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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 uses 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 is involved from exploratory research through the early clinical development stage (Phase II clinical trials). It develops new drugs targeting a wide range of fields including pain, gastrointestinal disorders, cancer, and immunological disorders. The company receives revenue from companies that in-license its products in the form of upfront payments, milestone payments, and post-launch royalties, as well as 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 FY12/21, revenue was JPY2.8bn, comprising royalty revenue (over 50%) and upfront and milestone payments (over 40%).

The company got its start as an independent entity when US-based Pfizer Inc. (NYSE: PFE) 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 the company was established in July 2008, after Pfizer transferred it 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 record them under operating expenses.

RaQualia has four products already commercialized by licensees (tegoprazan [launched as K-CAB® in South Korea], GALLIPRANT®, ENTYCE®, and ELURA®), 10 pipelines already out-licensed, and six 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)**. 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 CheilJedang Corporation (currently HK inno.N Corporation [KOSDAQ]). Since 2019, it has gradually expanded the territories covered, and has granted global rights excluding Japan to HK inno.N, which has launched K-CAB® in South Korea and aims to roll out the drug to 100 countries around the world by 2028. In April 2022, a sublicensee of HK inno.N launched tegoprazan in China, and sublicensees have also received approval in Mongolia and the Philippines, and are preparing for marketing.

* 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.
** 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.

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 plans 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 territories excluding Japan by FY12/21. The company is preparing to launch clinical pharmacological studies (equivalent to Phase I), which it intends to complete in FY12/23. It hopes to out-license tegoprazan in FY12/24, and is looking for a licensee. 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 complete preclinical studies by end-2023.

The company adopted a new management structure in March 2021 and expanded its disease coverage from pain and gastrointestinal diseases to include neurological diseases. As of FY12/22, it plans to focus 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 it difficult to find a licensing partner, 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)**.

* 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.
** Proof of concept (POC): The hypothesis (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, and there is a tendency for life-threatening side effects 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 just 5% of all drugs. RaQualia says it is the only company in the world to have out-licensed five drugs in the area.

Earnings trends

In FY12/21, revenue was JPY2.8bn (+150.7% YoY), operating profit JPY708mn (loss of JPY486mn in FY12/20), recurring profit JPY864mn (loss of JPY527mn), and net income attributable to owners of the parent JPY756mn (net loss of JPY607mn). Sales of GERD treatment tegoprazan (out-licensed to HK inno.N and sold under the brand name K-CAB®) grew, and sales of pet drugs by Elanco Animal Health (GALLIPRANT®, ENTYCE®, and ELURA®) were solid. In addition to strong royalty revenue from the above four commercialized drugs, the company received milestone payments for out-licensed programs and upfront payments from new license agreements, booking its first operating profit since its establishment in 2008.

The company made an upward revision to its FY12/22 earnings forecast on November 17, 2022. The revised forecast for FY12/22 calls for revenue of JPY3.1bn (+10.8% YoY), operating profit of JPY824mn (+16.4% YoY), recurring profit of JPY909mn (+5.2% YoY), and net income attributable to owners of the parent JPY724mn (-4.2% YoY). Taking probability of achievement into account, RaQualia assumed in its initial forecast that entry of the P2X7 receptor antagonist into Phase II clinical trials would generate milestone revenue of JPY250mn each in FY12/22 and FY12/23. RaQualia's revised forecast for FY12/22 assumes the entire USD4mn (JPY500mn) will be booked in FY12/22 and also factors in a JPY147mn boost from yen depreciation. The company revised its exchange rate assumption from JPY125/USD to JPY135/USD.

When revising its full-year FY12/22 earnings forecast on November 17, 2022, the company also made further revisions to its three-year medium-term business plan covering FY12/22 to FY12/24, citing as reason changes in its business climate and business progress. The revised plan targets FY12/24 revenue of JPY3.8bn (three-year CAGR of 10.6%), operating profit of JPY1.3bn (20.8%), recurring profit of JPY1.2bn (12.7%), and net income attributable to owners of the parent JPY990mn (9.4%). The lower growth rates from the recurring profit line down compared to projected operating profit growth reflect a JPY146mn forex gain in FY12/21. As the main reasons for the revision, RaQualia cited changes in projected milestone revenue in FY12/22 and FY12/23, and the impact of revising its exchange rate assumption from JPY125/USD to JPY135/USD to factor in recent exchange rates.

Strengths and weaknesses

Shared Research thinks the company has the following three strengths.

- Focus on ion channel drug discovery based on research processes and operating procedures on par with pharmaceutical companies
- Several hundred patents held
- Ability to efficiently identify candidate compounds from its massive compound library using SCARA robotic system

We think it has the following three weaknesses.

- 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.

- Lack of control over amount or timing of revenue, because milestone and royalty payments depend on development progress and earnings at licensees
- Difficulty in recruiting and training researchers due to high degree of specialization

Key financial data

Income statement	FY12/12	FY12/13	FY12/14	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22
(JPYmn)	Non-cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Est.
Operating revenue	**29**	**228**	**154**	**146**	**705**	**1,419**	**745**	**1,703**	**1,107**	**2,776**	**3,075**
YoY	-95.8%	687.0%	-32.5%	-5.5%	384.7%	101.2%	-47.5%	128.7%	-35.0%	150.7%	10.8%
Operating expenses	**2,666**	**2,366**	**2,276**	**2,010**	**1,465**	**1,570**	**1,820**	**1,719**	**1,593**	**2,068**	**2,251**
YoY	2.5%	-11.2%	-3.8%	-11.7%	-27.1%	7.1%	15.9%	-5.5%	-7.3%	29.8%	8.8%
Operating profit	**-2,637**	**-2,138**	**-2,123**	**-1,865**	**-760**	**-150**	**-1,075**	**-16**	**-486**	**708**	**824**
YoY	-	-	-	-	-	-	-	-	-	-	16.4%
Operating profit margin	-	-	-	-	-	-	-	-	-	25.5%	26.8%
Recurring profit	**-2,891**	**-1,820**	**-1,942**	**-1,795**	**-721**	**-81**	**-1,065**	**22**	**-528**	**864**	**909**
YoY	-	-	-	-	-	-	-	-	-	-	5.2%
Recurring profit margin	-	-	-	-	-	-	-	1.3%	-	31.1%	29.6%
Net income	**-2,905**	**-1,108**	**-465**	**-1,854**	**-728**	**-58**	**-1,105**	**5**	**-607**	**756**	**724**
YoY	-	-	-	-	-	-	-	-	-	-	-4.2%
Net margin	-	-	-	-	-	-	-	0.3%	-	27.2%	23.5%
Per-share data (split-adjusted; JPY)											
Shares issued at year-end (000 shares)	13,267	13,557	14,857	18,767	18,767	20,295	20,388	20,950	20,952	20,955	
EPS (JPY)	-219.0	-82.7	-45.7	-116.5	-38.8	-3.0	-54.2	0.3	-29.0	36.1	34.6
EPS (fully diluted; JPY)	-	-	-	-	-	-	-	0.3	-	36.0	
Dividend per share (JPY)	-	-	-	-	-	-	-	-	-	-	-
Book value per share (JPY)	400	424	315	240	201	240	189	220	191	228	
Balance sheet (JPYmn)											
Cash and cash equivalents	4,890	4,035	1,891	1,840	1,428	2,268	1,671	2,174	1,394	2,345	
Total current assets	**5,090**	**4,364**	**3,261**	**2,708**	**1,806**	**3,322**	**1,962**	**3,067**	**2,834**	**4,004**	
Tangible fixed assets	101	7	85	261	249	216	318	249	333	299	
Investments and other assets	289	2,266	1,844	1,769	1,951	1,516	1,738	1,488	1,051	897	
Intangible assets	21	12	12	14	13	10	34	32	33	34	
Total assets	**5,501**	**6,648**	**5,202**	**4,752**	**4,019**	**5,064**	**4,052**	**4,837**	**4,251**	**5,234**	
Short-term debt	-	-	-	-	-	-	1	1	18	22	
Total current liabilities	**183**	**233**	**262**	**200**	**190**	**149**	**164**	**183**	**187**	**401**	
Long-term debt	-	-	-	-	-	-	2	2	27	18	
Total fixed liabilities	**7**	**669**	**109**	**38**	**41**	**27**	**31**	**33**	**53**	**46**	
Total liabilities	**191**	**902**	**371**	**238**	**231**	**176**	**195**	**216**	**240**	**446**	
Shareholders' equity	5,310	5,713	4,821	4,503	3,773	4,871	3,845	4,608	3,999	4,777	
Total net assets	**5,310**	**5,746**	**4,831**	**4,514**	**3,788**	**4,888**	**3,857**	**4,621**	**4,011**	**4,788**	
Total interest-bearing debt	-	-	-	-	-	-	3	2	46	39	
Cash flow statement (JPYmn)											
Cash flows from operating activities	-2,729	-2,179	-2,081	-2,117	-681	-307	-404	-531	-289	366	
Cash flows from investing activities	3,741	952	-796	666	-441	534	-368	216	225	-279	
Cash flows from financing activities	-	309	762	1,702	-	1,007	99	696	-7	-16	
Financial ratios											
ROA (RP-based)	-41.7%	-30.0%	-32.8%	-36.1%	-16.4%	-1.8%	-23.4%	0.5%	-11.6%	18.2%	
ROE	-43.1%	-20.1%	-8.8%	-39.8%	-17.6%	-1.3%	-25.3%	0.1%	-14.1%	17.2%	
Equity ratio	96.5%	85.9%	92.7%	94.8%	93.9%	96.2%	94.9%	95.3%	94.1%	91.3%	

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

Joint research agreement with DWTI; progress in clinical trials of tamibarotene in AML patients being conducted by Syros (US) and development plans going forward

2022-12-12

On December 12, 2022, Raqualia Pharma Inc. announced the signing of a joint research agreement with D. Western Therapeutics Institute, Inc.

The company and D. Western Therapeutics Institute (TSE Growth: 4576, "DWTI") will utilize each other's technologies, resources, and know-hows in pharmaceutical R&D in joint research aimed at discovery and development of therapeutic agents for specific optic nerve disorders.

In the joint research, the company will draw on its ion channel drug discovery technology to synthesize a group of compounds that target specific ion channels ("the group of compounds"). DWTI, on the other hand, will utilize its evaluation technology in the field of ophthalmology to verify the potential of the group of compounds as therapeutic agents for eye diseases through pharmacological tests and other methods. Technological achievements and intellectual properties obtained from the joint research will be jointly owned by the company and DWTI, and even after the conclusion of the joint research, the two companies will hold discussions with an eye to the next stage of collaboration.

The company says this development will have only a marginal impact on its FY12/22 earnings, and hence it made no change to its earnings forecast. In the longer term, however, the company believes the joint research with DWTI will contribute to enhancing its R&D portfolio and fortifying its development pipeline.

On the same day, the company announced progress in clinical trials of tamibarotene in acute myeloid leukemia patients being conducted by Syros Pharmaceuticals Inc. (US) and development plans going forward.

Tamibarotene is a selective retinoic acid receptor alpha (RARα) agonist, that, due to its exhibition of strong differentiation-inducing activity, is expected to have a synergistic effect when used in combination with other antitumor agents. Consolidated subsidiary TMRC Co., Ltd. out-licensed RARα agonist (tamibarotene) to Syros Pharmaceuticals Inc. (NASDAQ: SRY, "Syros"). Syros is currently conducting clinical trials of the study compound in myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) patients in the US.

Syros commenced a Phase II clinical trial of tamibarotene + venetoclax + azacitidine three-drug combination therapy in RARα-positive newly diagnosed unfit AML patients (patients who are not suitable for standard chemotherapy, e.g., the elderly). Syros recently presented data from the safety lead-in part of the Phase II study at the 64th American Society of Hematology (ASH) Annual Meeting. According to Syros, the results of the study suggested that the use of tamibarotene in combination with existing standard of care can improve outcomes for approximately 30% of AML patients who are positive for RARα overexpression, and demonstrated 83% composite complete response rate*. Syros also announced that based on the data obtained, it will advance the study to the randomized part*2. The randomized part of the study is scheduled to commence in Q1 FY12/23, with data expected in 2023 or 2024.

TMRC entered into a license agreement with Syros in September 2015, granting Syros development and marketing rights to tamibarotene in North America and Europe. Based on the terms of the agreement, TMRC is entitled to receive milestone payments in accordance with development progress and royalties after tamibarotene is launched. The progress in clinical studies in AML patients outlined above will not trigger any one-time payment, and hence the company made no change to its consolidated earnings forecast for FY12/22. That being said, the company believes the progress will lead to enhancing the value of tamibarotene in the longer term.

*Composite complete response rate: total of complete response (CR) rate and CR with incomplete hematologic recovery (CRi) rate
*2In a randomized trial, trial subjects are randomly assigned to two or more groups using a method that is not associated with any specific intention, and the effects of treatment, etc. are verified. Also called randomized controlled trial or randomized control trial.

The start of a Phase II clinical trial on a P2X7 receptor antagonist and accompanying receipt of an upfront payment from Asahi Kasei Pharma; revisions to items related to its business plan and growth potential; revisions to consolidated earnings forecast for full-year FY12/22

2022-11-18

On November 17, 2022, RaQualia Pharma Inc. announced the start of a Phase II clinical trial on a P2X7 receptor antagonist and accompanying receipt of an upfront payment from Asahi Kasei Pharma.

In March 2018, RaQualia entered into a license agreement with Asahi Kasei Pharma Corporation (unlisted; subsidiary of Asahi Kasei [TSE Prime: 3407]) for a novel P2X7 receptor antagonist (RQ-00466479). Eli Lilly (NYSE LLY), with whom Asahi Kasei Pharma in turn has a license agreement, has initiated a Phase II clinical study in patients with chronic pain, signifying that a milestone has been met. With this, RaQualia will receive a USD4mn (JPY500mn) milestone payment from Asahi Kasei Pharma, which will be booked as operating revenue in Q4 FY12/22.

Under the terms of its license agreement with Asahi Kasei Pharma, RaQualia receives milestone payments corresponding to stages of development for the P2X7 receptor antagonist, and royalty payments in proportion to sales amounts after launch.

On the same day, RaQualia announced revisions to items related to its business plan and growth potential.

Based on recent changes in its business climate and business progress, the company revised its business plan as follows. As the main reasons for the revision, RaQualia cited changes in projected milestone revenue in FY12/22 and FY12/23, and the impact of revising its exchange rate assumption from JPY125/USD to JPY135/USD to factor in recent exchange rates.

