Business Conditions

ASKA Pharmaceutical

Creating new value as a leading company in female healthcare

Founded in 1920, ASKA Pharmaceutical began its business with the unique idea of developing hormone preparations from animal organs. Today, we concentrate management resources on the three priority areas of internal medicine, Ob/Gyn, and urology, and develop the pharmaceutical business with a focus on new drugs.

Our strengths lie in the trust and experience we have accumulated by conducting R&D with a focus on hormone-related areas, launching new products, ensuring quality and stable supply, and promoting dissemination of information on proper use.

In the Ob/Gyn area, in particular, we approach various issues according to women's life stages. We support women's health and lives with a wide variety of pharmaceuticals for dysmenorrhea, contraception, uterine fibroids and endometriosis, infertility, perinatal period disorders and menopause-related diseases, among other indications.

In the thyroid area, our domestic market share of pharmaceuticals for hypothyroidism and hyperthyroidism each exceeds 90%. We are fulfilling our mission of providing a stable supply of these products, which are indispensable in medical settings.

In the healthcare field, there has been growing public interest in Femtech, which is defined as the use of technology to address health issues specific to women, such as menstruation, pregnancy, childbirth, and menopause. There is increasing momentum toward creating an environment where everyone can work and live comfortably.

In light of this trend, in April 2023 we established the Femtech Business Promotion Unit, which is tasked with supporting women's health more broadly, beyond pharmaceuticals.

As women enter the workforce and their lifestyles change, we feel that now more than ever there is a need to address women's specific health issues.

As a leading company in female healthcare that responds to various needs, we will create innovative new drugs by accelerating open innovation through collaboration between industry, government, and academia in Japan and overseas. We will continue making efforts to raise awareness in various ways such as using the knowledge we have cultivated over the years to disseminate information. In doing so, we will create opportunities for women to make choices that lead to healthy and fulfilling lives.

While strengthening the core of our pharmaceutical business with a focus on new drugs, we aim to go beyond solely providing pharmaceuticals. We will take an integrated approach covering prevention, testing, diagnostics, treatment, and prognosis to become a total healthcare company while transforming into a competitive specialty pharma company.

Sohta Yamaguchi

President, Representative Director
ASKA Pharmaceutical

Strengths and Strategies

As a leading company in the Ob/Gyn area, ASKA Pharmaceutical is using its strengths in the fields of endocrinology and hormones to implement a range of strategies aimed at helping solve women's health issues.

Strengths

- Leading company in the Ob/Gyn area
- Leading company in the thyroid area
- Specializing in endocrine and hormone areas for over 100 years

Strategies

- Provide 21 pharmaceutical products that accommodate women's lifestyles
- Achieve penetration of agents for uterine fibroids, endometriosis, and dysmenorrhea
- Contribute to solving women's health issues through a variety of initiatives, including dissemination of information on women's health
- Contribute to raising awareness and treatment of thyroid-related diseases
- Maintain a stable supply of basic pharmaceutical products
- Conduct R&D with a focus on hormone-related areas, launch new products, ensure quality and stable supply, and promote dissemination of information on proper use
- Concentrate management resources on the three priority areas of internal medicine, Ob/Gyn, and urology, and develop the pharmaceutical business with a focus on new drugs
- Create innovative new drugs by accelerating open innovation through collaboration between industry, government, and academia in Japan and overseas
- Make efforts to raise awareness in various ways such as using the knowledge we have cultivated over the years to disseminate information

Main Products

• Internal Medicine

Hepatic encephalopathy agent
RIFXIMA
(rifaximin)

Hypothyroidism agent
THYRADIN
(levothyroxine)

Antihypertensive agent
CANDESARTAN "ASKA"
(candesartan)

• Ob/Gyn

Uterine fibroids and endometriosis agent
RELUMINA
(relugolix)

Dysmenorrhea agent
DroEthi "ASKA"
(drospirenone/ethinylestradiol)

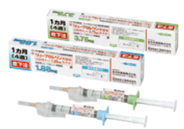
Dysmenorrhea agent
FREWELL "ASKA"
(norethisterone/ethinylestradiol)

Infertility agent
LUTEUM
(progesterone)

