth Possibilities"

Results trends

Net sales and profits decline in FY3/24 on delay in TLG-005 licensing and recognition of provision for loss on contracts for TLG-001

1. Overview of FY3/24 results

In the FY3/24 results, the Company reported ¥673mn in net sales (down 29.5% YoY), operating loss of ¥649mn (vs. an income of ¥167mn in the previous fiscal year), ordinary loss of ¥636mn (vs. an income of ¥144mn), and net loss of ¥641mn (vs. an income of ¥90mn). It missed period-start targets by ¥365mn in net sales and ¥680mnn in operating income.

FY3/24 results

(¥mn)

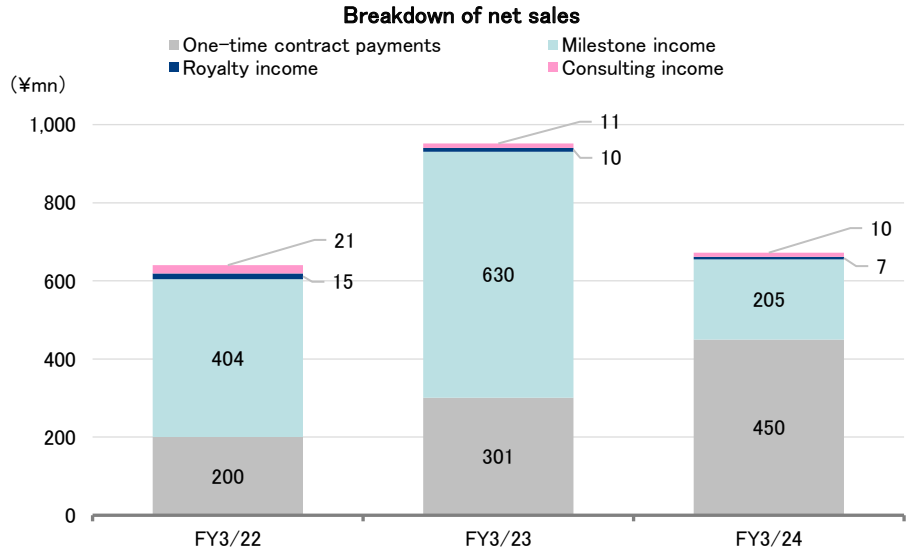
	FY3/23		FY3/24			YoY		Difference with the plan target
	Results	Ratio to net sales	Initial forecast	Results	Ratio to net sales	Change amount	Change (%)	
Net sales	954	-	1,039	673	-	-281	-29.5%	-365
Gross profit	719	75.3%	880	21	3.2%	-697	-97.0%	-858
SG&A expenses	552	57.8%	849	670	99.6%	118	21.5%	-178
(R&D expenses)	126	13.2%	-	205	30.5%	79	62.6%	-
Operating income	167	17.5%	31	-649	-	-816	-	-680
Ordinary income	144	15.1%	30	-636	-	-780	-	-666
Net income	90	9.4%	20	-641	-	-731	-	-661

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

Looking at the sales breakdown, one-time contract payments rose ¥148mn to ¥450mn due to a contract conclusion for TLM-018 with Rohto Pharmaceutical. Milestone income, however, decreased by ¥424mn to ¥205mn. This was due to posting ¥590mn in milestone income following the progress made in the myopia field pipeline in the previous fiscal year, and its milestone income fell to ¥180mn in FY3/24. Furthermore, royalty income declined ¥3mn to ¥7mn, and consulting income was down ¥1mn to ¥10mn. Sales results by major customers were ¥531mn from Rohto Pharmaceutical (up ¥149mn YoY) and ¥105mn from JINS Holdings (down ¥102mn). These two companies provided 94.5% of overall sales.

Main reasons for the ¥365mn shortfall versus period-start targets were missing out on a ¥600mn one-time contract payments due to delay in licensing TLG-005 to Sumitomo Pharma and loss of a roughly ¥200mn one-time contract payment for licensing TLG-001 in China and major Asian countries to Santen Pharmaceutical because of termination of the basic agreement. The Company was unable to fully offset the combined ¥800mn setback with the one-time contract payment from Rohto Pharmaceutical which was not included in the initial targets.

Results trends



Source: Prepared by FISCO from the Company's securities report

Gross profit declined ¥697mn YoY to ¥21mn due to weaker sales and recording ¥328mn in provision for loss on contracts under cost of sales. This was due to recording the cost overruns, resulting from extension of the TLG-001 clinical trial for roughly one year longer than planned, and the costs for clinical trials and subsequent statistical analysis were projected to exceed the contract value, and the excess loss has been accounted for as provision for loss on contracts. In other words, it accelerated booking of anticipated costs. Selling, general and administrative expenses increased ¥118mn YoY to ¥670mn. R&D expenses were up by ¥79mn, and fee expenses rose ¥39mn.