	FY12/21	FY12/22	FY12/23	FY12/24	FY12/23	FY12/24	3-year
(JPYmn)	Cons.	Revised forecast	Previous target	Previous target	Revised target	Revised target	CAGR
Operating revenue	**2,776**	**3,075**	**3,069**	**3,645**	**2,957**	**3,752**	
YoY	150.7%	10.8%	-0.2%	18.8%	-3.6%	26.9%	10.6%
Operating expenses	**2,068**	**2,251**	**2,675**	**2,478**	**2,691**	**2,504**	
YoY	29.8%	8.8%	18.8%	-7.4%	0.6%	-6.9%	6.6%
Operating expense ratio	74.5%	73.2%	87.2%	68.0%	91.0%	66.7%	
Operating profit	**708**	**824**	**393**	**1,167**	**266**	**1,248**	
YoY	-	16.4%	-52.3%	196.9%	-32.3%	369.2%	20.8%
Operating profit margin	25.5%	26.8%	12.8%	32.0%	9.0%	33.3%	
Recurring profit	**864**	**909**	**403**	**1,174**	**256**	**1,238**	
YoY	-	5.2%	-55.7%	191.3%	-36.5%	383.6%	12.7%
Recurring profit margin	31.1%	29.6%	13.1%	32.2%	8.7%	33.0%	
Net income	**756**	**724**	**327**	**970**	**204**	**990**	
YoY	-	-4.2%	-54.8%	196.6%	-37.6%	385.3%	9.4%
Net margin	27.2%	23.5%	10.7%	26.6%	6.9%	26.4%	

Source: Shared Research based on company data

RaQualia also announced revisions to its consolidated earnings forecast for full-year FY12/22.

Revisions to full-year FY12/22 forecast

- Revenue: JPY3.1bn (+10.8% YoY, previous forecast was JPY2.6bn)
- Operating expenses: JPY2.3bn (+8.8% YoY, JPY2.2bn)
- Operating profit: JPY824mn (+16.4% YoY, JPY420mn)
- Recurring profit: JPY909mn (+5.2% YoY, JPY420mn)
- Net income attributable to owners of the parent: JPY724mn (-4.2% YoY, JPY342mn)
- Earnings per share: JPY34.55 (JPY16.34)

Reasons for revisions

Taking probability of achievement into account, RaQualia assumed in its initial forecast that entry of the P2X7 receptor antagonist into Phase II clinical trials would generate milestone revenue of JPY250mn each in FY12/22 and FY12/23. RaQualia's revised forecast for FY12/22 assumes the entire USD4mn (JPY500mn) will be booked in FY12/22 and also factors in a JPY147mn boost from yen depreciation. The company revised its exchange rate assumption from JPY125/USD to JPY135/USD.

Phase III study of GERD treatment tegoprazan commences in the US

2022-10-21

On October 20, 2022, Raqualia Pharma Inc. announced the commencement of a Phase III clinical trial of tegoprazan, a drug indicated for gastroesophageal reflux disease (GERD), in the US.

The company announced that US-based Braintree Laboratories, Inc. (unlisted; hereafter "Braintree"), a sub-licensee of HK inno.N to which the company out-licensed GERD treatment tegoprazan (being marketed under the band name K-CAB® in South Korea), initiated a Phase III study of tegoprazan in patients with erosive esophagitis and non-erosive reflux disease (NERD).

HK inno.N signed a sublicensing agreement with Braintree in December 2021, and since then, Braintree has worked toward conducting late stage clinical trials. Before initiating the Phase III study, Braintree consulted with the US Food and Drug Administration (FDA) and obtained the agency's approval to skip Phase II and proceed straight to the Phase III study. Patients were enrolled in the Phase III study according to the FDA-approved clinical trial protocol, and the first patient has been dosed.

In the Phase III study, proton pump inhibitors (PPIs) will be used as control drugs to evaluate the efficacy and safety of tegoprazan. The company believes that the commencement of the Phase III study without conducting a Phase II study is significant in that it can lead to shortening of the clinical development period, and accordingly shorten the time required to launch the drug in the US.

According to the company, the US market for peptic ulcer drugs is one of the largest in the world, valued at roughly JPY400bn (as of 2021). In the US, P-CABs (potassium-competitive acid blockers) are currently not being marketed, and PPIs are primarily used to treat GERD. In terms of P-CAB competitor drugs, VOQUENZA™ (generic name: vonopurazan) was approved as a treatment for helicobacter pylori infection in 2022.

Based on the licensing agreement with HK inno.N, the company is entitled to milestone payments based on development progress of tegoprazan in the US and a predetermined percentage of the drug's sales in the country as royalties. While Raqualia will receive no one-off payment as a result of the commencement of the Phase III study, the company believes that if the study does lead to shortening of the time required to launch tegoprazan in the US, it will contribute to expanding the company's earnings in the medium to long term. This development will have no impact on the company's earnings forecast for FY12/22.

Marketing approval in Indonesia for GERD treatment tegoprazan

2022-10-13

On October 12, 2022, RaQualia Pharma Inc. announced marketing approval in Indonesia for tegoprazan, a treatment for gastroesophageal reflux disease (GERD).

RaQualia Pharma has out-licensed its GERD treatment tegoprazan to South Korea's HK inno.N Corporation, which markets the drug as K-CAB and has sublicensed it to Indonesia's PT Kalbe Pharma Tbk. Kalbe has obtained marketing approval for tegoprazan from the Indonesian National Agency of Drug and Food Control (NADFC), for the indication of non-erosive GERD. This makes Indonesia the fifth nation to issue approval, following South Korea, Mongolia, China, and the Philippines.

RaQualia had entered into a licensing agreement with HK inno.N, granting it an exclusive license with sublicensing rights for development, sales, and manufacturing of tegoprazan. HK inno.N has been marketing tegoprazan as K-CAB since 2019, and in 2021 the drug generated South Korean domestic sales (out-of-hospital prescription) of KRW109.6bn (about JPY10.96bn at JPY0.1/KRW), affording it the No. 1 market share for gastric ulcer drugs in South Korea.

In Indonesia, HK Inno.N entered into a sublicensing agreement with Kalbe in 2019, since which time Kalbe has been working to obtain marketing approval. According to HK Inno.N, the Indonesian market for gastric ulcer drugs was worth approximately USD170mn (about JPY21.3bn at JPY125/USD), making it the 19th largest market in the world.

Based on its licensing agreement with HK Inno.N, RaQualia is entitled to receive a certain percentage of the revenue that HK Inno.N receives from Kalbe. With this approval for tegoprazan in Indonesia, the company received a one-time payment

from HK Inno.N, which will be recorded as operating revenue for Q4 FY12/22. At this juncture, there is no change to RaQualia's full-year consolidated earnings forecast for FY12/22.

Trends and outlook

Quarterly trends and results

Earnings (cumulative)	FY12/20				FY12/21				FY12/22			FY12/22	
(JPYmn)	Q1	Q1–Q2	Q1–Q3	Q1–Q4	Q1	Q1–Q2	Q1–Q3	Q1–Q4	Q1	Q1–Q2	Q1–Q3	% of Est.	FY Est.
Operating revenue	124	373	574	1,107	656	1,321	1,623	2,776	339	1,447	1,904	61.9%	3,075
YoY	-64.5%	-31.7%	-19.0%	-35.0%	430.7%	254.3%	183.0%	150.7%	-48.3%	9.6%	17.3%		10.8%
Operating expenses	397	776	1,174	1,593	507	1,006	1,516	2,068	459	896	1,403	62.3%	2,251
YoY	-12.2%	-8.5%	-5.5%	-7.3%	27.6%	29.6%	29.1%	29.8%	-9.4%	-10.9%	-7.4%		8.8%
Operating expense ratio	321.3%	208.3%	204.7%	143.9%	77.3%	76.2%	93.4%	74.5%	135.3%	61.9%	73.7%		
R&D expenses	224	451	675	932	256	497	781	1,127	264	528	840		
YoY	6.7%	4.8%	5.7%	7.9%	14.4%	10.2%	15.6%	20.9%	3.0%	6.4%	7.6%		
R&D expense ratio	181.1%	120.9%	117.7%	84.2%	39.0%	37.6%	48.1%	40.6%	77.7%	36.5%	44.1%		
Operating profit	-273	-403	-601	-486	149	315	107	708	-120	551	501	60.8%	824
YoY	-	-	-	-	-	-	-	-	-	75.1%	367.6%		16.4%
Operating profit margin	-	-	-	-	22.7%	23.8%	6.6%	25.5%	-	38.1%	26.3%		26.8%
Recurring profit	-268	-403	-615	-528	268	433	238	864	-70	681	676	74.4%	909
YoY	-	-	-	-	-	-	-	-	-	57.4%	183.8%		5.2%
Recurring profit margin	-	-	-	-	40.9%	32.8%	14.7%	31.1%	-	47.1%	35.5%		29.6%
Net income	-328	-459	-699	-607	189	303	169	756	-121	469	467	64.5%	724
YoY	-	-	-	-	-	-	-	-	-	55.0%	175.9%		-4.2%
Net margin	-	-	-	-	28.8%	22.9%	10.4%	27.2%	-	32.4%	24.5%		23.5%
Earnings (quarterly)	**FY12/20**				**FY12/21**				**FY12/22**				
(JPYmn)	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**		
Operating revenue	124	249	201	534	656	665	302	1,153	339	1,108	457		
YoY	-64.5%	26.0%	23.6%	-46.3%	430.7%	166.9%	50.6%	116.0%	-48.3%	66.6%	51.1%		
Operating expenses	397	379	398	419	507	499	510	552	459	437	507		
YoY	157.7%	183.8%	165.0%	172.2%	27.6%	31.6%	28.2%	31.8%	-9.4%	-12.5%	-0.6%		
Operating expense ratio	321.3%	152.2%	198.2%	78.5%	77.3%	75.0%	168.7%	47.9%	135.3%	39.4%	111.0%		
R&D expenses	224	227	224	257	256	241	284	347	264	265	312		
YoY	6.7%	2.9%	7.5%	14.2%	14.4%	6.0%	26.6%	34.7%	3.0%	10.0%	9.8%		
R&D expense ratio	181.1%	91.1%	111.7%	48.2%	39.0%	36.2%	93.9%	30.1%	77.7%	23.9%	68.2%		
Operating profit	-273	-130	-197	115	149	166	-208	601	-120	671	-50		
YoY	162.3%	-34.4%	-14.7%	-77.9%	-	-	-	423.7%	-	304.5%	-		
Operating profit margin	-	-	-	21.5%	22.7%	25.0%	-	52.1%	-	60.6%	-		
Recurring profit	-268	-135	-213	88	268	165	-195	626	-70	751	-5		
YoY	180.9%	-36.5%	-3.5%	-84.2%	-	-	-	614.1%	-	356.5%	-		
Recurring profit margin	-	-	-	16.4%	40.9%	24.8%	-	54.3%	-	67.8%	-		
Net income	-328	-131	-239	92	189	114	-133	586	-121	590	-2		
YoY	218.8%	-36.6%	7.8%	-82.9%	-	-	-	539.8%	-	416.8%	-		
Net margin	-	-	-	17.2%	28.8%	17.2%	-	50.9%	-	53.3%	-		

Source: Shared Research based on company data

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

Q3 FY12/22 results (out November 11, 2022)

Earnings summary

Q3 FY12/22 (January–September 2022) results

- Revenue: JPY1.9bn (+17.3% YoY)
- Operating profit: JPY501mn (+367.6% YoY)
- Recurring profit: JPY676mn (+183.8% YoY)
- Net income attributable to owners of the parent: JPY467mn (+175.9% YoY)
- R&D expenses: JPY840mn (+7.6% YoY)

Progress against the company's full-year FY12/22 forecast was revenue 73.1%, operating profit 119.3%, recurring profit 161.1%, and net income 136.6%. Operating expenses fell 7.4% YoY to JPY1.4bn, with R&D expenses up JPY60mn (+7.6%) YoY at JPY840mn but other SG&A expenses down 15.3% YoY at JPY395mn. R&D spend amounted to 57.0% of the full-year forecast, suggesting that there were no material changes in R&D activities.

Factors behind higher revenue and profits

In pet drugs, sales were firm for GALLIPRANT® and ENTYCE®/ELURA®. In human drugs, sales in South Korea remained strong for tegoprazan (K-CAB®), buoyed by the launch of an orally disintegrating tablet formulation and approval for a fifth indication (maintenance therapy for healed erosive esophagitis). In China, Shandong Luoxin Pharmaceutical Group Stock Co., Ltd. (SHE: 002793), a licensee of HK inno.N, obtained marketing approval for tegoprazan and began sales. With regard to the cyclooxygenase (COX-2) inhibitor, Ask At Inc., to which RaQualia has out-licensed the rights to the drug, has entered into a license and development support agreement with US-based Velo-1, Inc. (unlisted). RaQualia received a lump-sum payment from AskAt as a result.

Pipeline

Launched products

In pet drugs, sales of GALLIPRANT® (generic name: grapiprant) for treatment of osteoarthritis in dogs and ENTYCE® (capromorelin) for treatment of anorexia in dogs, both out-licensed to Elanco, grew. Elanco also sells capromorelin under the brand name ELURA® as a drug for the management of weight loss in cats with chronic kidney disease in the US. Elanco applied for marketing approval for these drugs in Europe as well, and based on this development, RaQualia received a milestone payment of USD1mn from Elanco in Q1 (January–March 2022). According to RaQualia, sales of GALLIPRANT® continue to grow five years after its launch in 2017.

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 external prescriptions amounting to KRW31.6bn (+12.5% YoY) in Q3 FY12/22, and cumulative sales from external prescriptions of KRW92.2bn year to date for FY12/22. Furthermore, in July 2022, HK inno.N received manufacturing and marketing approval in South Korea for the product as a maintenance therapy for healed erosive esophagitis. As a result, there are now five indications for which the product has received manufacturing and marketing approval in South Korea: erosive esophagitis, non-erosive reflux disease, gastric ulcer, adjuvant therapy for Helicobacter pylori eradication, and maintenance therapy for healed erosive esophagitis.

In China, Luoxin, a licensee of HK inno.N, commenced sales of tegoprazan in April 2022. Preparations are under way for its launch in Mongolia and the Philippines. In addition, the product is under review or in preparation for approval in 29 other countries, including Indonesia, Thailand, and Mexico.

Out-licensed and pre-out-licensing programs

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

In pre-out-licensing programs, preclinical trials are underway on a ghrelin receptor agonist being developed in-house. With tegoprazan, the company is aiming at rapid approval in Japan and to that end is getting ready to launch clinical studies while also seeking potential out-licensing candidates.

At the exploratory research stage, RaQualia is steadily advancing joint research with ASKA Pharmaceutical Co., Ltd. (unlisted, subsidiary of ASKA Pharmaceutical Holdings Co., Ltd. [TSE Prime: 4886]), while also working on in-house discovery of development candidate compounds. In Q3 FY12/22, the company entered into a joint research agreement with STAND Therapeutics Co., Ltd. (unlisted) and started a joint research project to discover new drugs for intractable and rare diseases by utilizing the company's ion channel drug discovery technology and STAND's intracellular antibody production technology.

