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RaQualia Pharma

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Executive summary

Business overview

RaQualia Pharma Inc. is an R&D-focused drug discovery company. It primarily conducts exploratory research into small molecule compounds to discover the "seeds" of new drugs and out-licenses development and marketing rights to pharmaceutical companies and others. The company covers the drug discovery stage from exploratory research through early clinical development (Phase II clinical trials). It develops new drugs targeting various fields, including pain, gastrointestinal disorders, cancer, and immunological disorders. The company receives operating revenue from companies that in-license its products in the form of upfront payments, milestone payments, post-launch royalties, and joint development cooperation payments. Licensees have already launched four products, providing the company with stable long-term royalty revenue, its main source of earnings. In FY12/24, operating revenue was JPY3.1bn (+63.5% YoY), comprising royalty revenue (62.6%) and upfront and milestone payments (37.4%).

The company started as an independent entity when US-based Pfizer Inc. (NYSE: PFE; ranked third in terms of pharmaceuticals sales globally in 2023) decided to close its central research laboratory in Japan as part of a global research restructuring in 2007. The research lab spun off from Pfizer through an employee buyout, and RaQualia was established in July 2008, after Pfizer transferred its intellectual property rights covering a number of projects in the exploratory or development stages in June 2008. When RaQualia out-licenses rights for some compounds transferred from Pfizer, it pays royalties to Pfizer and records them under operating expenses.

RaQualia has four products already commercialized by licensees (K-CAB® [generic name: tegoprazan], GALLIPRANT®, ENTYCE®, and ELURA®), 13 programs already out-licensed, and seven at the pre-out-licensing stage. Human drug tegoprazan is a potassium-competitive acid blocker (P-CAB)*, with the main indication of gastroesophageal reflux disease (GERD)*2. In September 2010, the company reached an out-licensing agreement for marketing in South Korea, China (including Hong Kong), and Taiwan with South Korea's CJ Healthcare Corporation (currently HK inno.N Corporation [KOSDAQ: 195940]). Since 2019, the company has gradually expanded the licensed territories and has now granted global rights (excluding Japan) to HK inno.N.

* P-CAB: Potassium-competitive acid blockers act differently than the proton pump inhibitors (PPIs) used in existing therapies. While PPIs inhibit gastric acid secretion after being activated by acid in the body, P-CABs do not require acid activation. Instead they inhibit the binding of potassium ions necessary for gastric acid secretion, with a rapid and beneficial impact.
*2 Gastroesophageal reflux disease (GERD): A disease whereby stomach contents, in particular stomach acid, flow back into the esophagus (food pipe), causing characteristic symptoms such as heartburn. Non-erosive reflux disease (NERD) is a condition in which damage to the esophageal mucosa cannot be confirmed by endoscopy, despite symptoms such as heartburn and acid reflux caused by reflux of stomach acid and stomach contents.

HK inno.N has launched tegoprazan under the brand name K-CAB® in South Korea and aims to roll out the drug to 100 countries by 2028. HK inno.N and its sublicensees are working on development, manufacturing, and sales of tegoprazan in 48 countries. As of end-FY12/24, tegoprazan was sold in 15 countries (South Korea, China, Mongolia, the Philippines, Indonesia, Singapore, Mexico, Peru, Chile, Colombia, the Dominican Republic, Nicaragua, Honduras, Guatemala, and El Salvador), approved in two countries (Malaysia and Thailand), and under regulatory review in 10 countries (Vietnam and nine Latin American countries). Meanwhile, preparations were underway either to start Phase III clinical trials or to submit regulatory applications in the United States, Canada, Brazil, South Africa, some Eastern European nations, and various Middle Eastern and North African states. Under the licensing agreement with HK inno.N, RaQualia receives milestone payments based on development progress or a percentage of the revenue that HK inno.N earns from the sublicensee.

GALLIPRANT®, ENTYCE®, and ELURA® are drugs for pets. In December 2010, the company out-licensed worldwide rights to the three drugs to US-based Elanco Animal Health, Inc. (NYSE: ELAN) a former subsidiary of US-based Eli Lilly and Co. (NYSE: LLY). GALLIPRANT® revenue reached USD100mn (roughly JPY12.5bn) in FY12/21, becoming Elanco's tenth blockbuster drug.

RaQualia obtained approval for ELURA®, a weight loss management drug for cats with CKD, in Europe in 2023 and launched it in France in August 2024. It obtained approval in Japan in February 2024 and launched the drug domestically in November 2024. The company plans to expand ELURA® into other markets, having already secured approvals in the UK, several European countries, Brazil, and Canada. While the pet drug market is smaller than the human pharmaceuticals

market, the absence of regulated drug prices in Japan and other regions allows the company to maintain or increase prices more easily. Shared Research thinks this pricing flexibility supports stable royalty revenue and earnings.

RaQualia initially planned to conduct in-house development of two programs, tegoprazan (in Japan) and a ghrelin receptor agonist, to increase the probability of successfully commercializing new drugs and add value. It retains Japanese rights to tegoprazan after out-licensing it to HK inno.N in all markets excluding Japan by FY12/21. The company originally planned to complete clinical studies (equivalent to Phase I) in FY12/23, hoping to out-license tegoprazan in FY12/24 or later. However, during FY12/23, to launch the drug at the earliest possible date, the company decided to out-license the drug within the same year without conducting clinical pharmacological studies. However, due to lengthy negotiations with a potential licensee, the closing of the agreement is expected to be delayed until FY12/25. The company is also developing a ghrelin receptor agonist for the main indications of anorexia/cachexia syndrome associated with cancer and constipation associated with spinal cord injury. It plans to finalize the licensing agreement before initiating clinical studies.

The company expanded its disease coverage from pain and gastrointestinal diseases to include neurological diseases in March 2021. Since FY12/22, it has focused on areas with significant unmet medical needs* including neurodegenerative, genetic, and rare diseases, with the aim of consistently discovering new drugs. The previous management team focused on out-licensing drug candidates at the preclinical preparation stage. However, out-licensing at an early development stage, when the probability of commercialization is relatively low, not only makes finding a licensing partner challenging, but also results in lower upfront payments, milestone payments, and royalties. The company therefore changed its policy to out-licensing after developing drug candidates in-house until it can demonstrate proof of concept (POC)*2.

* Unmet medical needs: Medical needs involving diseases for which effective remedies are not yet available. This includes serious illnesses such as cancer, dementia, and multiple sclerosis as well as those that are not life-threatening but require innovative drugs to improve quality of life, such as insomnia and migraines.
*2 Proof of concept (POC): The hypothesis (clinical concept) that a new drug candidate substance under development can be a potential therapeutic agent for a disease (in terms of its usefulness and efficacy) is tested and validated through administration to humans. In the drug discovery process, Phase II of a three-stage clinical trial is used to demonstrate whether or not the candidate substance demonstrates a therapeutic effect during administration to a small number of patients, as measured using appropriate benchmarks.

The company has successfully out-licensed five drug discovery research programs targeting ion channels. Ion channels are membrane proteins that allow ions to pass into and out of cells. They are expressed in a variety of cells, and the type of ions that can pass through depend on the type of channels. Ion channels are vital to maintaining cell functions, and are deeply involved in a variety of physiological phenomena. Controlling the ion channels could help treat a wide range of diseases, but they are widely expressed in vital organs such as the heart and brain, increasing the risk of life-threatening adverse reactions such as cardiotoxicity and neurotoxicity. Few companies have entered the market due to the difficulty of drug discovery targeting ion channels, and such drugs account for under 10% of all drugs. RaQualia says it is the only company in the world to have out-licensed five drugs in the area.

In March 2024, the company acquired all shares in FIMECS, Inc. (unlisted) and made it a subsidiary (see the "Business" section below). FIMECS advances the research and development of new pharmaceuticals using targeted protein degradation (TPD) inducers, a new modality in drug discovery. Based on its unique drug discovery platform technology RaPPIDS™, it conducts joint research with Astellas Pharma Inc. (TSE Prime: 4503) and may receive milestone payments according to progress with development and royalties after product launch. The company expects to strengthen its drug discovery value chain, increase its earnings through a hybridized business model, and strengthen its presence in the field of cancer by making FIMECS a subsidiary.

Earnings trends

In FY12/24, RaQualia reported operating revenue of JPY3.1bn (+63.5% YoY), an operating loss of JPY213mn (compared to a loss of JPY337mn in FY12/23), a recurring loss of JPY362mn (compared to a loss of JPY293mn), and a net loss attributable to owners of the parent of JPY495mn (compared to a loss of JPY324mn). While the out-licensing agreement for tegoprazan in Japan was postponed to FY12/25, the global expansion of the gastric acid secretion inhibitor tegoprazan (out-licensed to HK inno.N and marketed as K-CAB®) drove earnings, and sales of pet drugs by Elanco, including GALLIPRANT®, ENTYCE®, and ELURA®, remained solid. Milestone payments, joint development payments, and option fees related to veterinary drugs also contributed to revenue growth.

For FY12/25, the company forecasts operating revenue of JPY3.9bn (+25.1% YoY), operating profit of JPY118mn (compared to a loss of JPY213mn in FY12/24), recurring profit of JPY73mn (compared to a loss of JPY362mn), and a net loss attributable to owners of the parent of JPY71mn (compared to a loss of JPY495mn). The company expects operating revenue to be driven by steady royalty revenue from tegoprazan, GALLIPRANT®, ENTYCE®, and ELURA®, along with upfront and milestone payments and research collaboration revenue from subsidiaries. The company forecasts standalone revenue for RaQualia at JPY3.1bn (+25.1% YoY), and combined revenue for subsidiaries FIMECS Inc. and TMRC Co. Ltd. at JPY767mn (+25.5% YoY). It expects total operating expenses of JPY3.8bn (+11.9% YoY).

The company revised the numerical targets of its medium-term management plan for the three-year period from FY12/24 to FY12/26, alongside its FY12/24 earnings forecast revision. The company lowered its FY12/25 operating revenue forecast by JPY498mn (-11.4%) from the previous target after deferring approximately half of the expected upfront payments from the tegoprazan license agreement in Japan, following a reassessment of milestone certainty. The company lowered the forecast for upfront and milestone payments at TMRC by a total of JPY900mn. The company lowered its FY12/26 operating revenue forecast by JPY2.0bn (-35.4%) from the previous target, reflecting downward revisions of JPY1.5bn at the subsidiary level and JPY400mn in upfront payments related to its license agreements, following a reassessment of milestone achievement likelihood. The business model, competitive edges, and investment strategy remain unchanged.

Strengths and weaknesses

Shared Research thinks the company has the following three strengths.

1) Focus on drug discovery based on research processes and operating procedures on par with pharmaceutical companies

2) Several hundred patents held

3) Ability to efficiently identify candidate compounds from its massive compound library using SCARA robotic system

We think it has the following three weaknesses.

1) Drug discovery modality* (methodology) relies on small molecule compounds

> * Drug discovery modality refers to the method of drug discovery, i.e., what kind of drug to make from what sources and by what method. Traditionally, most drugs have been small molecule drugs synthesized from chemical substances with molecular weights of under 500 Daltons. Currently there is a range of modalities including proteins (hormones, biological materials), antibody drugs, nucleic acid drugs, middle molecule drugs, and regenerative medicine.

2) Lack of control over amount or timing of revenue, because milestone and royalty payments depend on development progress and earnings at licensees

3) Difficulty in recruiting and training researchers due to high degree of specialization

Key financial data

Income statement	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24	FY12/25
(JPYmn)	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Company forecast
Operating revenue	**146**	**705**	**1,419**	**745**	**1,703**	**1,107**	**2,776**	**2,918**	**1,901**	**3,108**	**3,888**
YoY	-5.5%	384.7%	101.2%	-47.5%	128.7%	-35.0%	150.7%	5.1%	-34.8%	63.5%	25.1%
Operating expenses	**2,010**	**1,465**	**1,570**	**1,820**	**1,719**	**1,593**	**2,068**	**2,052**	**2,239**	**3,321**	**-**
YoY	-11.7%	-27.1%	7.1%	15.9%	-5.5%	-7.3%	29.8%	-0.8%	9.1%	48.4%	-
Operating profit	**-1,865**	**-760**	**-150**	**-1,075**	**-16**	**-486**	**708**	**866**	**-337**	**-213**	**118**
YoY	-	-	-	-	-	-	-	22.4%	-	-	-
Operating profit margin	-	-	-	-	-	-	25.5%	29.7%	-	-	3.0%
Recurring profit	**-1,795**	**-721**	**-81**	**-1,065**	**22**	**-528**	**864**	**904**	**-293**	**-362**	**73**
YoY	-	-	-	-	-	-	-	4.7%	-	-	-
Recurring profit margin	-	-	-	-	1.3%	-	31.1%	31.0%	-	-	1.9%
Net income	**-1,854**	**-728**	**-58**	**-1,105**	**5**	**-607**	**756**	**723**	**-324**	**-495**	**-71**
YoY	-	-	-	-	-	-	-	-4.3%	-	-	-
Net margin	-	-	-	-	0.3%	-	27.2%	24.8%	-	-	-
Per-share data (split-adjusted; JPY)											
Shares issued (year-end; '000)	18,767	18,767	20,295	20,388	20,950	20,952	20,955	20,977	21,623	21,839	
EPS (JPY)	-116.5	-38.8	-3.0	-54.2	0.3	-29.0	36.1	34.5	-15.0	-22.9	-3.3
EPS (fully diluted; JPY)	-	-	-	-	0.3	-	36.0	34.5	-	-	
Dividend per share (JPY)	-	-	-	-	-	-	-	-	-	-	-
Book value per share (JPY)	240	201	240	189	220	191	228	262	282	254	
Balance sheet (JPYmn)											
Cash and cash equivalents	1,840	1,428	2,268	1,671	2,174	1,394	2,345	3,675	3,715	3,340	
Total current assets	**2,708**	**1,806**	**3,322**	**1,962**	**3,067**	**2,834**	**4,004**	**4,822**	**4,957**	**4,539**	
Tangible fixed assets	261	249	216	318	249	333	299	391	574	529	
Investments and other assets	1,769	1,951	1,516	1,738	1,488	1,051	897	1,020	1,311	685	
Intangible assets	14	13	10	34	32	33	34	24	30	3,902	
Total assets	**4,752**	**4,019**	**5,064**	**4,052**	**4,837**	**4,251**	**5,234**	**6,258**	**6,872**	**9,655**	
Short-term debt	-	-	-	1	1	18	22	46	77	582	
Total current liabilities	**200**	**190**	**149**	**164**	**183**	**187**	**401**	**494**	**389**	**1,187**	
Long-term debt	-	-	-	2	2	27	18	177	291	2,870	
Total fixed liabilities	**38**	**41**	**27**	**31**	**33**	**53**	**46**	**267**	**362**	**2,897**	
Total liabilities	**238**	**231**	**176**	**195**	**216**	**240**	**446**	**761**	**752**	**4,085**	
Shareholders' equity	4,503	3,773	4,871	3,845	4,608	3,999	4,777	5,489	6,095	5,543	
Total net assets	**4,514**	**3,788**	**4,888**	**3,857**	**4,621**	**4,011**	**4,788**	**5,497**	**6,120**	**5,571**	
Total interest-bearing debt	-	-	-	3	2	46	39	222	368	3,452	
Cash flow statement(JPYmn)											
Cash flows from operating activities	-2,117	-681	-307	-404	-531	-289	366	1,480	-719	181	
Cash flows from investing activities	666	-441	534	-368	216	225	-279	-48	-135	-3,666	
Cash flows from financing activities	1,702	-	1,007	99	696	-7	-16	-30	793	2,982	
Financial ratios											
ROA (RP-based)	-36.1%	-16.4%	-1.8%	-23.4%	0.5%	-11.6%	18.2%	15.7%	-4.5%	-4.4%	
ROE	-39.8%	-17.6%	-1.3%	-25.3%	0.1%	-14.1%	17.2%	14.1%	-5.6%	-8.5%	
Equity ratio	94.8%	93.9%	96.2%	94.9%	95.3%	94.1%	91.3%	87.7%	88.7%	57.4%	

Source: Shared Research based on company data

Note: Figures may differ from company materials due to differences in rounding methods.

Note: Operating expenses include cost of operating revenue, R&D expenses, and other SG&A expenses.

Recent updates

Termination of license agreement between TMRC and Syros Pharmaceuticals

2025-04-11

RaQualia Pharma Inc. announced consolidated subsidiary TMRC canceled its license agreement with Syros Pharmaceuticals Inc. (NASDAQ: SYRS) on the retinoic acid receptor α agonist (tamibarotene).

In September 2015, TMRC signed a license agreement granting Syros Pharmaceuticals development and marketing rights for tamibarotene for cancer treatment in North America and Europe. Under this agreement, Syros conducted clinical trials, including the Phase III SELECT-MDS-1 trial targeting HR-MDS patients with overexpression of the RARA gene. On November 12, 2024, Syros announced it would discontinue the trial, citing failure to meet the primary endpoint of complete remission (CR) rate. On February 28, 2025, Syros announced plans to scale down its operations, limit spending, voluntarily delist from NASDAQ, and deregister its common stock with the SEC.

Both parties agreed to terminate the license agreement for tamibarotene following discussions on business strategy. Syros will return development and marketing rights to TMRC without compensation.

The company expects the conclusion of the agreement to have no impact on earnings for FY12/25. TMRC will consider further development of tamibarotene based on clinical trial data provided by Syros.

Subsidiary FIMECS achieves milestone in joint research with Astellas Pharma and receives lump-sum payment

2025-03-31

RaQualia Pharma Inc. announced that its subsidiary, FIMECS Inc., achieved a milestone in joint research with Astellas Pharma Inc. (TSE Prime: 4503). Consequently, FIMECS will receive a lump-sum payment from Astellas.

In 2022, FIMECS signed a joint research agreement with Astellas on targeted protein degraders (TPD) inducers. Since then, FIMECS has collaborated with Astellas to discover protein degraders for multiple oncology-related targets using its proprietary RaPPIDS™ platform. In May 2024, FIMECS achieved an initial milestone for a specific program within this collaboration. This time, FIMECS completed a predefined phase of a joint research project for the same program, paving the way for the next stage of research.

Consequently, FIMECS will receive JPY200mn from Astellas, which will be recorded as operating revenue in Q1 FY12/25. Moving forward, Astellas will focus on identifying development compounds for this program through further evaluation. If Astellas identifies a development candidate that leads to the commercialization of a new drug, FIMECS may receive over JPY15.0bn in milestone payments based on the progress of development, regulatory application filing and approval, and sales, along with royalties in the single-digit percentage range of product sales.

RaQualia factored the impact of this milestone payment into its full-year consolidated forecast for FY12/25, released on February 14, 2025. The company expects this achievement to contribute to the group's medium- to long-term growth and enhance corporate value through future development.

Issuance of new shares as share-based and performance-linked compensation for directors and executive officers

2025-03-25

RaQualia Pharma Inc. resolved at its Board of Directors meeting held on March 25, 2025 to issue new shares as share-based compensation with transfer restrictions for directors.

Starting April 24, 2025, the payment date, allocated directors must not transfer, pledge, or otherwise dispose of the allotted shares while they remain in their position as company directors.

Overview of the Issuance

Payment date	April 24, 2025
Type and number of shares to be issued	11,100 common shares
Issue price	JPY404 per share
Total issue amount	JPY4,484,400
Allottees	Two directors of the company (excluding directors who are members of the Audit & Supervisory Committee and outside directors)

Source: Shared Research based on company data

At the same meeting, the company resolved to issue new shares under its post-grant performance-linked compensation program.

The company will issue a total of 15,444 shares of common stock to three eligible directors and ten executive employees who served in those roles during the performance evaluation period from FY12/22 to FY12/24. The issuance corresponds to a total of JPY6,239,376 in monetary compensation claims (monetary claims for executive officers), which are granted based on the achievement level of performance targets during the evaluation period and contributed as payment in kind.

Overview of the Issuance

Allotment date	May 15, 2025
Number of shares to be issued	15,444 common shares
Issue price	JPY404 per share
Total issue amount	JPY6,239,376
Allottees	7,685 common shares for three directors of the company (excluding directors who are members of the Audit & Supervisory Committee and outside directors), 7,759 shares for ten executive officers

Source: Shared Research based on company data

Capital and business alliance, issuance of new shares through third-party allotment, and changes in major and largest shareholders

2025-03-21

RaQualia Pharma Inc. resolved at its Board of Directors meeting held on March 21, 2025, to issue new shares through a third-party allotment to HK inno.N Corporation, enter into a capital and business alliance agreement with HK inno.N, and execute a shareholders' agreement with HK inno.N and Mr. Yuichi Kakinuma, a major shareholder and Audit & Supervisory Committee member. The company expects this transaction to result in changes in major shareholders, including the largest shareholder.

1. Capital and Business Alliance

Purpose of the alliance

The company aims to raise funds through the third-party allotment and establish a strategic partnership with HK inno.N. The allottee is the licensee of tegoprazan, an acid suppressant developed by the company, and a strategic partner engaged in global business development for the compound. HK inno.N was the first to commercialize tegoprazan as a pharmaceutical product globally.

Details of the capital alliance

The company will allocate 2,592,100 common shares to HK inno.N, representing 10.62% of voting rights after the issuance. Based on 21,838,529 shares and 218,256 voting rights outstanding as of December 31, 2024, the dilution ratio is 11.87% (11.88% on a voting rights basis).

Planned areas of collaboration

1. Commercialization of tegoprazan in Japan

2. Value enhancement for development compounds
3. Joint research
4. Other R&D initiatives

2. Issuance of new shares through third-party allotment

Overview

Item details

Payment date	April 18, 2025
Number of shares to be issued	2,592,100 common shares
Issue price	JPY397 per share
Total proceeds	JPY1,029,063,700
Method	Third-party allotment
Allottee	HK inno.N Corporation (Pharmaceutical manufacture)

The company expects the funds raised to support high-level R&D investment aimed at maximizing growth potential, including strengthening its drug discovery infrastructure, expanding its development pipeline, and upgrading lab facilities such as testing equipment.

Net proceeds from the offering

- Total proceeds: JPY1.0bn
- Estimated issuance expenses: JPY11mn
- Estimated net proceeds: JPY1.0bn

Intended use of proceeds

The company will allocate the full amount of net proceeds to R&D investment aimed at building a sustainable drug discovery platform.

Use of proceeds and expected disbursement period

Use of proceeds	Amount (JPYmn)	Expected disbursement period
Strengthening drug discovery infrastructure (including development of new modalities)	341	May 2025–December 2027
Expanding the development pipeline	426	May 2025–December 2027
Upgrading lab facilities	250	May 2025–December 2027
Total	1,017	

3. Major shareholders before and after the offering

Name	Shareholding ratio (%)	
	Before (as of Dec 31, 2024)	
HK inno.N Corporation	–	10.61
Yuichi Kakinuma	10.92	9.76

The offering will make HK inno.N Corporation the company's largest shareholder, replacing Mr. Yuichi Kakinuma.

Licensing agreement for proprietary expertise with Nissan Chemical Corporation

2025-03-14

RaQualia Pharma Inc. has announced the signing of an exclusive global licensing agreement with Nissan Chemical Corporation (TSE Prime: 4021) for some of Nissan Chemical's proprietary know-how in the field of neurological disorders.

RaQualia is expanding its drug discovery research platform, a foundation for enhancing its growth potential as a biotech company, focusing on neurological diseases. The company aims to enhance new modalities and strengthen the drug discovery value chain. Meanwhile, Nissan Chemical has developed expertise and a portfolio of drug candidates through independent research on specific molecular pathways to create first-in-class treatments for neurological diseases.

This agreement aligns RaQualia's focus on neurological disease research with Nissan Chemical's goal of leveraging its expertise. Under the agreement, RaQualia will receive a sublicensable exclusive license to globally research, develop, and sell certain neurological disease-related expertise of Nissan Chemical to advance new drug candidates. Nissan Chemical will receive an upfront payment, milestone payments, and sublicensing royalties.

This partnership is part of a broader effort by both companies to integrate their strengths into a unified drug discovery value chain. By combining Nissan Chemical's expertise with RaQualia's R&D capabilities, the two companies aim to accelerate the development of new drug candidates. The company expects the agreement to have a minimal impact on its earnings in FY12/25 and has maintained its full-year earnings forecast announced on February 14, 2025. Over the medium to long term, it anticipates strengthening its R&D portfolio and expanding its drug development pipeline.

Patent review in China for TRPV4 antagonist (pyrimidin-4(3H)-one derivative)

2025-01-16

RaQualia Pharma Inc. has announced that it received a notification of patent grant in China for its TRPV4 antagonist (pyrimidin-4(3H)-one derivative) substance patent application (application number: 202180029570.1).

TRPV4 (Transient Receptor Potential Vanilloid 4) has been reported to function as an environmental sensor involved in various diseases. It is a temperature-sensitive TRP ion channel that served as a basis for the 2021 Nobel Prize in Physiology or Medicine. TRPV4 is activated by warm temperatures near body temperature, osmotic pressure changes, mechanical deformation, and other stimuli.

The company's TRPV4 antagonist acts specifically on TRPV4 ion channel receptors and has demonstrated high efficacy in multiple animal models of pain, inflammation, and ocular diseases. Since 2016, the company has conducted industry-academia collaborative research on ocular diseases with Gifu Pharmaceutical University. In April 2021, it established a joint research course at the university. Collaborative research with the Laboratory of Pharmacological Evaluation, led by Professor Masamitsu Shimazawa, resulted in a 2023 publication suggesting that TRPV4-targeted therapies could provide new treatment options for retinal vascular disorders in retinal diseases.

A patent is granted when a country's patent office determines that an invention is worthy of a patent. Upon payment of the patent fee, the patent becomes registered in that country. A patent grant represents the evaluation of an invention as worthy of patent protection by a country's patent office. Upon payment of the required fees, the patent is officially registered, granting the applicant patent rights in the relevant country. This patent grant covers pyrimidin-4(3H)-one derivatives, a novel group of compounds with TRPV4 antagonistic properties, marking the company's first patent for TRPV4 antagonists. It strengthens the company's intellectual property rights in China.

This patent grant highlights the company's expertise in ion channel drug discovery. RaQualia Pharma stated it will continue efforts to strengthen its intellectual property portfolio. The company does not expect this patent decision to impact its consolidated results for FY12/25. However, the company believes that the pyrimidin-4(3H)-one derivatives will contribute to its corporate value in the medium to long term through future development and related activities.

Trends and outlook

Quarterly trends and results

Earnings (cumulative)	FY12/23				FY12/24				FY12/24	
(JPYmn)	Q1	Q1–Q2	Q1–Q3	Q1–Q4	Q1	Q1–Q2	Q1–Q3	Q1–Q4	% of forecast	FY forecast
Operating revenue	370	1,014	1,495	1,901	649	1,411	2,369	3,108	99.1%	3,135
YoY	9.2%	-29.9%	-21.5%	-34.8%	75.1%	39.1%	58.4%	63.5%		64.9%
Operating expenses	479	1,037	1,604	2,239	604	1,565	2,397	3,321	98.6%	3,369
YoY	4.4%	15.8%	14.3%	9.1%	26.0%	50.9%	49.5%	48.4%		50.5%
Operating expense ratio	129.4%	102.3%	107.2%	117.7%	93.1%	110.9%	101.1%	106.9%		107.5%
R&D expenses	268	603	934	1,373	359	833	1,255	1,704		
YoY	1.7%	14.2%	11.2%	9.9%	33.8%	38.0%	34.3%	24.1%		
R&D expense ratio	72.4%	59.5%	62.5%	72.2%	55.4%	59.0%	53.0%	54.8%		
Operating profit	-109	-23	-108	-337	45	-154	-27	-213	-	-234
YoY	-	-	-	-	-	-	-	-		-
Operating profit margin	-	-	-	-	6.9%	-	-	-		-
Recurring profit	-110	37	-36	-293	-77	-278	-231	-362	-	-476
YoY	-	-94.6%	-	-	-	-	-	-		-
Recurring profit margin	-	3.6%	-	-	-	-	-	-		-
Net income	-148	25	-118	-324	-78	-324	-340	-495	-	-584
YoY	-	-94.6%	-	-	-	-	-	-		-
Net margin	-	2.5%	-	-	-	-	-	-		-
Earnings (quarterly)	**FY12/23**				**FY12/24**					
(JPYmn)	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**		
Operating revenue	370	644	481	406	649	762	958	738		
YoY	9.2%	-41.9%	5.3%	-60.0%	75.1%	18.5%	99.1%	81.9%		
Operating expenses	479	558	566	635	604	961	831	924		
YoY	4.4%	27.8%	11.6%	-2.1%	26.0%	72.2%	46.9%	45.6%		
Operating expense ratio	129.4%	86.7%	117.6%	156.5%	93.1%	126.1%	86.7%	125.2%		
R&D expenses	268	335	331	438	359	474	423	449		
YoY	1.7%	26.6%	6.2%	7.2%	33.8%	41.4%	27.6%	2.4%		
R&D expense ratio	72.4%	52.0%	68.8%	108.0%	55.4%	62.1%	44.1%	60.8%		
Operating profit	-109	85	-85	-229	45	-199	127	-186		
YoY	-	-87.3%	-	-	-	-	-	-		
Operating profit margin	-	13.3%	-	-	6.9%	-	13.3%	-		
Recurring profit	-110	147	-73	-257	-77	-200	46	-130		
YoY	-	-80.5%	-	-	-	-	-	-		
Recurring profit margin	-	22.8%	-	-	-	-	4.8%	-		
Net income	-148	174	-143	-206	-78	-246	-16	-155		
YoY	-	-70.6%	-	-	-	-	-	-		
Net margin	-	27.0%	-	-	-	-	-	-		

Source: Shared Research based on company data
Note: Figures may differ from company materials due to differences in rounding methods.

Pipeline

	Preclinical trials	Phase I	Phase II	Phase III
Out-licensed	Pet drugs using four compounds to Velovia	TRPM8 blocker (pain) to Xgene Pharmaceutical	EP4 receptor antagonist (pain) to AskAt	Tamibarotene (myelodysplastic syndromes) to Syros
	EP4 receptor antagonist (osteoarthritis and other diseases) to AskAt	CB2 agonist (chemotherapy induced peripheral neutoparhy) to AskAt/OCT	COX2 inhibitor (pain) to AskAt	
	COX-2 inhibitor (pain in pets) to AskAt	EP4 receptor antagonist (cancer/cancer immunology) to AskAt	Tamibarotene (acute myeloid leukemia) to Syros	
	5-HT4 partial agonist (intestinal motility disorder in pets) to Vetbiolix	5-HT4 partial agonist (Alzheimer's disease) to AskAt	P2X7 receptor antagonist (pain) to Asahi Kasei/Eli Lilly	
	Development phase not disclosed			
	Specific ion channel target (gastroenterology) to EA Pharma	Sodium channel blocker (pain) to Hisamitsu		
	Preclinical trials	**Phase I**	**Phase II**	**Phase III**
Pre-out-licensing	Motilin receptor agonist (gastroparesis and other diseases)	Tegoprazan (Japan) (gastroesophageal reflux disease (GERD) and other diseases)		
	Ghrelin receptor agonist (constipation, cachexia, anorexia)	5-HT4 partial agonist (gastroparesis and other diseases)		
	TRPM8 blocker (Japan) (chronic pain)	5-HT2B agonist (irritable bowel syndrome with diarrhea (IBS-D))		
	IRAK-M degradation inducer (cancer/cancer immunology)			

Source: Shared Research based on company data (as of December 2024)
* In addition to the above, the company is preparing to license out a selective sodium channel blocker currently under clinical development for analgesic and antipruritic applications.

Full-year FY12/24 results (out February 14, 2025)

Earnings summary

Full-year FY12/24 results (January–December 2024)

Operating revenue: JPY3.1bn (+63.5% YoY)

- Operating loss: JPY213mn (vs. a loss of JPY337mn in FY12/23)
- Recurring loss: JPY362mn (vs. a loss of JPY293mn)
- Net loss attributable to owners of the parent: JPY495mn (vs. a loss of JPY324mn)
- R&D expenses: JPY1.7bn (+24.1% YoY)

The company revised its full-year FY12/24 forecast on December 13, 2024. For FY12/24, the company achieved 99.1% of its revised full-year operating revenue forecast. This figure includes the results of FIMECS from Q2, following its consolidation.

Difference between initial forecasts and results

Operating revenue fell JPY1.4bn short of the initial forecast due primarily to the postponement of a license-out agreement for the development, manufacturing, and sale of tegoprazan in Japan, which deferred expected upfront payments of JPY1.0bn to FY12/25. In addition, operating revenue declined JPY400mn compared to the forecast, as FIMECS's new joint research contracts and TMRC's license negotiations did not progress as planned.

Operating expenses were JPY853mn below the initial forecast, reflecting a JPY679mn reduction in clinical development preparation costs and JPY174mn in lower expenses associated with a decline in cost of operating revenue and postponed contracts.

Factors behind higher operating revenue and lower profits

During FY12/24, royalties from four launched products, along with the steady global expansion of tegoprazan, resulted in royalty revenue of JPY1.9bn (+21.2% YoY). Other income, including upfront and milestone payments, totaled JPY1.2bn (+291.6% YoY). The company received option fee payments from Vetbiolix and milestone payments for the sodium channel blocker from Hisamitsu Pharmaceutical in Q4.

Total operating expenses were JPY3.3bn (+48.4% YoY), comprising cost of revenue at JPY626mn (+155.4% YoY), R&D expenses at JPY1.7bn (+24.1% YoY), and other SG&A expenses at JPY991mn (+159.6% YoY). Personnel and R&D expenses increased primarily due to the inclusion of FIMECS. The rise in R&D expenses was driven by higher clinical development preparation costs for the ghrelin receptor agonist and IRAK-M degradation inducer. These increased costs resulted in an operating loss of JPY213mn. The company recorded non-operating income of JPY39mn in foreign exchange gains and JPY5mn in interest income. Meanwhile, non-operating expenses included JPY43mn in interest expenses, JPY141mn in syndicated loan fees, and JPY22mn in loss on valuation of derivatives, resulting in a recurring loss and a net loss.

Breakdown of operating revenue

Earnings (cumulative)	FY12/23				FY12/24			
(JPYmn)	Q1	Q1–Q2	Q1–Q3	Q1–Q4	Q1	Q1–Q2	Q1–Q3	Q1–Q4
Operating revenue	370	1,014	1,495	1,901	649	1,411	2,369	3,108
YoY	9.2%	-29.9%	-21.5%	-34.8%	75.1%	39.1%	58.4%	63.5%
Royalties	350	732	1,198	1,605	551	998	1,493	1,944
YoY	90.2%	4.9%	10.6%	7.9%	57.4%	36.3%	24.6%	21.2%
% of total	94.5%	72.2%	80.1%	84.4%	85.0%	70.7%	63.0%	62.6%
Other (upfront and milestone payments)	20	282	297	297	97	413	876	1,163
YoY	-87.1%	-62.3%	-63.8%	-79.3%	385.0%	46.5%	194.9%	292.0%
% of total	5.4%	27.8%	19.9%	15.6%	15.0%	29.3%	37.0%	37.4%
R&D expenses	268	603	934	1,373	359	833	1,255	1,704
YoY	1.7%	14.2%	11.2%	9.9%	33.8%	38.0%	34.3%	24.1%
Research	219	485	780	-	-	-	-	-
YoY	-14.1%	0.6%	2.5%	-	-	-	-	-
% of total	81.6%	80.4%	83.5%	-	-	-	-	-
Development	49	118	154	-	-	-	-	-
YoY	512.5%	156.5%	94.9%	-	-	-	-	-
% of total	18.3%	19.6%	16.5%	-	-	-	-	-
Earnings (quarterly)(three months)	**FY12/23**				**FY12/24**			
(JPYmn)	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**
Operating revenue	370	644	481	406	649	762	958	738
YoY	9.2%	-41.9%	5.3%	-60.0%	75.1%	18.5%	99.1%	81.9%
Royalties	350	382	466	406	551	447	495	451
YoY	90.2%	-25.7%	21.0%	-	57.4%	17.0%	6.2%	11.1%
% of total	94.5%	59.4%	96.8%	100.1%	85.0%	58.6%	51.6%	61.1%
Other (upfront and milestone payments)	20	262	15	0	97	316	463	287
YoY	-87.1%	-55.8%	-79.2%	-	385.0%	20.6%	-	-
% of total	5.4%	40.7%	3.1%	-	15.0%	41.4%	48.3%	38.9%
R&D expenses	268	335	331	438	359	474	423	449
YoY	1.9%	26.4%	6.1%	-30.9%	34.0%	41.4%	27.6%	2.4%
Research	219	266	295	-	-	-	-	-
YoY	-14.1%	17.2%	5.7%	-	-	-	-	-
% of total	81.7%	79.4%	89.1%	-	-	-	-	-
Development	49	69	36	-	-	-	-	-
YoY	512.5%	81.6%	9.1%	-	-	-	-	-
% of total	18.3%	20.6%	10.9%	-	-	-	-	-

Source: Shared Research based on company data

Note: Figures may differ from company materials due to differences in rounding methods.