Emergency contraceptive
NORLEVO
(levonorgestrel)

• Urology

Endometriosis, uterine fibroids, and prostate cancer agent
LEUPRORELIN "ASKA"
(leuprorelin)

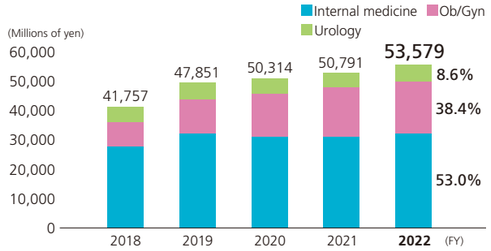


Business Conditions

Performance in FY2022

The pharmaceutical business, which focuses on the three priority areas of internal medicine, Ob/Gyn, and urology, remained strong overall despite the impact of NHI drug price revisions. Net sales increased to ¥53,579 million (up 5.5% year on year). By product, in the Ob/Gyn area, sales of RELUMINA (relugolix), a uterine fibroids and endometriosis agent, increased to ¥8,839 million (up 20.5% year on year), a significant increase following the previous year, and sales of FREWELL (norethisterone/ethinylestradiol, a dysmenorrhea agent), grew to ¥3,489 million (up 0.8% year on year) despite a price reduction of over 10% due to the NHI drug price revision in April 2022. Sales of DroEthi (launched in June 2022), a dysmenorrhea agent for which we acquired manufacturing and marketing approval as the only company, totaled ¥3,671 million. In addition, in the area of internal medicine, sales of our key product THYRADIN, a hypothyroidism agent, increased to ¥7,733 million (up 3.1% year on year). Sales of RIFXIMA, a hepatic encephalopathy agent for which we worked to establish clinical practice guidelines, rose to ¥5,397 million (up 11.2% year on year). In the urology field, sales of LEUPRORELIN, an endometriosis, uterine fibroids, and prostate cancer agent, decreased to ¥4,999 million (down 3.6% year on year). As a specialty pharma company focusing on the three areas of internal medicine, Ob/Gyn, and urology, we will continue to actively expand our development pipeline by further promoting drug discovery and alliances.

Net Sales in the Pharmaceutical Business



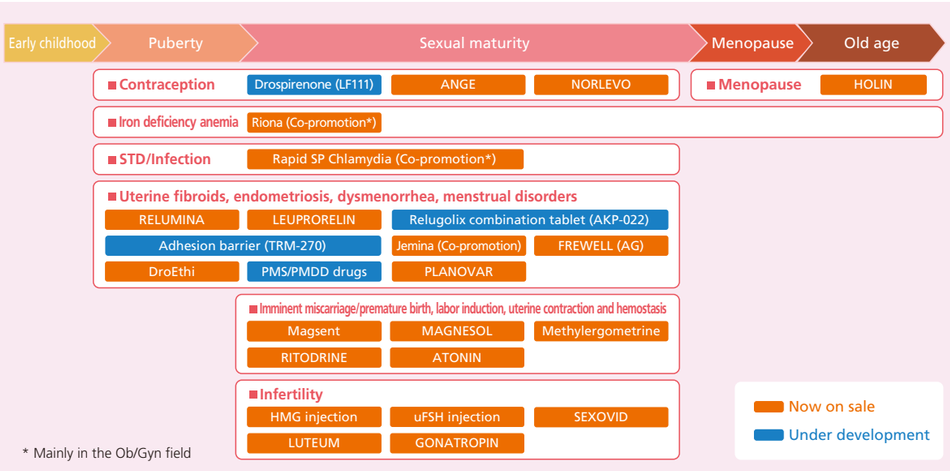
Note: Amounts are rounded down to the nearest million yen.