In addition, clinical trials for the treatment of myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) are under way in the US by Syros Pharmaceuticals Inc. (NASDAQ: SYRS) for a retinoic acid receptor alpha agonist (tamibarotene), which was discovered by consolidated subsidiary TMRC Co., Ltd. and licensed to Syros.

FY12/22 company forecast

	FY12/20			FY12/21			FY12/22		
(JPYmn)	1H Act.	2H Act.	FY Act.	1H Act.	2H Act.	FY Act.	1H Act.	2H Est.	FY Est.
Operating revenue	**373**	**735**	**1,107**	**1,321**	**1,456**	**2,776**	**1,447**	**1,628**	**3,075**
YoY	-31.7%	-36.5%	-35.0%	254.3%	98.2%	150.7%	9.6%	11.8%	10.8%
Operating expenses	**776**	**817**	**1,593**	**1,006**	**1,063**	**2,068**	**896**	**1,355**	**2,251**
YoY	-8.5%	-6.1%	-7.3%	29.6%	30.0%	29.8%	-10.9%	27.5%	8.8%
Cost of revenue	58	80	138	175	146	321	105		
YoY	-55.6%	-39.4%	-47.5%	201.8%	82.1%	132.4%	-40.2%		
R&D expenses	451	482	932	497	631	1,127	528		
YoY	4.8%	11.0%	7.9%	10.2%	30.9%	20.9%	6.4%		
R&D expense ratio	120.9%	65.6%	84.2%	37.6%	43.3%	40.6%	36.5%		
SG&A expenses	268	255	523	334	286	620	263		
YoY	-7.0%	-16.1%	-11.6%	24.9%	12.0%	18.6%	-21.4%		
SG&A ratio	71.8%	34.7%	47.2%	25.3%	19.6%	22.3%	18.2%		
Operating profit	**-403**	**-83**	**-486**	**315**	**393**	**708**	**551**	**273**	**824**
YoY	-	-	-	-	-	-	75.1%	-	16.4%
Operating profit margin	-	-	-	23.8%	27.0%	25.5%	38.1%	16.7%	26.8%
Recurring profit	**-403**	**-125**	**-528**	**433**	**431**	**864**	**681**	**228**	**909**
YoY	-	-	-	-	-	-	57.4%	-	5.2%
Recurring profit margin	-	-	-	32.8%	29.6%	31.1%	47.1%	14.0%	29.6%
Net income	**-459**	**-148**	**-607**	**303**	**453**	**756**	**469**	**255**	**724**
YoY	-	-	-	-	-	-	55.0%	-	-4.2%
Net margin	-	-	-	22.9%	31.1%	27.2%	32.4%	15.6%	23.5%

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.

FY12/22 company forecast (out November 17, 2022)

- Operating revenue: JPY3.1bn (+10.8% YoY; previously JPY2.6bn)
- Operating expenses: JPY2.3bn (+8.8% YoY; JPY2.2bn)
- Operating profit: JPY824mn (+16.4% YoY; JPY420mn)
- Recurring profit: JPY909mn (+5.2% YoY; JPY420mn)
- Net income attributable to owners of the parent: JPY724mn (-4.2% YoY; JPY342mn)

The company revised its FY12/22 earnings forecast on November 17, 2022. The revised forecast for FY12/22 calls for revenue of JPY3.1bn (+10.8% YoY), operating profit of JPY824mn (+16.4% YoY), recurring profit of JPY909mn (+5.2% YoY), and net income attributable to owners of the parent JPY724mn (-4.2% YoY). Taking probability of achievement into account, RaQualia assumed in its initial forecast that entry of the P2X7 receptor antagonist into Phase II clinical trials would generate milestone revenue of JPY250mn each in FY12/22 and FY12/23. RaQualia's revised forecast for FY12/22 assumes the entire USD4mn (JPY500mn) will be booked in FY12/22 and also factors in a JPY147mn boost from yen depreciation. The company revised its exchange rate assumption from JPY125/USD to JPY135/USD.

For FY12/22, RaQualia forecasts lower revenue and profits compared to the previous year. In FY12/21, in addition to steady royalty revenue from the sale of four launched products, the company received the following upfront and milestone payments from out-licensed programs: an upfront payment based on the license agreement entered with Asahi Kasei Pharma Corporation (unlisted; a group company of Asahi Kasei Corporation [TSE Prime: 3407]) for P2X7 receptor antagonist; a milestone payment from Maruho; a milestone payment from US-based Syros Pharmaceuticals, Inc. (NASDAQ: SYRS); and upfront payments from Hong-Kong based Xgene Pharmaceutical Co., Ltd. (unlisted) for concluding out-licensing agreements for a TRPM blocker and sodium channel blocker.

Assumptions underlying previous forecast

In FY12/22, the company expects operating revenue to be underpinned by solid sales of tegoprazan (a GERD treatment), GALLIPRANT® (a treatment for osteoarthritis in dogs), and ENTYCE® (a treatment for anorexia in dogs). In addition to royalty revenue of JPY1.4bn, it expects to generate additional JPY1.2bn through milestone payments from the launch of tegoprazan in China and other sources. In 1H, the company booked JPY698mn in royalties on sales of tegoprazan and pet drugs and JPY748mn in milestone payments and other revenue. In Q3, it anticipates JPY203mn in royalties on sales of pet drugs and other revenue, and in Q4, expects JPY956mn in operating revenue from sales royalties on pet drugs and other revenue.

In April 2022, HK inno.N's Chinese licensee Luoxin received marketing approval from the Chinese authorities for tegoprazan. Just 15 days later, it started sales of tegoprazan under the brand name Tai Xin Zan®. In Mongolia, HK inno.N's licensee Monos Pharma LLC (unlisted) received approval for tegoprazan, and plans to launch the product in Q3 FY12/22. In May 2022, HK inno.N's Philippines licensee, Metro Pharma Philippines, Inc. (unlisted), acquired approval in the Philippines. The company's operating revenue forecast for FY12/22 includes some royalty revenue from China, but none from Mongolia or the Philippines, so revenue may come in above forecast.

The operating revenue forecast for FY12/22 includes some royalty revenue anticipated from sales of tegoprazan in China, but sales in the country began about six months earlier than the company had initially expected. Moreover, the forecast does not include milestone payments or royalty revenue from Mongolia and the Philippines. In July 2022, AskAt, to whom the company out-licensed in-house discovered cyclooxygenase-2 (COX-2) inhibitor (RQ-00317076), concluded a licensing agreement with US-based Velo-1, Inc. (unlisted), granting it global rights to the drug for use in animals, as well as a two-year development support agreement with Velo-1. The company is entitled to a certain percentage of revenue AskAt earns from RQ-00317076, and will receive a one-time payment based on these agreements entered between AskAt and Velo-1, which it will record as operating revenue in Q3. Because above developments have not been factored into the FY12/22 forecast, Shared Research believes operating revenue may very well surpass the full-year projection.

RaQualia forecasts lower profits for FY12/22 because it expects to incur costs for in-house development of two pre-out-licensing programs, namely tegoprazan and a ghrelin receptor agonist. With the aim of maximizing the value of tegoprazan, the company is preparing to conduct clinical pharmacological studies in Japan by utilizing data obtained from South Korea for speedy and efficient development and approval process, and to this end began negotiating with the PMDA to start clinical trial consultations. For the ghrelin receptor agonist program, the company completed manufacturing APIs for use in preclinical studies, which have been ongoing at a contract research organization since Q4 FY12/21 (October–December 2021).

The company plans to spend a total of JPY1.5bn on R&D, broken down to JPY1.2bn for exploratory research and JPY311mn for preclinical development and clinical trials. Of the planned R&D expenditures, it plans to invest JPY271mn on preclinical trials for ghrelin receptor agonist and tegoprazan development, and JPY400mn on discovering candidate compounds and pioneering new territories and technologies. For Q3, the company plans cost of operating revenue of JPY47mn, R&D expenses of JPY340mn, and other SG&A expenses of JPY154mn; for Q4, it plans cost of operating revenue of JPY52mn, R&D expenses of JPY605mn, and other S&A expenses of JPY198mn. For the full-year, operating expenses are forecast to amount to JPY2.2bn.

Difference between initial company forecasts and results

Results vs. Initial Est.	FY12/12	FY12/13	FY12/14	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21
(JPYmn)	Non-cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.
Operating revenue (Initial Est.)	1,636～2,178	1,014	300	600	950	1,100	1,388	2,022	2,129	2,738
Operating revenue (Results)	29	228	154	146	705	1,419	745	1,703	1,107	2,776
Results vs. Initial Est.	-	**-77.5%**	**-48.7%**	**-75.8%**	**-25.8%**	**29.0%**	**-46.4%**	**-15.8%**	**-48.0%**	**1.4%**
Operating profit (Initial Est.)	-1,666 ～-1,168	-1,082	-1,684	-1,395	-819	-760	-698	187	70	420
Operating profit (Results)	-2,637	-2,138	-2,123	-1,865	-760	-150	-1,075	-16	-486	708
Results vs. Initial Est.	-	-	-	-	-	-	-	-	-	**68.5%**
Recurring profit (Initial Est.)	-1,647 ～-1,148	-1,071	-1,685	-1,415	-819	-761	-680	195	85	427
Recurring profit (Results)	-2,891	-1,820	-1,942	-1,795	-721	-81	-1,065	22	-528	864
Results vs. Initial Est.	-	-	-	-	-	-	-	**-88.9%**	-	**102.3%**
Net income (Initial Est.)	-1,700 ～-1,202	-1,075	-282	-1,661	-825	-767	-686	153	13	343
Net income (Results)	-2,905	-1,108	-465	-1,854	-728	-58	-1,105	5	-607	756
Results vs. Initial Est.	-	-	-	-	-	-	-	**-96.5%**	-	**120.3%**

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

In FY12/21, the company booked an operating profit for the first time since its founding in 2008. Sales of the four products on the market (tegoprazan [K-CAB®], GALLIPRANT®, ENTYCE®, and ELURA®) were solid, generating strong royalty revenue, and the company also received milestone payments for out-licensed programs and upfront payments for new license agreements. The significant difference between the initial forecast and results for recurring profit and net income owed to JPY146mn in forex gains due to yen depreciation.

Medium-term business plan (FY12/22 to FY12/24)

(JPYmn)	FY12/21 Cons.	FY12/22 Est.	FY12/23 Prev. plan	FY12/24 Prev. plan	FY12/23 New plan	FY12/24 New plan	3-year CAGR
Operating revenue	**2,776**	**2,605**	**2,926**	**3,362**	**3,069**	**3,645**	
YoY	150.7%	-6.2%	12.3%	14.9%	17.8%	18.8%	9.5%
Royalty revenue	-	1,554	1,718	1,887	1,855	2,007	
YoY	-	-	10.6%	9.8%	19.4%	8.2%	
% of total	-	59.7%	58.7%	56.1%	60.4%	55.1%	
Other	-	1,051	1,208	1,475	1,214	1,638	
YoY	-	-	14.9%	22.1%	15.5%	34.9%	
% of total	-	40.3%	41.3%	43.9%	39.6%	44.9%	
Operating expenses	**2,068**	**2,184**	**2,607**	**2,475**	**2,675**	**2,478**	
YoY	29.8%	5.6%	19.4%	-5.1%	22.5%	-7.4%	6.2%
Operating expense ratio	74.5%	83.8%	89.1%	73.6%	87.2%	68.0%	
R&D expenses	1,127	671	1,069	653	1,069	653	
YoY	20.9%	-40.5%	59.3%	-38.9%	59.3%	-38.9%	-16.6%
R&D expense ratio	40.6%	25.8%	36.5%	19.4%	34.8%	17.9%	
Operating profit	**708**	**420**	**318**	**886**	**393**	**1,167**	
YoY	-	-40.7%	-24.3%	178.6%	-6.4%	196.9%	18.1%
Operating profit margin	25.5%	16.1%	10.9%	26.4%	12.8%	32.0%	
Recurring profit	**864**	**420**	**313**	**874**	**403**	**1,174**	
YoY	-	-51.4%	-25.5%	179.2%	-4.0%	191.3%	10.8%
Recurring profit margin	31.1%	16.1%	10.7%	26.0%	13.1%	32.2%	
Net income	**756**	**342**	**206**	**678**	**327**	**970**	
YoY	-	-54.7%	-39.8%	229.1%	-4.4%	196.6%	8.7%
Net margin	27.2%	13.1%	7.0%	20.2%	10.7%	26.6%	
Assumed exchange rate (USD/JPY)	110.00	120.00 (1H) 125.00 (2H)	110.00	110.00	125.00	125.00	

Source: Shared Research based on company data

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

Targets through FY12/24

Aims at aggregate operating revenue of JPY9.3bn over three years while remaining profitable

In August 2022, the company made upward revisions to its three-year medium-term business plan covering FY12/22 to FY12/24 released back in February the same year. The revised plan targets FY12/24 revenue of JPY3.6bn (three-year CAGR of 9.5%), operating profit of JPY1.2bn (18.1%), recurring profit of JPY1.2bn (10.8%), and net income attributable to owners of the parent JPY970mn (8.7%). The lower growth rates from the recurring profit line down compared with projected growth in operating profit reflects a JPY146mn forex gain in FY12/21.

During the three years of the medium-term plan, the company targets aggregate operating revenue of JPY9.3bn and operating profit of 2.0bn, and aims to remain in the black throughout. In setting the targets, the company took into account growth of tegoprazan in a potential global peptic ulcer drug market of JPY2tn (company estimate) as well as strategic investments in products that could drive growth through expanding R&D. RaQualia also plans to invest heavily in growth driver products to facilitate ongoing new drug discovery, and forecasts aggregate R&D expenses of JPY2.4bn (three-year CAGR of 16.6%). In FY12/22 and FY12/23, the company expects profit to decline on higher operating expenses as it develops two programs in-house, but it looks for steady operating revenue and three consecutive years of operating profit.

Outlook for operating revenue

- FY12/22: In addition to sales royalties of JPY1.6bn on expanding sales of tegoprazan in South Korea, the company expects to generate additional JPY1.1bn through milestone payments from the launch of tegoprazan in China and other sources.
- FY12/23: The company expects to receive royalty revenue of JPY1.9bn from solid sales of tegoprazan and other already launched drugs as well as milestone and upfront payments of JPY1.2bn from programs it has already out-licensed.
- FY12/24: The company expects sales royalties of JPY2.0bn due to further growth in sales of tegoprazan in China and upfront payments of JPY1.6bn, including from out-licensing tegoprazan in Japan.

