September 28, 2023

Contributions to Women's Healthcare and Development Pipeline in the Obstetrics and Gynecology Field

Presentation for Investors



Securities code: 4886 (TSE)

ASKA Pharmaceutical Holdings Co., Ltd.

Forward Looking Statement

- The forward-looking statements contained in this presentation are based on the Company's assumptions and beliefs in the light of information currently available to it and involves known and unknown risks and uncertainties.
- Accordingly, there is a possibility that actual results and development programs may differ largely from these forecasts, due to a variety of factors.
- This report contains information on Pharmaceuticals Products (including those under development), and the content of this report is not intended for medical promotion or medical advice.
- This translation is provided solely as a reference material. In the case of any discrepancy between the two versions, the original Japanese version shall prevail.

Introduction



Sohta Yamaguchi,

Senior Managing Member of the Board of Directors, Representative Director

ASKA Pharmaceutical Holdings Co., Ltd.

We strive to empower women to reach their full potential and build a society where they can thrive and succeed.

Women's empowerment, being promoted as a national initiative, is closely related to women's health. We believe that We can significantly contribute to women's health as it is one of our material issues.

Contributions to Women's Healthcare

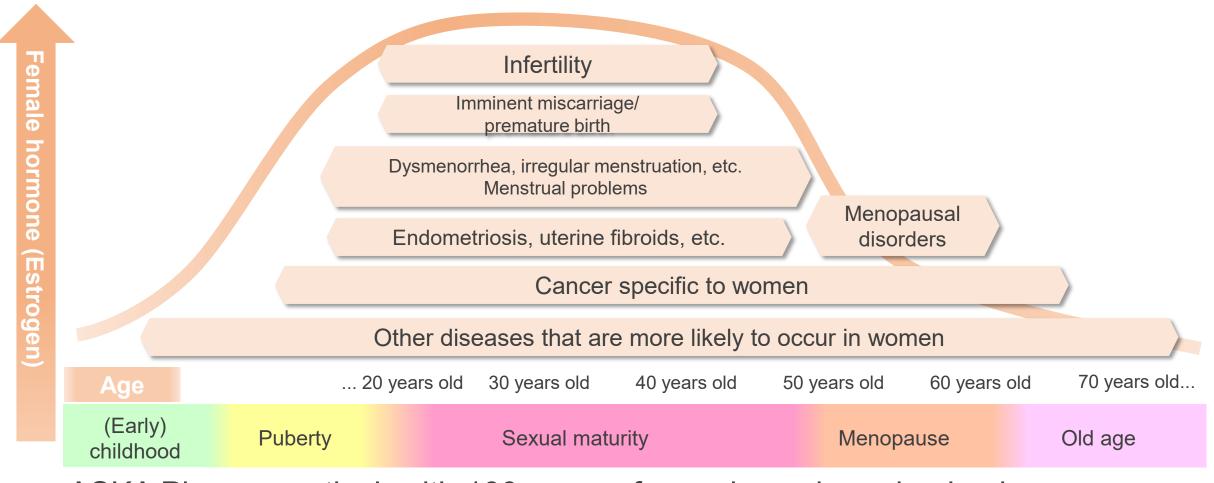


Maiko Mori,

Member of the Board of Directors, Executive Corporate Officer

ASKA Pharmaceutical Holdings Co., Ltd.

Estrogen Production and Women-specific Diseases at Different Stages of Women's Life



ASKA Pharmaceutical, with 100 years of experience in endocrine hormones, can offer valuable contributions in various areas.

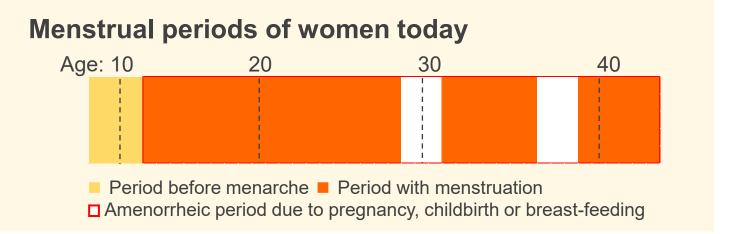
Increase in the Number of Menstrual Cycles due to Changes in Life Events

Women today experience their first menstruation earlier, tend to marry later, and experience fewer childbirths than women in past generations. The increase in the number of menstrual cycles (MCs) experienced in women's lifetime is considered a factor for the increase in dysmenorrhea and other menstrual problems.