Plans to conduct business activities using cash on hand for the time being

2. Financial conditions

Looking at financial conditions as of the end of FY3/24, total assets s decreased by ¥377mn from the end of the previous fiscal year to ¥2,295mn. Main decreasing factors were declines of ¥277mn in cash and deposits, ¥69mn in work in process and ¥32mn in fixed assets. Work in process books estimated value of milestone income and other income likely to be obtained from progress in the pipeline.

Total liabilities rose ¥205mn to ¥927mn. The increase was due to the recording of ¥328mn in provision for loss on contracts, which offset the steady decrease in interest-bearing debt, which was down ¥22mn to ¥116mn, and decreases of ¥44mn in contract liabilities and ¥36mn in income taxes payable. Total net assets decreased by ¥583mn to 1,367mn. Retained earnings decreased due to booking net loss of ¥641mn.

The equity ratio fell from 73.0% at the end of FY3/23 to 59.6%, though the Company has ¥1,766mn in net cash, a level that is sufficient to support business activities for the time being. However, the Company generates the majority of its income from one-time contract payments and milestone income, and there might be a point at which it needs to raise funds if these income sources do not materializes as planned.

Balance sheet

(¥mn)

	End of FY3/21	End of FY3/22	End of FY3/23	End of FY3/24	Change
Current assets	1,003	1,515	2,568	2,223	-344
(Cash and deposits)	610	1,174	2,161	1,883	-277
(Work in process)	223	308	355	285	-69
Fixed assets	74	102	104	71	-32
Total assets	1,078	1,617	2,672	2,295	-377
Total liabilities	487	873	722	927	205
(Interest-bearing debt)	242	223	139	116	-22
Total net assets	591	744	1,950	1,367	-583
(Soundness)					
Equity ratio	54.8%	46.0%	73.0%	59.6%	-13.4pt
Interest-bearing debt ratio	41.0%	30.1%	7.1%	8.6%	1.4pt
Net cash	368	951	2,021	1,766	-255

Note: Net cash = Cash and deposits – interest-bearing debt
Source: Prepared by FISCO from the Company's financial results

Expecting higher sales and profits in FY3/25 on an increase in one-time contract payments from multiple licensing deals

3. FY3/25 results outlook

In the FY3/25 results forecast, the Company projects ¥1,200mn in net sales, up 78.2% YoY, ¥131mn in operating income (vs. a loss of ¥649mnin the previous fiscal year), ¥130mn in ordinary income (vs. a loss of ¥636mn), and ¥100mn in net income (vs. a loss of ¥641mn). It aims to boost earnings by licensing multiple existing pipeline items and restore profits for the first time in two fiscal years. The anticipated larger increase in profit, than in net sales, reflects the non-recurrence of ¥328mn in provision for loss on contracts booked in the previous fiscal year.

FY3/25 forecast

(¥mn)

	FY3/24		FY3/25		YoY	
	Results	Ratio to net sales	Company forecast	Ratio to net sales	Change amount	Change (%)
Net sales	673	-	1,200	-	526	78.2%
(R&D expenses)	205	30.5%	410	34.2%	204	99.7%
Operating income	-649	-	131	10.9%	780	-
Ordinary income	-636	-	130	10.8%	766	-
Net income	-641	-	100	8.3%	741	-
Net income per share (yen)	-25.15		3.91			

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

Looking at unlicensed pipeline and regions for the existing pipeline, TLG-001 has openings in China, Asia, and Europe and will be seeking a new licensee for the US too as it opens up because the existing one is undergoing a dissolution. For TLM-003, China is an open region, though FISCO think it is likely to find a licensee considering the high level of interest from Chinese companies. For TLG-005, the Company plans to promote licensing activities in Asia and Europe. For TLM-007, it has started a designated clinical trial, and trial results should be clear by the first half of 2025. However, even if the results are positive, we at FISCO expect the timing of licensing to be in FY3/26 or later.