R&D and capex

- FY12/22: The company plans to invest JPY271mn on preclinical trials for its ghrelin receptor agonist and tegoprazan development, and JPY400mn on creating development candidate compounds and developing new territories and technologies.

- FY12/23: The company plans to spend JPY669mn on in-house clinical pharmacological trials for tegoprazan and research on a par with the previous year in a bid to expand its portfolio and technologies.
- FY12/24: The company plans to spend JPY372mn on creating development candidate compounds and enhancing technology, and JPY281mn on new development candidate compounds.

It plans to secure separate funding for clinical development after Phase II clinical trials are completed, and put in place its own in-house infrastructure. In fiscal years when it conducts clinical development, operating expenses will increase, but in other years it plans to spend JPY600mn–700mn on R&D. The above R&D expenses do not include personnel expenses.

Three-year research, development, and out-licensing targets

Research: Plans to discover one development candidate compound by FY12/24

Development: Complete preclinical studies for ghrelin receptor agonist and clinical pharmacological studies for tegoprazan

The company is developing two programs in-house (ghrelin receptor agonist [RQ-00433412] and tegoprazan) in a bid to increase the probability of successfully commercializing new drugs and increasing expected earnings, and intends to focus on out-licensing activities for the following three programs.

In-house development programs

- Ghrelin receptor agonist (RQ-00433412): Complete preclinical studies by end-2023
- Tegoprazan: Complete clinical pharmacological studies by end-2023

Programs RaQualia plans to out-license at current development stage

- 5-HT4 partial agonist (RQ-00000010, RQ-10): Complete Phase I clinical trials
- 5-HT2B antagonist (RQ-00310941, RQ-941): Complete Phase I clinical trials
- Motilin receptor agonist (RQ-00201894, RQ-894): Complete preclinical studies

Out-licensing: Aims to sign one new out-licensing agreement each year

The company was successful in signing two out-licensing agreements in 2H FY12/21, and aims to out-license at least one compound yearly on a consistent basis.

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 uses 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) 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 sold them after the company's initial public offering (IPO), and as of end-December 2021 it held about 3.5%.

In addition to six exploratory programs and six development programs, Pfizer transferred to the company 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.

* 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.

Business territory

Drug discovery from exploratory research to early clinical development

RaQualia Pharma is an R&D focused 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 it focuses on are from exploratory research of target molecules to early clinical development. Basically, the company's development processes are aimed at lessening R&D expenses and risk by conducting activities up to the early clinical trial (Phase II) stage, where efficacy and safety can be broadly evaluated. Under new management from March 2021, the company broadened its targets from pain and gastrointestinal diseases to include neurological diseases. The company plans to focus on areas with significant unmet medical needs including neurodegenerative, genetic, and rare diseases, with the aim of consistently creating new drugs.

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.

Drug development process

Generally, R&D into drugs goes through several stages. Basic research looks for new compounds ("seeds") that drugs will be based on; 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). First stage (Phase I) clinical trials check for safety and side effects in a small number of healthy individuals. Phase II clinical trials identify effective dosages and dosing regimens using a small number of patients. 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)

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.

Using expertise from Pfizer which had focused on compound synthesis and design, the company conducts experiments with the 100–150 compounds it synthesizes every week. It assigns an eight-digit compound code starting with 00000001 for all the compounds that it researches, develops, and evaluates. The number of digits in the codes attests to the company's ongoing exploratory research to find the seeds of new drugs using its vast stores of data. The compound database which 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.

Patent expiry management

Aims to extend life of its hundreds 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

Management renewal and fresh initiatives

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.

Below are the main initiatives in research, development, and out-licensing under new management since March 2021 (details not disclosed).

Research

- Next-generation growth: Investigating new modality concepts
- Streamlining compound creation: Building next-generation drug discovery value chain
- Expanding territories: Using AI to search for drug targets and diseases

Development

- Expanding territories: Recruitment of clinical development director
- Enhancing value of existing programs: Looking into added value, notably in-house development of tegoprazan and ghrelin receptor agonist

Out-licensing

- TRPM8 blocker: Out-licensed to Xgene Pharmaceutical (September 2021)
- Sodium channel blocker: Out-licensed to Hisamitsu Pharmaceutical (December 2021)

Higher funding demands due to strategy change under new management

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, upfront, milestone, and royalty payment rates tend 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 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 require more R&D spending than previously. Because the company intends to develop two projects in-house in FY12/23, it expects an increase of roughly 20% in operating expenses, and said it plans to raise funds through a combination of equity financing and commitment lines.

Trying new modality

Drugs can be broadly classified into two categories: chemically synthesized small molecule drugs and biopharmaceuticals (also called 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). This can lead to a price difference of 1.5 to 3.5 times between original and generic drugs with the same ingredients. 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 December 2024, the company is testing 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 that are challenging to develop with the technology and expertise it has accumulated thus far. It is also looking into AI and cloud collaboration initiatives for a structural biological approach to ion channels.

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.

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.

Earnings structure

RaQualia is an R&D focused drug discovery company. It primarily conducts exploratory research into development compounds ("seeds") for new drugs, and out-licenses development and marketing rights pharmaceutical companies and others to generate revenue. In general, revenue can be broken down based on drug development stage into: 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 revenue received once the drug under development is launched on the market.

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

	FY12/12	FY12/13	FY12/14	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21
(JPYmn)	Non-cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.
Total	29	228	154	146	705	1,419	745	1,703	1,107	2,776
YoY	-95.8%	687.0%	-32.5%	-5.5%	384.7%	101.2%	-47.5%	128.6%	-35.0%	150.7%
US	2	88	-	-	646	818	278	761	549	1,004
YoY	-88.9%	3,726.4%	-	-	-	26.5%	-66.0%	173.8%	-27.8%	82.7%
% of total	8.0%	38.8%	-	-	91.6%	57.6%	37.3%	44.7%	49.6%	36.2%
Japan	27	70	131	106	50	471	349	196	28	1,187
YoY	-55.6%	162.5%	86.9%	-19.4%	-52.6%	841.1%	-25.8%	-43.7%	-85.9%	4,175.6%
% of total	92.0%	30.7%	85.0%	72.5%	7.1%	33.2%	46.8%	11.5%	2.5%	42.8%
Asia	-	-	20	40	9	131	121	746	530	585
YoY	-	-	-	100.0%	-77.5%	1,355.0%	-7.8%	517.9%	-28.9%	10.3%
% of total	-	-	13.0%	27.5%	1.3%	9.2%	16.2%	43.8%	47.9%	21.1%
Europe	-	50	-	-	-	-	-	-	-	-
YoY	-	-	-	-	-	-	-	-	-	-
% of total	-	21.8%	-	-	-	-	-	-	-	-
Other	-	20	3	-	-	-	-	-	-	-
YoY	-	-	-84.7%	-	-	-	-	-	-	-
% of total	-	8.8%	2.0%	-	-	-	-	-	-	-

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

Licensees have already launched four products, providing the company with stable long-term royalty revenue, its main source of earnings. In FY12/21, revenue was JPY2.8bn, comprising royalty revenue (over 50%) and upfront and milestone payments (over 40%).

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: 10 already out-licensed, including ion channel projects, and six at the pre-out-licensing stage.

It also had nine programs in its exploratory research pipeline as of February 2022, and in addition to in-house research, it is conducting joint research with ASKA Pharmaceutical, Interprotein, Nagasaki University, and Gifu Pharmaceutical University. 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.

Out-licensed pipeline (human)

Out-licensed programs (human)

Program name	Generic name/compound code	Licensee	Key indication	Rollout area	Development stage
Tegoprazan (potassium-competitive acid blocker [P-CAB]; K-CAB®)	RQ-00000004 (tegoprazan)	HK inno.N (South Korea)	GERD	South Korea	On market (launched in March 2019)
				Mongolia	Approved, preparing to launch
				China	On market (launched in April 2022)
				US, Canada	Phase I complete
				Philippines	Approved (May 2022)
				Mexico, Thailand, Vietnam, Indonesia, Singapore	Application under review
				16 Latin American countries, Malaysia	Preparing for approval filing
Retinoic acid receptor alpha agonist	TamibaroteneTM-411/SY-1425	Syros Pharmaceuticals	Myelodysplastic syndrome (MDS)	US	Phase III underway
			Acute myeloid leukemia (AML)	US	Phase II underway
EP4 receptor antagonist	RQ-00000007 (grapiprant)	AskAt	Pain	US	Early Phase II completed
				China	Phase I complete
			Cancer	US	Phase I underway
				China	Phase I underway
5-HT4 partial agonist	RQ-00000009		Alzheimer's disease	US	Phase I complete
COX-2 inhibitor	RQ-00317076		Pain	US	Early Phase II completed
				China	Phase I underway
CB2 agonist	Not disclosed		Pain associated with IBS	-	Preclinical trials underway
Selective sodium channel blocker	Not disclosed	Maruho	Analgesic and antipruritic	-	Not disclosed
P2X7 receptor antagonist	Not disclosed	Asahi Kasei Pharma	Neuropathic pain	-	Phase I complete
Specific ion channel target	Not disclosed	EA Pharma	Gastroenterology	-	Not disclosed
TRPM8 blocker	RQ-00434739	Xgene Pharmaceutical (Hong Kong)	Chronic pain	-	Preparing for preclinical trials
Sodium channel blocker	RQ-00350215	Hisamitsu	Chronic pain	-	Preparing for preclinical trials

Source: Shared Research based on company data (as of end-May 2022)

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

Out-licensed worldwide (excluding Japan) to HK inno.N

Tegoprazan is primarily used to treat gastrointestinal reflux disease (GERD)*, and is an alternative to the existing mainstream therapy of proton pump inhibitors (PPIs). RaQualia inherited the development compound from Pfizer, and many of the employees who had been involved with development of tegoprazan were transferred to the company, so preclinical studies were launched soon after its establishment. 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.

*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.

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 current mainstream treatment,

proton pump inhibitors (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 progressively replaced PPIs and H2RAs (H2 blockers: histamine H2 receptor antagonists) and while the NHI price of TAKECAB® was cut by 4.1% in 2021, its revenue on an NHI price basis was still JPY111.1bn (+13.5% YoY), the third highest among domestic drugs.

No. 1 market share in South Korea

HK inno.N gained marketing approval for the company's out-licensed drug tegoprazan for South Korea in July 2018, and launched it in March 2019 as K-CAB®. Revenue of K-CAB® in South Korea in 2021 (non-hospital prescriptions) came to KRW109.6bn (roughly JPY11.0bn converted at KRW/JPY0.1) for a strong CAGR of 72% from 2019, and the No. 1 market share in South Korea for gastrointestinal disease treatments.

K-CAB® for sale in South Korea

Source: HK inno.N homepage

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, non-erosive reflux disease (NERD), gastric ulcer, adjuvant therapy for Helicobacter pylori eradication, and maintenance therapy for healed erosive esophagitis.

Characteristics of tegoprazan

Gastroesophageal reflux disease (GERD) is characterized by the reflux of stomach contents, especially stomach acid, into the esophagus with characteristic symptoms such as heartburn. The main symptoms are heartburn and acid regurgitation*, especially heartburn on an empty the stomach or during the night. The main differences between tegoprazan and existing drugs is the inhibition of acid secretion and speed of onset. Tegoprazan has the ability to inhibit acid secretion similar to vonoprazan (brand name TAKECAB®) and superior to PPIs. Like PPIs, tegoprazan is also indicated for non-erosive reflux disease (NERD), but vonoprazan is not. The pH value in the stomach is used as an indicator for onset of effect. PPIs require stomach acid for activation, so tend not to take effect on the first day (raising the intragastric pH level above 4) and vonoprazan takes about four hours, compared to about one hour for tegoprazan. Furthermore gastrin** levels tend to rise with vonoprazan, but less so with tegoprazan, which is similar to 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.
** 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.

Revenue increasing as tegoprazan sales territory expanded

Licensee HK inno.N's sales expansion plans

In September 2010, the company reached an out-licensing agreement with South-based HK inno.N Corporation for marketing tegoprazan in South Korea, China including Hong Kong, and Taiwan. It has gradually been expanding the territories covered, and since 2019, HK inno.N has 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. HK inno.N has started acquiring marketing approval in countries around the world under its global sales strategy, so the company thinks it is on the cusp of a long-term period where it can recoup its investment from FY12/22 onward.

In April 2022, HK inno.N completed Phase I clinical trials for tegoprazan in the US, and sub-licensee Braintree Laboratories plans to start the next phase by the end of 2022, with a view to gaining approval in the US and Canada. Also in April 2022, Luoxin Pharmaceutical, a sublicensee of HK inno.N, gained marketing approval from the Chinese authorities and launched the drug just 15 days later. In February 2022, HK inno.N reached a manufacturing supply agreement for Malaysia with the country's largest drug company, Pharmaniaga Logistics Sdn Bhd (PHARMA 7081), and in May 2022 it signed a licensing agreement covering India and six other countries with Dr. Reddy's Laboratories.

Royalty revenue expected to increase due to expansion of sales territories

As of June 2022, tegoprazan was for sale in South Korea and China, and in 34 countries it was at the development, approval review, or launch preparation stages. It had been approved in Mongolia, with a launch planned for June 2022. In May 2022, HK inno.N's sublicensee Metro received marketing approval for four indications in the Philippines, including erosive esophagitis. 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.

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 around the world by 2028. In addition to South Korea, it is working on development and filing for approval in 27 countries, the largest market being North America at JPY400bn, followed by China at JPY310bn. As mentioned, the sublicensee is preparing for the next stage of clinical trials in the US and Canada, sales have begun in China, preparations for launch are underway in Mongolia, and approval has been obtained for the Philippines. The product is under review in Mexico, with sales projected to start from 2023. 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	×	11% 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/regic	Development stage	Launch year (est.)	Market size
South Korea	On market	2019	JPY60,000mn (KRW600bn)
China	On market	2022	JPY350,000mn (CNY17bn)
US	Phase I completed	Not disclosed	JPY400,000mn
Mongolia	Approved, preparing to launch	2022	Not disclosed
South East Asia	Application under review	2022–2023	JPY46,000mn (USD370mn)
Latin America	Application under review (Mexico), Preparing for filing (other 16 countries)	2022–2023	Not disclosed

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

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, the number of GERD patients is also in an uptrend and it is likely that the market will also expand due to a growing share of patients in the population.

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 sales 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 royalty payments from Q3, reflecting sales.

EP4 receptor antagonist (RQ-00000007, grapiprant)

Grapiprant is an EP4 receptor antagonist that Pfizer was working on, and is the same compound as GALLIPRANT®, which is already being marketed as a pet drug. In January 2013, the company entered a business alliance with its then wholly-owned subsidiary AskAt, which has been developing the drug, mainly for the indications of cancer and pain. AskAt's US-based sublicensee Ikena Oncology Inc. (NASDAQ: IKNA) is conducting Phase Ib (expansion phase) clinical trials in the US as immunotherapy for cancer. Elsewhere, AskAt's China-based licensee 3D Medicines Co., Ltd. (unlisted) completed Phase I clinical trials in China for the indication of pain. Another licensee of AskAt, China-based Ningbo NewBay Medical Technology Development Co., Ltd. (unlisted), is conducting Phase I clinical trials in China in oncology.