Number of MCs experienced by women today

Number of lifetime MCs: Approx. 450

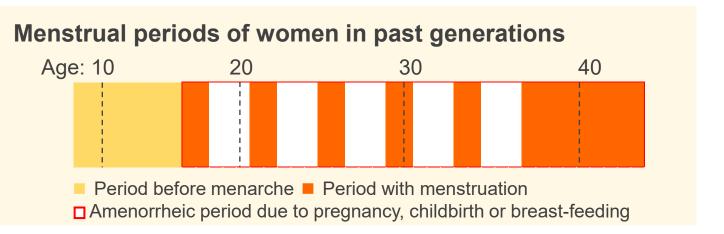
Number of lifetime childbirths: Approx. 2



Number of MCs experienced by women in past generations

Number of lifetime MCs: Approx. 50

Number of lifetime childbirths: Approx. 5



Changes in the Environment Surrounding Women (Examples)

Changes in the political environment

- ✓ Establishment of the Headquarters for Creating a Society in which All Women Shine in the Cabinet Secretariat, and formulation of the Women's Version of the Framework Policy
- ✓ Establishment of gynecologyspecific disease treatment and management fee, and insurance coverage of infertility treatment

Changes in the social environment

- ✓ Increase in the number of female employees and promotion of women to managerial positions through promotion of women's activities
- ✓ Increased awareness of health literacy through increased attention to women's specific health issues and increased exposure in the media and social media, etc.

Changes in the technological environment

- ✓ Development of pharmaceuticals and advances in medical technology related to diseases specific to women, such as treatment of dysmenorrhea and infertility
- ✓ Changes in access to medical care, including improved access to health information and expansion of online medical care due to the widespread use of the Internet

Obstetrics and Gynecology(Ob/Gyn) market is expanding in response to various changes in the environment surrounding women.

Ob/Gyn market in 2010: 49.5 billion yen^{*1} → Ob/Gyn market in 2025 (forecast): 94.5 billion yen^{*2}

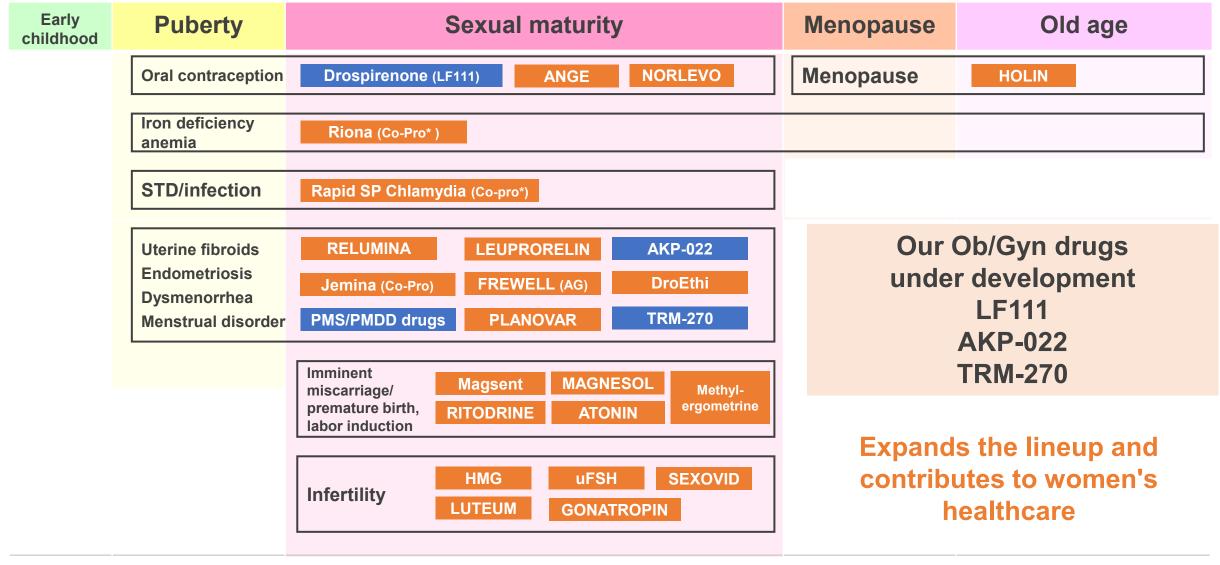
^{*1} Fuji Keizai Corporation 2018-2019 Ethical Drugs Databook No.4 All rights reserved.

^{*2} Fuji Keizai Corporation, "Trend Analysis and Future Forecast of Obstetrics and Gynecology Related Markets Attracting Attention through Insurance Coverage," All rights reserved.

The Value That ASKA Pharmaceutical Holdings Can Offer

- Contribution to the treatment of diseases specific to women through pharmaceutical drugs
- II. Contribution to improving health literacy about women through Mint*'s activities
- III. Contribution to the pharmaceutical peripheral field by utilizing Femtech

Our Ob/Gyn Pharmaceutical Products by Life Stage



Contribute to Improving Health Literacy about Women through Mint⁺

Established in 2020 on the occasion of the 100th anniversary of ASKA





女性のための健康ラボ Mint+

Health Lab Mint+ for Women's health

Key message

Knowing yourself, is protecting yourself

For the past 100 years, we have been dedicated to addressing women's concerns and their health. It is our fundamental responsibility to spread awareness, share accurate information, and relieve their worries.

Disseminating accurate information under physician supervision improves women's health literacy.