Pipeline

Brisk royalties from four commercialized products

Pet drugs

Sales of GALLIPRANT® (generic name: grapiprant), a treatment for osteoarthritis in dogs, ENTYCE® (generic name: capromorelin), a treatment for anorexia in dogs, and ELURA® (generic name: capromorelin), a treatment for weight management in cats with chronic kidney disease (CKD), continue to perform well. In Europe, ELURA® was launched in France in August 2024 following approval in 2023, securing a milestone payment for RaQualia. In February 2024, Elanco Japan obtained manufacturing and marketing approval from Japan's Ministry of Agriculture, Forestry, and Fisheries for ELURA®, launching the product in November 2024.

Development of tegoprazan in countries around the world

Sales of GERD treatment K-CAB® in South Korea by licensee HK inno.N continued to be robust, with sales from prescriptions outside hospitals amounting to KRW196.9bn (+24.4% YoY; roughly JPY21.7bn at JPY0.11/KRW) in FY12/24. HK inno.N's continues to lead the anti-ulcer drug market in South Korea with a share of 15%.

The company holds an exclusive license agreement with HK Inno.N to develop, market, and manufacture tegoprazan, including sublicense rights. HK Inno.N aims to expand tegoprazan's reach to 100 countries by 2028 and is actively pursuing this goal. As of end-FY12/24, tegoprazan was available or in preparation in 46 countries worldwide. HK Inno.N's sublicensees are advancing the development, manufacture, and sale of tegoprazan.

During FY12/24, tegoprazan was newly launched in Chile, Colombia, the Dominican Republic, Nicaragua, Honduras, Guatemala, and El Salvador. As of end-FY12/24, tegoprazan is marketed in 15 countries: South Korea, China, the Philippines, Mongolia, Mexico, Indonesia, Singapore, Peru, Chile, and the seven newly added countries. Under the licensing agreement with HK inno.N, RaQualia receives milestone payments based on development progress or a percentage of the revenue that HK inno.N earns from the sublicensee.

In China, tegoprazan has been marketed since 2022 by sublicensee Luoxin Pharmaceuticals and is now sold in 31 provinces and administrative regions. Luoxin has received regulatory approval from the National Medical Products Administration for clinical trials on an injectable formulation and has obtained marketing approval for combination therapy targeting

Helicobacter pylori infections. In the US, sublicensee Brainree is conducting a Phase III clinical trial. In January 2025, HK. Inno.N signed a sublicense agreement in Australia and New Zealand, expanding tegoprazan's reach to 48 countries.

Out-licensed and pre-out-licensing programs

For the out-licensed programs, RaQualia's partners and its sublicensees are advancing development in the preclinical or later stages.

In FY12/24, licensee Xgene commenced a Phase I clinical trial for the TRPM8 blocker in Australia, triggering a milestone payment. In December 2024, Vetbiolix exercised an option for a 5-HT4 agonist to develop veterinary pharmaceuticals, resulting in option fee payments and rights to milestone payments for development progress and royalty payments after product launch. Hisamitsu Pharmaceutical achieved a development milestone for a sodium channel blocker patch, leading to a milestone payment. The company and Maruho agreed to terminate their license contract for a sodium channel blocker in December 2024 following discussions on future development.

In April 2024, RaQualia signed an option and license agreement with Velovia Pharma for four development compounds targeting gastrointestinal, metabolic, and fibrotic diseases for veterinary use. If options are exercised, RaQualia is eligible to receive option fees, milestone payments, and sales royalties upon commercialization. If Velovia Pharma launches pet drugs containing the compounds, RaQualia is also eligible to receive sales royalties and sales-based milestone payments.

For pre-out-licensing programs, the company has accelerated business development efforts to secure large-scale licensing agreements. It is finalizing preclinical studies for its in-house developed ghrelin receptor agonist, while strategically shifting toward securing partnerships before entering clinical trials. The company has completed preclinical studies and is currently preparing the final report, including data verification, while actively pursuing out-licensing discussions under confidentiality agreements with multiple companies.

The company retains the development, manufacturing, and sales rights for tegoprazan in Japan. It decided to defer internal clinical development and prioritize out-licensing activities to enable an earlier market launch, and is currently in negotiations with potential partners. Although the company initially aimed to conclude a license agreement in FY12/24, this has been deferred to FY12/25. In parallel, it is also advancing other pre-out-licensing programs through in-person meetings and online discussions with prospective partners.

Exploratory and joint research

In the exploratory research phase, RaQualia is concentrating on research programs aimed at creating new development compounds. The company seeks to enhance technologies and pipelines by leveraging synergies between existing technologies and new initiatives, approached from four perspectives: modality, drug discovery targets, disease areas, and foundational technologies. By enhancing its next-generation drug discovery value chain through synergies of existing and new technologies, the company advances a critical development strategy to target previously unexplored drug opportunities, including genes and proteins once considered undruggable.

The company is developing targeted protein degradation inducers, a novel drug creation modality, primarily through FIMECS, which became a consolidated subsidiary in March 2024. FIMECS's RaPPIDS™ drug discovery platform strengthens the company and group's foundational technology while generating revenue through ongoing joint development efforts.

RaQualia entered an agreement with STAND Therapeutics (unlisted) to leverage STAND's technology for generating intracellular antibodies functional within cells, advancing drug discovery efforts. Additionally, the company conducts joint research with Veritas In Silico Inc. (TSE GRT: 130A) to develop breakthrough small-molecule drugs targeting messenger RNAs (mRNA). Through these initiatives, the company expanded its focus to include cancer. In 2023, RaQualia established a new research base at Shonan Health Innovation Park to advance drug discovery using new modalities.

Tamibarotene

Regarding the retinoic acid receptor α agonist (tamibarotene), which was out-licensed from subsidiary TMRC Co., Ltd. to Syros Pharmaceuticals Inc. (NASDAQ: SYRS), clinical trials are underway in the US targeting myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML).

In August 2024, an interim analysis of the SELECT-AML-1 trial for tamibarotene in combination with venetoclax and azacitidine indicated a low likelihood of the investigational drug demonstrating superiority in the final analysis, prompting Syros to halt new patient enrollment.

In Q1, Syros completed the patient enrollment required for the primary endpoint analysis in the Phase III clinical trial (SELECT-MDS-1) for tamibarotene and azacitidine. In November 2024, Syros announced that the trial did not meet its primary endpoint of complete response (CR) rate and that it would discontinue the trial.

FY12/25 company forecast

	FY12/23			FY12/24			FY12/25
(JPYmn)	1H results	2H results	FY results	1H results	2H results	FY results	FY forecast
Operating revenue	**1,014**	**887**	**1,901**	**1,411**	**1,697**	**3,108**	**3,888**
YoY	-29.9%	-39.7%	-34.8%	39.1%	91.2%	63.5%	25.1%
Operating expenses	**1,037**	**1,201**	**2,239**	**1,565**	**1,756**	**3,321**	
YoY	15.8%	3.9%	9.1%	50.9%	46.2%	48.4%	
Cost of revenue	122	123	245	227	399	626	
YoY	16.9%	-3.3%	5.8%	85.6%	224.8%	155.4%	
R&D expenses	603	769	1,373	833	871	1,704	
YoY	14.2%	6.8%	9.9%	38.0%	13.3%	24.1%	
R&D expense ratio	59.5%	86.7%	72.2%	59.0%	51.4%	54.8%	
SG&A expenses	312	309	621	506	486	991	
YoY	18.7%	0.1%	8.6%	62.1%	57.1%	59.6%	
SG&A ratio	30.8%	34.8%	32.7%	35.8%	28.6%	31.9%	
Operating profit	**-23**	**-314**	**-337**	**-154**	**-59**	**-213**	**118**
YoY	-	-	-	-	-	-	-
Operating profit margin	-	-	-	-	-	-	3.0%
Recurring profit	**37**	**-330**	**-293**	**-278**	**-84**	**-362**	**73**
YoY	-94.6%	-	-	-	-	-	-
Recurring profit margin	3.6%	-	-	-19.7%	-	-	1.9%
Net income	**25**	**-349**	**-324**	**-324**	**-171**	**-495**	**-71**
YoY	-94.6%	-	-	-	-	-	-
Net margin	2.5%	-	-	-	-	-	-

Source: Shared Research based on company data

Note: Figures may differ from company materials due to differences in rounding methods.

Note: The 1H FY12/22 forecast is for internal management purposes, and is not disclosed as the company's 1H forecast.

Full-year FY12/25 consolidated earnings forecast (out February 14, 2025)

- Operating revenue: JPY3.9bn (+25.1% YoY)
- Operating profit: JPY118mn (compared to a loss of JPY213mn in FY12/24)
- Recurring profit: JPY73mn (compared to a loss of JPY362mn)
- Net loss attributable to owners of the parent: JPY71mn (compared to a loss of JPY495mn)
- Negative EPS: JPY3.25 (compared to a loss of JPY22.87)

For FY12/25, the company expects royalty revenue from tegoprazan, GALLIPRANT®, ENTYCE®, and ELURA® to remain at the FY12/24 level while securing upfront payments, milestone payments, and research collaboration revenue, including contributions from subsidiaries. The company forecasts non-consolidated revenue at JPY3.1bn (+25.1% YoY), with subsidiaries contributing JPY767mn (+25.5% YoY), total operating expenses of JPY3.8bn (+11.9% YoY), and an assumed forex rate of JPY140/USD.

The company adopts a conservative forecasting approach at the beginning of each fiscal year due to quarterly fluctuations in royalty revenue. In Q1 FY12/25, it will record royalties from tegoprazan sales in China for the July–December 2024 period. The company will also receive upfront payments from a domestic license agreement for tegoprazan and a new agreement with FIMECS. Revenue from subsidiaries will include upfront payments, milestone payments, and research collaboration income from FIMECS, with no contribution expected from TMRC.

The company expects R&D expenses to remain flat YoY at JPY1.7bn, primarily reflecting costs related to clinical trial preparations for the ghrelin receptor agonist and the IRAK-M degradation inducer. Its medium-term management plan for FY12/25–FY12/27, announced alongside FY12/24 results, does not include clinical trial initiation as a target.

Catalyst forecast in 2025

Program	Indication	Country/ region	Development phase	Short-term (2025)	Licensee, partner
Tegoprazan	Gastroesophageal reflux disease and other diseases	US	Phase III	Approval filing	HK InnoN, Braintree
		Japan	Phase I	Signed license-out agreement	Licensee
P2X7 receptor antagonist	Pain and other diseases	US	Phase II	Review and resume of the development plan	Asahi Kasei, Eli Lilly
TRPM8 blocker	Chronic pain	Australia	Phase I	Progressed in preclinical trials	Xgene
Ghrelin receptor agonist	Constipation, cachexia	Worldwide	Preclinical trials	Preparing clinical trials, licensing-out activities	Licensee
IRAK-M degradation inducer	Cancer/cancer immunology	Worldwide	Preclinical trials	Preparing clinical trials, licensing-out activities	Licensee
Existing joint research programs	Cancer	Worldwide	Research	Progressed in joint research	Astellas
New joint research programs	TBD	Worldwide	Research	Signed a new contract	Partner

Source: Shared Research based on company data

*1 FIMECS, a subsidiary, is conducting the IRAK-M degradation inducer program and existing joint research programs.

*2 RaQualia and FIMECS are separately conducting new joint research programs.

Difference between initial company forecasts and results

Results vs. initial forecast	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24
(JPYmn)	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.
Operating revenue (initial forecast)	600	950	1,100	1,388	2,022	2,129	2,738	2,605	2,799	4,535
Operating revenue (Results)	146	705	1,419	745	1,703	1,107	2,776	2,918	1,901	3,108
Results vs. initial forecast	**-75.8%**	**-25.8%**	**29.0%**	**-46.4%**	**-15.8%**	**-48.0%**	**1.4%**	**12.0%**	**-32.1%**	**-31.5%**
Operating profit (initial forecast)	-1,395	-819	-760	-698	187	70	420	420	260	313
Operating profit (Results)	-1,865	-760	-150	-1,075	-16	-486	708	866	-337	-213
Results vs. initial forecast	**-**	**-**	**-**	**-**	**-**	**-**	**68.5%**	**106.2%**	**-**	**-168.2%**
Recurring profit (initial forecast)	-1,415	-819	-761	-680	195	85	427	420	242	290
Recurring profit (Results)	-1,795	-721	-81	-1,065	22	-528	864	904	-293	-362
Results vs. initial forecast	**-**	**-**	**-**	**-**	**-88.9%**	**-**	**102.3%**	**115.3%**	**-**	**-224.7%**
Net income (initial forecast)	-1,661	-825	-767	-686	153	13	343	342	183	236
Net income (Results)	-1,854	-728	-58	-1,105	5	-607	756	723	-324	-495
Results vs. initial forecast	**-**	**-**	**-**	**-**	**-96.5%**	**-**	**120.3%**	**111.5%**	**-**	**-309.8%**

Source: Shared Research based on company data

Note: Figures may differ from company materials due to differences in rounding methods.

Up to FY12/20, earnings was significantly below initial forecasts.

In FY12/21, the company booked an operating profit for the first time since its founding in 2008. Brisk sales of the four products on the market (tegoprazan [K-CAB®], GALLIPRANT®, ENTYCE®, and ELURA®) generated strong royalty revenue. Milestone payments for out-licensed programs and upfront payments for new license agreements also contributed to profitability. The significant difference between the initial recurring profit and net income forecasts and actual results is due to JPY146mn in forex gains stemming from yen depreciation.

In FY12/22, in addition to rising royalty revenue from the above four commercialized drugs, the company received a milestone payment accompanying the launch of a Phase II clinical trial on a P2X7 receptor antagonist and upfront payment from a new pet drug license agreement, aided by yen weakness, booking its second consecutive operating profit.

In FY12/23, the company lowered its earnings forecast on December 8, 2023, due to expected delays in finalizing the licensing agreement for the development, manufacture, and sale of tegoprazan in Japan, and the postponement of the approval and launch of ELURA®, a weight loss treatment for cats with CKD, in Europe until FY12/24. The company estimated these delays would negatively impact earnings by JPY900mn.

The company lowered its earnings forecast for FY12/24 in December 2024. It postponed its out-licensing agreement for the development, manufacture, and sales rights of the gastric acid secretion inhibitor tegoprazan in Japan to the following fiscal year. Additionally, no progress was made on new joint research agreements at FIMECS Inc. or licensing negotiations at TMRC Co. Ltd. However, royalty revenue from HK inno.N and Elanco's veterinary pharmaceuticals remained strong, while milestone income, research collaboration revenue, and option fees related to veterinary drugs contributed to increased other income.

Medium-term business plan

Revision of targets using a rolling approach

The company previously announced a medium-term business plan every three years, with the current plan covering FY12/24–FY12/26. However, it has shifted to a rolling update approach and released a new medium-term management plan

covering FY12/25–FY12/27 along with the announcement of its full-year FY12/24 earnings results.

The company targets operating revenue of JPY3.9bn (+25.1% YoY) and operating profit of JPY118mn for FY12/25, compared with an operating loss of JPY213mn in FY12/24. For FY12/26, it expects operating revenue of JPY3.6bn (-8.2% YoY) and operating profit of JPY258mn (+118.6% YoY), followed by operating revenue of JPY3.7bn (+2.3% YoY) and operating profit of JPY263mn (+1.9% YoY) in FY12/27. The company projects a three-year operating revenue CAGR of 5.5% and assumes an exchange rate of JPY140/USD for FY12/25–FY12/27. To remain responsive to changes in the business environment, it will update the plan annually on a rolling basis.

	FY12/21	FY12/22	FY12/23	FY12/24	FY12/25	FY12/26	FY12/27	3-year
(JPYmn)	Cons.	Cons.	Cons.	Cons.	Forecast	Targets	Targets	CAGR
Operating revenue	**2,776**	**2,918**	**1,901**	**3,108**	**3,889**	**3,571**	**3,653**	
YoY	150.7%	5.1%	-34.8%	63.5%	25.1%	-8.2%	2.3%	5.5%
Operating expenses	**2,068**	**2,052**	**2,538**	**3,321**	**3,769**	**3,312**	**3,389**	
YoY	29.8%	-0.8%	23.7%	30.9%	13.5%	-12.1%	2.3%	0.7%
Operating expense ratio	74.5%	70.3%	133.5%	106.9%	96.9%	92.7%	92.8%	
Operating profit	**708**	**866**	**-337**	**-213**	**118**	**258**	**263**	
YoY	-	22.4%	-	-	-	118.6%	1.9%	-
Operating profit margin	25.5%	29.7%	-	-	3.0%	7.2%	7.2%	
Recurring profit	**864**	**904**	**-293**	**-362**	**73**	**189**	**203**	
YoY	-	4.7%	-	-	-	158.9%	7.4%	-
Recurring profit margin	31.1%	31.0%	-	-	1.9%	5.3%	5.6%	
Net income	**756**	**723**	**-324**	**-495**	**-71**	**32**	**51**	
YoY	-	-4.3%	-	-	-	-	-	-
Net margin	27.2%	24.8%	-	-	-	0.9%	1.4%	

Source: Shared Research based on company data

Progress on the previous medium-term plan and targets in the new plan

Both operating revenue and out-licensing results fell short of the initial FY12/24 targets set for the company's previous medium-term management plan (FY12/24–FY12/26). Under its previous medium-term plan, the company sought to achieve three straight years of profitability from FY12/24. However, due to changes in the operating environment and the reduced likelihood of meeting the original targets, the company revised its goal to achieving operating profitability in FY12/25.

The company is continuing compound development and is integrating FIMECS's drug discovery capabilities, platform technologies, and business functions into its corporate group. In its development strategy, the company has revised the approach for the ghrelin receptor agonist, now aiming to secure a partnership agreement prior to initiating clinical trials. Preclinical studies are ongoing for FIMECS' IRAK-M degradation inducer.

While the company signed an option agreement related to a veterinary drug in FY12/24, it did not achieve its goal of concluding one licensing agreement per year from its out-licensing programs, including tegoprazan (Japan), nor one joint research agreement annually from FIMECS's platform business. For FY12/25, the company has designated the out-licensing of tegoprazan (Japan) and the signing of a new agreement at FIMECS as mandatory targets.

Targets covering FY12/25–FY12/27

Operating revenue	Operating profit for all fiscal years
	Total operating evenue of JPY11.1bn
Research	Developing two candidate compounds
	Advancing research on platform and pipeline programs through collaboration between RaQualia and FIMECS
Development	Licensing-out ghrelin receptor agonist and IRAK-M degradation inducer and initiation of clinical trials by licensee
	Initiation of preclinical trials of new pipeline programs
Out-licensing	One out-licensing agreement per year from its pre-out-licensing program including tegoprazan (Japan)
	One joint research agreement per year in FIMECS' platform business

Source: Shared Research based on company data

Operating revenue forecast: total of JPY11.1bn

FY12/25

The company projects royalties will remain at their FY12/24 level. It expects milestone payments, research collaboration income, and upfront payments from the license-out agreement for tegoprazan in Japan and new agreements at FIMECS. The company forecasts operating revenue of JPY3.9bn (+25.1% YoY), consisting of JPY3.1bn (+25.1% YoY) in standalone revenue from RaQualia and JPY767mn (+25.5% YoY) from subsidiaries FIMECS and TMRC.

FY12/26

The company expects royalties will increase YoY, driven by the expansion of tegoprazan's sales area. While it anticipates milestone and research collaboration income from within the group, it expects a YoY decline in upfront and milestone payments from new agreements. The company forecasts operating revenue of JPY3.6bn (-8.2% YoY), consisting of JPY2.6bn (-16.9% YoY) in standalone revenue from RaQualia and JPY978mn (+27.5% YoY) from subsidiaries FIMECS and TMRC.

FY12/27

The company projects royalties will increase YoY, driven by the expansion of countries where tegoprazan is sold. While it anticipates upfront payments, milestone payments, and research collaboration income, it conservatively assumes contributions from new agreements. The company forecasts operating revenue of JPY3.7bn (+2.3% YoY), consisting of JPY2.7bn (+3.9% YoY) in standalone revenue from RaQualia and JPY959mn (-1.9% YoY) from subsidiaries FIMECS and TMRC.

Status and allocation of funds

Fund	Use: investment aiming to enhance corporate value	Use: shareholder return
Estimated operating revenue from FY12/25 to FY12/27: JPY11.1bn	Exploratory investment, including personnel expenses for three years to expand research areas: JPY6.3bn	Dividend: to be implemented in line with efforts to strengthen the financial base
Cash and cash equivalents as of end-FY12/24: JPY3.9bn	Preclinical and clinical trials, including personnel expenses for three years to enhance project value : JPY400mn	Acquisition of own shares: consider flexibly
Commitment credit line agreement: JPY700mn	Capex (expanding existing facilities, investment in digital transformation)	
Equity financing (share subscription rights): JPY2.0bn	Strategic investment (acquisition of drug discovery technologies and pipeline programs)	

Source: Shared Research based on company data

(Reference) Revised former medium-term management plan (FY12/24–FY12/26)

	FY12/21	FY12/22	FY12/23	FY12/24	FY12/25	FY12/26	3-year
(JPYmn)	Cons.	Cons.	Cons.	Revised forecast	Revised target	Revised target	CAGR
Operating revenue	**2,776**	**2,918**	**1,901**	**3,135**	**3,888**	**3,571**	
YoY	150.7%	5.1%	-34.8%	64.9%	24.0%	-8.2%	23.4%
Operating expenses	**2,068**	**2,052**	**2,538**	**3,369**	**3,769**	**3,312**	
YoY	29.8%	-0.8%	23.7%	32.7%	11.9%	-12.1%	9.3%
Operating expense ratio	74.5%	70.3%	133.5%	107.5%	96.9%	92.7%	
Operating profit	**708**	**866**	**-337**	**-234**	**118**	**258**	
YoY	-	22.4%	-	-	-	118.6%	-
Operating profit margin	25.5%	29.7%	-	-	3.0%	7.2%	
Recurring profit	**864**	**904**	**-293**	**-476**	**73**	**189**	
YoY	-	4.7%	-	-	-	158.9%	-
Recurring profit margin	31.1%	31.0%	-	-	1.9%	5.3%	
Net income	**756**	**723**	**-324**	**-584**	**-71**	**32**	
YoY	-	-4.3%	-	-	-	-	-
Net margin	27.2%	24.8%	-	-	-	0.9%	

Source: Shared Research based on company data

*Figures may differ from company materials due to differences in rounding methods.

At the FY12/24 results announcement, The company revised its numerical targets for the medium-term management plan spanning the three-year period from FY12/24 to FY12/26.

The company now expects operating revenue for FY12/24 to decline by JPY1.4bn (-30.9%) compared to the previous forecast. This decrease primarily reflects delays in the licensing agreement negotiations for the development, manufacturing, and marketing rights for the gastric acid secretion inhibitor tegoprazan in Japan. While negotiations are ongoing, factors such as trends in the Japanese pharmaceutical market and challenges in securing funding for clinical development have pushed the agreement to FY12/25, reducing the operating revenue forecast by JPY1.0bn. Further, slower-than-expected progress in new collaboration agreements at subsidiary FIMECS and licensing negotiations at subsidiary TMRC has resulted in an additional JPY400mn decline in the operating revenue forecast.

The company expects operating expenses to drop by JPY853mn (-20.2%) compared to the previous forecast. The company reduced the estimates for upfront payments for a new license agreement and clinical trial preparation expenses by JPY1.0bn, while it increased projections for M&A-related expenses, including goodwill amortization, by JPY120mn.

The company projects FY12/25 operating revenue to decrease by JPY498mn (-11.4%) compared to the previous target. This decline reflects a total reduction of JPY900mn in upfront and milestone payments, following a review and reassessment at the subsidiary level. The company reviewed the negotiation progress of a new joint research agreement and reassessed the likelihood of milestone achievement at FIMECS. It also reassessed the clinical development progress of Syros

Pharmaceuticals, Inc. (NASDAQ: SYRS), the licensee of its subsidiary TMRC. In addition, the company deferred approximately half of the expected upfront payments carried over from FY12/24 license agreements after reassessing certainty. The company forecasts operating expenses to decline by JPY227mn (-5.7%) from the previous forecast, driven by a JPY400mn reduction in clinical development expenses at FIMECS, partially offset by an increase of JPY85mn following a review of goodwill amortization.

The company lowered the operating revenue forecast for FY12/26 by JPY2.0bn (-35.4%) compared to the previous target. This reduction primarily reflects a JPY1.5bn downward adjustment due to a reassessment of the progress in existing collaboration agreements and the likelihood of the receipt of milestone payments at subsidiaries. Additionally, the company reduced expected upfront payments from license agreements by JPY400mn, considering the certainty of milestone achievement. Operating expenses are expected to decrease by JPY1.1bn (-25.4%) compared to the previous projection. This reduction is driven by a combined JPY900mn decrease in clinical development expenses at the company and its subsidiary FIMECS, partially offset by a JPY96mn increase resulting from a review of goodwill amortization.

(Reference) Previous medium-term management plan (FY12/24–FY12/26)

	FY12/21	FY12/22	FY12/23	FY12/24	FY12/25	FY12/26	3-year
(JPYmn)	Cons.	Cons.	Cons.	Company forecast	Revised target	Targets	CAGR
Operating revenue	**2,776**	**2,918**	**1,901**	**4,535**	**4,386**	**5,524**	
YoY	150.7%	5.1%	-34.8%	138.5%	-3.3%	25.9%	42.7%
Existing businesses				3,435	3,036	3,574	
YoY				80.7%	-11.6%	17.7%	
% of total				75.7%	69.2%	64.7%	
FIMECS revenue				1,100	1,350	1,950	
YoY				-	22.7%	44.4%	
% of total				24.3%	30.8%	35.3%	
Operating expenses	**2,068**	**2,052**	**2,538**	**4,222**	**3,995**	**4,437**	
YoY	29.8%	-0.8%	23.7%	66.4%	-5.4%	11.1%	20.5%
Operating expense ratio	74.5%	70.3%	133.5%	93.1%	91.1%	80.3%	
Operating profit	**708**	**866**	**-337**	**313**	**391**	**1,086**	
YoY	-	22.4%	-	-	24.9%	177.7%	-
Operating profit margin	25.5%	29.7%	-	6.9%	8.9%	19.7%	
Recurring profit	**864**	**904**	**-293**	**290**	**371**	**1,072**	
YoY	-	4.7%	-	-	27.9%	188.9%	-
Recurring profit margin	31.1%	31.0%	-	6.4%	8.5%	19.4%	
Net income	**756**	**723**	**-324**	**236**	**295**	**834**	
YoY	-	-4.3%	-	-	25.0%	182.7%	-
Net margin	27.2%	24.8%	-	5.2%	6.7%	15.1%	

Source: Shared Research based on company data
Note: Figures may differ from company materials due to differences in rounding methods.

Aims at three straight years of operating profit

Along with the announcement of its full-year FY12/23 earnings results, the company also unveiled a three-year medium-term business plan covering FY12/24 to FY12/26. The plan targets FY12/26 operating revenue of JPY5.5bn (three-year CAGR of 42.7%), operating profit of JPY1.1bn, recurring profit of JPY1.1bn, and net income attributable to owners of the parent JPY834mn. The company targets operating profit in three consecutive years due to a doubling of operating revenue as a result of increased upfront and milestone payments and making FIMECS a subsidiary (see below). It assumes a forex rate of JPY135/USD in FY12/24, JPY125/USD in FY12/25, and JPY120/USD in FY12/26.

Three priority measures to improve corporate value and shareholder value

The company breaks down its price-to-book ratio (PBR) into price-per-earnings ratio (PER) and return on equity (ROE), and implements the three priority measures for improving corporate value and shareholder value outlined below to raise PER through growth expectations and increase PBR by recovering its investment.

1. Strengthen drug discovery value chain

Seek to improve growth potential (PER) by taking on new modalities and expanding focus disease areas

2. Expand development pipeline

Aim to improve growth potential (PER) by discovering new development candidate compounds and progressing clinical development to increase value

3. Expand scale of operating revenue

Improve growth potential (PER) and profitability (ROE) through a platform business and moving into areas with potential for large-scale licensing agreements

Key points of business plan

- M&A: Acquired FIMECS, which holds targeted protein degradation (TPD) technologies, to gain a platform business
- Operating revenue: Forecasts total operating revenue of JPY14.4bn in FY12/24–FY12/26, up 45.5% from the previously announced forecast. The company expects a steady increase in royalty revenue, new out-licensing agreements and upfront payments in FIMECS' platform business.
- Out-licensing: The company expects at least one out-licensing agreement per year from its pre-out-licensing program. For tegoprazan in Japan, it aims to conclude an out-licensing agreement in 1H FY12/24. It also expects at least one joint research agreement in FIMECS' platform business.
- R&D: To accelerate the strengthening of its drug discovery value chain centered on open innovation. Plans to discover two pipeline candidates by FY12/26, including new modalities.
- Ghrelin receptor agonist: Clinical trials scheduled for FY12/25

Outlook for operating revenue: Three-year total of JPY14.4bn

- FY12/24: The company looks for increased royalty revenue on solid sales of tegoprazan and pet drugs. It expects upfront payments and milestone payments from the launch of tegoprazan in Japan. Combined with revenue from newly acquired and ongoing joint research projects in FIMECS' platform business, the company forecasts total operating revenue of JPY4.5bn (+138.5% YoY).

- FY12/25: The company expects growth in global sales of tegoprazan and solid sales of pet drugs. It forecasts a total of JPY4.4bn (-3.3% YoY) in operating revenue including royalty revenue and upfront and milestone payments, and revenue from FIMECS' platform business.

- FY12/26: The company expects royalty revenue to remain stable, due to continued solid sales of tegoprazan and pet drugs. It also looks for upfront payments and milestone payments from ghrelin receptor agonist and other drugs. It forecasts a total of JPY5.5bn in operating revenue (+25.9% YoY), including revenue from FIMECS' platform business.

Growth strategy

Establishing drug discovery value chain through open innovation

The company thinks that it must organically combine basic technologies with drug discovery technologies if it is to continually create its development pipeline, and thus has a policy of actively working in collaboration with startups, drug discovery ventures, and academia to solve problems. Creating a drug development pipeline by combining its own technologies is possible with a plentiful supply of funds and human resources, but carries the risk of being limited by existing technologies and frameworks. Relationships of trust and ensuring rights are protected are important in open innovation between multiple companies and collaborations with academia, but this approach allows the application of technologies that a company does not own. The company seeks to establish a next-generation in-house drug discovery value chain by harnessing synergies between its own existing technologies and strengthened collaboration with startups and drug discovery ventures (see the "Business" section below).

1) Initiatives to expand drug discovery targets: Joint research with Veritas In Silico Inc. (TSE Growth: 130A)

2) Initiatives to harness AI: Joint research with Socium Inc.

3) Initiatives to expand modalities: Joint research with STAND Therapeutics Co., Ltd.

4) Initiatives to maximize value of pipeline: Joint research with D. Western Therapeutics Institute (TSE Growth: 4576)

5) Initiatives to utilize structural biology in ion channel drug discovery: Collaboration with leadXpro AG (Switzerland)

Business

Business overview

Predecessor was Pfizer's central research laboratory in Japan

RaQualia Pharma Inc. is an R&D focused drug discovery company. It primarily conducts exploratory research into small molecule compounds ("seeds") for new drugs, and out-licenses development and marketing rights to pharmaceutical and other companies. The company got its start when US-based Pfizer Inc. (NYSE: PFE; ranked third in terms of pharmaceuticals sales worldwide in 2023) decided to close its central research laboratory in Japan as part of global research restructuring in 2007. The research lab spun off from Pfizer through an employee buyout, and RaQualia Pharma was established in July 2008. Pfizer held 19% of the company's shares at its inception, but reduced its stake after the company's initial public offering (IPO), and as of end-December 2024 it held 3.40%.

Pfizer transferred intellectual property to the company covering six exploratory programs, six development programs, and Japanese rights to three products already approved and marketed in the US: GEODON® (ziprasidone), Dalvance® (dalbavancin), and ERAXIS® (anidulafungin)*. Under development at that time were tegoprazan and GALLIPRANT® (grapiprant), which the company continued developing and has already launched. Some compounds transferred from Pfizer are among the pre-out-licensing and out-licensed programs in the development pipeline. The company will pay royalties to Pfizer and record them as cost of operating revenue when licensing out certain compounds transferred from Pfizer.

* Programs transferred from Pfizer that are currently in RaQualia's development pipeline include a potassium-competitive acid blocker (tegoprazan), EP4 receptor antagonist (grapiprant), ghrelin receptor agonist (capromorelin), 5-HT_4, CB2, and 5-HT_{2B}, as well as those at a stage of research where the compound candidate has not yet been determined. Convinced of its value, the company was committed to developing tegoprazan, which it took over after Pfizer decided to withdraw from gastrointestinal diseases in 2007. Tegoprazan has been a key driver of the company's growth.

Earnings structure

In general, biotech company's revenue can be broken down based on drug development stage into: 1) upfront payments received when a contract is signed; 2) development milestone payments tied to predetermined achievements such as clinical trial initiation and application filings; 3) research cooperation payments when conducting joint research, and 4) royalty payments based on a percentage of sales from launched products, while one-time sales milestone payments are triggered when cumulative sales exceed predetermined thresholds.

Licensees have already launched four products, providing the company with stable long-term royalty revenue, its main source of earnings. In FY12/24, operating revenue was JPY3.1bn (+63.5% YoY), comprising royalty revenue (approximately 60%), as well as upfront and milestone payments and research cooperation payments (approximately 40%).

Types of company revenue

Upfront payment	Revenue received upon signing out-licensing or R&D cooperation contract.
	Compensation for value and potential of new drug candidate the company has developed.
Milestone payment	Revenue earned in line with R&D progress of out-licensee.
	Received when key barriers are crossed in process of transforming new drug candidate into a new drug such as moving to the next phase of clinical trials.
Royalty revenue	Revenue based on sales of out-licensee.
	Rate increases progressively with sales, depending on contract terms.
Research cooperation payment	Payment from partner for joint research to discover new drug candidate in early-stage alliance. Compensation for the company's drug discovery technology.

Source: Shared Research based on company data

Revenue by region

	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24
(JPYmn)	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.
Total	146	705	1,419	745	1,703	1,107	2,776	2,918	1,901	3,108
YoY	-5.5%	384.7%	101.2%	-47.5%	128.6%	-35.0%	150.7%	5.1%	-34.8%	63.5%
US	-	646	818	278	761	549	1,004	1,142	1,091	1,129
YoY	-	-	26.5%	-66.0%	173.8%	-27.8%	82.7%	13.8%	-4.5%	3.5%
% of total	-	91.6%	57.6%	37.3%	44.7%	49.6%	36.2%	39.1%	57.4%	36.3%
Japan	106	50	471	349	196	28	1,187	742	6	711
YoY	-19.4%	-52.6%	841.1%	-25.8%	-43.7%	-85.9%	4175.6%	-37.5%	-99.2%	-
% of total	72.5%	7.1%	33.2%	46.8%	11.5%	2.5%	42.8%	25.4%	0.3%	22.9%
Asia	40	9	131	121	746	530	585	1,034	801	1,256
YoY	100.0%	-77.5%	1355.0%	-7.8%	517.9%	-28.9%	10.3%	76.8%	-22.6%	56.8%
% of total	27.5%	1.3%	9.2%	16.2%	43.8%	47.9%	21.1%	35.4%	42.1%	40.4%
Europe	-	-	-	-	-	-	-	-	-	-
YoY	-	-	-	-	-	-	-	-	-	-
% of total	-	-	-	-	-	-	-	-	-	-
Other	-	-	-	-	-	-	-	-	4	12
YoY	-	-	-	-	-	-	-	-	-	249.5%
% of total	-	-	-	-	-	-	-	-	0.2%	0.4%

Source: Shared Research based on company data
Note: Revenue is based on customer location, and classified by country or region

Potential revenue from out-licensing products

Potential revenue from milestone and royalty payments from out-licensed programs totals JPY67.8bn. Development milestone payments are capped at JPY18.3bn, of which the company earned JPY4.5bn by end-FY12/24. Sales milestone payments are capped at JPY49.5bn, with no earnings recorded to date. Royalties have no upper limit; the company earned JPY8.3bn by end-FY12/24.

Business territory

Drug discovery from exploratory research to early clinical development

RaQualia Pharma is a drug discovery company that uses leading-edge technology with the aim of developing drugs for diseases with high unmet medical needs. The stages of drug discovery on which it focuses range from exploratory research of target molecules to early clinical development. When conducting development, the company aims to reduce R&D expenses and risk by advancing programs through early clinical trials (up to Phase II), where efficacy and safety can be broadly assessed. The company broadened its targets from pain and gastrointestinal diseases to include neurological diseases in FY12/21, and added oncology in FY12/24.