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), a business partner since November 2015, is conducting preclinical studies in the UK.

P2X7 receptor antagonist (RQ-00466479)

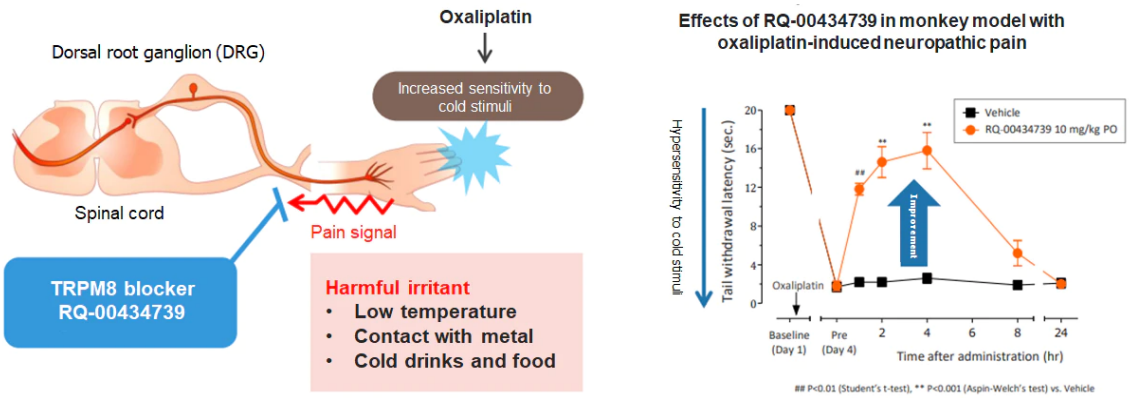
This is a P2X7 receptor antagonist created through joint research with Asahi Kasei Pharma, with a license agreement signed in March 2018. Phase I clinical trials targeting peripheral neuropathic pain have been completed and Eli Lilly, with whom Asahi Kasei Pharma has a license agreement, is preparing to launch Phase II clinical trials with an eye on global

development. The company has received a milestone payment from Asahi Kasei Pharma, and if the product is launched, it is set to receive royalty payments based on a certain percentage of Asahi Kasei Pharma's earnings. The company expects to receive a milestone payment once Eli Lilly begins Phase II clinical trials.

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.

Effect of TRPM8 blocker



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 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).

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 from FY12/22 onward. 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 sales 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.

The company has two other projects underway in addition to the above, although the development stages are undisclosed. These are a selective sodium channel blocker for analgesic and anti-pruritic indications out-licensed to Maruho and a compound for a specific ion channel target for gastrointestinal indications out-licensed to EA Pharma.

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 COX-2 inhibitors, 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 Co., Ltd. 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 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.

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 25% of patients with myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). Syros is currently conducting Phase III clinical trials for MDS and Phase II clinical trials for AML in the US. It plans to announce topline data from the Phase III clinical trial of tamibarotene administered in combination with azacitidine, the standard therapy for higher-risk MDS, in patients with newly diagnosed higher-risk MDS in Q4 FY12/23 or Q1 FY12/24, and file an NDA in 2024. It also plans to announce interim results of the Phase II clinical trial of tamibarotene + venetoclax + azacitidine three-drug combination therapy in elderly and other patients who are not suitable for standard chemotherapy by the end of 2022.

* Precision medicine: This 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.

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** 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.
** 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.

In Japan, RaQualia is conducting investigator-initiated Phase I/II clinical trials for tamibarotene as a pancreatic cancer treatment at Nagoya University. 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.

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 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.

Out-licensed programs (veterinary)

Program name	Generic name/compound code	Licensee	Key indication	Rollout area	Development stage
EP4 antagonist GALLIPRANT®	RQ-00000007 (grapiprant)	Elanco Animal Health Inc. (US)	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
COX-2 inhibitor	RQ-00317076	AskAt	Pain	—	Preparing for pilot test

Source: Shared Research based on company data (as of end-May 2022)

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.

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. There are 74.1mn pet cats in the US and 56.6mn in Europe, so the company thinks the potential market is significant.

Number of pet dogs and cats ('000)

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

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 COX-2 inhibitors, and AskAt believes it is a promising compound for treating acute pain, e.g., postoperative pain, and chronic pain associated with osteoarthritis.

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. In order 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 2021 round of price revisions, the dispensing price was reduced by 5.69% 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 veterinary 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.

Pre-out-licensing programs

The company has six 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
Potassium-competitive acid blocker (P-CAB)	tegoprazan RQ-00000004	GERD	Japan	Preparing for Phase I
5-HT4 partial agonist	RQ-00000010	Gastroparesis, functional dyspepsia, chronic constipation	Worldwide	Phase I complete
5-HT2B agonist	RQ-00310941	Irritable bowel syndrome with diarrhea (IBS-D)	Worldwide	Phase I complete
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, constipation from spinal cord injury	Worldwide	Preclinical trials underway
TRPM8 blocker	RQ-00434739	Pain	Japan	Preclinical trials under consideration

Source: Shared Research based on company data (as of end-May 2022)

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). It was out-licensed to HK inno.N in September 2010, but the company retains the rights for Japan. It is preparing to start pharmacological studies as part of Phase I clinical trials. It plans to complete the pharmacological studies by the end of FY12/23, and is looking for an out-licensee in Japan. It expects tegoprazan to drive domestic out-licensing revenue after it reaches a deal in FY12/24.

Preparing to file for domestic approval using South Korean 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 GERD, 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 in order to use South Korean data when filing for approval in Japan. It anticipates completing the clinical pharmacological studies in 2023 at a cost of JPY500mn.

Could become best in class

RaQualia's tegoprazan is the only P-CAB indicated for NERD. TAKECAB® is the frontrunner in Japan, China, and the US, but has not received approval for NERD. 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]). Another advantage of tegoprazan is that gastrin values tend to rise less than with vonoprazan (TAKECAB®). Shared Research thinks that if tegoprazan is approved in Japan, there is a high probability that it will replace TAKECAB®. The company says that there are some 17mn GERD patients in Japan as of 2020 (14% of the population) with a market size of JPY250bn.

5-HT4 partial agonist (RQ-00000010)

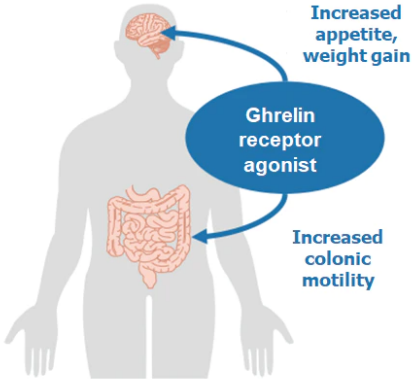
This compound is under development for target indications of gastrointestinal dysmotility including gastroparesis, functional dyspepsia, and chronic constipation. In January 2013, the company entered a business alliance with AskAt. Phase I clinical

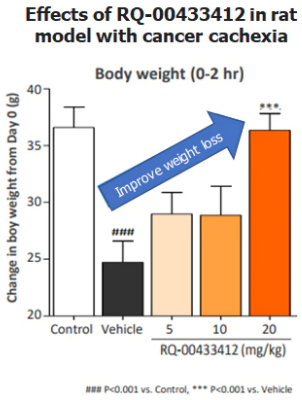
trials in the UK of healthy individuals and patients have been completed. In addition to moving forward with out-licensing activities, the company is looking into the next stage of development, Phase II clinical trials.

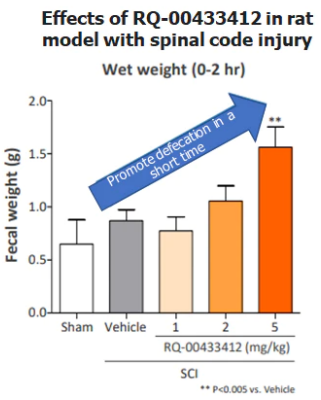
Ghrelin receptor agonist (RQ-00433412)

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 plans to out-license worldwide rights in 2024 after completing preclinical studies by the end of FY12/23, and is looking for a licensee.

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.







Ghrelin receptor agonist (RQ-00433412)

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).

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.

Exploratory and discovery phase pipeline

As of February 2022, the company had nine programs in exploratory and discovery research, four of which were joint research with companies or academia.

Joint research on specific protein-protein interaction inhibitor

The company is conducting joint research into a specific protein-protein interaction inhibitor for the main indication of pain with biotech company Interprotein Corporation (unlisted, formerly Inter Cyto Nano Science Co., Ltd.) which came out of

Osaka University.

Joint drug discovery research targeting specific ion channel

Joint research with ASKA Pharmaceutical Co., Ltd. is underway for a undisclosed indication.

Joint drug discovery research targeting idiopathic pediatric nephrotic syndrome

The company is conducting joint target discovery research with Epigeneron, Inc. (unlisted) for the main indication of idiopathic pediatric nephrotic syndrome.

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.

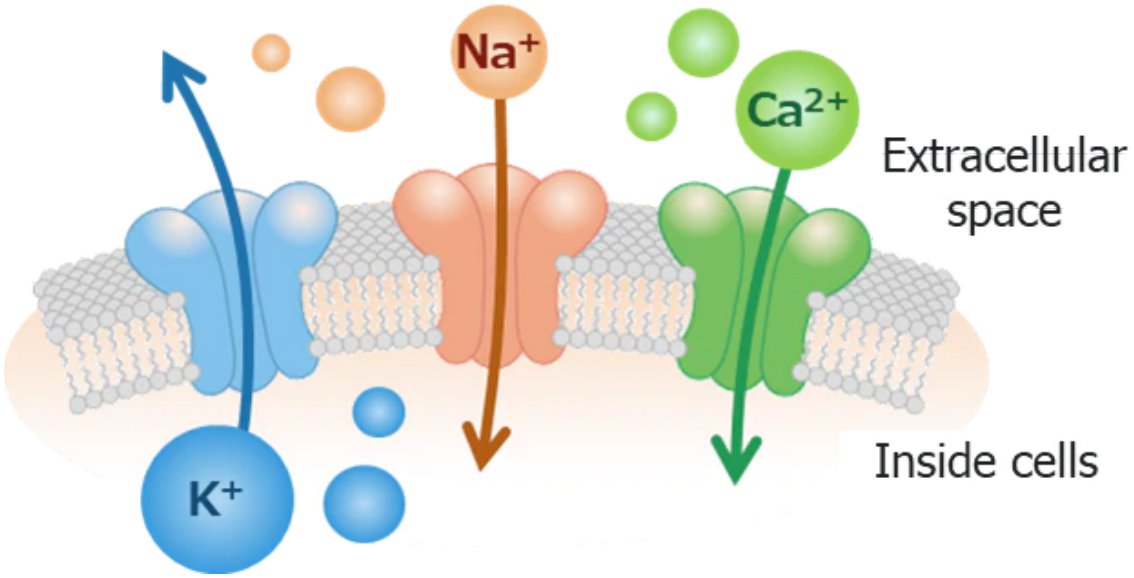
Ion channel drug discovery

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 are deeply involved in a variety of physiological phenomena. There are over 100 types. Controlling ion channels could help treat a wide range of diseases, but selective blocking is required to avoid strong side effects, as blocking one ion channel affects the entire body by simultaneously blocking another in a different location. Ion channels are widely expressed in vital organs such as the heart and brain, so there is a tendency for life-threatening side effects such as cardiotoxicity and neurotoxicity to emerge. 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 that target ion channels account for only 5% 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. In order 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 (ongoing)

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
				Preparing for preclinical trials
Sodium channel blocker	RQ-00350215	Chronic pain	Hisamitsu	Out-licensed in 2021
				Preparing for preclinical trials

Source: Shared Research based on company data

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.

Market and value chain

Global drug market

According to US-based IQVIA Holding Inc. (NYSE: IQV), global prescription drug sales in 2021 totaled USD1,424bn (JPY170.9tn, converted at JPY120.0/USD). It forecasts growth at a CAGR of 3–6% over the five years to 2026 and a global drug market of USD1,750–1,780bn (JPY210.0–213.6tn) in 2026.

Global drug sales

(USDbn)	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	CAGR
US	331	326	343	389	431	455	464	492	519	543	4.8%
Japan	112	109	91	85	79	89	86	86	89	89	2.4%
China	67	85	97	111	121	123	128	137	150	148	4.2%
Europe	263	246	258	266	239	245	260	282	286	303	4.9%
Latin America	67	71	73	65	75	87	95	67	67	62	-3.8%
Other	124	128	132	138	161	143	145	154	160	161	0.0%
Worldwide	963	964	994	1,056	1,104	1,141	1,178	1,216	1,272	1,305	3.4%

Source: Shared Research based on Japan Pharmaceutical Manufacturers Association (JPMA) DATA BOOK 2022 (data sourced from IQVIA)
Note: 5-year CAGRs are five years to 2020

Potential market for main target diseases

Disease	Number of patients	Market size	Region	Existing therapies	RaQualia's development pipeline
GERD	58mn (US)	JPY2tn	Worldwide	H2RA,	Tegoprazan
	17mn (Japan)	JPY450bn	US	PPI,	
		JPY250bn	Japan	vonoprazan	
Pain	50mn (US)	JPY2tn	Worldwide	Pregabalin,	EP4 receptor antagonist , COX-2 inhibitor,
	23mn (Japan)	JPY300bn	Japan	duloxetine,	TRPM8 blocker, P2X7 receptor antagonist,
				celecoxib, etc.	Sodium channel blocker
Cancer immunity	Approx. 12% of cancer patients respond to cancer immunotherapy	JPY10tn	Worldwide	Nivolumab,	EP4 receptor antagonist
				pembrolizumab, etc.	
Chronic constipation	42mn (US)	JPY660bn	Worldwide	Linaclotide,	5-HT4 partial agonist
		JPY60bn	Japan	lubiprostone, etc.	
Gastroparesis	80,000–400,000	JPY200bn	Worldwide	Metoclopramide, etc.	5-HT4 partial agonist
					Motilin receptor agonist
Irritable bowel syndrome	5–20% of Japanese/Western adults	JPY100bn	Worldwide	Rifaximin,	5-HT2B agonist
				ramosetron, etc.	
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)	JPY100bn	Worldwide	Azacitidine, etc.	Tamibarotene
Acute myeloid leukemia	160,000 (worldwide), 7,000 (Japan)	JPY100bn	Worldwide	Azacitidine,	Tamibarotene
	7,000 (Japan)			venetoclax, etc.	