Web site contents

- The Female Body: What You Should Know
- Mint ⁺'s useful columns that add a little something extra to my daily life
- Mint * for female teenagers: Know yourself

* Japanese version only

Mint⁺'s activities in figures

Number of page views (PV)

Monthly page views range from 400,000 to 600,000, with a maximum of around 900,000.

<u>Health and physical education supplementary materials for high school students</u>

Provided once a year starting in March 2020 Total of 640,000 copies were provided to 1,732 schools

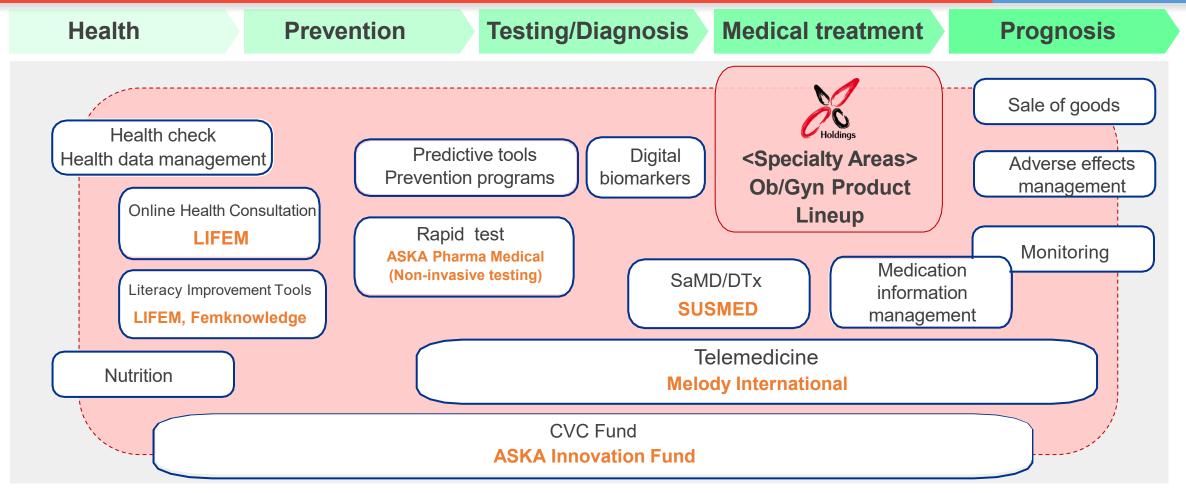
Seminars

Including online events, a total of 7 seminars were held with a total of 988 participants.

Social media posts

Posted 42 times on social media platform LINE and have 4,624 friends on LINE (as of August 28).

Contribute to the Peripheral Pharmaceutical Fields with Femtech



Contribute to women's health in the pharmaceutical peripheral areas by utilizing Femtech, focusing on the Ob/Gyn product lineup, and entering the Around-The-Pill field.

Contribute to the Peripheral Pharmaceutical Fields with Femtech

Signed an agreement for joint development and marketing of therapeutic applications in the field of obstetrics and gynecology.

* Japanese version only





Sustainable Medicine 2023年9月25日 あすか製薬株式会社 サスメド株式会社

各位

産婦人科領域における治療用アプリの共同研究開発及び販売に関する契約を締結

あすか製薬株式会社(本社:東京都港区、代表取締役社長:山口 惣大、以下「あすか製薬」)とサスメド株式会社(本社:東京都中央区、代表取締役社長:上野 太郎、以下「サスメド」)は、産婦人科領域における治療用アプリの共同研究開発及び販売に関する契約を締結しました。

ASKA Pharmaceutical Launches "Training Videos on Women's Health"