Neurological diseases: Newly added to the company's disease coverage, these involve damage to the brain, spinal cord, and nerves. A wide range of conditions comes under this category due to the number of bodily functions controlled by the nerves. Typical examples include cerebrovascular disease, Alzheimer's, epilepsy, and Parkinson's disease, as well as migraine and tension headaches.

The company has traditionally aimed at out-licensing at the preclinical stage, and many of the out-licensing deals to date have been in the early development stages. However, due to the low likelihood of market launch for pipeline drugs in the early development stage, upfront, milestone, and royalty payment rates tend to be lower. In FY12/21, the company shifted toward developing new drug candidate compounds until the proof of concept (POC) stage (which confirms the usefulness and efficacy of a new drug candidate compound under development through administration to humans) in a bid to enhance the value of its future pipelines. POC demonstration entails carrying on clinical trials until the Phase II stage, and requires more R&D spending than previously. The company plans to fund clinical trials through a combination of equity financing and commitment credit lines.

Following FIMECS' FY12/24 conversion into a subsidiary, the company adopted a hybrid business model and is now reconsidering early out-licensing, particularly during basic and exploratory research, as a strategic option. It also revised the development plan for its ghrelin receptor agonist, now aiming to secure a collaboration agreement before initiating clinical trials. The company has not scheduled clinical trials for the compound.

Making the undruggable druggable

The human genome includes approximately 25,000 genes, of which around 3,000 are associated with disease. Currently, only about 500 of these are considered druggable targets. The company focuses on neuroscience and oncology, areas with

high unmet medical needs, and aims to develop innovative drugs by targeting previously intractable disease-related genes through a reinforced drug discovery value chain.

*"Druggable" refers to the potential for modulating the function of target molecules, such as receptors, using compounds or antibodies. Target druggability significantly affects the likelihood of generating viable drug candidates.

Drug development process

Generally, R&D into drugs goes through several stages. Exploratory research looks for new compounds ("seeds") on which drugs will be based; nonclinical studies confirm the efficacy and safety of the compounds discovered through experiments on animals; clinical trials confirm efficacy and safety of administration to humans (healthy individuals and patients). Phase I clinical trials check for safety and adverse reactions in a small number of healthy individuals. Phase II clinical trials evaluate efficacy and safety and help determine appropriate dosages and dosing regimens in a limited patient population. Phase III clinical trials compare efficacy and safety with existing drugs using large numbers of patients.

Time required and success rates

Before a new drug is launched, applications are filed with regulatory authorities in individual countries based on huge volumes of trial data regarding its quality, efficacy, and safety. The drug is marketed following reviews and approval by experts. The process involves a long R&D period of roughly 10 to 15 years, and expenditure of tens of billions to hundreds of billions of yen. Few development pipelines succeed, as development may be halted during the long R&D period due to risks such as changes in the business environment and failure to obtain sought-after data. The difficulty of drug development continues to increase and likelihood of success has declined over time. The Japan Pharmaceutical Manufacturers Association puts the probability of success at 1 in 23,000 currently, versus 1 in 13,000 20 years ago.

Typical drug discovery processes and company's business territory

	Process		Duration	Details	RaQualia's business territory
Research	Exploratory (basic) research		3–5 years	Development of therapeutic concepts, compound synthesis and evaluation	✔
Development	Preclinical (nonclinical) studies		2–3 years	Evaluation of efficacy and safety mainly in animals	✔
	Clinical trials	Phase I	3–7 years	Evaluation of efficacy and safety in humans	✔
		Phase II			
		Phase III			
	Approval filing		approx. 1 year	Application and regulatory review	
	Time until launch		Total 9-16 years		

Source: Shared Research based on company data

Success rates in new drug development

	2000–2004	2005–2009	2010–2014	2015–2019
Preclinical trial launch	1:2,158	1:3,213	1:3,748	1:3,740
Clinical trial launch	1:3,653	1:8,698	1:9,622	1:10,301
Regulatory approval (own company)	1:12,888	1:31,064	1:24,553	1:22,749
Number of approvals (own company)	36	21	29	24

Source: Shared Research based on MHLW, Pharmaceutical Industry Vision 2021

RaQualia's drug discovery modality (methodology)

Expertise in small molecule drug development

The company is primarily engaged in R&D into small molecule compounds, and as of FY12/22, they comprise its entire development pipeline. The company got its start through an employee buyout of the central research laboratory in Japan of US-based Pfizer. When it was established in 2008, RaQualia took over research equipment and some research programs from Pfizer. As a result, it succeeded in out-licensing tegoprazan, its potassium-competitive acid blocker, less than two years after its founding.

Building on Pfizer's expertise, which had focused on compound synthesis and design, the company established an internal structure to conduct experiments with the 100–150 compounds it synthesizes every week. It assigns an eight-digit compound code (starting with 00000001) for all the compounds it researches, develops, and evaluates. The number of digits in the codes demonstrates the company's ongoing exploratory research aimed at finding the seeds of new drugs using its vast stores of data. The compound database it uses on a daily basis numbers approximately 800,000, including a library of about 300,000 compounds used for screening.

World's shortest research cycle: two weeks

The company uses a robotics system called SCARA (Selective Compliance Assembly Robot Arm) which allows it to evaluate 10,000 compounds a day from its vast compound library. New compounds that will become the seeds of new drugs are synthesized by analyzing multidimensional data, with designs based on empirical rules and computational methods according to an efficient synthesis plan based on accumulated expertise. Synthetic samples (including impurities) synthesized by company chemists are delivered promptly to pharmacologists in solution form with purity guaranteed through the company's CAP (Centralized Analysis & Purification) system that automates the purification, weighing, dissolution, and dispensing processes. The company says that using CAP increases the SCARA robotic system's efficiency by roughly 10 times, enabling it to supply 200 compounds per week.

All information concerning compounds is managed using two-dimensional barcodes in a database and used for the structure-activity relationship (SAR)* research. Barcode-controlled 384-hole plates conduct rapid, accurate pharmacological, safety, metabolic, and other studies. Results are promptly recorded in a database and reported to design and synthesis staff. This research cycle takes two weeks, which the company says is the fastest in the world.

* Structure-activity relationship: Refers to the statistical relationship between the structure of a chemical substance and its biological (pharmacological or toxicological) activity. In the drug discovery process, researchers conduct studies aimed at making predictions about the efficacy of structurally similar compounds.

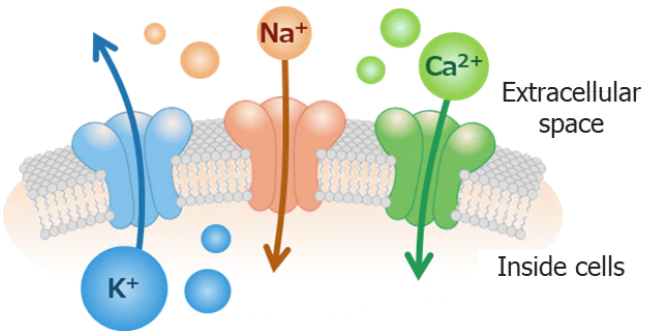
Ion channel drug discovery

The company has already out-licensed five drug discovery programs targeting ion channels. Ion channels are membrane proteins which allow the passage of ions across cell membranes. Expressed in a range of cells, each has a specific ion that can pass through it; examples include the sodium channel, calcium channel, potassium channel, and chloride ion channel.

Ion channels are vital for the maintenance of cell functions and deeply involved in a variety of physiological phenomena. There are over 100 types. Controlling ion channels may offer therapeutic potential across a wide range of diseases; however, selective blocking is essential to avoid serious adverse effects, as simultaneous inhibition of different ion channels in distinct tissues can lead to unintended outcomes. Ion channels are widely expressed in vital organs such as the heart and brain, increasing the risk of life-threatening adverse reactions, including cardiotoxicity and neurotoxicity. Compound design expertise and systems enabling constant high throughput screening* to evaluate compounds are necessary, so this is a niche territory where few companies operate. Consequently, drugs targeting ion channels account for under 10% of all drugs, and RaQualia is the only company in the world to have out-licensed five drugs in the area.

* High throughput screening (HTS) is a technology used to select useful drug candidates from a vast number of compounds rapidly and efficiently. Fast, efficient screening requires a systematic approach covering all processes, including compound storage, structural diversity, solution preparation, plate preparation, assay technology, robotic assays, measurement methodologies, data processing, and database building.

Ion channel mechanism



Source: Company data

Key physiological phenomena involving ion channels

Nerve signaling	➡	**Cognition, memory, five senses**	➡	**Psychiatric and neurological disorders**
Myocardial contraction	➡	Arrhythmia	➡	**Cardiovascular disease**
Skeletal muscle contraction	➡	Quadriplegia, muscle atrophy	➡	**Muscular disorders**
Hormone secretion	➡	Blood sugar, diuresis	➡	**Metabolic and urological diseases**

Source: Shared Research based on company data

Researchers originally involved when the company was under the Pfizer umbrella are conducting a large number of drug discovery research programs targeting ion channels based on advanced technology and abundant experience. To improve screening efficiency, the company teamed up with Hamamatsu Photonics K.K. (TSE Prime: 6965) to develop a voltage-gated ion channel assay system (EFS-FRET Assay System). The system acquires about 1,000 data points per day, enabling highly accurate, low-cost ion channel assays. It enables the company to conduct electrophysiological* research in-house, allowing it to distinguish its assays.

* Electrophysiology refers to both a branch of physiology and an experimental technique that elucidates the electrical properties of nerves, the brain, muscles, and other tissues or cells, and their effects on the body. The interior of cell membranes in living cells maintains an electrically charged state against the outside, and stimuli and information received by sensory cells and nerve cells from outside the cells change the membrane's potential. Neurophysiology in particular focuses on electrophysiological research, and conducts molecular-level research on ion channels and receptors.

The company has a track record of collaborative research in ion channel drug discovery with companies in Japan and overseas, which has resulted in some out-licensed programs.

- Eli Lilly & Company (US): 2010–2014
- Ajinomoto Pharmaceuticals Co., Ltd. (currently EA Pharma Co., Ltd., Japan): 2012–2017
- Asahi Kasei Pharma Corporation (Japan): 2013–2018
- XuanZhu Pharma Co., Ltd. (China): 2015–2018
- ASKA Pharmaceutical Co., Ltd. (Japan): Since 2019–2023

Development candidate compounds created by the company and licensees

Program	Compound code	Main indications	Licensee	Development stage
P2X7 receptor antagonist	RQ-00466479/AK1780	-	Asahi Kasei Pharma	Joint research in 2013
				Eli Lilly running Phase II trials
Selective sodium channel blocker	Not disclosed	Analgesic and antipruritic	Maruho	Out-licensed in 2017
				Not disclosed
Specific ion channel target	Not disclosed	Specific gastrointestinal disorders	EA Pharma	Joint research in 2012
				Not disclosed
TRPM8 blocker	RQ-00434739	Chronic pain	Xgene	Out-licensed in 2021
				Xgene (Hong Kong) running Phase I trials
Sodium channel blocker	RQ-00350215	Chronic pain	Hisamitsu	Out-licensed in 2021
				Not disclosed

Source: Shared Research based on company data (as of December 2024)

The TRPM8 blocker and sodium channel blocker programs were out-licensed in FY12/21, and are drug discovery programs targeting ion channels.

Expanding coverage to neurological diseases

The company has decided to shift the direction of in-house development from a line-up focused mainly on pain and gastrointestinal diseases to include neurological diseases. From FY12/22 onward, RaQualia plans to focus on areas with significant unmet medical needs including neurodegenerative, genetic, and rare diseases, and continue to discover new drugs by searching for target molecules and collaborating with academia in its disease models. The company has been working on pain, which is a nervous system related disorder, for many years, and with growing needs related to nervous system diseases among rare diseases, it decided that its technology and facilities were suitable.

Patent expiry management

Aims to extend life of patents

RaQualia applies for basic patents (substance patents) and obtains rights in major countries around the world on an ongoing basis. While the regions and expiry dates differ, the company has several hundred patents, with some effective until around 2040. After filing for a basic patent, the company aims to extend the effective life of patents by seeking extensions and applying for peripheral patents. Compound patents are effective for 20 years, which may be extended by as much as five years, and filing for peripheral patents (such as use patents and manufacturing process patents) can extend exclusivity for a further 20 years. The company has extended the life of patents that Pfizer originally applied for until the mid-2030s via extensions and peripheral patent applications. The aim is to ensure revenue over the long term by delaying the launch of lower-priced generic drugs with the same ingredients and efficacy after the basic patent for a new drug has expired.

Examples of patent types

Patent	Coverage	Example
Substance patent	Substance structure only	Compound as indicated in chemical formula X
Process patent	Substance manufacturing method	Method of producing substance C through reaction of substance A and substance B
Use patent	Uses and target diseases	Agents for treating specific diseases containing substance A
Dosage and administration patent	Dosage and administration method	Administering xx mg per dose x times daily
Formulation patent	Formulation technology	Compressed solid preparation containing substance A, disintegrant B, and binder C
Compound in combination patent	Multiple active ingredients	Pharmaceutical composition containing substance A and substance B
Crystal patent	Substance crystal structure	Crystal of substance A (definition of diffraction angle)

Source: Shared Research based on company data

Trying new modality

Drugs can be broadly classified into two categories: chemically synthesized small molecule drugs and biopharmaceuticals made from biological materials. Small molecule drugs are generally less expensive to produce because they have smaller molecules, a fixed chemical structural formula, and are easy to mass produce. Biopharmaceuticals have active ingredients derived from proteins, such as growth hormones, insulin, or antibodies, and are manufactured from cells, yeast, or bacteria. The molecules of biopharmaceuticals are large and complex, and their properties and characteristics depend on the manufacturing process, boosting costs. Biopharmaceuticals launched as new drugs tend to be more expensive, and the market is also larger.

When the Ministry of Health, Labour and Welfare puts a new prescription drug on the national health insurance (NHI) price list, the price of the newly developed drug is based on a comparison with drugs already in use with similar efficacy (comparable drug method). If the new drug is more effective or novel, a premium is added, boosting the price. If there is no comparable drug with similar efficacy, the price is based on costs such as raw materials and manufacturing (cost accounting method). There are more existing drugs in the company's main therapeutic areas of pain and gastrointestinal diseases than neurodegenerative diseases, genetic diseases, and rare diseases, which have significant unmet medical needs. This means that the price at time of launch for the former tends to be low, as does royalty revenue.

In its medium-term plan up to FY12/24, the company mentioned conducting tests of new modality concepts. Its strength lies in small molecule drug discovery. It plans to try out new modalities involving collaborations with university start-ups and others for drugs challenging to develop with the technology and expertise it has accumulated thus far. The company is engaged in initiatives such as protein structure analysis using cryo-electron microscopy and informatics-driven drug discovery for a structural biological approach to ion channels.

Collaboration with drug discovery start-ups and others

Using AI to look for treatments for intractable and rare diseases

In May 2022, the company and Socium Inc. (unlisted) signed a joint research agreement to look for indications for RaQualia's compounds to treat intractable and rare diseases. Socium's intractable and rare disease program has a database of gene expression patterns for all intractable and rare diseases registered at the Intractable Disease Information Center. Socium can estimate compounds' possible indications based on their gene expression pattern. Estimating indications based on gene expression patterns can identify novel indications in a few months that could not be predicted from the conventional pharmacological mode of action of the compound. The company thinks this will help maximize the value of the compound.

Disease-focused approach using new modality (intracellular antibodies)

In August 2022, RaQualia entered into an agreement with STAND Therapeutics (unlisted) to explore the possibility of applying STAND's technologies to drug discovery, and began collaborating with STAND with the aim of discovering treatments for intractable and rare diseases. Many target molecules of drugs and other medical therapies exist within cells; however, because antibodies cannot function within cells as they become unstable and aggregate in the cytosol, antibody drugs until now have focused on targets in the extracellular space. By utilizing STAND's technology to generate intracellular antibodies that can function within cells, the company believes it can stabilize antibody drugs by attaching stabilizing peptide tags to them and have them approach target molecules in the intracellular space without aggregating.

Aims at mRNA-targeted small-molecule anti-cancer drug discovery

In December 2022, the company announced a joint research agreement with Veritas In Silico Inc. (TSE GRT: 130A, VIS) to discover breakthrough small-molecule drugs targeting messenger RNAs (mRNA). VIS has proprietary platform technologies specialized in mRNA-targeted drug discovery. Through joint research over multiple years, the company and Veritas In Silico will target a number of genes associated with cancer specified by the company and identify target structures on corresponding mRNA; identify hit compounds by high-throughput screening; identify lead compounds by synthesizing analogues (hit expansion); and determine development candidate compounds through lead optimization.

Looking for compounds targeting ion channels to treat eye diseases

In December 2022, the company announced a joint research agreement with D. Western Therapeutics Institute, Inc. (TSE Growth: 4576, DWTI). The partners will use their respective technologies, resources, and expertise in pharmaceutical R&D in joint research aimed at discovering and developing therapeutic agents for specific optic nerve disorders. The company will draw on its ion channel drug discovery technology to synthesize a group of compounds that target specific ion channels. DWTI will verify the compounds' potential as therapeutic agents for eye diseases through pharmacological tests and other methods using its evaluation technology in the field of ophthalmology. Technological achievements and intellectual property obtained from the joint research will be jointly owned by the company and DWTI, and after the research program finishes, the partners plan to hold discussions on the next stage of collaboration.

Structural biology analysis of ion channels

The company announced that it has partnered with leadXpro AG (unlisted), a Swiss company with expertise in membrane protein biochemistry, to accelerate drug discovery research targeting membrane proteins, a challenging area for drug development. RaQualia has a strong track record in ion channel drug discovery targeting membrane proteins and aims to accelerate drug discovery projects in this area through collaboration with leadXpro. leadXpro is a biotech company specializing in membrane protein structure-based drug discovery with expertise in structural biology, ligand design*1, and biophysical characterization of membrane proteins. By using structural biology techniques such as cryogenic electron microscopy*2 to observe how ligands bind to proteins at the atomic level, the company believes it is possible to logically design drug candidates (i.e., improve drug activity and selectivity) and accelerate drug discovery research.

*1 A ligand is a substance that binds specifically to a particular receptor, such as an amino acid, protein, or small molecule. Drug development involves identifying receptors that are targets for specific diseases and developing drugs that exert therapeutic effects through interactions with ligands or selective actions of ligand-based drugs.

*2 Cryogenic electron microscopy is a device used to observe and analyze the three-dimensional structure of biomolecules such as proteins by irradiating them with an electron beam while cooled with liquid nitrogen to -196°C.

Joint research and technologies held by startups and drug discovery companies

	Proprietary technologies	Start date	Joint research overview
Socium	Proprietary database of intractable and rare diseases and AI drug discovery platform	May 2022	Exploratory research on the applicability of the company's compounds to intractable and rare diseases
STAND	Proprietary technology (STAND technology) to generate antibodies in cells and approach target molecules	August 2022	Feasibility study on the application of STAND technology for drug discovery targeting intractable and rare diseases
Veritas In Silico	Informatics technology to find target substructures on mRNA	December 2022	Discovery of small-molecule drugs targeting mRNA
DWTI	Expertise in ophthalmic drug discovery (glaucoma drug: Glanatec®)	December 2022	Discovery of treatments for ophthalmic diseases
LeadXpro	Technology for structural analysis of membrane proteins using cryo-electron microscopy	December 2022	3D structural analysis of membrane proteins

Source: Shared Research based on company materials

Business model change

To a hybridized business model

M&A aiming to raise corporate value and shareholder value

In February 2024, the company announced it would acquire all shares in FIMECS, Inc. (unlisted) and make it a subsidiary, because it needs to create a new source of earnings to follow tegoprazan and pet drugs. FIMECS advances the research and development of new pharmaceuticals using targeted protein degradation (TPD) inducers, a new modality in drug discovery. Based on its unique drug discovery platform technology RaPPIDS™, it conducts joint research with Astellas Pharma Inc. (TSE Prime: 4503) and may receive milestone payments according to progress with development and royalties after product launch. The company expects to strengthen its drug discovery value chain, increase its earnings through a hybridized business model, and strengthen the cancer disease area by making FIMECS a subsidiary.

Synergies expected from M&A

Management resources	• Acquire pipelines • Acquire skilled personnel • New corporate cultures and innovation engines
Increased growth potential	• Strengthen drug discovery value chain • Acquire new modalities • Further advance into cancer disease area
Increased profitability	• Increase earnings opportunities • Expand into platform businesses

Source: Shared Research based on company data

Taking on untouched drug discovery targets

Existing small molecule drugs treat diseases by binding to disease-related proteins, which are the drug discovery targets, and inhibiting their function. Proteins with structures that prevent binding have been considered "undruggable" (impossible to discover drugs to treat the condition). However, new modalities and application of new technologies such as informatics and AI in drug discovery have opened up the possibility of creating new candidate drugs that target disease-related proteins that were previously believed to be "undruggable."

Founded in 2018, FIMECS is a drug discovery bio-venture engaged in research and development of new pharmaceuticals using targeted protein degradation (TPD) inducers, a new modality in drug discovery. TPD works by directly breaking down "undruggable" target proteins. The human body naturally breaks down and removes unnecessary proteins through metabolism, but TPD stimulates the breaking down of the target protein by bringing E3 ligase, an enzyme that adds ubiquitin to mark the target protein to help break it down.

Based on its unique E3 ligase binding molecule and drug discovery platform technology RaPPIDS™, it aims to create innovative medicines for diseases that have been considered extremely difficult to treat using medications ("undruggable"). FIMECS has established a technology to identify the optimal E3 ligase for each target from over 600 known E3 ligases and acquire novel E3 ligase binders by improving and evolving RaPPIDS™.

Platform-type business model enables revenue generation from early-stage of the development

The company operates as a pipeline-type drug discovery company, developing drug candidate compounds, conducting preclinical and clinical trials in-house, and licensing out these assets. It generates revenue through upfront and milestone payments, as well as royalties based on a percentage of sales from launched products. In contrast, FIMECS follows a platform-type model.

Platform-type biotech companies provide their proprietary technology at the exploratory stage and license it out prior to preclinical trials, generating revenue through upfront payments and research collaboration fees. Licensees are responsible for conducting preclinical studies and subsequent development. Platform-type companies earn milestone payments based on development progress and receive royalties based on a percentage of sales from launched products. In contrast with pipeline-type companies, platform-type companies avoid development risk but tend to receive smaller upfront payments, milestones, and royalties. However, they generate more stable income from the early stages of product development.

Through the acquisition of FIMECS, RaQualia aims to establish a hybrid model that combines platform- and pipeline-type approaches.

In 2022, FIMECS entered into a research collaboration agreement with Astellas Pharma Inc. (TSE Prime: 4503) on multiple targets. Based on this agreement, FIMECS received an upfront payment of JPY500mn and research funding. After the identification of candidate compounds, Astellas Pharma will conduct development, and FIMECS will receive milestone payments based on the progress of development for each target program. Furthermore, after commercialization, FIMECS may receive single-digit sales milestones and royalties at a single-digit rate based on sales revenue. Operating revenue in FIMECS in FY12/24 was JPY601mn.

FIMECS is also advancing several first-in-class new drug development programs targeting proteins associated with cancer diseases as its main in-house pipeline. The most advanced program, the IRAK-M program (compound code: FIM-001), aims to develop a new cancer immunotherapy based on the mechanism of action of immune suppression relief and is currently in the preclinical stage.

FIMECS' pipeline

Target	Target disease	Research stage	Partner
IRAK-M	Non-small cell lung cancer, pancreatic cancer, other	Preclinical studies	
TRIB1	Cancer	Exploratory	
Undisclosed	Undisclosed	Exploratory	Astellas Pharma
Undisclosed	Undisclosed	Exploratory	Astellas Pharma

Source: Shared Research based on FIMECS website (as of December 2024)

Reason for the acquisition

RaQualia is focused on enhancing corporate and shareholder value by reinforcing its growth foundation, while aiming to improve profitability through the signing of large contracts. In pursuit of growth enhancement, updating the drug discovery value chain and M&A are positioned as key strategies. By making FIMECS a subsidiary, RaQualia expects business expansion in the following three areas:

1. Enhancing the drug discovery value chain to improve growth potential and competitiveness

Traditionally, RaQualia has specialized in drug discovery research of small molecules targeting ion channels and GPCRs, generating many drug candidate compounds. Since 2022, aiming to establish the next-generation in-house drug discovery value chain from four perspectives: modality, drug discovery target, disease area, and core technology, RaQualia has been advancing collaborations with several startups and drug discovery companies. Acquiring FIMECS's RaPPIDS™ platform technology to venture into new modalities, such as targeted protein degradation (TPD) inducers, allows targeting molecules and disease areas previously considered undruggable. The acquisition of FIMECS is expected to significantly advance the strengthening of RaQualia's next-generation in-house drug discovery value chain.

*The human body eliminates unnecessary proteins through natural intracellular degradation systems. Targeted protein degraders (TPDs) are small molecules that harness these systems to selectively eliminate disease-related proteins. By inducing degradation, TPDs inhibit protein function through a mechanism of action distinct from that of conventional enzyme inhibitors or receptor antagonists.

2. Adopt a hybridized business model: Increase its earnings through platform business

The company is a "pipeline-type" drug discovery company, which discovers new drug candidate compounds and develops them in-house, and undertakes the later stages of clinical development by out-licensing, through joint research, or independently. FIMECS is a "platform-type" drug discovery company, which focuses on exploratory research, with technology that it out-licenses and ability to create drug discovery seeds. The company that in-licenses its technology undertakes development from the preclinical studies stage onward. The earnings structure of platform-type companies is based on joint research from the exploratory research stage to obtain upfront payments, research cooperation payments, and milestone payments early on, as well as royalty revenue. For pipeline-type companies on the other hand, exploratory research through to out-licensing is an investment phase, and the investment recovery phase comes after out-licensing in the form of upfront and milestone payments and royalty revenue. By making FIMECS a subsidiary, the company has hybridized its business model so it can earn revenue from the exploratory research stage.

Currently, FIMECS is conducting joint research with Astellas Pharma on multiple targets, which may yield milestone payments, royalties, and sales milestones based on the progress of these joint research projects. The interest in targeted protein degradation inducers is particularly high abroad, with similar companies in the US (e.g., Arvinas [NASDAQ: ARVN], C4 Therapeutics [NASDAQ: CCCC], Kymera Therapeutics [NASDAQ: KYMR], Nurix Therapeutics [NASDAQ: NRIX]) building their platforms and securing substantial contracts from the early stages of collaboration. FIMECS plans to continuously acquire new joint research partners both domestically and internationally around its core platform technology, RaPPIDS™, expecting further expansion of revenue opportunities.

3. Further strengthening and expansion in the oncology field

RaQualia has developed marketed pharmaceuticals such as the gastric acid secretion inhibitor tegoprazan (brand name: K-CAB®) and the dog osteoarthritis treatment grapiprant (brand name: GALLIPRANT®). While many of its out-licensed programs are being developed by pharmaceutical companies and belong mainly to the pain and gastrointestinal disease areas, the company has initiated exploratory research targeting cancer as part of strengthening its drug discovery value chain. The acquisition of FIMECS, adding pipelines including the IRAK-M program, will strengthen the group's pipeline targeting cancer.

Consideration and method for the acquisition

RaQualia plans to acquire all issued shares of FIMECS from the current shareholders on March 26, 2024, making FIMECS a consolidated subsidiary. The consideration for the acquisition consists of an upfront payment (the closing consideration) paid at the time of the share acquisition and payments based on future revenues earned by FIMECS (the earn-out consideration).

1. Closing consideration

RaQualia will pay a closing consideration of JPY4.5bn in cash to the sellers on March 26, 2024. In March 2024, the company decided to borrow a syndicated loan of JPY3.5bn (loan period: seven years) to fund the share acquisition.

2. Earn-out consideration

From FY12/24 to FY12/28, based on contract upfront payments, milestone payments, royalty revenue, and revenue from commissioned work generated from contracts with third parties, an amount calculated using a predetermined calculation method will be paid to the sellers.

This arrangement mitigates the risk of RaQualia paying a large one-time consideration by avoiding payment of the entire consideration at the time of the acquisition execution, instead paying part of it as earn-out consideration based on the revenue of FIMECS. It also serves as an incentive for some sellers involved in FIMECS's operations to continue contributing to research and development activities and revenue expansion.

Pipeline overview

Ample pipeline based on pharmaceutical company standard research processes and operating procedures

The company took over the expertise and methodology in drug discovery R&D from its predecessor, the Pfizer central research laboratory, and has continued with the research projects it inherited. Accordingly, it has a large number of "seeds," and has been able to create a series of candidate compounds. It has advanced technological capabilities based on its standard operating procedures (SOP) equivalent to those of pharmaceutical companies, and is engaged in difficult drug discovery targeting ion channels, and has out-licensed five projects at an early stage. The company has four products already commercialized (tegoprazan, GALLIPRANT®, ENTYCE®, and ELURA®), and an ample pipeline: 15 project compounds already out-licensed, including ion channel projects, and seven at the pre-out-licensing stage.

It also had 11 programs in its exploratory research pipeline as of December 2024, and in addition to in-house research, it is conducting joint research with other companies and academia. In March 2018, the company signed an agreement with Nagoya University to establish the RaQualia Pharma Industry-Academia Collaborative Research Center (RARC) within the university which houses the Department of Pharmacology and Department of Pharmaceutical Sciences. It conducts research aimed at discovering drug candidate compounds and aims to accelerate drug discovery with industry-academia collaboration. The company thinks that it can continually discover innovative compounds as development candidates by always having 7–10 exploratory research programs underway.

Out-licensed pipeline (human)

Out-licensed programs (human)

Program name	Generic nameCompound code	Key indication	Out-licensing region	Development stage
Tegoprazan (potassium-competitive acid blocker [P-CAB]; K-CAB®)	RQ-00000004 (tegoprazan)	GERD	South Korea	On market (Mar 2019)
			China	On market (Apr 2022)
			Philippines	On market (Oct 2022)
			Mongolia	On market (Oct 2022)
			Mexico	On market (May 2023)
			Indonesia	On market (July 2023)
			Singapore	On market (Sep 2023)
			Peru	On market (Oct 2023)
			Chile	On market (Sep 2024)
			Colombia	On market (Oct 2024)
			Dominican Republic, Nicaragua, Honduras, Guatemala, El Salvador	On market (Dec 2024)
			Malaysia	Marketing approval obtained
			Thailand, Vietnam	Application under review
			6 countries in Latin America	Preparing for approval filing
			Brazil	Preparing for approval filing
			US, Canada	Phase III underway in US (2022-)
			7 countries including India	Phase III underway, preparations underway
Retinoic acid receptor alpha agonist	Tamibarotene TM-411/SY-1425	High-risk MDS	North America, Europe	Phase III complete (US)
		Acute myeloid leukemia (AML)		Phase II complete (US)
EP4 receptor antagonist	RQ-00000007 (grapiprant)	Pain	Worldwide	Phase II complete (US)
				Phase I complete (China)
		Cancer	Worldwide	Phase I complete (US)
				Phase I underway (China)
	RQ-00000008	Osteoarthritis, zautoimmune disorders, etc.	Worldwide	Preclinical trials complete
5-HT4 partial agonist	RQ-00000009	Alzheimer's disease	Worldwide	Phase I complete (US)
COX-2 inhibitor	RQ-00317076	Pain	Worldwide	Phase IIa complete (US)
				Phase I underway (China)
CB2 agonist	RQ-00202730	Pain relief, etc.	Worldwide	Phase I underway (UK)
Selective sodium channel blocker	Not disclosed	Analgesic and antipruritic	Worldwide	Not disclosed
P2X7 receptor antagonist	RQ-00466479 AK1780	Neuropathic pain	Worldwide	Phase II complete (US and others)
Specific ion channel target	Not disclosed	Gastroenterology	Worldwide	Not disclosed
TRPM8 blocker	RQ-00434739	Chronic pain	Worldwide, except Japan	Phase I underway (Australia)
Sodium channel blocker	RQ-00350215	Chronic pain	Worldwide	Phase I underway
IRAK-M degradation inducer	FIM-001	Cancer	Worldwide	Preclinical trials ongoing

Source: Shared Research based on company data (as of December 2024)

Potassium-competitive acid blocker: P-CAB (generic name: tegoprazan)

Characteristics of tegoprazan

Tegoprazan is primarily used to treat gastroesophageal reflux disease (GERD)* and serves as an alternative to conventional proton pump inhibitors (PPIs). The company initiated preclinical trials upon its establishment, having received tegoprazan as a development candidate from Pfizer and with many Pfizer researchers involved in tegoprazan transferring to the company.

*GERD: A disease whereby stomach contents, in particular stomach acid, flow back into the esophagus (food pipe), causing characteristic symptoms such as heartburn. GERD can be classified as non-erosive reflux disease (NERD) or erosive esophagitis. NERD is a condition in which damage to the esophageal mucosa cannot be confirmed by endoscopy, despite symptoms such as heartburn and acid reflux.

GERD is a condition in which stomach contents, especially gastric acid, reflux into the esophagus and cause symptoms such as heartburn. The primary symptoms are acid regurgitation* and heartburn, which often occurs during fasting or at night. Tegoprazan and the existing drug vonoprazan (brand name: TAKECAB®) primarily differ in their mechanisms of acid secretion inhibition and speed of onset. According to the company, tegoprazan provides acid suppression comparable to vonoprazan and superior to PPIs.

In South Korea, tegoprazan and PPIs are approved to treat NERD, whereas vonoprazan is not approved for this indication in Japan. Intragastric pH is used as an indicator of onset of action. Tegoprazan raises intragastric pH above 4 within one hour, whereas vonoprazan takes approximately four hours to reach the same level. PPIs require activation by gastric acid and therefore generally do not take effect on the first day of administration. While gastrin*2 levels tend to increase with vonoprazan, the elevation is less pronounced with tegoprazan and PPIs.

* Acid regurgitation is a symptom of the backward flow of stomach acid into the esophagus, followed by downward flow that causes a sour or bitter sensation in the mouth and throat.
*2 Gastrin is a hormone secreted mainly from cells in the pyloric antrum of the stomach. Under normal conditions, it temporarily rises after meals and promotes gastric acid secretion. When abnormally secreted, causing extreme hyperacidity, if the serum gastrin level is maintained at an elevated level over an extended period, this increases the risk of developing peptic ulcers and neuroendocrine tumor development and should be carefully monitored. Medication is sometimes discontinued due to high gastrin levels.

Frontrunner was Takeda Pharmaceutical's TAKECAB®

Vonoprazan (brand name: TAKECAB®) is a potassium-competitive acid blocker (P-CAB) launched by Takeda Pharmaceutical Company Limited (TSE Prime: 4502) in February 2015, and has a different action than the then-mainstream treatment, PPIs. PPIs are activated by acid in the body, and inhibit gastric acid secretion. Vonoprazan does not require activation by acid, and is fast acting and effective at preventing gastric acid secretion by inhibiting the binding of potassium ions needed for secretion (source: Takeda).

P-CABs have largely replaced PPIs and histamine H2 receptor antagonists (H2RAs, H2 blockers). In 2021, despite a 4.1% reduction in the NHI price of TAKECAB®, its revenue on an NHI price basis totaled JPY111.1bn (+13.5% YoY), ranking third among domestic prescription drugs. In 2024, revenue rose to JPY120.1bn (+3.9% YoY), placing fourth among domestic prescription drugs. P-CABs have continued to achieve YoY revenue growth for 10 consecutive years since launch, whereas most drugs typically peak five to six years after market entry. TAKECAB® was initially listed in February 2015 at an NHI price of JPY160.12 for a 10mg tablet and JPY240.20 for a 20mg tablet. As of April 1, 2025, the prices had decreased to JPY94.30 for a 10mg tablet and JPY141.00 for a 20mg tablet, including orally disintegrating formulations.

Maintained No. 1 market share in South Korea, the first launch country following global out-licensing (excluding Japan)

In June 2010, after Phase I trials in the US were completed, the company entered a strategic alliance with South Korea-based HK inno.N in gastrointestinal diseases, and reached an out-licensing agreement covering South Korea, China including Hong Kong, and Taiwan for the commercialization of tegoprazan in September 2010. The geographic regions covered gradually increased from 2019, and currently HK inno.N has been granted rights to cover the entire world except Japan.

HK inno.N gained marketing approval for the company's out-licensed drug tegoprazan for South Korea in July 2018, and launched it as K-CAB® tablets in March 2019. Revenue of K-CAB® in South Korea in 2024 (non-hospital prescription data) remained brisk, totaling KRW196.9bn (+24.4% YoY, roughly JPY21.7bn converted at JPY0.11/KRW). From 2019 to 2024, total prescriptions reached KRW705.4bn (JPY77.6bn), with a CAGR of 45.9%. As of end-December 2024, the product held the top market share in South Korea for gastrointestinal disease treatments at 15%.