Results trends

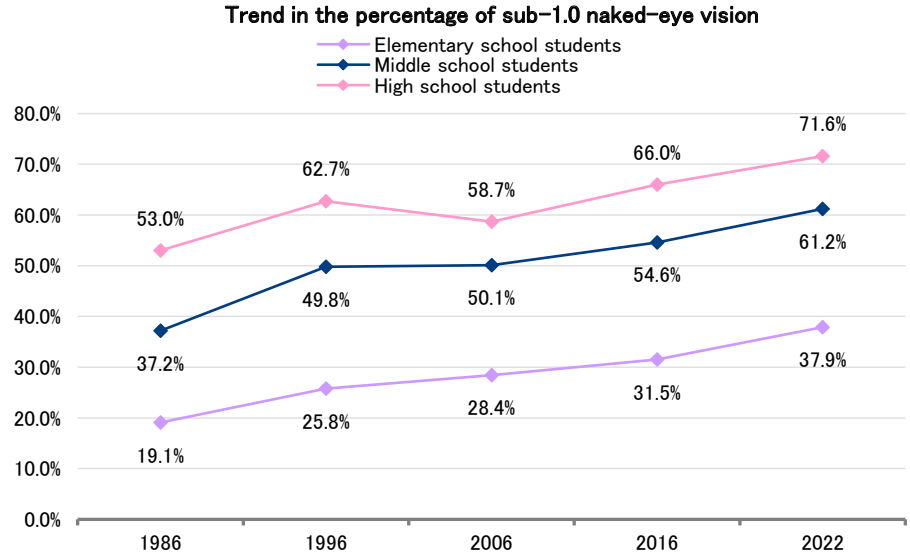
While the Company is targeting multiple licensing contracts from FY3/26 too, its important management goals are is steadily advancing pipeline R&D and enhancing pipeline value by publishing academic papers and acquiring patents, and adding one to two new additions annually and further expand the pipeline.

Licensing situation for major pipeline items (○ indicates open regions)

Pipeline	Japan	China	Asia	Europe	United States
TLG-001 (Myopia progression curtailment VL eyeglasses)	JINS Holdings	○	○	○	Twenty Twenty Therapeutics*
TLM-003 (Sclera thinning curtailment eyedrop drug)	Rohto Pharmaceutical	○	Rohto Pharmaceutical	Laboratoires Théa	Laboratoires Théa
TLG-005 (Brain stimulation VL eyeglasses)	Sumitomo Pharma	Sumitomo Pharma	○	○	Sumitomo Pharma
TLM-001 (MGD therapeutic drug)	Maruho	Maruho	Maruho	Maruho	Maruho
TLM-007 (Myopia progression curtailment)	○	○	○	○	○
TLM-018 (Eyedrop drug)	Rohto Pharmaceutical	○	○	○	○

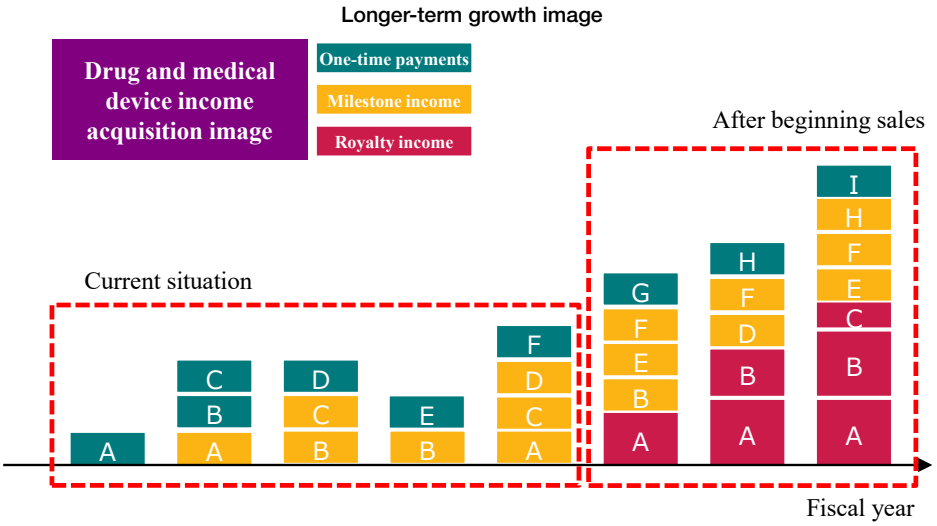
* While the Company provided a license to Twenty Twenty Therapeutics, this region is likely to be open because of the dissolution process.
Source: Prepared by FISCO from the Company's results briefing materials

As the longer-term growth image, the Company is targeting dramatic growth from acquisition of one-time contract payments and milestone income related to licensing the development pipeline along with accumulation of post-release royalty income. There is a possibility of launching sales of TLG-001, the first item likely to reach the market as a medical device or drug, as soon as 2027 if the situation proceeds smoothly. According to a Ministry of Health, Labour and Welfare survey, myopic student prevalence continues to rise and was 37.9% among elementary school students and 61.2% among middle school students in 2022. Since myopia advancement for the younger generation has become a societal issue, adoption of VL eyeglasses offers a way to curtail myopia progression.



Source: Prepared by FISCO from the Ministry of Health, Labour and Welfare's "Survey of School Health Statistics"

Results trends



Source: The Company's results briefing materials

FISCO

Disclaimer

FISCO Ltd. (“FISCO”) offers 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 inquiries, 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