Press Release

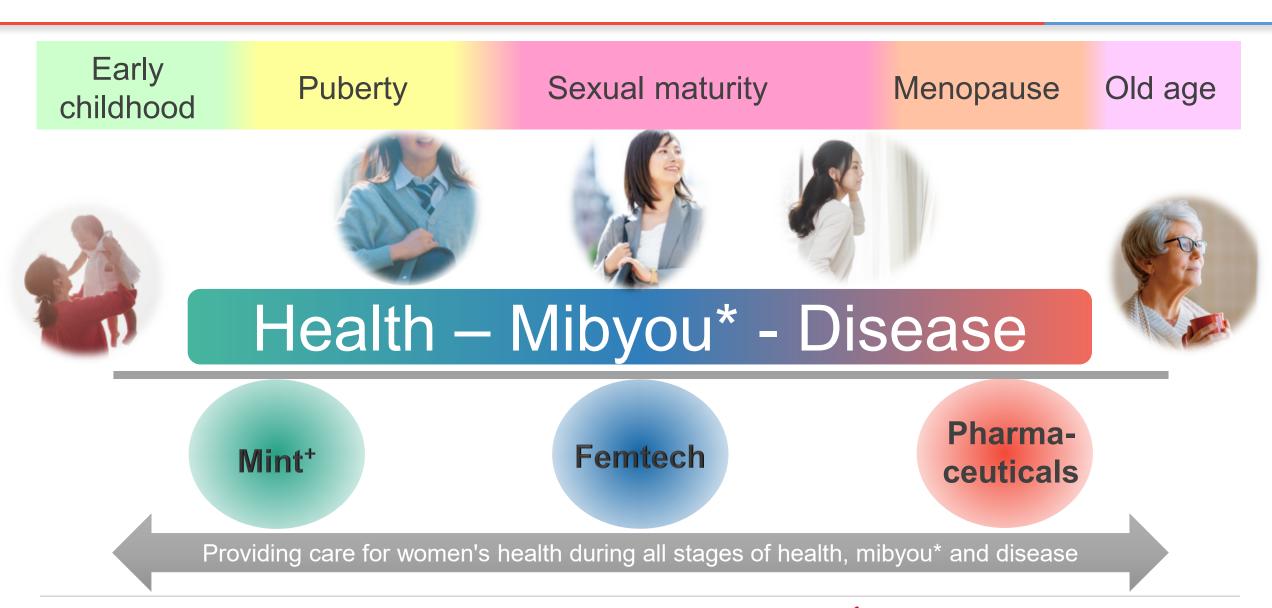


ASKA Pharmaceutical Launches "Training Videos on Women's Health"

TOKYO, **September 21**, **2023** - ASKA Pharmaceutical Co., Ltd. (Head Office: Minato-ku, Tokyo; President: Sohta Yamaguchi; hereinafter "ASKA"), a subsidiary of ASKA Pharmaceutical Holdings Co., Ltd., established the Femtech Business Promotion Unit in April of this year to make a broad contribution to women's healthcare. ASKA is pleased to announce that it will start selling "training videos on women's health" as the first step of the Unit.



Contribute to Solving Health Issues for All Kinds of Women



^{*} Mibyou refers to a pre-symptomatic state.

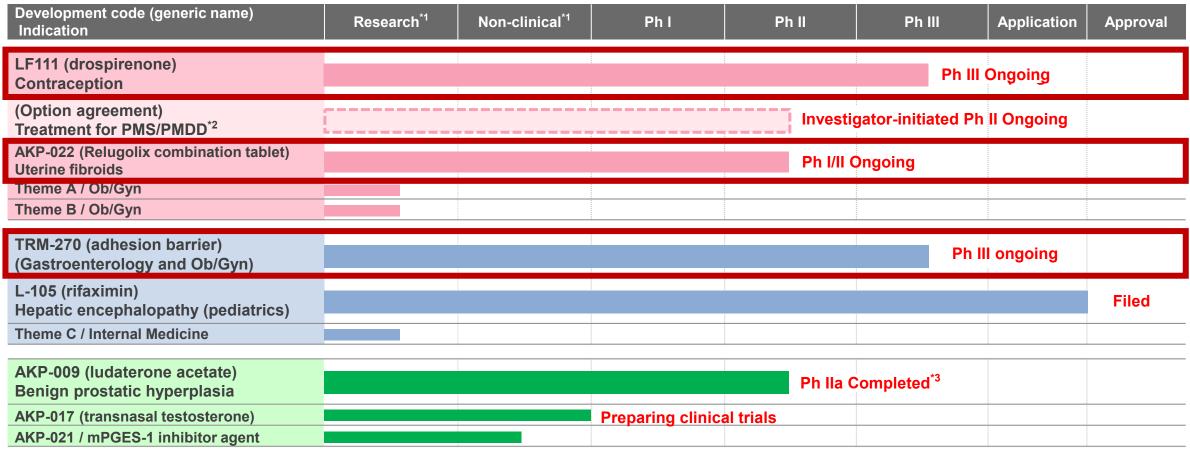
Development Pipeline in the Obstetrics and Gynecology Field



Masaya Takanashi,
Corporate Officer, Development Division Director
ASKA Pharmaceutical Co., Ltd.

Development Pipeline

R&D Status (as of August 2023)



^{*1} Details of research are not disclosed because it was non-clinical. *2 Premenstrual syndrome / premenstrual dysphoric disorder

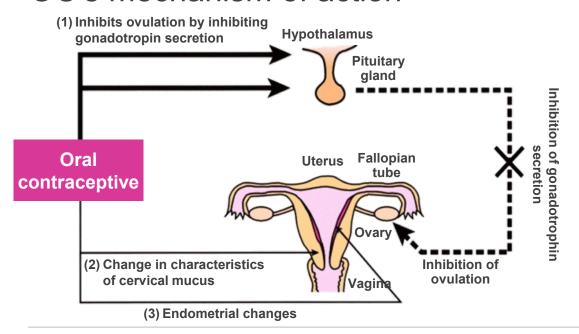
^{*3} After receiving the results of the additional Phase I study, we are again conducting a Phase I study to reconfirm the data.



What is an oral contraceptive?

In general, the term oral contraceptive refers to an oral combination of progesterone (corpus luteum hormone) and estrogen (follicular hormone) with a contraceptive mechanism in which the main action is ovulation inhibition. Oral contraceptives are also referred to as OCs, the Pill, and combined oral contraceptives (COCs).