K-CAB® for sale in South Korea

Source: HK inno.N homepage

Expanding market share in South Korea through broadened indications and OD tablets

In February 2022, HK inno.N gained manufacturing and marketing approval for orally disintegrating K-CAB® tablets, and launched sales in May 2022. These can be taken by elderly who have trouble swallowing tablets, those with restricted fluid intake, or those unable to drink water because they are away from home. The company expects that improved dosing convenience and expanded patient population will boost HK inno.N's earnings and be reflected in royalty revenue.

In July 2022, HK inno.N obtained approval for K-CAB® as maintenance therapy for healed erosive esophagitis. This makes K-CAB® the most widely indicated P-CAB marketed in South Korea. The five indications for which tegoprazan received marketing approval in South Korea are erosive esophagitis, NERD, gastric ulcer, adjuvant therapy for Helicobacter pylori eradication, and maintenance therapy for healed erosive esophagitis. Following its approval for health insurance coverage in January 2023, a new formulation used in maintenance therapy for erosive esophagitis was launched. The new formulation contains half of the tegoprazan volume of existing medicines, and maintains the condition of the patient once healed. This means that tegoprazan is the only P-CAB marketed in South Korea able to be used in all stages from the onset of erosive esophagitis to the post-treatment stage.

Global expansion of tegoprazan

The company granted HK inno.N the global rights to out-license tegoprazan outside Japan, including the right to sublicense. HK inno.N aims to expand tegoprazan into 100 countries by 2028. HK inno.N and its sublicensees are engaged in global business activities related to tegoprazan, with the product currently marketed in 15 countries and preparations underway for development, manufacturing, and commercialization in an additional 48 countries.

HK inno.N's sales expansion plans

HK inno.N has gradually expanded its licensed territories and, since 2019, holds global rights excluding Japan. Since its establishment in 2008, RaQualia Pharma carried on with and invested in R&D into tegoprazan, one of Pfizer's development programs. Under its global strategy, HK inno.N has started acquiring marketing approval in countries around the world under its global sales strategy. The company believes it is on the cusp of a long-term period where it can recoup its investment.

In China, tegoprazan has been marketed by sublicensee Luoxin Pharmaceuticals since 2022, making it the second country after South Korea to launch the product. Luoxin sells tegoprazan across 31 provinces and administrative regions. Luoxin has received regulatory approval from the National Medical Products Administration (NMPA) to conduct clinical trials on an injectable formulation and has also obtained marketing approval for a combination therapy targeting Helicobacter pylori infections.

In May 2022, HK inno.N's sublicensee Metro received marketing approval for four indications in the Philippines, including erosive esophagitis, and launched sales in November 2022. The peptic ulcer medicine market in the country is over USD60mn (about JPY7.5bn), making it the fourth largest market in Southeast Asia. Metro has successfully marketed proton pump inhibitors (PPIs) in the Philippines and has sales infrastructure and marketing expertise in the field of peptic ulcers, so the company hopes it will be able to make quick inroads in the market with tegoprazan. As of March 2023, in addition to being on sale in South Korea, China, and the Philippines, tegoprazan has been rolled out to 36 countries, where it is in the

development, awaiting approval, or preparing to launch stage. It has received approval in Mongolia, and product supply has begun, with plans to put the drug on sale during FY12/23.

In the US, sublicensee Brainree is conducting Phase III clinical trials. As of end-FY12/24, the trial targeting NERD has been completed, while the clinical trial for erosive esophagitis remains ongoing.

Royalty revenue expected to increase due to expansion of sales territories

As of end-December 2024, HK Inno.N's sublicensees are advancing the development, manufacture, and sale of tegoprazan in 45 countries excluding South Korea. In January 2025, HK. Inno.N signed a sublicense agreement in Australia and New Zealand, expanding tegoprazan's reach to 48 countries.

As of end-December 2024, tegoprazan is marketed in 15 countries: South Korea, China, Mongolia, the Philippines, Mexico, Indonesia, Singapore, Peru, Chile, Colombia, the Dominican Republic, Nicaragua, Honduras, Guatemala, and El Salvador. Under the licensing agreement with HK inno.N, RaQualia receives milestone payments based on development progress or a percentage of the revenue that HK inno.N earns from the sublicensee.

The company says that the global peptic ulcer market is potentially worth JPY2tn, and HK inno.N aims to roll out tegoprazan to 100 countries by 2028. The largest market is North America at JPY400bn, followed by China at JPY310bn. Assuming a global market share of 10% for tegoprazan and a royalty rate of 5%, the company could potentially receive annual royalty payments of JPY10bn.

Estimate of company royalties

Potential global market size		Share captured		Royalty rate		Maximum royalties company can receive
JPY2bn	×	15% in South Korea	×	Generally 1–10%	=	

Source: Shared Research based on company data

Development status and market size for HK inno.N by key country/region

Country/region	Licensee*	Sales and development status	Market size (JPYmn)
South Korea	HK inno.N	Launched in 2019, maintaining No. 1 market share	120,000
China	Luoxin	Launched in April 2022	450,000
Philippines	MPPI	Launched in October 2022	5,000
Mongolia	Monos	Launched in October 2022	-
Mexico	Carnot	Launched in May 2023	66,000
Indonesia	Kalbe	Launched in July 2023	50,000
Singapore	UITC	Launched in September 2023	50,000
Peru	Carnot	Launched in October 2023	66,000
Thailand, Vietnam, Malaysia	Pond's, Lyhn farma, Pharmaniaga	Approval obtained and sales preparation in Thailand and Malaysia, application under review in Vietnam	50,000
Argentina and 15 other Latin American countries	Carnot	Application under review in eight Latin American countries, approval obtained in seven Latin American countries, including Chile	66,000
Brazil	Eurofarma	Filing in preparation	88,000
US, Canada	Braintree	Phase III study in progress	460,000
7 countries including India	Dr.Reddy	Phase III study in progress/preparation	140,000

Source: Shared Research based on company data (as of December 2024)
Note: Licensees include HK inno.N sublicensees
Note: Market sizes from HK inno.N data (September 2022). Calculated at JPY0.1/KRW

Growth potential for peptic ulcer drug market in China

According to Scientific Reports, in 2020 there were 58mn GERD patients in China (4.2% of the population), with an estimated market size of JPY350bn. The mainstream treatments are conventional PPIs and H2RAs (H2 blockers), with treatment costs per patient of JPY6,000. With the entry of P-CAB, prescription costs per patient in Japan and South Korea have risen to JPY14,000 and JPY20,000 respectively, and the company thinks that prescription costs per patient in China will also increase as PPIs and H2RAs are replaced. Furthermore, due to the adoption of Western dietary habits and the aging of the population, GERD patients are also increasing, and the market is likely to expand as their share in the population grows.

GERD patient numbers and peptic ulcer drug market size

Country/region	No. of patients (% of population)	Market size (JPYmn)	Treatment costs per patient	Mainstream treatment
China	58mn (4.2%)	350,000	JPY6,000	PPI, H2RA
US	67mn (21.0%)	450,000	JPY6,700	PPI, H2RA
South Korea	3mn (5.8%)	60,000	JPY20,000	PPI, H2RA, P-CAB
Japan	17mn (14.0%)	250,000	JPY14,000	PPI, H2RA, P-CAB

Source: Shared Research based on company data
Note: Calculated at JPY0.1/KRW, JPY19.6/CNY, JPY125/USD

Sales plans in China

Luoxin Pharmaceutical is selling tegoprazan under the brand name Tai Xin Zan® in China. After receiving Category 1 approval in China, designating it an innovative drug, on April 13, 2022, it launched the drug just 15 days later, on April 28. In addition to selling it at major hospitals and retail drugstores in China, it is also selling it over the internet via online medical services, and is targeting revenue of CNY1.0bn (roughly JPY19.6bn converted at JPY19.6/CNY) in 2023, and CNY3.0bn in the longer term (roughly JPY58.8bn). In Q2 FY12/22, the company received a milestone payment of JPY300mn, and is set to receive further royalty payments based on a percentage of sales from launched products. Because Luoxin is a sublicensee, royalty revenue will come through HK inno.N, so the company expects a time lag of about six months.

EP4 receptor antagonist (RQ-00000007, grapiprant)

Grapiprant is an EP4 receptor antagonist originally developed by Pfizer and later transferred to RaQualia. It is the same compound as GALLIPRANT®, which is already marketed as a pet drug. In January 2013, the company transferred the intellectual property rights for grapiprant to AskAt (a wholly-owned subsidiary at the time) in return for a set percentage of royalty AskAt receives. AskAt has been developing grapiprant since the IP transfer, mainly for the indications of cancer and pain. In December 2017, AskAt concluded a licensing agreement with Arrys Therapeutics (unlisted, a subsidiary of Ikena) for global rights to grapiprant, excluding China and Taiwan. Subsequently, Ikena took over rights from Arrys and has been conducting clinical trials.

Ikena started a US expansion phase I clinical trial (Phase Ib) in October 2018, targeting patients with unresectable or advanced microsatellite stable colorectal cancer. However, in November 2022, Ikena announced it had suspended in-house development and was considering alternative strategic plans. In September 2023, AskAt announced the cancellation of its worldwide license agreement for the EP4 receptor antagonist in cancer immunology, reflecting a shift in its R&D strategy. An investigator-initiated clinical trial that began in September 2021 is ongoing at the University of Texas MD Anderson Cancer Center to evaluate concurrent treatment with grapiprant and Halaven® (eribulin) for metastatic inflammatory breast cancer since September 2021.

In addition, Chinese licensee 3D Medicines Co., Ltd. (unlisted) concluded Phase I trials of grapiprant for pain management. Another licensee in China, Ningbo NewBay Medical Technology Development Co., Ltd. (unlisted), is conducting Phase I clinical trials for oncological applications.

CB2 agonist (RQ-00202730)

The CB2 agonist is a compound the company originated after inheriting the theme from Pfizer. AskAt's UK-based licensee Oxford Cannabinoid Technologies Ltd. (LSE: OCTP), is a business partner since November 2015. In January 2023, OCTP submitted an application for a Phase I clinical trial to the UK Medicines and Healthcare products Regulatory Agency (MHRA) and Research Ethics Committee (REC). After receiving approval, it started dosing patients in July 2023. OCTP's Phase I clinical trial for the CB2 agonist mainly targets chemotherapy induced peripheral neuropathy (CIPN). OCTP plans to proceed with clinical development of the CB2 agonist, and commenced the Phase I trial in the UK in Q3 FY12/23. As of December 2024, OCTP is conducting a single-dose clinical trial.

The human body has cannabinoid receptors known as CB1 and CB2, but targeting CB1 entails risks of central nervous system adverse reactions on behavior or psychology. However, CB2 is attracting interest as a target for drugs to treat pain, inflammatory diseases, and cancer. Because the company's CB2 agonist is a compound that selectively acts on CB2, it avoids adverse reactions via CB1, and is thought promising as a highly tolerable treatment. The global CIPN market is worth about USD1.6bn (roughly JPY241.5bn at JPY150/USD), and is expected to grow to USD2.4bn (roughly JPY355.5bn) by 2027.

P2X7 receptor antagonist (RQ-00466479)

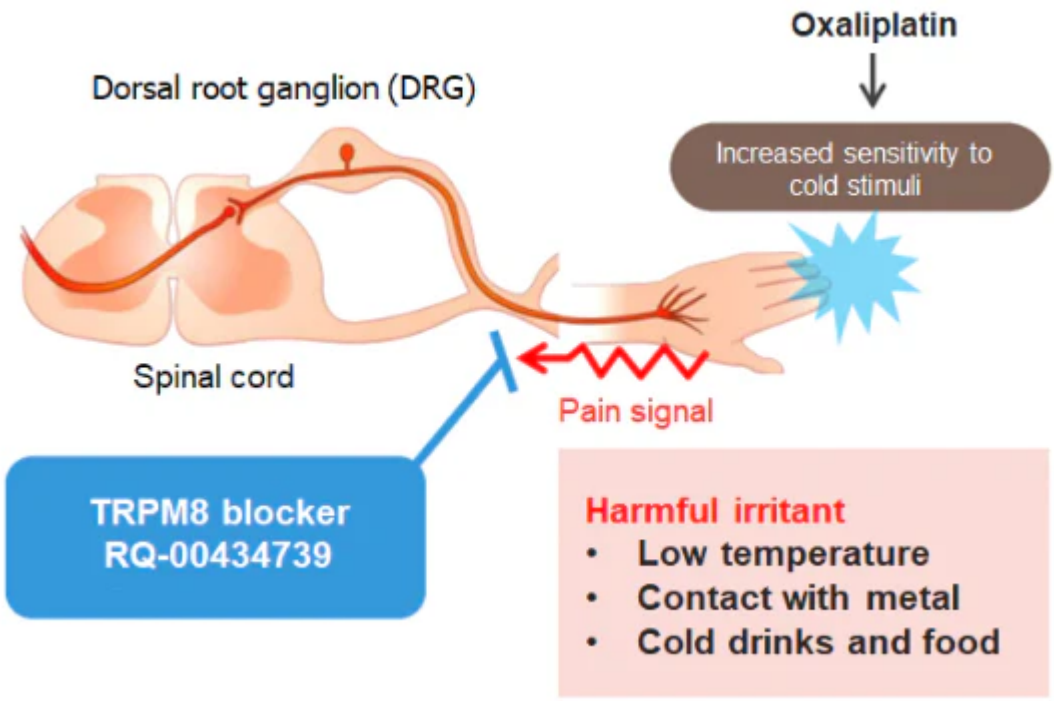
The company created a P2X7 receptor antagonist through joint research with Asahi Kasei Pharma (a license agreement signed in March 2018). Phase I clinical trials targeting peripheral neuropathic pain have been completed. Eli Lilly, with whom Asahi Kasei Pharma has a license agreement, will take over global development from Phase II. Based on the licensing agreement with Asahi Kasei Pharma, the company will receive royalty payments based on a certain percentage of Asahi Kasei Pharma's earnings. With the start of Phase II by Eli Lilly in November 2022, RaQualia achieved the development milestone and received an upfront payment of USD4mn (JPY500mn based on JPY125/USD translation).

In August 2024, sublicensee Eli Lilly announced the results of Phase II clinical trials conducted in the US for three diseases (knee pain due to osteoarthritis, chronic low back pain, and diabetic neuropathic pain). Although the safety profile of the investigational drug was favorable with no major concerns, its efficacy did not meet the primary endpoints. Eli Lilly is currently reviewing future development plans.

TRPM8 blocker (RQ-00434739)

The TRPM8 blocker is a program RaQualia created. TRPM8 is a temperature-sensitive ion channel activated by cold stimuli under 28°C or by menthol (mint) and its involvement has been suggested in a variety of chronic disorders, including chronic pain. In-house discovered selective TRPM8 blocker (azaspiro derivative) demonstrated a different mechanism of action in animal models of chronic pain from existing drugs, and the company hopes it will be a breakthrough drug. For example, about 90% of patients who receive cancer treatment using oxaliplatin are susceptible to cold pain. The company's TRPM8 blocker blocks TRPM8 (the cold receptor) directly, suppressing the transmission of pain signals.

TRPM8 blocker and pain mechanisms



Source: Company data

In September 2021, RaQualia entered a licensing agreement with Hong Kong-based Xgene Pharmaceutical Co. Ltd. (unlisted), granting it exclusive global rights (excluding Japan) to develop, manufacture, and sell the TRPM8 blocker. Xgene has moved to the preclinical study phase in its quest to develop a pain therapy, and In March 2024, it received approval to begin Phase I clinical trials from the Australian Therapeutic Goods Administration (TGA). The company is set to receive milestone payments as research moves through development stages and royalties based on sales if the product is launched (specific target conditions and amounts have not been disclosed).

In May 2024, Xgene initiated a Phase I clinical trial in Australia without a one-time payment at initiation. The trial involves a dose-escalation study in healthy volunteers to evaluate the tolerability and pharmacokinetics of a TRPM8 blocker to gather critical data. Xgene will advance to Phase II clinical trials targeting cancer-related and neuropathic pain in China and the US.

Sodium channel blocker (RQ-00350215)

Sodium channels, along with other ion channels such as potassium channels, control the generation and transmission of nerve action potentials, and are deeply involved in neurotransmission. The company hopes that the sodium channel blocker it developed will become a breakthrough new drug for chronic pain (that existing drugs to not provide sufficient analgesic effect for) by selectively blocking the function of specific sodium channels involved in pain signal transmission.

In December 2021, RaQualia entered a licensing agreement with Hisamitsu Pharmaceutical Co., Inc., (TSE Prime: 4530) granting it exclusive worldwide development, manufacturing, and marketing rights. Although the out-licensing occurred in the early development stage, the company received JPY600mn as an upfront payment and may receive up to JPY3.0bn in milestone payments as development progresses. Further, if drugs containing the sodium channel blocker the company developed are approved and launched, it has the right to receive sales royalties with a royalty rate in the range of 5–10%, and milestone payments in line with revenue to a maximum of over JPY10bn. Hisamitsu Pharmaceutical plans to develop transdermal medication (one of its strengths) for pain containing the sodium channel blocker RaQualia developed, starting with the preclinical trial phase.

In October 2024, the company received a milestone payment of JPY100mn from Hisamitsu upon achieving a pre-determined target. Although the company has not disclosed its development status, Shared Research believes that a Phase I clinical trial has commenced.

The company has additional projects underway, though the development stages remain undisclosed. It has out-licensed a compound targeting a specific ion channel for gastrointestinal indications to EA Pharma. In December 2017, the company out-licensed a selective sodium channel blocker for analgesic and anti-pruritic indications to Maruho and received a milestone payment in March 2021 upon achieving a pre-determined target. However, it terminated the license agreement in December 2024.

Cyclooxygenase-2 (COX-2) inhibitor (RQ-00317076)

The company discovered a cyclooxygenase-2 (COX-2) inhibitor from a compound with a different type of chemical structure from existing COX-2 inhibitors.

In January 2013, the company signed an agreement to transfer all intellectual property rights, related data, and the drug substance for RQ-00317076 to AskAt in return for a percentage of the revenue AskAt earns from RQ-00317076 as royalties. AskAt has positioned RQ-00317076 as a third-generation COX-2 inhibitor. In early-stage Phase II clinical trials conducted in the US targeting postoperative pain, RQ-00317076 was shown to have superior efficacy, more rapid response, and longer-lasting effect, as well as higher safety and tolerability compared to ibuprofen, the standard treatment. As of FY12/22, AskAt's China-based licensee 3D Medicines Co., Ltd. (unlisted) was conducting a Phase I clinical trial of the drug for human use.

In July 2022, AskAt entered into a license agreement with US-based Velo-1 for global rights to RQ-00317076 as a drug for animals, as well as a two-year development support agreement with Velo-1. Signing of these agreements meant that RQ-00317076 was being developed not only for human use, but also for animals. RQ-00317076 has lower risk of adverse effects when used in dogs compared with existing NSAIDs, and AskAt believes it is a promising compound for treating acute pain, e.g., postoperative pain, and chronic pain associated with osteoarthritis.

Pipeline of TMRC (consolidated subsidiary)

Tamibarotene (TM-411) (retinoic acid receptor alpha agonist: anticancer agent)

The company's consolidated subsidiary TMRC is a drug discovery company specializing in the field of cancer.

TMRC was established in January 2002 as a contract research organization (CRO) specializing in cancer. In February 2004, it obtained exclusive manufacturing and marketing rights in Japan and overseas for tamibarotene (TM-411) as an antineoplastic (anticancer) drug. In March 2009 it spun off the CRO business and established it as a subsidiary, and transferred 100% of the shares to Sugi Medical Co., Ltd. (unlisted, subsidiary of Sugi Holdings Co., Ltd. [TSE Prime: 7649]). In February 2017, TMRC became a wholly-owned subsidiary of RaQualia.

Tamibarotene, a selective retinoic acid receptor alpha (RARα) agonist, is TMRC's main pipeline. In February 2004, TMRC obtained exclusive development and marketing rights in Japan and overseas for tamibarotene as an anticancer drug. In April 2005, licensee Toko Pharmaceutical Industries Co., Ltd. (unlisted) received manufacturing and marketing approval in Japan and launched the drug as an orphan drug* (for rare diseases) for acute promyelocytic leukemia (APL). The drug is sold by Nippon Shinyaku Co., Ltd. (TSE Prime: 4516) as Amnolake® tablets.

* Orphan drugs are drugs used to treat rare diseases, and they are called so because they are often not actively developed, i.e., ignored or rarely adopted by pharmaceutical companies, due to their limited market and accompanying difficulty in recouping development costs.

Generic name	Tamibarotene
Mechanism of action	TM-411 has a high affinity for RAR alpha, and inhibits leukemia cell differentiation and cancer cell proliferation by regulating gene expression. The inhibitory effect includes suppression of IL-6 production and IL-6R expression, enhancement of IGFBP-3 expression, and suppression of VEGF-dependent angiogenesis, and may be applicable to a range of cancer tumors.
	Meanwhile, it acts on hematopoietic stem cells (CDK-activating kinase (CAK)-RAR alpha) in the bone marrow to promote differentiation into neutrophils via progenitor cells, induces granule formation and reactive oxygen species (ROS), and displays antibacterial activity.
	It is expected to be more effective when used in combination with the G-CSF preparations used to treat neutropenia.
Indications	Myelodysplastic syndrome, acute myelogenous leukemia, breast cancer, childhood cancers, acute promyelocytic leukemia, neuroblastoma, and neutropenia.
Administration	Oral (tablets, capsules)
Licensor	Toko Pharmaceutical Industry, Chemfizz

Source: Shared Research based on company data

Out-licensed to US-based Syros Pharmaceuticals

In September 2015, TMRC granted development and marketing rights in Europe and North America for tamibarotene as a cancer therapy to US-based Syros Pharmaceuticals, Inc. (NASDAQ: SYRS) in exchange for rights to receive milestone payments in accordance with development progress and sales royalties after launch. Syros aims to file a new drug application for tamibarotene as a precision medicine* for RAR alpha gene (RARA)-positive patients. RARA is expressed as a biomarker in patients with myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). Syros has been conducting clinical trials targeting MDS and AML in the US.

* Precision medicine: Also known as cancer gene therapy, it is cutting-edge medicine that entails analyzing cancer at the genetic level to provide the optimal treatment for that particular cancer. It is most advanced in the field of oncology, but can be used for all diseases. It is a kind of tailor-made, personalized medicine that entails analyzing cancer cell genes using a next-generation sequencer (a device for high-speed, large-scale decoding of the base sequences that represent the order in which the bases that make up DNA are bound together) to find the cancer-causing genetic mutation. It uses a molecular targeted drug designed to be effective against that particular gene mutation.

Analysis shows that approximately 50% of MDS patients and 30% of AML patients have RAR alpha overexpression. When tamibarotene is used in combination with an anticancer agent, tamibarotene binds to RAR alpha, controlling the expression of differentiation factor genes, for an anti-tumor effect inducing cancer cell death. A patent review regarding the use of tamibarotene with anticancer drugs in Japan was conducted in July 2023.

Tamibarotene received fast-track designation from the US Food and Drug Administration for higher-risk myelodysplastic syndrome (HR-MDS) in January 2023, and for acute myeloid leukemia (AML) in April 2024. Companies whose drug candidates obtain fast-track designation can hold more frequent meetings to discuss development plans with the FDA, and may be eligible for priority and fast-track review if the plan can be supported by clinical data.

RaQualia is entitled to receive milestone payments from Syros in line with the development stages and royalties once tamibarotene is launched on the market. Tamibarotene has received orphan drug designation* for MDS and AML in the US and for AML in Europe. In addition, in July 2022 the company obtained a use patent (jointly filed with the National Institute of Advanced Industrial Science and Technology [AIST]) for tamibarotene as a growth inhibitor for cancer stem cells*[2] in Europe. In August the same year, Syros announced that the European Medical Agency (EMA) indicated it was in favor of granting orphan drug designation to tamibarotene for MDS.

* Orphan drug designation: A system designed to support development of drugs for life-threatening, rare diseases that affect only a small number of people (diseases that affect less than 200,000 [inclusive] patients in the US; less than five [exclusive] patients out of 10,000 persons in Europe; and less than 50,000 [exclusive] patients in Japan). Drugs that have obtained orphan drug designation enjoy various benefits, including preferential treatment in approval review, development funding, and guaranteed time-limited first mover advantage (market exclusivity) from the start of sales.
*2 Cancer stem cells are cancer cells that have the characteristics of stem cells (i.e., self-renewal ability to divide and produce identical cells and multilineage differentiation ability to differentiate into various types of cells). They are malignant cells that self-renew and serve as the source of cancer cells. Cancer stem cells are either 1) normal stem cells that have become cancerous or 2) cells that have differentiated to some degree and become cancer stem cells through long-term inflammation. The former is often seen in childhood cancers such as osteosarcoma and hematologic cancers, and is thought to be the cause of disease recurrence and metastasis, as its slow cell division makes it difficult to respond to radiotherapy and anticancer drugs.

Clinical trials by Syros

Syros conducted a Phase III clinical trial (SELECT-MDS-1) of tamibarotene administered in combination with azacitidine, the standard treatment for high-risk MDS, targeting previously untreated high-risk MDS patients. Patient enrollment necessary for analyzing the primary endpoint was completed during Q1 FY12/24. The company initially planned to release pivotal data by mid-Q4 and subsequently submit an NDA. However, in November 2024, Syros announced that the trial failed to meet its primary endpoint, the complete response (CR) rate, and that it would discontinue the trial while conducting a detailed analysis of the clinical trial data to determine the next steps.

In December 2022, Syros published data from the safety lead-in phase of the Phase II clinical trial (SELECT-AML-1), which studied the combination therapy consisting of tamibarotene, venetoclax, and azacitidine. The trial was conducted in AML patients, including elderly individuals, who are ineligible for standard chemotherapy. The trial then progressed to the randomized phase, and the results of this phase were announced in December 2023. In August 2024, an interim analysis, including a non-binding futility analysis, was conducted using data from 51 patients enrolled in the Phase II clinical trial. The analysis concluded that the probability of demonstrating superiority in the final analysis with data from 80 patients was low, leading Syros to decide to halt new patient enrollment. No new safety concerns were identified in the combination therapy of tamibarotene, venetoclax, and azacitidine. Syros presented these findings at the 12th Annual Meeting of the Society of Hematologic Oncology (SOHO) in September 2024.

*A futility analysis is a statistical assessment used to predict trial outcomes based on prespecified hypotheses and evaluation criteria, helping to determine whether the trial should continue.

Regarding MDS, Syros completed patient enrollment necessary for the primary endpoint analysis during Q1 FY12/24 for the Phase III clinical trial evaluating the combination therapy of tamibarotene and azacitidine. In November 2024, Syros announced that the trial failed to meet its primary endpoint, the complete response (CR) rate. Syros also disclosed its decision to discontinue the trial while conducting a detailed analysis of the clinical trial data to determine the next steps. Additionally, the company stated that the failure to meet the primary endpoint in the Phase III clinical trial constitutes a default event under its existing secured loan agreement.

Separately, a clinical research/investigator-initiated clinical trial of tamibarotene for pancreatic cancer and upper urinary tract cancer (led by Nagoya University) has been underway since March 2023, as a Japan Agency for Medical Research and Development (AMED) project. RaQualia has rights for Asia, and aims to out-license rights for treatment of MDS in Japan and China and pancreatic cancer in Japan as development in the US progresses.

Out-licensed pipeline (pet drugs)

Three products on the market

Two of the pet drugs the company has already launched, EP4 receptor antagonist grapiprant and ghrelin receptor agonist capromorelin, are compounds inherited from Pfizer. In December 2010, it granted US-based Aratana Therapeutics Inc. (acquired by Elanco in 2019) an exclusive global license with sublicensing rights to develop, market, and manufacture veterinary drugs. The three products on the market are currently sold by Elanco.

Out-licensed programs (veterinary)

Program name	Generic name/compound code	Key indication	Rollout area	Development stage
EP4 antagonist GALLIPRANT®	RQ-00000007 (grapiprant)	Osteoarthritis in dogs	US	On market
			Europe	On market
			Japan	On market
Ghrelin receptor agonistENTYCE®	RQ-00000005 (capromorelin)	Anorexia in dogs	US	On market
Ghrelin receptor agonistELURA®		Weight loss in cats with CKD	US	On market
			Europe	Approved, on market
			Japan	Approved, preparing for launch
COX-2 inhibitor	RQ-00317076	Pain	—	Exploratory research completed
EP4 receptor antagonist	RQ-00000008	Osteoarthritis, etc.	Worldwide	Preclinical trial ongoing
5-HT4 agonist	RQ-00000010	Intestinal motility disorder (dogs, cats)	Worldwide (Veterinary)	POC trial ongoing
Four specific compounds	Not disclosed	Under evaluation	Worldwide	Under evaluation

Source: Shared Research based on company data (as of November 2024)

GALLIPRANT® (EP4 receptor antagonist, generic name: grapiprant)

This compound was launched in the US in January 2017 as GALLIPRANT® for osteoarthritis in dogs by US-based Elanco and is now being sold in over 20 countries around the world by Elanco (US). The nonsteroidal anti-inflammatory analgesic and first-in-class (breakthrough)* drug was launched in Japan in October 2020, and sales are growing steadily. Sales reached USD100mn (roughly JPY12.5bn) in FY12/21, becoming Elanco's tenth blockbuster drug.

* A first-in-class (breakthrough) drug is one that is highly novel and useful, and groundbreaking in that it significantly changes existing treatments. It often has a new chemical structure or therapeutic concept. Best-in-class (improved) drugs compensate for shortcomings of first-in-class drugs and have a clear advantage over existing drugs.

ENTYCE®, ELURA® (ghrelin receptor agonist, generic name: capromorelin)

Elanco sells ENTYCE® in the US as a treatment for anorexia in dogs. It is also sold under the brand name ELURA® in the US as a drug for the management of weight loss in cats with chronic kidney disease (CKD). Elanco filed for approval in Europe in March 2022. The company received an associated milestone payment of JPY115mn in Q1 FY12/22. The company receives milestone payments as set out in its contract and royalties in line with sales when there is progress such as expanding sales territories. The company said that sales of ENTYCE® and ELURA® were tracking well due to the absence of similar products.

The company filed for approval of ELURA® in March 2022 in Europe, and the Committee for Veterinary Medicinal Products (CVMP) of the European Medical Agency (EMA) indicated that it was in favor of approval in May 2023. Approval was granted in 2023; the product was launched in August 2024 in France and the company received a milestone payment. In February 2024, Elanco obtained manufacturing and marketing approval for ELURA® from Japan's Ministry of Agriculture, Forestry, and Fisheries and launched the product in November. The company will not receive an upfront payment for the launch.

Potential for ELURA®

According to the company, over 30% of cats aged 10 and over and over 9% overall (roughly 648,000 cats) in Japan have CKD. Cats with CKD may show ongoing weight loss and reduced life expectancy due to loss of appetite and repeated vomiting as the disease progresses. Over 80% of the cats with CKD that were administered ELURA® for 56 days gained weight. In 2022, there are 74.1mn pet cats in the US and 56.6mn in Europe, so the company thinks the potential market is significant (source: Global Market Insights Research Inc. [unlisted]).

Cyclooxygenase-2 (COX-2) inhibitor (RQ-00317076)

RaQualia's in-house discovered cyclooxygenase-2 (COX-2) inhibitor has a different type of chemical structure than those of existing COX-2 inhibitors. In January 2013, the company signed an agreement to transfer all intellectual property rights, related data, and the drug substance for RQ-00317076 to AskAt, in return for a percentage of the revenue that AskAt earns from RQ-00317076 as royalties. AskAt had been developing RQ-00317076 as a human drug, but in July 2022, signed a

license agreement with US-based Velo-1 for global rights to the drug for use in animals, as well as a two-year development support agreement with Velo-1. Signing of these agreements signaled the start of RQ-00317076 development as an animal drug. RQ-00317076 has lower risk of adverse effects when used in dogs compared with existing NSAIDs, and AskAt believes it is a promising compound for treating acute pain, e.g., postoperative pain, and chronic pain associated with osteoarthritis.

New licensing agreement

5-HT4 agonist (RQ-00000010)

In April 2023, the company signed an option and license agreement with Vetbiolix SAS (unlisted) for the development of a veterinary drug targeting gastrointestinal motility disorders in dogs and cats, based on its proprietary 5-HT$_4$ agonist RQ-00000010 (RQ-10). Under the agreement, the company granted Vetbiolix an exclusive, global, and sublicensable option to license RQ-10 for development, manufacturing, and commercialization. In December 2024, the company received an option fee following Vetbiolix's exercise of the option. The company is entitled to receive milestone payments based on RQ-10's development progress, as well as sales-based royalties from product revenue or sublicensing income earned by Vetbiolix following market launch.

Four development compounds

In April 2024, the company entered into an option and license agreement with US-based Velovia Pharma, LLC (unlisted) for the development of veterinary drugs containing the company's four pipeline compounds. Based on the terms of the agreement, the company granted Velovia option for the exclusive rights to evaluate, develop, manufacture, and sell veterinary drugs containing its four pipeline compounds. If Velovia exercises its option right for one or more of the compounds, the company is entitled to receive option exercise fees as well as milestone payments based on Velovia's subsequent development progress. Further, if veterinary drugs containing the compounds reach the market, the company may receive sales royalties and sales milestone payments based on product sales from Velovia.

Royalty revenue stable for pet drugs, as not affected by drug price revisions

In Japan, the Ministry of Health, Labour and Welfare (MHLW) sets uniform nationwide prices (NHI prices) for human prescription drugs. However, in the distribution chain, pharmaceutical wholesalers sell drugs to medical institutions and insurance pharmacies at wholesale prices that are different from the NHI prices. To reduce the burden on the insurance scheme, the MHLW surveys sales prices and volumes for each individual drug, and revises (lowers) prices based on its findings every year (every second year until April 2018). On the five occasions leading up to the April 2024 round of price revisions, the price was cut by 1.18% on a medical fee basis and reduced and by 5.51% on a drug fee basis on average. Expensive drugs are covered by public insurance and are thought to have a significant impact on the insurance budget, leading to this arrangement for stepwise reductions. This means it is difficult for pharmaceutical companies to generate expected profits for drugs that they launch following prolonged periods of development and massive investments.

The market for pet drugs for which the company receives royalty revenue is smaller than that for human drugs, but there is no similar NHI drug price system either in Japan or overseas. This enables prices to be maintained or lifted, and Shared Research thinks royalty revenue, which is a percentage of sales, tends to be stable and resilient to downward pressure as a result.

Pet drugs versus human drugs

	Pet drugs	Human drugs
Curtailing medical expenses/price revisions	Basically deregulated treatment with no price-setting system. Manufacturers have the right to set prices.	In countries with national drug price systems, the government (insurers in countries without such systems) influences price setting.
Generic drugs	A small number of companies enter market with slightly lower prices once patent expires. Japanese government provides little administrative guidance to promote generics.	Many companies enter market with lower prices once patent expires. Japanese government promotes use of generics.
Consumer behavior	Pet owners (consumers) have strong focus on brand/quality, and tend to keep using the same product after patent expiry.	Price is an important consideration, and consumers tend to shift to low-priced generic products after patent expiry.

Source: Shared Research based on company data

Pre-out-licensing programs

The company has seven pre-out-licensing programs (i.e., pipelines in preparation for out-licensing). This includes some that have been out-licensed outside Japan such as tegoprazan and a TRPM8 blocker.

Pre-out-licensing programs

Program name	Generic name/ compound code	Key indication	Target market	Development stage
tegoprazan	tegoprazan RQ-00000004	GERD, others	Japan	
5-HT4 partial agonist	RQ-00000010	Gastroparesis, functional dyspepsia, chronic constipation	Worldwide (human)	Phase I completed
5-HT28 agonist	RQ-00310941	Irritable bowel syndrome with diarrhea (IBS-D)	Worldwide	Phase I completed (UK)
Motilin receptor agonist	RQ-00201894	Gastroparesis, functional dyspepsia, post-operative ileus	Worldwide	Preclinical trials completed
Ghrelin receptor agonist	RQ-00433412	Cancer-related anorexia/cachexia syndrome, contipation from spinal cord	Worldwide	Preclinical trials underway
IRAK-K degradation inducer	FIM-001	Cancer (NSCLC, pancreatic cancer)	-	Preclinical trials underway
TRPM8 blocker	RQ-00434739	Pain	Japan	Preclinical trials underway

Source: Shared Research based on company data (as of December 2024)

Potassium ion-competitive acid blocker: P-CAB (generic name: tegoprazan)

Tegoprazan is primarily used to treat gastrointestinal reflux disease (GERD), and is an alternative to the existing mainstream therapy of proton pump inhibitors (PPIs).