Source: Shared Research based on company data

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 (JPY0.6tn converted at JPY120.0/USD) in 2020 to USD5.9bn (JPY0.7tn) in 2027. It projects the market for proton pump inhibitors (PPIs) that suppress gastric acid secretions to reach USD4.2bn (JPY0.5tn, CAGR of 2.5%) in 2027.

Japanese drug market

According to IQVIA, prescription drug sales in Japan in 2021 reached JPY10.6tn (+2.2% YoY), the seventh consecutive year above JPY10tn. Sales of antacids, flatulence agents, and ulcer agents came to JPY351.6bn (+1.3% YoY) with sales of Takeda's antiulcer drug TAKECAB® at JPY111.1bn (+13.5% YoY), the third highest among domestic drugs.

Prescription drug sales in Japan

JPYmn	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
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	8,873,623
YoY	0.0%	3.8%	1.2%	4.1%	2.1%	7.5%	-0.6%	4.6%	2.6%	7.2%	0.2%
Antacids, flatulence/ulcer agents	391,242	400,632	383,713	392,301	395,660	418,112	408,593	422,148	427,027	446,651	429,890
YoY	-1.0%	2.4%	-4.2%	2.2%	0.9%	5.7%	-2.3%	3.3%	1.2%	4.6%	-3.8%
	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Prescription drug sales in Japan	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	10,371,733	10,599,031
YoY	6.9%	0.7%	3.1%	1.4%	6.2%	0.2%	-1.0%	-1.7%	2.8%	-2.4%	2.2%
Antacids, flatulence/ulcer agents	434,997	408,604	418,289	397,394	389,788	376,365	377,550	349,783	351,329	347,142	351,640
YoY	1.2%	-6.1%	2.4%	-5.0%	-1.9%	-3.4%	0.3%	-7.4%	0.4%	-1.2%	1.3%

Source: Shared Research based on company 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). This can lead to a price difference of 1.5 to 3.5 times between original and generic drugs with the same ingredients.

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). In order 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 2021 price revisions, the dispensing price was reduced by 5.69% 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 1.44% 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.

NHI price revisions and average deviation

	1994	1996	1998	2000	2002	2004	2006	2008
NHI price revisions (drug fee basis)	-6.6%	-4.4%	-9.7%	-7.0%	-6.3%	-4.2%	-6.7%	-5.2%
NHI price revisions (medical fee basis)	-2.0%	-1.3%	-2.7%	-1.6%	-1.3%	-0.9%	-1.6%	-1.1%
Average deviation	17.8%	13.1%	9.5%	7.1%	6.3%	8.0%	6.9%	8.4%
	2010	2012	2014	2016	2018	2019	2020	2021
NHI price revisions (drug fee basis)	-5.75%	-6.00%	-5.64%	-5.57%	-7.48%	-4.35%	-4.38%	-6.69%
NHI price revisions (medical fee basis)	-1.23%	-1.26%	-1.22%	-1.22%	-1.65%	-0.93%	-0.99%	-1.44%
Average deviation	8.4%	8.2%	8.8%	9.1%	7.2%	8.0%	8.0%	7.6%

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

Global pet drug market

Global Market Insights Research Inc. (unlisted) estimates the value of the global pet drug market at about USD11.8bn (JPY1.4tn converted at JPY120.0/USD) in 2020, and projects a CAGR of about 6% through 2027. The market continues to expand as the number of pets is increasing due to growth in emerging economies and a burgeoning middle class.

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.

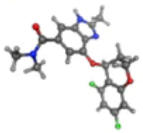
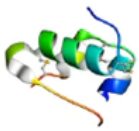
Difference between small molecule drugs and biopharmaceuticals

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

Number of approvals by FDA (US)

	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
New Molecular Entities (NMEs)	23	19	28	47	34	25	33	25	19	11	15	31	18	18	16
% of total	92.0%	90.5%	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%
Biologics License Applications (BLAs)	2	2	1	6	5	5	2	2	5	6	6	5	2	4	2
% of total	8.0%	9.5%	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%
	2008	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	
New Molecular Entities (NMEs)	21	20	15	24	33	25	30	33	15	34	42	38	40	36	
% of total	87.5%	76.9%	71.4%	80.0%	84.6%	92.6%	73.2%	73.3%	68.2%	73.9%	71.2%	79.2%	75.5%	72.0%	
Biologics License Applications (BLAs)	3	6	6	6	6	2	11	12	7	12	17	10	13	14	
% of total	12.5%	23.1%	28.6%	20.0%	15.4%	7.4%	26.8%	26.7%	31.8%	26.1%	28.8%	20.8%	24.5%	28.0%	

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

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 high at 72.0% of the total in 2021.

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	Operating profit margin	ROE	
		(JPYmn)	(%)	(%)	
4579	RaQualia	2,776	25.5%	17.2%	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	12,690	12.8%	11.6%	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	Sosei Group	17,712	21.3%	1.9%	A biotech start-up engaged in membrane protein GPCR-targeted drug discovery. Founded by Shinichi Tamura, former president of Genentech's Japanese subsidiary. The mainstay of its business is a UK acquisition, Heptares.
4571	NanoCarrier	264	-780.6%	-29.1%	Biotech start-up focused on oncology. Aims at new drugs with few side effects using its ultrafine micellar nanoparticle technology.
4572	Carna Biosciences	2,018	-26.3%	-10.2%	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	8,257	12.3%	39.6%	Main focus on oncology, hematology, and rare diseases. In-licenses drug candidate compounds which it develops and commercializes.
4587	PeptiDream	9,366	47.2%	15.6%	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. Developing COVID-19 treatment drugs.
4597	Solasia Pharma	559	-432.7%	-79.4%	Biotech venture that in-licenses development rights for candidate substances and uses in clinical development, focusing on cancer. Fabless operations. Outsources manufacturing to overseas companies.
4883	Modalis	1	-112,676.7%	-12.6%	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)			Sosei Group (4565)		
	FY12/19	FY12/20	FY12/21	FY12/19	FY12/20	FY12/21	FY12/19	FY12/20	FY12/21
	Cons.	Cons.	Cons.	IFRS, Cons.	IFRS, Cons.	IFRS, Cons.	IFRS, Cons.	IFRS, Cons.	IFRS, Cons.
Revenue	1,703	1,107	2,776	7,446	9,774	12,690	9,726	8,842	17,712
Gross profit	1,440	969	2,456	6,395	8,228	11,090	8,875	8,081	16,779
R&D expenses	864	932	1,127	758	1,243	2,016	4,292	3,793	5,931
SG&A expenses	592	523	620	4,334	5,181	7,959	3,614	3,435	3,940
Operating profit	-16	-486	708	1,302	1,870	1,625	384	928	3,775
Recurring profit	22	-528	864	1,197	1,806	1,107	534	1,622	433
Net income	5	-607	756	182	1,366	55	1,432	1,479	1,017
ROE	0.1%	-14.1%	17.2%	1.8%	7.1%	11.6%	3.3%	3.0%	1.9%
ROA (RP-based)	0.5%	-11.6%	18.2%	6.3%	8.2%	4.1%	0.9%	2.4%	0.5%
Operating profit margin	-0.9%	-43.9%	25.5%	17.5%	19.1%	12.8%	3.9%	10.5%	21.3%
Total assets	4,837	4,251	5,234	20,607	23,219	30,297	56,680	76,465	96,985
Net assets	4,621	4,011	4,788	13,096	12,769	19,266	45,078	52,381	57,468
Equity ratio	95.3%	94.1%	91.3%	51.9%	47.4%	62.3%	79.5%	68.5%	59.3%
Operating CF	-531	-289	366	789	1,378	552	3,441	4,672	7,095
Investing CF	216	225	-279	-153	570	-261	-246	-150	278
Financial CF	696	-7	-16	2,218	801	2,853	-6,964	20,278	11,123
Cash and deposits	2,174	1,394	2,345	7,674	10,322	14,352	15,375	40,008	60,087
Interest-bearing debt	2	46	39	2,038	1,747	1,126	3,368	1,834	1,831
Net debt	-2,172	-1,349	-2,306	-5,636	-8,575	-13,226	-12,007	-38,174	-58,256
	NanoCarrier (4571)			Carna Biosciences (4572)			SymBio (4582)		
	FY03/20	FY03/21	FY03/22	FY12/19	FY12/20	FY12/21	FY12/19	FY12/20	FY12/21
	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.
Revenue	553	313	264	3,207	1,133	2,018	2,838	2,987	8,257
Gross profit	475	275	223	3,000	941	1,882	865	867	5,800
R&D expenses	1,152	1,173	1,530	1,281	1,474	1,841	2,442	2,267	1,736
SG&A expenses	506	405	503	2,022	1,998	2,413	5,166	5,373	4,784
Operating profit	-1,106	-1,303	-2,061	978	-1,057	-531	-4,302	-4,506	1,016
Recurring profit	-1,144	-1,279	-1,925	957	-1,077	-523	-4,377	-4,616	1,001
Net income	-2,010	-2,836	-1,882	828	-1,111	-534	-4,376	-4,090	2,032
ROE	-27.8%	-35.2%	-29.1%	26.8%	-21.1%	-10.2%	-107.4%	-104.7%	39.6%
ROA (RP-based)	-13.1%	-15.3%	-25.7%	35.1%	-29.0%	-13.2%	-76.0%	-79.9%	13.6%
Operating profit margin	-200.0%	-415.9%	-780.6%	30.5%	-93.3%	-26.3%	-151.6%	-150.9%	12.3%
Total assets	8,945	7,821	7,136	5,377	4,835	5,433	5,274	6,275	8,453
Net assets	8,769	7,500	5,567	3,854	3,824	4,316	4,400	4,657	6,746
Equity ratio	97.0%	94.8%	77.6%	71.5%	79.0%	79.3%	83.4%	74.2%	79.8%

Operating CF	-1,139	-1,247	-1,753	1,478	-1,261	-1,537	-4,351	-4,122	140
Investing CF	-112	-872	-244	-41	-70	-42	-216	-160	-71
Financial CF	2,162	-11	1,146	2,122	724	1,065	3,740	4,222	-72
Cash and deposits	4,471	3,892	3,545	4,915	4,299	3,818	3,911	3,849	3,860
Interest-bearing debt	0	0	1,150	729	430	540	0	0	0
Net debt	-4,471	-3,892	-2,395	-4,186	-3,869	-3,278	-3,911	-3,849	-3,860
	PeptiDream (4587)			Solasia Pharma (4597)			Modalis (4883)		
	FY12/19	FY12/20	FY12/21	FY12/19	FY12/20	FY12/21	FY12/19	FY12/20	FY12/21
	IFRS, Cons.	IFRS, Cons.	IFRS, Cons.	IFRS, Cons.	IFRS, Cons.	IFRS, Cons.	Cons.	Cons.	Cons.
Revenue	1,037	11,677	9,366	1,310	454	559	645	342	1
Gross profit	366	9,529	7,008	1,244	244	373	-	-	-
R&D expenses	893	1,460	1,638	1,138	1,928	845	304	532	1,010
SG&A expenses	360	1,078	952	1,868	2,432	1,948	184	208	231
Operating profit	-887	6,991	4,418	-1,762	-4,116	-2,419	157	-398	-1,239
Recurring profit	-707	6,976	4,774	-1,797	-4,159	-2,442	146	-440	-745
Net income	-488	4,448	3,606	-1,867	-4,127	-2,478	141	-448	-739
ROE	-2.9%	23.4%	15.6%	-26.7%	-78.1%	-79.4%	5.6%	-8.9%	-12.6%
ROA (RP-based)	-3.7%	31.6%	18.1%	-22.9%	-60.6%	-54.8%	5.7%	-8.6%	-16.6%
Operating profit margin	-85.5%	59.9%	47.2%	-134.5%	-906.6%	-432.7%	24.4%	-116.5%	-112,676.7%
Total assets	17,817	26,267	26,619	7,946	5,775	3,144	3,938	6,277	6,069
Net assets	16,978	21,217	24,999	6,917	3,652	2,587	3,843	6,207	5,549
Equity ratio	94.8%	80.5%	93.8%	87.0%	63.2%	82.3%	97.6%	98.9%	91.4%
Operating CF	242	1,733	6,655	-828	-2,789	-2,473	224	-377	-747
Investing CF	-138	-1,200	-2,283	-735	-171	-164	-62	-830	172
Financial CF	-	-237	66	1,641	1,829	361	2,491	2,778	73
Cash and deposits	6,987	7,149	11,747	4,116	2,964	714	3,857	5,421	4,936
Interest-bearing debt	0	0	0	68	1,039	84	0	0	0
Net debt	-6,987	-7,149	-11,747	-4,048	-1,925	-630	-3,857	-5,421	-4,936

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 side effects. 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 only 5% 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 high at 72.0% of the total in 2021.

In its medium-term plan through FY12/24, the company is testing new modality concepts it hopes will drive the next generation of growth. However, Shared Research believes that it will take time to establish the necessary sophisticated platform technologies, 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 once the drug under development is launched on the market. 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. Barring a 3.6% YoY increase in 2010, enrolments in graduate doctoral programs have been in a downtrend since peaking in 2003. Furthermore, most biopharmaceutical drug discovery occurs overseas, and there are relatively few researchers in Japan. Shared Research thinks that the company's future growth will depend on its ability to hire personnel who match its particular requirements.