OC's mechanism of action



*Pearl index:

Number of pregnancies (per 100 woman-years) in 100 women using the contraceptive method for one year (13 cycles)

Pearl index for various methods of contraception*

Method	In ideal use*1 (%)	In typical use *2 (%)
Oral contraceptives	0.3	9
Levonorgestrel-releasing IUS	0.2	0.2
Copper IUD	0.6	0.8
Condom	2	18
Rhythm method (Ogino method, etc.)	0.4 - 5	24
Female sterilization	0.5	0.5
Male sterilization	0.10	0.15
No contraception	85	85

IUS: Intrauterine system

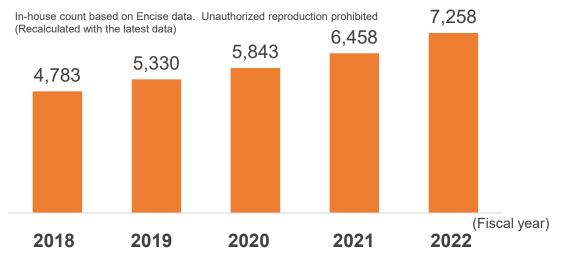
IUD: Intrauterine device

^{*1} Cases in which pregnancy occurred even though the selected method of contraception was used correctly and continuously

^{*2} Cases in which pregnancy occurred even though the selected method of contraception was used (For oral contraceptives, failure rates includes cases in which the woman forgot to take them)

Change in COC market over time

(unit: 1000 sheets)



The domestic market is tending to expand

Percentage of women who use OCs in each country*

France	33.1%	Germany	31.7%
Canada	28.5%	United States	13.7%
Korea	3.3%	Japan	2.9%

What are the major risks associated with COCs?

Quoted from our company's treatment support tool

Although the frequency of occurrence is low, thrombosis (a disease in which a blood vessel in a limb, lung, heart, brain, retina, etc. is blocked by a blood clot) may occur as a severe life-threatening adverse reaction.

Note: The incidence of venous thrombosis is generally about 5 cases per 100,000 persons per year in persons who do not take COCs, but according to an overseas report, the risk increases 3.25 to 4-fold when COCs are taken. The proportion of patients with venous thrombosis due to pregnancy is estimated to be 60 per 100,000 women per year.

Precautions before administration

Quoted from our company's treatment support tool

1. Smoking

Smoking while taking oral contraceptives has been reported to increase the risk of side effects such as venous thrombosis, pulmonary embolism, myocardial infarction, and stroke. This risk is said to increase with age (35 years or older) and smoking volume (15 cigarettes or more per day). Therefore, persons 35 years old or older who will be taking this drug need to stop smoking.

- 2. The following persons should not take oral contraceptives (*Partial excerpt)
 - Persons who are 35 or older and smoke 15 cigarettes or more per day
- 3. The following persons should **consult a physician before receiving a prescription.** If you have any concerns even after receiving a prescription, consult a physician or pharmacist (*Partial excerpt)
 - Women aged 40 years or older
 - Women who smoke
 - Women who are obese

^{*} United Nations: Contraceptive Use by Method 2019 "Estimated prevalence of contraceptive use among women of reproductive age (15-49 years), 2019"



LF 111 Overview (planned)

Nonproprietary name	Drospirenone
Therapeutic category	Oral contraceptive
Indication	Contraception
Characteristics	Progesterone-only pill (POP*) with the ingredient drospirenone. Conventional oral contraceptives contain two female hormones, estrogen and progesterone. Although the frequency of occurrence is low, there is a risk of thrombosis due to estrogen. Since this is a progestogen-only oral contraceptive, the risk of thrombosis can be expected to be lower.
Significance of development	Provides a new option for women who desire contraception and are not suitable candidates for COC use for reasons of age, smoking, and obesity.

Status of overseas approval of LF 111 (drospirenone POP)

LF has been approved in 54 countries throughout the world, including France (2019), Italy (2019), Germany (2021), USA (2019), and Canada (2021).

LF 111 Overview of Ph III

Research objectives	To evaluate the efficacy and safety of 13 cycles of LF 111 4 mg in Japanese women who desire contraception.	
Study phase	III	
Study period	December 1, 2021 to September 30, 2024 Status of progress: Recruitment has ended	
Planned number of subjects	260	
Study design	Single-arm, open-label, uncontrolled, single-group comparison	
Details of intervention	Subjects will receive one 4-mg LF111 tablet per day for the first 24 days and one LF111 placebo tablet per day for the subsequent 4 days (oral administration). Subjects will receive 13 consecutive treatment cycles, each consisting of 28 days. In the case of continuous administration, administration will be continued up to 24 cycles.	
Primary endpoint	General Pearl Index* *Pearl index: Number of pregnancies (per 100 woman-years) in 100 women using the contraceptive method for one year (13 cycles)	

LF 111 Future outlook

The study is progressing smoothly, and we aim to launch the product as part of the current mid-term business plan.