Could become best in class

The existing drug TAKECAB®, approved for erosive esophagitis, has not received approval for NERD in Japan. In Japan, NERD accounts for 60% of GERD cases (source: Osaka City Medical Association, "Pathophysiology and treatment of gastroesophageal reflux disease and related disorders" [2016]). Gastrin levels tend to rise less with tegoprazan than with vonoprazan (TAKECAB®). Shared Research thinks that, if approved in Japan, tegoprazan has a high probability of replacing TAKECAB®. The company says that there were some 17mn GERD patients in Japan as of 2020 (14% of the population) with a market size of JPY250bn.

Extended negotiations for out-licensing tegoprazan in Japan

The company retains the rights for Japan for tegoprazan, which was out-licensed to HK inno.N in September 2010. It had planned to complete pharmacological studies as part of Phase I clinical trials in FY12/23 and out-license in FY12/24 onward. However, having been approached by a licensee candidate, the company decided not to conduct its own pharmacological studies and out-license in FY12/23 so that the product could go on sale as soon as possible. It began negotiations with the licensee candidate in FY12/23 and expected to conclude an agreement by end-2023, but the following issues have required more time to resolve.

In the negotiations with the licensee candidate for tegoprazan in Japan, RaQualia identified three discussion points: 1) accelerating development and reducing the risk, 2) ensuring the supply of APIs and formulations, and 3) potential drug price cuts.

The company leverages overseas clinical trial information through frequent consultation with its partners, HK Inno.N and Braintree to address the first issue. HK inno.N, currently marketing in countries including Korea and China, will supply APIs and formulations to the company. These two issues were resolved early in 2023. However, discussions on the third issue persist. To maintain price elasticity in anticipation of future drug price reductions, negotiations with licensee candidates

continue. The discussions focus on key terms such as license fees and supply costs. The company missed its initial target of signing an agreement in FY12/24, as the prospective licensee had not reached a final decision. Negotiations are ongoing, with both parties sharing the goal of an early launch in Japan. The company now aims to conclude the license agreement by end-FY12/25.

Use of South Korean and US data

The company is working to maximize the value of tegoprazan. It is aiming at rapid and efficient development and approval in Japan using South Korean data and is getting ready to launch clinical pharmacological studies. RaQualia is investigating the study protocol based on advice from medical experts and is in discussions with the Pharmaceuticals and Medical Devices Agency (PMDA) concerning the trial. Tegoprazan has already been approved in South Korea for erosive esophagitis, non-erosive reflux disease (NERD), gastric ulcers, and adjuvant therapy for Helicobacter pylori eradication. The company thinks it needs to evaluate ethnic differences between Japanese and Korean people to use South Korean data when filing for approval in Japan.

5-HT4 partial agonist (RQ-00000010)

This compound is under development for target indications of gastrointestinal dysmotility including gastroparesis, functional dyspepsia, and chronic constipation. Phase I clinical trials in the UK of healthy individuals and patients have been completed. In addition to moving forward with out-licensing activities, the company is looking into the next stage of development, Phase II clinical trials.

Ghrelin receptor agonist (RQ-00433412)

The compound is under development for the target indication of cancer-related anorexia and cachexia syndrome and constipation resulting from spinal cord injury. The company originated the compound after its establishment. The manufacturing of APIs for preclinical study has been completed, and an outsourced preclinical study began in Q4 FY12/21. The company initially planned to out-license worldwide rights in 2024 after completing preclinical studies by end-FY12/23. As of end-FY12/24, the studies were nearly complete, having taken longer than expected. The company is awaiting final reports from part of the studies. It has already manufactured APIs for clinical trials and is prepared to initiate subsequent clinical studies. The company remains committed to concluding a license-out agreement before the start of clinical trials.

Cancer cachexia is a complication seen in about 50% of patients with advanced cancer at the time of initial diagnosis and 80% at the terminal stage. The main symptoms are weight loss, skeletal muscle loss, and anorexia. It calls for aggressive treatment because it can weaken the effect of chemotherapy, exacerbate side-effects, interrupt treatment, and ultimately impact survival rates. The ghrelin receptor agonist works on the hypothalamus to increase appetite, stimulate the release of growth hormone from the pituitary gland, and increase muscle mass and body weight. Many spinal cord injury patients live with defecation disorders due to autonomic neuropathy. Conventional laxatives may cause diarrhea, so the healthcare community is calling for easier-to-use drugs to promote defecation. The ghrelin receptor acts directly on the sacral spinal defecation center to promote colonic motility and voluntary defecation.

TRPM8 (RQ-00434739)

TRPM8 is a temperature-sensitive ion channel activated by cold stimuli under 28°C or menthol (mint) and its involvement has been suggested in a variety of chronic disorders, including chronic pain. The company discovered a selective TRPM8 blocker (azaspiro derivative) that demonstrated a different mechanism of action in animal models of chronic pain and cystitis than existing drugs, and hopes it will be a breakthrough new drug in the pain and urological disease fields. RaQualia entered an agreement with Hong Kong-based Xgene, granting it exclusive global (excluding Japan) development, manufacturing, and marketing rights for its TRPM8 blocker in September 2021 (see TRPM8 blocker in the out-licensed pipeline (human) section). The company still holds the rights in Japan.

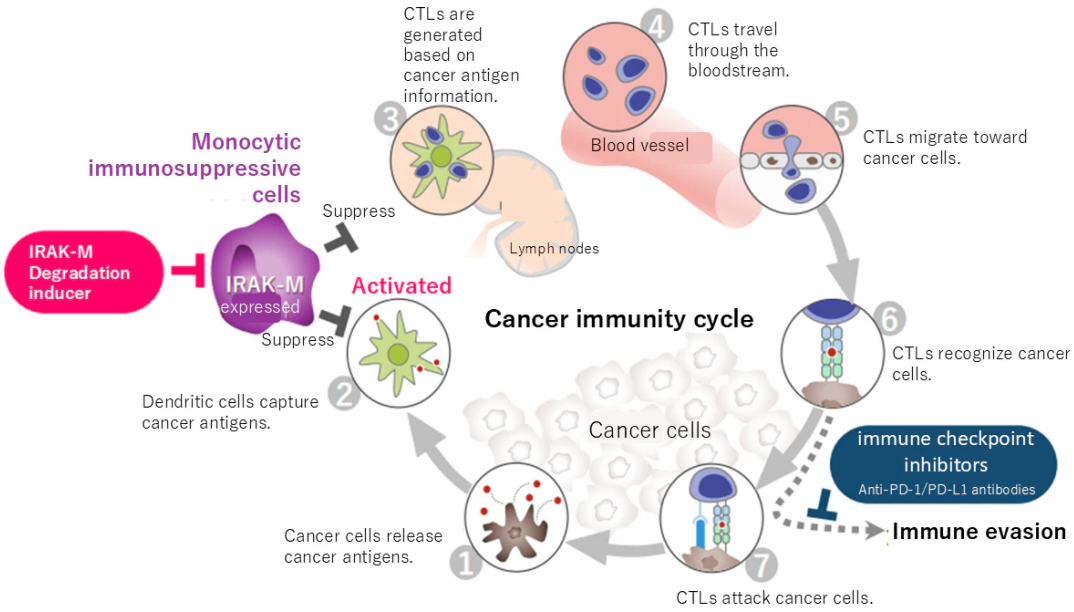
Motilin receptor agonist (RQ-00201894)

The compound is under development for the target indication of gastrointestinal dysmotility including gastroparesis, functional dyspepsia, and post-operative ileus, and the preclinical studies required for Phase I clinical trials have been completed. In addition to moving forward with licensing activities, the company is considering conducting Phase I clinical trials, the next development phase.

IRAK-M degradation inducer (FIM-001)

A targeted protein degradation inducer developed by FIMECS, FIM-001 serves as a caner immunotherapy that operates by degrading IRAK-M to disrupt immunosuppressive mechanisms. It inhibits a novel systemic immunosuppressive mechanism through a pathway distinct from that of immune checkpoint inhibitors (see below). For this reason, the company believes the investigational drug may help overcome resistance (a condition in which the drug becomes ineffective due to mutations in the drug's target protein) to immune checkpoint inhibitors. Preclinical studies and out-licensing activities are ongoing for the primary target indications of non-small cell lung cancer and pancreatic cancer.

Target and mechanism of action of IRAK-M degradation-inducing agents



Source: The company materials.

Exploratory and discovery phase pipeline

As of the beginning of FY12/25, the company had 11 discovery-stage programs, focusing on oncology and neurological disorders through novel modalities such as TPDs.

Beginning of 2024: nine programs	Small molecule compound	TPD	Other new modalities	Total
Cancer	0	0	1	1
Neurology	4	0	1	5
Ocular diseases	2	0	0	2
Other diseases	1	0	0	1
Beginning of 2025: 11 programs	**Small molecule compound**	**TPD**	**Other new modalities**	**Total**
Cancer	0	4	1	5
Neurology	2	0	2	4
Ocular diseases	2	0	0	2
Other diseases	0	0	0	0

Source: Shared Research based on company data

Drug discovery research targeting specific ion channel

The company has been conducting joint research with ASKA Pharmaceutical Co., Ltd. (unlisted; subsidiary of ASKA Pharmaceutical Holdings Co., Ltd. [TSE Prime: 4886]) since July 2019, with the goal of developing new drugs targeting specific ion channels (main indication undisclosed). After extensive discussions on the future development based on the results achieved to date, the two companies have agreed to terminate the joint research agreement in June 2023. Upon termination of the agreement, the research results of the joint research will belong to RaQualia and the company will continue to develop new drugs independently.

RaQualia is also conducting joint research with Gifu Pharmaceutical University for the main indication of retinal vein occlusion (details not disclosed). By constantly conducting seven to ten programs in exploratory and discovery phases, the company thinks it will be able to continue to create groundbreaking development compounds.

Market and value chain

Global drug market

According to US-based IQVIA Holding Inc. (NYSE: IQV), global prescription drug sales in 2023 totaled USD1.6tn (JPY239.9tn, converted at JPY150.0/USD). It forecasts global market growth of USD2.3tn (JPY345tn) in 2028, with a five-year CAGR of 5–8%. In Japan, prescription drug sales totaled USD72.3bn (JPY10.8tn) in 2023, reflecting a five-year CAGR of -3.0%.

Global drug sales

(USDbn)	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	5-year CAGR
US	389.4	430.6	455.4	464.7	492.8	521.0	544.6	588.9	645.9	727.4	8.1%
YoY	13.6%	10.6%	5.8%	2.0%	6.0%	5.7%	4.5%	8.1%	9.7%	12.6%	
Japan	85.4	78.8	89.1	84.8	84.2	87.9	87.4	86.7	74.8	72.3	-3.0%
YoY	-5.8%	-7.7%	13.1%	-4.8%	-0.7%	4.4%	-0.6%	-0.8%	-13.7%	-3.3%	
China	111.4	120.5	122.6	127.7	136.7	150.5	148.5	171.4	162.8	160.8	3.3%
YoY	14.5%	8.2%	1.7%	4.2%	7.0%	10.1%	-1.3%	15.4%	-5.0%	-1.2%	
Europe	266.2	238.5	244.5	258.5	273.7	281.8	298.4	334.7	327.9	360.1	5.6%
YoY	3.1%	-10.4%	2.5%	5.7%	5.9%	3.0%	5.9%	12.2%	-2.0%	9.8%	
Latin America	65.1	74.7	86.9	97.9	59.8	60.5	56.3	68.7	76.5	83.5	6.9%
YoY	-10.2%	14.7%	16.3%	12.7%	-38.9%	1.2%	-6.9%	22.0%	11.4%	9.2%	
Other	138.4	160.9	142.8	145.7	156.0	163.3	164.9	188.8	192.1	195.5	4.6%
YoY	4.5%	16.3%	-11.2%	2.0%	7.1%	4.7%	1.0%	14.5%	1.7%	1.8%	
Worldwide	1,055.9	1,104.0	1,141.3	1,179.3	1,203.2	1,265.0	1,300.1	1,439.2	1,480.0	1,599.6	5.9%
YoY	6.2%	4.6%	3.4%	3.3%	2.0%	5.1%	2.8%	10.7%	2.8%	8.1%	

Source: Shared Research based on Japan Pharmaceutical Manufacturers Association (JPMA) DATA BOOK 2025 (data sourced from IQVIA World Review)
Note: 5-year CAGR s are five years to 2023

According to the Ministry of Health, Labour and Welfare's 2023 Pharmaceutical Production Statistics, the domestic pharmaceutical market rose 2.7% YoY to JPY13.1tn (excluding foreign exchange effects), while domestic prescription drug shipments increased 4.5% YoY to JPY12.4tn. The domestic pharmaceutical market has returned to growth in recent years, supported by increased vaccine imports in response to the COVID-19 pandemic. This recovery occurred despite a prior downturn driven by annual NHI drug price revisions introduced in 2018 and the promotion of lower-cost generics aimed at curbing rising public healthcare expenditures resulting from Japan's aging population.

Pharmaceutical market in Japan

(JPYbn)	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	5-year CAGR
Pharmaceutical market in Japan	9,652.1	10,616.7	10,393.6	9,992.7	9,866.6	11,787.4	11,629.4	11,650.9	12,747.7	13,092.8	5.8%
YoY	-1.9%	10.0%	-2.1%	-3.9%	-1.3%	19.5%	-1.3%	0.2%	9.4%	2.7%	

Source: Shared Research based on Statistics of Production by Pharmaceutical Industry, Ministry of Health, Labour and Welfare
* Pharmaceutical market size = domestic production value - export value + import value

(JPYbn)	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Drug											
Domestic production	6,894	6,590	6,748	6,624	6,721	6,908	9,486	9,305	9,180	9,982	10,033
YoY	-1.2%	-4.4%	2.4%	-1.8%	1.5%	2.8%	37.3%	-1.9%	-1.3%	8.7%	0.5%
Import	3,077	3,188	4,022	3,945	3,438	3,148	2,753	2,853	3,093	3,414	3,773
Export	130	126	154	176	167	189	443	513	563	649	713
Internal shipping							11,224	10,897	11,203	11,823	12,360
YoY								-2.9%	2.8%	5.5%	4.5%
Medical devices											
Domestic production	1,905	1,989	1,946	1,915	1,990	1,949	2,568	2,426	2,602	2,583	2,675
YoY	0.5%	4.4%	-2.2%	-1.6%	4.0%	-2.1%	31.8%	-5.5%	7.2%	-0.7%	3.6%
Import	1,301	1,369	1,425	1,556	1,650	1,620	2,723	2,637	2,815	2,918	3,322
Export	530	572	623	584	619	668	1,009	991	1,003	1,094	1,126
Internal shipping							3,986	3,935	4,233	4,186	4,549
YoY								-1.3%	7.6%	-1.1%	8.7%
Quasi-drug											
Domestic production	925	923	922	947	951	1,000	1,343	1,405	1,400	1,407	1,425
YoY	15.6%	-0.2%	-0.2%	2.7%	0.5%	5.1%	34.4%	4.6%	-0.4%	0.5%	1.3%
Regenerative medicine											
Domestic production							6	6	7	7	11
YoY								0.0%	25.5%	-2.9%	58.2%

Source: Shared Research based on Statistics of Production by Pharmaceutical Industry, Ministry of Health, Labour and Welfare

Peptic ulcer drug market

Global Industry Analysts, Inc. forecasts that the market for peptic ulcer drugs will grow at a CAGR of 2.6% from USD4.9bn (JPY0.7tn converted at JPY150.0/USD) in 2020 to USD5.9bn (JPY0.9tn) in 2027. It projects the market for PPIs that suppress gastric acid secretions to reach USD4.2bn (JPY0.6tn, CAGR of 2.5%) in 2027.

Potential market of main target diseases

Disease	Number of patients	Market size	Region	Existing therapies	RaQualia's development pipeline
GERD	58mn (US), 17mn (Japan)	JPY2tn JPY450bn JPY250bn	Worldwide US Japan	H2RA, PPI, vonoprazan	Tegoprazan
Pain	50mn (US), 23mn (Japan)	JPY2.4tn JPY300bn	Worldwide Japan	Pregabalin, duloxetine, celecoxib, etc.	EP4 receptor antagonist , COX-2 inhibitor, TRPM8 blocker, P2X7 receptor antagonist, sodium channel blocker
Cancer immunity	Approx. 12% of cancer patients respond to cancer immunotherapy	JPY10tn	Worldwide	Nivolumab, pembrolizumab, etc.	EP4 antagonist
Chronic constipation	42mn (US)	JPY660bn JPY60bn	Worldwide Japan	Linaclotide, lubiprostone, etc.	5-HT_4 partial agonist
Gastroparesis	80,000-400,000	JPY200bn	Worldwide	Metoclopramide, etc.	5-HT_4 partial agonist, motilin receptor agonist
Irritable bowel syndrome	5-20% of Japanese/Western adults	JPY100bn	Worldwide	Rifaximin, ramosetron, etc.	5-HT_{2B} agonist
Cancer cachexia	Over 20% of cancer patients develop cachexia	JPY200bn	Worldwide	Anamorelin	Ghrelin receptor agonist
Constipation associated with spinal cord injury	300mn	Over JPY20bn	Worldwide	Laxatives	Ghrelin receptor agonist
Myelodysplastic syndrome	60,000-170,000 (US), 20,000 new cases annually (US, Europe)	JPY100bn	Worldwide	Azacitidine, etc.	Tamibarotene
Acute myeloid leukemia	160,000 (worldwide), 25,000 new cases annually (US, Europe), 7,000 (Japan)	JPY1tn	Worldwide	Azacitidine, venetoclax, etc.	Tamibarotene

Source: Shared Research based on company data

Japanese drug market

According to IQVIA, prescription drug sales in Japan in 2024 reached JPY11.5tn (+2.0% YoY), the tenth consecutive year above JPY10tn. Sales of antacids, flatulence agents, and ulcer agents were not disclosed as the product did not rank among the top 10 therapeutic categories. Sales of Takeda's antiulcer drug TAKECAB® were JPY120.1bn (+3.9% YoY), the fourth highest among domestic drugs.

Prescription drug sales in Japan

(JPYmn)	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Prescription drug sales in Japan	6,455,972	6,698,087	6,775,152	7,056,186	7,203,310	7,745,509	7,696,972	8,047,859	8,254,290	8,851,647
YoY	0.0%	3.8%	1.2%	4.1%	2.1%	7.5%	-0.6%	4.6%	2.6%	7.2%
Antacids, flatulence/ulcer agents	391,242	400,632	383,713	392,301	395,660	418,112	408,593	422,148	427,027	446,651
YoY	-1.0%	2.4%	-4.2%	2.2%	0.9%	5.7%	-2.3%	3.3%	1.2%	4.6%
	2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
Prescription drug sales in Japan	8,873,623	9,481,578	9,547,314	9,846,641	9,983,426	10,597,934	10,623,980	10,514,878	10,337,471	10,625,631
YoY	0.2%	6.9%	0.7%	3.1%	1.4%	6.2%	0.2%	-1.0%	-1.7%	2.8%
Antacids, flatulence/ulcer agents	429,890	434,997	408,604	418,289	397,394	389,788	376,365	377,550	349,783	351,329
YoY	-3.8%	1.2%	-6.1%	2.4%	-5.0%	-1.9%	-3.4%	0.3%	-7.4%	0.4%
	2020	**2021**	**2022**	**2023**	**2024**					
Prescription drug sales in Japan	10,371,733	10,599,031	10,939,481	11,280,631	11,503,713					
YoY	-2.4%	2.2%	3.2%	3.1%	2.0%					
Antacids, flatulence/ulcer agents	347,142	351,640	331,675	278,425	-					
YoY	-1.2%	1.3%	-5.7%	-16.1%	-					

Source: Shared Research based on IQVIA data

Note: Figures may differ from company materials due to differences in rounding methods.

Impact of Japan's NHI drug price revisions

The Ministry of Health, Labour and Welfare (MHLW) sets uniform nationwide prices (NHI prices) for human drugs. The price of a newly developed drug is based on a comparison with drugs already in use with similar efficacy (comparable drug method). If the new drug is more effective or novel, a premium is added, boosting the price. If there is no comparable drug with similar efficacy, the price is based on costs such as raw materials and manufacturing (cost accounting method).

However, the distribution process involves free price competition. Medical institutions and insurance pharmacies charge drug costs based on NHI prices, but the prices of drugs sold from drug companies to wholesalers and wholesalers to medical institutions and insurance pharmacies are freely set wholesale prices, resulting in differences from the NHI price (i.e., drug-price margins). To reduce the insurance benefit burden, the MHLW surveys sales prices and volumes for each individual drug, and revises (lowers) prices based on its findings every year (every second year until April 2018). Expensive drugs are covered by public insurance and are thought to have a significant impact on the insurance budget, leading to this arrangement for stepwise reductions. On the five occasions leading up to the April 2024 price revisions, the price was cut by 1.18% on a medical fee basis and reduced and by 5.51% on a drug fee basis on average.

Japan's arrangements to set NHI drug prices make it difficult for pharmaceutical companies to generate expected profits after launching drugs following extended periods of development and massive investments. The April 2022 drug price revisions featured a cut of 1.35% on a medical fee basis and a cut of 6.69% on a drug fee basis. This acted to shrink the domestic drug market by over JPY600bn in FY2022.

According to an August 2022 survey by MHLW, there were shortages, suspended shipments, or limited shipments for 28.2% of drugs overall and 41.0% of generic drugs due to a sharp rise in demand during the pandemic and steep cost increases due to the Russia-Ukraine war and yen weakness. As a consequence, in the off-year price revisions for FY2023, the ministry took limited extraordinary measures to reassess unprofitable products, resulting in price hikes to 1,100 relevant items. In the FY2023 revisions, prices were cut for 48% of all listed drugs (9,300) items, maintained for 46% (9,000), and raised for 6% (1,100).

The April 2024 NHI drug price revision called for cuts of 0.97% on a medical fee basis and 4.67% on a drug fee basis, with the expectation of a JPY120.0bn reduction in healthcare spending. The 2024 price revision reviewed the drug reimbursement price system to resolve the issue of drug lag and loss and ensure a stable supply. It overhauled the Drug Price Standard, including the way drugs are evaluated for early adoption in Japan and the way premiums such as innovation premium, value premium (for usefulness), pediatric premium (to encourage development of pediatric drugs), and repricing for market expansion are calculated by doing away with corporate indicators and increasing the number of items for evaluation. To ensure stable supply, price revisions reflected the reassessment of unprofitable products and the evaluation of the supply system for generic drugs.

The 2025 NHI drug price revision, the third interim-year revision, differs from the previous two in that price adjustments were determined by drug category. In earlier revisions, all products with a price divergence exceeding 0.625× the average were uniformly subject to revision. The 2025 revision classifies drugs into five categories: products eligible for the premium to promote the creation of new drugs, new drugs not eligible for the premium, long-listed products, generic drugs, and others. Pricing adjustments were relaxed for all categories except long-listed products, for which the scope of revision was expanded. A total of 9,320 products, accounting for 53% of all listed drugs, were subject to revision, with projected medical cost savings of JPY246.6bn. However, due to the reduced number of applicable products and a narrower divergence rate, the overall cost reduction is expected to be smaller than in the previous two interim-year revisions.

NHI price revisions and average deviation

	1994	1996	1998	2000	2002	2004	2006	2008	2010
NHI price revisions (drug fee basis)	-6.6%	-4.4%	-9.7%	-7.0%	-6.3%	-4.2%	-6.7%	-5.2%	-5.75%
NHI price revisions (medical fee basis)	-2.0%	-1.3%	-2.7%	-1.6%	-1.3%	-0.9%	-1.6%	-1.1%	-1.23%
Average deviation	17.8%	13.1%	9.5%	7.1%	6.3%	8.0%	6.9%	8.4%	8.4%
	2012	2014	2016	2018	2019	2020	2022	2024	
NHI price revisions (drug fee basis)	-6.00%	-5.64%	-5.57%	-7.48%	-4.35%	-4.38%	-6.69%	-4.67%	
NHI price revisions (medical fee basis)	-1.26%	-1.22%	-1.22%	-1.65%	-0.93%	-0.99%	-1.35%	-0.97%	
Average deviation	8.2%	8.8%	9.1%	7.2%	8.0%	8.0%	7.0%	5.2%	

Source: Shared Research based on MHLW "NHI drug price revisions"

* The average differential between the NHI drug price and prevailing market price was around 6.0%.

Global pet drug market

Global Market Insights Research Inc. (unlisted) estimates the global pet drug market at USD43.3bn (JPY6.5tn, at JPY150/USD) in 2024 and USD46.3bn (JPY6.9tn) in 2025, and forecasts it will reach USD78.9bn (JPY11.8tn) by 2032, with a CAGR of approximately 6.1%. The market continues to expand as pets are increasing (estimated at 522mn dogs and 445mn cats) due to growth in emerging economies and a burgeoning middle class. Although the market for pet drugs is smaller than that of human pharmaceuticals, the company can maintain or increase prices more easily in the absence of regulated drug prices in Japan and elsewhere.

Number of pet dogs and cats (in thousands)

Number of pet dogs			Number of pet cats	
US	69,929	1	US	74,059
China	27,400	2	China	53,100
Russia	12,520	3	Russia	17,800
Japan	12,000	4	Brazil	12,466
Philippines	11,600	5	France	11,480
India	10,200	6	Germany	8,200
Argentina	9,200	7	UK	8,000
UK	9,000	8	Italy	7,400
France	7,570	9	Ukraine	7,350
South Africa	7,400	10	Japan	7,300

Source: Shared Research based on The Hollard Insurance Company Pty Ltd., A Guide to Worldwide Pet Ownership

Changes to drug discovery modalities

Traditionally, small molecule compounds accounted for the bulk of drug discovery in the pharmaceutical industry, but starting in the 1990s, biopharmaceuticals (made from antibodies, enzymes, hormones, and other substances) produced using biotechnology started being approved. Currently modalities span a diverse range including middle molecule drugs, antibody drugs, nucleic acid drugs, gene therapies, and regenerative medicine.

Difference between small molecule drugs and biopharmaceuticals

Small molecule drugs have a molecular weight of under 500 Daltons, stable chemical structures, and are produced by chemical synthesis. Manufacturing and development costs are comparatively low, and there is a wide variety of dosage forms, not just tablets. Biopharmaceuticals have large molecular weights ranging from several thousand to 150,000 Daltons, complex structures, and are nonuniform. They are made from cells and microorganisms, and manufacturing and development costs are much higher than small molecule drugs. Because they are proteins that are broken down by digestive enzymes if taken orally, they are mainly administered by injection.

Biopharmaceuticals are made within cells using genetic recombination technology. The manufacturing process is extremely complicated, and slight variations in temperature, oxygen concentration, agitation speed, and cell density can affect the quality. Establishing manufacturing methods requires advanced technology and significant costs. While chemically synthesized small molecule drugs entail about 50 in-process tests, biopharmaceuticals require about 250. In some cases, culture methods have not been established for biopharmaceuticals, and in other cases, overseas companies may hold the patents even if the culture method has been established, and Japan has a lack of specialists. Regulators demand compliance with exacting quality control standards (good manufacturing practice or GMP) and stipulated standards, to constantly maintain the safety and efficacy of products during mass production.

Characteristics of small molecule drugs, medium molecule drugs, and biopharmaceuticals

Type of drug		Small molecule drugs	Medium molecule drugs, biopharmaceuticals		
			Peptide	Nucleic acid	Antibody
Shape (image)					
Molecular weight		100–500	100–10,000	Up to 10,000	About 100,000 or more
Manufacturing method		Chemical synthesis	Chemical synthesis/culture	Chemical synthesis/culture	Culture
Target molecule	Protein	○	○		○
	Nucleic acid (DNA/RNA)	○		○	○
Target molecule location	Intracellular	○	○	○	
	Extracellular	○	○	○	○
Administration route	Oral	○			
	Other	○	○	○	○

Source: Shared Research based on company data

The advantage of biopharmaceuticals is their ability to target molecules that are difficult for small molecule drugs, but their disadvantage is that they are difficult to administer orally. The share of small molecule drugs in FDA approvals was 64.0% in 2024, and remained the most common.

Number of approvals by FDA (US)

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
New Molecular Entities (NMEs)	28	47	34	25	33	25	19	11	15	31	18	18	16	21	20
% of total	96.6%	88.7%	87.2%	83.3%	94.3%	92.6%	79.2%	64.7%	71.4%	86.1%	90.0%	81.8%	88.9%	87.5%	76.9%
Biologics License Applications (BLAs)	1	6	5	5	2	2	5	6	6	5	2	4	2	3	6
% of total	3.4%	11.3%	12.8%	16.7%	5.7%	7.4%	20.8%	35.3%	28.6%	13.9%	10.0%	18.2%	11.1%	12.5%	23.1%
	2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
New Molecular Entities (NMEs)	15	24	33	25	30	33	15	34	42	38	40	36	22	34	32
% of total	71.4%	80.0%	84.6%	92.6%	73.2%	73.3%	68.2%	73.9%	71.2%	79.2%	75.5%	72.0%	59.5%	61.8%	64.0%
Biologics License Applications (BLAs)	6	6	6	2	11	12	7	12	17	10	13	14	15	21	18
% of total	28.6%	20.0%	15.4%	7.4%	26.8%	26.7%	31.8%	26.1%	28.8%	20.8%	24.5%	28.0%	40.5%	38.2%	36.0%

Source: Shared Research based on company data

Note: New Molecular Entities (NMEs) are drugs containing new active ingredients and refer to small molecule drugs. Biologics License Applications (BLAs) are for new biopharmaceuticals

Competition

The Ministry of Economy Trade and Industry (METI) categorizes biotech start-ups into three broad groups. RaQualia can be classified as a "pipeline-type" as it is involved in the exploratory research, preclinical study, and early clinical trial stages. It looks for seed compounds in the fields of pain and gastrointestinal diseases and its development pipeline is based on its core ion channel drug discovery technology.

Types of biotech start-up business model

Business model		Japanese company example
Drug discovery platform technology-type (platform-type)	Has technology to create drug discovery seeds, which it out-licenses	PeptiDream, Carna Biosciences
Drug discovery pipeline-type (pipeline-type)	Integrated from seed exploration through in-house development and sales	NanoCarrier, RaQualia
Pipeline acquisition-type (In-licensing-type)	Acquires promising pipeline drugs through corporate acquisitions or in-licensing	Sosei Group, Solasia Pharma

Source: Shared Research based on Ministry of Economy, Trade and Industry, 2017, "Business models and financing activities of biotech startups" and company data
Note: The drug discovery pipeline model employs a variety of strategies, such as partial out-licensing for particular indications and selling territories, and development and sales through alliances.

Latest full-year results from biotech start-ups

Stock code	Company	Latest full-year results			Key characteristics
		Revenue (JPYmn)	Operating profit margin (%)	ROE (%)	
4579	RaQualia	3,108	-6.9%	-8.5%	Predecessor was Pfizer's central research laboratory in Japan. Business focuses on revenue from out-licensing new development compounds. Expanding from pain and gastrointestinal diseases to include neurological diseases.
2160	GNI Group	23,612	5.9%	3.1%	Vertically integrated company based in China, involved in drug discovery, clinical development, and manufacturing through sales. Has a leading share in idiopathic pulmonary fibrosis drugs in China. Has R&D locations in US and China.
4565	Nxera Pharma (former Sosei Group)	28,835	-18.8%	-7.2%	A biotech start-up engaged in membrane protein GPCR-targeted drug discovery. The mainstay of its business is a UK acquisition, Heptares. Acquired the pharmaceutical business in Japan and the Asia-Pacific region (excluding China) from Switzerland-based Idorsia and will also conduct late-stage clinical trials and commercialization.
4571	NANO MRNA (former NanoCarrier)	136	-637.9%	-20.4%	Biotech start-up focused on oncology. Aims at new drugs with few adverse reactions using its ultrafine micellar nanoparticle technology.
4572	Carna Biosciences	636	-326.3%	-68.6%	Revenue stable. Sells kinase proteins and provides early stage drug discovery support services such as screening under contract. Also engaged in drug discovery using BTK inhibitors.
4582	SymBio	2,453	-158.1%	-70.9%	Main focus on oncology, hematology, and rare diseases. In-licenses drug candidate compounds which it develops and commercializes.
4587	PeptiDream	46,677	45.2%	30.9%	Biopharmaceutical company using proprietary Peptide Discovery Platform System to produce specialty peptide drug candidates, which it creates with major drug companies and licenses technology for. Many alliances with major overseas drug companies. Moved into radiopharmaceuticals by M&A.
4597	Solasia Pharma	316	-615.7%	-128.1%	Biotech venture that in-licenses development rights for candidate substances and uses in clinical development, focusing on cancer. Re-out-licenses drug candidates it has in-licensed and developed, and sells pharmaceutical products. Fabless operations. Outsources manufacturing to overseas companies.
4883	Modalis	0	-	-54.0%	Biotech start-up that creates therapeutic drugs for rare genetic disorders through drug discovery using unique non-cleaving genome editing technology. Has research base in US.

Source: Shared Research based on company data

(JPYmn)	RaQualia (4579)			GNI group (2160)			Nxera Pharma (4565)		
	FY12/22 Cons.	FY12/23 Cons.	FY12/24 Cons.	FY12/22 IFRS, Cons.	FY12/23 IFRS, Cons.	FY12/24 IFRS, Cons.	FY12/22 IFRS, Cons.	FY12/23 IFRS, Cons.	FY12/24 IFRS, Cons.
Revenue	2,918	1,901	3,108	17,419	26,011	23,612	15,569	12,766	28,835
Gross profit	2,686	1,670	2,482	14,745	22,431	18,037	14,643	9,664	21,219
R&D expenses	1,249	1,373	1,704	2,545	2,558	2,812	7,454	10,075	11,816
SG&A expenses (excluding R&A expense)	572	621	991	10,966	15,293	15,772	4,377	9,965	16,015
Operating profit	866	-337	-213	1,378	13,109	1,402	3,436	-9,526	-5,423
Pre-tax recurring profit	904	-293	-362	768	12,613	238	645	-10,680	-4,662
Net income	723	-324	-495	-868	9,504	-10	382	-7,193	-4,838
ROE	14.1%	-5.6%	-8.5%	2.0%	29.6%	3.1%	0.7%	-11.5%	-7.2%
ROA (RP-based)	15.7%	-4.5%	-4.4%	2.4%	26.2%	0.4%	1.1%	-8.3%	-3.0%
Operating profit margin	29.7%	-17.7%	-6.9%	7.9%	50.4%	5.9%	22.1%	-74.6%	-18.8%
Total assets	6,258	6,872	9,655	33,907	63,394	71,943	99,417	157,198	151,498
Net assets	5,497	6,120	5,571	19,811	36,053	39,714	57,936	66,810	68,518
Equity ratio	87.7%	88.7%	57.4%	61.8%	54.2%	50.7%	58.3%	42.5%	45.2%
Operating CF	1,480	-719	181	393	6,549	-3,164	9,952	-5,273	-7,718
Investing CF	-48	-135	-3,666	-4,116	-9,843	-10,361	1,043	-63,791	-4,763
Financial CF	-30	793	2,982	-646	10,687	694	-4,887	48,329	-6,854
Cash and deposits	3,675	3,715	3,340	11,049	21,633	10,115	66,557	49,065	32,268
Interest-bearing debt	222	368	3,452	537	3,699	7,206	1,753	73,973	67,900
Net debt	-3,453	-3,347	112	-10,512	-17,934	-2,909	-64,804	24,908	35,632
	NANO MRNA (4571)			Carna Biosciences (4572)			SymBio (4582)		
	FY03/22 Cons.	FY03/23 Cons.	FY03/24 Cons.	FY12/22 Cons.	FY12/23 Cons.	FY12/24 Cons.	FY12/22 Cons.	FY12/23 Cons.	FY12/24 Cons.
Revenue	264	202	136	1,387	1,626	636	10,008	5,590	2,453
Gross profit	223	160	111	1,215	1,451	466	7,600	4,411	1,873
R&D expenses	1,924	1,121	647	1,882	1,903	1,886	2,555	2,638	3,379
SG&A expenses(excluding R&A expense)	360	285	328	2,485	2,568	2,542	5,636	5,223	2,371
Operating profit	-2,061	-1,246	-864	-1,270	-1,117	-2,076	1,964	-812	-3,877
Pre-tax recurring profit	-1,925	-1,105	-750	-1,279	-1,126	-2,081	2,000	-736	-3,690
Net income	-1,882	-1,311	-780	-1,350	-1,153	-2,179	1,179	-1,963	-3,833
ROE	-29.1%	-27.0%	-20.4%	-34.0%	-30.7%	-68.6%	14.6%	-26.1%	-70.9%
ROA (RP-based)	-25.7%	-17.0%	-13.8%	-26.4%	-26.1%	-58.4%	19.2%	-7.9%	-56.2%

Operating profit margin	-780.6%	-616.3%	-637.9%	-91.6%	-68.7%	-326.3%	19.6%	-14.5%	-158.1%
Total assets	7,136	5,784	5,071	4,266	4,350	2,772	10,433	8,170	4,968
Net assets	5,567	4,253	3,421	3,642	3,878	2,475	8,506	7,210	4,198
Equity ratio	77.6%	73.5%	67.2%	85.0%	89.1%	89.3%	77.6%	84.9%	78.1%
Operating CF	-1,753	-1,087	-585	-708	-1,677	-1,375	1,614	-195	-3,417
Investing CF	-244	1,208	793	-126	-11	-13	-47	-377	-4
Financial CF	1,146	0	4	367	1,182	567	628	680	708
Cash and deposits	3,545	2,812	2,078	3,379	2,889	2,108	6,283	6,517	3,964
Interest-bearing debt	1,150	0	0	300	183	61	0	0	0
Net debt	-2,395	-2,812	-2,078	-3,079	-2,706	-2,047	-6,283	-6,517	-3,964
	PeptiDream (4587)			Solasia Pharma (4597)			Modalis (4883)		
	FY12/22	FY12/23	FY12/24	FY12/22	FY12/23	FY12/24	FY12/22	FY12/23	FY12/24
	IFRS, Cons.	IFRS, Cons.	IFRS, Cons.	IFRS, Cons.	IFRS, Cons.	IFRS, Cons.	Cons.	Cons.	Cons.
Revenue	26,852	28,712	46,677	1,092	617	316	41	0	0
Gross profit	18,113	17,218	34,504	662	337	185	-	-	-
R&D expenses	2,915	3,155	4,003	883	403	414	1,862	2,103	1,092
SG&A expenses (excluding R&A expense)	6,218	7,256	9,110	2,250	1,073	1,721	242	268	245
Operating profit	8,980	6,773	21,114	-2,470	-1,139	-1,951	-2,063	-2,371	-1,338
Pre-tax recurring profit	6,653	4,353	20,889	-2,492	-1,135	-1,961	-1,996	-2,352	-1,303
Net income	7,554	3,036	15,015	-2,548	-1,112	-1,941	-2,703	-2,392	-1,318
ROE	26.3%	8.4%	30.9%	-97.1%	-49.0%	-128.1%	-63.8%	-111.9%	-54.0%
ROA (RP-based)	14.6%	6.5%	25.8%	-79.4%	-42.3%	-109.2%	-43.4%	-91.2%	-45.6%
Operating profit margin	33.4%	23.6%	45.2%	-226.1%	-184.6%	-615.7%	-5094.3%	-	-
Total assets	63,865	69,464	92,770	3,134	2,229	1,362	3,130	2,026	3,692
Net assets	32,041	40,350	56,762	2,662	1,875	1,156	2,941	1,380	3,548
Equity ratio	50.2%	58.1%	61.2%	84.9%	84.1%	84.9%	93.4%	66.8%	95.5%
Operating CF	-83	12,421	23,845	-2,074	-359	-1,033	-1,896	-2,254	-1,432
Investing CF	-27,377	1,303	8,371	-418	0	0	-186	-40	-188
Financial CF	20,789	264	-2,995	2,571	275	1,180	64	1,216	3,045
Cash and deposits	5,248	19,508	48,118	803	728	886	2,933	1,883	3,575
Interest-bearing debt	21,048	22,221	20,154	37	33	25	0	413	0
Net debt	15,801	2,713	-27,964	-766	-695	-861	-2,933	-1,471	-3,575

Source: Shared Research based on company data

Note: Figures may differ from company materials due to differences in rounding methods. Pre-tax profit for companies that use IFRS is shown as recurring profit.