Historical results and financial statements

Income statement

Income statement	FY12/12	FY12/13	FY12/14	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21
(JPYmn)	Non-cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.
Operating revenue	**29**	**228**	**154**	**146**	**705**	**1,419**	**745**	**1,703**	**1,107**	**2,776**
YoY	-95.8%	687.0%	-32.5%	-5.5%	384.7%	101.2%	-47.5%	128.7%	-35.0%	150.7%
Operating expenses	**2,666**	**2,366**	**2,276**	**2,010**	**1,465**	**1,570**	**1,820**	**1,719**	**1,593**	**2,068**
YoY	2.5%	-11.2%	-3.8%	-11.7%	-27.1%	7.1%	15.9%	-5.5%	-7.3%	29.8%
Cost of revenue	-	0	3	-	118	150	89	263	138	321
YoY	-	-	731.3%	-	-	27.1%	-40.2%	193.9%	-47.5%	132.4%
R&D expenses	1,804	1,518	1,480	1,302	796	849	1,075	864	932	1,127
YoY	8.6%	-15.9%	-2.5%	-12.0%	-38.9%	6.6%	26.6%	-19.6%	7.9%	20.9%
R&D expense ratio	6,225.5%	665.7%	961.7%	895.2%	112.9%	59.8%	144.3%	50.7%	84.2%	40.6%
SG&A expenses	862	848	794	708	551	572	656	592	523	620
YoY	-7.2%	-1.6%	-6.3%	-10.9%	-22.1%	3.7%	14.7%	-9.7%	-11.6%	18.6%
SG&A ratio	2,974.2%	371.7%	515.9%	486.4%	78.2%	40.3%	88.1%	34.8%	47.2%	22.3%
Operating profit	**-2,637**	**-2,138**	**-2,123**	**-1,865**	**-760**	**-150**	**-1,075**	**-16**	**-486**	**708**
YoY	-	-	-	-	-	-	-	-	-	-
Operating profit margin	-	-	-	-	-	-	-	-	-	25.5%
Non-operating income	28	327	187	99	94	85	45	49	35	177
Interest income	4	1	3	4	13	4	9	9	4	2
Interest on securities	2		31	78	52	35	32	35	28	21
Foreign exchange gains		55	27	14		1			-	146
Gain on valuation of compound financial instruments			20		8			4	1	0
Gain on sale of securities				1						
Subsidy income	11				20	44	1	0	2	6
Dividend received				0						
Reversal of allowance for investment loss		261								
Rent income	5									
Gain on sale of intermediates, etc.	3									
Other	3	10	6	1	2	1	3	1	1	3
Non-operating expenses	282	9	7	29	55	85	35	12	76	21
Interest expenses									0	1
Interest on bonds										
Foreign exchange losses	5				55		33	0	76	-
Share issuance expenses		8	7	6		13	1	12	0	0
Loss on valuation of derivatives									-	10
Settlement package									-	10
Loss on valuation of compound financial instruments				21		2	1			
Loss on redemption of securities				2						
Provision of allowance for investment loss	261									
Other	17	1	-	-	-	0	-	-	-	-
Recurring profit	**-2,891**	**-1,820**	**-1,942**	**-1,795**	**-721**	**-81**	**-1,065**	**22**	**-528**	**864**
YoY	-	-	-	-	-	-	-	-	-	-
Recurring profit margin	-	-	-	-	-	-	-	1.3%	-	31.1%
Extraordinary gains		801	1,549	66		21	5	6	9	17
Gain on sale of fixed assets			6						1	-
Gain on sale of investment securities		801	1,544	66		18	5	6	8	14
Gain on redemption of investment securities										2
Extraordinary losses	10	83	65	119	2	0	18		9	
Impairment losses		58							3	
Loss on sales of investment securities						0			0	
Loss on redemption of investment securities				6	2				7	
Special retirement expenses	10		10	69						
Office relocation expenses			54	43						
Loss on cancellation of lease contract		24								
Other	-	1	-	-	-	-	-	-	-	-
Income taxes	4	6	7	6	5	-2	26	22	79	125
Implied tax rate	-0.1%	-0.6%	-1.5%	-0.3%	-0.7%	2.9%	-2.4%	80.4%	-15.0%	14.2%
Net income attributable to owners of the parent	**-2,905**	**-1,108**	**-465**	**-1,854**	**-728**	**-58**	**-1,105**	**5**	**-607**	**756**
YoY	-	-	-	-	-	-	-	-	-	-
Net margin	-	-	-	-	-	-	-	0.3%	-	27.2%

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	FY12/12	FY12/13	FY12/14	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21
(JPYmn)	Non-cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.
Assets										
Cash and deposits	4,890	4,035	1,891	1,840	1,428	2,268	1,671	2,174	1,394	2,345
Notes and accounts receivable	10	60	20	73	58	449	1	747	531	1,205
Securities			1,184	503	9	329	168	26	719	314
Inventories	48	47	9	7	7	5	6	6	7	11
Advances paid	101		58	179	205	190	9	6	36	16
Prepaid expenses	21		55	65	56	62	72	69	50	90
Other	21	222	43	40	43	20	35	39	97	22
Total current assets	**5,090**	**4,364**	**3,261**	**2,708**	**1,806**	**3,322**	**1,962**	**3,067**	**2,834**	**4,004**
Buildings and structures	54	83	80	140	141	142	143	143	153	154
Tools, furniture, and fixtures	47	370	349	394	452	488	677	742	872	944
Lease assets							3	3	49	60
Accumulated depreciation		-464	-363	-273	-344	-415	-505	-639	-741	-859
Machinery, equipment, and vehicles	0	17	2							
Total tangible fixed assets	**101**	**7**	**85**	**261**	**249**	**216**	**318**	**249**	**333**	**299**
Trademark	2	4	3	2	6	5	5	5	4	4
Software	18		6	8	7	4	28	27	28	29
Other	1	8	3	4	0	-	1	1	1	1
Total intangible assets	**21**	**12**	**12**	**14**	**13**	**10**	**34**	**32**	**33**	**34**
Investment securities	476	2,221	1,800	1,752	1,937	1,503	1,717	1,474	1,038	888
Long-term prepaid expenses	4		4	5	3	2	10	2	0	0
Deferred tax assets									3	-
Guarantee deposits	70									
Allowance for investment loss	-261									
Other	-	45	39	12	11	11	12	12	10	9
Investments and other assets	**289**	**2,266**	**1,844**	**1,769**	**1,951**	**1,516**	**1,738**	**1,488**	**1,051**	**897**
Total fixed assets	**411**	**2,284**	**1,941**	**2,044**	**2,213**	**1,742**	**2,090**	**1,769**	**1,417**	**1,230**
Total assets	**5,501**	**6,648**	**5,202**	**4,752**	**4,019**	**5,064**	**4,052**	**4,837**	**4,251**	**5,234**
Liabilities										
Notes and accounts payable						2		34	42	46
Short-term debt	-	-	-	-	-	-	1	1	18	22
Accounts payable–other	91	142	119	123	126	63	99	67	53	113
Accrued expenses	72		63	57	40	44	48	50	50	63
Income taxes payable	16	17	16	15	1	21	14	20	21	80
Consumption taxes payable						14			-	37
Deferred tax liabilities					1					
Advances received			14		14	1		7		
Deposits	4		5	5	3	4	3	3	3	29
Other	-	74	46	-	5	-	-	-	-	10
Total current liabilities	**183**	**233**	**262**	**200**	**190**	**149**	**164**	**183**	**187**	**401**
Long-term debt	-	-	-	-	-	-	2	2	27	18
Asset retirement obligations				12	12	12	12	12	12	12
Deferred tax liabilities	7	669	109	26	29	16	16	19	14	16
Other	-	-	-	-	-	-	-	-	-	-
Total fixed liabilities	**7**	**669**	**109**	**38**	**41**	**27**	**31**	**33**	**53**	**46**
Total liabilities	**191**	**902**	**371**	**238**	**231**	**176**	**195**	**216**	**240**	**446**
Net assets										
Capital stock	8,490	8,628	8,952	9,806	2,238	2,741	2,793	2,255	2,255	2,257
Capital surplus	3,774	3,912	4,236	5,090	2,238	2,931	2,983	2,445	2,445	2,447
Retained earnings	-6,965	-8,074	-8,567	-10,421	-728	-786	-1,890	-99	-706	50
Share subscription rights		33	11	11	15	17	13	12	12	11
Total net assets	**5,310**	**5,746**	**4,831**	**4,514**	**3,788**	**4,888**	**3,857**	**4,621**	**4,011**	**4,788**
Total liabilities and net assets	**5,501**	**6,648**	**5,202**	**4,752**	**4,019**	**5,064**	**4,052**	**4,837**	**4,251**	**5,234**
Working capital	57	107	29	80	65	452	7	718	496	1,170
Total interest-bearing debt	-	-	-	-	-	-	3	2	46	39
Net debt	-4,890	-4,035	-1,891	-1,840	-1,428	-2,268	-1,668	-2,172	-1,349	-2,306

Source: Shared Research based on company data

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

Cash flow statement

Cash flow statement	FY12/12	FY12/13	FY12/14	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21
(JPYmn)	Non-cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.	Cons.
Cash flows from operating activities (1)	-2,729	-2,179	-2,081	-2,117	-681	-307	-404	-531	-289	366
Pre-tax profit	-2,902	-1,102	-632	-1,848	-723	-60	-1,078	27	-528	881
Depreciation	28	68	21	53	80	86	126	140	124	142
Impairment losses									3	-
Gain and loss on sale and disposal of fixed assets									-1	-
Change in working capital	-112	-50	78	-51	15	-377	445	-711	223	-674
Cash flows from investing activities (2)	3,741	952	-796	666	-441	534	-368	216	225	-279
Purchase of intangible/tangible fixed assets	-54	-26	-101	-200	-37	-88	-221	-94	-156	-105
Proceeds from sale of intangible/tangible fixed assets		4	2						1	-
Free cash flow (1+2)	1,013	-1,227	-2,877	-1,451	-1,122	226	-772	-315	-64	87
Cash flows from financing activities	-	309	762	1,702	-	1,007	99	696	-7	-16
Net change in short-term borrowings									-	-
Net change in long-term borrowings	-	-	-	-	-	-	-	-	-	-
Proceeds from issuance of, and redemption of, bonds	-	-	140	-	-	-	-	-	-	-
Proceeds from share issuance exercising share subscription rights		272	640	1,686		996	100	692	0	2
Proceeds from issuance of share subscription rights		38	15	15		11		4		
Proceeds from issuance of shares										
Repayments of lease obligations							-1	-1	-7	-18
Change in cash and cash equivalents	1,013	-855	-2,031	252	-999	1,229	-644	371	-139	179
Cash and cash equivalents (year-end)	4,890	4,035	2,004	2,243	1,244	2,474	1,830	2,200	2,061	2,241

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

In FY12/21, cash flows from operating activities increased by JPY655mn, from outflows of JPY289mn in FY12/20 to inflows of JPY366mn. This was mainly due to JPY880mn in pre-tax profit and JPY141mn in depreciation, offsetting an outflow from a JPY674mn increase in trade receivables.

Cash flows from investing activities

Cash outflows from investing activities came to JPY279mn, an increase of JPY504mn versus cash inflows of JPY225mn in FY12/20. This was mainly attributable to JPY200mn used for the purchase of securities and JPY200mn used for the purchase of investment securities, which absorbed JPY221mn proceeds from sales of investment securities.

Cash flows from financing activities

Cash outflows from financing activities came to JPY16mn, an increase of JPY9mn versus cash outflows of JPY7mn in FY12/20. This was mainly attributable to repayments of lease obligations of JPY18mn.

Historical performance

1H FY12/22 results (out August 15, 2022)

Earnings summary

1H FY12/22 (January–June 2022) results

- Revenue: JPY1.4bn (+9.6% YoY)
- Operating profit: JPY551mn (+75.1% YoY)
- Recurring profit: JPY681mn (+57.4% YoY)
- Net income attributable to owners of the parent: JPY469mn (+55.0% YoY)
- R&D expenses: JPY497mn (+0.0% YoY)
- Progress against full-year forecast: Revenue 55.6%, operating profit 131.3%, recurring profit 162.2%, and net income 137.3%

Factors behind higher revenue and profits

In 1H FY12/22, operating revenue came to JPY1.4bn (+9.6% YoY), comprising royalty revenue of JPY699mn (+43.2% YoY), milestone payments of JPY434mn (-42.0% YoY), which included a one-time payment of JPY300mn from approval and launch

of tegoprazan in China, and other revenue of JPY314mn (+XX% YoY).

In pet drugs, while sales of GALLIPRANT® were sluggish in Europe due to inclement weather among other factors, sales of the drug maintained double-digit growth in the US. ENTYCE® and ELURA® also performed strong. In human drugs, orally disintegrating tablet formulation of tegoprazan (K-CAB®) was launched, and the drug was approved for its fifth indication, maintenance therapy for healed erosive esophagitis, with sales in South Korea remaining strong. In China, Shandong Luoxin Pharmaceutical Group Stock Co., Ltd. (SHE: 002793), a licensee of HK inno.N, obtained marketing approval for tegoprazan and began sales, triggering a milestone payment of JPY300mn.

R&D expenses totaled JPY528mn (+6.4% YoY, 35.8% of the full-year plan), consisting of JPY481mn for discovery of development candidate compounds and JPY46mn for preclinical studies of a ghrelin receptor agonist and preparation of clinical pharmacological studies of tegoprazan. All profit categories exceeded their respective full-year targets as of end-1H, but the company maintained its forecast as it expects to incur R&D and other expenses in 2H.

Pipeline

Launched products

In pet drugs, sales of GALLIPRANT® (generic name: grapiprant) for treatment of osteoarthritis in dogs and ENTYCE® (capromorelin) for treatment of anorexia in dogs, both out-licensed to Elanco, grew. Elanco also sells capromorelin under the brand name ELURA® as a drug for the management of weight loss in cats with chronic kidney disease in the US. Elanco applied for marketing approval for these drugs in Europe as well, and based on this development, RaQualia received a milestone payment of USD1mn from Elanco in Q1 (January–March 2022).

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 amounting to KRW60.6bn (approximately JPY6.0bn, converted at JPY0.10/KRW; +21.2% YoY). HK inno.N obtained marketing approval for and launched the new orally disintegrating tablet formulation of tegoprazan in South Korea. In China, Luoxin, a licensee of HK inno.N in the country, obtained marketing approval for tegoprazan from the Chinese authorities in April 2022 and began sales in the same month. Luoxin targets sales of CNY1.0bn (approximately JPY19.6bn, converted at JPY19.6/CNY) for 2023 and CNY3.0bn (JPY58.8bn) in the medium to long term. The company will receive royalty payments from HK inno.N after the latter confirms its revenue from the drug.

In April 2022, HK inno.N completed Phase I clinical trial of tegoprazan in the US, and sublicensee Braintree Laboratories (unlisted) had pre-clinical trial consultations with the US FDA with the goal of commencing clinical trials within 2022. In May 2022, HK inno.N entered into a license agreement with India-based Dr. Reddy's Laboratories (NSD: DRREDDY), covering marketing rights in seven countries including India in Asia, Eastern Europe, and Africa. Also in May 2022, Metro, a sublicensee of HK inno.N in the Philippines, obtained marketing approval for tegoprazan for erosive esophagitis and three other indications.

Out-licensed pipeline

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

- EP4 receptor antagonist: US-based Ikena Oncology (NASDAQ: IKNA), a sublicensee of the company's licensee AskAt Inc. (unlisted), is conducting a Phase Ib clinical trial of the pipeline drug as cancer immunotherapy in the US. In China, Ningbo NewBay Medical Technology Development Co., Ltd. (unlisted), a licensee of AskAt, is conducting a Phase I study in the oncology field.
- CB2 agonist: UK-based Oxford Cannabinoid Technologies Ltd. (LSE: OCTP), a licensee of AskAt, is conducting preclinical studies in the UK.
- P2X7 receptor antagonist: US-based Eli Lilly is preparing to conduct a Phase II study.
- TRPM8 blocker: Hong Kong-based Xgene Pharmaceutical commenced preclinical studies.
- Sodium channel blocker: Hisamitsu Pharmaceutical is preparing to conduct preclinical studies.