What are uterine fibroids?

Benign tumors that develop in the myometrium.

Estrogen is thought to cause them to grow larger.

In rare cases, uterine fibroids may become malignant.

Depending on where they form, they are classified as submucosal fibroids, intramural fibroids, or subserosal fibroids. Fibroids are not always solitary, and more than one may develop.

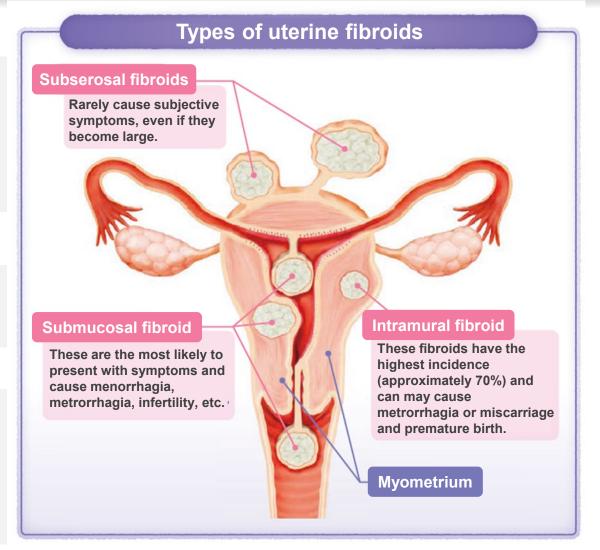
Symptoms of uterine fibroids

Prolonged menstruation, menorrhagia, anemia, metrorrhagia, lower abdominal pain, low back pain, infertility, pollakiuria/constipation due to compression, etc.

Prevalence of uterine fibroids*

The prevalence is reported to be 4.5% to 68.6% depending on race and age.

According to the population estimates in Japan, the population of women aged 20 to 49 years in 2021 was approximately 21.8 million, among which 6.55 million may have uterine fibroids. (On the assumption that the prevalence of uterine fibroids is 30%)

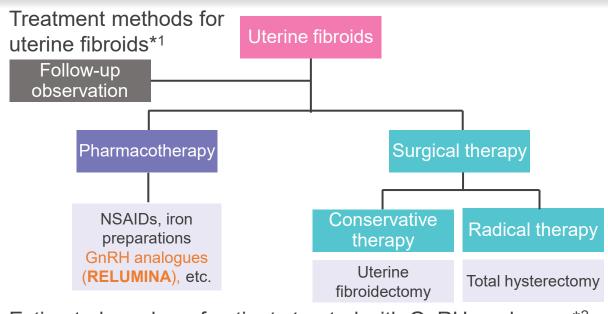


Quoted from our company's treatment support tool



^{*} Koga, K, Fukui, M, Fujisawa, M, Suzukamo, Y. Impact of diagnosis and treatment of uterine fibroids on quality of life and labor productivity:

The Japanese online survey for uterine fibroids and quality of life (JOYFUL survey). J Obstet Gynaecol Res. 2023. https://doi.org/10.1111/jog.15758



Estimated number of patients treated with GnRH analogues*2



Follow-up observation

If there is no symptoms and the fibroid is not large, follow-up observation will be performed periodically without treatment.

Pharmacotherapy

This is a method of treating fibroids with drugs to suppress symptoms such as menorrhagia, anemia, and menstrual pain.

GnRH analogues

Improve symptoms by reducing the production of female hormones.

Since bone loss may occur owing to the estrogenlowering effect, these products should not be administered for more than 6 months in principle.

Surgical therapy

Surgery includes both open surgery and laparoscopic surgery.

^{*1} Prepared with our company's treatment support tool

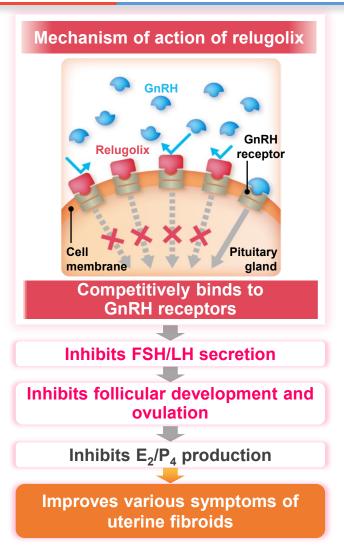
^{*2} Sum of estimated number of patients treated with the drugs per month, based on the actual quantity of RELUMINA + LEUPRORELIN 1.88 mg formulation

Overview of AKP-022 (planned)

Nonproprietary name	Relugolix, ethinylestradiol, norethisterone acetate
Therapeutic category	GnRH antagonist
Indication	Uterine fibroids
Characteristics	These drugs combine relugolix, which inhibits the production of estradiol and progestogen, with ethinylestradiol, which inhibits bone loss, and norethisterone acetate, which inhibits endometrial proliferation.
Significance of development	This drug is now under development. The relugolix in this combination improves symptoms associated with uterine fibroids, the ethinylestradiol keeps E2 levels within the range where symptoms of uterine fibroids are not exacerbated and menopausal symptoms (hot flashes, bone density decreased) do not occur, and the progestogen inhibits the development of E2-induced endometrial proliferation. Together, these actions are expected to make long-term administration possible. This drug represents a new option for the treatment of uterine fibroids.