Strengths and weaknesses

Strengths

Focus on ion channel drug discovery based on research processes and operating procedures on par with pharmaceutical companies

The company took over drug discovery R&D expertise and methodologies from its predecessor, Pfizer's central research laboratory in Japan, following an employee buyout, and carried on with its research programs. It is able to create numerous drug candidates from its compound library, which includes hundreds of thousands of compounds. Advanced technological capabilities based on pharmaceutical company standard research processes and operating procedures have enabled it to discover drugs targeting ion channels with the potential to treat a wide range of diseases. It has already out-licensed five ion channel projects at an early stage.

Ion channels are widely expressed in vital organs needed for life, such as the heart and brain. There are over 100 types. Blocking one ion channel affects the entire body by simultaneously blocking ion channels in a different location, selective blocking is required to avoid strong adverse reactions. Ion channel drug discovery is difficult as compound design expertise and systems enabling constant screening to evaluate compounds are necessary. As a result, drugs that target ion channels account for under 10% of all prescription drugs. According to the company, this is a niche territory with few companies operating in it, and RaQualia is the only company in the world to have out-licensed five drugs in the area.

The company has four products already commercialized by licensees, 10 pipelines (including those targeting ion channels) already out-licensed, and six at the pre-out-licensing stage. The value of biotech companies is generally considered to be the sum total of its pipelines. Shared Research thinks that RaQualia's corporate value is also backed by its alliances with major companies in Japan and overseas and joint research outcomes in both commercialized products and out-licensed projects, in addition to its ability to generate a series of candidate compounds.

Several hundred patents held

The company applies for basic patents (substance patents) and obtains rights in major countries around the world on an ongoing basis. It has several hundred patents (including peripheral patents) in various regions with different expiry dates (some effective until as late as 2040). After filing for a basic patent, the company aims to extend its life cycle of a compound it has created by seeking extensions and peripheral patents. Compound patents are effective for 20 years, and may be extended by up to five years, and peripheral patents (such as use patents and manufacturing process patents) can extend the exclusive period for a further 20 years. The company has extended patents that Pfizer originally applied for until the mid-2030s via extensions and peripheral patent applications.

Patent expirations are a matter of life and death for drug companies. Pfizer's major restructuring came about after its failure to develop a successor for its hyperlipidemia drug Lipitor® (which generated more than JPY1tn in revenue worldwide), despite investing JPY80bn. RaQualia's strategy aims to ensure revenue over the long term by delaying the launch of lower-priced generic drugs with the same ingredients and efficacy after the patent for a new drug has expired. In addition to obtaining strong patents with broad coverage, the timing of filing patent applications is important to avoid gaps. Some former Pfizer patent experts have come over to the company and are managing patent life cycles using pharmaceutical company expertise. This is a strength for the company.

Ability to efficiently identify candidate compounds from its massive compound library with SCARA robotic system

Many Japanese biotech startups find difficulty creating their next candidate compound seeds following establishment. RaQualia's ability to continuously create candidate compounds rests on its technology. The company screens compounds from its library of 800,000 on a daily basis using a robotics system called SCARA (Selective Compliance Assembly Robot Arm). It is able to evaluate 10,000 compounds a day using the system.

New compounds that will become the seeds of new drugs are synthesized by analyzing multidimensional data, with designs based on empirical rules and computational methods according to an efficient synthesis plan based on accumulated expertise. Synthetic samples (including impurities) synthesized by company chemists are delivered promptly to pharmacological evaluators in solution form with purity guaranteed through the company's CAP (Centralized Analysis & Purification) system, which automates the purification, weighing, dissolution, and dispensing processes. The company says that these technologies enhance the efficiency by roughly 10 times compared to chemists performing it manually, enabling it to supply 150 compounds per week.

All information concerning compounds is managed using two-dimensional barcodes in a database and used for structure-activity relationship (SAR) research. Barcode-controlled 384-hole plates conduct rapid, accurate pharmacological, safety, and metabolic studies. Results are promptly recorded in a database and reported to design and synthesis staff. This research cycle takes two weeks, which the company says is the fastest in the world.

Weaknesses

Drug discovery modality (methodology) relies on small molecule compounds

Small molecule drugs are generally less expensive to produce than biopharmaceuticals because they have a fixed chemical structural formula and are easy to mass-produce. Biopharmaceuticals have active ingredients derived from proteins, such as growth hormones, insulin, or antibodies, and are manufactured from cells, yeast, or bacteria. Their molecules are large and complex, and their properties and characteristics depend on the manufacturing process, boosting costs. Biopharmaceuticals launched as new drugs tend to be more expensive, and the market is also larger.

The company has an abundant development pipeline, with four products already commercialized, 10 pipelines (including those targeting ion channels) already out-licensed, and six at the pre-out-licensing stage. However, these are all small molecule drugs. The chances of launching a new drug are said to be one in 30,000, and developing a small molecule drug candidate compound takes about 72 months, and the market size in comparison to the time and cost involved is smaller than for biopharmaceuticals. The advantage of biopharmaceuticals is that they enable an approach to targets that are difficult for small molecule drugs, but the disadvantage is that they cannot be administered orally. The share of small molecule drugs in FDA approvals remained greater than that of biopharmaceuticals, at 64.0% of the total in 2024.

The company is pursuing small-molecule drug discovery alongside new modality-based approaches to create synergies between existing and emerging technologies. Under its medium-term management plan through FY12/27, it aims to strengthen the drug discovery value chain by expanding small-molecule capabilities and advancing new modality initiatives. These efforts include the subsidiarization of FIMECS and ongoing joint research with VIS and STAND. Shared Research surmises establishing the sophisticated platform technologies will take time, as the development, manufacturing processes, and quality control for biopharmaceuticals are difficult.

Lack of control over amount or timing of revenue, because milestone and royalty payments depend on development and earnings at licensees

The company's revenue comes from: 1) upfront payments received when a contract is signed; 2) milestone payments that depend on pipeline progress such as launching clinical trials; 3) research cooperation payments when conducting joint research, and 4) royalty payments received based on a percentage of sales from launched products. Upfront payments

depend on the licensee's assessment of the company's development products, and are decided by negotiation. Milestone payments are sometimes delayed due to stalled development at the licensee. Research cooperation payments are insignificant compared to other payments. Finally, because royalty payments are based on a certain percentage of licensees' sales, the company's revenue depends on their marketing and sales capabilities.

The company has traditionally aimed at out-licensing at the preclinical preparation stage, and many of the out-licensing deals to date have been in the early development stages. However, due to the low likelihood of market launch for pipeline drugs in the early development stage, there is a tendency for upfront, milestone, and royalty payment rates to be lower. For this reason, the new management team has decided to carry on development of new drug candidate compounds until the proof of concept (POC) stage, which confirms usefulness and efficacy of a new drug candidate compound under development through administration to an animal or human, in a bid to enhance the value of its future pipelines. Obtaining POC confirmation generally requires reaching Phase II, entailing an investment of JPY2.0–5.0bn in general, which will require more funding than previously. If expenditures do not match the timing of revenue received from licensees, the company may need to raise funds.

Difficulty in recruiting and training specialist researchers

The company mainly hires researchers with abundant R&D experience at pharmaceutical companies. From FY12/22 onward, it plans to recruit holders of doctorates in a bid to stand shoulder to shoulder with the world's top companies. However, researchers in biopharmacology have high levels of expertise, and focus on specific disease areas. The company will need to hire personnel with experience in researching neurological diseases professionally as it branches out from its traditional areas of pain and gastrointestinal diseases.

According to the Ministry of Education, Culture, Sports, Science and Technology data, students starting PhD programs (usually five years) at graduate schools peaked in FY2003 and continued to decline until the downward slide has reached a nadir in FY2015. The number has since increased slightly, reaching 15,000 (+0.9% YoY) in FY2018, of which 6,000 specialized in health (medicine, dentistry, pharmaceutical science, and health science). The number remained flat at 15,000 in FY2021 and 14,000 in FY2022, but the overall trend is downward. We also note bio-pharma drug discovery mostly takes place overseas and Japan has relatively few researchers. In the most recent fiscal year, the US has the largest number of PhD holders in this field (92,000), followed by China (66,000) and Germany (26,000), and numbers have doubled in South Korea, China, and the US since 2000. Shared Research concludes attracting personnel who fit the company's needs holds the key to its future growth.

Historical results and financial statements

Income statement

Income statement	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24
(JPYmn)	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.
Operating revenue	**146**	**705**	**1,419**	**745**	**1,703**	**1,107**	**2,776**	**2,918**	**1,901**	**3,108**
YoY	-5.5%	384.7%	101.2%	-47.5%	128.7%	-35.0%	150.7%	5.1%	-34.8%	63.5%
Gross profit	146	588	1,270	655	1,440	969	2,456	2,686	1,656	2,482
YoY	-3.9%	303.9%	116.1%	-48.4%	119.8%	-32.7%	153.3%	9.4%	-38.4%	49.9%
Gross profit margin	100.0%	83.3%	89.5%	88.0%	84.6%	87.5%	88.4%	92.1%	87.1%	79.9%
Operating expenses	**2,010**	**1,465**	**1,570**	**1,820**	**1,719**	**1,593**	**2,068**	**2,052**	**2,239**	**3,321**
YoY	-11.7%	-27.1%	7.1%	15.9%	-5.5%	-7.3%	29.8%	-0.8%	9.1%	48.4%
Cost of revenue	-	118	150	89	263	138	321	232	245	626
YoY	-	-	27.1%	-40.2%	193.9%	-47.5%	132.4%	-27.8%	5.8%	155.4%
R&D expenses	1,302	796	849	1,075	864	932	1,127	1,249	1,373	1,704
YoY	-12.0%	-38.9%	6.6%	26.6%	-19.6%	7.9%	20.9%	10.8%	9.9%	24.1%
R&D expense ratio	895.2%	112.9%	59.8%	144.3%	50.7%	84.2%	40.6%	42.8%	72.2%	54.8%
SG&A expenses	708	551	572	656	592	523	620	572	621	991
YoY	-10.9%	-22.1%	3.7%	14.7%	-9.7%	-11.6%	18.6%	-7.9%	8.6%	59.6%
SG&A ratio	486.4%	78.2%	40.3%	88.1%	34.8%	47.2%	22.3%	19.6%	32.7%	31.9%
Operating profit	**-1,865**	**-760**	**-150**	**-1,075**	**-16**	**-486**	**708**	**866**	**-337**	**-213**
YoY	-	-	-	-	-	-	-	22.4%	-	-
Operating profit margin	-	-	-	-	-	-	25.5%	29.7%	-	-
Non-operating income	99	94	85	45	49	35	177	77	88	68
Interest income	4	13	4	9	9	4	2	1	3	5
Interest on securities	78	52	35	32	35	28	21	13	7	3
Foreign exchange gains	14		1			-	146	44	52	39
Gain on valuation of compound financial instruments		8			4	1	0		3	-
Gain on sale of securities	1									
Subsidy income		20	44	1	0	2	6			
Dividend received	0									
Reversal of allowance for investment loss										
Other	1	2	1	3	1	1	3	6		
Non-operating expenses	29	55	85	35	12	76	21	39	44	216
Interest expenses						0	1	6	7	43
Commitment fees								6	9	7
Foreign exchange losses		55		33	0	76	-			
Syndicated loan fees										141
Share issuance expenses	6		13	1	12	0	0	16	4	1
Loss on valuation of derivatives						-	10	-	25	22
Settlement package						-	10			
Loss on valuation of compound financial instruments	21		2	1				11		2
Loss on redemption of securities	2									
Other	-	-	0	-	-	-	-	-	-	-
Recurring profit	**-1,795**	**-721**	**-81**	**-1,065**	**22**	**-528**	**864**	**904**	**-293**	**-362**
YoY	-	-	-	-	-	-	-	4.7%	-	-
Recurring profit margin	-	-	-	-	1.3%	-	31.1%	31.0%	-	-
Extraordinary gains	66		21	5	6	9	17	14	-	9
Gain on sale of fixed assets						1	-			
Gain on sale of investment securities	66		18	5	6	8	14	10		9
Gain on redemption of investment securities							2	4		
Extraordinary losses	119	2	0	18		9		68	1	6
Impairment losses						3				
Loss on sales of investment securities			0			0				6
Loss on redemption of investment securities	6	2				7		50	1	
Retirement benefits for officers								18	-	
Special retirement expenses	69									
Office relocation expenses	43									
Loss on cancellation of lease contract										
Other	-	-	-	-	-	-	-	-	-	-
Income taxes	6	5	-2	26	22	79	125	128	30	137
Implied tax rate	-0.3%	-0.7%	2.9%	-2.4%	80.4%	-15.0%	14.2%	15.0%	-10.1%	-38.4%
Net income attributable to owners of the parent	**-1,854**	**-728**	**-58**	**-1,105**	**5**	**-607**	**756**	**723**	**-324**	**-495**
YoY	-	-	-	-	-	-	-	-4.3%	-	-
Net margin	-	-	-	-	0.3%	-	27.2%	24.8%	-	-

Source: Shared Research based on company data
Note: Figures may differ from company materials due to differences in rounding methods.

In June 2008, the company received intellectual property rights from Pfizer covering a number of projects that were in the exploratory or development stages. When the company out-licenses rights for compounds transferred from Pfizer, it pays a certain percentage of the revenue it receives (upfront, milestone, and royalty payments) as royalties to Pfizer and record them under operating expenses.

The bulk of the upfront, milestone, and royalty payments the company receives from out-licensing is in US dollars, so it books foreign exchange gains or losses each fiscal year depending on currency fluctuations, which affect earnings.

Balance sheet

Balance sheet	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24
(JPYmn)	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.
Assets										
Cash and deposits	1,840	1,428	2,268	1,671	2,174	1,394	2,345	3,675	3,715	3,340
Notes and accounts receivable	73	58	449	1	747	531	1,205	602	603	689
Securities	503	9	329	168	26	719	314	251	50	2
Inventories	7	7	5	6	6	7	11	9	148	168
Advances paid	179	205	190	9	6	36	16	90	67	27
Prepaid expenses	65	56	62	72	69	50	90	109	188	194
Other	40	43	20	35	39	97	22	87	186	120
Total current assets	**2,708**	**1,806**	**3,322**	**1,962**	**3,067**	**2,834**	**4,004**	**4,822**	**4,957**	**4,539**
Buildings and structures	140	141	142	143	143	153	154	154	158	159
Tools, furniture, and fixtures	394	452	488	677	742	872	944	964	1,125	1,371
Lease assets				3	3	49	60	255	398	434
Accumulated depreciation	-273	-344	-415	-505	-639	-741	-859	-982	-1,107	-1,435
Total tangible fixed assets	**261**	**249**	**216**	**318**	**249**	**333**	**299**	**391**	**574**	**529**
Trademark	2	6	5	5	5	4	4	4	5	4
Software	8	7	4	28	27	28	29	20	26	33
Goodwill										3,865
Other	4	0	-	1	1	1	1	0	0	0
Total intangible assets	**14**	**13**	**10**	**34**	**32**	**33**	**34**	**24**	**30**	**3,902**
Investment securities	1,752	1,937	1,503	1,717	1,474	1,038	888	988	1,231	547
Long-term prepaid expenses	5	3	2	10	2	0	0	24	64	15
Deferred tax assets						3	-		6	78
Other	12	11	11	12	12	10	9	8	11	45
Investments and other assets	**1,769**	**1,951**	**1,516**	**1,738**	**1,488**	**1,051**	**897**	**1,020**	**1,311**	**685**
Total fixed assets	**2,044**	**2,213**	**1,742**	**2,090**	**1,769**	**1,417**	**1,230**	**1,436**	**1,915**	**5,117**
Total assets	**4,752**	**4,019**	**5,064**	**4,052**	**4,837**	**4,251**	**5,234**	**6,258**	**6,872**	**9,655**
Liabilities										
Notes and accounts payable			2		34	42	46	128	54	59
Short-term debt	-	-	-	1	1	18	22	46	77	582
Accounts payable–other	123	126	63	99	67	53	113	206	159	194
Accrued expenses	57	40	44	48	50	50	63	60	54	69
Income taxes payable	15	1	21	14	20	21	80	31	20	28
Consumption taxes payable			14			-	37			
Deferred tax liabilities		1							-	186
Advances received		14	1		7					
Deposits	5	3	4	3	3	3	29	19	4	19
Other	-	5	-	-	-	-	10	4	22	50
Total current liabilities	**200**	**190**	**149**	**164**	**183**	**187**	**401**	**494**	**389**	**1,187**
Long-term debt	-	-	-	2	2	27	18	177	291	2,870
Asset retirement obligations	12	12	12	12	12	12	12	12	12	15
Deferred tax liabilities	26	29	16	16	19	14	16	3	-	
Other	-	-	-	-	-	-	-	75	59	13
Total fixed liabilities	**38**	**41**	**27**	**31**	**33**	**53**	**46**	**267**	**362**	**2,897**
Total liabilities	**238**	**231**	**176**	**195**	**216**	**240**	**446**	**761**	**752**	**4,085**
Net assets										
Capital stock	9,806	2,238	2,741	2,793	2,255	2,255	2,257	2,266	2,668	2,721
Capital surplus	5,090	2,238	2,931	2,983	2,445	2,445	2,447	2,455	2,857	2,910
Retained earnings	-10,421	-728	-786	-1,890	-99	-706	50	773	449	-46
Share subscription rights	11	15	17	13	12	12	11	8	26	27
Total net assets	**4,514**	**3,788**	**4,888**	**3,857**	**4,621**	**4,011**	**4,788**	**5,497**	**6,120**	**5,571**
Total liabilities and net assets	**4,752**	**4,019**	**5,064**	**4,052**	**4,837**	**4,251**	**5,234**	**6,258**	**6,872**	**9,655**
Working capital	80	65	452	7	718	496	1,170	483	697	798
Total interest-bearing debt	-	-	-	3	2	46	39	222	368	3,452
Net debt	-1,840	-1,428	-2,268	-1,668	-2,172	-1,349	-2,306	-3,453	-3,347	112

Source: Shared Research based on company data
Note: Figures may differ from company materials due to differences in rounding methods.

As of end-FY12/24, total assets increased JPY2.8bn YoY to JPY9.7bn, up 40.5% from end-FY12/23. The rise was primarily driven by a JPY3.9bn increase in intangible assets, reflecting higher goodwill following the full acquisition of FIMECS in March 2024. This was partially offset by a JPY374mn decrease in cash and deposits and a JPY684mn decline in investment securities.

Total liabilities rose by JPY3.3bn to JPY4.1bn, up 443.6% YoY, mainly due to a JPY2.6bn increase in long-term borrowings, a JPY500mn rise in the current portion of long-term borrowings, and a JPY185mn increase in contract liabilities.

Total net assets declined JPY549mn to JPY5.6bn, down 9.0% YoY, primarily reflecting a JPY495mn net loss attributable to owners of the parent and a JPY162mn decrease in valuation difference on marketable securities, partially offset by a JPY105mn increase in capital stock and capital surplus through a third-party allotment.

As a result, the equity ratio declined 31.3pp YoY to 57.4%.

Cash flow statement

Cash flow statement	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24
(JPYmn)	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.
Cash flows from operating activities (1)	-2,117	-681	-307	-404	-531	-289	366	1,480	-719	181
Pre-tax profit	-1,848	-723	-60	-1,078	27	-528	881	851	-294	-358
Depreciation	53	80	86	126	140	124	142	148	176	198
Impairment losses						3	-			
Gain and loss on sale and disposal of fixed assets						-1	-			
Change in working capital	-51	15	-377	445	-711	223	-674	687	-214	-78
Cash flows from investing activities (2)	666	-441	534	-368	216	225	-279	-48	-135	-3,666
Purchase of intangible/tangible fixed assets	-200	-37	-88	-221	-94	-156	-105	-32	-222	-116
Proceeds from sale of intangible/tangible fixed assets						1	-			
Free cash flow (1+2)	-1,451	-1,122	226	-772	-315	-64	87	1,432	-854	-3,485
Cash flows from financing activities	1,702	-	1,007	99	696	-7	-16	-30	793	2,982
Net change in short-term borrowings						-	-			
Net change in long-term borrowings	-	-	-	-	-	-	-	12	40	2,970
Proceeds from issuance of, and redemption of, bonds	-	-	-	-	-	-	-	-	-	-
Proceeds from share issuance exercising share subscription rights	1,686		996	100	692	0	2	4	4	0
Proceeds from issuance of share subscription rights	15		11		4				783	80
Repayments of lease obligations				-1	-1	-7	-18	-45	-52	-68
Change in cash and cash equivalents	252	-999	1,229	-644	371	-139	179	1,439	-15	-523
Cash and cash equivalents (year-end)	2,243	1,244	2,474	1,830	2,200	2,061	2,241	3,679	3,665	3,142

Source: Shared Research based on company data

Note: Figures may differ from company materials due to differences in rounding methods.

Cash flows from operating activities

Cash inflows from operating activities increased by JPY899mn YoY, turning from an outflow of JPY718mn in FY12/23 to an inflow of JPY180mn in FY12/24. This improvement was primarily driven by a pre-tax loss of JPY357mn, depreciation of JPY198mn, amortization of goodwill of JPY203mn, a JPY73mn decrease in advance payments, and a JPY74mn decrease in consumption taxes receivable.

Cash flows from investing activities

Cash outflows from investing activities increased JPY3.5bn YoY, rising from JPY135mn in FY12/23 to JPY3.7bn in FY12/24. This was mainly due to a JPY3.9bn outflow for the acquisition of shares in a subsidiary following a change in the scope of consolidation, and a JPY200mn outflow for payments into time deposits. These were partially offset by inflows of JPY100mn from withdrawal of time deposits, JPY258mn from sales of investment securities, and JPY200mn from distributions from investment partnerships.

Cash flows from financing activities

Cash inflows from financing activities increased JPY2.2bn YoY, rising from JPY793mn in FY12/23 to JPY3.0bn in FY12/24. This was primarily due to an inflow of JPY3.4bn from long-term borrowings and JPY79mn from share issuance. These were partially offset by outflows of JPY387mn for repayments of long-term borrowings and JPY68mn for lease obligation repayments.

Historical performance

Cumulative Q3 FY12/24 results (out November 14, 2024)

Earnings summary

Cumulative Q3 FY12/24 (January–September 2024) results

- Operating revenue: JPY2.4bn (+58.4% YoY)
- Operating loss: JPY27mn (vs. a loss of JPY108mn in cumulative Q3 FY12/23)
- Recurring loss: JPY231mn (vs. a loss of JPY36mn)
- Net loss attributable to owners of the parent: JPY340mn (vs. a loss of JPY118mn)
- R&D expenses: JPY1.3bn (+34.3% YoY)

In cumulative Q3, the company achieved 52.2% of its full-year operating revenue forecast. This figure includes the results of FIMECS from Q2 FY12/24, following its consolidation.

Factors behind higher revenue and lower profits

In cumulative Q3, royalty revenue from four launched products, along with the steady global expansion of tegoprazan, generated royalty revenue of JPY1.5bn (up 36.3% YoY). Other income, including upfront and milestone payments, totaled JPY876mn (up 195.2% YoY). Royalty revenue for pet drugs remains stable at its peak, with the increase in royalty revenue primarily driven by tegoprazan. Revenue in South Korea continues to perform well. Revenue in cumulative Q3 rose by 24.6% YoY. HK inno.N continues to lead the anti-ulcer drug market in South Korea with a share of 15%. In Q3, the company recorded royalty revenue from sales in China during 1H FY12/25.

In addition to royalty revenue, the company confirmed the receipt of a milestone payment following the launch of Eluracat® in France in August 2024, with USD2mn to be recorded as operating revenue in Q3. Additionally, in September 2024, the company will receive a milestone payment from HK inno.N after a sublicensee obtained marketing approval for tegoprazan in Colombia, which will also be recorded as Q3 operating revenue. The company also records research cooperation payments received by FIMECS each quarter.

Total operating expenses were JPY2.4bn (+49.5% YoY), including the cost of revenue at JPY397mn (+109.5% YoY), R&D expenses at JPY1.3bn (+34.3% YoY), and other SG&A expenses at JPY745mn (+55.2% YoY). The increase in costs led to an operating loss of JPY27mn. The company also recorded non-operating income, including interest income of JPY3mn and derivative valuation gains of JPY4mn. However, it booked non-operating expenses such as interest expenses of JPY29mn and arrangement fees of JPY141mn related to a syndicated loan, resulting in a recurring loss and a net loss for the quarter.

Pipeline

Brisk royalties from four commercialized products

Pet drugs

Sales of GALLIPRANT® (generic name: grapiprant), a treatment for osteoarthritis in dogs, ENTYCE® (generic name: capromorelin), a treatment for anorexia in dogs, and ELURA® (generic name: capromorelin), a treatment for weight management in cats with chronic kidney disease (CKD), continue to perform well. In Europe, Elanco secured manufacturing and marketing approval in 2023 and launched the product in France in August 2024, resulting in the confirmation of a milestone payment to RaQualia. In February 2024, Elanco obtained manufacturing and marketing approval for ELURA® from Japan's Ministry of Agriculture, Forestry, and Fisheries and launched it in November 2024. The company will not receive an upfront payment for the launch.

Development of tegoprazan in countries around the world

Sales of GERD treatment K-CAB® in South Korea by licensee HK inno.N continued to be robust, with sales from prescriptions outside hospitals amounting to KRW142.2bn (+24.6% YoY; roughly JPY15.6bn at JPY0.11/KRW) in cumulative Q3 FY12/24. HK inno.N continues to lead the anti-ulcer drug market in South Korea with a share of 15%. HK inno.N has not disclosed a peak sales forecast for K-CAB, as the product has already received marketing approval for five indications, with the potential for obtaining further approvals in other gastric acid-related diseases. Additionally, the anti-ulcer drug market in South Korea has expanded since the product's launch in 2019.

The company holds an exclusive license agreement with HK inno.N to develop, market, and manufacture tegoprazan, including sublicense rights. HK inno.N aims to expand tegoprazan's reach to 100 countries by 2028 and is actively pursuing this goal. As of end-Q3, tegoprazan was available or in preparation in 46 countries worldwide. HK inno.N's sublicensees are advancing the development, manufacturing, and sales of tegoprazan.

In Q3, Laboratories Carnot (unlisted), an out-licensee of HK inno.N, obtained marketing approvals and launched the product in October 2024 in Colombia. With the approval from Colombian authority, tegoprazan is now approved for sale in nine Latin American countries: Mexico, Peru, Chile, the Dominican Republic, Honduras, Nicaragua, Guatemala, El Salvador, and Colombia. As of end-Q3, tegoprazan is marketed under the brand name Ki-CAB® in Mexico, Peru, and Chile. Carnot commenced sales in October 2024 in Colombia and in December 2024 in the remaining five approved countries.

Additionally, Pharmaniaga Logistics Sdn Bhd (KLSE: 7081), a sublicensee of HK inno.N Corporation, obtained marketing approval for tegoprazan from the National Pharmaceutical Regulatory Agency (NPRA) of Malaysia. Shandong Luoxin

Pharmaceutical Group Co., Ltd. (002793: SHE) obtained approval from Chinese authorities to conduct a clinical trial for injectable tegoprazan development in China.

At the Q3 announcement in November 2024, tegoprazan is currently marketed in ten countries: South Korea, China, the Philippines, Mongolia, Mexico, Indonesia, Singapore, Peru, Chile, and Colombia. The company receives sales royalties through HK inno.N. Regulatory reviews are underway in several Southeast Asian and Latin American countries, including Thailand, Vietnam, and Argentina. Additionally, clinical development is ongoing in the United States, Canada, and other countries.

Out-licensed and pre-out-licensing programs

For the out-licensed programs, RaQualia's partners and its sublicensees are advancing development in the preclinical or later stages. The company out-licensed P2X7 receptor antagonist to Asahi Kasei Pharma (unlisted, a subsidiary of Asahi Kasei Corp. [TSE Prime: 3407]). Eli Lilly, with whom Asahi Kasei Pharma has a license agreement, is taking over global development. In August 2024, sublicensee Eli Lilly announced the results of Phase II clinical trials initiated in November 2022 for three diseases (knee pain due to osteoarthritis, chronic low back pain, and diabetic neuropathic pain). Although the safety profile of the investigational drug was favorable with no major concerns, its efficacy did not meet the primary endpoints and no advantage over placebo was observed. Eli Lilly is currently reviewing future development plans.

In its pre-out-licensing programs, the company is advancing preclinical trials for a ghrelin receptor agonist in-house. Manufacturing of APIs for clinical trials scheduled in 2H FY12/25 has been completed. Regarding tegoprazan, the company retains the rights for development, manufacturing, and sales in Japan, and actively negotiated with potential licensing partners during Q2 and Q3. For other pre-out-licensing programs, the company has conducted business development activities aimed at acquiring partners, utilizing a flexible combination of in-person meetings and online conferences.

In the exploratory research phase, RaQualia is concentrating on research programs aimed at creating new development compounds. The company seeks to enhance technologies and pipelines by leveraging synergies between existing technologies and new initiatives, approached from four perspectives: modality, drug discovery targets, disease areas, and foundational technologies. By enhancing its next-generation drug discovery value chain through synergies of existing and new technologies, the company advances a critical development strategy to target previously unexplored drug opportunities, including genes and proteins once considered undruggable.

The company is developing targeted protein degradation inducers, a novel drug creation modality, primarily through FIMECS, which became a consolidated subsidiary in March 2024. FIMECS's RaPPIDS™ drug discovery platform strengthens the company and group's foundational technology while generating revenue through ongoing joint development efforts.

RaQualia entered an agreement with STAND Therapeutics (unlisted) to leverage STAND's technology for generating intracellular antibodies functional within cells, advancing drug discovery efforts. Additionally, the company conducts joint research with Veritas In Silico Inc. (TSE GRT: 130A) to develop breakthrough small-molecule drugs targeting messenger RNAs (mRNA). Through these initiatives, the company expanded its focus to include cancer.

Tamibarotene

Regarding the retinoic acid receptor α agonist (tamibarotene), which was out-licensed from subsidiary TMRC Co., Ltd. to Syros Pharmaceuticals Inc. (NASDAQ: SYRS), clinical trials are underway in the US targeting myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML).

In August 2024, an interim analysis was conducted using data from 51 patients enrolled in the SELECT-AML-1 trial for tamibarotene in combination with venetoclax and azacitidine. The interim analysis concluded the likelihood of the investigational drug's demonstrating superiority in the final analysis was low, leading Syros to halt new patient enrollment. No new safety concerns were identified in the combination therapy of tamibarotene, venetoclax, and azacitidine. Syros presented the results at the 12th Annual Meeting of the Society of Hematology and Oncology (SOHO) in September 2024.

In Q1, Syros completed the patient enrollment required for the primary endpoint analysis in the Phase III clinical trial (SELECT-MDS-1) for tamibarotene and azacitidine. In November 2024, Syros announced that the trial did not meet its primary endpoint of complete response (CR) rate and that it would discontinue the trial while analyzing the clinical data in detail to evaluate next steps. Syros also disclosed that the SELECT-MDS-1 trial's failure to meet the primary endpoint constitutes a default event under its secured loan agreement.

Key progress events expected for the next six months

Tegoprazan (gastroesophageal reflux disease [GERD])

- US: Phase III clinical trials in progress → Conclude the study.
- Japan: Licensing activities are ongoing → An out-licensing agreement expected in December 2025.

Tamibarotene (antitumor drug)

- MDS: Phase III clinical trials in progress → Considering the next step in response to the results of Phase III (failed to meet primary end points).
- AML: Phase II clinical trial ongoing → Stopped new patient enrollment, reviewing future development plans.

P2X7 receptor antagonist (pain)

Analysis of Phase II clinical trial data ongoing → Considering the new development plan in response to the results of Phase II clinical trials in FY12/24

CB2 agonist (pain associated with CIPN/IBS)

Phase I clinical trials in progress → The next phase of clinical trials starts.

TRPM8 blocker (chronic pain)

Commenced Phase I clinical trials in Australia in FY12/24, received milestone payments from Xgene in Q1 → Results of Phase I study will be announced.

Ghrelin receptor agonist (constipation, cachexia)

Preclinical trials and investigational drug manufacturing in progress → Concluded preclinical trials, with signing license-out agreements expected in FY12/25 onward.

1H FY12/24 results (out August 14, 2024)

Earnings summary

1H FY12/24 (January–June 2024) results

- Operating revenue: JPY1.4bn (+39.1% YoY)
- Operating loss: JPY154mn (vs. loss of JPY23mn in 1H FY12/23)
- Recurring loss: JPY278mn (vs. JPY37mn)
- Net loss attributable to owners of the parent: JPY324mn (vs. JPY25mn)
- R&D expenses: JPY833mn (+38.0% YoY)

In 1H, operating revenue was 31.1% of the full-year forecast. In March 2024, the company acquired all outstanding shares and stock options of FIMECS, making it a consolidated subsidiary. As a result, FIMECS's financial performance has been reflected in the company's results from Q2. According to the company, both revenue and expenses were largely in line with forecasts.