Major Initiatives

❶ Specialty Areas

We have established a specialty area system, which we introduced to conduct information provision activities focusing on the Ob/Gyn area and RIFXIMA. Under this system, we will continue to provide high-quality information and pursue efficient sales activities such as through webinars. We work to further enhance our presence in the Ob/Gyn area through the provision of information on products that contribute to business performance, mainly RELUMINA and DroEthi (launched in June 2022), as well as Jemina and Riona for which we are conducting co-promotion activities. In addition, with the revision of guidelines, RIFXIMA has established its status as a standard agent for hepatic encephalopathy. As a result, we will further promote the dissemination and penetration of the agent. In addition, THYRADIN, which holds a domestic market share of over 90%, is an indispensable pharmaceutical in the medical setting. As a leading company in thyroid disease-related medicines, we will maintain a stable supply system and continue to engage in activities to raise awareness of thyroid diseases.

Ob/Gyn Pharmaceuticals by Life Stage



* Mainly in the Ob/Gyn field

❷ Endometriosis Treatment

Promoting the penetration of RELUMINA as a treatment for endometriosis

We launched RELUMINA in 2019 as the first oral GnRH antagonist agent for the treatment of uterine fibroids in 20 years. Since then, the switch from the standard injectable formulation of comparable drugs with similar efficacy is progressing steadily. In December 2021, it received approval for an additional indication as an endometriosis agent. We are working to promote the penetration of RELUMINA as a treatment for endometriosis as well as for uterine fibroid treatment with the aim of providing a new option in pharmaceuticals for endometriosis. In FY2022, sales increased significantly to ¥8,839 million (up 20.5% year on year). By accelerating the penetration of RELUMINA for the treatment of uterine fibroids and endometriosis, we plan to significantly increase sales to ¥10,128 million (up 14.6% year on year) in FY2023. In this way, we expect to achieve our target of over ¥10 billion for the final year of the current medium-term management plan ahead of schedule.

Note: Amounts are rounded down to the nearest million yen.

❸ Dysmenorrhea Treatments

Achieved No.1 share in the LEP market by selling DroEthi as the company with sole sales rights

The dysmenorrhea market is rapidly expanding due to factors such as women's advancement in the workforce and increased health literacy. In this area, we have three products in our lineup: FREWELL (authorized generic) and Jemina (a co-promotion with Nobelpharma), and DroEthi (a generic drug) launched in June 2022 for which we have the sole sales rights. As such we provide a range of options for people suffering from dysmenorrhea. The combined market share of the three LEP* formulations (pharmaceuticals) is 42.7%, and we expect this to continue to grow in line with market expansion. In addition to provision of pharmaceutical products, we also operate Health Lab Mint* for Women's health as an initiative to support women's health. We continue striving to contribute to women's health through dissemination of a variety of information.

* Low-dose estrogen/progestin combination

❹ Thyroid Disease Treatments

Domestic thyroid pharmaceutical market share of 95% with THYRADIN, MERCAZOLE, etc.

Abnormal thyroid function can cause a variety of physical and mental symptoms. Thyroid disease is a common disorder among women and said to be related to menstrual disorders and infertility. Through a wide range of activities to raise disease awareness among medical professionals and the general public, we are working to be able to identify patients in need of treatment at an early stage. In addition to activities to provide information, lengthening the administration period by extending life expectancy has also contributed to sales growth of roughly 2-3% each year. We will work to ensure stable supply through daily production, stocking, and business continuity planning (BCP) measures so that we can continue to deliver pharmaceuticals to patients even in the event of an emergency. In doing so, we will fulfill our mission as a leading company in the thyroid area.

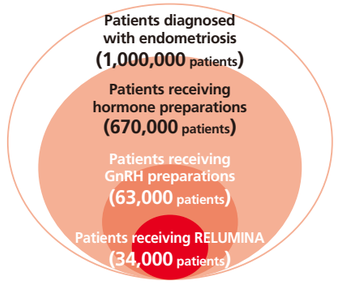
Note: Amounts are rounded down to the nearest million yen.

❺ Hepatic Encephalopathy Treatment

Contribution to unmet medical needs through RIFXIMA

Hepatic encephalopathy is a condition in which liver function is significantly reduced, which can give rise to psychoneurological symptoms such as loss of consciousness. It is a rare disease with fewer than 50,000 patients, and as such RIFXIMA is designated as an orphan drug. In addition, *the Clinical Practice Guidelines for Cirrhosis* strongly recommend RIFXIMA for treating hepatic encephalopathy. We are working to raise awareness of these guidelines with the aim of promoting the penetration of RIFXIMA. In June 2023, we additionally applied for dosage and administration approval for RIFXIMA as an agent for the treatment of hepatic encephalopathy in children. We will continue to address unmet medical needs so that we can contribute to society.