Overseas approval status of AKP-022 (relugolix combination tablet)

It has been approved in 35 countries worldwide, including the United States (2021), the United Kingdom (2021), and EU member states (2021).



AKP-022 Overview of Ph I/II

Research objectives	The objective of this study is to evaluate the pharmacokinetics, pharmacodynamics, and safety of multiple oral doses of AKP-022 or relugolix in healthy premenopausal Japanese adult women.
Study phase	1/11
Study period	July 1, 2023 to July 31, 2024
Planned number of subjects	48
Study design	Randomized controlled, double-blind, active-control, parallel-group comparison study
Details of intervention	A total of two tablets (one tablet of AKP-022 and one tablet of relugolix placebo, or one tablet of relugolix and one tablet of AKP-022 placebo) are orally administered once daily for 6 weeks. The first dose should be given within 1 to 5 days of the start of menstruation.
Primary endpoint	 Pharmacokinetics: Concentration and pharmacokinetic parameters of relugolix, NET, E2, and E1 Pharmacodynamics: endocrinological tests and bone metabolism markers Safety

AKP-022 Future outlook

We aim to provide a new treatment option and further enhance corporate value by developing and launching AKP-022 as a successor to RELUMINA.



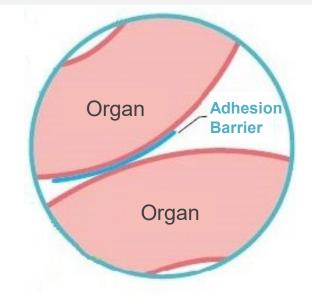
TRM-270 (Adhesion Barrier)

Postoperative adhesion and Adhesion Barriers

When tissues are sutured during surgery, it is normal for the tissues to join together and heal spontaneously, but tissues of adjacent organs may adhere during the healing process. This is called postoperative adhesion. Complications resulting from postoperative adhesions are known to include small intestinal obstruction, secondary infertility, and chronic pelvic pain. The Adhesion Barrier is applied to the affected area after surgery to prevent postoperative adhesion.

Market for Adhesion Barriers (in-house estimate)

The market for Adhesion Barriers is estimated to be about 14 billion yen. It has been tending to grow in recent years.



TRM-270 (Adhesion Barrier)

Overview of TRM-270 (planned)

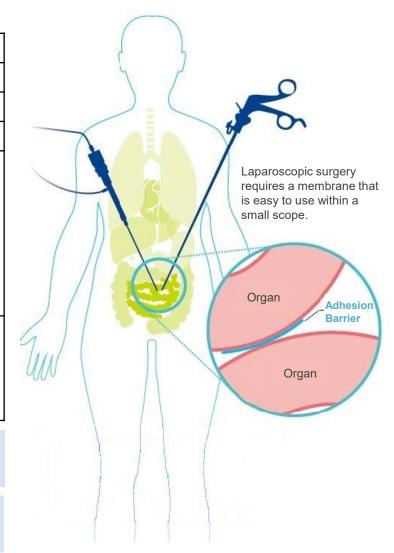
Nonproprietary name	Resorbable Adhesion Barrier
Therapeutic category	Adhesion Barrier
Dosage form	Sheet
Indication	Reduction of postoperative adhesion
Characteristics	It has a two-layer structure consisting of an Adhesion Barrier layer and a support layer. The Adhesion Barrier layer is made of biodegradable polylactic resin that is degraded and absorbed by the body. The support layer is a gauze-like structure made of water-soluble resin, and it reinforces the Adhesion Barrier layer, which is only a few hundred nanometers thick and is difficult to handle. Since the support layer dissolves in water, it does not need to be retrieved. This characteristic can be expected to improve maneuverability during surgery.
Significance of development	This product offers good maneuverability while exerting an Adhesion Barrier effect equivalent to that of existing products. It is being developed as a medical device designed to promote ease of handling in laparoscopic surgery and robot-assisted surgery, which have been increasing in recent years.

Configuration of TRM-270

Adhesion Barrier layer
Biodegradable polylactic resin

Support layer
Gauze-like structure made of watersoluble resin

With adhesion supplied by the Adhesion Barrier layer and flexibility supplied by the supporting layer, it is expected to provide both adhesiveness and maneuverability.