Factors behind higher revenue and lower profits

In 1H, royalty revenue from three pet products, along with the steady global expansion of tegoprazan, generated royalty revenue of JPY998mn (+36.3% YoY). Other income, including upfront and milestone payments, totaled JPY413mn (+46.5% YoY). Other revenue includes a lump-sum payment related to the sublicensing of tegoprazan in the Middle East and North Africa, as well as a JPY200mn milestone payment FIMECS received from Astellas Pharma in May 2024.

Total operating expenses were JPY1.6bn (+50.9% YoY), including cost of revenue at JPY227mn (+85.6% YoY), R&D expenses at JPY833mn (+38.0% YoY), and other SG&A expenses at JPY506mn (+62.1% YoY). The increase in expenses, driven by higher R&D expenses and the consolidation cost of FIMECS, resulted in operating loss of JPY154mn. The company also recorded non-operating income, including foreign exchange gains of JPY75mn. However, it booked non-operating expenses such as derivative valuation losses of JPY52mn and arrangement fees of JPY140mn related to a syndicated loan, resulting in a recurring loss and a net loss.

Pipeline

Brisk royalties from four commercialized products

Pet drugs

Sales of GALLIPRANT® (generic name: grapiprant), a treatment for osteoarthritis in dogs, ENTYCE® (generic name: capromorelin), a treatment for anorexia in dogs, and ELURA® (generic name: capromorelin), a treatment for weight management in cats with chronic kidney disease (CKD), continue to perform well. In February 2024, Elanco obtained manufacturing and marketing approval for ELURA® from Japan's Ministry of Agriculture, Forestry, and Fisheries, and is now preparing for its launch. In Europe, Elanco secured manufacturing and marketing approval in 2023 and launched the product in France in August 2024, resulting in the confirmation of a milestone payment to RaQualia.

Development of tegoprazan in countries around the world

Sales of the GERD treatment K-CAB® in South Korea by licensee HK inno.N remained robust. K-CAB® held a 14% share of the anti-ulcer drug market in South Korea, maintaining its top position. Prescription sales outside hospitals reached KRW91.9bn (+24.1% YoY; approximately JPY10.1bn at JPY0.11/KRW) in 1H FY12/24. Notably, sales of orally disintegrating tablets (OD tablets) grew, accounting for about 27% of total sales. In July 2024, HK inno.N launched a low-dose (25 mg) OD tablet for maintenance therapy following the treatment of erosive esophagitis, and the company expects the share of OD tablet sales to increase further.

In South Korea, a negative patent scope confirmation trial* was filed against tegoprazan's compound patents, but all claims were dismissed in June 2024. The company believes that this outcome will strengthen the protection of K-CAB®'s exclusive commercialization rights.

*A negative scope confirmation trial in South Korea is a legal proceeding requested by a third party who is not the patent holder. The third party seeks confirmation that the technology or actions it implements do not fall within the scope of the patent. The patent term for tegoprazan in South Korea is 20 years from the application date, with a possible extension of up to five years. As a result, HK inno.N holds exclusive marketing rights until 2031.

The company holds an exclusive license agreement with HK inno.N to develop, market, and manufacture tegoprazan, including sublicense rights. HK inno.N aims to expand tegoprazan's reach to 100 countries by 2028 and is actively pursuing this goal. During 1H, Laboratories Carnot (unlisted) obtained marketing approvals in Chile, the Dominican Republic, Honduras, and Nicaragua. As a result, RaQualia received a lump-sum payment from HK inno.N in accordance with their agreement.

As of end-1H, tegoprazan was available or in preparation in 46 countries worldwide. It is currently marketed in eight countries: South Korea, China, the Philippines, Mongolia, Mexico, Indonesia, Singapore, and Peru. Regulatory reviews are underway in several Southeast Asian and Latin American countries, including Thailand, Vietnam, and Argentina. Additionally, clinical development is ongoing in the United States, Canada, and other countries.

The company records royalties from tegoprazan sales on a quarterly basis in South Korea and semi-annually in China, with sales from July to December of the previous year recorded in Q1, and sales from January to June of the current year recorded in Q3. Although contributions from other countries remain small, sales in these markets are steadily increasing.

Out-licensed and pre-out-licensing programs

For the out-licensed programs, RaQualia's partners are advancing development in the preclinical or later stages.

For the TRPM8 antagonist (RQ-00434739/XG2002), the company's licensee, Xgene Pharmaceutical Co. Ltd. (unlisted), received approval from the local research ethics committee in Australia to conduct a Phase I clinical trial. Consequently, RaQualia received a milestone payment from Xgene. The Phase I trial will evaluate the tolerability and pharmacokinetics of TRPM8 blockade in a dose-escalation study in healthy volunteers.

In April 2024, the company entered into an option and license agreement with Velovia Pharma, LLC (unlisted) for the development of animal health products using four compounds with potential applications in gastrointestinal, metabolic, and fibrotic diseases. If Velovia Pharma exercises its option on one or more of the compounds, the company will receive an option exercise fee. Additionally, the company is eligible to receive milestone payments based on subsequent development

progress, as well as royalties and sales milestone payments from Velovia Pharma once the animal health products containing the compounds become commercially available.

Sublicensee Eli Lilly completed Phase II clinical trials in the US for a P2X7 receptor antagonist targeting three diseases and has published the results. While the safety profile was favorable with no major concerns, the efficacy failed to meet the primary endpoints. Eli Lilly is currently reviewing its future development plans.

Status of the out-license preparation pipeline:

In its pre-out-licensing programs, the company is advancing preclinical trials for a ghrelin receptor agonist in-house. Following the completion of these preclinical trials by end-2024, the company expects to launch Phase I clinical trials in 2H FY12/25. Regarding tegoprazan, the company retains the rights for development, manufacturing, and sales in Japan and is actively negotiating with potential licensing partners. For other pre-out-licensing programs, the company has conducted business development activities aimed at acquiring partners, utilizing a flexible combination of in-person meetings and online conferences.

Programs in the exploratory research stage

In the exploratory research phase, RaQualia is concentrating on research programs aimed at creating new development compounds. The company seeks to establish its next-generation drug discovery value chain by leveraging synergies between existing technologies and new initiatives, approached from four perspectives: modality, drug discovery targets, disease areas, and foundational technologies. In addition to its independent research efforts, RaQualia is also expanding collaborations with startups and drug discovery ventures.

To strengthen its expertise in small molecule drug discovery, the company is conducting joint research with Veritas In Silico Co., Ltd. (TSE Growth: 130A, VIS) to develop small molecule drugs targeting mRNA for cancer treatment, leveraging technologies such as AI-driven compound design and iPS cell-derived neural cells. In 1H, the company made significant progress in exploring compounds, resulting in the discovery of several small molecules exhibiting the desired properties at the cellular level. The company is focusing on drug discovery using novel modalities at its new research facility, established in 2023 at the Shonan Health Innovation Park (Fujisawa, Kanagawa Prefecture). Additionally, it is collaborating with STAND Therapeutics Co., Ltd. (unlisted) to apply intracellular antibody technology in developing treatments for intractable and rare diseases.

Tamibarotene

Regarding the retinoic acid receptor α agonist (tamibarotene), which was out-licensed from subsidiary TMRC Co., Ltd. to Syros Pharmaceuticals Inc. (NASDAQ: SYRS), clinical trials are underway in the US targeting myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML). In Q1, Syros completed the patient enrollment required for the primary endpoint analysis in the Phase III clinical trial (SELECT-MDS-1), which targets patients with high-risk myelodysplastic syndromes (HR-MDS) exhibiting an overexpression of the RAR alpha gene. Complete remission rate data are expected to be available by mid-Q4.

In August 2024, Syros announced it would halt patient enrollment in the Phase II clinical trial (SELECT-AML-1) for untreated AML patients who overexpress the RAR alpha gene and are ineligible for conventional chemotherapy. The decision was based on an interim analysis of 51 patients, which indicated a low likelihood that the final analysis of 80 patients would demonstrate significantly superior efficacy of the investigational drug. Syros presented the results at the 12th Annual Meeting of the Society of Hematology and Oncology (SOHO) in September 2024.

Acquisition of FIMECS

In March 2024, the company acquired all issued shares and share subscription rights of FIMECS Inc., making it a wholly owned subsidiary. FIMECS is a drug discovery startup that advances the R&D of new pharmaceuticals using targeted protein degradation inducers, a novel modality in drug discovery. Leveraging its unique E3 ligase-binding molecules and the RaPPIDS™ drug discovery platform technology, FIMECS aims to develop innovative medicines for diseases previously considered "undruggable."

The figures include FIMECS' results from Q2 FY12/24, following its consolidation. In line with the joint research agreement for targeted protein degraders, FIMECS received JPY200mn from Astellas Pharma Inc., which was recorded as operating revenue in Q2 FY12/24.

FIMECS's business model is a hybrid that combines revenue generation from out-licensing its in-house developed pipeline with collaborative research partnerships with pharmaceutical companies. The acquisition of FIMECS not only strengthens the company's drug discovery value chain through the acquisition of platform technologies but also enhances earnings through the hybridization of its business model, and the expansion and strengthening of its oncology business.

When the company converted FIMECS into a subsidiary, the closing consideration amounted to JPY4.5bn, funded in part by a JPY3.5bn syndicated loan, with disbursement completed in March 2024. The acquisition significantly increased the company's assets and liabilities, resulting in an equity ratio of 55.6%, a decrease of 33.1pp from end-FY12/23.

Q1 FY12/24 results (out May 15, 2024)

Earnings summary

Q1 FY12/24 (January–March 2024) results

- Operating revenue: JPY649mn (+75.1% YoY)
- Operating profit: JPY45mn (vs. loss of JPY109mn in Q1 FY12/23)
- Recurring loss: JPY0.77mn (vs. loss of JPY110mn)
- Net loss attributable to owners of the parent: JPY78mn (vs. loss of JPY148mn)
- R&D expenses: JPY359mn (+33.8% YoY)

In Q1, the company's rate of progress toward its full-year forecast was 14.3% for operating revenue and 14.2% for operating profit.

Factors behind higher revenue and profits

In Q1, the company received one-time payments in addition to royalties of JPY551mn (+57.4% YoY) from its four marketed products. The one-time payments were for the approval of tegoprazan in four countries in Latin America and the approval to conduct a Phase I clinical trial of a TRPM8 blocker in Australia. Other revenue, including the one-time payments, was JPY97mn (+385.0% YoY).

Total operating expenses were JPY604mn (+26.0% YoY), including cost of revenue at JPY61mn (+1.9% YoY), R&D expenses at JPY359mn (+33.8% YoY), and other SG&A expenses at JPY185mn (+21.8% YoY). The increase in R&D expenses was mainly due to progress in preclinical studies of ghrelin receptor agonist and manufacture of APIs. Despite the increase in costs, the rise in operating revenue led to operating profit of JPY44mn. The company also recorded non-operating income, including foreign exchange gains of JPY42mn. However, it booked non-operating expenses such as derivative valuation losses of JPY27mn and arrangement fees of JPY140mn related to a syndicated loan, resulting in a recurring loss and a net loss for the quarter.

Pipeline

Brisk royalties from four commercialized products

Pet drugs

Sales of GALLIPRANT® (generic name: grapiprant), a treatment for osteoarthritis in dogs, ENTYCE® (generic name: capromorelin), a treatment for anorexia in dogs, and ELURA® (generic name: capromorelin), a treatment for weight management in cats with chronic kidney disease (CKD), continue to perform well. In February 2024, Elanco secured manufacturing and marketing approval from the Ministry of Agriculture, Forestry, and Fisheries in Japan for ELURA®. Following the approval received in Europe in 2023, Elanco is progressing with preparations to launch the product.

In April 2024, the company entered into an option and license agreement with US-based Velovia Pharma, LLC (unlisted) for the development of veterinary drugs containing the company's four pipeline compounds. Based on the terms of the agreement, the company granted Velovia option for the exclusive rights to evaluate, develop, manufacture, and sell veterinary drugs containing its four pipeline compounds. If Velovia exercises its option right for one or more of the compounds, the company is entitled to receive option exercise fees as well as milestone payments based on Velovia's subsequent development progress. Further, if veterinary drugs containing the compounds reach the market, the company may receive sales royalties and sales milestone payments based on product sales from Velovia.

Development of tegoprazan in countries around the world

Sales of GERD treatment K-CAB® in South Korea by licensee HK inno.N continued to be robust, with sales from prescriptions outside hospitals amounting to KRW45.2bn (+26.8% YoY; roughly JPY5.0bn at JPY0.11/KRW) in FY12/23. Co-promotions with Boryung Pharmaceutical Co., Ltd. (KRX: 003850) initiated in January 2024 and a change in sales channels proved successful. HK inno.N's continues to lead the anti-ulcer drug market in South Korea with a share of 14%.

In April 2024, HK inno.N entered into an exclusive license agreement with Tabuk Pharmaceutical Manufacturing Company (unlisted) of Saudi Arabia, granting the latter sublicensing rights to tegoprazan in 10 countries. As of end-Q1, companies licensed by HK inno.N (sublicensees) are advancing development, manufacturing, and sales initiatives for tegoprazan in 46 countries, including South Korea. During Q1, the sublicensee, Laboratories Carnot (unlisted), obtained marketing approvals in Chile, the Dominican Republic, Honduras, and Nicaragua. Consequently, RaQualia received a lump-sum payment from HK inno.N based on their agreement. As of May 2024, tegoprazan was being marketed in eight countries: South Korea, China, Mongolia, the Philippines, Mexico, Indonesia, Singapore, and Peru.

Out-licensed and pre-out-licensing programs

For the out-licensed programs, RaQualia's partners are advancing development in the preclinical or later stages.

For the TRPM8 antagonist (RQ-00434739/XG2002), the company's licensee, Xgene Pharmaceutical Co. Ltd. (unlisted), received approval from the local research ethics committee in Australia to conduct a Phase I clinical trial in March 2024. Consequently, RaQualia received a milestone payment from Xgene. In April the same year, Xgene announced the enrollment of the first patient and commenced the Phase I trial. Based on the license agreement with Xgene, the company is entitled to receive milestone payments in accordance with development progress and royalties on product sales after the product's launch.

In its pre-out-licensing programs, the company is advancing preclinical trials for a ghrelin receptor agonist in-house. Regarding tegoprazan, the company retains the rights for development, manufacturing, and sales in Japan and is actively negotiating with potential licensing partners. For other pre-out-licensing programs, the company has conducted business development activities aimed at acquiring partners, utilizing a flexible combination of in-person meetings and online conferences.

In the exploratory research phase, RaQualia is concentrating on research programs aimed at creating new development compounds. The company seeks to establish its next-generation drug discovery value chain by leveraging synergies between existing technologies and new initiatives, approached from four perspectives: modality, drug discovery targets, disease areas, and foundational technologies. In addition to its independent research efforts, RaQualia is also expanding collaborations with startups and drug discovery ventures.

Development status of tamibarotene

Regarding the retinoic acid receptor α agonist (tamibarotene), which was out-licensed from subsidiary TMRC Co., Ltd. to Syros Pharmaceuticals Inc. (NASDAQ: SYRS), a Phase III clinical trial in myelodysplastic syndromes (MDS) patients and a Phase II trial in acute myeloid leukemia (AML) patients are ongoing in the US. In Q1, Syros completed the patient enrollment required for the primary endpoint analysis in the Phase III clinical trial (SELECT-MDS-1), which targets patients with high-risk myelodysplastic syndromes (HR-MDS) exhibiting an overexpression of the RARA gene. Syros expects to disclose pivotal data on complete remission (CR) by mid-Q4 FY12/24.

In April 2024, tamibarotene was awarded a fast-track designation by the US FDA for the treatment of AML. In December 2023, Syros released data from the randomized part of the Phase II clinical trial being conducted in AML patients (SELECT-AML-1). Complete remission/complete remission with incomplete blood cell recovery (CR/CRi) rate was 70% (seven out of 10 patients) for the current standard of care, the venetoclax/azacitidine combination therapy, whereas the CR/CRi rate was 100% (nine out of all nine patients enrolled in the study) for the three-drug combination therapy including tamibarotene (venetoclax/azacitidine/tamibarotene) in a short time. Syros plans to release additional data in Q4 FY12/24.

Acquisition of FIMECS

In March 2024, the company acquired all issued shares and share subscription rights of FIMECS Inc., making it a subsidiary. FIMECS is a drug discovery startup that advances the R&D of new pharmaceuticals using targeted protein degradation inducers, a novel modality in drug discovery. Leveraging its unique E3 ligase-binding molecules and the RaPPIDS™ drug discovery platform technology, FIMECS aims to develop innovative medicines for diseases previously considered

"undruggable." Its business model is a hybrid that combines revenue generation from out-licensing its in-house developed pipeline with collaborative research partnerships with pharmaceutical companies.

The company believes that the acquisition of FIMECS not only strengthens the company's drug discovery value chain through the acquisition of platform technologies but also enhances earnings through the hybridization of its business model, and the expansion and strengthening of its oncology business. The company financed this acquisition by raising JPY3.5bn through a syndicated loan. As a result, the equity ratio fell 32.8pp from end-FY12/23 to 55.9%. FIMECS's financial results will be reflected in the consolidated income statement starting Q2. The balance sheet was consolidated from the deemed acquisition date of March 31, 2024, resulting in assets expanding 55.6% from end-FY12/23 and liabilities ballooning 524.8%.

Full-year FY12/23 results (out February 14, 2024)

Earnings summary

Full-year FY12/23 (January–December 2023) results

- Operating revenue: JPY1.9bn (-34.8% YoY)
- Operating loss: JPY337mn (compared to profit of JPY866mn in the previous year)
- Recurring loss: JPY293mn (compared to profit of JPY904mn)
- Net loss attributable to owners of the parent: JPY324mn (compared to net income of JPY723mn)
- R&D expenses: JPY1.4bn (+9.9% YoY)

On December 8, 2023, the company revised its earnings forecast for FY12/23 downward, attributing this to anticipated delays in finalizing the license agreement for developing, manufacturing, and selling tegoprazan in Japan, as well as postponement of the approval and launch of ELURA®, a weight loss treatment for cats with CKD, in Europe until FY12/24. Against this revised forecast, full-year operating revenue reached 98.1%.

Factors behind lower revenue and operating loss

In the previous fiscal year, the company reported royalty revenue of JPY1.5bn and other revenue (mainly from upfront and milestone payments) totaling JPY1.4bn. In comparison, FY12/23 revenue decreased by 34.8%, primarily due to the deferral of tegoprazan's out-licensing in Japan and the milestone achievement related to ELURA® to FY12/24. Royalty revenue also fell short of the company's assumption due to the delayed launch of tegoprazan in China and slowing growth of sales in South Korea, where tegoprazan has been on the market for over five years. Operating revenue for Q4 alone (October–December 2023) was JPY406mn, which did not meet the revised forecast of JPY443mn for combined royalty and other revenues.

Operating expenses totaled JPY2.2bn (+9.1% YoY), with cost of revenue increasing by JPY13mn to JPY245mn (+5.8% YoY), R&D expenses increasing by JPY124mn to JPY1.4bn (+9.9% YoY), and other SG&A expenses amounting to JPY621mn (+8.6% YoY). The increase in costs amid declining operating revenue resulted in an operating loss of JPY337mn. Operating expenses were below the initial forecast of JPY2.5bn due to the delayed booking of outsourcing expenses for a ghrelin receptor agonist and reduced personnel expenses associated with the company's hiring plan. However, with a 9.1% YoY increase in operating expenses and lower operating revenue, the company recorded a JPY337mn operating loss. Although the company recorded non-operating income including foreign exchange gains of JPY52mn, this was offset by an increase in non-operating expenses, including derivative valuation losses of JPY25mn. As a result, the company recorded a recurring loss and a net loss.

Pipeline

Brisk royalties from four commercialized products

Pet drugs

Sales of GALLIPRANT® (generic name: grapiprant), a treatment for osteoarthritis in dogs, ENTYCE® (capromorelin), a treatment for anorexia in dogs, and ELURA® (capromorelin), a treatment for weight loss in cats with CKD, continued to be solid. All three products are out-licensed to Elanco.

Development of tegoprazan in countries around the world

Sales of GERD treatment K-CAB® in South Korea by licensee HK inno.N continued to be robust, with sales from prescriptions outside hospitals amounting to KRW158.2bn (+19.8% YoY; roughly JPY17.4bn at JPY0.11/KRW) in FY12/23. HK inno.N's leads

the anti-ulcer drug market in South Korea with a share of 13%.

As of end-December 2023, HK inno.N's sublicensees are advancing the development, manufacturing, and sales of tegoprazan in 35 countries. In China, which became the second country to launch tegoprazan in 2022 following South Korea, the product is now available across 31 provinces and administrative regions. Additionally, in Peru, the sublicensee has received marketing approval for tegoprazan for four conditions, including erosive esophagitis. Tegoprazan is marketed in eight countries, namely South Korea, China, Mongolia, the Philippines, Mexico, Indonesia, Singapore, and Peru. Moreover, regulatory reviews are in progress in over 20 countries, including Argentina. In the US, Braintree, a sublicensee, is conducting Phase III clinical trials of tegoprazan, with plans to apply for approval in 2024.

Out-licensed and pre-out-licensing programs

Out-licensed programs are in the preclinical development stage or later at licensees.

In FY12/23, Oxford Cannabinoid Technologies Ltd. (LSE: OCTP, hereafter "OCT") initiated Phase I clinical trials of a cannabinoid CB2 receptor agonist (RQ-00202730/AAT-730/OCT46120), which was out-licensed to OCT from AskAt Inc. (unlisted), a licensee of RaQualia. With plans to develop the CB2 agonist for the lead indication of chemotherapy-induced peripheral neuropathy (CIPN), OCT began dosing patients in July 2023.

Xgene Pharmaceutical Co., Ltd. (unlisted) completed preclinical trials for the TRPM8 antagonist (RQ-00434739/XG2002), which was out-licensed from RaQualia, and had been preparing for Phase I clinical trials. In March 2024, it received approval to begin clinical trials from the Australian Therapeutic Goods Administration (TGA). Additionally, the company's licensees are engaged in both preclinical and clinical trials for other out-licensed programs.

In April 2023, RaQualia signed an option and license agreement with Vetbiolix SAS, an unlisted French company, for the development of pet drugs using the company's 5-HT_4 agonist (RQ-10). Under the agreement, the company grants Vetbiolix an exclusive option for a sublicensable license to develop, manufacture, and sell veterinary drugs containing RQ-10 with worldwide exclusivity. If Vetbiolix exercises the exclusive option, RaQualia will receive an option fee from Vetbiolix and will also be eligible to receive development milestones and sales royalties.

In pre-out-licensing programs, the company has engaged in business development activities, flexibly combining in-person and online meetings to seek potential licensing partners. As for tegoprazan, the company holds the rights for development, manufacturing, and sales in Japan, and continues to negotiate with potential licensing partners. In addition, RaQualia is advancing the development of its ghrelin receptor agonist with the goal of securing a major licensing agreement. Preclinical studies and API manufacturing has been underway for the ghrelin receptor agonist.

In the exploratory research phase, RaQualia is focusing on research programs to create new development compounds, while also working on strengthening its drug discovery research capabilities. The company is aiming to establish its own next-generation drug discovery value chain by creating synergies between existing technologies and new initiatives. This approach is taken from four perspectives: modality, drug discovery targets, disease areas, and basic technology. In addition to its own independent research, the company is also advancing collaborations with startups and drug discovery companies. As part of these efforts, from December 2022, the company has been advancing joint research with Veritas In Silico Inc. (unlisted) aimed at creating mRNA-targeted small molecule drugs that target multiple genes related to cancers. In December 2023, a predetermined milestone was achieved.

In the US, Syros Pharmaceuticals Inc. (NASDAQ: SYRS) is conducting clinical trials for a retinoic acid receptor alpha agonist (tamibarotene), aimed at treating myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). This compound, discovered by TMRC Co., Ltd., a consolidated subsidiary, has been licensed to Syros. Currently, a Phase III clinical trial is in progress, focusing on patients with high-risk myelodysplastic syndromes (HR-MDS) that show overexpression of the RARA gene. In December 2023, Syros published preliminary results from the randomized segment of a Phase II clinical trial for AML patients. As a result, the company earned fees related to the clinical development conducted by Syros.

News and topics

Sublicensing of tegoprazan in Australia and New Zealand

2025-01-06

RaQualia Pharma Inc. announced a sublicense agreement concerning its gastric acid secretion inhibitor, tegoprazan, in Australia and New Zealand.

HK inno.N Corporation (KOSDAQ: 195940), the licensee of RaQualia, disclosed it has concluded a license agreement for tegoprazan with Southern XP IP Pty. Ltd. (unlisted), a pharmaceutical company in Australia.

With over 20 years of experience, Southern X specializes in the registration and distribution of pharmaceuticals in Australia and New Zealand. Through this agreement, Southern XP has obtained exclusive rights to distribute and sell tegoprazan products in these regions. According to HK inno.N, the pharmaceutical market in Australia and New Zealand was valued at approximately KRW22tn (JPY2.4tn, based on a conversion rate of JPY0.11/KRW) in 2023, with the peptic ulcer treatment market accounting for KRW150bn (JPY16.5bn).

Tegoprazan, developed by RaQualia, is a gastric acid secretion inhibitor with a novel mechanism of action, classified as a potassium-competitive acid blocker (P-CAB). Unlike proton pump inhibitors (PPIs), which are the first-line drugs for gastroesophageal reflux disease (GERD), tegoprazan suppresses gastric acid secretion more rapidly and persistently, offering a next-generation therapeutic option. In South Korea, where tegoprazan was first launched globally in 2019 under the brand name "K-CAB®" by HK inno.N, it has maintained the leading share in the gastric acid secretion inhibitor market for out-of-hospital prescriptions for five consecutive years. Domestic sales reached KRW177.7bn (JPY19.5bn) from January to November 2024.

The company has granted HK inno.N an exclusive license, including sublicensing rights, for the development, manufacture, and sale of tegoprazan worldwide, excluding Japan. HK inno.N and its sublicensees conduct business activities related to tegoprazan in various countries under this license. With tegoprazan currently sold in 15 countries, this new agreement will expand its reach to 48 countries, including South Korea, the US, and China. HK inno.N aims to roll out tegoprazan to 100 countries worldwide by 2028.

Under the terms of its license agreement with HK inno.N, RaQualia is entitled to receive a portion of the revenue generated by HK inno.N from its sublicensees. Although the company will not receive a lump sum payment as part of this agreement, the company believes that the further global expansion of tegoprazan will contribute to enhancing its corporate value over the medium to long term.

Receipt of upfront payment from Vetbiolix SAS (France) for option exercise on 5-HT$_4$ agonist

2024-12-18

RaQualia Pharma Inc. announced that Vetbiolix SAS, an unlisted French company, has exercised its option to develop veterinary drugs containing the 5-HT$_4$ agonist RQ-00000010 (RQ-10). The company confirmed it will receive an option fee from Vetbiolix.

In April 2023, RaQualia entered into an option and license agreement with Vetbiolix to develop pet drugs targeting intestinal motility disorders in dogs and cats using RQ-10. The agreement grants Vetbiolix an exclusive, sublicensable license to develop, manufacture, and sell veterinary drugs containing RQ-10 worldwide.

Following Vetbiolix's exercise of the option, RaQualia will receive an option fee and become eligible for development milestone payments, royalties based on sales, and/or license fees. RaQualia will recognize the lump sum payment from Vetbiolix as operating revenue in Q4 FY12/24.

RaQualia has factored the impact of this matter into its revised full-year consolidated forecast for FY12/24, released on December 13, 2024.

Revisions to the full-year FY12/24 forecast, updates to target figures under the three-year medium-term management plan, and the termination of the license agreement with Maruho for a selective sodium channel blocker

2024-12-13

RaQualia Pharma Inc. announced the revision for the full-year FY12/24 earnings outlook, updates to target figures under the three-year medium-term management plan, and the termination of the license agreement with Maruho for a selective sodium channel blocker.

Revision to full-year FY12/24 (January–December 2024) forecast

- Operating revenue: JPY3.1bn (+64.9% YoY; JPY4.5bn at the previous forecast)
- Operating loss: JPY234mn (compared to a loss of JPY337mn in FY12/23; JPY313mn)
- Recurring loss: JPY476mn (a loss of JPY293mn; JPY290mn)
- Net loss attributable to owners of the parent: JPY584mn (a loss of JPY324mn; JPY236mn)
- Net loss per share: JPY26.76 (a loss of JPY14.98; a profit of JPY10.91)

The company forecasts a JPY1.4bn (-30.9%) decrease in operating revenue compared to the previous forecast, the primary factor behind the revised earnings outlook.

Negotiations for a licensing agreement for the development, manufacturing, and marketing rights to the acid suppressant tegoprazan in Japan are ongoing. However, due to trends in the Japanese pharmaceutical market and challenges in securing funding for clinical development, the company now expects the agreement to conclude in FY12/25, resulting in a JPY1.0bn reduction from the previous operating revenue forecast. Additionally, progress stalled on new collaboration agreements at subsidiary FIMECS Inc. and licensing negotiations at subsidiary TMRC Co. Ltd., leading to a further JPY400mn reduction in the projected operating revenue compared to the previous forecast.

Updates to target figures under the three-year medium-term management plan

On the same day, the company also announced updates regarding its business plan and growth potential.

	FY12/21	FY12/22	FY12/23	FY12/24	FY12/25	FY12/26	3-year
(JPYmn)	Cons.	Cons.	Cons.	Revised forecast	Revised target	Revised target	CAGR
Operating revenue	**2,776**	**2,918**	**1,901**	**3,135**	**3,888**	**3,571**	
YoY	150.7%	5.1%	-34.8%	64.9%	24.0%	-8.2%	23.4%
Operating expenses	**2,068**	**2,052**	**2,538**	**3,369**	**3,769**	**3,312**	
YoY	29.8%	-0.8%	23.7%	32.7%	11.9%	-12.1%	9.3%
Operating expense ratio	74.5%	70.3%	133.5%	107.5%	96.9%	92.7%	
Operating profit	**708**	**866**	**-337**	**-234**	**118**	**258**	
YoY	-	22.4%	-	-	-	118.6%	-
Operating profit margin	25.5%	29.7%	-	-	3.0%	7.2%	
Recurring profit	**864**	**904**	**-293**	**-476**	**73**	**189**	
YoY	-	4.7%	-	-	-	158.9%	-
Recurring profit margin	31.1%	31.0%	-	-	1.9%	5.3%	
Net income	**756**	**723**	**-324**	**-584**	**-71**	**32**	
YoY	-	-4.3%	-	-	-	-	-
Net margin	27.2%	24.8%	-	-	-	0.9%	

Source: Shared Research based on company data

The company revised its target figures for the medium-term management plan spanning the three-year period from FY12/24 to FY12/26.

The company now expects operating revenue for FY12/24 to decline by JPY1.4bn (-30.9%) compared to the previous forecast. This decrease primarily reflects delays in the licensing agreement negotiations for the development, manufacturing, and marketing rights for the acid suppressant tegoprazan in Japan. While negotiations are ongoing, factors such as trends in the Japanese pharmaceutical market and challenges in securing funding for clinical development have pushed the agreement to FY12/25, reducing the operating revenue forecast by JPY1.0bn. Further, slower-than-expected progress in new collaboration agreements at subsidiary FIMECS Inc. and licensing negotiations at subsidiary TMRC Co. Ltd. has resulted in an additional JPY400mn decline in the operating revenue forecast.

The company expects operating expenses to drop by JPY853mn (-20.2%) compared to the previous forecast. The company reduced the estimates for upfront payments for a new license agreement and clinical trial preparation expenses by JPY1.0bn, while it increased projections for M&A-related expenses, including goodwill amortization, by JPY120mn.

The projection for FY12/25 operating revenue shows a decline of JPY498mn (-11.4%) versus the previous target. This decline reflects a total decrease of JPY900mn in received upfront and milestone payments. FIMECS Inc., a subsidiary, reviewed the negotiation progress of a new collaboration research contract and reassessed the likelihood of receiving milestone payments, contributing to this reduction. TMRC Co. Ltd., another subsidiary, reassessed the clinical development progress of its licensee, Syros Pharmaceuticals, Inc. (NASDAQ: SYRS), which further impacted the operating revenue forecast. The company also deferred approximately half of the expected upfront payments for license contracts carried over from FY12/24 after reassessing the certainty of milestone achievement. The company forecasts operating expenses to decrease by JPY227mn (-5.7%) compared to the previous forecast, driven by a JPY400mn reduction in clinical development expenses, partially offset by a projected increase of JPY85mn after reviewing goodwill amortization.

The company revised down the target operating revenue for FY12/26 by JPY2.0bn (-35.4%) compared to the previous target. This reduction primarily reflects a JPY1.5bn downward adjustment due to a reassessment of the progress in existing collaboration agreements and the likelihood of the receipt of milestone payments at subsidiaries. Additionally, the company reduced expected upfront payments from license agreements by JPY400mn, considering the certainty of milestone achievement. Operating expenses are expected to decrease by JPY1.1bn (-25.4%) compared to the previous projection. This reduction is driven by a combined JPY900mn decrease in clinical development expenses at the company and its subsidiary FIMECS Inc., partially offset by a JPY96mn increase resulting from a review of goodwill amortization.

The business model, competitive edges, and investment strategy remain unchanged.

Termination of the license agreement with Maruho for a selective sodium channel blocker
RaQualia Pharma announced that its Board of Directors, in a meeting held on December 13, 2024, resolved to terminate the licensing agreement with Maruho Co., Ltd. (unlisted) regarding a selective sodium channel blocker.

Reason for Termination

RaQualia and Maruho signed an exclusive licensing agreement on December 25, 2017, granting Maruho worldwide rights to develop, manufacture, and commercialize a selective sodium channel blocker developed by RaQualia, with sublicensing rights included. Maruho advanced the development of a therapeutic drug using this compound as the active ingredient. In March 2021, Maruho achieved a pre-determined milestone specified in the licensing agreement, and RaQualia received an upfront payment. Subsequently, Maruho continued development efforts; however, after discussions regarding the compound's future development, both companies mutually agreed to terminate the agreement.

Terms of Termination

With the termination of the agreement, RaQualia will regain the rights to develop, manufacture, and commercialize the compound and therapeutic drugs using the compound as the active ingredient, from Maruho. Additionally, RaQualia will obtain from Maruho the rights, data, information, and materials necessary to advance the development and commercialization of the compound and its related therapeutic drugs, including various data obtained from Maruho's development efforts. There will be no financial transactions associated with the termination of this agreement.

RaQualia plans to pursue licensing activities to secure a new partner using the rights, information, and materials obtained from Maruho to advance the commercialization of the compound. According to RaQualia, this matter will not impact the company's consolidated earnings forecast for FY12/24.

Launch of gastroesophageal reflux disease treatment, tegoprazan, in five Latin American countries

2024-12-12

RaQualia Pharma Inc. announced the launch of its gastroesophageal reflux disease (GERD) treatment, tegoprazan, in five Latin American countries.

The company licensed the rights to tegoprazan to HK inno.N Corporation (KOSDAQ:195940). Laboratorios Carnot (unlisted), a sublicensee of HK inno.N, launched tegoprazan in these markets.

Tegoprazan, developed by RaQualia, is a novel potassium-competitive acid blocker (P-CAB). It offers a distinct mechanism compared to traditional proton pump inhibitors (PPIs), which are typically the first treatment for GERD. Unlike PPIs, P-CABs inhibit gastric acid secretion more rapidly and sustainably, positioning them as a new generation of GERD therapy.

RaQualia has signed an exclusive license agreement with HK inno.N, granting HK inno.N sublicensing rights for the development, manufacture, and sale of tegoprazan worldwide, excluding Japan. Under this agreement, HK inno.N and its sublicensees are actively conducting business activities involving tegoprazan across various countries. In Latin America, HK inno.N has sublicensed tegoprazan to two companies, including Carnot, for commercialization in 18 countries.

Carnot launched tegoprazan under the brand name Ki-CAB® in Mexico and Peru in 2023, followed by launches in Chile and Colombia in September and October 2024. Ki-CAB® holds the third-largest market share in the peptic ulcer drug segment in Mexico, its initial launch market. In 2024, Carnot further expanded tegoprazan's presence with launches in the Dominican Republic, Nicaragua, Honduras, Guatemala, and El Salvador, bringing its total reach to 15 countries. Carnot actively markets Ki-CAB® across its territory, and RaQualia expects sales to continue growing.

Under the license agreement with HK inno.N, RaQualia will receive a percentage of the revenue generated by HK inno.N from Carnot's sales. However, the company will not receive a milestone payment from these launches. RaQualia anticipates that tegoprazan will contribute to medium- to long-term revenue growth and enhance corporate value.

Issuance of shares through third-party allotment

2024-12-04

RaQualia Pharma Inc. announced the issuance of shares through a third-party allotment to the directors of its subsidiary, FIMECS Inc.