In addition to the above, although development stage is undisclosed, a selective sodium channel blocker is being developed by Maruho Co., Ltd. (unlisted), and a candidate compound targeting a specific ion channel is under development by EA

Pharma Co., Ltd. (unlisted; former Ajinomoto Pharmaceuticals Co., Ltd.; consolidated subsidiary of Eisai Co., Ltd. [TSE Prime 4523]).

Pre-out-licensing pipeline

- Tegoprazan (Japan): Consultations with PMDA and discussions with candidate licensing partners ongoing with an eye toward starting clinical development
- Ghrelin receptor agonist: Preclinical studies underway at a contract research organization
- 5-HT4 partial agonist, 5-HT2B antagonist, motilin receptor agonist: Out-licensing activities ongoing

Q1 FY12/22 results

Earnings summary

Q1 FY12/22 (January–March 2022) results

- Revenue: JPY339mn (-48.3% YoY)
- Operating loss: JPY120mn (profit of JPY149mn in Q1 FY12/21)
- Recurring loss: JPY70mn (profit of JPY268mn)
- Net loss attributable to owners of the parent: JPY121mn (net income of JPY189mn)
- R&D expenses: JPY264mn (+3.0% YoY)
- Progress against full-year forecast: Revenue 13.0%, R&D expenses 17.9%

In Q1 FY12/22, the company generated revenue of JPY339mn, comprising royalty revenue of JPY184mn (+36% YoY), milestone payments of JPY115mn accompanying the approval of ELURA® in Europe, and other revenue of JPY40mn. Revenue declined versus Q1 FY12/21, when the company received a total of JPY516mn in milestone payments from Asahi Kasei Pharma Corporation (unlisted, subsidiary of Asahi Kasei Corporation [TSE Prime 3407]) and Maruho Co., Ltd. (unlisted).

The company spent JPY264mn on R&D, primarily exploratory research. It conducted preclinical studies into its ghrelin receptor agonist and prepared to start clinical pharmacological studies of tegoprazan.

Revenue came in at 13.0% of the full-year forecast. Royalty payments for tegoprazan are twice yearly, and booked in Q2 and Q4, so progress was largely in line with the company forecast. At the time of the Q1 results announcement, the company maintained its full-year FY12/22 forecast.

Pipeline

Launched products

Sales of K-CAB® (GERD treatment) in South Korea by licensee HK inno.N remained strong, with revenue from prescriptions outside hospitals up 23.5% YoY. HK inno.N received manufacturing and marketing approval for a new orally disintegrating tablet formulation of tegoprazan in South Korea. In China, HK inno.N's Chinese licensee Luoxin Pharmaceutical received manufacturing and marketing approval from Chinese authorities in April 2022. In Malaysia, HK inno.N signed a drug product supply agreement with Pharmaniaga.

In pet drugs, sales of GALLIPRANT® (grapiprant; treatment for osteoarthritis in dogs) and ENTYCE® (capromorelin; treatment for anorexia in dogs) remained in an uptrend for licensee Elanco. Elanco also sells capromorelin under the brand name ELURA® as a drug for the management of weight loss in cats with CKD. Elanco filed for manufacturing and marketing approval for capromorelin in Europe, and the company received a milestone payment of USD1mn in Q1.

Out-licensed pipeline

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

Pre-out-licensing pipeline

The company plans to develop tegoprazan in Japan and aims at efficient development and approval in Japan using South Korean data. It decided to conduct clinical pharmacological studies to evaluate ethnic differences between Japanese and Korean people. In February 2022, by mutual consent, the company and Meiji Seika Pharma Co., Ltd. terminated a license agreement signed in March 2011 granting the latter exclusive rights to develop and market the schizophrenia drug ziprasidone in Japan. The company decided to return the license to the licensor, US-based Viatris Inc. (NASDAQ: VTRS).

FY12/21 results

Earnings summary

FY12/21 (January–December 2021) results

- Revenue: JPY2.8bn (+150.7% YoY)
- Operating profit: JPY708mn (loss of JPY486mn in FY12/20)
- Recurring profit: JPY864mn (loss of JPY528mn)
- Net income attributable to owners of the parent: JPY756mn (loss of JPY607mn)
- R&D expenses: JPY1.1bn (+20.9% YoY)
- Progress against revised full-year forecast: Revenue 99.2%, operating profit 100.1%, recurring profit 101.9%, and net income 100.8%

Sales of K-CAB® (tegoprazan; GERD treatment; out-licensed to HK inno.N) continued to grow, and sales of pet drugs by Elanco Animal Health (GALLIPRANT®, ENTYCE®, and ELURA®) were solid. In addition to strong royalty revenue from the above four commercialized drugs, the company received milestone payments from out-licensed programs and upfront payments from new license agreements, booking the first operating profit since its founding in 2008.

A new management structure including a new representative director was put in place following the approval of a shareholder proposal at the ordinary general meeting of shareholders held on March 25, 2021.

Milestone and upfront payments received in FY12/21

- Upfront payment from Asahi Kasei Pharma relating to license agreement for P2X7 receptor antagonist
- Milestone payment from Maruho
- Milestone payment from Syros
- Upfront payment from Xgene relating to license agreement for TRPM blocker and sodium channel blocker

Pipeline

Launched products

Sales of K-CAB® (GERD treatment) in South Korea by licensee HK inno.N remained strong, as they were in FY12/20. Following the impact of inventory adjustments in Q1, growth resumed from Q2 onward, and royalty revenue increased significantly. In November 2021, tegoprazan used as a gastric ulcer treatment became covered by health insurance in South Korea. This was the third indication approved for the drug, following GERD and nonerosive reflux disease (NERD). HK inno.N plans to apply to the South Korean Ministry of Food and Drug Safety (MFDS) for an additional indication as a maintenance treatment for patients who have been cured of GERD.

Regarding global development of tegoprazan, in China, a new drug application (NDA) that HK inno.N's licensee Luoxin Pharmaceutical filed with the Chinese authorities in 2020 was under review. HK inno.N hopes to gain approval in China in 1H 2022. HK inno.N launched Phase I clinical trials of tegoprazan in the US and concluded a sublicense agreement with US-based Braintree in December 2021.

In Asia, tegoprazan acquired approval in Mongolia, and in the Philippines, Thailand, Vietnam, Singapore, and Indonesia, sublicensees were preparing to submit new drug applications. In South and Central America, in Mexico, tegoprazan passed screening by the Comite de Moleculas Nuevas, an organization involved in that country's pharmaceutical approval process, and sublicensees were working on preparations aimed at obtaining approval in FY2023. HK inno.N aims to roll out the drug to 100 countries around the world by 2028, and is looking for sublicensees in other regions.

Sales of drugs out-licensed to Elanco, GALLIPRANT® (treatment for osteoarthritis in dogs) and ENTYCE® (treatment for anorexia in dogs) remained solid overall. Elanco launched capromorelin under the brand name ELURA® for the management of weight loss in cats with CKD in the US.

Out-licensed pipeline

In ion channel drug discovery, where the company's strengths lie, five of its programs made steady progress: a P2X7 receptor antagonist created through joint research with Asahi Kasei Pharma, a compound created through joint research with EA Pharma, a selective sodium channel blocker out-licensed to Maruho, a joint research project with ASKA Pharmaceutical, and a TRPM8 blocker out-licensed to Xgene.

Asahi Kasei Pharma and Eli Lilly concluded a license agreement covering the P2X7 receptor antagonist. Eli Lilly is preparing to launch Phase II clinical trials with the aim of global development.

The company received a lump sum payment after achieving a milestone in July 2021 in the joint research project with ASKA Pharmaceutical, and concluded a new joint research contract in November 2021.

In Q3, the company concluded a license agreement with Hong Kong-based Xgene for a TRPM8 blocker with the aim of developing a treatment for chronic pain. The company granted Xgene an exclusive global license for development, manufacture, and marketing excluding Japan. Xgene will be responsible for development beyond the preclinical trial phase.

In December 2021, the company and Hisamitsu concluded a license agreement regarding a sodium channel blocker, with the aim of developing a treatment for chronic pain. The company granted Hisamitsu an exclusive global license for development, manufacture, and marketing. Hisamitsu plans to conduct preclinical trials and beyond with the aim of developing transdermal drugs, one of its strengths.

The company's consolidated subsidiary TMRC out-licensed a retinoic acid receptor alpha (RARA) agonist (tamibarotene) to Syros Pharmaceutical, which in Q1 launched Phase III clinical trials for newly diagnosed RARA-positive patients with higher risk myelodysplastic syndrome (MDS). In Q3, it launched Phase II clinical trials of a triple drug therapy in combination with venetoclax and azacitidine in newly diagnosed unfit* RARA-positive patients with acute myeloid leukemia (AML). The company received milestone payments as these benchmarks were met.

*Unfit here means patients such as the elderly for whom standard chemotherapy treatment is not suitable.

Pre-out-licensing pipeline

The company was looking into launching clinical trials with a view to early commercialization of tegoprazan in Japan, and considering how to collaborate with HK inno.N.

The company's consolidated subsidiary RaQualia Innovations Inc. determined that continuing to operate in the recent business environment would be difficult and decided to dissolve on January 22, 2021, with liquidation complete on April 1, 2021.

Cumulative Q3 FY12/21 results

Earnings summary

Cumulative Q3 FY12/21 (January–September 2021) results

- Revenue: JPY1.6bn (+183.0% YoY)
- Operating profit: JPY107mn (loss of JPY601mn in cumulative Q3 FY12/20)
- Recurring profit: JPY238mn (loss of JPY615mn)
- Net income attributable to owners of the parent: JPY169mn (loss of JPY699mn)
- R&D expenses: JPY781mn (+15.6% YoY; about 63% of full-year budget)
- Progress against full-year forecast: Revenue 72.3%, operating profit 175.4%, recurring profit 129.3%, net income 143.2%

In cumulative Q3 FY12/21, operating expenses of JPY1.5bn (+29.1% YoY) broke down to cost of operating revenue of JPY268mn (+176.4% YoY), R&D expenses of JPY781mn (+15.6% YoY) and other SG&A expenses of JPY466mn (+16.0% YoY). The main reason for the rise in other SG&A expenses was that the cost of running the ordinary general meeting of shareholders, at JPY60mn, was more than double that of normal years due to shareholder proposals.

Pipeline

Launched products

Revenue from pet drugs was up 11.1% YoY, and royalty revenue came to JPY152mn. Sales of tegoprazan (K-CAB®) in South Korea were strong, with revenue from prescriptions outside hospitals of KRW78.1bn.

Out-licensed pipeline

In September 2021, the company signed an out-license agreement with Hong Kong-based Xgene regarding its TRPM8 blocker, and booked an upfront payment. Consolidated subsidiary TMRC's licensee Syros Pharmaceutical administered drugs to its first patient in Phase II clinical trials of a triple drug therapy of tamibarotene, venetoclax, and azacitidine in newly diagnosed unfit patients with AML. The company received a payment of USD1mn for reaching this milestone.

Pre-out-licensing pipeline

The company completed the manufacture of active pharmaceutical ingredients (APIs) for preclinical studies into its ghrelin receptor agonist, which it planned to launch in Q4.

In November 2021, the company concluded a new joint research project with ASKA Pharmaceutical. The partners plan to conduct advanced R&D based on the results of their joint efforts to date.

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®, veterinary 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®, veterinary 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

Source: Shared Research based on company data

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
Chairperson of Audit & Supervisory Committee	Outside director
Other	
Participation in electronic voting platform	In place
Providing convocation notice in English	In place
Implementation of measures regarding director incentives	Performance-linked remuneration; stock option
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

President and CEO: Hirobumi Takeuchi (born December 21, 1971)

Apr 1994	Joined Kyowa Co., Ltd.
Feb 2004	Joined Skylight Biotech Inc as general manager of sales department
Sep 2005	Director in charge of business promotion and finance, Skylight Biotech Inc.
Jul 2006	Director and CFO in charge of administrative division, Skylight Biotech Inc.
May 2009	Joined Sumisho Realty Management Co., Ltd. as manager of administration department
Jan 2013	Joined Cyfuse Biomedical K.K. as director in charge of corporate planning and business administration
Jan 2014	Joined RaQualia Pharma Inc. as deputy general manager of accounting department
Apr 2014	General manager of accounting department, RaQualia Pharma Inc.
Oct 2014	General manager of finance and accounting department, finance and corporate planning division, RaQualia Pharma Inc.
Apr 2018	President and CEO, UBiENCE Inc.
Mar 2021	President and CEO, RaQualia Pharma Inc. (current position)
Jun 2021	Director, UBiENCE Inc. (current position)

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). In order 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 in order to separate the management and execution functions and strengthen and invigorate execution.

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 an 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 ('000)	Shareholding ratio
Yuichi Kakinuma	2,385	11.38%
SBI Securities Co., Ltd.	951	4.54%
MSIP CLIENT SECURITIES (Standing proxy: Morgan Stanley MUFG Securities Co., Ltd.)	806	3.85%
Pfizer Japan Inc.	743	3.55%
Central Tanshi Co., Ltd.	580	2.77%
au Kabucom Securities Co., Ltd.	182	0.87%
Matsui Securities Co., Ltd	169	0.81%
Takahiro Tanago	167	0.79%
Yukio Uemura	146	0.70%
SBC Co., Ltd.	122	0.58%
SUM	6,250	29.83%

Source: Shared Research based on company data (as of December 31, 2021)

Number of employees

	FY12/12	FY12/13	FY12/14	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21
Number of employees (consolidated)		74	72			60	63	68	70	67
Number of employees (parent)	81	70	70	64	50	55	58	62	64	62
Average age	42.8	43	43.6	44.1	44.8	45.5	45.5	46.3	47.3	46.5
Average years of service	3.8	4.7	5.5	5.9	6.6	7.0	6.9	7.4	8.1	8.7
Average annual salary (JPY'000)	8,497	8,024	7,971	8,124	7,242	7,391	7,408	7,237	7,510	7,369

Source: Shared Research based on company data

In FY12/21, roughly 50 of the parent's 62 employees were involved in research and development, and over 10 were involved in out-licensing and other business development and management duties.

Profile

Company Name

Raqualia Pharma Inc.

Phone

052-446-6100

Established

2008-02-19

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http://www.raqualia.co.jp

IR Contact

https://www.raqualia.com/contact/

IR Phone

-

Head Office

Meieki Southside Square, 1-21-19 Meieki Minami, Nakamura-ku, Nagoya City

Listed On

Tokyo Stock Exchange, Growth Market

Exchange Listing

2011-07-20

Fiscal Year-End

Dec

IR Web

https://www.raqualia.com/ir/

IR Email

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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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