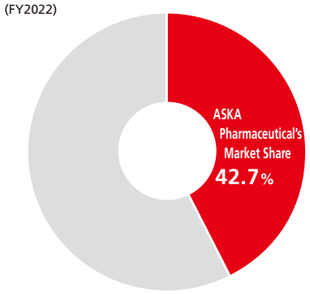
Reality of Treatment for Endometriosis



Source: Survey results by JMDC Inc. (March 2023)
Note: Estimation from electronic health insurance claims data

Product Share in the LEP Formulation Market

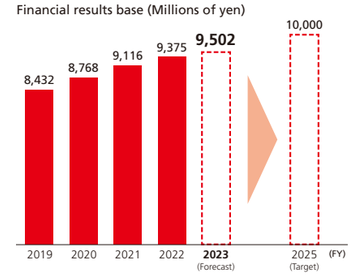
(FY2022)



Note: Estimated based on Encise data

Sales of Thyroid-Related Pharmaceuticals*

Financial results base (Millions of yen)



* THYRADIN, MERCAZOLE, PROPACIL

Business Conditions

6 Development Pipeline

In clinical development, four clinical trials are currently in progress. A Phase III trial is under way for LF111 (drospirenone), which is being developed for the indication of contraception. In September 2021, we started a domestic Phase I/II clinical trial for Relugolix (for which we have obtained exclusive development and sales rights in Japan from Takeda Pharmaceutical Company Limited) combination tablet (development code: AKP-022) for the treatment of uterine fibroids. In addition, after the completion of a Phase IIa clinical trial of AKP-009 (ludaterone acetate), which is being co-developed with Kyorin Pharmaceutical Co., Ltd., we conducted an additional Phase I clinical trial to confirm the maximum efficacy. We are carrying out another Phase I clinical trial to reconfirm the data based on the results. For TRM-270, which we are developing jointly with Toray Industries, Inc., we are currently conducting a Phase III clinical trial. In addition, a Phase II/III clinical trial for L-105 (rifaximin), for which we are seeking an additional dosage and administration approval for the treatment of hepatic encephalopathy (pediatric), has been completed and an application has been submitted to the regulatory authorities.

One theme we are pursuing in preparation for development is transnasal testosterone (AKP-017), for which we aim to begin clinical trials at an early date. In addition, we are pursuing several themes in the non-clinical setting through the acquisition of drug discovery seeds through open innovation in addition to our own technologies.

In terms of out-licensing and in-licensing activities during FY2022, in June 2022 ASKA Pharmaceutical signed a license agreement with Hyundai Pharm. Co., Ltd. concerning the development and commercialization rights in South Korea for the oral contraceptive drospirenone, which is currently under clinical trials in Japan.

In February 2023, we entered into a joint R&D agreement with Epsilon Molecular Engineering, Inc. (EME) for new drug creation of next-generation VHH antibodies in the Ob/Gyn area using EME's proprietary humanized VHH discovery platform "The Month." We will continue to expand our development pipeline by promoting drug discovery research activities.

R&D Status (As of August 2023)

Development code (generic name) / Indication		Research[1]	Non-clinical[1]	Phase I	Phase II	Phase III	Application	Approval
LF111 (drospirenone)	Contraception					Phase III ongoing		
(Option agreement)	PMS/PMDD[2] drugs under development at Renascience Inc.				Investigator-initiated Phase II ongoing			
AKP-022 (Relugolix combination tablet)	Uterine fibroids				Phase I/II ongoing			
Theme A	Ob/Gyn							
Theme B	Ob/Gyn							
TRM-270 (adhesion barrier)	Gastroenterology and Ob/Gyn					Phase III ongoing		
L-105 (rifaximin)	Hepatic encephalopathy (pediatric)						Filed	
Theme C	Internal medicine							
AKP-009 (ludaterone acetate)	Benign prostatic hyperplasia				Phase IIa completed[3]			
AKP-017 (transnasal testosterone)	Urology			Preparing development				
AKP-021 (mPGES-1 inhibitor agent)	Urology							

The reference to a cervical dysplasia agent has been deleted because a decision not to exercise the option was made.
1. Details of research are not disclosed because it is non-clinical. 2. PMS: Premenstrual syndrome/PMDD: premenstrual dysphoric disorder
3. After receiving the results of the additional Phase I clinical trial, we are again conducting a Phase I clinical trial to reconfirm the data.