The company resolved to issue new shares through a third-party allotment to Yusuke Tominari, CEO of FIMECS Inc., a subsidiary, and Kanae Gamo, CSO of FIMECS, during a meeting on December 4, 2024. The issuance aims to align the directors' medium- and long-term interests with those of shareholders by enhancing corporate value, stock value, and shared value. The allottees will pay the subscription amount and acquire 167,000 ordinary shares of RaQualia. The company and the allottees will execute a share allotment agreement, including provisions on share transfer restrictions and share transfer reservations.

Overview of issuance

Payment due date	December 20, 2024
Type and number of newly issued shares	167,000 ordinary shares of RaQualia
Issuance price per share	JPY478
Total issue price	JPY79,826,000
Planned allottees	Two directors of FIMECS

Source: Shared Research based on company data

In March 2024, RaQualia acquired all issued shares and share subscription rights of FIMECS Inc., making it a wholly owned subsidiary. FIMECS, a drug discovery startup, specializes in advancing R&D for new pharmaceuticals using targeted protein degradation inducers, a novel modality in drug discovery. Its proprietary Rappid Protein Proteolysis-Induced Discovery System (RaPPIDS™) significantly strengthens the group's core technology and supports business development. The two allottees are both founders, shareholders, and current directors of FIMECS, actively leading its operations.

The company intends to allocate the funds raised through this financing to drug discovery, the foundation of the group's business, with a focus on FIMECS' R&D. The use of funds and the scheduled payment date are as follows.

Use of fund raised	Amount (JPYmn)	Scheduled payment date
R&D for the RaPPIDS™ drug discovery platform technology of FIMECS	40	January–December 2025
R&D for existing and new programs of FIMECS	39	January–December 2025
Total	79	

Source: Shared Research based on company data

Launch of a ghrelin receptor agonist drug ELURA in Japan

2024-11-22

RaQualia Pharma Inc. announced the launch of ELURA, a ghrelin receptor agonist, in Japan.

On November 20, 2024, Elanco Japan K.K., a subsidiary of Elanco Animal Health Inc. (NYSE: ELAN, "Elanco"), launched ELURA® for cats in Japan. This product is based on the ghrelin receptor agonist capromorelin (RQ-00000005/AT-002), which the company out-licensed to Elanco. In October 2010, the company entered into a licensing agreement with Aratana Therapeutics Inc. (now Elanco), granting it global marketing rights for capromorelin as an animal therapeutic. Elanco has marketed the agonist as ENTYCE®, an anorexia treatment for dogs in the US, and as ELURA® and Eluracat®, a weight-loss management drug for cats with chronic diseases, in the US and Europe. With the launch of ELURA® in Japan, it is now available domestically as well.

ELURA® is the first selective ghrelin receptor agonist for cats, mimicking ghrelin, the hunger hormone that stimulates appetite. Chronic diseases in cats often lead to weight loss, negatively affecting energy levels, immune function, wound recovery, and survival. Appetite and weight loss caused by diseases also create significant stress for pet owners. ELURA®, the first veterinary drug developed to promote weight gain in cats suffering from appetite and weight loss due to chronic diseases, is expected to stimulate appetite and enhance metabolism to support weight gain.

The company will not receive a milestone payment from this launch, and therefore, the consolidated results for FY12/24 will remain unaffected. RaQualia anticipates that increased sales of ELURA® will contribute to medium- to long-term revenue growth and corporate value.

Syros discontinues Phase III clinical trials for treatment of myelodysplastic syndrome (MDS)

2024-11-13

RaQualia Pharma Inc. announced the results and subsequent plans for the ongoing Phase III clinical trial (SELECT-MDS-1 trial) targeting myelodysplastic syndrome (MDS). Syros Pharmaceuticals, Inc. (NASDAQ: SYRS, US), an out-licensee of RaQualia's subsidiary TMRC Co. Ltd., conducted the trial.

Tamibarotene (TM-411/SY-1425) is a selective agonist of the retinoic acid receptor alpha (RARα), specifically targeting its alpha subtype. In September 2015, TMRC signed a licensing agreement with Syros, granting it development and marketing rights for tamibarotene as an oncology treatment in North America and Europe. TMRC is entitled to receive milestone payments based on development progress and royalties following commercialization.

Syros is conducting a Phase III clinical trial of tamibarotene combined with azacitidine in higher-risk myelodysplastic syndrome (HR-MDS) patients with RARA gene overexpression. On November 12, 2024 (EST), Syros announced that the trial did not meet its primary endpoint of complete response (CR) rate and that it would discontinue the trial while reviewing the clinical data in detail to evaluate next steps. Syros also disclosed that the SELECT-MDS-1 trial's failure to meet the primary endpoint constitutes a default event under its secured loan agreement.

RaQualia expects this development to have a minimal impact on its consolidated earnings forecast for FY12/24 and does not plan to revise the full-year forecast announced on February 14, 2024. The company will consult closely with Syros to gather information, assess the medium- to long-term impact, and promptly announce any necessary revisions to its financial forecasts and plans upon determination.

Milestone payment received for development progress of the novel sodium channel blocker

2024-10-30

RaQualia Pharma Inc. announced that it received a milestone payment following the achievement of a pre-determined development target for a transdermal formulation containing the novel sodium channel blocker RQ-00350215, which it out-licensed to Hisamitsu Pharmaceutical Co., Inc. (TSE Prime: 4530).

RQ-00350215, a novel sodium channel blocker, selectively blocks the function of specific sodium channels involved in pain signal transmission. Hisamitsu is currently advancing clinical development of a transdermal formulation containing the compound.

In December 2021, the company entered into a licensing agreement granting Hisamitsu exclusive worldwide development, manufacturing, and marketing rights to the compound. The company received an upfront payment of JPY600mn and retains the rights to receive milestone payments based on development progress, in addition to sales royalties and sales-based

milestone payments. On this occasion, the company received a milestone payment of JPY100mn from Hisamitsu, which it will record as operating revenue in Q4 of FY12/24.

The company does not intend to revise its consolidated earnings forecast for FY12/24 at this time. If a revision becomes necessary, the company will promptly disclose it.

Helicobacter pylori eradication added to indications for tegoprazan in China

2024-10-22

RaQualia Pharma Inc. announced the addition of Helicobacter pylori infection as a new indication for the gastric acid secretion inhibitor tegoprazan in China.

Shandong Luoxin Pharmaceutical Group Stock Co., Ltd. (SHE: 002793, "Luoxin"), RaQualia's sublicensee in China, received marketing approval from the National Medical Products Administration to add Helicobacter pylori infection as an indication for tegoprazan (trade name in China: Tai Xin Zan®) in combined Helicobacter pylori eradication therapy. RaQualia out-licensed tegoprazan to HK inno.N (former CJ Healthcare Corporation; KOSDAQ: 195930) in South Korea, and Luoxin manufactures and sells the drug in China under a sublicense agreement with HK inno.N. This is the third indication approved in China, following erosive esophagitis and duodenal ulcers.

Tegoprazan is a gastric acid secretion inhibitor with a new mechanism of action, classified as a potassium-competitive acid blocker (P-CAB), developed by RaQualia. Characteristic of P-CABs is their suppression of gastric acid secretion through a mechanism that is different, faster and more persistent than proton pump inhibitors (PPIs), which are the first-line drugs for gastric acid secretion inhibition. According to Luoxin, studies indicate that the Helicobacter pylori infection rate in the Chinese population is high, ranging from 40% to 60%. As Helicobacter pylori contributes to diseases such as peptic ulcers and gastric cancer, Chinese and international guidelines recommend eradication therapy for confirmed cases.

In Helicobacter pylori eradication therapy, it is important to maintain a high pH level in the stomach and prevent a decrease in antibiotic activity. According to the company, the characteristics of P-CABs provide an advantage over PPIs in this regard. In a Phase III clinical trial in China, Luoxin's tegoprazan-containing bismuth-based quadruple therapy demonstrated an eradication rate of 93.5%, surpassing the 86.4% rate achieved by the esomeprazole-containing (a typical PPI) bismuth-based quadruple therapy.

Under the licensing agreement with HK inno.N, RaQualia has the right to receive a percentage of the revenue that HK inno.N earns from the sublicensee. Although RaQualia will not receive any upfront payments in connection with this matter, and the impact on the consolidated results for FY12/24 is expected to be immaterial, the company believes that the expanded use of tegoprazan in China will contribute to future sales growth and thus improve operating revenue and corporate value in the medium to long term.

Approval of GERD treatment tegoprazan in Malaysia

2024-09-26

RaQualia Pharma Inc. announced that its potassium-competitive acid blocker (P-CAB), tegoprazan, has received marketing approval in Malaysia.

The company stated that Pharmaniaga Logistics Sdn Bhd (KLSE: 7081), a sublicensee of HK inno.N Corporation (KOSDAQ: 195940), obtained marketing approval for tegoprazan from the National Pharmaceutical Regulatory Agency (NPRA) of Malaysia.

Tegoprazan, developed by RaQualia, represents a novel acid suppressant that operates via the P-CAB mechanism. Unlike proton pump inhibitors (PPIs), which are currently the first-line therapy for gastroesophageal reflux disease (GERD), P-CABs offer more rapid and sustained suppression of gastric acid secretion, providing a more advanced treatment option.

RaQualia holds an exclusive license agreement with HK inno.N, granting them sublicensing rights for the development, manufacture, and marketing of tegoprazan worldwide, excluding Japan. Under this agreement, HK inno.N and its sublicensees have been advancing the development and commercialization of tegoprazan, which is currently available in

nine countries, including South Korea, Mongolia, China, the Philippines, Indonesia, Singapore, Mexico, Peru, and Chile. Marketing preparations, regulatory approvals, and clinical trials are underway in 37 additional countries, including the US.

In Malaysia, HK inno.N entered into a product supply agreement with Pharmaniaga in 2021, and Pharmaniaga has since worked toward obtaining marketing approval. Following the regulatory review, the NPRA approved the marketing of tegoprazan for four indications: erosive esophagitis, non-erosive esophagitis, peptic ulcers, and as an adjunct therapy for the eradication of Helicobacter pylori. The product will be sold under the brand name K-CAB®, with sales scheduled to commence in 1H FY12/25.

The peptic ulcer market in Southeast Asia is valued at USD520mn (JPY72.0bn, at an exchange rate of JPY140/USD), with further growth anticipated. Tegoprazan is currently marketed in the Philippines, Singapore, and Indonesia, with regulatory reviews ongoing in Thailand and Vietnam. With the addition of Malaysia, the drug is expanding into the six largest markets in Southeast Asia.

Under the license agreement with HK inno.N, RaQualia has the right to receive a percentage of the revenue that HK inno.N earns from Pharmaniaga. The company expects no milestone payments from the approval in Malaysia. RaQualia believes that the expansion of tegoprazan's sales territories will contribute to operating revenue growth and enhance its corporate value over the medium to long term. The company remains committed to strengthening its collaboration with HK inno.N, supporting development and sublicense agreements, and expanding treatment options for acid-related disorders to improve quality of life for patients.

Issuance of stock options (share acquisition rights)

2024-09-13

Raqualia Pharma Inc. has decided to issue share acquisition rights as stock options.

At the Board of Directors meeting held on September 13, 2024, the company resolved to issue share acquisition rights as stock options to its employees and those of its subsidiaries, as detailed below. The stock options will be issued without charge, aiming to incentivize employees to drive earnings growth and enhance corporate value, and to promote value-sharing with shareholders. The company will finalize any undecided matters by the planned allocation date of September 30, 2024.

Overview

Type and number of shares	209,000 shares of the company's common stock
Allottees and the number of share acquisition rights to be allotted	66 employees of the company: 1,570 rights 21 employees of the company's subsidiaries: 520 rights
Allotment date	September 30, 2024
Exercise period	From September 14, 2026, to September 13, 2034

Approval of GERD Treatment tegoprazan in Colombia

2024-09-02

RaQualia Pharma Inc. announced the approval of its gastroesophageal reflux disease (GERD) treatment, tegoprazan, for sale in Colombia.

Laboratorios Carnot (unlisted), RaQualia's sublicensee, obtained marketing approval for tegoprazan from the Instituto Nacional de Vigilancia de Medicamentos y Alimentos (INVIMA), the Colombian regulatory authority. RaQualia has out-licensed tegoprazan, a gastric anti-secretory drug, to HK inno.N Corporation (KOSDAQ: 195940), which subsequently sublicensed it to Carnot.

Tegoprazan, developed by RaQualia, is a novel potassium-competitive acid blocker (P-CAB). It offers a distinct mechanism compared to traditional proton pump inhibitors (PPIs), which are typically the first treatment for GERD. Unlike PPIs, P-CABs inhibit gastric acid secretion more rapidly and sustainably, positioning them as a new generation of GERD therapy.

RaQualia has signed an exclusive license agreement with HK inno.N, granting HK inno.N sublicensing rights for the development, manufacture, and sale of tegoprazan worldwide, excluding Japan. Under this agreement, HK inno.N and its sublicensees are actively conducting business activities involving tegoprazan across various countries. In Latin America, HK inno.N has sublicensed tegoprazan to two companies, including Carnot, for commercialization in 18 countries.

With the approval from INVIMA, tegoprazan is now approved for sale in nine Latin American countries: Mexico, Peru, Chile, the Dominican Republic, Honduras, Nicaragua, Guatemala, El Salvador, and Colombia. Tegoprazan was launched under the brand name Ki-CAB® in Mexico and Peru in 2023 and in Chile in 2024. Carnot aims to commence sales in the remaining six approved countries within this year.

RaQualia reports that the market for ulcer drugs in the 17 Latin American countries where Carnot sells tegoprazan is approximately KRW574.0bn (approximately JPY63.1bn, converted at JPY0.11/KRW). To expand tegoprazan's reach in Latin America, HK inno.N and Carnot have been conducting intensive promotional activities, including hosting academic conferences for healthcare professionals. Tegoprazan has garnered significant attention, particularly in Mexico, where it is ranked top 10 anti-ulcer drugs within seven months of its launch and is expected to rank among the top five this year. The recent update to Mexico's gastroenterology guidelines, recommending P-CABs as a first treatment for GERD, is anticipated to further enhance tegoprazan's market presence in Latin America.

Under the license agreement with HK inno.N, RaQualia is set to receive a percentage of the revenue generated by HK inno.N from Carnot. Additionally, RaQualia will receive a lump sum payment from HK inno.N following the product launch in Colombia, which the company plans to recognize as operating revenue in Q3 FY12/24. RaQualia has already incorporated the impact of this approval into its full-year consolidated forecast for FY12/24, with no current plans to revise the full-year earnings forecast. However, should a revision become necessary, RaQualia will promptly disclose any changes.

Milestone payment received following the launch of Eluracat, a ghrelin receptor agonist by Elanco in France

2024-08-29

Raqualia Pharma Inc. announced that Elanco Animal Health Inc. (NYSE: ELAN) has notified them of the launch in France of Eluracat® (capromorelin/RQ-00000005/AT-002), a ghrelin receptor agonist, for treating weight loss in cats with chronic medical conditions. As a result of the launch of the product licensed to Elanco by Raqualia in France, the company has confirmed that it will receive a milestone payment.

This medication is an oral solution containing capromorelin, the active ingredient that mimics ghrelin, the hunger hormone responsible for stimulating appetite and promoting gastrointestinal motility. The weight gain in cats treated with this medication is believed to result from a combination of enhanced food intake and metabolic changes due to its mechanism of action. In the US, it has been marketed since 2021 under the product name Elura® for the management of weight loss in cats with chronic kidney disease. In Europe, Elanco secured manufacturing and marketing authorization for the drug in 2023 and had been preparing for its launch. Recently, Elanco released it in France under the product name Eluracat®. With the launch in France, this medication is now available in two countries. It has also received approval in Japan, the UK, other European countries, Brazil, and Canada, and the company anticipates further expansion into additional markets.

In 2010, the company entered into an out-licensing agreement with Aratana Therapeutics Inc. (now Elanco) for the global commercialization of capromorelin as a veterinary drug. As a result of this agreement, the company will receive a milestone payment of USD2mn, which will be recorded as operating revenue in Q3 FY12/24.

The company stated that it will not revise its earnings forecast for FY12/24, which was announced on February 14, 2024, at this time. However, if any changes become necessary, it will promptly disclose an updated forecast.

Syros suspends enrollment of new patients in clinical trials for AML in the US

2024-08-14

RaQualia Pharma Inc. announced today that Syros Pharmaceuticals, Inc. (NASDAQ: SYRS, "Syros"), a licensee of its consolidated subsidiary TMRC Co., Ltd., has decided to end the enrollment of new patients in its ongoing Phase II clinical trial of tamibarotene (TM-411/SY-1425), a retinoic acid receptor alpha (RAR alpha) agonist, for the treatment of acute myeloid leukemia (AML).

Tamibarotene, a selective activator of the RAR alpha subtype, which was licensed out by TMRC to Syros, exhibits strong differentiation-inducing activity and is expected to have synergistic effects when combined with other anti-tumor agents to enhance the effectiveness of anti-tumor therapies. Since September 2021, Syros has been conducting the SELECT-AML-1

Phase II clinical trial, a triplet regimen study involving venetoclax and azacitidine in patients with AML and RAR alpha positivity, including elderly patients and others for whom standard chemotherapy is unsuitable.

On August 9, 2024, an interim analysis of the SELECT-AML-1 trial was conducted using data from 51 patients. As a result of this analysis, which included a non-binding futility analysis, Syros decided to stop enrolling new patients, as the probability of demonstrating superiority in the final analysis with data from 80 patients was considered low. A futility analysis statistically predicts the outcome of a study based on prespecified hypotheses and evaluation criteria to determine whether the study should continue. Importantly, no new safety concerns were identified with tamibarotene in combination with venetoclax and azacitidine. Syros plans to present data from the SELECT-AML-1 study at the 12th annual meeting of the Society of Hematology and Oncology (SOHO) in September 2024.

Meanwhile, Syros is advancing its Phase III SELECT-MDS-1 trial of tamibarotene in combination only with azacitidine, the standard of care, the standard treatment for high-risk myelodysplastic syndrome (MDS) patients with RARA gene overexpression. The trial is progressing on schedule, with a futility analysis cleared in Q1 FY12/24 and pivotal CR data expected by mid-Q4.

In September 2015, TMRC entered into a license agreement granting Syros the rights to develop and commercialize tamibarotene for the treatment of cancer in North America and Europe, with the right to receive milestone payments and post-marketing royalties based on the development stage. According to the company, this agreement will have no impact on its full-year consolidated results for FY12/24.

Patent review in Japan for XIAP inhibitor (heterocyclic compound)

2024-07-22

RaQualia Pharma Inc. announced the receipt of notification for a Japanese substance patent application (application number: JP-A2020-534723) for a X-linked inhibitor of apoptosis (XIAP) inhibitor (heterocyclic compound) developed by its consolidated subsidiary, FIMECS, Inc.

A patent is granted when a country's patent office determines that an invention is worthy of a patent. Upon payment of the patent fee, the patent becomes registered in that country. The recently patented heterocyclic derivative is an XIAP inhibitor with a novel structure designed by FIMECS, that is expected to bind to XIAP, an E3 ligase, and exhibit antitumor activity. XIAP belongs to the inhibitor of apoptosis protein (IAP) family. XIAP is up-regulated in many cancers and is positively correlated with malignant transformation and poor prognosis. Therefore, inhibition of XIAP is expected to exhibit anti-cancer activity. XIAP is widely known as one of the E3 ligases, along with VHL and CRBN, that can be used as inducers of target protein degradation.

FIMECS focuses on techniques that induce target protein degradation by utilizing E3 ligase binding compounds. FIMECS is developing these inducers using this group of compounds.

This is the second patent issued to FIMECS, following the issuance of a patent in the US last year (application number: 17/263,580). Currently, similar patents have been filed or are pending in Europe, China, and other countries. The company expects FIMECS's intellectual property rights to continue to strengthen in the future.

The company does not expect this patent decision to impact its consolidated results for FY12/24. However, the company believes that the XIAP inhibitor (heterocyclic compound) for which the patent decision was issued will contribute to its corporate value in the medium to long term through future development and related activities.

Patent review in the US for Nav1.7 and Nav1.8 sodium channel blockers (heterocyclic derivatives)

2024-07-17

RaQualia Pharma Inc. has announced that it received a notice of patent review (a decision for patent grant) on the same day for its Nav1.7 and Nav1.8 sodium channel blockers (heterocyclic derivatives), which the company developed and were under review in the US (Application No. 17/417,182).

The heterocyclic derivatives that received this patent review are a novel group of compounds with blocking effects on Nav1.7 and Nav1.8 sodium channels, based on a new molecular framework different from those previously granted patents by the company. A patent review is an evaluation indicating that the patent office of the relevant country has determined that a patent should be granted for the applied invention. Upon payment of the patent fees, the patent is registered, and patent rights are created in the respective country. With this patent review, the company's intellectual property rights have been strengthened in the US.

Sodium channels are a type of ion channel predominantly expressed on the surface of the cell membrane in excitable cells such as muscle and nerve cells. They open in response to changes in membrane potential, selectively allowing sodium ions to pass into the cell. The opening of sodium channels generates action potentials, responsible for pain transmission in sensory nerves. To date, nine types (Nav1.1–Nav1.9) of sodium channels have been reported, and sodium channel blockers are anticipated to be therapeutic agents for various diseases, including pain.

The sodium channel blockers created by the company specifically target the Nav1.7 and Nav1.8 sodium channels and have demonstrated high efficacy in multiple animal models of pain. Furthermore, due to their good selectivity for the Nav1.5 sodium channel, which is critical for cardiac function, they are expected to be revolutionary new drugs capable of suppressing side effects in the cardiovascular system, thus meeting various medical needs.

According to the company, the patent review will have no impact on the financial results for FY12/24. The company believes that the heterocyclic derivatives that have received patent review will contribute to improving its corporate value over the medium to long term through future development.

Subsidiary FIMECS achieves initial milestone in joint research with Astellas Pharma and receives lump-sum payment

2024-05-13

RaQualia Pharma Inc. announced that its subsidiary, FIMECS Inc., has achieved an initial milestone in joint research with Astellas Pharma Inc. (TSE Prime: 4503). As a result, FIMECS will receive a lump-sum payment from Astellas.

In 2022, FIMECS signed a contract with Astellas for joint research on targeted protein degraders. Based on this contract, FIMECS has been collaborating with Astellas to discover protein degraders for multiple targets related to oncology, utilizing its proprietary RaPPIDS™ platform. The milestone achieved pertains to one specific program within this collaboration.

As a result of the milestone achievement, FIMECS will receive JPY200mn from Astellas, which will be recorded as operating revenue for Q2 FY12/24. Moving forward, both companies will accelerate the search for development compounds through further optimization by FIMECS and technological collaboration from Astellas. Should a development candidate be identified and lead to the commercialization of a new drug, FIMECS may receive more than JPY15bn in milestone payments based on the progress of development, regulatory approvals, and sales, as well as royalties in the single-digit percentage range of product sales.

RaQualia acquired all shares in FIMECS on March 26, 2024, making it a wholly-owned subsidiary. The impact of this event on the consolidated financial results for FY12/24 has been accounted for in the company's initial earnings forecast.

RaQualia's novel TRPM8 blocker enters Phase I trial in Australia

2024-05-08

RaQualia Pharma Inc. announced that its licensee, Xgene Pharmaceutical Co. Ltd., (headquartered in Hong Kong; unlisted) has announced the enrollment of the first subject in the Phase I clinical trial in Australia for a novel TRPM8 blocker.

In September 2021, RaQualia entered into an exclusive license agreement with Xgene to grant the exclusive rights for development, manufacturing, and sales of the TRPM8 blocker (RQ-00434739/XG2002) globally, excluding Japan.

TRPM8 is an ion channel expressed in peripheral sensory neurons and is highly expressed in various pain conditions and cancer cells. Preclinical studies conducted by Xgene have shown that this compound inhibits TRPM8 and exhibits significant analgesic effects while maintaining a favorable safety profile. Xgene is hopeful that this compound will serve as a potential treatment for various types of acute and chronic pain, including neuropathic pain such as migraine and diabetic pain. The Phase I clinical trial aims to evaluate the tolerability and pharmacokinetics of the compound in a dose-escalation study in healthy volunteers, providing essential information for subsequent clinical trials.

Based on the license agreement with Xgene, RaQualia has the right to receive milestone payments and royalties based on the product's sales after launch. There are no upfront payments associated with the initiation of the Phase I trial and it will not impact the financial results for FY12/24, but RaQualia believes that the development progress by Xgene will contribute to the long-term value enhancement of the compound.

Sublicensing of tegoprazan in the Middle East and North Africa

2024-04-24

RaQualia Pharma Inc. announced a sublicense agreement established between licensee HK inno.N of South Korea and Tabuk Pharmaceutical Manufacturing Company in Saudi Arabia. This agreement concerns the company's gastric acid secretion inhibitor, tegoprazan (marketed in South Korea under the brand name K-CAB®) and applies to the Middle East and North Africa region.

Tabuk Pharmaceutical, a leading pharmaceutical company in Saudi Arabia, distributes pharmaceuticals across 17 countries in the Middle East and North Africa. Through this agreement, Tabuk Pharmaceutical has acquired the rights to sell tegoprazan products in these regions. Due to Tabuk's strong market presence, RaQualia anticipates significant acceleration in the deployment of tegoprazan in this emerging market with high growth potential.

RaQualia has an exclusive license agreement (including sublicensing rights) with HK inno.N for the development, manufacture, and sale of tegoprazan worldwide, excluding Japan. Under this agreement, HK inno.N and sublicensees conduct business activities related to tegoprazan in various countries. The conclusion of this new sublicense agreement with Tabuk Pharmaceutical has enabled tegoprazan to be introduced into 46 countries. Currently, tegoprazan is marketed in eight countries: South Korea, China, the Philippines, Mongolia, Mexico, Indonesia, Singapore, and Peru. The drug has also received approval in Chile, the Dominican Republic, Honduras, and Nicaragua, with regulatory reviews underway in other Latin American countries. Clinical development is in progress in countries such as the US and Canada. HK inno.N aims to roll out tegoprazan to 100 countries worldwide by 2028.

Under its license agreement with HK inno.N, RaQualia has the right to receive a percentage of the revenue that HK inno.N earns through Tabuk Pharmaceutical. RaQualia will also receive a lump sum payment from HK inno.N as a result of the sublicense agreement, which it will recognize as operating revenue in Q2 FY12/24. The company has already incorporated the impact of this agreement into its full-year consolidated earnings forecast for FY12/24.

Other information

History

Feb 2008	Company established in Chita, Aichi to conduct R&D into pharmaceuticals
Jul 2008	Accompanying the closure of Pfizer's central research laboratory in Japan, RaQualia's business launched with the transfer of some employees and purchase of laboratory equipment
Sep 2010	Reached out-licensing agreement for marketing potassium-competitive acid blocker (P-CAB) in South Korea, China including Hong Kong, and Taiwan with South Korea's CJ CheilJedang Corporation (currently HK inno.N Corporation)
Dec 2010	Reached agreement to grant global rights to commercialize EP4 receptor antagonist and ghrelin receptor agonist as veterinary drugs to US-based Aratana Therapeutics Inc. (currently Elanco Animal Health Inc.)
Jul 2011	Listed shares on Osaka Securities Exchange JASDAQ Growth market (currently Tokyo Stock Exchange Growth)
Feb 2014	Signed agreement with Nagoya University to establish joint industry-academia research department
Sep 2014	Biological Research Department, Drug Discovery Research Division was moved to the premises of Nagoya University
Nov 2014	Signed out-licensing agreement with CJ HealthCare Corporation (currently HK inno.N Corporation) for marketing P-CAB in Southeast Asia
Aug 2015	Scientific Research Department, Drug Discovery Research Division was moved to the premises of Nagoya University
Jan 2017	Aratana Therapeutics, Inc. (currently Elanco Animal Health Inc.) began marketing EP4 receptor antagonist (GALLIPRANT®, pet drug) in the US
Dec 2017	Out-licensed selective sodium channel blocker to Maruho Co., Ltd.
Mar 2018	Signed out-licensing agreement with Asahi Kasei Pharma for P2X7 receptor antagonist targeting peripheral neuropathic pain
Mar 2019	CJ CheilJedang Corporation (currently HK inno.N Corporation) began marketing P-CAB (tegoprazan, K-CAB®) in South Korea
Mar 2019	Aratana Therapeutics, Inc. (currently Elanco Animal Health Inc.) began marketing ghrelin receptor agonist (ELURA®, pet drug) in the US
Nov 2019	Signed agreement with CJ CheilJedang Corporation (currently HK inno.N Corporation) on expanding global partnership
Sep 2021	Signed out-licensing agreement with Hong Kong-based Xgene Pharmaceutical Co. Ltd. covering TRPM8 blocker
Dec 2021	Signed out-licensing agreement with Hisamitsu Pharmaceutical Co., Inc., covering sodium channel blocker
Apr 2022	Listed on Growth market under new Tokyo Stock Exchange classifications
Mar 2024	Acquired all shares in FIMECS, Inc., making it a wholly owned consolidated subsidiary.

Source: Shared Research based on company data

Predecessor was Pfizer's central research laboratory in Japan

The company was established as an independent entity following the closure of Pfizer Inc.'s central research laboratory in Japan, part of a global research restructuring in 2007. Pfizer Inc. (NYSE: PFE), ranked third globally in pharmaceutical sales in 2023, allowed the research lab to spin off through an employee buyout. RaQualia was founded in July 2008, following the transfer of intellectual property rights from Pfizer in June 2008, covering multiple projects in the exploratory and development stages. Pfizer held 19% of the company's shares at its inception, but reduced its stake after the company's initial public offering (IPO), and as of end-December 2024 it held about 3.40%. When RaQualia out-licenses compounds originally transferred from Pfizer, it pays royalties to Pfizer, which are recorded under cost of operating revenue.

New R&D base established at Shonan iPark

The company conducts drug discovery research primarily at the RaQualia Industry-Academia Collaborative Research Center located on the premises of the Higashiyama Campus of Nagoya University. In January 2023, the company opened a new research center at Shonan Health Innovation Park (Fujisawa, Kanagawa Prefecture; Shonan iPark) and commenced research activities there. Established in April 2018, Shonan iPark is Japan's first pharma-led science park, where more than 2,000 people from over 150 companies and organizations (as of January 2023), including pharmaceutical companies, experts and researchers in next-generation medicine and AI, startups, and administrative agencies, form an ecosystem. The Park hosts a variety of networking events, and the company seeks opportunities to collaborate with companies conducting cutting-edge clinical trials or possessing advanced technologies for novel modalities, target search, and AI-driven drug discovery, further enhancing its drug discovery value chain and portfolio.

Top management and corporate governance

Form of organization and capital structure	
Form of organization	Company with Audit & Supervisory Committee
Controlling shareholder and parent company	None
Directors and Audit & Supervisory Committee members	
Number of directors under Articles of Incorporation	1200.00%
Number of directors	7
Directors' term of office under Articles of Incorporation	1 year
Chairperson of Board of Directors	President
Number of outside directors	4
Number of independent outside directors	3
Number of Audit & Supervisory Committee members under Articles of Incorporation	3
Number of Audit & Supervisory Committee members	3
Number of outside directors on Audit and Supervisory Committee	3
Other	
Participation in electronic voting platform	In place
Providing convocation notice in English	In place
Implementation of measures regarding director incentives	Performance-linked compensation system
Eligible for stock option	Employees
Disclosure of directors' compensation	None
Policy to determine amount and calculation method of remuneration	In place
Corporate takeover defenses	None

Source: Shared Research based on company data

Top management

At the ordinary general meeting of shareholders held in March 2021, a shareholder resolution for a management renewal put forth by current board member Yuichi Kakinuma (the largest shareholder with an 11% stake), was adopted with the approval an overwhelming majority (about 85%) of individual shareholders. Mr. Kakinuma had three concerns: that the company's initial forecast was lowered for three consecutive years starting in FY12/19, that the existing pipeline development program was halted, and that the company was unable to out-license its new pipeline. In addition, in 2017, former president Naoki Tani had pledged that the company would have a market capitalization of JPY100bn in 2020, but as of end-2020 it was significantly below this figure, at about JPY20bn.

In February 2025, the company announced the resignation of former Representative Director Hirofumi Takeuchi, with formal approval scheduled at the Annual General Meeting of Shareholders on March 25, 2025. Prior to this, in January 2025, Masaki Sudo was appointed as the new Representative Director. Sudo brings extensive experience and expertise in drug discovery research and has contributed to company-wide strategy formulation and execution as Director and Executive Officer in charge of corporate management. His responsibilities have included oversight of human resources, general affairs, medium-term management planning, and investor relations. He holds 21,247 shares of the company.

Representative Director: Masaki Sudo (born in July 29, 1971)

1996	Apr	Joined Teijin Ltd.
1999	Sep	Pfizer Japan (current Pfizer Japan Inc.) Joined
2004	Apr	Senior Research Scientist, Department of Chemical Research, Central Research Laboratories, Pfizer Japan
2006	Apr	Principal Research Scientist, Department of Chemical Research, Central Research Laboratories, Pfizer Japan
2008	Jul	Principal Researcher, Department of Research, the company
2012	Oct	Executive officer, Chemical Research division, Drug Discovery department, the company
2016	Apr	Associate Professor (special appointment), Institute of Transformative Bio-Molecules, Nagoya University
2018	Jul	Visiting Professor, Nagoya University
	Jul	Head of Business Planning Office, Stem Cell & Device Laboratory,
2020	Jan	General Manager, Business Development Department, Stem Cell & Device Laboratory, Inc.
2021	Jun	Stem Cell & Device Laboratory, Inc. as General Manager, Business Strategy Department, the company
	Oct	Executive Officer (administration and management), the company
2022	Mar	Director, the company
2023	Apr	Executive Officer, the company (management)
2024	Mar	Director, TMRC Co., Ltd. (current)
2025	Jan	Representative Director, the company (current)

Source: Shared Research based on company data

Corporate governance

RaQualia Pharma employs a company with Audit & Supervisory Committee structure, and has a board of directors, an Audit & Supervisory Committee, and a corporate internal audit office. The board of directors has seven members (including four outside directors). To strengthen the board's monitoring functions, the company chooses outside board members who are

familiar with the pharmaceutical industry and corporate management. Furthermore, the company has an executive officer system to separate the management and execution functions and strengthen and invigorate execution.
In March 2023, the company established a nomination and remuneration committee to enhance the fairness, transparency, and objectivity of procedures related to the nomination and remuneration of directors and strengthen corporate governance.

Dividends

The company sees returning profits to shareholders as an important management issue, but it has continued to make upfront investments since its establishment and recorded net losses, so has not yet paid a dividend. In FY12/21, it posted operating profit for the first time and will consider paying a dividend in the future if it is able to maintain business profits, depending on the strength of its financial position.

Top shareholders

Top shareholders	Shares held (shares)	Shareholding ratio
Yuichi Kakinuma	2,384,700	10.92%
Pfizer Japan Inc.	743,000	3.40%
BOFAS INC SEGREGATION ACCOUNT (Standing proxy: BofA Securities Japan Co., Ltd.)	687,579	3.15%
Ueda Yagi Tanshi Co., Ltd.	286,000	1.31%
The Tokyo Tanshi Co., Ltd.	270,200	1.24%
Chen Yuan	258,000	1.18%
SBC Co., Ltd.	237,000	1.09%
Advanced Media, Inc.	223,800	1.02%
Kazunari Ono	199,500	0.91%
Takahiro Tanago	177,900	0.81%
SUM	5,467,679	25.03%

Source: Shared Research based on company data (as of December 31, 2024)
Note: Shareholding ratio is calculated excluding 181 treasury shares.

The company reported 21,838,529 issued shares as of end-December 2024.

Number of employees

	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24
Number of employees (consolidated)	-	-	60	63	68	70	67	65	67	85
Number of employees (parent)	64	50	55	58	62	64	62	62	64	64
Average age	44.1	44.8	45.5	45.5	46.3	47.3	46.5	47.5	46.4	48.2
Average years of service	5.9	6.6	7.0	6.9	7.4	8.1	8.7	10.7	8.9	10.4
Average annual salary (JPY'000)	8,124	7,242	7,391	7,408	7,237	7,510	7,369	7,033	7,264	

Source: Shared Research based on company data; omissions reflect undisclosed data.

In FY12/24, consolidated employees increased following the consolidation of FIMECS in March 2024. Roughly 50 of the parent's 64 employees were involved in research and development, and over 10 were involved in out-licensing and other business development and management duties. Female accounted for 4.7% of management positions.

Profile

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Established

2008-02-19

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Listed On

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Exchange Listing

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Fiscal Year-End

Dec

About Shared Research Inc.

We offer corporate clients comprehensive report coverage, a service that allows them to better inform investors and other stakeholders by presenting a continuously updated third-party view of business fundamentals, independent of investment biases. Shared Research can be found on the web at https://sharedresearch.jp.

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