TRM-270 (Adhesion Barrier)

TRM-270 Overview of Phase III gastroenterology study

Research objectives	To evaluate the efficacy, safety and maneuverability of TRM-270 in patients undergoing laparoscopic or robot-assisted surgery for rectal cancer.
Study phase	
Study period	November 1, 2022 to February 28, 2025
Planned number of subjects	260
Study design	Randomized controlled, single-blind, active-control, parallel-group comparison study
Details of intervention	At the time of the first stage of surgery, when resection of the primary focus and colostomy are performed, resorbable Adhesion Barrier "TRM-270" or "Seprafilm" is applied under the small incision wound.
Primary endpoint	Incidence of adhesion in small incision wounds

TRM-270 Future outlook

In addition to the gastroenterology studies, we are preparing clinical trials in the fields of obstetrics and gynecology.

Development Pipeline - Summary of Characteristics

✓ LF111

Progesterone only oral contraceptive. Under development with the expectation of reducing the risk of thrombosis.

✓ AKP-022

Combines estrogen and progesterone with relugolix. Under development with the expectation that long-term administration for 6 months or longer will be possible.

✓ TRM-270

Under development with the expectation that it will be an Adhesion Barrier with good maneuverability, with a special focus on handling in laparoscopic surgery and robot-assisted surgery.

ASKA Pharmaceutical Holdings Group Corporate Message

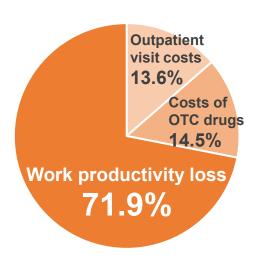
For a Healthy Tomorrow and Future.



Appendix

Women's Health Issues

The annual economic burden of menstrual symptoms in Japanese women



Detail	Estimated amount
Outpatient visit costs	93.0 billion yen
Costs of OTC drugs	98.7 billion yen
Work productivity loss	491.1 billion yen

Total 682.8 billion yen

OTC drugs: Over The Counter drugs

Made based on Tanaka E, Momoeda M, Osuga Y et al J Med Econ 2013; 16(11): 1255-1266

Current challenges for women's health in the workplace

Challenges in occupations with a relatively large number of women

Ex) Mental health and smoking rate increase in occupations such as hospitality, standing work, call center, etc.

Challenges in menstruation

Ex) Loss due to presenteeism, lack of literacy, etc.

Challenges in women's specific diseases

Ex), such as the presence or absence of compatibility and gynecological examination

Challenges in pregnancy and childbirth

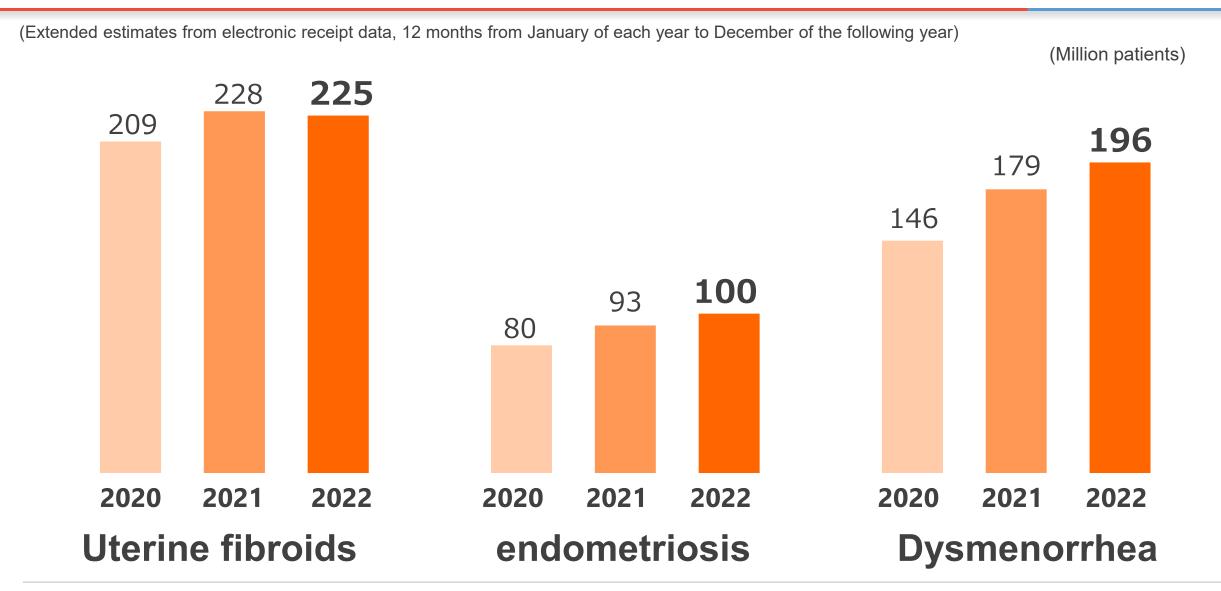
Ex) loss of career opportunities, etc.

Challenges in menopause

Ex) Balancing work and long-term care, loss of opportunities in the workplace, etc.

Source: Ministry of Economy, Trade and Industry, Health Care Industry Division, "Women's Health Initiatives in Health Management.

Number of Uterine Fibroids/Endometriosis/Dysmenorrhea Patients



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