Drug Discovery and Alliance Activities

Relugolix combination tablet (AKP-022), the successor product to RELUMINA as a treatment for uterine fibroids and endometriosis started domestic clinical trials

In July 2023, we started a domestic Phase I/II clinical trial of Relugolix combination tablet. By proposing the Relugolix combination tablet as a successor to RELUMINA, we expect to be able to offer a new option as an agent for the treatment of uterine fibroids (estimated number of patients in Japan: about 2 million). This formulation is a gonadotropin-releasing hormone (GnRH) receptor antagonist created by Takeda Pharmaceutical Company Limited. Treatment with Relugolix single tablet (RELUMINA) is effective due to its estrogen-lowering effects. However, since one side effect can be a decrease in bone mass, dosing for more than 6 months is generally avoided. Relugolix combination tablet contains estrogen to suppress the decrease of bone mass and progestin to suppress the growth of the endometrium caused by estrogen. We are developing it with the aim of enabling long-term treatment for more than 6 months.

7 Overseas Business Development

The International Business Division is working to develop our overseas business, particularly in Southeast Asia, a region where economic development is continuing. The new plant construction project (in compliance with PIC/S GMP Guidelines) with our strategic partner Hataphar, a Vietnamese pharmaceutical company, will be completed in August 2023. We are preparing to obtain PIC/S GMP certification by using the expertise the Group has accumulated through our domestic business. To achieve early operation and profitability of the new plant, we will actively carry out collaborative efforts between our two companies to further strengthen our framework for cooperation.

With regard to the marketing of our original health supplement in Jordan, in the Middle East, which we have been working on since 2021, we have submitted the export application to the relevant authorities in each country and are continuing activities to obtain approval and start sales at an early date.

Going forward, we will continue to boldly take on the challenge of expanding our overseas business to further improve our presence in the Southeast Asia region for the growth and development of the Company.

Illustration of the new plant in Vietnam

TOPICS

Establishment of the Femtech Business Promotion Unit

The term "Femtech," blending the words "female" and "technology," refers to products and services that use technology to solve various health issues that women face in their various life stages.

There are many focus areas within Femtech, including menstruation, pregnancy, infertility, childbirth, postpartum care, childcare, gynecological diseases, among other issues that women face, as well as items related to sexual wellness.

In Japan, although this domain has not yet been fully established, it has been attracting particular attention in recent years. In 2021, for example, the promotion of Femtech was specified for the first time in government documents such as the *Honebuto no Houshin* ("big-boned policies").

According to a research report (issued by the Ministry of Economy, Trade and Industry), into the effects (and related challenges) that changes in the way we work and live will have on the Japanese economy in the future, the economic effect of Femtech that facilitates women's participation in the workforce will be approximately ¥2 trillion/year as of 2025 (menstruation field: approx. ¥240.0 billion; pregnancy and infertility field: approx. ¥300.0-500.0 billion; menopausal field: approx. ¥1.3 trillion.)

Tomohito Nagao
Corporate Officer, Director of Femtech Business Promotion Unit
ASKA Pharmaceutical

For around a century since its establishment in 1920, ASKA Pharmaceutical has been devoted to supporting women's health, mainly by providing sex hormone agents. The Femtech Business Promotion Unit, which we newly established in April 2023, will use the knowledge and network cultivated in the Ob/Gyn field to offer options for solving women's health issues and concerns, which are becoming increasingly diverse and apparent.

Through our efforts in Femtech, we aim to broadly support women's health, to help as many women as possible improve their quality of life and play an active role in society, and to launch new businesses in this area.

Exhibited at the first Femtech Tokyo

Femtech Tokyo